
﴿ قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ ﴾
(٣٢ البقرة)
وآه إسلاما

MINERALS

BY

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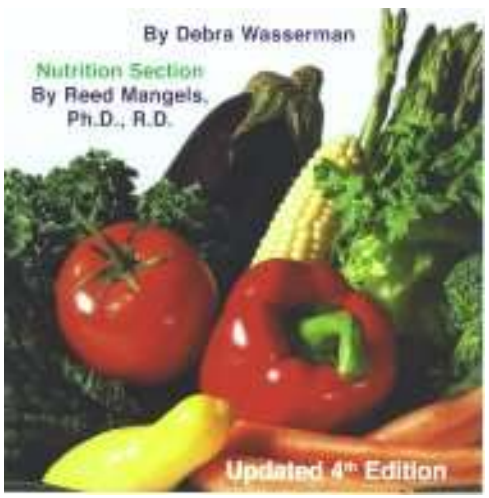
MINERALS

- The minerals, form a small portion of the total body weight, are nonetheless of great importance in tile vital economy.
- Most of the minerals are essential components of an adequate diet.
- The principal sources of the mineral elements are fruits, vegetables and cereals.
- Certain foods are particularly outstanding for their contribution of particular minerals *e.g.*1 milk products which are depended on to supply the majority of the calcium and phosphorous in the diet.



The mineral elements present in the animal body are classified into three groups

Major components

Carbon, hydrogen, oxygen, nitrogen and sulpher.

Principal elements (macronutrients) (major e1ements)

Calcium, magnesium, sodium, potassium, phosphorous, and chlorine.
They constitute 60-80% of all the inorganic material in the body
They required in amount greater than 100 mg/day

Trace elements (micronutrients) (microelements)

Iron, iodine, copper, cobalt, chromium, manganese, molybdenum, selenium and fluorine
They required in amount less than 100 mg/day

Non essential elements

Arsenic, cadmium, nickel, silicon, tin and vanadium
no essential function in the body

Toxic elements

lead, and mercury

N.B.:

1. Although in respect to their amounts the mineral elements are relatively minor components of the tissues, they are essential to many vital processes *e.g.* blood calcium exerts an important role in blood clotting and in neuromuscular irritability. despite the relative low content of this element in extracellular fluid.
2. The balance (*i.e.* the ratio of one to another) of the ions in the tissues if often of physiological importance *e.g.*:
   * Normal ossification demands a proper ratio of calcium to phosphorus.
   * Normal activity of muscle requires a normal ratio between potassium and calcium.
3. In. discussing the metabolism of a mineral the following points must be covered: sources, requirements, absorption, excretion and effects of alterations in their blood level (*i.e.* their deficiency or their overdosage).

CALCIUM

Calcium is the major cation present in the body Almost all of it is in the bones and the teeth. the very small (10/o) not in the skeletal structures is in the body fluids and is in part ionized. The total body content of an average 70 kg adult is about 1200 g. 99% of them in the skeleton.

Functions of calcium

1. **Enters in the structure of bones and teeth.**
2. **Maintenance of normal excitability of heart muscles arid nerves.**
3. **Essential for blood cloning, and milk curdling.**
4. **Maintenance of integrity of capillary walls and decreases their permeability.**
5. **Activation of certain enzymes as pancreatic lipase and glycogen phosphorylase.**
6. **A normal blood calcium is essential for release of almost all hormones. The only two hormones that are released in response to low blood calcium are: glucagon and parathyroid hormone (PTH).**
7. **May play a role in mediating the action of some hormones, in this respect they act as a third messenger, (cyclic AMP is the second messenger and the hormone is the first messenger).**
8. **It involves in the regulation and secretion of insulin.**

Sources:

1. **The richest sources of calcium are milk and cheese.**
2. **Most other foods contribute smaller amounts *e.g.* egg yolk, beans, lentiles, nut, figs, cabbages, cauliflower and turnip.**

Requirements:

- **Children : 0.8 – l.2 g/day**
- **Adults: 0.8 g/day.**
- **Pregnancy and lactation 1.2 g/day.**

Absorption of calcium :

This occurs by an active transport mechanism in the upper part of small intestine.

Factors Affecting Absorption

1- pH of duedenum:

- **An acidic duedenal pH is essential for normal absorption as calcium is insoluble and non-ionized in alkaline pH.**
- **An acidic pH is provided by the acid chyme, on its arrival for stomach.**

2- Phosphate in diet:

- **Increasing the amount of phosphate in diet precipitates calcium and decreases its absorption.**
- **The Ca : P ratio in diet must be 1 : 2 or 1:1 for optimum absorption, this is the ratio present in human milk. (*animal milk contains higher phosphate content and this may produce hypocalcaemia after absorption of phosphate lending to tetany and convulsions in infants*)**

3- Forms of calcium in Diet:

- The organic forms *i.e.* calcium gluconate, lactate or citrate are soluble and readily absorbed.
- The inorganic forms *e.g.* calcium carbonate and calcium phosphate are insoluble and poorly absorbed.

4- Other constituents of diet:

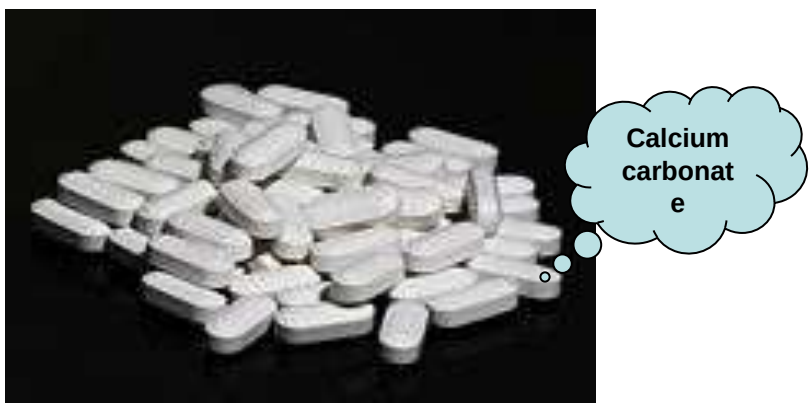
- **Phytic acid (in cereal grains) interfere with calcium absorption by forming the insoluble calcium phytate.**
- **Oxalates in food (*e.g.* in spinach) has a similar effect by forming calcium oxalate**
- **High protein diet increases calcium absorption.**

5- Vitamin D:

- **This is essential for and promotes absorption of calcium from the intestine (see its role later on).**

6- Parathyroid hormones: **essential for formation of the active form of vitamin D (1, 25 dibydroxy cholecalciferol or calcitriol).**

Excretion of Calcium: This occurs in: milk, urine and stools.



Blood Calcium

- **The normal plasma level = 9-11 mg% (average 10 mg%).**
- **The erythrocytes not contain calcium.**
- **The plasma calcium exists in 2 forms:**

1- Non-diffusible (45%):

- **This form of calcium is bound to plasma proteins maily albumin.**
- **It is physiologically mactive.**

2- Diffusible (55%)

This form of calcium may be:

A) Ionizable (50%)

- **This mostly in the form of chloride salt.**
- **It is the only physiologically active.**
- **If it decreases tetany occure.**

B) non-Ionizable (5%)

- **This mostly in the form of citrate salt.**
- **It is physiologically inactive.**

Factors Affecting Blood Calcium:

1. **Parathyroid hormone (PTH) which is a hypercalcaemic hormone *i.e.* increases blood calcium by**
   - **Increased mobilization of calcium from bones.**
   - **Keeps Ca X P solubility product constant (10 x 5 = 50).**
   - **Increased calcium absorption from intestine (by activation of vitamin D).**
2. **Calcitonin which is a hypocalcaemic hormone that decreases blood calcium by increasing calcium deposition in bones and also it inhibits the osteoclastic activity. On the kidney it increases calcium excretion.**
3. **3. Ca X P solubility product which must be kept constant (at 50 mg) i.e. if phosphates are increased in blood, calcium level will decrease, and vice versa.**
4. **4. Vitamin D (active from) which increases calcium absorption from intestine. The active from of vitamin D *i.e.* 1.25 dihydroxy cholecalciferol enters the intestinal mucosal cells (after being synthesized in kidney) where it acts on the DNA of the mucosal cell nuclei to stimulate the synthesis of a specific messenger RNA (mRNA). This specific messenger RNA will be transported to the ribosomes in the cytoplasm of the mucosal cells to stimulate the synthesis of a calcium-binding protein that it will trigger the transport of calcium, from the intestinal lumen to the blood.**
5. **5. Blood pH : calcium is soluble and ionized at the normal blood pH (7.4). On the other hand, alkalosis decreases ionization of calcium.**

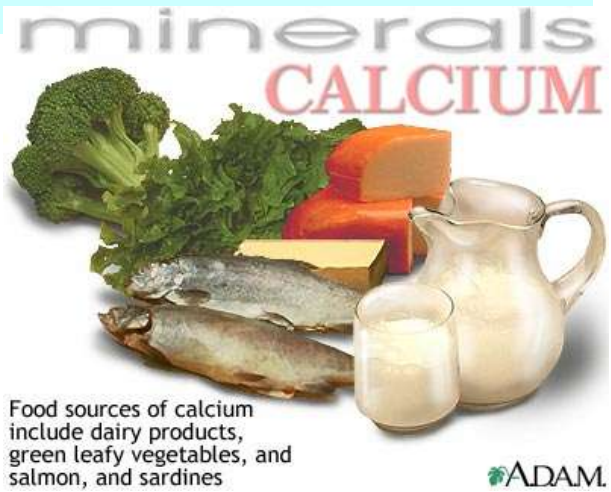
N.B.:

The hormones that regulate blood calcium (calcitropic hormones) are:

1. **Parathyroid hormone.**
2. **Calcitonin.**
3. **1, 25 dihydroxy cholecalciferol (active vitamin D or calcitriol).**

Notes on parathyroid Hormone (PTH) Action:

1. **Parathyroid hormone produces proliferation of osteolytic cells in bone (mainly osteoclasts), which produce bone resorption involving bone matrix and mineral crysia. and leading to a net mobilization of calcium from bone.**
2. **The stimulus for parathyroid hormone release is the decreases in serum calcium level (hypocalcaemia).**
3. **The action of parathyroid hormone is possibly mediated through cyclic AMP.**



Food sources of calcium include dairy products, green leafy vegetables, and salmon, and sardines

ALTERATIONS IN SERUM CALCIUM LEVELS

Hypercalcaemia, which can be produced by:

1. Primary hyperparathyroidism:

- **This results from increased secretion of PTH than what is needed.**
- **This usually occurs due to single adenoma in the gland (85-90%) and less frequently due to hyperplasia of all four parathyroid glands (5-10%).**

2. Secondary hyper parathyroidism:

- **This is a state characterized by an increased release of PTH to compensate for a decreased serum ionized calcium i.e. secondary to the decrease in calcium level.**
- **The decreased serum calcium level usually results from renal failure, osteomalacia, steatorrhea,, or post-gasteroctomy malabsorption.**

3. Hypercalcaemia of malignancy:

- **The most common from of this type occurs due to direct infiltration of bone by malignant tissue which produces oesteolysis and increased mobilization of calcium to blood.**
- **Other forms include hypercalcaemia associating breast cancer and multiple myeloma where pararthyroid hormone-like peptides are possibly released from the tumors to produce hypercalcaemia.**

4. Milk-alkali syndrome:

- **This occurs in patients who take antiacids and drink milk for peptic ulcer disease.**
- **In such condition there is an increased calcium absorption (from the ingested milky which is not balanced by increased renal excretion.**

Hypocalcaemia and Tetany:

Tetany is a condition characterized by increased neuromuscular irritability (excitability) due to a decrease in ionized calcium in blood that may result form: (causes of hypocalcaemia):

1. **Hypoparathyroidism.**
2. **Alkalosis (which decreases serum ionized calcium).**
3. **Decreased dietary intake or poor absorption from intestine.**
4. **Kidney disease (nephritis) that increases renal excretion of calcium and inhibits vitamin D activation** in kidney.

PHOSPHORUS

- **Phosphorus is found in every cell of the body.**
- **It presents in 2 forms:**
  A) Inorganic form *e.g.* Na, K and Mg salts.
  B) Organic form esters of phosphoric acid with organic compounds *e.g.* G.6.p and phospholipids.
- **70% of food phosphates are absorbed.**
- **Aluminum hydroxide (ant-acid) inhibit absorption due to the formation of aluminum phosphate.**
- **Total body phosphorus averages 0.80 kg/70 kg.**
- **80% of the total body P is in the skeleton.**
- **Blood phosphorus:**
  A) Erythrocytes:
    1- Most of the phosphorus in the form of organic phosphates.
    2- Very little is inorganic salts of potassium phosphate.
  B) Plasma:
    1- Part of plasma P is organic in the form of phosphlipids.
    2- The inorganic phosphates is of sodium phosphate type.
- **Renal function effect plasma inorganic phosphate which increased in renal failure due to defect in excretion.**
- **Normal serum inorganic phosphate level is 2.5-4.5 mg% (0.9-1.5 mEq/L).**

Forms and Function:

1. Enters in bone and teeth formation.
2. Enters in structure of phospholipids.
3. Enters in structure of nucleic acid (DNA and RNA).
4. Enters in structure of coenzymes as NAD and FAD.
5. Present as phosphorylated intermediates of carbohydrates and lipids *e.g.* glucose-6-phosphate and glycerol-3-phosphate.
6. Enters in structure of high energy phosphate containing compounds *e.g.* ATP, GDTP, CTP, …..etc.
7. Enters in structure of cyclic AMP and cyclic GMP.
8. Enters in the formation of buffers.

Sources, Absorption and Excretion:

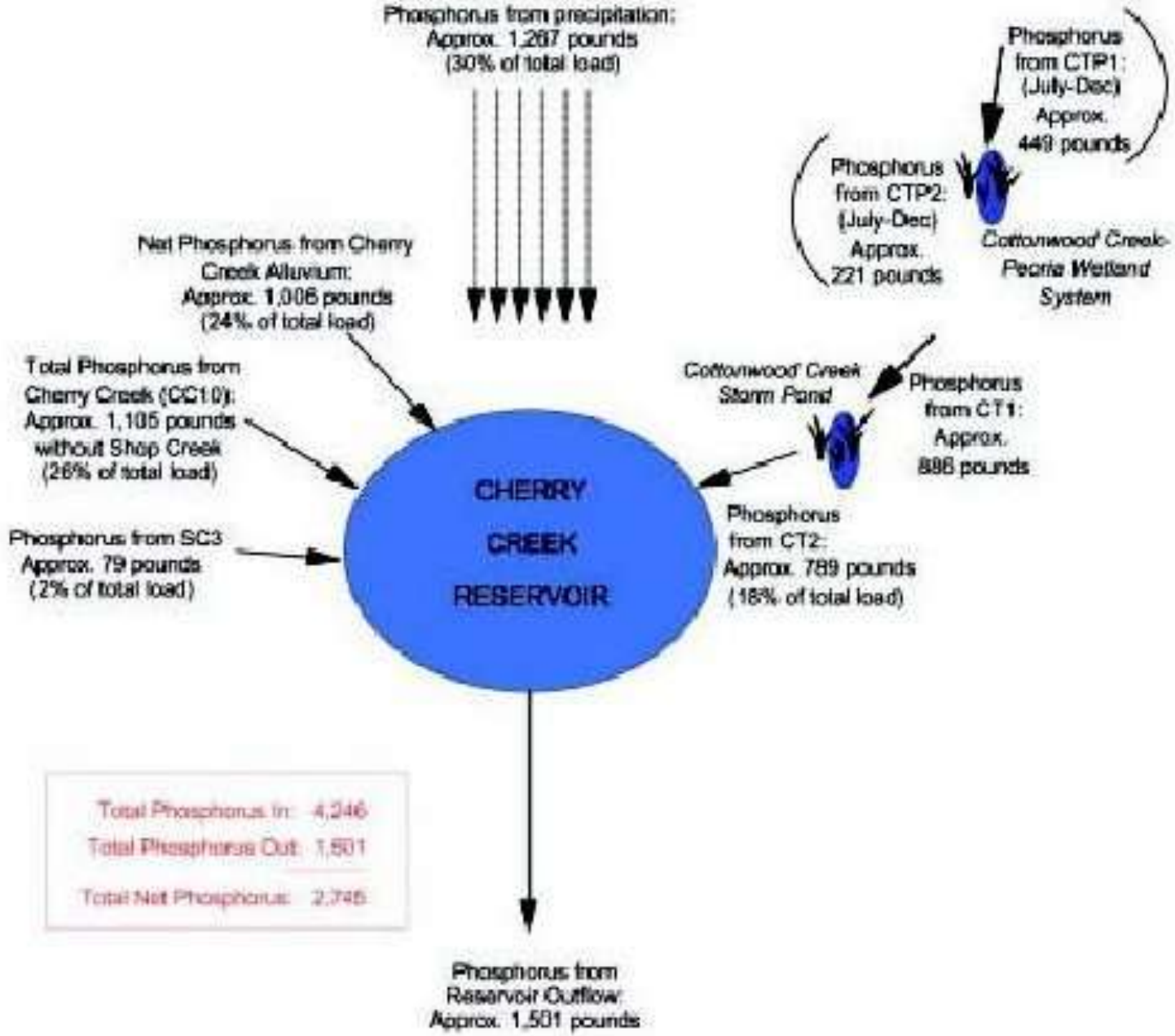
The same as that for calcium.

High Energy Phosphate Compounds: These are:

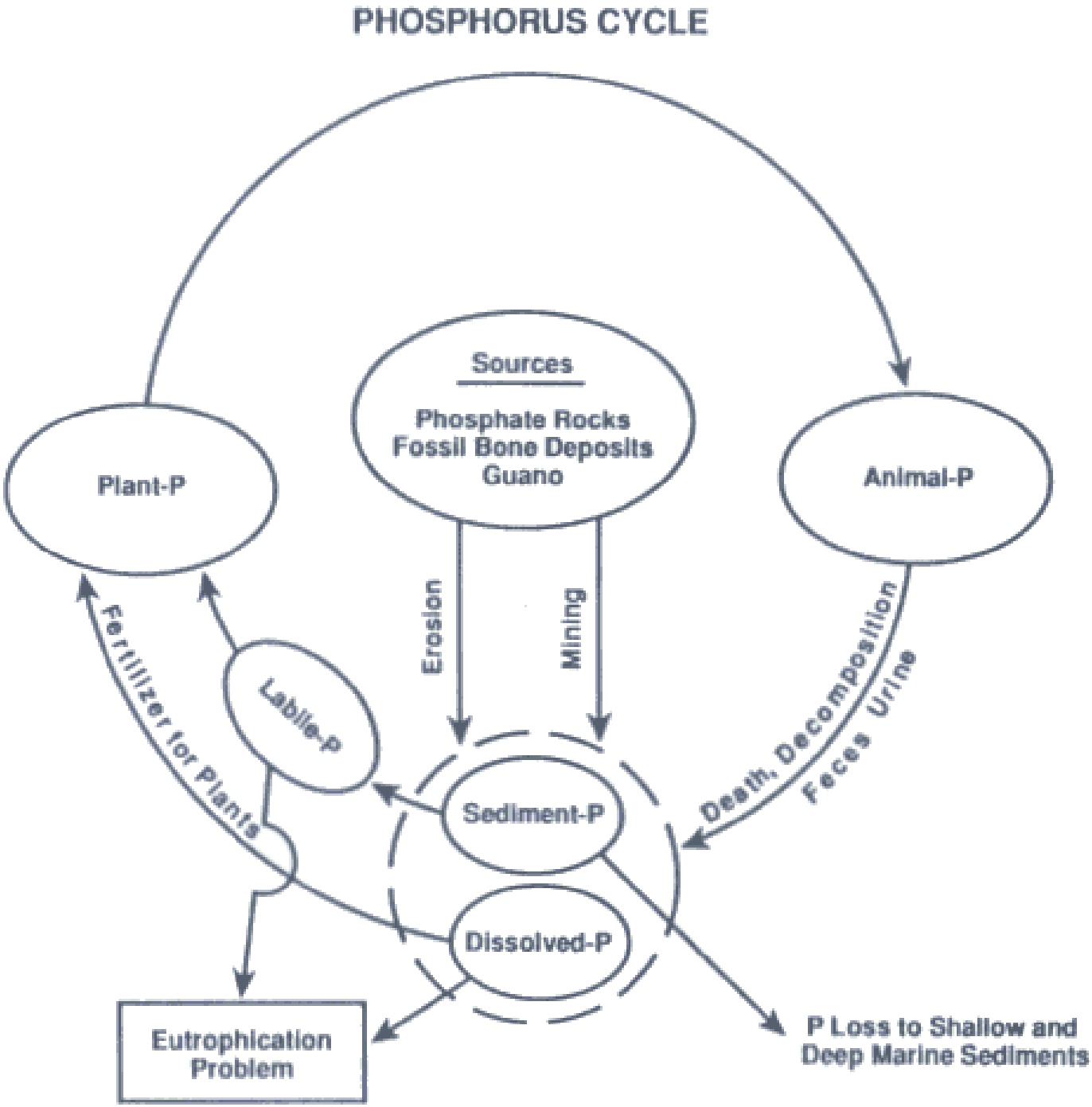
1. **ATP and its relatives *e.g.* GTP and CTP.**
2. **Creatine phosphate.**
3. **Carboxyl phosphate *e.g.* the phosphate bond at C-I in 1, 3 diphosplioglyceric acid.**
4. **Enol phosphate *e.g.* phosphoenol pyruvic.**
5. **Carbamoyl phosphate (urea cycle).**

N.B.:

High energy compounds include:
1- High energy phosphate.
2- High energy sulfate (see sulfur).



Mass balance diagram of phosphorus loading in Cherry Creek Reservoir, 2002.


PHOSPHORUS CYCLE
Sources
Phosphate Rocks
Fossil Bone Deposits
Guano
Plant-P
Animal-P
Erosion
Mining
Fertilizer for Plants
Labile-P
Death, Decomposition
Feces Urine
Sediment-P
Dissolved-P
Eutrophication Problem
P Loss to Shallow and Deep Marine Sediments

MAGNESIUM

- Magnesium is one of the principal elements (macroelements).
- It is a divalent cation.
- The total body content of magnesium is about 21 gm.
- 70% is combined with calcium and phosphorous in bone and the remainder 30% is present in soft tissues and body fluids

Sources:

- Excellent sources are cocoa derivatives, soybeans and various nuts.
- Other sources include whole grains, raw dried beans, and peas.
- The major source is the chlorophyll of plants.

Distribution:

- 70% in the skeleton.
- 30% in the other tissues and body fluids.
- It mostly intracellular.
- Its concentration in muscle cells is about 10 times in plasma.

Blood magnesium:

- Plasma Mg normally 2.40±0.60 mg/dl.
- 80% of them is diffusible.
- 20% is non-diffusible bound to plasma proteins.
- Erythrocyte Mg is 2-3 times of plasma.

Factors affecting plasma magnesium:

- ***Aldosterone:***
  - Decrease plasma Mg by increasing its urinary excretion.
- ***Parathyroid hormone:***
  - Increase plasma Mg by increasing its mobilization.
- ***Kidney function:***
  - Hypermagnesaemia in renal failure due to defect in excretion.

Requirements:

350 mg/day for men and 300 mg/day for women.

Absorption:

This occurs in upper small intestine – Normally about 40% of the ingested.

Factors affected mg absorption:

1. **Amount of Mg in diet.**
2. **Amount of Ca in diet due to Ca competes with Mg absorption.**
3. **Vit. D.**
4. **Parathyroid hormone.**
5. **Solubility of Mg as high and excess phosphate, phytic acid and unabsorbed fatty acids effect its solubility and absorbababability.**

Excretion:

- **In urine and milk.**
- **Aldosterone increases the renal excretion of magnesium as it do also with potassium.**

Function:

1. Activation of many enzymes as kinases, adenylate cyclase, gunnylate cyclase, phosphorylase and some decroxylase.
2. Acts to depress neuromuscular and central transmission.
3. Enter in the formation of skeleton.
4. Important for normal contraction of muscles. It decreases neuromuscular excitability.

a) Hypermagnesamia leads to muscle weakness and paralysis this action antagonized with calcium.
b) Hypomagnesemia leads to tetany which can't be treated with calcium.

Alterations in serum Mg^{++}:

1. Magnesium deficiency, this is characterized by confusion, neuromuscular irritability, and seizures similar to the symptoms of hypocalcaemia.
2. Hypermagnesemia may produce hypotension, loss of tendon reflexes, stupor, and coma, and it rarely occurs following increased intake of magnesium in laxatives and as magnesium sulfate given in the treatment of eclampsia.

SULFUR

Sources:

The major sources of sulfur are the sulfur containing amino acids: cysteine, cystine and methionine.

Form of sulfur in body:

1- Sulfur containing amino acids present in structure of tissue proteins. plasma proteins, enzymes and hormones.

*** These include cysteine, cystine and methionine.**

2- Sulfur containing vitamins: thiamine (B_1), biotin and lipoic acid.

3- Sulfur containing coenzymes: TPP, lipoic, biocytin, COASH and glutathione.

4- Sulfolipids.

5- Bile salts (sodium and potassium salts of taurocholic acid).

6- Sulfated mucopolysaccharides as heparin and chondroitin sulfate.

7- Lipoic acid derivatives *e.g.* acetyl lipoate atd succinyl lipoate.

8- COA derivatives *e.g.* active acetate, active succinate...etc.

9- Active sulfate

10- Ergothionine is found in liver, RBCS and semen.

High energy sulfur containing compounds include:

1- **COA derivatives e.g. active acetate, active succinate …..etc.**

2- **Lipoate derivatives *e.g.* acetyl lipoate and succinyl lipoate.**

3- **Active methionine (used for transmethylation reactions).**

4- **Active sulfate (used in detoxication).**

Excretion:

A- In urine:

- This is the principle rout of excretion.
- About 1 gm excreted daily in the form of:

1- Inorganic (80%):

- Na and K sulphate related to protein intake and catabolism.

2- Neutral sulpher compounds (10%):

- Sulpher containing vitamins and amino acids.
- Thiocyanates and urochrome.

3- Ethereal sulphate (10%):

- Include
  - * indican (K-indoxyl sulphate)
  - * Skatoxle K-sulphate.
  - * Phenol sulphate.
  - * Steroid hormone sulphate.

-They relatively constant exception increased intestinal purification.

4- In addition there are some S-containing compounds as taurine, taurocholic acid and thiosulphate.

SODIUM

- Sodium (Na^+) is the major cation of the extracellular fluid and is largely associated with chloride and bicarbonate in the regulation of acid-base balance.
- The plasma sodium concentration is about 142 m.Eq/litre (330 mg %).
- The main dietary source of sodium is table salt (NaCl) used in cooking and seasoning. Meats contain more sodium than vegeratbles.
- Requirements: about 5 g/day.
- Absorption readily occurs in ileum, and little is present in stools.
- Excretion occurs in urine and sweat.
- In susceptible individuals, there is a clear relationship between Na^+ intake and diastolic blood pressure.
- Thus the excessive and wasteful intake of NaCl may lead to or aggrevate pre-existing hypertension.
- Sodium intake must be decreased in hypertension. renal failure and some cardiac diseases.

Factors affecting plasma level of Na, K and chloride:

1. Rapid and prolonged transfusion for injected fluids.
2. Acid-base balance.
3. Vomiting and Diarrhia.
   Vomiting short period → alkalosis and hypochloremia
   Prolonged vomiting and diarrhea → hypernatremia, acidosis and hypokalemia.
4. Excessive sweating and diabetes insipidus lead to hypernatremia and hyperchloremia.
5. Renal functions.
   Chronic renal failure leads to hyponatremia without hyperkolemia.
6. Diuretics
   Leads to hyponatremia and hypokalemia.
7. Adrinocortical function:
   a) hyperfunction (cusing disease) → hypokalemia-hypo-Cl leads to alkalosis and hyper-Na leads to increase blood volum and pressure.
   b) Hypofunction (Addison disease) → hyper-K and hyper-Cl leads to acidosis and hypo-Na leads to decrease blood volume and pressure.
8. Intravenous injection of glucose.
   Each gram glycogen stored –0.36 mol of K enters the cell leads to hypo-K.

Function of sodium:

A- Regulation of:

1. **Osmotic pressure of extracellular fluid.**
2. **Acid-base balance (formation of buffers).**
3. **Water balance.**

B- Plays a significant role in neuromuscular excitation process by preserving the normal irritability of muscles and permeability of cells.

Sodium depletion (hyponatraemia):

The plasma sodium concentration may be decreased in the following disorders:

1. **<u>Renal diseases characterized by failure of renal tubular reabsorption</u> mechanisms with an increased loss of Na+ in urine e.g. sodium losing nephritis.**
2. **<u>Addison's disease:</u> due to deficiency of aldosterone (aldosterone normally stimulates Na+ tubular reabsorption in distal tubules).**
3. **<u>Excessive loss in gastrointestinal fluids</u> as in severe vomiting and diarrhae (the gastrointestinal secretions are rich in Na+ and K+).**
4. **<u>By the excessive action of diuretics</u> that block tubular sodium reabsorptive mechanisms.**

Effects of hyponatraemia:

1. Neuromuscular weakness.
2. Lethargy, confusion, coma and death in severe cases.

Sodium intoxication (hypernatremia):

Sodium may be retained in high concentration in the body in the following states.

1. Cushing's syndrome: the excessive glucorticoids present in such state will increase sodium reabsorption in distal tubules.
2. Excessive cortisone intake.
3. Hyperaldosteronism.

Effects of hypernatremia:

The major effect is cellular dehydration, and dehydration of brain cells will lead to lethargy, convulsions, coma and even death, if not treated.

POTASSIUM (KALIUM)

- Potassium is the principal cation (K^+) of the intracellular fluid.
- The plasma concentration is about 5 m.Eq/litre (20 mg %).
- The main dietary sources are meats, vegetables and fruits (especially lemons, oranges and banana).
- Absorption readily occurs in upper part of small intestine.
- The daily requirement is about 3-4 g/day.

Function of potassium:

A high intracellular potassium is required for.

1. Protein synthesis by the ribosomes.
2. Activation of some enzymes as pyruvate kinase and sodium-potassium adenosine triphosphatase ($Na^+ + K^+$ ATPase, of sodium pump).
3. Maintenance of membrane potential of excitable tissues notably cardiac muscle.
4. Regulates intracellular: acid-base balance, osmotic pressure and water balance.

Potassium depletion (Hypokalemia):

This occurs in:

1. Cushing's disease (adrino cortical hyperfunction).
2. Hyperaldosteronism.
3. Excessive steroid intake.
4. Alkalosis: the decreased H+ concentration in plasma will result in shift of H^+ from intracellular fluid (ICF) into extracellular fluid (ECF), with a reverse shift of K^+ (from plasma into cells) to keep the concentration of intracellular cations. This will result in decreased serum K^+ concentration (hypokalaemia).
5. Dietary deficiency specially in elderly persons who live on tea and toast.
6. Duiretics that increases K^+ loss.
7. Increased losses by vomiting and diarrhea.

Effects of hypokalemia:

1. Tenderness, weakness and hyporeflexia.
2. Cardiac arrhythmias.
3. Renal tubular damage (in prolonged cases) with polyuria and failure to concentrate urine.

Causes of hyperkalemia:

1. Excessive intake specially in the presence of impaired renal function.
2. Increased tissue damage (due to the release of the high K^+ content).
3. Addison's disease (due to absence of aldosterone, which normally increase K^+ and H^+ excretion in exchange for the reabsorbed Na^+).
4. Renal failure; due to failure of filtration at glomeruli and/or secretion by tubules.
5. Acidosis: The intracellular shift of H^+ for buffering will lead to extracellular shift of K^+ (from buffering will lend to extracellular shift of K^+ (from within cells into plasma).
6. Hemolysis: intracellular cation.

Effect of hyperkalemia:

1. Generalized neuromuscular irritability with hyperreflexia.
2. Myocardial irritability leading to arrhythmia and cardiac arrest.

The sodium-potassium pump:

- The mechanism responsible for the active transport of sodium out of the cell and potassium into the cell is a sodium-potassium pump (simply known as sodium pump).
- The pump is located in the membrane and the energy for pumping is provided by ATP generated during metabolic reactions in the cell
- An enzyme intimately related to the active transport of Na^+ and K^+ across cell membrane has been recently described.
- This enzyme hydrolyses ATP to adenosine disphosphate (ADP), and it is activated by Na^+ and K^+. It is therefore known as the sodium-potassium activated adensine triphosphatase (Na^+ -K^+ ATPase or transport ATPase).
- The enzyme is absolutely dependant upon the presence of Na+ for its activity, but other ions as lithium (Li^+ can substitute for K^+ to some extent).
- Also the enzyme requires Mg^{++} for its activity and so it is called Mg^{++}-activated ATPase.
- Tissues with high transport activity, including nervous and secretory tissues possess high Na^+-K^+ ATPase activity.
- The transport mechanism is inhibited by ouabian (cardiac glycoside = drug used in treatment of heart failure). Also it is inhibited by metabolic poisons which prevent the formation of ATP.

CHLORIDE

- This is the main anion of extracellular fluid.
- Its concentration in plasma is about 103 m.Eq/litre.
- It is always present associated with sodium (as NaCl) and so its sources are the same as sodium.
- Absorption occurs in the upper part of small intestine.
- Excretion occurs in urine and sweat.
- Requirements 5-15 g/day (in the form of NaCl).

Functions:

A- Togerher with sodium it is essential for:

1. Regulation of water balance.
2. Regulation of acid-base balance (by chloride shift).
3. Regulation of osmotic pressure.

B- Essential for production of HCl of gastric juice.

Hypochloremic alkalosis:

- **This condition mainly occurs after prolonged vomiting (as in pyloric obstruction) where there is loss of chloride in excess of sodium.**
- **This leads to a decrease of plasma chloride, with a compensatory increase of plasma bicarbonate and a resultant hypochloremic alkalosis results.**
- **Other causes for such condition include:**
  1. **Cushing's disease.**
  2. **Excessive intake of ACTH or glucocorticoids.**
- **In these two later condition there is also hypokalemia.**

Chloride increase in case of:

- ❑ **Acute renal failure: decrease excretion.**
- ❑ **Dehydration.**
- ❑ **Diabetes insipidus.**
- ❑ **Acidosis: lead to diarrhea**
- ❑ **Hyperventillation: lead to alkalosis**

TRACE ELEMENTS

IRON

- Iron is one of the trace elements.
- The total body iron ranges between 3-5 g :
- Iron present in the body in 2 forms:-

A) Functional form (75%):

These are mostly hemoproteins responsible for cellular respiration they include:

1- Hemoglobin (67%):

- The main form of iron in the body,
- It carries O_2 from lung to tissues.
- Help in carriage of CO_2 in opposite direction.

2- Myoglobin (7.5%):

- A hemoprotein found in muscles.
- Temporary carry oxygen.

3- Respiratory enzymes (0.5%):

- Including cytochromes and cytochrome oxidase (in respiratory chain).
- Catalase and peroxidase important in detoxication of hydrogen peroxide.
- Tryptophan pyrrolase in tryptophane metabolism.
- Flavo-protein enzymes contain non-heme iron as NADH-dehyrogenase and succinate dehydrogenase.

B) Non functional form (25%) (transport and storage of iron):

- Transferrin → transport form in plasma.
- Ferritin → shelf storage form in liver, kidney, bone morrow.
- Hemosidrin → when body contain excess iron

Function of iron:

- Iron is the element of great importance regarding oxygen metabolism.
- Its role in this respect can be classified as follows:
  1. Oxygen carriage by hemoglobin.
  2. Oxygen storage: by myoglobin
  3. Oxygen utilization: by respiratory chain.
- Important for hemopiosis and hematopiosis.

Sources of iron:

1. Organs meat: liver, heart, kidney and spleen.
2. Egg yolk and fish.
3. Plant sources as whole wheat, dates, nuts, artichoke, beans and figs.

Requirements:

- 10-20 mg/day for normal adults (only 1-2 mg/day are absorbed which is the actual requirement).
- This is increased during period of increased demand *e.g.* pregnancy, lactation and after blood loss.

Absorption:

1. Iron is present in diet as ferric organic complex. By action of HCl in the stomach ferric ions (Fe^{+++}) are liberated.
2. Ferric ions are reduced to ferrous (only ferrous ions can be absorbed). This reduction is carried out by H+ of HCl, SH groups of proteins and by vitamin (C).
3. Ferrous ions (Fe^{++}) are absorbed to be oxidized again inside the intestinal mucosal cells to ferric (Fe^{+++}) ions,. then the ferric ions combine with apoferritin (mucosal cell protein) to form Ferritin.
4. Ferritin liberates ferric ions into the plasma and apoferritin is regenerated.

Iron binding by transferrin:

- Ferric iron couples to transferrin only in the company of an anion (usually carbonate) that serves as a bridging ligand between metal and protein.
- Without the anion cofactor, iron binding to transferring is negligible.
- With it, ferric transferring is resistant to most potent chelators.

Distribution and kinetics of body iron:

Percent of total	Iron (grams)	Compartment
66%	2.7	Hemoglobin
3%	0.2	Myoglobin
0.1	0.008	Heme Enzymes
--	<0.0001	Non-heme Enzymes
30%	1.0	Intracellular Storage (Ferritin)
1%	0.07(?)	Interacellular Labile Iron (Chelatable Iron)
0.1%	0.003	Intercellular Transport (Transferrin)

Mucosal block:

- This theory described the intestinal control of iron absorption.
- It states that the intestinal content of apoferritin is limited, and so once saturated with (to form Ferritin), block or inhibition of further iron absorption is carried out.

Factors regulating iron absorption:

1- Requirements of body:

- **An increased rate of erythropoiesis (*e.g.* after hemorrhage increases the need for more absorption of iron.**

2- Forms of iron in diet:

- **Organic iron e.g. iron citrate, lactate and gluconate and more soluble and readily absorbed.**
- **Inorganic iron as iron phosphate, carbonate are insoluble and poorly absorbed.**

3- Other constituents of diet:

- **Vitamin (C) and proteins increase iron absorption.**
- **Increased phosphate and oxalate precipitate iron and hinders its absorption. Also phytic acid produces the same effect i.e. decreases absorption.**

N.B.:

Absorption of iron occurs mainly in the stomach and duodenum. So after gasterectomy (removal of stomach) the patient is liable to iron deficiency anemia.

Blood iron:

1- In red blood cells:

- It contains Hb which contain 3.40 mg of Fe/g.
- There are 15 g of Hb/100 ml blood.
- That amount of Hb = 50 mg Fe/100 ml blood.

2- In plasma:

- Plasma Fe concentration – is 50-150 µg/dl.
- Fe carried on glycoprotein (transferrin).
- Each molecule of transferrin carried 2 atoms of ferric.
- Transferrin is synthesized in liver.
- Transferrin may carry up to 250-450 µg of Fe/dl of plasma which is the total iron binding capacity (TIBC).
- This means that on the average only about 30% of TIBC is saturated.
- In iron deficiency anemia plasma Fe decreased and TIBC tends to increases.
- In liver diseases plasma Fe and TIBC are decreased.
- Plasma contain-s only low concentrations of ferritin which is the index of Fe storage.
- Ferritin decreased in iron deficiency anemia and increased in hemosiderosis.

Storage of iron:

Iron is stored as ferritin (mainly) in the following organs and tissues:

1- Liver.	**2- Intestine.**
3- Spleen.	**4- Bone marrow.**
5- Kidney.	**6- Heart.**

Excretion of iron:

- **This amounts to 1-2 mg/day mainly in stools but also in sweat, hairs and menstrual blood in females.**

Iron differs from most other minerals in that its quantity in the body is controlled by regulation of absorption rather than its excretion.

1- In stool (90-95%):

- **Fecal Fe mostly unabsorbed Fe.**
- **Only few amount excreted in bile after absorption.**

2- In urine and sweat (5-10%):

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3- In menstruation and milk (5-10%):

- **About 15-30 mg of iron (Hemoglobin) are lost in menstruation per month *i.e.* 0.5-1.0 mg/day.**
- **Breast feeding accounts for the loss of 0.5-1.0 mg/day.**

4- The body is unable to excrete a large load of iron.

N.B.:

After intake of excess amounts of iron the stools are rendered black due to oxidation of iron in colon with excretion of iron oxide (black) in stools which must be differentiate from meleana (gasterointestimal bleeding).

Bronz diabetes: (Hemosiderosis-hemochromatosis).

This is an abnormal condition characterized by uncontrolled iron absorption resulting in increased rate of iron absorption, the absorbed iron will be deposited in the form of hemosidrin in:

1. **Subcutaneous tissues → bronz colour.**
2. **Pancreas → destroy B-cells → diabetes.**
3. **Brain → mental disturbances**
4. **When serum Fe is elevated: transferrin becomes 70-90% saturated similar condition in patients with a plastic or hemolytic anemia who recovered repeated blood transfusion.**

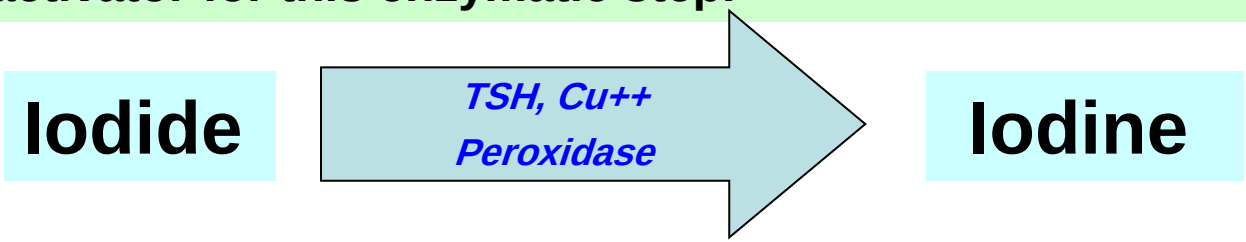
N.B.:

1. **Iron deficiency results in hypochromic microcytic anemia due to low intake of iron.**
2. **Iron balance is at equilibrium in normal adults *i.e.* intake = excretion n = 1-2 mg which equals the amount excreted).**
3. **Hemochromatosis – due to iron overload for long time there are hemosidrive deposits in liver, pancrease skin and joints.**

IODINE

- **Total body contain <u>25-50 mg</u>.**
- **Iodine is one of the trace elements.**
- **Source vegetable and fish.**
- **The only known function of iodine is synthesis of the thyroid hormones which proceeds by the following steps:**

1. **Trapping of inorganic iodide are oxidized by iodine peroxidase enzyme to molecular iodine (elemental or organic iodine), copper is needed as activator for this enzymatic step.**



TSH = thyroid stimulating hormone.

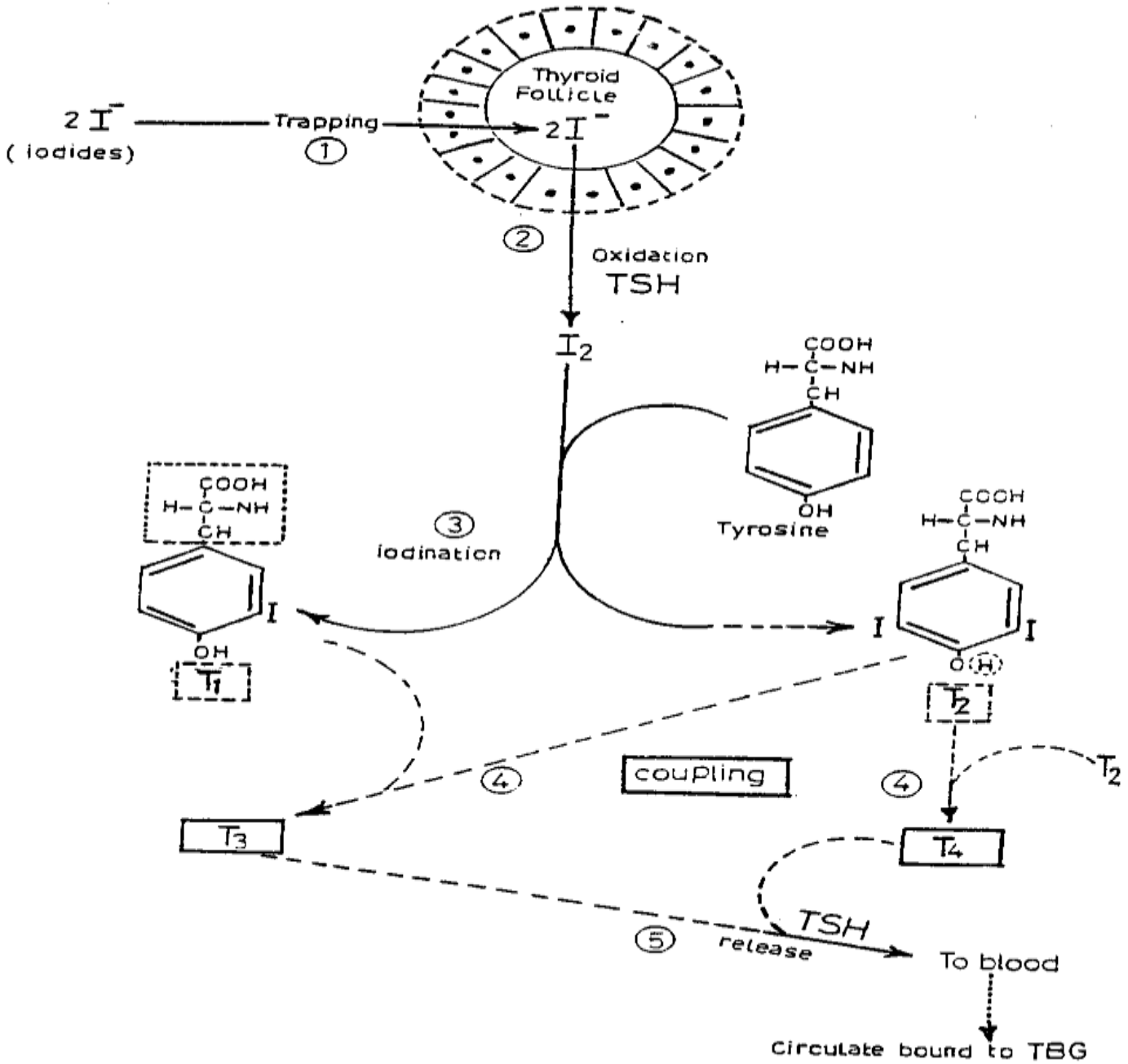
2. Iodination of tyrosine:

- This is carried out while the tyrosine molecules are attached to thyroglobulin (thyroid protein).
- The result of iodination is the formation of:
- T1 = monoiodo-tyrosine.
- T2 = diiodo-tyrosine.

3. Coupling (conjugation) of:

$T_1 + T_2$ → forms T_3 = triiodo-thyronine.
$T_2 + T_2$ → forms T_4 = tetra-iodothyronine = thyroxin →
in peptide linkage.
Both T_3 and T_4 are the thyroid hormones.

4. Release T_3 and T_4 from thyroglobulin contain 115 tyrosin residue into plasma occurs by a proteolytic enzyme and is activated by TSH. The released thyroid hormones are transported bound to plasma proteins known as thyroxine binding globulins (TBG).



Synthesis of thyroid hormones

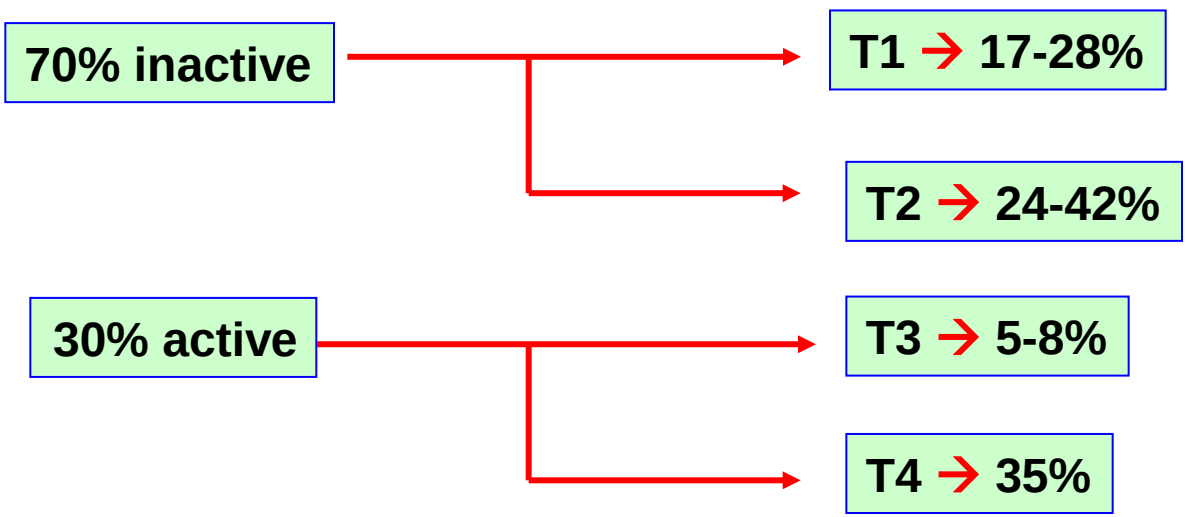
Absorption:

Readily absorbed in skin, lung, intestine converted to inorganic iodide before absorption intestine + stomach

Iodine in the body:

- 25-50 mg.
- 10-15 mg in thyroid.
- 2 mg/g dried thyroid
- 100 : 1 – 10:1 ratio of thyroid iodine.

Distribution of organic iodine in the gland:



N.B.:

1. T_3 is more active, more rapidly acting and more rapidly excreted than T_4.
2. 80 % of thyroid hormones stored in the thyroid gland is in the form of T_4, the remaining 20 % are present as T_3.
3. Plasma free levels of free T_3 is relatively more higher than that of T_4, due to the poor binding of T_3, to plasma proteins.
4. Both T_3 and T_4 are metabolized in the peripheral tissues by demination and decarboxylation to produce.
   * TRIAC: triiodoacetic acid.
   * TeTRAC: tetraiodoacetic acid.
5. Tetrac and Triac possess 25% of activity of T_3 and T_4.
6. Thyroid hormones are conjugated in liver with glucuronic acid and sulfate, and the conjugated products are excreted in bile and urine.

Excretion → mainly in urine and sometimes in stool, saliva lungs and milk.

COPPER

- **High concentration in liver.**
- **Copper is one of the trace elements.**
- **Whole body content is <u>100-150 mg</u>.**
- **Although its exact function is not yet understood but copper is known to be:**

1. **Essential for hemoglobin synthesis (and hence normal erythropoiesis), normal bone formation and the maintenance of myelin within the nervous system**
2. **Enters in structure of many metalloproteins *e.g.*:**
   Cerulopasmin = Plasma copper
   Erythrocuprin = Red cell copper
   Hepatocuprin = Liver copper.
   Cerebrocuprin = Brain copper.
3. **Enters in structure of a chromprotein know as hemocyanin or cuprocyanin which is the equivalent of haemoglobin in red cells of invertebrate and snak.**
4. **Enters in and is essential. for activity of ceratin enzymes *e.g.* ascrobic acid oxidase, tyrosinase, cytochrome oxidase, uricase, iodine peroxidase and superoxide dismutase.**

Requirements: 2.5 mg/day.

Sources: Nuts, liver, kidney and dried legumes.

N.B.: Milk is a poor source for iron.

Metabolism:

- Absorption of copper occurs in small intestine. The cupric ions Cu^{2+} are insoluble. Certain carrier low M.W. keep it soluble in water at intestinal pH is present in saliva and gastric juice of human. It complexes with Cu^{2+} to keep it soluble. In the intestinal mucosa copper is bound to a binding protein called "metallothionein".
- Copper in plasma binds to amino acids (especially histidine) and serum albumin. Plasma copper is rapidly removed from the circulation by the liver.

Plasma → 90% carried in cerulopasmin (α 2 glob glycoprotein)

Plasma → 10% carried in albumin.

RBC → bind to erythrocuprin (superoxide dimutase)

In the liver copper enters one of two routes:

1. **Excretion in bile.**
2. **Integration into ceruloplasmin. Ceruloplasmin contains 6-8 atoms of copper, half as (Cu^{2+}). Ceruloplasmin copper is not available for exchange with copper ions or bound copper (it is not the transport form of copper).**

Normal plasma level of copper is 100 µg/100 ml, in RBC, 100 µg/g.

a) **Copper toxicity may occur due to excess intake, it is manifested by green diarrhea, green saliva and acute haemolysis.**
b) **Menske's disease. This is a defective absorption of copper. The defect occurs at the transport of copper from the intestinal serosa to plasma.**

C- Willson's disease: (Hepato-lenticular degeneration).

This is a disease characterized by:

1. Increased copper absorption from intestine.
2- Increased deposition of copper in liver which may result in liver cirrhosis.
3- Deposition of excessive amounts of cooper in lenticular nucleus of brain with mental disturbances.
4- Low levels of copper and of ceruloplasmin in plasma.
5- Deposition of copper in kidney leading to increased urinary excretion of amino acids ((alninoncidurin) and maybe of glucose (glucosurin).

Excretion → **in stool through bile.**

ZINC

Function:

a) It helps crystallization and storage of insulin in B cells of the pancreas.
b) Component of some enzymes *e.g.* carbonic anhydrase, carboxypeptidase, retinal reductase and alcohol dehydrogenase.
c) Important for wound healing.

Sources:

Animal protein, citrus fluid and leafy vegetables.

Metabolism:

- Zinc is absorbed in the intestine by the help of a zinc binding factor, then binds inside the intestinal cell to zinc binding protein that transferes it to albumin.
- Copper interfere with zinc absorption by competing for the biniding sites on albumin. Also high plasma calcium prevents binding of zinc to albumin. Phytic acid complexes with zinc and prevents its absorption.
- In high zinc intake, it is bound by liver metallothionein.

Zinc deficiency occurs due to:

1- Malabsorption.
2- Sickle cell disease.

In zinc deficiency there is multisystem disfunction due to its presence in many enzymes.

Excretion:

1- Stool.
2- Urine.
3- Sweat.

MANGANESE (Mn^{2+})

Function:

1. Component of many enzymes *e.g.* arginase, carboxylases and superoxide dismutase.
2. Important for growth.
3. Important for the metabolism of nervous system.
4. Important for spermatogenesis and ovulation.

Sources:

Animal meats.

Metabolism:

Absorption of Mn^{2+} occurs in intestine by the help of a binding factor that makes it soluble. In the intestinal cell it is bound to a binding protein that transfers it to plasma albumin.

Excretion:

Mainly in stool.

CHRONIUM

Functions:

1. Important for glucose metabolism (it potentiates insulin action).
2. Important for lipoprotein metabolism.

Sources:

Yeast, grains and cereals. It is contributed in diet if cooking is done in stainless steel containers.

Metabolism:

Absorption occurs in small intestine in share with zinc. It is transported in blood to transferring.

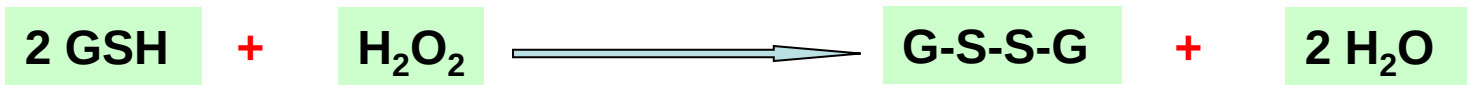
Excretion:

Mainly in urine.

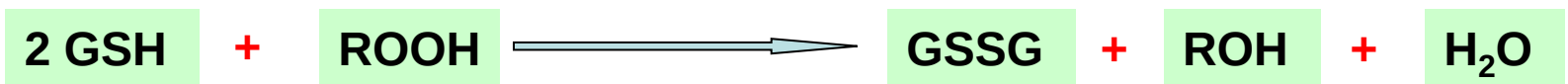
SELENIUM

Functions:

- **Selenium spares vitamin E or reduces its requirements. It is an essential component of glutathione peroxidase enzyme.**
- **This enzyme catalyzes the oxidation of reduced glutathione to oxidized glutathione as shown below:**



- **Reduced glutathione protects membrane lipids and other cell constituents (e.g. haemoglobin) against oxidative damage by destroying peroxide and fatty acid hyperperoxides through reactions catalyzed by glutathione peroxidase, thus:**



FLUORINE

Function:

Involved in a modification of hydroxyapatite crystals in the enamel of the tooth to produce fluoroapatite that prevents dental caries.

Sources:

Drinking water in many areas is enough.

Metabolism:

Absorption occurs in small intestine. Excess fluorine leads to fluorosis in which the teeth are brittle and mottled with white patches. Also fluorine is toxic to enzymes activated by magnesium *e.g.* enolase.

Excretion:

Mainly in urine.

COBALT

Function:

It is a constituent of vitamin B_{12}. So it is essential for erythroposis. In excess administration polycythemia may occur.

MOLYBDENUM

Function:

It is a component of flavoprotein enzyme *e.g.* aldehyde oxidase, xanthine oxidase (used for uric acid synthesis) and sulfite oxidase.