# Essential and trace ions

- **1- Iron:-**
- It is essential to the elementary metabolic processes in the cell
- In the respiratory chain , iron functions as an electron carrier
- Iron is responsible for the transport of molecular oxygen in higher organisms
- both of these functions depend on the ability of iron to exist in coordination compounds in different states of oxidation and bonding

| occurrence | iron bound as | mode of linkage | function |
|---|---|---|---|
| Blood system | Hemoglobin | Heme | O2 Transport |
| | Plasma | Transferrin | Fe Transport |
| Tissue | Functional iron ( myoglobin, cell hemes) | Heme | Cell respiration |
| | Storage iron | Ferritin hemosiderin | Iron pool Detoxication |

- Hemglobin consists of four protein chains, each of which contains a heme unit of a porphyrin ring and ferrous iron.
- Ferritin and hemosiderin are iron storage proteins found in the liver, spleen, and bone marrow
- Ferritin is a water soluble, crystallizable iron protein built up from apoferritin and micelles of a colloidal ferric hydroxide-phosphate complex
- Although the iron in ferritin is stored in the Fe+3 form it is incorporated and released in the Fe+2 form
- Hemosiderin is water insoluble and is considered by some to be a dehydrated ferritin.
- The major iron transport protein of blood plasma is a glycoprotein known as transferrin

- Iron transport into the intestinal mucosa is facilitated by ascorbic acid, fructose, and other organic molecules which tend to hold iron in a soluble ferrous state.
- The response of the intestine to iron depletion is more rapid when erythropoiesis (RBc production)is stimulated than when storage sites in the liver are reduced
- This has lead to the concept that as transferrin becomes depleted of iron during RBc formation, transferrin returns to the intestinal wall to pick up more iron , thereby signalling the intestine to absorb more iron.

- A person deficient in iron will become anaemic.
- Anaemia is a general term for a condition in which:

1. circulating red blood cells are deficient in number.
2. or deficient in total haemoglobin content per unit of blood volume.

- The net result is lower oxygen carrying capacity by the blood.
- Anaemia can be caused by excessive loss of blood or destruction or they may be due to decreased blood formation.
- Excessive blood loss can be caused by bleeding ulcer, haemorrhaging and menstrual flow.

- Blood destruction is caused by haemolytic agents (drug therapy, infections, toxins )or defective haemoglobins(sickle cell anaemia, thalassemia).
- Anaemia due to decreased blood formation can be caused by deficiencies of key materials (cobalamine, folic acid, pyridoxine and iron ), infections, renal insufficiency, malignancy, and marrow failure.
- Iron compound used for replacement therapy must meet two requirements:

1. it must be biologically available, usually water soluble, ferrous sulphate is the standard to which other iron salts are compared.
2. must be not irritant .

- Sustained released iron formulation have been utilized to minimize the irritant property of iron.
- Parenteral iron preparations are indicated only in:

1. defect in iron absorption as in partial gastroctomy, steatorrhea .
2. iron salt may irritate GIT so not used as in ulcerative colitis, peptic ulcer.

- Overdosage of oral iron is serious and can cause death, particularly in young children
- The human lethal dose is considered to be 150 to 200 mg iron / kg body weight.
- Ingestion of 10-15 (300mg ferrous sulfate tablet)may be lethal to a child, with a mortality rate near 50%

- Iron poisoning progresses in three to four stages
- Stage one begins 30 to 40 minutes after ingestion and includes gastrointestinal distress due to the astringent action of ionized iron, developing into cardiovascular collapse, shock and possible death in six hours.
- In stage two recovery seems apparent and may continue for 10 to 14 hours
- Stage three may then develop with a recurrent cardiovascular collapse, convulsions, metabolic acidosis, shock, coma, liver damage, and possible death occurring in one to three days.
- If the patient survives, stage four may occur one to two months later with gastrointestinal complications ( scarring, pyloric obstruction) due to the necrotizing effect (cell death) of the iron.

- Treatment usually includes

1- gastric lavage

2- and administration of salts (sodium bicarbonate and sodium dihydrogen phosphate) to form insoluble iron salts.

3-Oral administration of deferoxamine will prevent iron absorption. Provided kidney damage has not occurred.

- Deferoxamine can be given parenterally to chelate the iron and allow it to pass out in the urine.

4- Peritoneal dialysis has also been tried with poor results.

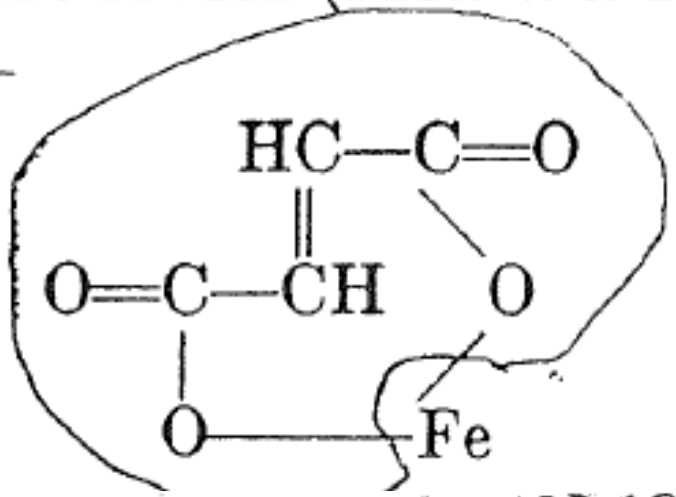
- A recent report suggests lavage of the stomach with a phosphate salt to bind all unabsorbed iron that was not expelled by emesis.
- Chelation by deferoxamine mesylate (desferal mesylate) is indicated only when there is unbound iron demonstrated in the serum.
- Orally administered iron has been shown to interfere with absorption of tetracycline presumably by forming a 1:1 chelate.
- Oral ferrous salts may aggravate gastrointestinal diseases such as peptic ulcer , regional enteritis, and ulcerative colitis.

- Official iron product:
- There are three officially approved iron salts available for the oral administration of iron.
- 1.Ferrous sulphate FeSo4.7H2O
- Ferrous sulfate U.S.P occurs as pale, bluish green crystals or granules which are odorless.
- it is oxidizes readily in moist air to form brownish yellow basic ferric sulphate [Fe4(OH)2(SO4)5 ]
- Ferrous sulphate is the most widely used oral iron preparation and is considered as the drug of choice for treating uncomplicated iron deficiency anaemia.
- It can be irritating to GIT mucosa due to the astringent action of soluble iron but iron salt equivalent doses are used.

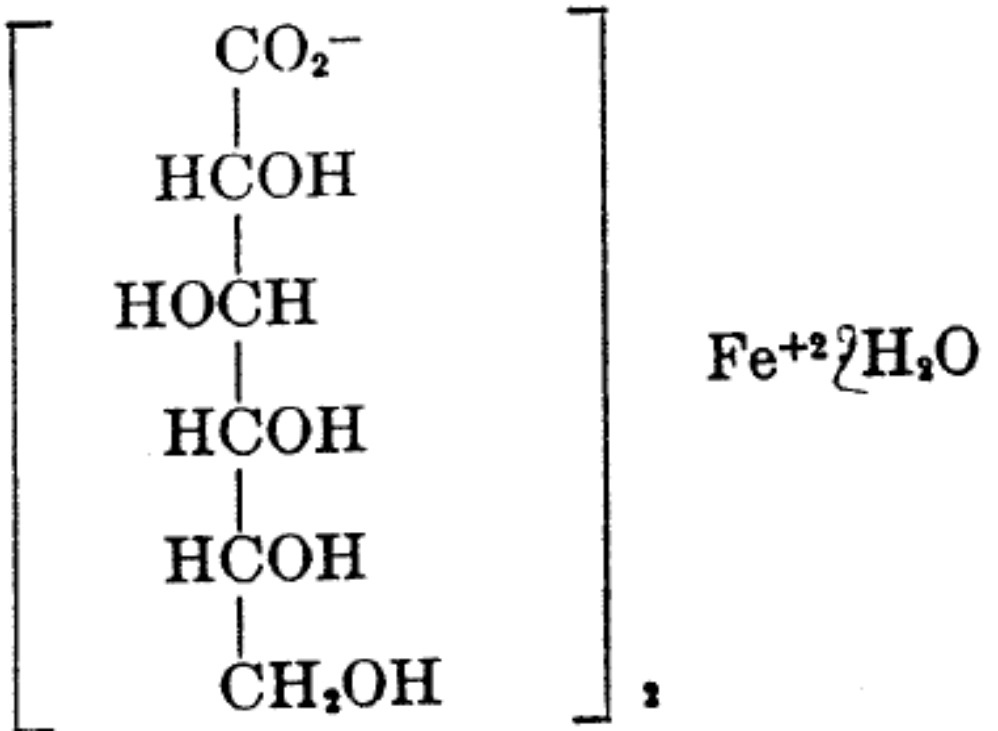
- Usual dose : 300mg, the equivalent of 60mg of elemental iron, two or three times a day.
- Dosage forms: dried ferrous sulfate tablets, and syrup.
- 2.Ferrous fumarate.
- Ferrous fumarate U.S.P occurs as a reddish orange to red-brown, odorless powder.
- It is resistant to oxidation on exposure to air so it may be superior to both ferrous sulphate and gluconate.
- Usual dose : 200mg, the equivalent of 60mg of elemental iron, two or three times a day.
- Dosage forms: ferrous fumarate tablets

- 3.Ferrous gluconate.
- Ferrous gluconate N.F. occurs as a yellowish gray or pale greenish yellow, fine powder or as granules having a slight odor.
- It has a good bioavailability .
- Usual dose : 300mg, the equivalent of 35mg of elemental iron, three times a day.
- Dosage forms: ferrous gluconate tablets
- It is doubtful if it is any less irritating than ferrous fumarate or sulfate when equivalent doses of iron are administered why?? (H.W.)

**Ferrous Fumarate,** U.S.P. XVIII (Mol. Wt. 169.9)



**Ferrous Gluconate,** N.F. XIII (Mol. Wt. 482.18)



- Parenteral administration of iron:
- 1-Iron dextran injection, U.S.P. (Imferon)
- is a sterile , colloidal solution of ferric hydroxide [Fe(OH)3] complexed with partially hydrolyzed dextran (glucose polymer) of low M.wt., in Water for Injection.
- The PH will between 5.2 and 6.5. prior to mixing, it is a dark brown, slightly viscous liquid.
- It is for I.M. injection only.
- It is used only in confirmed cases of severe iron deficiency anemia where oral therapy is contraindicated or ineffective, or if the patient cannot be relied upon to take oral medication.
- Usual dose: intramuscular, the equivalent of 100mg of iron once a day.

- 2- Iron sorbitex injection. U.S.P. (Jectofer)
- Is a sterile solution of a complex of iron , sorbitol, and citric acid that is stabilized with the aid of dextrin and an excess of sorbitol.
- The PH is between 7.2 and 7.9. by itself, iron sorbitex is a dark brown, clear liquid.
- Is to be administered by the I.M. route only.
- Usual dose: intramuscular, the equivalent of 100mg of iron once a day.
- the concurrent administration of oral iron is contraindicated
- The patient “s urine can become dark on standing due to the formation of iron sulfide.

## 2.Copper:

- It is required for many enzymes, for synthesis of haemoglobin and for normal bone formation.
- Unlike iron it is believed that most of the population obtain the sufficient amount of copper from food, water, and cooking utensils.
- Copper supplements are probably not necessary.
- The adult human is estimated to contain about 2mg/kg of copper, distributed mostly in enzymes and other proteins.
- The average daily intake is estimated at 2-5 mg per day.
- Copper is solubilized in stomach acid and absorbed from the stomach and upper small intestine,

- From intestine copper moves into the blood where it exists first as copper albumin complex, then goes to the liver where the copper become part of copper protein, ceruloplasmin .
- Ceruloplasmin copper is not released until the protein is catabolized
- Copper is found in the brain in form of cerebrocuprein, in blood cells as erythrocuprein.

Several roles in metabolism have been attributed to copper :

1. haemoglobin formation.

- copper is required to prevent anaemic conditions through:

a. facilitate iron absorption.

b. Stimulates enzymes involve haeme and globin biosynthesis.

c. Could involve in metabolism of stored iron .

2. It is important in oxidative phosphorylation (ATP production by cellular respiration )

Copper is a constituent of cytochrome oxidase.

3. It is associated with the formation of aortic elastin.

It may be that copper is necessary for amine oxidase activity and may play a role in the formation of cross linkages of elastin .

4. It is a component of tyrosinase , an enzyme responsible for conversion of tyrosine to the black pigment, melanin.

A copper deficiency in animals may cause loss of hair color which can be attributed to reduced tyrosinase activity.

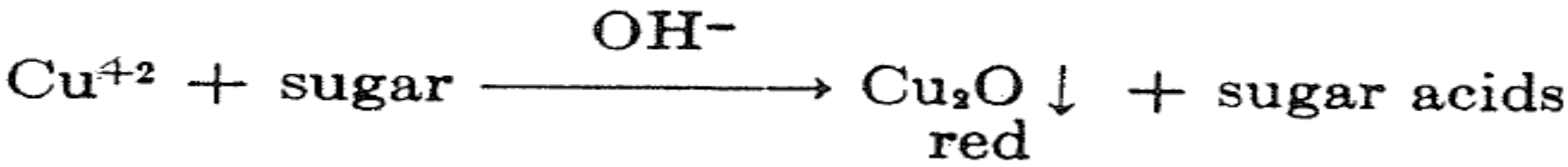
Albinisim is associated with either an absence of or an inactive form of tyrosinase.

- **Wilson disease a condition of excess copper storage.**
- Is of genetic origin, being transmitted by an autosomal recessive gene
- There is a decrease in ceruloplasmin conc. which lead to a decrease in total blood copper ,and characterized by presence of large amounts of copper in the brain along with an excessive urinary output ,increased copper levels in liver, brain, kidney, and cornea.
- **Pencillamine is the drug of choice which is a chelating agent , in addition to diet restriction.**

- **Uses of Copper**

1. Topically as fungicide and astringents.
2. Antidote for phosphorous poisoning.
3. Essential component of Fehling and benedict solutions which are used for determination of glucose.

- a positive test is the production of cuprous oxide.



## 3.zinc :

- Zinc essential for:

1. Several enzymes as alcohol dehydrogenase, alkaline phosphatase, carbonic anhydrase, glutamic dehydrogenase and others.
2. Zinc bound to RNA stabilizing secondary and tertiary structures.
3. For normal growth and reproduction.
4. It has a beneficial effect on tissue repair and wound healing.
5. Zinc complexes with insulin present in B cells of pancreas.
6. Necessary for vitamin A mobilization from liver and vit. A metabolism affected by zinc deficiency.

**Low plasma zinc level is found in:**

1. Alcoholic cirrhosis (progressive liver disease).
2. Uremia.
3. Myocardial infarction.
4. Cystic fibrosis with growth retardation.

- Food sources of zinc includes : seafood, nuts, meat, eggs, and milk.
- A person on vegetable diet may not receive a sufficient amount of zinc (10-15 mg daily) because phytic acid which found in vegetable proteins such as soya bean combine with zinc and decrease its absorption.
- Zinc sulfate is official as a topical astringent.

- 4- Selenium :
- The main function of selenium is to mediate the activity of the enzyme glutathione peroxidase, which acts as an antioxidant.
- The oral administration of large doses of selenium salts produce intestinal irritation and interference with the functioning of small blood vessels and blood-forming organs.
- It may be of therapeutic value in the treatment of kwashiorkor, a protein deficiency affecting large numbers of children and infants in south america, africa and asia

- Selenium has been implicated in cellular respiration and as an antioxidant in conjunction with vitamin E.
- Selenium is official as Selenium sulfide N.F., a suspension for the treatment of seborrheic dermatitis of the scalp (dandruff).

- 5- Sulfur:
- **Sulfur is widely distributed throughout the body in:**
- 1. Proteinase a. Sulfhydryl groups of cysteine.
  b. Disulfide linkages in protein from cystine
- 2. Mucopolysaccharides and sulfolipids as sulphate salts and esters.
- Dietary sulfur comes from these same groupings found in plant and animal foodstuffs.
- **Sulphur has been used therapeutically as :**
- 1.Cathartic action.
- 2.Parasiticide in scabies.
- 3.Stimulant in alopecia

- 6- Iodine(Iodide):
- Iodide is an essential ion necessary for the synthesis of two hormones produced by thyroid gland, triiodothyronine T3 and thyroxineT4.
- Internally iodine or iodide can be administered, since iodine is reduced to iodide in the intestinal tract but more common iodide salts are administer because of solubility reasons.

- Iodine have :

1. biochemical role in thyroid hormone formation.
2. pharmacological action as:

- a. Fibrinolytic agent.
- b. Expectorant .
- c. Bactericidal agent.
- The usual daily iodine requirement for an average male is 140 micrograms and female about 100 micrograms.
- Lack of sufficient iodine in diet result in an enlargement of thyroid gland.

- When iodine is administered its uptake is governed by three principle factors:

1. The character of local thyroid tissue because abnormal thyroid tissue (tumorous) has a slower uptake of iodide and a lower content of iodine than normal tissue.
2. Blood level of inorganic iodide ,because a high level keeps the iodine at high level in the colloids thus using up only a small part of the administered iodide.
3. The level of TSH in blood which is hormone secreted by anterior pituitary gland because the thyrotropin content has a direct bearing on the complete utilization of iodine in the formation of of the iodinated hormones, and thyrotropin also controls the release of thyroid hormone from the thyroid gland .

- Excess of iodide inhibit release of TSH and decrease production of thyroid hormones.
- The effect of such antithyroid drugs as propylthiouracil is not to inhibit iodine uptake but rather to block the enzyme system that iodinates the amino acid precursor .
- **Thyroid gland regulates:**

1.metabolism of the body.

2. affect growth and development of the body.

- **Iodide therapeutically used as :**
- Improving agent in hyperthyroidism.
- Radioactive iodide used which administered in the form of sodium iodide .the body converts the inorganic radioactive iodide into thyroglobin in the thyroid gland ,thus subjecting the gland to radiation that will cut down its activity.
- Official iodine product
- Strong iodine solution U.S.P. (Lugol ‘s solution)
- Contains 5g of iodine and 10g of potassium iodide per 100ml total volume
- It is a transparent liquid having a deep brown color and odor of iodine.
- Usual dose: 0.1 to 0.3 ml three times a day