teeth. About 50% of the daily intake is excreted through urine.

Functions

Fluoride is required for the proper formation of bone and teeth. Fluoride becomes incorporated into hydroxyapatite, the crystalline mineral of bones and teeth to form fluoroapatite, which increases hardness of bone and teeth and provides protection against dental caries and attack by acids.

Deficiency Symptoms

Deficiency of fluoride leads to ***dental caries*** and ***osteoporosis.***

Toxicity

- Excessive amounts of fluoride can result in ***dental fluorosis.*** This condition results in teeth with a patch, dull white, even chalk looking appearance. A brown mottled appearance can also occur.
- It is known to ***inhibit*** several enzymes especially ***enolase*** of glycolysis.

IODINE (I_2)

The adult human body contains about 50 mg of iodine. Nearly half of this is present in muscles. Thyroid gland in which the concentration is highest contains 20% of the body iodine; skin and skeleton also contain small amounts. The blood plasma contains 4-8 µg of protein bound iodine (PBI) per 100 ml.

Dietary Food Sources

Seafood, drinking water, iodized table salt, onions, vegetables, etc.

Recommended Dietary Allowance Per Day

150 µg.

Functions

The most important role of iodine in the body is in the synthesis of thyroid hormones, ***triiodothyronine (T_3)*** *and* ***tetraiodothyronine (T_4),*** *which influence a large number of metabolic functions.*

Absorption and Excretion

Iodine in the diet absorbed rapidly in the form of iodide from small intestine. Normally, about 1/3rd of dietary iodide is taken up by the thyroid gland, a little by the mammary and salivary glands. The rest is excreted by the kidneys.

Nearly 70 to 80% of iodine is excreted by the kidneys, small amounts are excreted through bile, skin and saliva. Milk of lactating women also contains some iodine.

Deficiency Manifestation

Deficiency of iodine occurs in several regions of the world, where the iodine content of soil and therefore of plants is low. A deficiency of iodine in children leads to ***cretinism*** and in adults endemic ***goitre.***

Cretinism

Severe iodine deficiency in mothers leads to intrauterine or neonatal hypothyroidism results in cretinism in their children, a condition characterized by mental retardation, slow body development, dwarfism and characteristic facial structure.

Goitre

A goitre is an enlarged thyroid with decreased thyroide hormone production. An iodine deficiency in adults stimulates the proliferation of thyroid epithelial cells, resulting in enlargement of the thyroid gland. The thyroid gland collects iodine from the blood and uses it to make thyroid hormones. In iodine deficiency the thyroid gland undergoes compensatory enlargement in order to extract iodine from blood more efficiently.

IRON (Fe)

A normal adult possesses 3 to 5 gm of iron. This small amount is used again and again in the body. Iron is called a ***one way substance,*** because very little of it is excreted. Iron is not like vitamins or most other organic or even inorganic substances which are either inactivated or excreted in course of their physiological function.

Dietary Food Sources

The best sources of food iron include liver, meat, egg yolk, green leafy vegetables, whole grains and cereals. There are two types of food iron:

- **Haem iron:** Iron associated with porphyrin is found in green leafy vegetables
- **Non-haem iron:** Iron without porphyrin, and present as a prosthetic group of a substance, is found in meat, poultry and fish.

Recommended Dietary Allowance Per Day

- Adult men and post menopausal women: 10 mg
- Premenopausal women: 15 to 20 mg
- Pregnant women: 30 to 60 mg

Women require greater amount than men due to the physiological loss during menstruation.

Functions

Iron is required for the,

- Synthesis of haem compound like haemoglobin, myoglobin, cytochromes, catalase and peroxidase

- Synthesis of non-haem iron (NHI) compounds, e.g., iron-sulfur proteins of flavoproteins, succinate dehydrogenase and NADH dehydrogenase

Thus iron helps mainly in the ***transport, storage*** and ***utilization of oxygen.***

Absorption **(Figure 17.3)**

The normal intake of iron is about 10 to 20 mg/day. Normally, about 5 to 10% of dietary iron is absorbed by the active transport process. Most absorption occurs in the duodenum. Haem of food is absorbed directly from the intestine and non-haem iron (inorganic iron) is absorbed in the ferrous (Fe^{2+}) state into the mucosal cell as follows:

- The gastric acid, HCl and organic acids in the diet convert organic ferric compound of the diet into free ferric (Fe^{3+}) ions
- These free ferric ions are reduced with ascorbic acid and glutathione of food to more soluble ferrous (Fe^{2+}) form which is more readily absorbed than Fe^{3+}
- After being taken up by the intestinal mucosa iron, is either stored in the form of ***ferritin*** in the mucosal cells or transported across the mucosal cells to the plasma in the form of ***transferrin. Mucosal cell storage is influenced by the body's iron status, being reduced in iron depletion and increased in states of iron overload.***

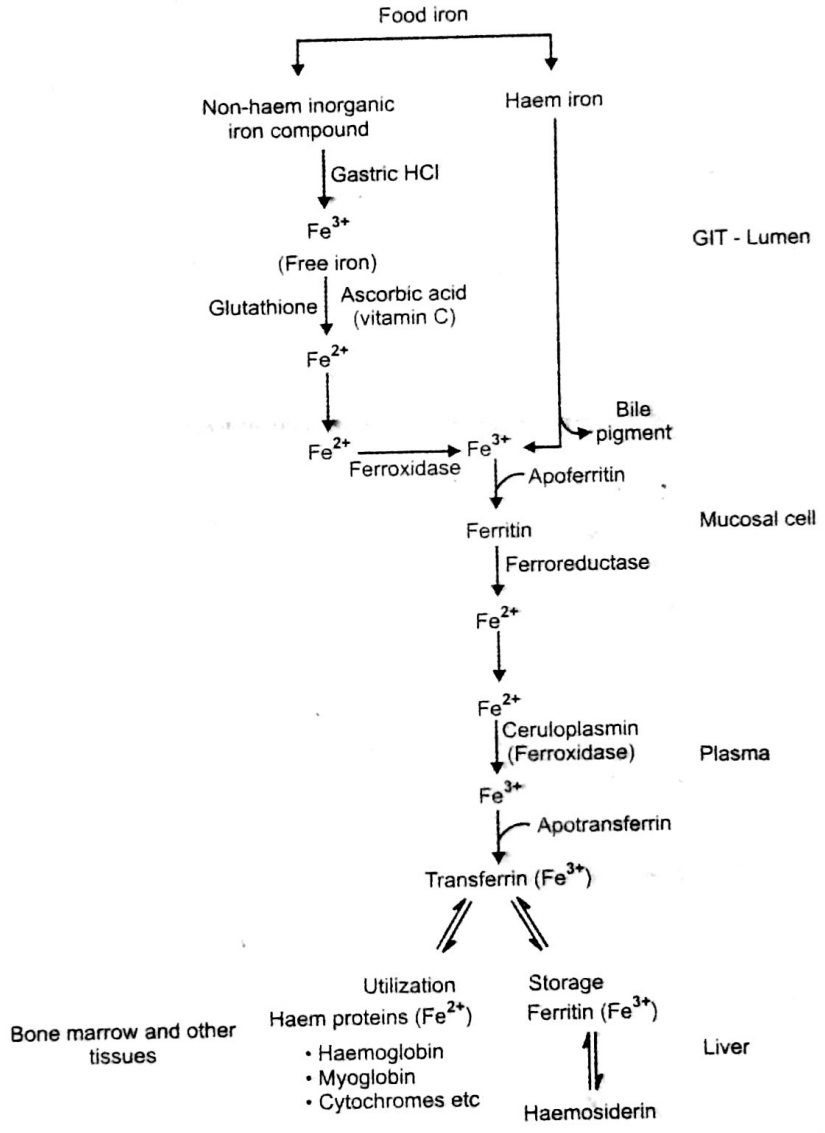

Figure 17.3: Absorption, storage and utilization of food iron

Factors Affecting Iron Absorption

- **State of iron stores in the body:** Absorption is increased in iron deficiency and decreased when there is iron overload. The mechanism is not known
- **Rate of erythropoiesis** (the process of red blood cell production). When rate of erythropoiesis is increased, absorption may be increased even though the iron stores are adequate or overloaded
- **The contents of the diet:** Substances that form soluble complexes with iron, e.g. ascorbic acid (vitamin C) facilitates absorption. Substances that form insoluble complexes, e.g. phosphate, phytates and oxalates, inhibit absorption.
- **Nature of gastrointestinal secretions and the chemical state of the iron:** Iron in the diet does not usually become available for absorption unless released in free form during digestion. This depends partly on gastric acid (HCl) production. Ferrous (Fe^{2+}) is more readily absorbed than ferric form (Fe^{3+}) and the presence of HCl, helps to keep iron in the Fe^{2+} form.

Transport

- Iron is transported in plasma bound to the specific glycoprotein, ***apotransferrin***, each molecule of which binds two Fe^{3+} ions together with bicarbonate as an anion
- Iron is always transported in the ***ferric form***. The transfer of iron from the storage ferritin (Fe^{3+} form) to plasma involves reduction of Fe^{3+} to Fe^{2+} in the mucosal cell with the help of ***ferrireductase***
- Fe^{2+} then enters the plasma where it is reoxidized to Fe^{3+} by a copper protein, ***ceruloplasmin*** or serum ferroxidase
- Fe^{3+} is then incorporated into transferrin by combining with apotransferrin.

Storage

Iron in plasma is taken up by cells and either incorporated into heme or stored as ***ferritin*** or ***haemosiderin.***

Ferritin

- Ferritin is the major iron storage compound and readily available source of iron for metabolic requirements
- The protein component of ferritin is apoferritin
- Each apoferritin molecule can take up about 4500 iron atoms
- Storage of iron occurs in most cells but predominantly in cells of liver, spleen and bone.

Haemosiderin

- In addition to storage as ferritin, iron can also be found in a form of ***haemosiderin***. The precise nature of haemosiderin is unclear
- It may be formed as a result of the partial degradation of the protein of ferritin by lysosomal proteases; followed by the release of ***iron oxide*** to ***form insoluble aggregates***
- In contrast to ferritin haemosiderin is insoluble in aqueous solution. Iron is released only slowly from haemosiderin
- Normally, very little haemosiderin is to be found in the liver, but the quantity increases steadily during iron overload and haemosiderin formation may represent a secondary protective mechanism against iron overload.

Excretion

- Iron is not excreted in the urine, but is lost from the body via the ***bile, faeces*** and in ***menstrual blood***
- Iron excreted in the faeces is exogenous, i.e. dietary iron that has not been absorbed by the mucosal cells is excreted in the faeces
- In male, there is an average loss of endogenous iron of about 1 mg/day through desquamated cells of the skin and the intestinal mucosa
- Females may have additional losses due to menstruation or pregnancy.

Disorders of Iron Metabolism

Iron deficiency *and* **iron overload** are *the major disorders of iron metabolism.*

Iron deficiency

A deficiency of iron causes a reduction in the rate of haemoglobin synthesis and erythropoiesis, and can result in ***iron deficiency anaemia.*** Anaemia is a condition characterised by a reduced number of circulating red cells or a reduced amount of haemoglobin in the cells or both. Iron deficiency anaemia is the commonest of all single-nutrient deficiencies. The main causes are:

- **Deficient intake,** including reduced bioavailability of iron from dietary fibre, phytates, oxalates, etc.
- **Impaired absorption,** e.g. in intestinal malabsorptive disease and abdominal surgery
- **Excessive loss,** e.g. menstrual blood loss in women and in men from gastrointestinal bleeding (in peptic ulcer, diverticulosis or malignancy)

Iron deficiency causes low haemoglobin resulting in ***hypochromic microcytic anaemia*** in which the size of the red blood cells are much smaller than normal and have much reduced haemoglobin content.

Clinical features of anaemia

Weakness, fatigue, dizziness and palpitation. Nonspecific symptoms are nausea, anorexia, constipation, and menstrual irregularities. Some individuals develop pica, a craving for unnatural articles of food such as clay or chalk.

Iron overload

Haemosiderosis *and* **haemochromatosis** *and* **iron poisoning** *are conditions associated with iron over load.*

Haemosiderosis

Haemosiderosis is a term that has been used to imply an increase in iron stores as haemosiderin **without associated tissue injury.** Haemosiderosis is an initial stage of iron over load.

Haemochromatosis

Haemochromatosis is a clinical condition in which excessive deposits of iron in the form of haemosiderin are present in the tissues, **with injury** to involved organs. The causes of haemochromatosis may be genetic (primary) or acquired (secondary).

Primary or genetic haemochromatosis

Primary haemochromatosis is a hereditary disorder, due to an unregulated increase in the intestinal absorption of iron from normal diet. Patients with haemochromatosis absorb about 4 mg of iron per day rather than 1 mg from gastrointestinal tract. Iron is deposited as haemosiderine in liver, pancreas, heart and other organs. After accumulating for years, the excessive amounts of intracellular iron lead to tissue injury and ultimately organ failure. At this stage the amount of storage iron may exceed ***20 gm rather than the normal 3-4 gm.***

Secondary or acquired haemochromatosis

The main causes of acquired haemochromatosis are:

- **Chronic overload:** Which occurs when the diet contains excess absorbable iron, e.g. acid containing food cooked in iron pot
- ***Parenteral administration of iron or*** **chronic blood transfusion** *for blood disorders, e.g., thalassaemia*
- **Alcohol abuse** due to an ethanol induced increase in iron absorption.

Clinical symptoms of haemochromatosis are related to the involved organ systems as follows:

- **Liver:** Leading, to cirrhosis
- **Pancreas:** Leading to fibrotic damage to pancreas with diabetes mellitus
- **Skin:** Skin pigmentation, bronzed diabetes
- **Endocrine organ:** leading to hypothyroidism, testicular atrophy
- **Joints:** Leading to arthritis
- **Heart:** Leading to arrhythmia and heart failure.

At least 90% of affected individuals are male, suggesting that iron losses in menstruation and pregnancy may protect females.

Iron Poisoning

Acute overdose, mainly occurring in children may cause severe or even fatal symptoms due to toxic effect of free iron in plasma which may be life threatening. Symptoms include:

- Nausea
- Vomiting
- Abdominal pain
- Diarrhoea and
- Haematemesis.

In severe cases, hypotension, liver damage, and coma can result.

MANGANESE (Mn)

Manganese is present in biological systems bound to protein. It is associated with connective and bony tissue, growth and reproductive functions and carbohydrate and lipid metabolism.

Dietary Food Sources

Meat (liver and kidney), wheat germs, legumes and nuts.

Recommended Dietary Allowance Per Day

2.5 to 5.0 mg.

Functions

- Manganese is a constituent of metalloenzymes and an enzyme activator
- Important manganese containing enzymes include:
  - arginase
  - pyruvate carboxylase and
  - mitochondrial manganese superoxide dismutase
- Manganese activated enzymes include
  - hydrolases
  - kinases
  - decarboxylases and
  - transferases.

Many of these activations are nonspecific in that other metal ions, such as magnesium, iron or copper can replace manganese as the activator. Such activation can mask the effect of manganese deficiency, that is why the deficiency of manganese in humans appear to be very rare.

- Manganese specific activating enzymes are:
  - glycosyltransferases
  - phosphoenolpyruvate caroboxykinase and
  - glutamine synthetase
- Manganese also functions with vitamin K in the formation of prothrombin.

Absorption and Excretion

Dietary manganese is absorbed poorly from the small intestine. Most of the manganese is excreted rapidly in the bile and pancreatic secretion in the faeces.