Iron Metabolism

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- Iron is one of the most essential trace element
- Total body iron content is 3 to 5 g.
- 75% present in blood, the rest is in liver, bone marrow & muscles.
- Iron is present in almost all cells.
- Heme is the most predominant iron-containing substance.
- It is a constituent of proteins/enzymes (hemoproteins)-Hb, myoglobin, cytochromes,

- catalase, xanthine oxidase, tryptophan pyrrolase, peroxidase.
- Non-heme iron-transferrin, ferritin, hemosiderin.
- Sources:
- The best sources of food iron include liver, meat, egg yolk, green leafy vegetables, dates, whole grains and cereals.

- In a typical Indian diet, the major quantity of iron is received from cereals because of the bulk quantity taken, although they contain iron only in moderate amounts.
- Jaggery is a good source of iron.
- Milk is a very poor source of iron, containing less than 0.1 mg/100 ml.

RDA

- **Adult man & postmenopausal women:** 10 mg
- **Premenopausal women:** 15 to 20 mg
- **Pregnant women:** 30 to 60 mg
- **Women require greater amount than men due to physiological loss during menstruation.**

Biochemical functions

- Iron is a component of several functionally important molecules.
- Iron is required for the synthesis of hemoglobin, myoglobin, cytochromes, catalase and peroxidase.
- Cytochromes & certain non-heme proteins are necessary for ETC & oxidative phosporylation.
- Peroxidase, the lysosomal enzyme is required for phogocytosis & killing of bacteria.

- Iron is also essential for the synthesis of non heme iron (NHI) compounds like, succinate dehydrogenase, iron-sulfur proteins of flavoproteins, NADH dehydrogenase.
- Iron helps mainly in the transport, storage and utilization of oxygen.
- Iron is associated with effective immuno-competence of body.

Metabolism of iron

- **Absorption:**
- ***Iron is called as one way substance, because it is absorbed and excreted from small intestine.***
- **Iron is absorbed from upper small intestine.**
- **Iron is absorbed in three forms: (1) ferrous iron (2) ferric iron (3) heme iron.**
- **Iron is absorbed mainly in the ferrous form.**

- Ferric ions are reduced with ascorbic acid & glutathione of food to more soluble ferrous (Fe^{2+}) form which is more readily absorbed than Fe^{3+}
- After 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.

Factors affecting iron absorption

- **Factors increasing the iron absorption:**
- **Iron is mainly absorbed in the ferrous form.**
- **Ascorbic acid & cysteine favors the reduction of ferric form of iron to ferrous form.**
- **Cystatin C & HCL also favors the reduction of ferric form of iron to ferrous form.**
- **In iron deficiency state, the iron absorption is increased to 2-10 times that of normal.**

Factors decreasing iron absorption

- Phytates and phosphates in the food decreases iron absorption.
- Achlorohydria:
- The deficiency of HCL results in impaired conversion of ferric form of iron to ferrous form of iron.
- Iron absorption is deceases in the presence of gastrointestinal diseases.

Transport

- **Iron in the mucosal cells:**
- **The iron (Fe^{2+}) entering the mucosal cells by absorption is oxidized to ferric form (Fe^{3+}) by the enzyme ferroxidase (ferroxidase activity of ceruloplasmin)**
- ***Major sources of iron in the plasma is from degraded erythrocytes.***
- **Fe^{3+} combines with apoferritin to form ferritin, which the temporary storage form of iron.**

- From the mucosal cells, iron may enter the blood stream.
- Transport of iron in the plasma:
- Iron enters plasma in ferrous state.
- It is oxidized to ferric form by a copper containing protein, ceruloplasmin - ferroxidase activity.
- Ferric iron binds with a specific iron binding protein-transferrin or siderophilin.
- Transport form of iron is transferrin.
- It is a glycoprotein, synthesized in liver.

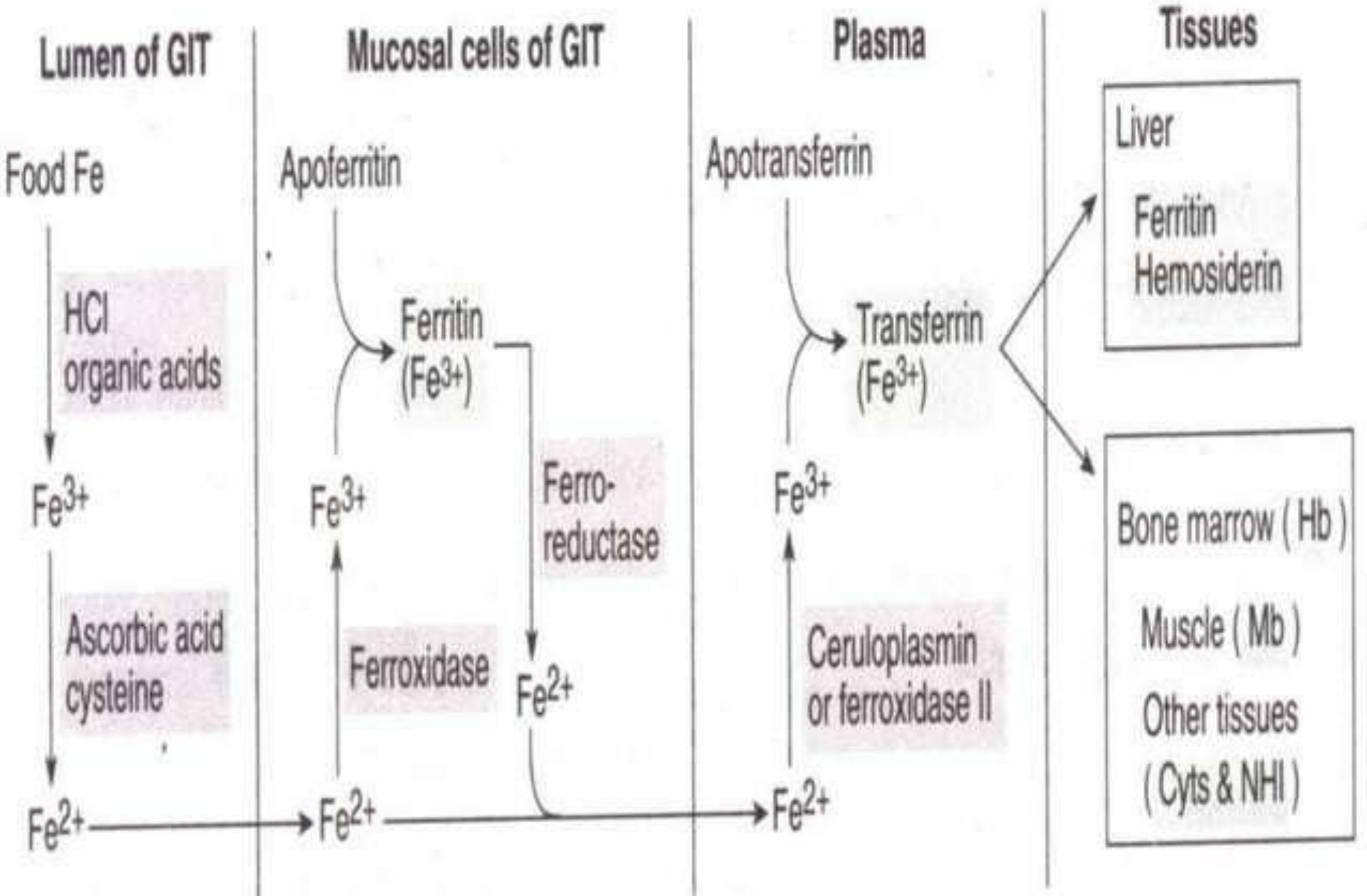
- Normal plasma level of transferrin is 250 mg/dl.
- One molecule of transferrin can transport 2 ferric atoms and the half-life of transferrin is 7-10 days.
- Serum iron and serum iron binding capacity:
- Total iron binding capacity (TIBC) of transferrin is 250-450 µg/dl;
- In iron deficiency anemia, serum iron level is decreased and TIBC is increased.

Storage

- Iron is stored in liver, spleen & bone marrow in the form of ferritin.
- In the mucosal cells, ferritin is the temporary storage form of iron.
- Ferritin contains about 23% iron.
- Ferritin in plasma level is elevated in iron over load.

- **Ferritin level in blood is an index of body iron stores.**
- **Ferritin is an acute phase reactant protein, elevated in inflammatory diseases.**
- **Hemosiderin:**
- **It is another iron storage protein, which can hold about 35% of iron by weight.**
- **Hemosiderin accumulates when iron levels are increased.**

Summary – iron absorption and transport



Excretion

- The normal Iron excretion is about 1mg/day.
- The major excretory pathway is through intestine.
- Iron is not excreted in urine, but in nephrotic syndrome loss of transferrin may lead to increased loss of iron in urine.

Disorders of iron metabolism

- Iron deficiency & iron overload are the major disorders of iron metabolism.
- Iron deficiency
- Iron deficiency causes a reduction in the rate of haemoglobin synthesis & erythropoiesis.
- It can result in iron deficiency anemia.

- **Causes:**
- **Iron deficiency is caused by inadequate intake, impaired absorption, chronic blood loss & increased demand.**
- **Iron deficiency anemia mostly occurs in growing children, adolescent girls, pregnant & lactating women.**

Clinical features

- Microcytic hypochromic anemia in which the size of the red blood cells are smaller than normal and have much reduced haemoglobin content.
- Weakness, fatigue, dizziness and palpitation,
- Nonspecific symptoms are nausea, anorexia, constipation, and menstrual irregularities.

Iron over load

- Haemosiderosis and haemochromatosis and iron poisoning are conditions associated with iron over load.
- Haemosiderosis:
- It refers to accumulation of hemosiderin in liver & other reticulo-endothelial system.
- There is no significant tissue destruction.
- Haemosiderosis is an initial stage of iron over load.

Haemochromatosis

- Haemochromatosis is a clinical condition in which iron is directly deposited in the tissues (liver, spleen, pancreas & skin).
- Haemochromatosis may be genetic (primary) or acquired (secondary)

Genetic or primary haemochromatosis

- It is a hereditary disorder, due to an unregulated increase in the intestinal absorption of iron from normal diet.
- Iron is deposited as haemosiderin in liver, pancreas, heart and other organs.
- After accumulation, excessive amounts of intracellular iron lead to tissue injury and organ failure.

Acquired or secondary haemochromatosis

- It is caused by excess intake of iron, increased hemolysis and repeated blood transfusions.

Clinical features

- 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 organs: leading to hypothyroidism, testicular atrophy

- **Joints**: leading to arthritis
- **Heart**: leading to arrhythmia & heart failure
- **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 life threatening.
- **Symptoms**:
- Nausea, vomiting, abdominal pain, diarrhoea.

Thank You