Haematinic agents

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Haematinic agents

Haematinic agents are which stimulate the production of RBCs or increase the amount of hemoglobin in the blood.

These includes :

- ✓ Iron,
- ✓ Vitamin B12
- ✓ Folic acid.

Haematinic agents antianemics. They are used to treat and various types of anemias.

Iron

- Iron is an essential haematinic agent that is required for human life.
- Iron stored in the body as ferric form(Fe3+) with apoferritin. Major storage of iron is Reticulo endothelial cells of liver. Others are spleen, bone marrow & hepatocytes.
- An adult body contains about 3-4 g of iron. About 66% of iron is present in hemoglobin.

☆ Sources of Iron :

Animal sources : Liver, egg yolk, chicken ,fish, milk &dairies.

Plant sources : Banana, apple, dry bean, peas, lentils, dry fruits etc.

☆ RDA :

Adult male : 0.5-1.0 mg

Adult female : 1-2 mg

Infant : 50 mcg

Pregnant woman : 3-5 mg.

☆ Role of Iron in our body :

1.The primary function of iron is to form haemoglobin. Iron forms the nucleus of iron-porphyrin heme ring, which together with globin chains forms hemoglobin.

2. It is necessary for the formation & maturation of RBC.

3.It s responsible for the transport of oxygen from the lungs to rest of the body, in the form of oxyhaemoglobin. Iron is the central atom of heam. The heam binds with Oxygen, transporting it from lungs to tissues.

4.Cytochrome is an iron containing enzyme. It is concerned with the oxidation of metabolites in the cell.

5.Myoglobin is an iron containing chromoprotein. It combines with O2 & acts as an oxygen store for muscle.

6.The chromatin of the nucleus contains iron and thus helps in the functioning of nuclei.

7. Iron helps convert food to energy

8. Iron helps to maintain normal cognitive function.

- **Risk factors associated with Iron :**

Inadequate supply of iron in our body can lead to Iron deficiency. Major symptoms include - Nausea, Vomiting,metabolic acidosis, Abdominal pain, Bloody diarrhea, shock.

Causes of Iron deficiency:

1. Inadequate dietary intake of iron.
2. Chronic blood loss.
3. Conditions that produce increased requirement of iron.
4. Abnormalities of GIT
5. In premature babies, since they are born with low iron stores.
6. It may also occur due to parasite infection

- **Iron absorption :**

There are 3 hypothesis proposed for iron absorption-

1. Mucosa block hypothesis.
2. Iron chelation hypothesis.
3. Active transport hypothesis.

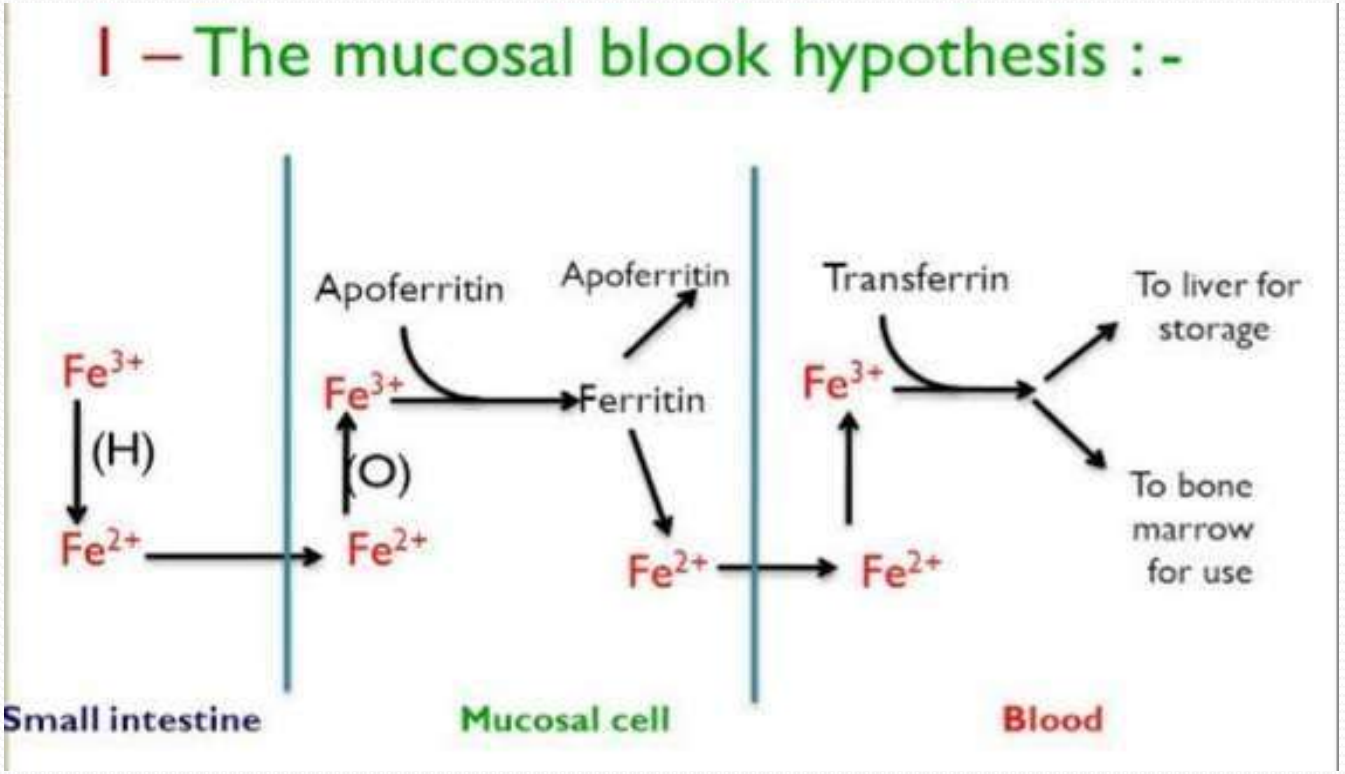
Among them Mucosa block hypothesis is widely accredited.

- **Mucosa block hypothesis**:

1. Mostly, Iron in food particles is in Fe3+(ferric) form. When Fe3+ ions are in stomach, it is reduced with ascorbic acid & glutathione of food to more soluble Fe2+(ferrous) form by means of ferric reductase enzyme.
2. Then it's absorbed from the small intestine & crosses the intestinal mucosal cells.
3. The Fe2+ entering the mucosal cells by absorption is oxidised to Fe3+ by ferric oxidase.
4. Fe3+ combines with apoferritin to form ferritin, which acts as the temporary storage form of iron.
5. The ferritin may be transported across the mucosal cells to the blood plasma in the form of transferrin.

6. The transferrin stored in the liver is used in different purposes like catalyst action, synthesis of Hb & myoglobin.

7. When the iron stored in the body is depleted absorption is enhanced.



☆ Factors facilitating Iron Absorption :

1. **Acid** : Acid enhances dissolution and reduction of ferric iron.
2. **Reducing Substances**: Ascorbic acid reduces ferric iron and forms absorbable complexes
3. **Meat**: Meat also facilitates iron absorption by increasing HCl secretion
4. **Pregnancy/ Menstruation** : Due to increased iron requirement

☆ Iron preparations:

1. **Oral preparations** : Ferrous sulfate, Ferrous fumarate, Ferrous gluconate.
2. **Parenteral preparations** : Iron-dextran, Iron-sucrose, Iron-sorbitol-citric acid comple

☆ Ferrous Fumarate :

▪ Ferrous fumarate is one of the most common & available form of oral iron preparation.

It's a tablet dosage form. It contains 33% of Iron as API.

▪ Dose : 200mg two or three times a day.

▪Ferrous fumarate is made by the interaction of hot, aqueous solution of ferrous sulfate &sodium fumarate. Here sodium fumarate is generally added to the ferrous sulfate.

$$FeSO_4 + Na_2C_4H_2O_4 \rightarrow FeC_4H_2O_4 + Na_2SO_4$$

The precipitate of ferrous fumarate is removed by filtration. Then it is washed, dried & reduced to a powder.

- **Advantages :**

1. It is resistant to oxidation on exposure to air.
2. It provides good haematologic responses in iron deficiency from any other available preparations.
3. It is less irritating to the GIT than other commonly used ferrous salts.
4. It does not cause staining to teeth.

- **Disadvantages :**

1. Some side effects such as heartburn , nausea, vomiting, colic constipation or diarrhea may occur.
2. Like other iron preparations this drug may increase GIT diseases, especially ulcer.
3. It can not be dispersed in solution dosage form which is necessary for use especially for old persons & children.
4. It's relatively expensive.

Vitamin B12

- Vit B12 is a Complex cobalt containing molecule to which various groups are linked covalently to form cobalamine.
- Vit B12 is a water soluble vitamin. It is synthesized in nature by only microorganisms ; plants &animals acquire it from them.
- It Consists of a Porphyrin like ring with central cobalt atom attached to anucleotide
- Sources : Liver, kidney, Sea fish, egg yolk, meat &dairy products.
- RDA : 1-3 mcg for an adult.

☆ Pharmacokinetics :

- ✓ Absorption of Vit B12 occurs in small intestine by active transport.
- ✓ When it passed the stomach, it binds to specific intrinsic receptors present on intestinal mucosal cells at the ileum.
- ✓ The intrinsic factor-vitamin B complex is subsequently absorbed in the distal ileum & later It is transported in blood in combination with transcobalamin ll.
- ✓ It is stored in the hepatic cells of liver & excreted mainly through bile &urine.

☆ Role of Vit B12 in body :

1. Essential for conversion of homocysteine to methionine.
2. Essential for purine &pyrimidine synthesis.
3. Essential for cell growth &multiplication.
4. Essential for DNA synthesis, fatty acid metabolism
5. Essential for RBC production.

- **☆ Role of Vit B12 in DNA synthesis:**

- Vitamin B12 is important for DNA synthesis . B12 contains cobalamin, is essential for the synthesis of methionine, which is an essential amino acid for the synthesis of DNA. .
- Cobalamin acts as a methyl-donor, it participates in the monocarbonic acid metabolic pathway & plays a critical role in DNA methylation.
- DNA-methylation is catalyzed by DNA methyl-transferases that transfer methyl groups from methionine to cytosine.

- Vitamin B12 & folate, are necessary as coenzymes of methyltransferase & lead to the remethylation of homocysteine to methionine, which is a essential amino acid for the synthesis of DNA. So without cobalamin the synthesis of DNA will not work correctly.
- Low dietary consumption of B12 results in respectively low serum levels, which induce alterations in DNA synthesis. Thus, deficiency of B12 may lead to DNA damage.

Folic acid

Folic acid is a yellow crystalline, water soluble vitamin essential for cell growth &reproduction.

It functions as coenzyme with vitamins B12 in the metabolism &in the formation of RBCs..

- Folic acid consists of 3 components- PABA, Pteridine ring &Glutamic acid.
- Sources : Liver, kidney, cereals, yeasts, egg, meat, grains,
- RDA : o.2 mcg for an adult.

☆ Pharmacokinetics :

- ✓ Folic acid is present in food as polyglutamate. The additional glutamate residues are split off primarily in the upper intestine before being absorbed.
- ✓ It is transported in blood mostly as methyl THFA which is partly bound to plasma protein.
- ✓ It is stored in cell as polyglutamates..

☆ Role of Folic acid in body :

1. Conversion of homocysteine to methionine.
2. Conversion of serine to glycine.
3. Needed for protein synthesis.
4. Needed for DNA synthesis.
5. Essential for RBC production.
6. Essential for Histidine metabolism.

☆ Role of haematinics in RBC production :

- ✓ Erythropoiesis is the process in which new erythrocytes are produced. These new erythrocytes replace the oldest erythrocytes that are phagocytosed and destroyed each day.
- ✓ Vit B12, FA & iron have crucial roles in erythropoiesis. Erythroblasts require Vit B12 & FA for proliferation during their differentiation.
- ✓ Deficiency of Vit B12 & FA inhibits purine and pyrimidine synthesus that impairs DNA synthesis & causes erythroblast apoptosis, resulting destruction of RBCs.

- Erythroblasts require large amounts of iron for hemoglobin synthesis. Large amounts of iron are recycled daily with hemoglobin breakdown from destroyed old erythrocytes.
- Therefore, in case of formation of RBC combination of Folic acid, Vit B12&Iron is important. If any single is absent, RBC will be immature.