**HAEMATOLOGY 5  
IRON DEFICIENCY**

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**Learning Objectives**

* Describe the role of iron in erythropoiesis, dietary sources of iron, absorption of iron, causes of iron deficiency, clinical and haematological features of iron deficiency and the diagnosis and management of iron deficiency.
* Describe the clinical and haematological features of anaemia of chronic disease and explain how this is distinguished from iron deficiency.

**IRON METABOLISM**

Iron is an essential component of many haem-containing molecules including **enzymes** and the oxygen carrying compounds **haemoglobin** and **myoglobin.**

Dietary iron is found in large amounts in red meat, offal and to a lesser extent other animal products. It is also found in relatively large amounts in green vegetables. Because free iron is toxic and because there is no mechanism for excretion of iron the absorption of iron from food is strictly regulated by the intestinal mucosa and this is governed by the amount of iron in the body.

Other factors that affect iron absorption include the form of iron. Haem consists of a protoporphyrin ring with an iron atom at its centre. Haem is better absorbed than free iron (up to 10% absorption) and its absorption is not adversely affected by other food components. In contrast, non-haem iron (i.e. Fe2+ and Fe3+) from vegetable sources are less well absorbed (1-2% absorption) and may be affected by other dietary factors. Factors which improve non-haem iron absorption include acid pH, ascorbic acid (e.g. glass of orange juice) and digestive enzymes, whilst those that inhibit iron absorption include alkaline pH, phytates and phosphates (e.g. cups of tea).

The total amount of iron in an adult is between 3-5 grams. This is divided into three pools:   
(i) a metabolic pool in haemoglobin and myoglobin (2-3 grams), (ii) a storage pool in ferritin and haemosiderin of up to 1 gram and (iii) a proportionately small but extremely important transit pool which consists mainly of plasma protein-bound iron of which the most important component is transferrin-bound iron (about 3 milligrams).

Iron compounds in the body

Metabolic pool

Haemoglobin 2500 mg

Myoglobin 500 mg

Storage pool

Ferritin and haemosiderin 0-1000 mg

Transit pool

Plasma protein-bound iron 3 mg   
e.g. transferring -bound

**Transferrin** is a glycoprotein made in the liver with two binding sites for iron. It interacts with a **transferrin receptor** on the surface of erythroblasts. The complex is internalised; the iron is removed from the transferrin, which is then recirculated. Iron itself will act as a positive regulator of erythropoiesis and expression of the gene that codes for ferritin. Iron is a negative regulator for expression of the gene that codes for transferrin receptor.

**Hypochromic microcytic anaemias**

This is a term used to describe an anaemia where the red cells contain less haemoglobin than normal [low mean cell haemoglobin (MCH)], have a lower concentration of haemoglobin [hypochromia, low mean cell haemoglobin concentration (MCHC)] and are small (microcytic low mean cell volume MCV). The three commonest causes for this type of anaemia are **iron deficiency, anaemia of chronic disease** and **the thalassaemias.**In milder forms of thalassaemia there is often microcytosis without anaemia.

**Iron deficiency anaemia (IDA):**

Iron deficiency is the most important cause of anaemia on a worldwide basis. The major cause of iron deficiency is **BLOOD LOSS**. Additional causes are **dietary deficiency, increased needs** and **malabsorption.** . Often there is more than one cause of deficiency such as a poor diet in menstruating women or in growing children.

**Blood loss.** The main sources of **blood loss** are uterine in women of childbearing age group, followed by gastrointestinal blood loss, which may be overt or occult.

**Dietary deficiency** occurs in vegans and vegetarians with unbalanced diets poor in iron but can also occur in non-vegetarians.

**Increased needs** occur during childhood and especially during the pubertal growth spurt and during child bearing.

**Malabsorption** is a less common cause of iron deficiency

**Treatment:** iron replacement is simply, effectively and cheaply effected with oral iron compounds and the most commonly used is ferrous sulphate. Side effects include constipation and indigestion and may reduce compliance. Compounds containing less iron (ferrous fumarate or ferrous gluconate) may be better tolerated. In case of difficulties, iron can be given parenterally (IM or IV).

**Assessment of iron status:**

Several parameters can be useful including serum iron, total iron binding capacity (TIBC), transferrin saturation, serum ferritin and a visualisation of haemosiderin in bone marrow aspirates using the Prussian blue reaction.

***The serum ferritin*** is PARTICULARLY USEFUL in clinical practice as it is low in uncomplicated iron deficiency and normal in thalassaemia trait and normal or raised in anemia of chronic disease. As ferritin is an acute phase reactant, however, it may be normal or increased in patients where iron deficiency co-exists with chronic inflammatory conditions.

Anaemia of chronic disease. Typically the serum iron is low but the ferritin is normal or raised. Total iron binding capacity is normal or reduced.

Iron deficiency. Typically the serum iron is low and the ferritin is also low. The total iron binding capacity is increased.

Thalassaemia trait. Iron levels, total iron binding capacity and ferritin levels are all normal.

Anemia of chronic disease plus iron deficiency. This is not uncommon. Additional tests which may help to establish whether a patient is iron deficient are:-

1. blood film….you may see changes of iron deficiency, such as elliptocytes
2. bone marrow aspirate….slides can be stained to see whether or not iron stores are present

**FILL IN THE MISSING SECTIONS**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Iron deficiency** | **ACD** | **Thalassaemia Trait** |
| Hb |  |  |  |
| MCV |  | Low or normal |  |
| Serum Iron |  |  |  |
| Ferritin | Low |  |  |
| Transferrin |  |  |  |
| Transferrin saturation |  |  | Normal |

**Anaemia of chronic disease (ACD)**

This is an anemia associated with chronic inflammatory, infectious or neoplastic conditions. ACD can cause a mild to moderate normocytic or microcytic hypochromic anaemia. In ACD the inflammatory markers such as CRP (C-reactive protein) and ESR (erythrocyte sedimentation rate) are raised. The serum ferritin may also be raised and there is accumulation of excess iron in the bone marrow storage pool but with a block in iron incorporation into erythroblasts, which may lead to reduced haemoglobin synthesis and hypochromia. Difficulties arise in differentiating between ACD and IDA and in certain cases the two coexist; in these patients the serum ferritin may be within the low normal range.   
A bone marrow aspirate may be required to distinguish between the two conditions.   
The pathogenesis of ACD is complex but it usually responds to treatment of the underlying disorder.

(Handout modified from a previous version from Dr. Saad Abdalla)