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Iron Deficiency

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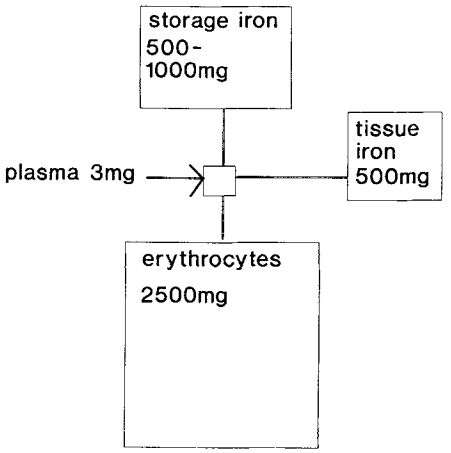
THE SUBJECT IS DIVIDED INTO THE FOLLOWING PARTS:

1. Distribution
2. Turnover
3. Stages of deficiency
4. Diagnosis
5. Clinical aspects
6. Is iron deficiency a big problem?
7. Discussion.

1. IRON DISTRIBUTION

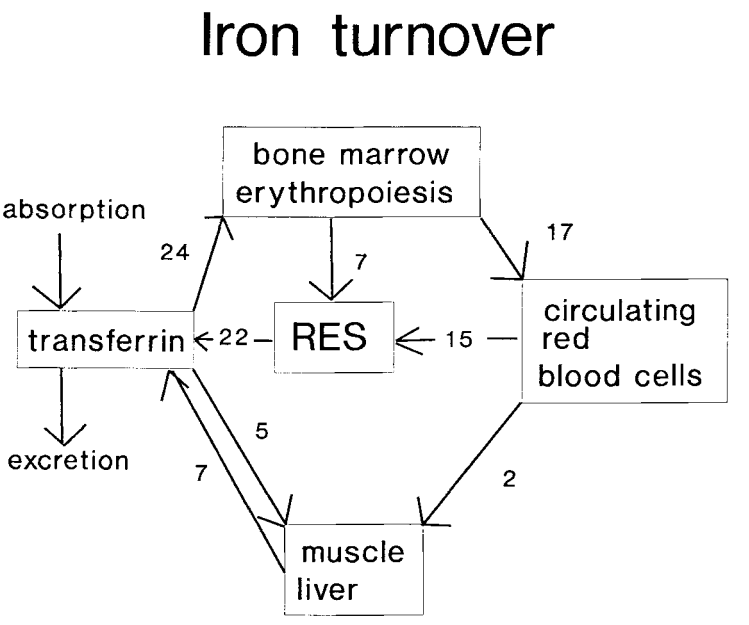
Iron is required for the normal function of haemoglobin, myoglobin and some enzymes, e.g. cytochromes and catalases. The total amount of iron in an adult human is around 3-4 g (54-71 mmol), most of which is bound to haemoglobin. Iron is stored as ferritin and haemosiderin in the reticuloendothelial system (RES; mainly bone marrow, liver and spleen), hepatic parencymal cells and in skeletal muscle. Part of the ferritin of the RES is secreted into plasma.

Iron distribution



2. IRON TURNOVER

In plasma, approximately 3 mg (54 μmol) of iron bound to transferrin is circulating, and plasma iron turnover is around 30 mg per day. Small changes in iron turnover give large changes in plasma iron concentrations. Furthermore, there is a diurnal variation with higher plasma iron concentration in the morning and lower in the evening.

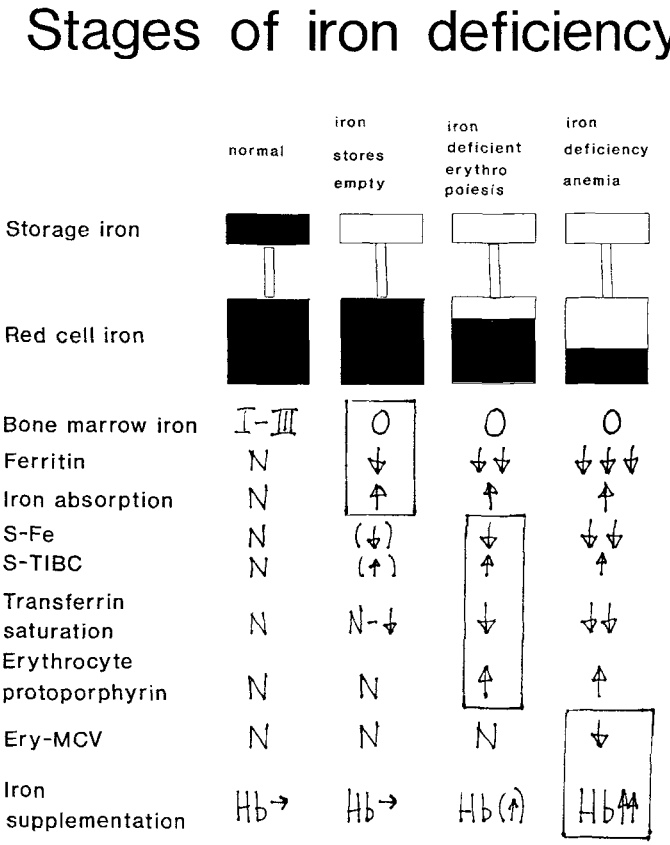


Figures indicate mg iron per day

3. IRON DEFICIENCY

Iron deficiency is commonly defined as a situation in which the amount of iron in the body is decreased to such an extent that the iron stores are empty, which leads to inadequate supply to iron-dependent tissues, e.g. the bone marrow.

Different stages of iron deficiency may be defined, as this figure illustrates, with the use of different methods. When the iron stores are empty, the serum ferritin concentration decreases and the iron absorption increases. No storage iron can be demonstrated in the bone marrow. Blood hemoglobin and MCV are still normal. In iron deficient erythropoiesis, the transferrin saturation decreases and the free erythrocyte protoporphyrin levels increase. MCV is still within reference limits, and the subject is not anemic. In frank iron deficiency anemia, MCV decreases and all the variables will be abnormal as well.



All the methods have, however, limitations, as shown in this figure. In addition, a therapeutic trial with iron requires good patient compliance, that continuing blood loss does not occur. The limitations of all these methods become evident in some clinical situations, particularly when dealing with patients in whom iron deficiency is associated with other disorders.

Limitations of some methods for diagnosing iron deficiency

Bone marrow reticular iron:
- requires good specimens
- invasive, laborioius
- expensive

Serum ferritin:
- difficult to interpret in some situations
- inflammation
- catabolic states
- cell damage. e.g. hepatic cells
- iron supplementation

Iron absorption tests:
- expensive, laborious
- limited availibility

S-Fe, transferrin saturation:
- diurnal variation
- influenced by inflammation
  iron medication

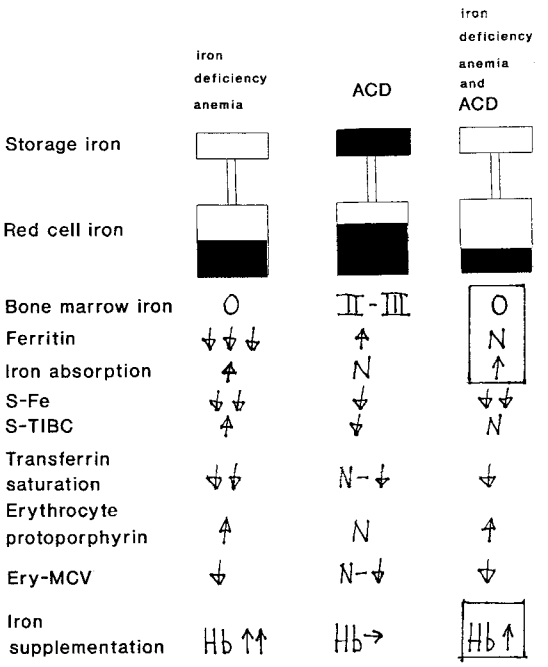
Ery-MCV:
- late stage of iron deficiency
- low in thalassemia
  sideroblastic anemia

5. CLINICAL ASPECTS

The anemia seen in different inflammatory states has been defined as anemia of chronic disease, ACD. This is characterized by a moderate anemia, a low serum iron concentration and sometimes even a decreased MCV. However, serum transferrin or total iron binding capacity is also decreased, which leads to a normal or possibly only slightly diminished transferrin saturation. Serum ferritin is elevated, and bone marrow iron is abundant.

ACD and iron deficiency may be co-existing, not least among hospital patients. For example, patients with rheumatoid arthritis may become iron deficient due to gastric hemhorrhage caused by aspirin and other antiinflammatory drugs. Patients with hematological disorders who are treated with high doses of prednisolone is another example of this. On the other hand, old patients with chronic disorders may be subject to long term iron medication when the diagnosis was ACD instead of iron deficiency. Thus, the definition of iron deficiency in subjects with anemia of chronic disease is often important.

Anemia of chronic disease and iron deficiency



In the differential diagnosis between these two entities, the following methods may be employed. A biopsy is the "godlen standard". If storage iron can be demonstrated, iron deficiency is excluded. A low normal serum ferritin concentration in the presence of signs of inflammatory response may indicate iron deficiency. Iron absorption tests have limited availibility. A therapeutic trial with iron may be useful.

Is iron deficiency a big problem? Indeed, anemia and iron deficiency is a global problem. In 1985, WHO estimated that 500-600 million people in the world were suffering from iron deficiency anemia.

Diagnosis of iron deficiency in the presence of ACD

1. Tissue biopsy (bone marrow, liver)
2. S-Ferritin not high in spite of inflammation
3. Iron absorption test
4. Therapeutic trial with iron

7. DISCUSSION

In Sweden, the prevalence of iron deficiency has varied somewhat during the years. The diminishing prevalence of iron deficiency among fertile women has been explained by a more widespread use of oral contraceptives, ascorbic acid supplements and iron tablets, as well as by increased food iron fortification. It has been shown that elderly subjects have increased iron stores, possibly due to a shift of iron from skeletal muscle and red cells to the RES.

Iron deficiency in an industrialized country like Sweden should, at least among adults, be regarded as a sign of gastrointestinal blood loss. This has in most instances clinical implications in terms of further investigation of the patient, and a correct diagnosis of iron deficiency is thus essential.

Prevalence of iron deficiency

Iron deficiency anemia in Swedish women aged 44 - 46 years

1963 - 64 25%
1968 - 69 8%
1974 - 75 7%
(Hallberg 1967; Garby 1967, 1969; Bengtsson 1978; Tibblin 1979)

Absence of bone marrow reticular iron in women aged 38 years

1984 32% (Rybo 1984)

Iron deficiency in subjects aged 70 - 81

Men 7 - 8% (of which 1 - 4% anemic)
Women 7 - 9% (of which 2 - 3% anemic)
(Nilsson-Ehle 1988)

Iron deficiency anemia in long term care patients aged 45 - 95 years: 7%

I would like to finish by pointing at some aspects of diagnosing iron deficiency, of which I believe point 2 is particularly relevant for this meeting.

Aspects of diagnosing iron deficiency

1. **Quantitative**
   when and how thoroughly should we assess iron status?
   * Target groups
     Anemic patients
     Women of fertile age?
     Pregnancy?
     Children?
     Elderly?

2. **Qualitative**
   which combination of methods are optimal in the clinical setting?
   * To define the different stages of iron deficiency
   * To define iron deficiency in the presence of other disorders
   * To evaluate iron supplementation

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