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# IRON Metabolism and its Importance in Child Development - Review

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**Abstract:** ***Anemia is a decrease in the total amount of red blood cells or hemoglobin in the blood, or a lowered ability of the blood to carry oxygen. Globally, anaemia affects 1.62 billion people. Symptoms of anemia are related to its severity and speed of installation. Iron deficiency anemia (IDA) is a microcytic, hypochromic and hypoprolipherative condition. The physiological balance of iron in the body depends on getting through diet and loss. A balanced diet should contain enough iron for the body's requirements. Iron deficiency (ID) is a systematic condition that harms physical stability, work capacity, psychomotor development of children and decreases their immunity. Morbidity against infectious diseases is increased in populations that suffer from iron deficiency. Depletion of iron stores into the brain may damage the activity of iron-dependent enzymes that are required for the synthesis, function and degradation of neurotransmitters such as dopamine, serotonin and noradrenaline, causing changes in behavior and reduction in test results of cognitive test in children.***

**Keywords:** Iron, anemia, children, ferritin

## 1. Introduction

The physiological balance of iron in the body depends on getting through diet and loss. A balanced diet should contain enough iron for the body's requirements. About 10% of 10-20 mg iron taken from the diet is absorbed daily and this is sufficient to balance daily loss of sweats, epithelial desquamation, urine and gastrointestinal losses [1].

The composition of iron in the diet can also affect its absorption. The iron is found in two forms: heme iron and non heme iron. Food sources of heme iron (fish, poultry, meat) have a higher bioaffinity than food sources of non heme iron (plant origin). Heme iron is normally absorbed about 30%, while non heme iron about 10%. It is also important the association of iron with other foods. Ascorbic acid which is mainly found in fruits and citrus can form complexes with iron that enhances its absorption, while tannates which are mainly found in tea, whole grain foods rich in phosphate may reduce iron absorption [2]–[5].

Gastrointestinal mucosa plays an important role in the regulation of iron absorption. The dietary iron can be found in two forms: most of it is in the form of ferric iron (Fe ++ +) which is very slightly soluble in ph above 3, and ferrous iron (Fe ++) which is more soluble even in ph 7-8 that is in the duodenum. Duodenal microvilli contain ferric reductase to promote the absorption of ferrous iron (Fe ++).

Iron is absorbed primarily in the duodenum and upper jejunum. DMT1 (divalent metal transporter 1) facilitates the transport of iron through intestinal epithelial cells. Iron passes in to the blood through enterocytes with the help of ferroportin. DMT1 and ferroportin are found in several cells involved in iron transport. It is caught in the blood by transferrin which is a transport glycoprotein. The gene for apotransferrin is located on the long arm of chromosome 3. It codes for a protein (molecular weight 80 kDa) that strongly binds one or two ferric molecules (Fe +++). Transferrin is the largest transporter of iron in plasma. The most part of transferrin, which has a half-life of eight days, is synthesized in the liver, its synthesis increased due to the absence of iron by unknown mechanisms. [6]–[7].

Most of the iron in the body is recycled. Old red blood cells are destroyed and release iron, which is captured by the phagocytic cell and is again released mainly for the interest of erythropoiesis.

Iron stores in the body are:
-Ferritin
-Hemosiderin

Iron can be stored in the form of a soluble complex protein such as Ferritin. Dysfunctional ferritin can accumulate like Hemosiderin, which is an insoluble protein complex accumulated in lysosomes. Ferritin and hemosiderin are found mainly in the bone marrow, spleen, liver, skeletal muscle. Small amounts of ferritin circulate in the plasma. In healthy people the iron is stored in the form of ferritin, and small amounts in the form of hemosiderin [8].

Ferritin is also a protein of the acute phase of inflammation. In general ferritin is a good indicator of iron status in the body, but it should be considered carefully because being a protein of the acute phase of inflammation, increases in other pathologies such as liver disease, inflammation, malignant neoplasms. Duodenal absorption of iron and its distribution in the body is regulated by hepcidin. It is a peptide hormone that is mainly produced in the liver. Hepcidin was first detected in serum and human urine samples as small bactericidal peptides (defensin and cathelicidin) and was called antimicrobial peptide (LEAP-1). The origin of the

name "hepcidin" comes from the place of synthesis in hepatocyte (hep-) and its antimicrobial activity (-cidin) [9]–[10]–[11].

The body of the newborn infant contains about 0.5 g of iron while the body of adults about 5g. To compensate for this discrepancy the organism should absorb about 0.8 mg each day for the first 15 years of life [12].

The iron content in the body is in the following forms:

- Hemoglobin (contains iron) in circulating red blood cells and in all precursors during erythropoiesis (about 2.5g) or about 75% of the amount of iron found in the body.
- Iron-containing proteins (myoglobin, cytochrome, catalase-about 400 mg) or about 10% of the amount of iron in the body.
- Binded to transferin (about 3-7 mg) or about 1-2% of the amount of iron in the body.
- Ferritin and Hemosiderin (in the form of store) about 10-20% of the amount of iron that is in the body.

The regulation of iron metabolism involves the interaction of specific proteins that participate in the process of absorption, recycling and iron loss [13].

Iron is an essential microelement which serves to maintain the functions and structure of the body's cells. It is a component of many proteins (and hemoglobin) so it is very important for oxygen transport throughout the body. Oxygen is poorly soluble in plasma, the iron atoms in heme group of hemoglobin can be bound to reversible manner with oxygen molecules, making transportation of 98.5% of total oxygen to body tissues.

## 2. Clinical manifestations of Iron deficiency anemia (IDA)

Symptoms of anemia are related to its severity and speed of installation. Iron deficiency anemia (IDA) is a microcytic, hypochromic and hypoprolipherative condition. During the lack of iron the iron stores begin to diminish but have enough iron in circulation (from red blood cells turnover) for normal hemoglobin synthesis, unless its continuous loss occurs. Anemia develops only at the final stage of iron deficiency. Vice versa, when iron therapy begins, anemia is first corrected and then normalization of iron stores is done, which requires time to fully correct. The most common clinical presentation of iron deficiency anemia is an asymptomatic, well-fed baby or child who has an mild or moderate microcytic, hypochromic anemia. Rarely are children with severe anemia, appearing drowsy, pale, nervous, with cardiomegaly, poorly fed, and with tachypnea. The main cause of iron deficiency anemia (IDA) is iron deficiency with diet. In some cases it may be due to a medical problem that leads to gastrointestinal bleeding, malabsorption syndrome, chronic inflammatory disease etc. [14]–[15]–[16]–[17].

A quickly installed anemia gives more dramatic symptoms. In the case of a chronic anemia, the clinical signs of anemia are slowly installed, expressing in general its gravity. The symptoms of iron deficiency anemia are pale skin, lips and hands, increased heart rate, asthenia, fatigue, disturbance of taste, flat nails (koilonychia). The nails become thin, concave (spoon-like) and breakable in their distal half [18].

Tinnitus, cold hands and feet, decreased exercise tolerance, Pica (the desire to eat substances that have no nutritional value (e.g. dirt or ice) [18].

Children with severe iron deficiency are often described as nervous, apathetic, and decreased appetite [12]–[19].

### 2.1 Neurological development

In children, iron deficiency anemia (IDA) is associated with neurological disorder, including slower visual and auditory processing [20]–[21]–[22]–[23]–[24]–[25]–[26]–[27].

In low and middle-income countries, iron-treating trial studies in these children have brought benefits to psychomotor development [28]–[29]–[30]–[31]–[32]–[33]–[34].

In one study were involved 81 teenage girls in America who had ferritin levels ≤12 micrograms / L but normal hemoglobin values. They were randomly divided into two groups. One group was treated with ferrous sulfate orally for 8 weeks and the placebo group. It was observed that iron treated girls increased the level of ferritin and had a better performance in the memory test [35].

However, there is some evidence that psychomotor development does not always recover after treatment with ferritin [36]–[37]–[38]–[39].

### 2.2 Febrile Seizure

Several studies have shown a link between febrile seizures and iron deficiency or iron deficiency anemia (IDA). No cause has been found, but the level of ferritin is significantly lower in children with febrile seizures compared to children without febrile seizures.Therefore the screening of iron deficiency in these children would be very necessary [40]–[41]–[42]–[43]–[44].

### 2.3 Breath holding spells

In some studies to evaluate the prognosis of breath holding spells in children, oral iron treatment was tested for 2 to 3 months. There has been noticed reduction in the frequency of breath holding spells in these children [45]–[46]–[47]–[48]–[49]–[50].

### 2.4 Immunity and infections

There are various data on the impact of iron supplements on the functioning of the immune system and sensitivity to infections. In one hand the iron deficiency appears to be associated with mild to moderate defects in leukocyte and lymphocyte function including defective production of IL-2 and IL-6 [62]–[63]–[64]–[65].

On the other hand iron supplements paradoxically increase the risk of some infections, especially bacterial infections.This is because the proteins that bind iron (transferrin and lactoferrin) have bacteriostatic effect, which is lost when they are bound to iron [56].

### 2.5 Physical ability

The moderate iron deficiency anemia (IDA) is associated with a decrease in physical capacity, partly because iron is a cofactor in aerobic metabolism.Reduction of iron stores in the absence of anemia is associated with reduced physical performance in laboratory experiments on animals. Similar data were observed even in children, especially teenagers involved in sport activities.

### 2.6 Thrombosis

Iron deficiency anemia (IDA) is associated with cerebral vein thrombosis. The mechanism for this uncommon complication is unclear, but may be associated with thrombocytosis that is often present in iron deficiency anemia (IDA) or as a result of abnormal body conditions in children suffered from iron deficiency anemia (IDA) [57]–[58].

### 2.7 Conclusions

Iron deficiency (ID) is a systematic condition that harms physical stability, work capacity, psychomotor development of children and decreases their immunity.Morbidity against infectious diseases is increased in populations that suffer from iron deficiency. Depletion of iron stores into the brain may damage the activity of iron-dependent enzymes that are required for the synthesis, function and degradation of neurotransmitters such as dopamine, serotonin and noradrenaline, causing changes in behavior and reduction in test results of cognitive test in children [59]–[60]–[61].

It still remains unresolved the question whether only iron deficiency (ID) is capable of causing a delay in child development, but still remains a public health problem that needs multidimensional interventions.

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