Spotlight on hematology

Iron Deficiency Anemia

MQZH

Causes of iron deficiency

- Lacking/not enough supply (nutrition)
- Limited absorption in the gastrointestinal tract (e.g. with celiac disease, Crohn's disease)
- Increased consumption, e.g. during growth, pregnancy, competitive
- sports, etc.
- Increased loss of iron, primarily through blood loss (hypermenorhea, gastrointestinal blood loss due to ulcers/ tumors in men and postmenopausalwomen).

Note! Chronic blood loss causes iron deficiency anemia.

Effects of an Iron Deficiency

In its most dramatic form, an iron deficiency first leads to iron deficiency anemia with decreased hemoglobin and hypochromic microcytic erythrocytes – this because the availability of iron in the erythropoiesis is so essential for the supply of oxygen. Thus, the erythropoiesis is supplied the longest and preferably with iron even with decreasing stored iron.

Important proteins, such as oxygen carriers, proteins of the respiratory chains, cytochromes and DNA-synthesis and repair enzymes contain iron. For this reason, patients can already be suffering from symptoms associated with an iron deficiency, even if there is still no iron deficiency anemia. Symptoms due to an iron deficiency in the somatic cells are, e.g.

- Chronic fatigue/ lethargy
- Concentration /sleeping disorders
- Brittle nails / hair loss
- Angular cheilitis
- Restless Leg Syndrome

Unborn, children, and youths

Iron deficiency conditions during pregnancy may cause premature births, a low birth weight, and growth delays. In children and youth, impacts to brain development, concentration disorders, and disorders of the menstrual cycle may occur.

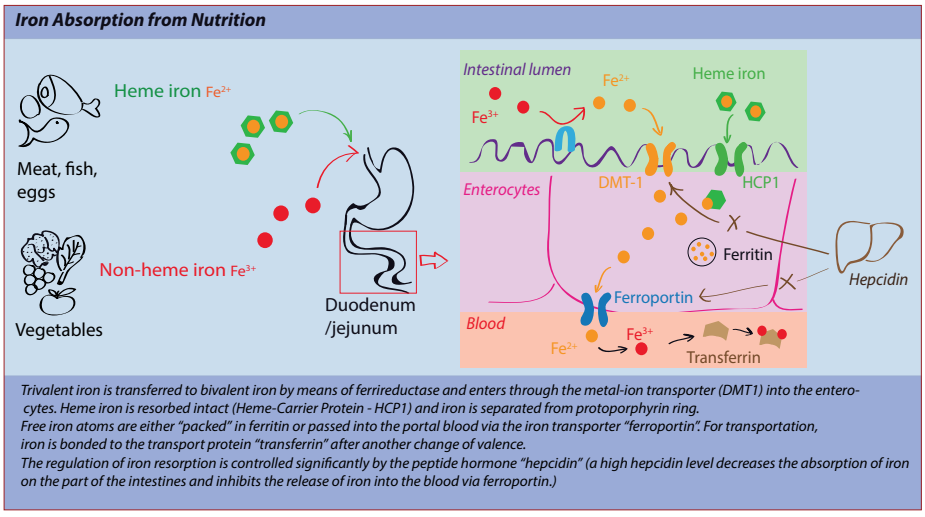
Introduction

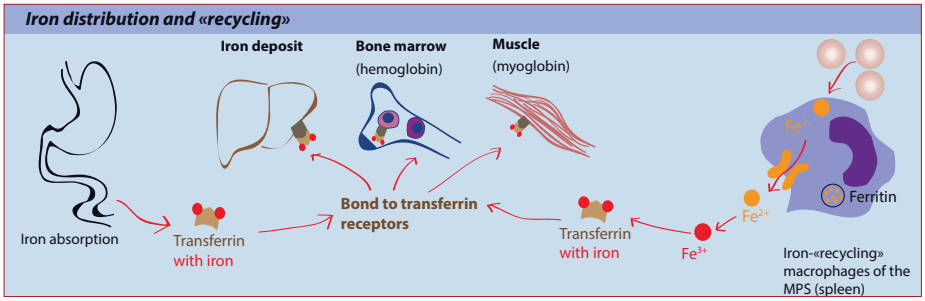
In the case of an iron deficiency, there is a decrease of iron in the whole body. Iron is an essential trace element. It participates in a wide variety of metabolic processes. Among other things, it is a component of hemoglobin and myoglobin, where it enables the transportation of oxygen. With around 75%, iron consumption in erythropoiesis is the highest percentage. A reduction of the supply (nutrition, resorption disorder) as well as increased consumption (e.g. growth, pregnancy, increased menstrual bleeding) leads to a depletion of the iron stored in the body, iron-deficient erythropoiesis, and ultimately to iron deficiency anemia. Microcytic anemia with abnormal erythrocyte forms then occurs in the blood count.
Iron deficiency is primarily ascertained through the determination of ferritin. Ferritin in serum is proportional to the iron in the whole body without inflammation and without hepatopathy.
Our proficiency test survey specimen 2018-02 H3A originates from a 17-year old female patient with iron deficiency anemia.

Biological Function and Iron Metabolism

Biological Function of Iron
Oxygen (O2) is transported in the erythrocyte by bonding to the heme group of hemoglobin. As a central atom, iron lies in a porphyrin molecule (heme group of hemoglobin). Myoglobin, which likewise contains heme, is responsible for intramuscular oxygen transportation. Compounds of iron and sulfur (clusters) are involved in the transportation of electrons in the mitochondria («energy producer» of cells). As a free ion, iron is toxic. It cannot be excreted in a controlled manner, so an iron overload can lead to organ damage in the case of genetic iron regulation defects (hemochromatosis).

Iron Metabolism
Nutritional iron is resorbed in the duodenum and upper jejunum. Heme iron from animal sources supplied with food is highly resorbable (20-30%), while non-heme iron from vegetables has a low resorption rate. Vitamin C benefits and tannins (coffee, black tea, red wine) diminish the absorption of iron. However, a large portion of circulating iron does not come from food, but rather from a «recycling» process in the body. Erythrocytes are removed in the macrophages of the spleen and liver and the iron being released in this way from the heme becomes bonded to ferritin in an intracellular manner. From there, it is provided into the bloodstream as needed, where – bonded to transferrin – it is once again available for delivery to the erythropoiesis in bone marrow. The peptide hormone, hepcidin, produced in the liver plays an important role in the regulation of iron absorption.





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Iron Metabolism Diagnostics

Ferritin
Protein shell «apoferritin» with approx. 4500 stored iron atoms. Ferritin represents the stored iron in the body.

Reference ranges:
M 30.0 - 400.0 µg/l
F 13.0 - 150.0 µg /l

30-50 or 13-50 µg /l gray area
≥ 50 µg /l iron deficiency unlikely
≥ 100 µg /l even with acute phase reaction (CRP ↑) iron deficiency unlikely.

Transferrin
Transport protein for iron. Value increased with iron deficiency. Negative acute phase reaction.
Reference range: 25-50 µmol/l

Transferrin Saturation
Determination from serum iron and transferrin. Blood sampling due to the circadian rhythm and nutritional dependency of iron in the morning and on an empty stomach. The «transferrin loaded with iron» is calculated.
Reference ranges: M 20-55% / F 15-50%

Value decreased with iron deficiency, increased with iron overload (e.g. hemochromatosis).

Soluble Transferrin Receptor (sTfR)
Reflects the «iron craving» of cells. Lacking standards for the sTfR determination made the assessment difficult. Thus, in 2011 the standardization was made in accordance with the Swiss Iron Health Organization (SIHO) / newsletter 11/9.
Reference range: M 2.2 - 5.0 mg/l
F 1.9 - 4.4 mg/l

Value increased with iron deficiency (other causes for an increase are also possible).

Transferrin Receptor - Ferritin Index (sTfR / log ferritin)
Quotient from soluble transferrin receptor and ferritin. Increases with iron storage deficiency.
for CRP <5 mg/l: < 3.8
for CRP >5 mg/l: < 2.0

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Laboratory Diagnostics of Iron Deficiency

If an iron deficiency is suspected, first and foremost the ferritin in serum is determined, which acts proportionally to the iron in the whole body. In addition, parameters affecting iron metabolism are normally determined in the case of special questions. An iron deficiency anemia is referred to if the iron deficit in the erythropoiesis leads to a decrease of hemoglobin. Here, there are typically hematogram and blood count changes as well as characteristic findings with the reticulocyte parameters.

Clinical-chemical parameters in serum

Initial assessment of the iron supply	• Ferritin (represents stored iron in the liver, bone marrow, spleen) • CRP (↑ CRP with acute phase reaction may lead to a false, normal or high ferritin value despite iron deficiency)
Further assessment, special questions	• Transferrin, transferrin saturation, soluble transferrin receptor, and transferrin receptor ferritin quotient

Hematological parameters in whole blood

Hematogram with iron deficiency anemia	• Hemoglobin, hematocrit and erythrocyte count ↓ MCV ↓ MCHC ↓ (Microcytosis, hypochromasia) • Histogram: Erythrocyte curve moved to the left, with status after iron substitution a "shoulder", or even potentially a second population curve is visible on the right side of the curve. (This represents the newly formed erythrocytes) • Special parameters on larger devices: %Hypochromic Ec, reticulocyte count, MCHC of reticulocytes • Thrombocytes ↑ reactive • hypersegmented neutrophils (1)
Blood count	• Hypochromasia, microcytosis • anisocytosis, poikilocytosis • ovalocytes, potentially anulocytes

1) Neutrophil hypersegmentation in iron deficiency anaemia: A case-control study; British Journal of Haematology, 107(3):512-5, January 2000, Westerman DA1, Evans D, Metz J.

Morphology of Erythrocytes with Iron Deficiency Anemia