



## **Features of Anemia in Children**

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**Abstract:** *The article presents various deficiency anemias in children (iron deficiency, vitamin deficiency, micronutrient deficiency, protein deficiency anemias) and also considers the epidemiology, etiology, clinical manifestations, treatment and prevention.*

**Keywords:** *hematopoiesis, iron deficiency anemia, erythroid, inflammation, ferritin, vegetarianism.*

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Iron deficiency anemia (IDA) is a clinical-hematological syndrome, which is based on a violation of heme synthesis due to iron deficiency (ID), which develops as a result of various acquired or genetically determined pathological processes. Iron is one of the essential factors for erythroid bone marrow progenitor cells, which ensure normal bone marrow hematopoiesis.

Iron is one of the essential factors for erythroid bone marrow progenitor cells (ECPCs), which ensure normal bone marrow hematopoiesis:

- 1) absolute iron deficiency (AID);
- 2) functional iron deficiency and
- 3) iron deposition against the background of inflammation.

Iron deficiency is associated with IDA. Functional (relative) iron deficiency develops in patients with normal iron stores in conditions of an increased need for EPO in iron. Iron deposition syndrome, which is related to increased production of hepcidin against the background of inflammation, leads to the development of anemia of chronic diseases (ACD), synonym anemia of inflammation (AI).

AID develops due to a significant decrease (up to a complete absence) of iron stores in the depot and is manifested by a reduced level of serum ferritin. There are three ID stages:

- iron stores depletion (prelate ID) - a stage of increased iron absorption, with an increased concentration of circulating transferrin and a reduced content of serum ferritin (SF);
- iron deficiency erythropoiesis (latent ID) - characterized by a decrease in the iron transferrin saturation coefficient (ITS), a low SF level and an increase in the concentration of serum transferrin receptor (cSTR) at a normal Hb level;
- iron deficiency anemia - the final stage of ID, characterized by a decrease in Hb levels and ineffective erythropoiesis with an increased level of endogenous EPO.

In the IDA development, a key role belongs to the absolute ID that develops for one reason or another, which leads to hemoglobin synthesis violation, the iron-deficient erythropoiesis formation and bone marrow hematopoiesis ineffectiveness with a high level of endogenous erythropoietin

(EPO) adequate to the anemia severity. Thus, an absolute iron deficiency, a decrease in the hemoglobin (Hb) concentration in erythroid cells with preserved adequate EPO production in the kidneys are the characteristic features of IDA.

IDA occupies the leading place among anemias in the general population, but the IDA prevalence varies significantly depending on age and sex. Up to 6 months of age, IDA is extremely rare, with the preterm infants' exception, in which the IDA risk increases significantly after doubling the birth weight. The highest IDA prevalence is observed in children aged 6 months to 3 years (1 peak incidence) and adolescent girls over 12 years of age (2 peak incidence). Tables 1 and 2 present the main causes and risk groups for the IDA development in children less than 3 years of age and adolescents.

**Table 1. Groups of children and adolescents at high IDA developing risk**

<b>Children under 12 years old</b>	<b>Teenagers</b>
<ul style="list-style-type: none"> <li>➤ Prematurity / low birth weight (&lt;2500g)</li> <li>➤ Children of migrants</li> <li>➤ Children over 6 months of age who are only breastfed and not receiving iron prophylactic</li> <li>➤ Children receiving cow's milk under 1 year of age</li> <li>➤ Helminthic invasions</li> </ul>	<ul style="list-style-type: none"> <li>➤ History of heavy menstrual blood loss (&gt; 80 ml / month)</li> <li>➤ Significant physical activity (playing sports)</li> <li>➤ Disorders of iron absorption</li> <li>➤ Vegetarianism</li> <li>➤ Hungry diets</li> <li>➤ Helminthic invasions</li> </ul>

**Table 2. The main reasons for the IDA development**

<b>ID Development Factor</b>	<b>Causes</b>
Dietary iron deficiency	<ul style="list-style-type: none"> <li>➤ Malnutrition</li> <li>➤ anorexia of various origins</li> <li>➤ vegetarianism</li> </ul>
Increased need for iron	<ul style="list-style-type: none"> <li>➤ doing sports</li> <li>➤ intense growth in early and adolescence</li> <li>➤ pregnancy</li> </ul>
Chronic or acute blood loss	<ul style="list-style-type: none"> <li>➤ bleeding from the organs of the female reproductive system (heavy menstruation, swelling)</li> <li>➤ bleeding from the gastrointestinal tract (diverticulosis and intestinal polyposis, rectal fissure, erosive and ulcerative process, chronic inflammatory diseases, tumors)</li> <li>➤ recurrent nosebleeds</li> <li>➤ donation</li> <li>➤ long-term use of non-steroidal anti-inflammatory drugs - feeding with cow's milk (in young children)</li> <li>➤ helminthic invasions</li> <li>➤ trauma, surgical intervention</li> </ul>
Impaired iron absorption	<ul style="list-style-type: none"> <li>➤ celiac disease (IDA may be the only manifestation of the disease)</li> <li>➤ Helicobacter pylori - infection</li> <li>➤ autoimmune atrophic gastritis</li> </ul>

Currently, a number of studies have shown that long-term ID in young children can contribute to impaired myelination of nerve fibers, the brain structures formation, and a delay in mental and motor development, which can be irreversible. In adolescents, iron deficiency states are manifested by increased fatigue, muscle weakness, decreased memory, decreased emotional tone, etc. IDA in children with Hb <105 g/l is associated with psychomotor and cognitive impairments, as well as poor school performance.

IDA treatment in frequently ill children has been shown to reduce the upper respiratory tract infections incidence. However, the causal relationship between IDA and the listed negative effects on the child's health has not been conclusively established. At the same time, anemia, including IDA, is an independent factor of increased mortality in patients with chronic diseases. And IDA in pregnant women is associated with an increased risk of low birth weight and preterm birth, as shown in randomized controlled trials and meta-analyses.

Most children with moderate IDA are clinically absent. However, in some cases, sideropenic and anemic syndromes manifestations can be observed. Sideropenic syndrome is characterized by:

- dry skin;
- changes in the mucous membranes: "sticking" in the corner of the mouth, glossitis, atrophic gastritis and esophagitis;
- dyspeptic symptoms from the gastrointestinal tract;
- breakage and hair loss;
- changes in nails - transverse striation of the nails thumbs (in severe cases, and toes), fragility, delamination into plates;
- change in the smell sense - the patient's addiction to the pungent smells of varnish, paint, acetone, car exhaust gases, concentrated perfumes;
- changes in taste - the patient's addiction to clay, chalk, raw meat, dough, etc.;
- increased susceptibility to infection (frequent colds)
- pain in the calf muscles
- restless legs syndrome.

Sideropenia symptoms may appear as early as the latent ID (LID) stage. The anemic severity syndrome is determined by the development and progression rate of the decrease in the Hb content in erythrocytes, as well as the anemic syndrome severity, which usually develops when the Hb level is <70-80 g/l and can manifest itself with the following symptoms:

- pallor of the skin and visible mucous membranes
- dyspnea
- tachycardia
- flashing spot before the eyes
- muffled heart tones
- systolic murmur at the apex of the heart
- weakness, lethargy, dizziness, irritability
- fainting
- poor exercise tolerance

- decreased performance, inability to perform usual work
- muscle hypotension, the bladder muscles hypotension with the urinary incontinence development.

The main goal of IDA treatment is to reimburse the ID in the patient's body and eliminate the underlying disease cause (for example, eliminate the blood loss source, etc.). The main principles of IDA treatment are: It is impossible to eliminate IDA without iron supplementation, just diet. Treatment should be carried out primarily with oral iron supplementation. The iron preparation dose and the therapy course duration should be adequate to the patient's body weight and the anemia severity. The criterion for cure from IDA is not Hb level, but the physiological threshold achievement of iron stores in the depot. You should not resort to blood transfusions for IDA without vital indications. Treatment for mild to moderate IDA is carried out in a polyclinic or day hospital. It is recommended to start treatment of severe IDA in a hospital (day hospital) setting. Initial IDA therapy should be with ferrous ionic saline, of which ferrous sulfate is the most commonly used.

When treating children of early childhood, preference should be given to liquid dosage forms (drops, syrup). Taking iron salt preparations is recommended 1 hour before meals. The daily drug dose is divided into 2-3 doses. It is allowed to take a single daily drug dose at night. At the same time, as has been shown in randomized trials, the number of side effects does not increase. On the first day, it is advisable to use a salt preparation of iron in a half dose. It is allowed to gradually increase the drug dose to the daily dose within 7 days. The absorption of iron salt preparations is negatively affected by tea, coffee, milk, food products (cheese, cottage cheese, milk) and antacids containing calcium and aluminum, salicylates, tetracyclines.

Parents should be warned about the reversible darkening possibility of the teeth enamel, dark feces staining and the dyspeptic disorders appearance, as well as an accidental inadmissibility or deliberate increase in the daily iron preparation dose indicated by the doctor (in order to avoid overdose and poisoning). For this reason, iron supplements should be kept out of the reach of children. In cases of poor tolerance, it is recommended to change the drug. An alternative to ferrous salts are ferric preparations based on a hydroxide-polymaltose complex (HPC). They have better tolerance and fewer side effects, can be taken with food, and do not stain the teeth enamel and feces. However, differences in efficacy and frequency of side effects between iron salts and HPA-based drugs have not been confirmed by the results of randomized controlled trials and meta-analyzes.

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