S. N. KOZAREZOV, A. K. DZIHOYEVA

АНЕМИИ У ДЕТЕЙ
ANEMIA IN CHILDREN

Minsk BSMU 2021

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
2-я КАФЕДРА ДЕТСКИХ БОЛЕЗНЕЙ

С. Н. Козарезов, А. К. Дигоева

АНЕМИИ У ДЕТЕЙ
ANEMIA IN CHILDREN

Учебно-методическое пособие

Минск БГМУ 2021

УДК 616.155.194-053.2(075.8)-054.6
ББК 57.33я73
К59

Рекомендовано Научно-методическим советом университета в качестве учебно-методического пособия 23.06.2021 г., протокол № 6

Р е ц е н з е н т ы: канд. мед. наук, доц. 1-й каф. детских болезней Белорусского государственного медицинского университета И. А. Козыро; каф. детской онкологии, гематологии и иммунологии Белорусской медицинской академии последипломного образования

Козарезов, С. Н.

К59 Анемии у детей = Anemia in children : учебно-методическое пособие / С. Н. Козарезов, А. К. Дигоева. – Минск : БГМУ, 2021. – 20 с.

ISBN 978-985-21-0896-6.

Издание посвящено актуальной проблеме педиатрии – анемиям детского возраста. В нем объединены и систематизированы современные сведения, касающиеся этиопатогенеза, классификации, клиники и диагностики наиболее часто встречаемых анемий у детей. Особое внимание уделено диагностике, профилактике и лечению железодефицитных состояний.

Предназначено для студентов 5-го курса медицинского факультета иностранных учащихся, изучающих педиатрию на английском языке.

УДК 616.155.194-053.2(075.8)-054.6
ББК 57.33я73

ISBN 978-985-21-0896-6

ABBREVIATIONS

DNA — deoxyribonucleic acid

EPO — erythropoietin

G-6-PD — glucose-6-phosphate dehydrogenase

GI — gastrointestinal

Hb — hemoglobin

IDA — iron deficiency anemia

MCH — mean corpuscular hemoglobin

MCHC — mean corpuscular hemoglobin concentration

MCV — mean corpuscular volume

RBC — red blood cell

RDW — red cell distribution width

RES — reticuloendothelial system

RI — reticulocyte index

SF — serum ferritin

SI — serum iron

Tf — transferring

TfR — transferrin receptor

DEFINITION

Anemia is a syndrome defined as a reduction of the hemoglobin (Hb) concentration below the range of values occurring in healthy persons, more often with a simultaneous decrease in the number of red blood cells (RBC), which leads to the development of hypoxia.

So to diagnose anemia, we need to investigate and evaluate the hemoglobin level for a specific age.

Table 1

Lower normal Hb values depending on age

Age	Hb level (g/L)
1–3 days	180
4–14 days	160
2–4 weeks	120

End of table 1

Age	Hb level (g/L)
1–6 months	115
6 months – 6 years	110
Older than 6 years	120

Table 2

Lower normal serum ferritin values depending on age

Age	Serum ferritin level (mcg/L)
1 month	150
2–3 months	80
Older than 3 months	30
Pregnant	20–40

CLASSIFICATION

There is no single international classification of anemia. But all anemias could be classified according **to severity** and **pathogenesis**.

Classification of anemia according to severity: ***mild*** (90 g/L ≤ Hb < N g/L), ***moderate*** (70 g/L ≤ Hb < 90 g/L), ***severe*** (Hb < 70 g/L).

Classification of anemia according to the pathogenesis:

I. Acute blood loss.

Considering the fact that about 40 % of the blood volume is presented by RBC, significant acute blood loss will naturally lead to the development of anemia.

II. Inadequate production of red blood cells.

There are a number of entities commonly associated with an inadequate production of red blood cells:

1. ***Iron deficiency anemia*** is the most common cause of anemia globally.

2. ***Anemia of renal disease*** results from erythropoietin (EPO) deficiency. The synthesis of this hormone is regulated by the oxygen tension in the periglomerular cells of the kidney. Hypoxia drives the synthesis of EPO and its release into the bloodstream, which stimulates the maturation and development of erythrocyte precursors in the bone marrow. These activities result in an increase in red blood cell mass, bringing additional oxygen to the kidney, and ultimately completing the feedback loop by downregulating production of EPO. A reduction in renal function is generally accompanied by a reduction of EPO production.

3. ***Endocrine anemias*** result from deficiencies or excess of hormones that contribute to blood cell development. Hypothyroidism may be associated with a mild to moderate anemia sometimes associated with macrocytosis. Adrenal cortical insufficiency may be accompanied by a normocytic anemia. Decreased levels of serum testosterone may lead to a mild anemia in males.

4. ***Pure red cell aplasia*** in children may be the result of heritable disorders, such as congenital hypoplastic anemia (Diamond-Blackfan anemia), or may be

the apparent result of infection with a virus (e.g., Parvovirus B19) or an immunologic phenomenon (e.g., as seen in systemic lupus erythematosus). In contrast to aplastic anemia, in which two or more cell lineages are affected, pure red cell aplasia is characterized by preservation of the white blood cell count and platelet count.

5. ***Bone marrow replacement*** is also known by the term myelophthisis. In this case, the blood forming bone marrow space is taken over by cells or material that should not be there. Causes of bone marrow replacement include hematologic malignancies such as leukemia or lymphoma, metastatic cancer, infection with fungi or other microorganisms, and fibrosis such as that which may occur in conjunction with primary myelofibrosis.

6. ***Sideroblastic anemias*** represent an uncommon group of hereditary and acquired disorders in which iron is not effectively used in hemoglobin synthesis leading to iron accumulation in the mitochondria of red blood cell precursors. The deposition of iron in mitochondria leads to the morphologic entity of ringed sideroblasts in the bone marrow when it is stained for iron. Exactly as the name implies, ringed sideroblasts are cells in which ironladen mitochondria encircle at least one-third of the circumference of the erythroblast nucleus (Fig. 1). Usually at least five iron-laden mitochondria need to be seen encircling the nucleus to make diagnostic criteria.

Hereditary forms of sideroblastic anemia are rare and may be X-linked, autosomal dominant, or recessive. Acquired forms may occur after exposure to drugs (e.g., cyclosporine, vincristine) or toxins (ethanol).

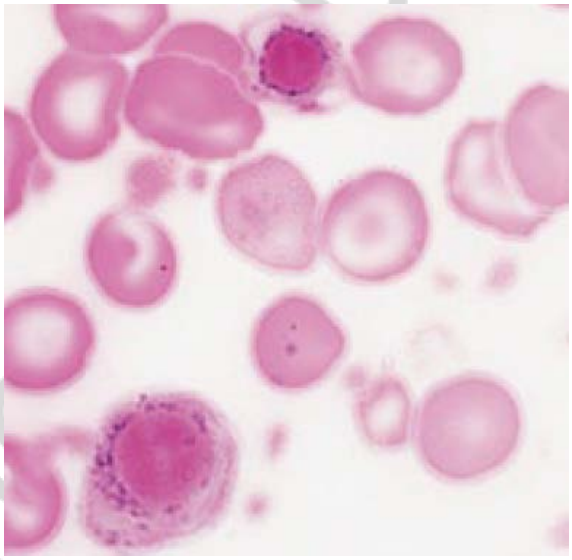

Fig. 1. The bone marrow smear shows ring sideroblasts with complete or nearly complete rings of iron granules around their nuclei

7. ***Anemia of inflammation (also known as the anemia of chronic disease)*** is commonly encountered in association with a variety of conditions, including serious infections, rheumatologic diseases, diabetes mellitus, and malignancy.

Cytokines lead to an increase in hepcidin levels. Hepcidin in turn reduces iron absorption in the gastrointestinal tract and increase iron retention in the reticuloendothelial system. Both reduce iron availability in the erythron and lead to anemia. In addition, cytokines reduce the production of erythropoietin and response to it, proliferation of erythron and RBC half-life (Fig. 2).

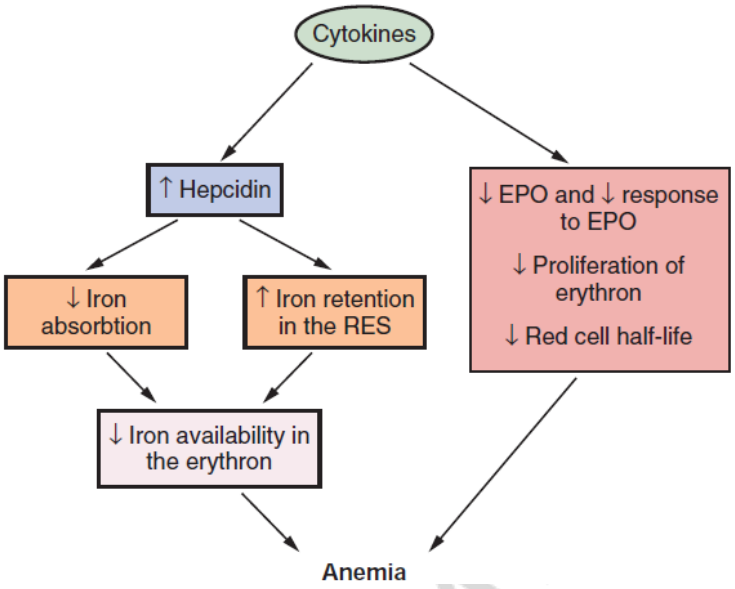

Fig. 2. Anemia of inflammation (pathogenesis)

8. ***Folate and vitamin B_{12} deficiency*** are two types of megaloblastic anemia that lead to maturation abnormalities in all three cell lineages. These disorders share in common the pathophysiology of impaired synthesis of DNA.

Folate deficiency is generally related to inadequate dietary intake or to increased requirements due to red blood cell hemolysis. The situation for vitamin B_{12} (also called cobalamin) is more complex. Vitamin B_{12} is released from food in the acidic environment of the stomach and binds to the intrinsic factor that is secreted by the parietal cells in the stomach. The intrinsic factor vitamin B_{12} complex then travels to the terminal ileum where it is absorbed.

Vitamin B_{12} deficiency (Fig. 3) may result from several different causes including inadequate stomach acidity, pernicious anemia (an autoimmune phenomena destroying the parietal cells that synthesize intrinsic factor), structural lesions in the terminal ileum due to conditions such as Crohn's disease, and from surgical resection of portions of the GI tract. Inadequate dietary intake is generally only observed in vegans.

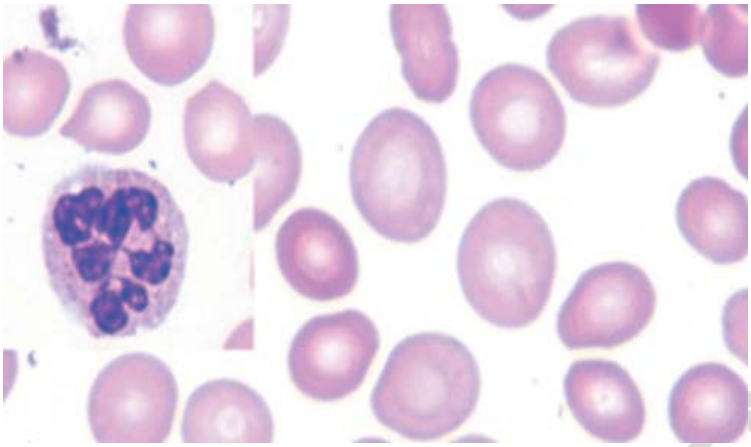

Fig. 3. Vitamin B_{12} deficiency anemia. The peripheral smear exhibits macro-ovalocytosis and hypersegmented polys

III. Destruction of red blood cells (hemolytic anemia).

Normally red blood cells circulate for about 100 to 120 days before they are cleared by the RES. Premature RBC destruction may result from intrinsic defects such as abnormal hemoglobin molecules, cytoskeletal proteins, or enzymes. It may also result from defects extrinsic to the erythrocyte, including mechanical forces and antibody or complement-mediated red cell breakdown.

1. Intrinsic defects:

– ***Hemoglobinopathies include structural mutations (sickle cell anemia) or defects in the synthesis of the globin chain (alpha- and beta-thalassemia).***

Hemoglobin is a tetramer consisting of 2 pairs of globin chains. Abnormalities in these proteins are named hemoglobinopathies. From 9 wk of fetal life, the major hemoglobin is HbF ($\alpha 2\gamma 2$). HbA ($\alpha 2\beta 2$) first appears at approximately 1 mo. of fetal life, but does not become the dominant hemoglobin until after birth, when HbF levels start to decline. HbA2 ($\alpha 2\delta 2$) is a minor hemoglobin that appears shortly before birth and remains at a low level after birth. The final hemoglobin distribution pattern that occurs in childhood is not achieved until at least 6 mo. of age and sometimes later. The normal hemoglobin pattern is $\geq$ 95 % HbA, $\leq$ 3,5 % HbA2 and < 2,5 % HbF.

Among the most commonly encountered structural mutations is a glutamine to valine substitution at position 6 of the beta globin gene. This change results in the production of hemoglobin S, which tends to polymerize in its deoxygenated state. Heterozygotes with one copy of hemoglobin S (sickle cell trait) are relatively protected against infection with the malaria parasite. This structural mutation thus provides a survival advantage, and selective pressure leads to persistence of the mutation. Homozygotes with two copies of hemoglobin S have sickle cell anemia (Fig. 4), a serious life-defining hematologic disorder.

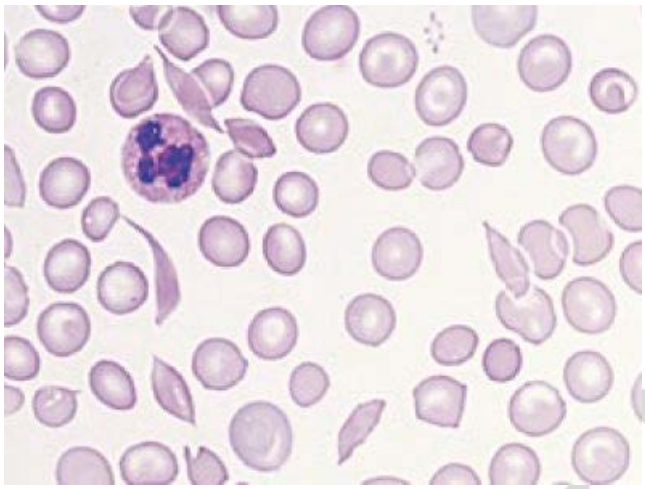

Fig. 4. Sickle cell anemia: peripheral blood films showing deeply staining sickle cells with target cells and polychromasia

The thalassemia syndromes are a heterogeneous group of inherited anemias characterized by defects in the synthesis of one or more globin chain subunits of the Hb tetramer. Clinical manifestations are diverse, ranging from asymptomatic hypochromia and microcytosis to profound anemia, which can be fatal in utero or in early childhood if untreated. Thalassemia trait is common in individuals from Africa, Asia, and the Mediterranean Basin.

– ***Red blood cell membrane defects*** result from a variety of different defects affecting the red blood cell cytoskeleton or the membrane itself.

Defects in any of the proteins lead to changes that reduce the resiliency of red blood cells as they pass through the narrow passageways in the spleen. This initially leads to the formation of spherocytes and ultimately resulting in hemolysis. The resulting disorder, hereditary spherocytosis, is most common in individuals of Northern European descent.

Liver disease is the most common cause of an acquired red cell membrane defect and results in abnormal cells noted on examination of the blood smear (codocytes or target cells).

Abnormalities in the lipid composition of the RBC membrane result in cells that are abnormally stiff and unable to rebound from deformities that arising from transit of the circulation. Paroxysmal nocturnal hemoglobinuria represents a rare type of acquired membrane defect that is derived from a stem cell defect leading to the reduction or absence of phosphatidylinositol glycan-linked membrane proteins and is associated with the hemolysis of RBC through the unopposed constitutive activation of components of the complement cascade.

– ***Red blood cell enzyme defects*** are potentially the most common red cell abnormalities globally. Glucose-6-phosphate dehydrogenase (G-6-PD) is the enzyme required for function of the hexose monophosphate shunt in the RBC. This pathway provides the RBC with reduction capacity against oxidant stress. Mutations in G-6-PD are very common and have been preserved in populations

because of their relative protection against infection with the malaria parasite, like sickle cell anemia. Those carrying mutations in G-6-PD (especially males, since this is an X-linked trait) have RBC that are susceptible to hemolysis under conditions of oxidant stress (for example medications: antimalarials, nitrofurans and sulfonamides).

2. Extrinsic to the erythrocyte defects:

– ***Mechanical causes of hemolysis.***

Microangiopathic hemolytic anemias include disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome. In these conditions abnormalities in the microvasculature result in shearing of the RBC and the formation of RBC fragments called schistocytes.

Infections (malaria, clostridia) can lead to mechanical disruption of the RBC membrane.

Malignant hypertension and vasculitis are additional etiologies producing mechanical destruction of RBC.

Malfunctioning mechanical valves, as well as long-distance running can also result in the mechanical destruction of RBC.

– **Autoimmune hemolytic anemia** results from the formation of antibodies that bind to the RBC and either fix complement resulting in its destruction in the circulation (intravascular hemolysis) or result in clearance in the reticuloendothelial system (extravascular hemolysis).

Warm and cold autoantibodies are often idiopathic but may be associated with hematologic malignancies such as chronic lymphoid leukemia or rheumatologic disorders such as systemic lupus erythematosus.

– **Alloimmune hemolytic anemia** results from exposure of an individual to foreign RBC. In children this most commonly results from blood transfusion in which there are mismatched minor antigens.

Classification of anemia according to the type of erythropoiesis: **normoblastic** (IDA, acute blood loss) or **megaloblastic (**folate and vitamin B_{12} deficiency).

Classification of anemia according to the volume of RBC (MCV): **microcytic** (IDA, thalassemia), **normocytic** (acute blood loss, anemia of renal disease), or **macrocytic** (folate and vitamin B_{12} deficiency, aplastic anemia, myelodysplasia, chronic liver disease).

Classification of anemia according to the amount of HB in RBC (color index, MCH, MCHC): **hypochromic** (IDA, sideroblastic anemia, thalassemia), **normochromic** (acute blood loss, sickle cell anemia), or **hyperchromic** (folate and vitamin B_{12} deficiency).

Classification of anemia according to the ability of the erythroid bone marrow to regenerate.

The reticulocyte count measures the production and release of newly formed RBC. In the presence of anemia, the absolute reticulocyte count should be at least 100,000/μL. This value corresponds to a reticulocyte index of at least

2 % and represents an appropriate response to blood loss or to hemolysis (**regenerative**). If reticulocyte index is more than 5 % it means that anemia is **hyperregenerative.**

Alternatively, normal (0,2–2 % — **hyporegenerative**) or decreased (< 0,2 % — **aregenerative**) reticulocyte count indicates the presence of a red blood cell maturation abnormality (sideroblastic anemia, folate and vitamin B_{12} deficiency) or a hypoproliferative process (IDA without treatment, anemia of renal disease, endocrine anemias, pure red cell aplasia, bone marrow replacement, anemia of inflammation).

IRON METABOLISM

Iron is essential for cellular function, and iron-containing compounds are found in all cells. Most of the body's iron is contained within the heme moiety of hemoglobin, with smaller amounts in myoglobin and other heme proteins and cellular enzymes. Storage iron is sequestered in a nontoxic form in ferritin and hemosiderin within the reticuloendothelial system and liver. A small but essential amount of iron circulates in the plasma bound to transferrin.

Iron-containing compartments

– **Hemoglobin iron** (≈ 65 %).

– **Tissue iron** — myoglobin and other heme proteins and cellular enzymes, such as cytochromes, catalase and peroxidase (≈ 10 %).

– **Storage iron** — ferritin and hemosiderin (≈ 25 %).

– **Transport iron** — a small but essential amount of iron circulates in the plasma bound to transferrin (< 1 %).

Most body iron is taken up by RBC precursors in the bone marrow and incorporated into hemoglobin. Hemoglobin iron is removed from senescent RBCs taken up at the end of their lifespan by macrophages. The iron is removed from the heme ring and recycled to the bone marrow for hemoglobin production. Thus, iron is continuously recycled between the RES and the bone marrow, and this recycling system supplies most of the iron needed for RBC production. The majority of circulating iron derives from destruction of approximately 20 mL of RBC daily in the RES, which liberates about 20 mg of iron. Iron from senescent RBCs is transported from the RES via the plasma, bound to transferrin.

Release of iron from macrophages is mediated by ferroportin, the only known cellular iron exporter. In turn, the abundance of ferroportin on the macrophage plasma membrane is regulated by hepcidin, a liver-derived polypeptide hormone that binds ferroportin, leading to its internalization and degradation. Hepcidin levels are reduced in iron deficiency and increased in certain other conditions such as iron overload and inflammation.

A further 1–2 mg of iron per day is derived from dietary iron absorption and is also transported via the plasma. The iron taken up from dietary sources replaces small amounts of iron lost daily from the body, mainly by exfoliation of epithelial cells. Circulating iron is rapidly removed from the plasma, primarily by nascent RBC precursors in the bone marrow, with smaller portions going to other cells and to iron stores.

The average iron content of the Western diet is 10–20 mg/day, of which only about 10 % is absorbed. Heme iron is absorbed more efficiently than nonheme iron and is the best source of dietary iron. Heme is absorbed intact in the duodenum, and the iron is removed from the heme ring within the enterocytes and enters the same pool as nonheme iron.

Nonheme iron is less well absorbed. Ferric (Fe^{3+}) iron in food must be reduced to ferrous (Fe^{2+}) iron before absorption. The low-pH environment in the stomach solubilizes the iron and helps maintain it in the ferrous state during transport to the proximal duodenum. Nonheme iron absorption is enhanced by formation of complexes with peptides from meat. Vitamin C enhances absorption of nonheme iron by chelating ferrous iron at acid pH in the stomach and maintaining its solubility in the alkaline pH of the duodenum, where iron absorption takes place. Nonheme iron can be bound to food phytates in vegetable fiber and polyphenols in tea, which impair absorption.

Iron absorption is influenced by iron stores, and absorption is enhanced in patients with iron deficiency. This modulation is mediated by the circulating hormone hepcidin, the central regulator of iron metabolism. Hepcidin binds to ferroportin on the basolateral membrane of duodenal enterocytes, causing it to be internalized and degraded. Ferroportin is more abundant when hepcidin levels are lower, leading to increased transfer of iron to the systemic circulation. Hepcidin production is increased in the presence of excess iron stores or inflammation and decreased in iron deficiency or hypoxia. Increased erythropoietic activity, as occurs in hemolytic conditions, increases iron absorption especially when accompanied by increased ineffective erythropoiesis.

Transferrin-bound iron is delivered primarily to red cell precursors in the bone marrow via binding of transferrin to specific transferrin receptors on the outer cell membrane. Smaller amounts are delivered to other cells throughout the body. The Tf-TfR complex is internalized, after which the iron is released into the cytosol, and apo-Tf is recycled intact to the plasma.

Iron utilization and storage

– Most iron is incorporated into hemoglobin, myoglobin, and cytochromes.

– A small amount is incorporated into nonheme enzymes (e.g., ribonucleotide reductase).

– The remaining iron is stored as ferritin and hemosiderin, mainly in cells that specialize in iron storage (macrophages and hepatocytes). Ferritin is the major form of storage iron, which can be mobilized for increased demands. Hemosiderin is composed of aggregates of ferritin molecules that have partially lost their protein shells. It is a more stable and less soluble form of storage iron. However, all the iron stored in both ferritin and hemosiderin can be mobilized if needed to replace losses.

– Iron normally is removed from the body only when cells are lost, especially epithelial cells of the GI tract, skin and renal tubules, and decidua from menstrual cycles. In some pathological conditions, e.g., GI blood loss or hemoglobinuria, iron is lost from the body in the form of heme in hemoglobin. There is no physiologic mechanism for regulating iron excretion. Therefore, body iron balance is maintained by control of intestinal iron absorption.

STAGES OF IRON DEPLETION

1. **Prelatent iron deficiency.**

Initially, when iron stores become depleted, sufficient iron is still available for RBC production, and Hb levels remain normal. Tissue iron levels also remain normal, although the serum ferritin concentration begins to fall, indicating diminishing iron stores.

Diagnostic criteria: ↓ SF, no clinical manifestations.

2. **Latent iron deficiency.** As iron levels continue to decrease, tissue iron may start to become depleted. At this stage, serum ferritin and serum iron concentrations are low; serum Tf is increased, and the percent of saturation of the transferrin with iron is decreased.

Hb and MCV remain within normal limits, but there may be a few hypochromic red cells visible on peripheral smear; the RDW may become elevated, as the first sign of developing iron deficiency anemia.

Diagnostic criteria: ↓ SF, ↓ SI, ↑ Tf, clinically manifested by the appearance of iron deficiency syndrome.

3. **IDA.** In the last phase, once iron stores have been fully depleted, there is no longer sufficient iron to maintain RBC production and, as losses continue, anemia results. RBCs become progressively hypochromic and microcytic (Fig. 5).

Diagnostic criteria: ↓ Hb, normal or ↓ RBC, ↓ MCV, ↓ MCH, ↑ RDW, RI < 2 %, ↓ SF, ↓ SI, ↑ Tf, clinically manifested by the appearance of anemic syndrome and amplification of iron deficiency syndrome.

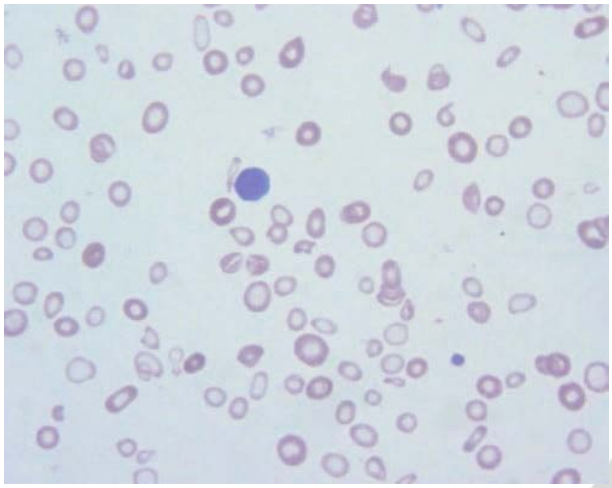

Fig. 5. Blood smear from a 16-year-old male who had a hemoglobin of 65 g/L, MCV 55 fL, and a positive fecal occult blood test. A normal red blood cell is about the size of a lymphocyte nucleus. The area of central pallor occupies about one-third of the overall diameter. Note the very microcytic red cells in relation to the small lymphocyte in the center of the picture. The red cells are also hypochromic, with an increased area of central pallor and a narrow rim of hemoglobin

CAUSES OF IRON DEFICIENCY

1. Deficient intake. Iron stores can be inadequate at birth as a result of maternal iron deficiency or prematurity, as half of the infant's iron stores accumulate in the last month of fetal life. A newborn infant is fed predominantly on milk. Breast milk and cow's milk contain 0.5–1.5 mg/L. Although cow's milk and breast milk are equally poor in iron, breast-fed infants absorb about 50 % of the iron, in contrast to the approximately 10 % that is absorbed from cow's milk. The bioavailability of iron in breast milk is much greater than in cow's milk. The amount of iron in the newborn is about 75 mg/kg. If low iron is present in the diet, the iron stores present at birth will be depleted by 1–2 months in a premature infant and by 4 months in a full-term infant. So even breast-fed infants are at high risk for ID and should take iron supplements from 1–2 months in premature infants and from 4 months in full-term infants.

2. Increased demand: growth (low birth weight, prematurity, multiple births, adolescence), cyanotic congenital heart disease. The most common cause of IDA is inadequate intake during the rapidly growing years of infancy and puberty.

3. Blood loss: perinatal (transplacental bleeding, fetofetal bleeding, ruptured umbilical cord); postnatal (chronic gastritis, erosions and ulcers of GI tract, intestinal parasites, recurrent epistaxis, menstrual loss, hematuria, bleeding disorders).

4. Impaired absorption: malabsorption syndrome, celiac disease, inflammatory bowel disease.

CLINICAL MANIFESTATIONS OF IRON DEFICIENCY

Iron deficiency syndrome

1. Pica — obsessive consumption of substances with no nutritional value such as ice (pagophagia); sand, starch and dirt (geophagia), clay, paper.

2. Changes in the skin and its appendages due to the fact that epithelial tissues have high iron requirements because of rapid rates of growth and turnover and thus are affected in many patients with iron deficiency. They are characterized by a decrease in the elasticity and dryness of the skin, the presence of lichenification on the extensor surfaces of large joints; dryness, brittleness and increased hair loss, the appearance of striation and deformation of nails – spooning of the nails (Fig. 6), in which the nails are concave instead of convex (koilonychia).

3. Atrophic changes in the mucosal epithelium manifested by atrophic gingivitis, stomatitis, glossitis, angular cheilitis (Fig. 7) — ulcerations or fissures at the corners of the mouth), esophagitis (dysphagia, characterized by difficulty swallowing dry food).

4. Muscle weakness is manifested by a decrease in muscle strength, primarily of the sphincters (enuresis, urinary and gas incontinence when coughing and laughing, etc.) and limbs.

5. Immunologic system. Patients with ID have an increased risk of infection, especially of the respiratory system.

6. Central nervous system. Children with iron deficiency are characterized by: irritability, decreased attentiveness, significantly lower academic performance, reduced cognitive performance. **In addition, iron deficiency in children can lead to impaired psychomotor and mental development, not reversible by subsequent iron repletion.**

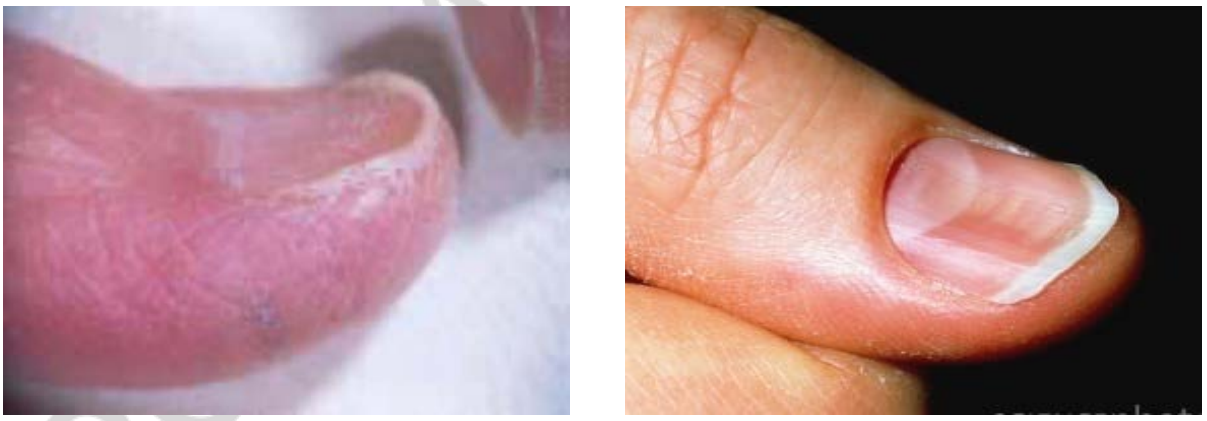

Fig. 6. Spooning of the nails (koilonychia)

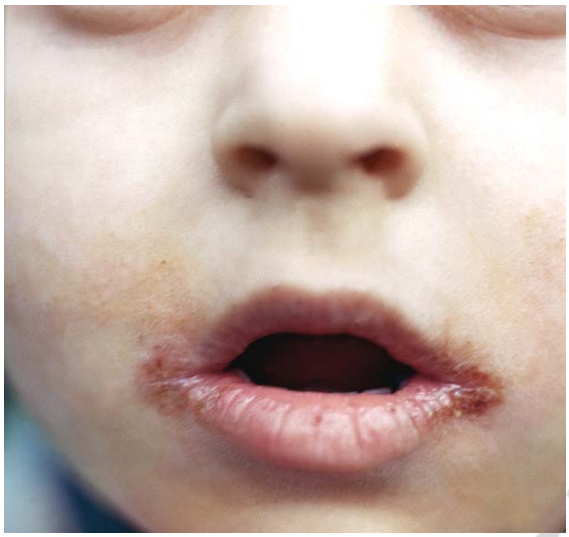

Fig. 7. Iron deficiency syndrome (angular cheilitis)

DIAGNOSTIC TESTS FOR IRON-DEFICIENCY ANEMIA

1. Hb is decreased, RBC is normal or decreased.
2. Hypochromic microcytic RBC, confirmed by indices: MCV, MCH, MCHC less than normal for the patient`s age.
3. RDW greater than 14,5 %, RI less than 2 %.
4. Serum ferritin is decreased.
5. Therapeutic responses to oral iron:

– Reticulocytosis with peak 5–10 days after starting of therapy.

– Following peak reticulocytosis hemoglobin level rises on average by 2,5–4,0 g/L/day, further 1,0–1,5 g/L/day.

The most reliable criterion of iron-deficiency anemia is the hemoglobin response to an adequate therapeutic trial of oral iron. A reticulocytosis followed by a significant rise in hemoglobin level occurs. The absence of these changes implies that iron deficiency is not the cause of anemia or treatment recommendations are violated. Iron therapy should then be discontinued and further diagnostic studies implemented.

GENERAL PRINCIPLES OF IRON DEFICIENCY THERAPY

1. A diet balanced in iron, proteins, rich in vitamins and essential microelements. Maintain breast-feeding for at least 6 months, if possible or use an iron-fortified infant formula until 1 year (formula is preferred to whole cow’s milk).
2. The optimal age-appropriate regimen of the day (walking in the fresh air, limiting physical and psycho-emotional overloads).
3. Identification and elimination the cause of ID.
4. Iron therapy. Anemia should not be treated with iron unless a diagnosis of iron deficiency has been confirmed.

Principles of iron therapy

1. It is impossible to treat ID only by a diet, since iron absorption from food is strictly limited. That is why we need to use iron therapy.

2. The minimum duration of iron therapy is 12 weeks and it consists of 2 steps:

– Anemia treatment is carried out in a full therapeutic dose for 4–10 weeks (until Hb level and the RBC indices becomes normal).

– Replenishment of storage iron, carried out at half the daily dose, for at least 8–16 weeks. This can be confirmed by measurement of serum ferritin concentration demonstrating a return to normal levels.

3. Oral iron replacement is usually the treatment of choice. Parenteral iron drugs are used only in the presence of malabsorption or poor compliance, as oral therapy is otherwise just as effective and it is much cheaper and less toxic.

4. The daily dose of oral iron is calculated based on the content of elemental iron in the drug, depending on the severity of the anemia and the age (body weight) of the child (Table 3).

5. Drug of choice is Iron (III)-hydroxide polymaltose complex. It has similar efficacy, good tolerability and rarely causes side effects than drugs containing iron salts.

6. Iron salts such as ferrous sulfate are associated with a high incidence of GI side effects such as nausea, vomiting, constipation and diarrhea. Also treatment with drugs containing iron salts could lead to permanent staining of tooth enamel.

7. Notice that iron therapy is contraindicated in case of an active infectious process.

Table 3

Dosage of oral iron drugs depending on age (body weight) and severity of IDA

Age/body weight	**Severity of IDA**		
	Mild	**Moderate**	**Severe**
0–3 year	5 mg/kg/day	6–7 mg/kg/day	8–10 mg/kg/day
≥ 4 years and < 50 kg	3–5 mg/kg/day	5 mg/kg/day	6–7 mg/kg/day
≥ 50 kg	2–4 mg/kg/day		

PROPHYLAXIS OF IRON DEFICIENCY

– Iron loses of 500–700 mg are typical with pregnancy: 250 mg transferred to the fetus and the remainder lost with the placenta and via hemorrhage. Pregnant women thus need additional iron supplementation with 20–30 mg/day orally. Further iron is required to replace losses during lactation (50 mg/day orally).

Adequate prevention of ID during pregnancy and lactation is the key to creating adequate iron stores in the newborn and maintaining them in the first year of life.

– Infants at high risk for ID should take iron supplements at a daily dose of 2 mg/kg (from 1–2 months of age in premature infants and from 4 months in full-term) until they receive iron-rich food.

– All full-term infants without risk factors who are breastfed or mixed-fed should take iron supplements at a daily dose of 1 mg/kg from 4 months and until they receive iron-rich food.

– Children over one year of age with ID risk factors (low-iron formula, low meat intake, low socioeconomic status) should take iron supplements at a daily dose of 1 mg/kg in courses of 6–8 weeks.

– When a child reaches a body weight of 50 kg, the maximum daily prophylactic dose of the iron is 50 mg.

– Seven-day courses of iron therapy are indicated for girls with severe or prolonged menstruation at a daily dose of 50 mg/day after each cycle.

Infants at high risk for iron deficiency

1. Increased iron needs: low birth weight, prematurity, multiple gestation, high growth and weight rate, chronic hypoxia — cyanotic heart disease, low Hb at birth.

2. Blood loss: perinatal bleeding.

3. Dietary factors: early cow's milk intake, early solid food intake, low-iron formula, frequent tea intake (inhibits iron absorption), low vitamin C intake reduces iron absorption), low meat intake, breast-feeding > 6 months without iron supplements, frequent infections, low socioeconomic status.

LITERATURE

Main

1. *Paramonova,* N. S. Pediatrics : textbook for students of the Faculty of Foreign Students / N. S. Paramonova, V. A. Zhemoytiak, P. R. Gorbachevsky. Grodno : GrSMU, 2010. 264 p.

Additional

2. *Nelson* Textbook of Pediatrics : 2-Volume Set / ed. by R. M. Kliegman, J. St. Geme. 21th ed. USA, 2020. P. 9865–1094.

CONTENTS

Учебное издание

Козарезов Станислав Николаевич
Дигоева Альбина Казбековна

АНЕМИИ У ДЕТЕЙ

ANEMIA IN CHILDREN

Учебно-методическое пособие

На английском языке

Ответственная за выпуск И. И. Саванович
Переводчик С. Н. Козарезов
Компьютерная вёрстка С. Г. Михейчик

Подписано в печать 07.09.21. Формат 60×84/16. Бумага писчая «Xerox office».
Ризография. Гарнитура «Times».
Усл. печ. л. 1,16. Уч.-изд. л. 0,91. Тираж 40 экз. Заказ 450.

Издатель и полиграфическое исполнение: учреждение образования
«Белорусский государственный медицинский университет».
Свидетельство о государственной регистрации издателя, изготовителя,
распространителя печатных изданий № 1/187 от 18.02.2014.
Ул. Ленинградская, 6, 220006, Минск.

ISBN 978-985-21-0896-6