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CURRENT MODERN ETIOLOGY OF ANEMIA

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Abstract
Anemia is a syndrome of many diseases encountered in the practice of primary care physicians of all specialties. The main manifestations of anemic syndrome are symptoms of hypoxia - increased fatigue, weakness, dizziness, tachycardia, shortness of breath, which are nonspecific and often observed in many chronic diseases. This is often the cause of hypodiagnosis and delayed therapy of this condition, which leads to worsening of the course of the underlying disease and prognosis. Anemic syndrome is diverse in its etiology [1,2].

Keywords: anemia, iron deficiency anemia, anemic syndrome, anemia chronic diseases.

Today, one in five patients has anemic syndrome. However, it is impossible to judge the frequency of anemic syndrome in real practice: statistical records are kept on the main disease, and anemia is almost always secondary and falls out of the field of vision of doctors in the provision of primary health care in outpatient and narrow specialists. The current epidemiological situation on the incidence of anemia indicates its high prevalence. According to WHO data, anemia is present in almost 2 billion inhabitants of the planet. The proportion of iron deficiency anemias (IDA) is 70 to 80% of all anemias [3,4]. Iron deficiency is the most frequent and widespread nutrient deficiency, even in industrialized countries, and affects approximately two billion people worldwide. Iron deficiency with or without anemia is found in patients with chronic diseases such as cancer (43% among various tumors), inflammatory bowel disease (45%), chronic kidney disease (24-85%), chronic heart failure (43-100%), and other chronic inflammatory diseases. Anemia of chronic disease (ACD) is the second most common anemia after iron deficiency anemia and is seen in patients with acute or chronic activation of the immune system due to a variety of both infectious and non-infectious diseases [5,6]. The prevalence of ACEs in old age and senility ranges from 2.9 to 61% in men and 3.3 to 41% in women, and in young adulthood it is more frequently detected in women. In hospitalized 27 elderly patients its frequency reaches 36-80% (in outpatients 5-14%). Among patients with systemic connective tissue diseases, anemia occurs in almost half of patients, with ACE predominating. According to WHO, 1.62 billion people were affected by anemic syndrome in 1993-2005, representing 24.8% of the world's population. For comparison, a similar analysis in 2010 showed - 1.9 billion people suffering from anemic syndrome and it is already 27.9%. The prevalence of various forms of anemia is different in developing and industrialized countries. Vegetarian

diets with cereals as the staple food are common in today's developing world. Fish or meat as a source of digestible iron and fruits and vegetables as a source of vitamin C remain rare in the diet. Foods based on green plant parts are rich in folate, polyphenols and, rich in oxalic acid. These compounds form complexes with iron that are poorly absorbed in the intestinal lumen and impair iron availability. According to WHO experts, the prevalence of iron deficiency in the population can be moderate - from 5 to 19.9%, moderate - from 20 to 39.9% and high - 40% or more. According to WHO estimates, the prevalence of anemia among women of reproductive age is 30.2%, in adolescents it is 25.4%, and its cause is mainly iron deficiency. Among the elderly, the prevalence of anemia is 23.9%. The prevalence of anemia among patients with cardiovascular disease is relatively well studied [7,8]. Among patients with coronary heart disease (CHD), anemia ranges from 10 to 30%, and in the example of CVD, it varies widely from 4 to 61% (average 18%), depending on the severity of the underlying disease and the anemia criteria used. Numerous studies have shown that anemia is an independent risk factor for mortality. In a large-scale study of 6880 elderly patients in primary care clinics, even mild anemia (defined as >10 g/dL) was associated with nearly double the risk of all-cause mortality in men [9].

In order to understand the mechanisms of iron deficiency, it is necessary to have an understanding of iron metabolism in the body. A healthy person's body contains 3-4 g of iron on average: 72.9% is a part of hemoglobin (Hb); 3.3% is a part of myoglobin; 16.4% is in stores (depots): in the form of ferritin (80%) and hemosiderin (20%). The largest part of ferritin is contained in plasma and its level can be used to estimate the iron content in the depot. The daily iron requirement of the organism is 22-24 mg and is mainly covered by heme iron of decaying erythrocytes. Physiologic loss of iron with urine, feces, sloughing epidermis is 0.6- 1.2 mg/day in men and 1.5- 2 mg/day in women (taking into account blood loss during menstrual cycle - 25 mg/month), and is covered by iron from food, which in a normal diet contains about 14 mg. In foodstuffs, iron is present either as a component of heme (meat, fish) or as non-heme iron (vegetables, fruits). Organic iron (Fe^{2+}) is well absorbed (up to 20-30%), while inorganic iron (Fe^{3+}) is absorbed by no more than 5%. In just one day, 1-2 mg (or 8-15%) of dietary iron is absorbed in the upper small intestine [10]. Depending on the causes of iron deficiency, there are 5 groups of iron deficiency anemias:

1. chronic posthemorrhagic iron deficiency anemia;
2. Iron deficiency anemias associated with impaired absorption and intake of iron from food;
3. iron deficiency anemias associated with insufficient initial levels of iron in the body (more often in children);
4. Iron deficiency anemias due to increased body iron requirements (without blood loss);
5. Iron deficiency anemias associated with impaired iron transport.

The most frequent chronic posthemorrhagic WDA occurs in women of childbearing age, which is associated with heavy and prolonged menstruation (in 30%-50% of women) and frequent childbirth (more than once every 3 years), which is characteristic of the inhabitants of Asia, Africa and Latin America. The most frequent chronic posthemorrhagic WDA occurs in women of childbearing age, which is associated with heavy and prolonged menstruation (in 30%-50% of women) and frequent childbirth (more than once every 3 years), which is characteristic of the inhabitants of Asia, Africa and Latin America. In 50% of women menorrhagia have organic causes: polyps, endometritis, myomas, adenomyosis opening into the uterine cavity. A certain proportion of women with menorrhagia are patients with ovarian dysfunction. Therefore, all women with menstrual irregularities in the form of hyperpolymenorrhea and menometrorrhagia should definitely be examined by a gynecologist. Often the cause of menorrhagia can be a disorder of hemostasis:

thrombocytopenia and thrombocytopathies, Willebrand's disease, hereditary or acquired deficiencies of coagulation factors VII, X, V and II [9,10,11,12].

Blood loss from the gastrointestinal (GI) tract is the main cause of iron deficiency in men and non-menstruating women. Even a small blood loss (5-10 ml per day) leads to a monthly loss of 200-250 ml of blood, which corresponds to 100-125 mg of iron. In such a situation, it takes 1-1.5 years for DALYs to develop. Gastrointestinal bleeding (GI bleeding), characteristic of gastrointestinal diseases: erosive gastritis, hernia of the esophageal orifice of the diaphragm, ulcerated Meckel's diverticulum (blind pouch of the small intestine), nonspecific ulcerative colitis, Crohn's disease, polyps of the gastrointestinal tract, diverticulosis of the large intestine, bleeding from hemorrhoidal veins. One of the frequent causes of blood loss from the GI tract are gastric and intestinal tumors, gastric and duodenal ulcers, ankylostomidosis (one ankylostoma consumes 0.3 ml of blood). Therefore, all patients with detected GID should be examined by a gastroenterologist to rule out GI diseases. The next cause of GAD development is bleeding from dilated mucous membrane vessels with thinning wall (Rendu-Osler disease), which are most often detected in the nasal mucosa and cause chronic nasal bleeding [13,14].

Latent iron deficiency and DALD may be observed in blood donors. In rare cases, posthemorrhagic HDA may be associated with hemorrhage into closed cavities with subsequent impaired heme iron reutilization of destroyed erythrocytes. Such blood loss occurs in glomic (vascular) tumors, in endometriosis not associated with the uterine cavity. A similar mechanism of anemia development occurs in isolated pulmonary siderosis, since pulmonary siderophages are unable to deliver iron to erythroblasts. WDD in malabsorption syndrome is seen in chronic enteritis (gluten enteropathy, tropical and non-tropical sprue), Turner syndrome, gastric resection complicated by dumping syndrome. It should be remembered that DALD does not develop as a result of achylic gastritis, since organic iron is perfectly absorbed in complete achyllia. In adolescents, especially girls, during puberty, DALD, or "juvenile chlorosis" is the result of a combination of several causes: increased iron requirements due to rapid growth of girls and the onset of menstruation, initially low iron levels, and poor nutrition (lack of meat products in the diet). Rare cases of iron deficiency due to hereditary impairment of transferrin production (hereditary atranferrinemia) have been described. Over time, iron deficiency progresses, goes latent for many years, and then, after complete depletion of iron stores in the depot, develops ALD [7,8,9,10,11,12].

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