CLINICAL-LABORATORY DIAGNOSIS AND TREATMENT METHODS OF HEMOLYTIC ANEMIA

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Hemolytic anemia in systemic diseases is a widely observed type of anemia that develops in patients with hematological, infectious, or oncological diseases. The characteristic feature of anemia in systemic diseases is a decrease in iron content in the blood. However, unlike true iron deficiency, it is stored in macrophages, which can lead to an increase in iron deposits in the body. Therefore, another term is suggested - "anemia of reticuloendothelial siderosis with iron deficiency."

Anemia in systemic diseases is one of the most common types of anemia and occurs in the second place after iron deficiency anemia.

The etiology of hemolytic anemia in systemic diseases is diverse and often unclear. Hemolytic anemia is associated with hematological, rheumatic, neoplastic diseases, systemic lupus erythematosus (SLE), systemic vasculitis, diabetic mellitus, liver cirrhosis, and others (Table 1).

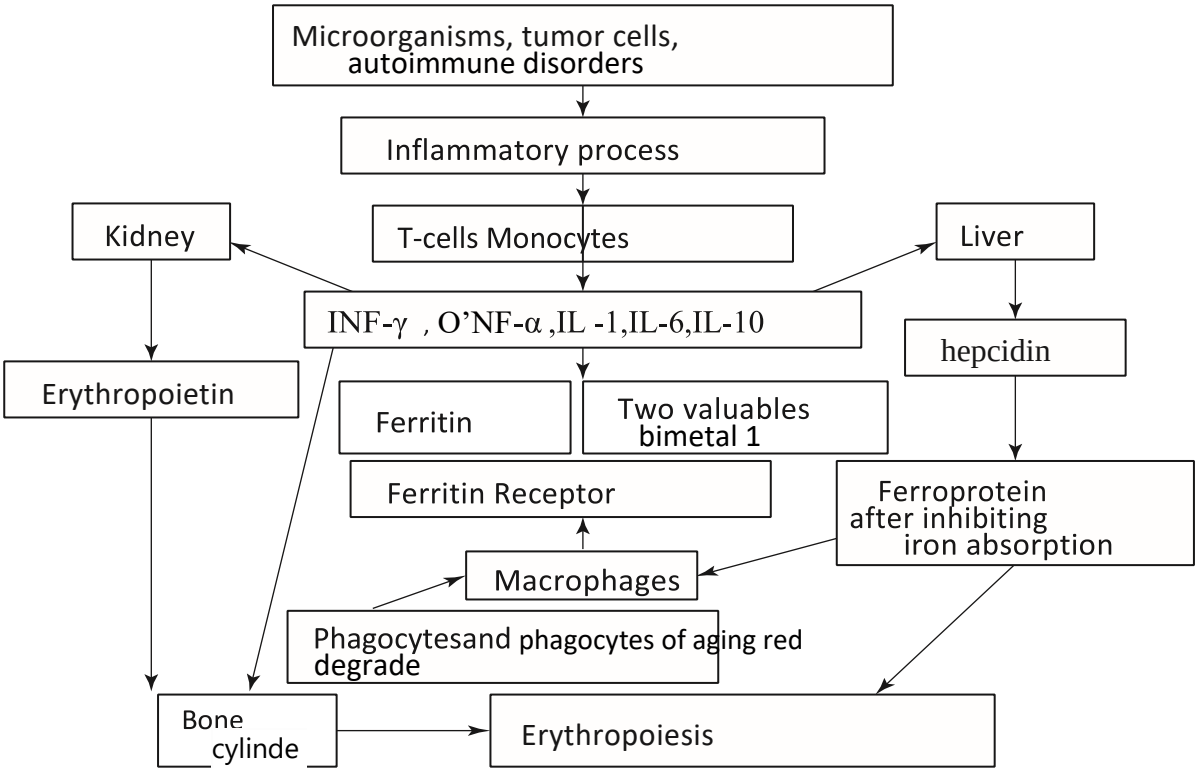
Table 1. Suri nary diseases are the main causes of anemia.

Anemia-related diseases	Approximate spread of anemia in these diseases
Acute and chronic viral, bacterial, fungal infections Parasitic diseases	18-95
Poor quality growths Hemoblastosis	30-77
Autoimmune diseases: systemic reddish-brown, connective tissue diffuse diseases, vasculitis, sarcoidosis, intestinal diseases	8-71
Reaction 'against transplant ant boss’ after organ transplant	8-70
Kidney chronic diseases	23-50

Recent research in the past decade has shed light on the multifactorial pathophysiological mechanisms underlying hemolytic anemia in systemic diseases. During acute infection or systemic disease, the secretion of cytokines against inflammation can alter the regulated iron homeostasis by increasing the excessive synthesis of the main iron regulatory hormone, hepcidin. Additionally, hepcidin inhibits the release of iron from cells, blocks the activity of ferroportin, and the excessive levels of hepcidin in the blood are the main cause of impaired iron metabolism and subsequent disruption of normal erythropoiesis observed in hemolytic anemia of systemic diseases.

A key characteristic of hemolytic anemia in systemic diseases is the sequestration of iron in macrophages, which are part of the reticuloendothelial system, leading to a decrease in the amount of iron in the blood. As a result, iron is redistributed to other macrophage stores that are not available for erythropoiesis, resulting in inadequate or high levels of functional iron deficiency in the body.

Another important factor in the development of hemolytic anemia is the excessive production of pro-inflammatory cytokines, which leads to a significant reduction in erythropoietin production.



1. Scheme. Pathophysiological mechanisms of hemolytic anemia in systemic diseases.

Abbreviations: IL - interleukin, INF-γ - interferon-gamma, TNF-α - tumor necrosis factor-alpha

Clinical manifestations specific to this form of anemia are not present. In most cases, the signs of the underlying disease overshadow anemia, but sometimes anemia syndrome can be its initial manifestation. In hemolytic anemia of systemic diseases, fatigue, general weakness, pale skin, palpitations, shortness of breath, and decreased exercise tolerance may be observed. It should be emphasized that there are other factors that may contribute to the development of anemia syndrome in some systemic diseases, such as iron deficiency, vitamin B12 deficiency, folate deficiency, recurrent bleeding, hemolysis, functional iron deficiency due to absolute erythropoietin deficiency, and bone marrow infiltration by malignant cells or extramedullary metastases.

The diagnostic algorithm includes necessary tests for identifying the underlying disease-causing anemia and systemic disease.

The mandatory range of medical services includes:

- Initial appointment with a general practitioner (examination, consultation);
- Determination of leukocyte levels in the blood;
- Determination of platelet levels in the blood;
- Determination of leukocyte ratio in the blood (calculation of blood formula);
- Examination of blood smears to analyze morphological abnormalities in red blood cells, platelets, and leukocytes;
- Determination of the color index;
- Determination of total hemoglobin and erythrocyte levels in the blood;
- Determination of iron deficiency in the blood without hemoglobin;
- Esophagogastroduodenoscopy;
- Endoscopy of the small intestine.

If the mandatory range of information is insufficient or treatment is ineffective, additional medical services are utilized (a series of tests are performed in specialized hematological clinics):

- Determination of transferrin levels in the blood;
- Determination of ferritin levels in the blood;
- Determination of total iron-binding capacity of transferrin;
- Assessment of transferrin saturation;
- Measurement of C-reactive protein;
- Determination of erythroid transferrin receptor levels in the blood (eTfR);
- Identification of side oblasts and siderocytes;
- Measurement of blood loss volume through radioactive chromium via the fecal-oral route;
- Cytological examination of bone marrow smears (myelogram);
- Determination of endogenous erythropoietin.

An example of a complete blood analysis for hemolytic anemia is as follows: hemoglobin - 82 g/l; erythrocytes - 2.5×10^12/l, hematocrit - 22%, MCV - 90 fl, MCH - 28 pg, leukocytes - 9.9×10^9/l. Leukocyte formula: neutrophils - 60%, lymphocytes - 31%, monocytes - 9%, platelets - 200×10^9/l.

Differential diagnosis for hemolytic anemia in systemic diseases is performed with iron deficiency anemia (Table 2).

Table 2. Differential diagnosis of iron deficiency anemia (TTA) and chronic disease anemia (SKA) and their combinations

Indicator	SKA	TTA	SKA & TTA Combinations
Hemoglobin	Decreases	Decreases	Decreases
The amount of iron in the whey	Decreases	Decreases	Decreases
The ability to bind a common iron in a blood vessel	Decreases	Increased	Decreases

Saturation of the transferrin	Decreases	Decreases	Decreases
The amount of ferritin in the bloodstream	Normally or increases	Decreases	Increased
Level of soluble transferrin receptors in blood whey (sTfR)	Normally	Increased	Normally or increases
Ratio of soluble transferrin receptors to log ferritin (sTfR index)	Normally (ratio <1)	Increased (ratio >2)	Normally (ratio >2)
The amount of gepsidin	Increased	Normally	Increased

Inadequate treatment of the underlying disease is the most effective way to treat chronic disease anemia. However, all chronic diseases that are difficult to treat anemia (systemic connective tissue diseases, chronic inflammatory intestinal diseases, HIV infections, etc.) are difficult to treat, because anemia significantly worsens the prognosis and outcomes of these diseases and is an independent risk factor for increased mortality.

The partial effect of oral iron preparations may be in patients with advanced chronic disease anemia against the background of iron deficiency. The most effective scheme to treat the anemia of chronic disease is the joint use of epoetin beta (Erythropoietin♠) and iron preparations (table 3).

Table 3. Drug preparations in chronic disease anemia

Name of the international non-patented name	Average delivery frequency	Unit	Average daily dose	Average course dosage
Blood-affecting drugs				
Anti-anemia preparations				
Epoetin alpha (Recombinant man alpha erythropoietin)	0,9	Ampoule	5,000 ed.	180,000 ed.
Iron preparation				
Polyethylene compound iron oxide	0,9	Vial	200 mg	1000 mg

Epoetin alfa (recombinant human erythropoietin) is used to treat anemia when the hemoglobin level is less than 100 g/L. Contraindications for use include:

- Hematocrit greater than 0.6
- Leukocytosis greater than 40 x 10^9/L
- Thrombocytosis greater than 700 x 10^9/L
- Individual intolerance to the medication

Treatment with epoetin alfa can last up to 12 weeks. The dosing regimen is as follows: subcutaneous injection 3 times a week at a dose of 150-300 IU/kg. Therapeutic regimen:

- Initial dose - 150 IU/kg

- Additional iron preparations should be prescribed orally or intravenously in a daily dose not exceeding 5 mg/kg to correct functional iron deficiency.

Laboratory monitoring includes monitoring the total number and level of erythrocytes, reticulocytes, and platelets in the blood. Hemoglobin and hematocrit levels should be checked every 7-10 days before and during treatment.

The desired target for hemoglobin levels is 110 g/L.

The continuation of monitoring depends on the symptomatic characteristics of the anemia syndrome and is determined by the clinical presentation of the underlying disease.

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