МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
КАФЕДРА ПОЛИКЛИНИЧЕСКОЙ ТЕРАПИИ

ДИФФЕРЕНЦИАЛЬНАЯ ДИАГНОСТИКА АНЕМИЧЕСКОГО СИНДРОМА. АМБУЛАТОРНЫЕ АСПЕКТЫ ДИАГНОСТИКИ И ЛЕЧЕНИЯ АНЕМИЙ, ОБУСЛОВЛЕННЫХ ДЕФИЦИТОМ ЖЕЛЕЗА, ВИТАМИНОВ B12 И ФОЛИЕВОЙ КИСЛОТЫ

DIFFERENTIAL DIAGNOSIS OF ANEMIC SYNDROME. OUTPATIENT ASPECTS OF DIAGNOSIS AND TREATMENT OF ANEMIAS CAUSED BY IRON, VITAMIN B12, AND FOLIC ACID DEFICIENCY

Учебно-методическое пособие

Минск БГМУ 2026

УДК [616-071-08:616.155.194]:616.155.194.8+577.164(075.8)=111
ББК 54.11я73
Д50

Рекомендовано Научно-методическим советом университета в качестве учебно-методического пособия 18.03.2026 г., протокол № 7

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Дифференциальная диагностика анемического синдрома. Д50 Амбулаторные аспекты диагностики и лечения анемий, обусловленных дефицитом железа, витаминов B12 и фолиевой кислоты = Differential diagnosis of anemic syndrome. Outpatient aspects of diagnosis and treatment of anemias caused by iron, vitamin B12, and folic acid deficiency : учебно-методическое пособие / Е. С. Алексеева, Н. М. Ерёмина, М. В. Зюзенков, Е. А. Каразей. – Минск : БГМУ, 2026. – 32 с.

ISBN 978-985-21-2213-9.

Рассматриваются причины и механизмы развития, этапы диагностического поиска и дифференциальной диагностики анемического синдрома в амбулаторных условиях, а также диагностика и лечение анемий, обусловленных дефицитом железа, витаминов B12 и фолиевой кислоты

Предназначено для студентов, обучающихся по специальности «Лечебное дело» по учебной дисциплине «Поликлиническая терапия» на английском языке.

УДК [616-071-08:616.155.194]:616.155.194.8+577.164(075.8)=111
ББК 54.11я73

ISBN 978-985-21-2213-9

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ABBREVIATIONS

ACD — anemia of chronic diseases
ACTH — adrenocorticotropic hormone
AG — autoimmune hemolytic anemia
APHA — acute posthemorrhagic anemia
CBC — complete blood count
CL — color index (CL)
CRP — C-reactive protein
ECG — electrocardiography
ECHO-CG — echocardiography
EGD — esophagogastroduodenoscopy
ESR — erythrocyte sedimentation rate
FDA — folate deficiency Anemia
G6PDH — glucose-6-phosphate dehydrogenase
HA — hemolytic anemia
HGA — hereditary hemolytic anemia
HM-EKG — Holter ECG monitoring
HR — heart rate
IDA — cholestatic anemia
LIBC — latent iron-binding capacity of serum
MSE — medical and social examination
PNH — paroxysmal nocturnal hemoglobinuria
RR — respiratory rate
TF — transferrin
TIBC — total iron-binding capacity of serum
URA — complete urinalysis

MOTIVATIONAL CHARACTERISTICS OF THE TOPIC

Lesson Topic: «Iron deficiency anemia, Vitamin B12 deficiency anemia and Folate deficiency anemia. Differential Diagnosis of Anemic Syndrome».

Lesson Duration: 6 Academic Hours.

Anemic syndrome is a clinical and hematological syndrome that remains a pressing public health problem worldwide. Various types of anemia occur in 10–25 % of the population, and any population group can be affected, regardless of gender, age, region of residence, or occupation. Clinical manifestations of anemic syndrome can be caused by both the anemia itself and various manifestations of hypoxia and hypercapnia, leading to dysfunction of all organs and systems of the body. Anemic syndrome is often a symptom of another disease, both medical and

surgical. Due to the similarity of clinical manifestations, physicians of various specialties face the complex task of differential diagnosis of anemic syndrome. Mastering differential diagnostic skills is an integral part of any physician's work. When analyzing clinical data obtained during an initial consultation, it is often necessary to use differential diagnostic methods to determine the stages of the diagnostic examination, establish a diagnosis, and determine treatment strategies. Assessing the clinical situation requires identifying the primary symptom (syndrome), correlating it with other manifestations of the disease, and supplementing the picture with objective, laboratory, and instrumental examination data. This process requires extensive knowledge not only in the physician's specialty but also in related fields.

Therefore, a detailed study of this topic during the training of future general practitioners will deepen and systematize their knowledge in the field of diagnosis and personalized management of patients with anemia.

The purpose of the lesson: to deepen, systematize, and consolidate students' knowledge of the diagnosis and differential diagnosis of diseases associated with anemic syndrome.

Objectives of the lesson: acquire practical skills in interpreting examination data, determining treatment strategies, assessing disability, conducting clinical trials, and preventing anemia caused by iron, vitamin B12, and folate deficiency.

Basic Knowledge Required: to fully master the topic in the «Normal and Pathological Physiology» section, students must study the process of erythropoiesis, understand the biological substances involved in red blood cell maturation, the causes of erythropoiesis disorders, and understand hemogram parameters and their significance.

Test questions from related disciplines:

1. The main stages of erythropoiesis.
2. Factors that stimulate and inhibit erythropoiesis.
3. Causes of erythropoiesis disorders.
4. Pathological conditions associated with erythropoiesis disorders.
5. Hemogram parameters and their significance.

Test questions on the topic of the lesson:

1. Definition of anemic syndrome.
2. Classification of anemias by pathogenesis (posthemorrhagic, dyserythropoietic, hemolytic), by color index, red blood cell size and volume, hemoglobin oxygen saturation, bone marrow regenerative capacity, and severity.
3. Stages and algorithm for diagnosing anemic syndrome.
4. Differential diagnosis of anemia: hypochromic (iron deficiency and iron-deficiency), hyperchromic (B12 and folate deficiency), normochromic (hypo- and aplastic, hemolytic, mixed).

5. Iron deficiency anemia: patient examination plan, outpatient treatment, assessment of temporary disability, monitoring, prevention.

6. B12 and folate deficiency anemia: patient examination plan, treatment strategy, outpatient treatment, assessment of temporary disability, medical examination, prevention.

Assignments for independent student work. To better understand the topic, the student is offered an in-depth study of iron, vitamin B12, and folate metabolism, the role of these compounds in the functioning of various body systems, and the development of pathological mechanisms that can result from their deficiency.

GENERAL PROVISIONS

Anemic syndrome (anemia, blood hypoformation) is a clinical and hematological condition caused by an absolute decrease in hemoglobin levels and a reduced red blood cell count (hemoglobin — less than 130 g/L in men and 120 g/L in women, less than 110 g/L in pregnant women; red blood cell count — 4.0×10^{12}/L in men and 3.8×10^{12}/L in women) per unit volume of blood. Qualitative changes in red blood cells (size, shape, residual nuclei, color change, etc.) may also be detected in the peripheral blood.

Common causes of anemia include the following factors:

– physical: penetrating radiation (X-rays, gamma radiation, and neutrons, acute or chronic exposure exceeding maximum permissible doses);

– chemicals (varnishes, paints, benzene derivatives, insecticides, heavy metal salts — lead, etc.);

– infections caused by cytomegalovirus, herpes viruses, hepatitis, etc.;

– medication intake (chloramphenicol, salicylic acid and its derivatives, analgesics, anti-tuberculosis drugs, etc.);

– nutritional factors (deficiency in hematopoietic factors in the diet: iron, cobalt, vitamins B12, B6, folic acid); chronic alcohol consumption;

– genetic disorders of erythropoiesis, inherited as an autosomal dominant, less commonly recessive, or sex-linked disorder;

– physical and mental trauma;

– many somatic diseases and/or their complications (bleeding of various etiologies, gastrointestinal diseases, connective tissue diseases, immunodeficiency states, malignant neoplasms, uterine fibroids, infectious diseases, etc.);

– surgical interventions (gastrectomy, ileectomy, bowel resection, etc.).

Red blood cell synthesis is one of the most powerful cell-forming processes in the body. 2,000,000 red blood cells are produced per second, 173,000,000,000 per day, 63,072,000,000,000 per year, and 4,415,040,000,000,000 over 70 years. Approximately 140 g of red blood cells are produced per day, 51 kg per year, and

3.5 tons over 70 years. In adults, erythropoiesis occurs in the bone marrow and flat bones, while in fetuses and in certain pathological conditions, hematopoietic islets are located in the liver, spleen, and other organs (extramedullary hematopoiesis).

The process of erythropoiesis is shown in fig. 1.

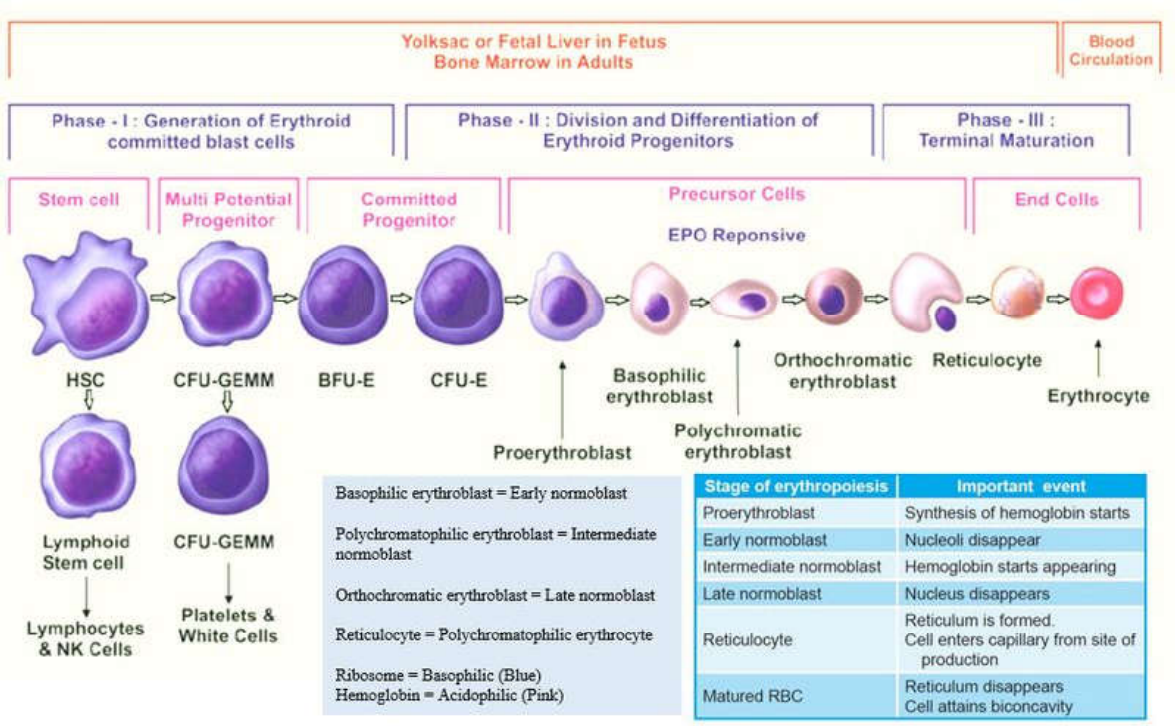

Fig. 1. Hematopoiesis diagram
(https://epomedicine.com/medical-students/erythropoiesis-simplified)

The proliferation of young erythropoietic progenitor cells requires the presence of granulocyte-macrophage colony-stimulating factor, stem cell factor, and interleukin-3. Differentiated erythropoietic progenitor cells formed through cell division gradually lose sensitivity to these factors and acquire sensitivity to erythropoietin.

Erythropoietin is a glycoprotein hormone, 90 % of which is produced in the kidneys and synthesized by juxtaglomerular cells and glomerular epithelial cells. In healthy individuals, plasma erythropoietin levels range from 0.01 to 0.03 IU/μL, increasing 100- to 1000-fold with hypoxia of any origin. Vitamin B12 and folate, necessary for DNA synthesis, are also important elements of cell division.

Erythropoiesis is inhibited by ACTH, corticosteroids, androgens, thyroxine, insulin, and vasopressin.

ANEMIA CLASSIFICATIONS

In general practice, the main criteria for assessing anemia and its severity are hemoglobin and red blood cell levels, which allow for the classification of anemia by severity to determine treatment strategies and indications for hospitalization. Thus, anemia is classified as follows:

– mild — Hb 110–90 g/L; red blood cells 3.8–3.0 × 10^{12}/L;
– moderate — Hb 90–70 g/L; red blood cells 3.0–2.0 × 10^{12}/L;
– severe — Hb less than 70 g/L; red blood cells less than 2.0 × 10^{12}/L.

The most common pathogenetic forms are:

I. Anemias caused by acute blood loss.

II. Anemias caused by erythropoiesis failure.

II.I. Anemias due to impaired maturation (mainly microcytic):
– impaired iron absorption and utilization (IAU);
– impaired iron transport (atransferrinemia);
– impaired iron utilization (thalassemia, sideroblastic anemia);
– impaired iron reutilization (anemias in chronic diseases).

II. II. Due to impaired differentiation (mainly normocytic type):
– aplastic anemias (congenital and acquired);
– congenital dyserythropoietic anemias.

II. III. Due to impaired proliferation (mainly macrocytic type):
– vitamin 12 deficiency anemia;
– folic acid deficiency anemia (FDA).

III. Anemias caused by increased destruction of erythroid cells:

III.I. Hemolysis caused by intrinsic erythrocyte abnormalities:
– membranopathies;
– enzymopathies;
– hemoglobinopathies.

III.II. Hemolysis caused by external factors:
– autoimmune hemolytic anemias;
– traumatic anemias;
– paroxysmal nocturnal hemoglobinuria (PNH).

The morphological classification of anemias is based on the values of the red blood cell indices (erythrocyte indices) of the peripheral blood. The following forms are distinguished:

1. *Microcytic hypochromic anemia* — color index less than 0.80, red blood cell diameter less than 6.5 μm, MCV less than 80 μm3, MCH less than 27 pg, MCHC less than 30 g/dL (less than 30 %), RDW — normal or elevated. Hypochromic anemias include:

– chronic iron deficiency;
– anemia of chronic disease;

– sideroblastic;

– anemias caused by impaired porphyrin synthesis (including anemia caused by lead poisoning and vitamin B6 deficiency);

– thalassemia.

2. *Macrocytic hyperchromic anemia:* color index greater than 1.1; red blood cell diameter greater than 8 μm; MCV greater than 100 μm^3; MCH greater than 32 pg; MCHC greater than 36 g/dL (36 %) or normal; RDW increased. Sometimes MCHC is normal, in which case macrocytic anemia is normochromic. Macrocytic anemias are divided into megaloblastic and non-megaloblastic. Megaloblastic anemia is more common:

– with vitamin B12 or folate deficiency;

– with aplastic anemia, myelodysplasia;

– with liver disease, hypothyroidism, alcoholism;

– with anemia of pregnancy and neonates;

– with the use of hydroxyurea and antimetabolites.

3. *Normochromic normocytic anemia:* all vital signs are within normal limits. A normal red blood cell count is characteristic of:

– acute posthemorrhagic anemia;

– hereditary hemolytic anemia (except thalassemia);

– acquired autoimmune hemolytic anemia;

– anemias associated with hemoblastoses and bone marrow metastases;

– mixed deficiencies (e. g., iron and vitamin B12).

Depending on the functional state of the bone marrow and its ability to regenerate, anemias are classified as:

– hyperregenerative (reticulocyte production index greater than 3) — with normoblastic impairment of red blood cell maturation and megaloblastic erythropoiesis;

– hyporegenerative (reticulocyte production index less than 2);

– normoregenerative (reticulocyte production index 2–3);

– areregenerative (absence of reticulocyte production).

STAGES OF DIAGNOSTIC SEARCH FOR ANEMIA SYNDROME

Diagnosis of anemia syndrome involves several stages.

Stage I is the determination of the presence of anemia syndrome and the development of a primary diagnostic hypothesis. This includes an analysis of the patient's complaints, medical history, examination data, and hemogram.

Anemia syndrome, as a clinical and laboratory condition, rarely brings a patient to a general practitioner. Most often, the physician actively identifies this pathology by analyzing information at the initial stage of patient management.

However, patients with anemia syndrome of any etiology may experience a complex of nonspecific complaints caused by the severity of hemic hypoxia in organs and tissues, underlying pathology, the clinical picture of comorbidities, as well as specific symptoms characteristic of a particular type of anemia. During the interview, it is important to pay attention to symptoms that indicate the presence of:

– *general anemic syndrome*: general weakness, malaise, headache and dizziness, tinnitus, memory and concentration impairment, rapid heartbeat, shortness of breath when walking quickly and climbing stairs, decreased performance, and sleep disturbances. Frequently detected symptoms include pale skin and mucous membranes, tachycardia, tachypnea, hypotension, enlarged heart, muffled heart sounds, and a functional systolic murmur at all standard cardiac auscultation points;

– *sideropenic syndrome*: taste perversion — desire to eat chalk, clay, coal, sand, tooth powder, raw ground meat, dough, cereals; addiction to unusual odors — acetone, varnish, paint, kerosene, fuel oil, exhaust fumes, shoe polish, mothballs; Severe general weakness disproportionate to the degree of anemia. Objective examination reveals trophic disorders: dry skin and premature wrinkles, cracks on the hands and feet; cracks in the corners of the mouth; dry, brittle nails, their thinning, flattening, in severe cases flat spoon-shaped nails (koilonychia); dry, brittle and falling out hair, its premature graying; atrophy of the mucous membrane of the tongue, smoothing of the papillae of the tongue, burning of the tongue, its redness (atrophic glossitis), cracks in the mucous membrane of the pharynx and esophagus, sideropenic dysphagia (Plummer-Vinson syndrome); atrophy of the gastric mucosa, sometimes with histamine-resistant achylia, impaired absorption of fats and glucose in the intestine; «sideropenic subfebrile condition»;

– *jaundice syndrome*: lemon-yellow skin tone, changes in stool color (dark brown) and urine (intense yellow);

– enlarged lymph nodes and hepatosplenomegaly;

– hemorrhagic syndrome, signs of external bleeding;

– dyspepsia and abdominal pain;

– edema syndrome;

– symptoms of nervous system damage;

– hyperthermia, recurrent infections of various organs and systems.

When collecting the anamnesis, the following is determined:

1. Age. For example, iron deficiency is common in children under 6 months, adolescents, pregnant women, and elderly patients; anemia of chronic diseases (ACD) — more often in the elderly, senile, etc.;

2. Gender. Iron deficiency in women, glucose-6-phosphate dehydrogenase (G6PD) deficiency in men.

3. Ethnicity. Thalassemia syndrome is typical among Arabs, while G6PD deficiency is more common among Sephardic Jews, Filipinos, Greeks, Kurds, and Sardinians.

4. Neonatal, childhood, and adolescent history. Hereditary hemolytic anemias, iron deficiency, infections, and helminthiasis.

5. Family history.

6. Dietary habits. Can identify deficiencies in iron, vitamins E, B12, and folate.

7. Past (especially infections, surgeries, etc.) and diagnosed chronic diseases.

8. Medication intake. Plays a significant role in the development of anemias such as hemolytic and aplastic.

9. Professional history. Work with chemicals capable of causing hemolysis, ionizing radiation, etc.

Analysis of clinical manifestations is not always informative, so differential diagnosis of anemia in an outpatient setting is usually performed using the most accessible indicator for the physician — red blood cell indices, i.e., morphological signs of anemia: microcytic hypochromic, normocytic normochromic, and macrocytic hyperchromic.

The main red blood cell mass indices required for analysis when anemia syndrome is suspected are presented in tables 1 and 2.

Table 1

Hemogram indicators

Indicator	Normal Values
RBC — (Red Blood Cells) red blood cell count ($\times 10^{12}$/L)	Lower Limit 4.0×10^{12}/L in men 3.8×10^{12}/L in women
HGB — hemoglobin level	Lower Limit Men 130 g/L Women 120 g/L
HCT — hematocrit	Men 0.4–0.48 % Women 0.36–0.42 %
MCV — (Mean Corpuscular Volume) red blood cell volume	80–98 (100) μm^3
MCH — (Mean Corpuscular Hemoglobin) average hemoglobin level in red blood cells	27–32 picograms
MCHC — (Mean Corpuscular Hemoglobin Concentration) average hemoglobin concentration in red blood cells	cells 30–36 g/L or 30–36%
RDW — (Red Blood Cell Distribution Width) an indicator of red blood cell distribution by volume	11,0–14,5 %.
Color index: Hb (g/L) × 0.03 : Er (L)	0,85–1,0
Red blood cell diameter	7,2–7,5 μm

Table 2

Blood Plasma Analysis Parameters

Parameter	Normal Values
Serum Iron (μmol/L)	Men 13–30 μmol/L Women 11.5–25 μmol/L
Total Iron-Binding Capacity (TIBC) — the amount of iron that can bind one liter of serum	50–84 μmol/L
Ferritin	20–200 μg/L (in men ≈ 94 μg/L, in women ≈ 34 μg/L)

Additional plasma parameters used to diagnose anemia:

1. *TIBC minus serum iron = latent TIBC (LIBC)*. Normal range: 46–54 μmol/L.

2. Transferrin (TF) is the main plasma protein, an iron carrier, and the primary iron donor for hemoglobin synthesis. It is the primary clinical parameter for differentiating between iron deficiency anemia (IDA↑) and hemolytic anemia (IDA↓). Normal range: 2–3.6 g/L.

3. *Transferrin iron saturation ratio* is a calculated parameter expressed as the ratio of the patient's blood iron level to TIBC. Normal range: 17.8–43.3 %. Decreased transferrin iron saturation is a sign of iron deficiency anemia. An increased saturation ratio may indicate excessive iron accumulation in the body, which can be deposited in organs and tissues, causing pathological processes.

4. Determination of plasma vitamin B12 levels, measured in pg/mL. The normal range is 193–982 pg/mL.

5. Determination of *plasma folic acid levels (serum folate)*, measured in ng/mL. The normal range is 1.5–20 ng/mL.

6. Determination of *plasma erythropoietin levels*, measured in IU/μL. The normal range is 0.01–0.03 IU/μL.

7. *Anti-intrinsic factor antibodies* are autoantibodies to gastric cells that produce both intrinsic factor and hydrochloric acid. Their detection during testing indicates autoimmune gastritis, leading to impaired absorption of vitamin B12 and the development of anemia.

8. *Soluble transferrin receptor (sTfR)* is an indicator of iron levels and erythropoiesis activity. Used as a supplemental test for anemia of chronic disease. The sTfR value is proportional to the amount of transferrin. As serum iron concentration decreases, sTfR concentration increases simultaneously with transferrin. An increase in sTfR is independent of the degree of inflammation but indicates iron deficiency and increased erythropoiesis. Normal range: 1.9–5 mg/L.

Primary clinical significance: assessment of erythropoiesis in chronic kidney disease, aplastic anemia, and after chemotherapy; monitoring erythropoiesis after bone marrow transplantation; assessing the effectiveness of recombinant

erythropoietin therapy in anemia associated with renal failure; assessing the severity of changes in iron stores in the body. To identify the cause of anemia, it is necessary to determine the number of leukocytes, reticulocytes, platelets, and ESR in capillary blood. Serum acute-phase reactants (CRP), bilirubin and transaminase levels, urea, creatinine, glucose, total protein, electrolytes, and lipid profile should also be determined, and the glomerular filtration rate (GFR) calculated. A complete list of tests for diagnosing anemia is presented in table 1.

Mandatory tests also include:

– general urinalysis, including microscopic examination of the sediment;
– fecal occult blood enzyme immunoassay;
– stool test for helminth eggs and protozoa;

Instrumental tests:

– chest X-ray;
– electrocardiography, echocardiography;
– ultrasound of the abdominal organs, pelvis, and thyroid gland;
– FGDS with gastric biopsy (2 biopsies from the body of the stomach — along the lesser and greater curvatures); 2 biopsies from the antrum — along the lesser and greater curvatures and 1 biopsy from the angle of the stomach and the duodenum (at least 3 biopsies, including a biopsy from the postbulbar region). Diagnosis of Helicobacter pylori infection (histological method or 13C-breath test);
– colonoscopy (for patients over 50 years old);
– specialist consultations: gynecologist, hematologist (as indicated), oncologist (as indicated).

Stage II of the diagnostic search involves determining the leading pathogenetic/morphological variant of anemia based on hemogram analysis.

As already mentioned, to optimize the diagnostic search based on hemogram parameters, it is necessary to classify the patient's anemia into one of its morphological variants (table 3).

Table 3

Morphological forms of anemia

Type of anemia		
Microcytic/ hypochromic	**Normocytic/ normochromic**	**Macrocytic/ hyperchromic**
MCV less than 80 μm^3	MCV 80–100 μm^3	MCV greater than 100 μm^3
MCH less than 27 pg	MCH 27–32 pg	MCH greater than 32 pg
MCHC less than 30 g/dL (less than 30 %)	MCHC 30–36 g/dL	MCHC greater than 36 g/dL (36 %) or normal
RDW — normal or elevated	RDW normal	RDW — elevated
CI less than 0.8	CI 0.8–1.1	CI greater than 1.1

Stage III of the diagnostic search involves determining the nosological affiliation, i. e., identifying the underlying disease-causing anemia in a given patient, with the selection of additional examination methods presented above to confirm the final diagnosis.

This stage can be divided into several substages:

1. Differential diagnosis of microcytic anemias
2. Differential diagnosis of normocytic anemias
3. Differential diagnosis of macrocytic anemias

Differential diagnosis of microcytic anemias (tables 4, 5).

The nosological causes of these anemias are:

– iron deficiency anemia (IDA);
– anemia of chronic diseases (ACD);
– sideroblastic anemia;
– anemias caused by lead poisoning and vitamin B6 deficiency;
– thalassemia.

Table 4

Differential features of microcytic anemias

Signs	IDA	ACD	thalassemia	sideroblastic anemia	Lead poisoning
Anam-nesis, reasons	Acquired, causes include malabsorption, increased iron requirement, and blood loss. Women and children are more commonly affected	Acquired, causes include chronic infections, systemic connective tissue diseases, cancer, liver and kidney disease, etc.	Hereditary, caused by impaired synthesis of α- or β-globin. Both sexes are affected	Hereditary, defects in the genes responsible for the synthesis of porphyrin metabolism enzymes. Young men are more commonly affected	Acquired, causes include a history of lead exposure
Clinical signs	Sideropenic syndrome	Clinical presentation of the underlying disease	Skeletal abnor-malities, osteoporosis, infantilism, signs of hemolysis, enlarged spleen	Impaired attention, memory, itchy skin, dry skin, hair loss, brittle nails, attacks of shortness of breath, rhythm disturbances, hepatosple-nomegaly	Abdominal pain, constipation, sallow pallor, leaden rim, polyneuritis, encepha-lopathy

End of the table 4

Signs	IDA	ACD	thalassemia	sideroblastic anemia	Lead poisoning
Hemogram	Hypochromic, microcytosis, aniso- and poikilocytosis	Hypochromic or normo-chromic at onset	Hypoch-romic, schistocytes, target cells	Hypo- or normochromic anemia, often leukopenia and thrombocyto-penia, target cells, schisto-cytes, increased content in erythrocytes	Hypochromic anemia, basophilic punctu-ration of erythrocytes, sometimes Jolly bodies, reticulo-cytosis
Serum iron	Reduced	Reduced	Norm	Increased	Increased
TIBC	Increased	Reduced	Reduced	Reduced	Reduced
Ferritin	Reduced	Normal or elevated	Normal or elevated	Normal or elevated	Normal or elevated
Transferrin	Normal or elevated	Reduced	Reduced or normal	Reduced	Reduced
CRP and other inflam-mation markers	Normal or slightly increased	Increased	Normal or slightly increased	Normal or slightly increased	Normal or slightly increased
Signs of hemolysis	No	No	Expressed	Insignificant	Insignificant
Bone marrow	A decrease in the number of sideroblasts — erythrocytes containing iron granules, hemosiderin is sharply reduced.	Inhibition of erythro-poiesis — proliferation and diffe-rentiation of erythroids, increased hemosiderin	Erythro-poiesis hyperplasia, elevated hemosiderin	Erythropoiesis hyperplasia with a left shift, a large number of sideroblasts, and a sharp increase in hemosiderin	Erythro-poiesis hyperplasia, binucleated erythroblasts, increased sideroblasts

Table 5

Differential diagnosis of microcytic anemias by serum iron level

IDA	ACD	Thalassemia and other hemoglobi-nopathies	Sideroblastic anemia
Serum iron			
Decreased < 11.5 μmol/L		Normal (11.5–30 μmol/l)	Increased > 30 μmol/L
Ferritin			
< 20 mcg/l	> 20 mcg/l	> 20 mcg/l	> 20 mcg/l
Transferrin			
> 3,6 g/l	< 2 g/l	< 2 g/l	< 2 g/l

Differential Diagnosis of Normocytic Anemias (tables 6, 7).

Nosological causes of these anemias:

– acute posthemorrhagic anemia (APHA);
– hereditary hemolytic anemia (except thalassemia) (HHA);
– acquired autoimmune hemolytic anemia (AAH);
– anemias associated with hemoblastoses and bone marrow metastases;
– mixed deficiencies (e. g., iron and vitamin B12).

Table 6

Differential Features of Normocytic Anemias

Signs	APHA	HHA	AAH	Hemoblastoses
Anamnesis, reasons	External and internal bleeding	Hereditary hemolytic anemias caused by a biochemical defect in the membrane and enzyme systems of red blood cells. Childhood	Acquired hemolytic anemias caused by extraerythrocyte (autoimmune) factors that cause the destruction of normal red blood cells. Adults, more often women	Any age and gender Complex of hereditary, environmental, industrial, and infectious factors
Clinical signs	Rapidly increasing signs of general anemic syndrome in combination with signs of external (trauma) or internal (melena, vomiting with «coffee grounds», blood, etc.)	Constitutional skeletal deformities, hemolytic (suprahepatic) jaundice, splenomegaly, possible fever, and abdominal pain. Development of cholelithiasis and signs of mechanical jaundice are possible	Hemolytic (suprahepatic) jaundice, splenomegaly, fever, pale skin, weight loss, shortness of breath, possible hepatomegaly, lymphadenopathy, edema, cyanosis of the lips, wings of the nose, ears, associated with impaired microcirculation	General anemic syndrome, recurrent, complicated infections, lymphadenopathy, splenomegaly, hemorrhagic and pain syndromes, fever, damage to the nervous system
Hemogram	Normochromic, reticulocytosis	Normochromic, morphologically altered erythrocytes (spherocytes, pycnocytes, schistocytes, stomatocytes, etc.), reticulocytosis	Normochromic, reticulocytosis, possible leukocytosis, accelerated ESR syndrome	Normochromic, leukopenia, neutropenia, agranulocytosis, thrombocytopenia, accelerated ESR syndrome

End of the table 6

Signs	APHA	HHA	AAH	Hemoblastoses
Bioche-mical blood test	Most often without any special features	Increased indirect fraction of bilirubin, free hemoglobin, decreased haptoglobin	Increased indirect bilirubin fraction, increased CRP and other inflammatory markers	Increased CRP and other inflammatory markers
Hemolysis markers (Coombs test, erythrocyte osmotic resistance, Price-Jones curve)	Negative	Often sharply positive	positive	Negative
Bone marrow	No changes	Compensatory hyperplasia of the red germ with a pronounced erythronormoblastic reaction (leukoerythropoiesis ratio of 1:1 or more, normally 3:1)	Compensatory hyperplasia of the red germ with pronounced erythronormoblastic reaction	Bone marrow infiltration with cellular tumor substrate depending on the type of hemoblastosis

Table 7

Differential diagnosis of normocytic anemia depending on the level of reticulocytes and signs of hemolysis

Reticulocytes The norm is 2–10 reticulocytes out of 1000 red blood cells (2–10 ppm (‰), or 0.2–1%).			
Reticulocytosis			*Norm*
Signs of hemolysis		No hemolysis	No hemolysis
Morphologically altered erythrocytes, childhood	Leukocytosis, accelerated ESR syndrome, adults	Other hemogram parameters are normal	Neutropenia, thrombocytopenia
HHA	AAH	APHA	Hemoblastoses

Differential Diagnosis of Macrocytic Anemias (table 8):

- vitamin B12 or folate deficiency (megaloblastic);
- aplastic anemia, myelodysplasia;
- liver disease, hypothyroidism, alcoholism;
- anemia of pregnancy and neonatal disease;
- with the use of hydroxyurea and antimetabolites.

Table 8

Differential Features of Normocytic Anemias

Signs	Megaloblastic		Non-megaloblastic
	Vitamin B12 deficiency	**folic acid deficiency**	**aplastic anemia, anemia associated with liver disease, hypothyroidism, and alcoholism**
Anam-nesis, reasons	Vegetarianism, poor nutrition, chronic alcoholism, insufficient secretion of Castle's intrinsic factor, impaired absorption in the small intestine, medication intake (methotrexate, sulfasalazine, zidovudine)	Poor nutrition, chronic alcoholism, malabsorption in the small intestine, pregnancy, medication intake: methotrexate and other cytostatics; purine and pyrimidine analogues; anticonvulsants, contraceptives	Taking medications: amidopyrine, methylthiouracil, mercazolyl, sulfonamide drugs, cytostatic drugs, gold preparations, antibiotics (chloramphenicol, streptomycin sulfate), ionizing radiation, chemical substances (benzene, arsenic, heavy metals, infectious agents (hepatitis viruses, infectious mononucleosis and influenza, herpes, cytomegaloviruses, mycobacteria, HIV infection), alcoholism, thyroid pathology, pregnancy
Clinical signs	Anemic syndrome, gastrointestinal tract damage (loss of appetite, belching, feeling of heaviness in the epigastric region, diarrhea, pain, burning sensation in the tongue), damage to the nervous system (paresthesia, impaired sensitivity, pain and feeling of cold in the extremities, tabetic pain, severe muscle weakness, impaired vibration sensitivity, areflexia, ataxia, positive Babinski and Oppenheimer reflexes, spastic paralysis, dysfunction of the pelvic organs.	Anemic syndrome, dyspepsia. Characterized by the absence of nervous system damage and glossitis.	Anemic, hemorrhagic (petechial rashes on the skin, bruises, nose and gum, gastrointestinal bleeding, menorrhagia) syndromes, increased risk of developing infectious complications (stomatitis, pneumonia, otitis, pyelitis, possible development of sepsis), jaundice, edema syndrome.

End of the table 8

Signs	Megaloblastic		Non-megaloblastic
	Vitamin B12 deficiency	**folic acid deficiency**	**aplastic anemia, anemia associated with liver disease, hypothyroidism, and alcoholism**
Hemo-gram	MCV > 110, aniso- and poikilocytosis of erythrocytes, their basophilic puncturation, macrocytosis, megalocytosis, Jolly bodies, Cabot rings, leukopenia and thrombocytopenia, a shift to the right in the leukocyte formula, hypersegmentation of neutrophils, a decreased number of reticulocytes	MCV > 110, macrocytosis, macroovalocytosis, poikilocytosis, anisocytosis of erythrocytes, hypersegmentation of neutrophils, sometimes reticulo-, leuko- and thrombocytopenia (without hemorrhagic syndrome)	MCV < 110, no neutrophil hypersegmentation, pancytopenia (leukopenia, agranulocytosis, reticulocytopenia, thrombocytopenia
Bioche-mical blood test	Hyperbilirubinemia, normal or slightly elevated iron levels	As a rule, without any peculiarities	Syndromes of cytolysis, mesenchymal inflammation, cholestasis, hepatocellular insufficiency
B12 and folate levels	Decreased B12 levels	Decreased folic acid levels	Norm
Bone marrow	Irritation of the red germ, presence of megaloblasts, giant metamyelocytes, band cells, decrease in the number of megakaryocytes	The presence of megaloblasts, giant metamyelocytes, band cells	Aplasia, low cell counts in the puncture, predominance of fatty degeneration

In the fig. 2 you can see a scheme of the algorithm for diagnosing anemic syndrome.

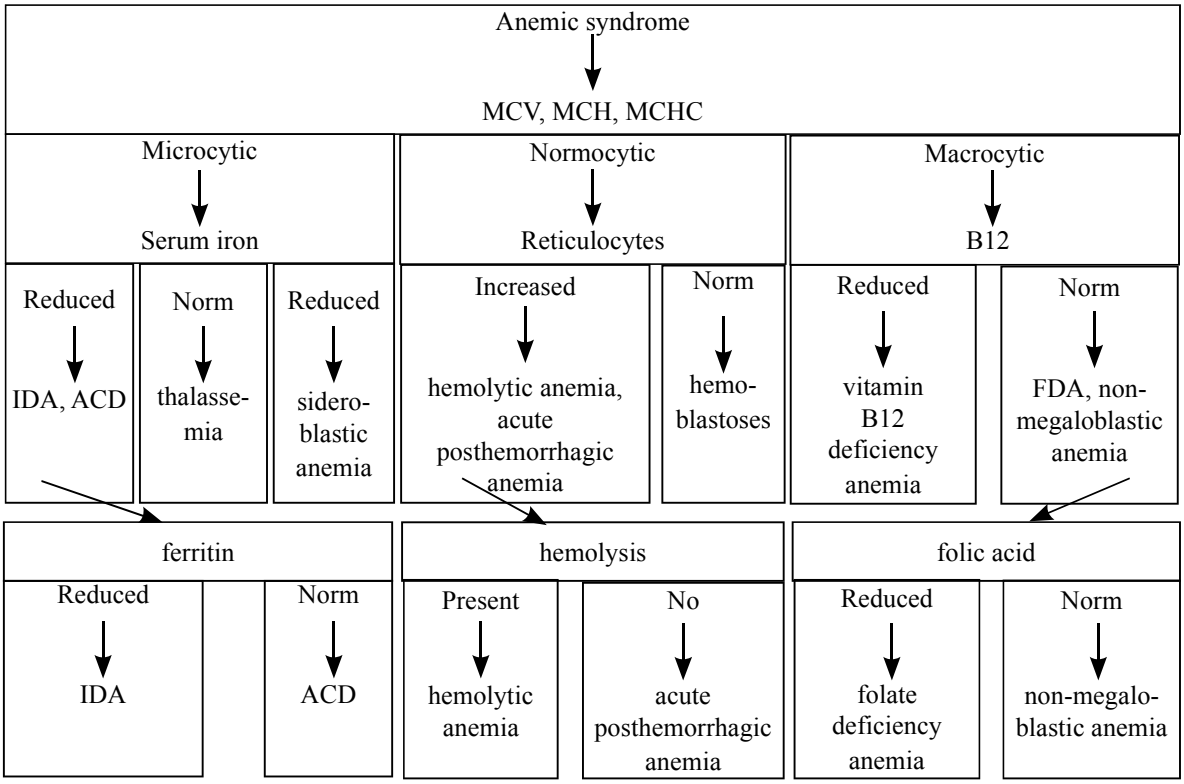

Fig. 2. Algorithm of diagnostic search for anemic syndrome.

TREATMENT OF ANEMIA CAUSED BY IRON, VITAMIN B12, AND FOLIC ACID DEFICIENCY

Treatment of Cholestatic Anemia

Indications for hospitalization of patients with cholestatic anemia (IDA) include: hemoglobin levels below 70 g/L; hemoglobin levels below 80 g/L; and the patient's severe general condition, including hemodynamic compromise.

Diet: It is recommended to consume beef, fish, organ meats, eggs, cereals (oatmeal, buckwheat), beans, peas, grains (wheat, rye, oats, barley), vegetables (apples, peaches, raisins, prunes), parsley, sorrel, various berries, porcini mushrooms, cocoa, chocolate, honey, etc.

Outpatient drug treatment for patients with IDA includes oral iron supplements at a dose of up to 200 mg/day, calculated as elemental iron, for 4–6 weeks until hemoglobin levels are normalized, followed by continued supplementation at a dose of up to 100 mg/day, calculated as elemental iron, for 2–3 months until ferritin levels reach at least 40 μg/L.

In cases of iron absorption disorders and/or conditions in which the use of oral iron supplements is contraindicated or limited (including patients with gastrointestinal diseases and malabsorption syndrome), parenteral (intramuscular or intravenous) iron supplementation is indicated. The optimal dosage regimen

and choice of administration route depend on the form of the iron preparation, the dose of elemental iron in the ampoule (vial), and the patient's hemoglobin level. These are determined individually by the physician based on the indications, the patient's age, the clinical situation, and in accordance with the instructions for medical use (package insert) of the specific iron-containing medicinal product for parenteral use.

Indications for prescribing iron-containing medicinal products for parenteral use may include: ineffectiveness of oral forms of iron; intolerance to oral forms of iron; severe gastrointestinal side effects of oral therapy that cannot be eliminated by other means; the presence of inflammatory diseases of the gastrointestinal tract, which may be aggravated by the use of oral iron-containing preparations; iron deficiency conditions refractory to therapy, including those associated with poor patient compliance with the oral iron-containing preparation regimen; iron absorption disorders in intestinal pathology (peptic ulcer of the stomach and duodenum in the acute phase, enteritis, malabsorption syndrome, small bowel resection, Billroth II gastric resection with exclusion of the duodenum, ulcerative colitis); constant blood loss, in which the need for iron exceeds the physiological ability to absorb iron from oral preparations: uterine bleeding, hereditary hemorrhagic hemostasis, telangiectasia.

The main groups of iron-containing preparations are ionic and non-ionic. Ionic preparations include ferrous iron (II) salts (sulfate, fumarate, gluconate, succinate, glutamate, lactate, chelate, and others) and ferric iron (III) salts. Non-ionic iron preparations (based on organic iron compounds) include iron protein succinylate and iron polymaltose. The average daily dose of iron-containing preparations is no more than 200 mg, calculated as elemental iron. The criteria for the effectiveness of treatment for patients with IDA are: normalization of blood parameters: hemoglobin >120 g/L in women, >130 g/L in men, >110 g/L in pregnant women; normalization of blood ferritin levels to at least 30 μg/L.

Treatment of the underlying condition causing iron deficiency is also necessary. Prophylactic administration of iron-containing drugs is indicated for patients with a risk of developing their deficiency, including: pregnant and lactating women; women with an interval between pregnancies of less than 2 years; with hereditary hemorrhagic hemostasiopathies with ongoing or recurrent bleeding; with chronic kidney disease with established iron deficiency; with a blood ferritin content of less than 40 μg / l (tissue iron deficiency); women with a menstrual period lasting more than 5 days. 20. Therapeutic prophylaxis of IDA in an effective therapeutic dosage of an oral iron-containing drug is carried out according to one of the options: 80–100 mg / day for 3 months once a year; 80–100 mg / day for 6 weeks 2 times a year, one of the courses in spring; 80–100 mg 1 time per week for 1 year.

Treatment of Vitamin B12 Deficiency Anemia

Medical indications for hospitalization of patients with vitamin B12 deficiency anemia include: hemoglobin level below 70 g/L; thrombocytopenia less than 30×10^9/L and/or the presence of hemorrhagic syndrome; hemoglobin level below 80 g/L and the patient's severe general condition, including hemodynamic compromise.

The diet is similar to that for iron deficiency anemia. Alcohol consumption is strictly prohibited.

Treatment methods for patients with vitamin B12 deficiency anemia in outpatient and/or day hospital settings include: cyanocobalamin 500 mcg/day for 30 days until hemoglobin and/or vitamin B12 levels are normalized, after which the patient is transferred to maintenance therapy; Parenteral administration of cyanocobalamin intramuscularly or intravenously at 500–1000 mcg once a week for 2 months, and then twice a month for 2 months (maintenance therapy); Parenteral administration of cyanocobalamin intramuscularly or intravenously at 500 mcg once a month for 2–3 years, and if necessary, lifelong (for patients with gastrectomy, with removal of large sections of the small intestine, and elderly patients with atrophic gastritis); Enteral administration of vitamin B12 preparations: an initial dose of 1–2 tablets of 1000 mcg twice a day daily for 4 weeks, followed by maintenance therapy of 1 tablet of 1000 mcg once a day for 2 weeks.

If the cause of vitamin B12 deficiency cannot be eliminated, treatment is prescribed for life.

The criteria for effective treatment are: subjective improvement in the first days of treatment; reticulocytosis, most pronounced (up to 20%) on the 5th–7th day of treatment; an increase in hemoglobin and the number of red blood cells, starting from the 2nd week of treatment; normalization of the number of red blood cells, the number of white blood cells and platelets after 3–4 weeks of treatment; normalization of the level of vitamin B12 (the normal range of serum vitamin B12 may decrease during pregnancy to 99 pg/ml).

Ineffective treatment indicates an incorrect diagnosis.

Measures to prevent vitamin B12 deficiency include: deworming; surgical intervention to correct anatomical defects (including blind pockets, diverticulosis); discontinuation of drugs that impair the absorption of vitamin B12. Prophylactic administration of vitamin B12 is indicated for patients at risk of developing its deficiency, namely: elderly age; with gastric resection; with atrophic gastritis; With autoimmune gastritis; After resection of large sections of the small intestine (more than 60 cm); After cholecystectomy; In strict vegetarians; In those taking H2 receptor blockers, proton pump inhibitors, or metformin for a long time (at least 12 months) (more than 4 months).

Preventive treatment includes long-term (lifelong) vitamin B12 supplementation at a dose of 500 mcg once a month.

Treatment of Folate Deficiency Anemia

The medical indications for hospitalization of patients with folate deficiency anemia and nutritional recommendations are the same as for patients with B12 deficiency anemia.

Outpatient treatment options for patients with folate deficiency anemia (FDA) include folic acid at a dosage of 6–15 mg/day for 4–6 weeks until blood counts return to normal. Folic acid is administered orally until blood counts return to normal, after which the patient is transferred to maintenance therapy: 5–10 mg of folic acid orally once a week for 2 months, then twice a month for 2 months.

The criteria for treatment success are the same as for patients with B12 deficiency anemia, plus normalization of folate levels.

MEDICAL MONITORING AND MEDICAL AND SOCIAL EXAMINATION FOR ANEMIA CAUSED BY IRON, VITAMIN B12, AND FOLIC ACID DEFICIENCY

Medical Monitoring and Medical-social Examination for Cholestatic Anemia

A complete blood count (CBC) for patients with IDA is performed by a general practitioner (GP) or a specialist at the patient's place of residence once a month for three months after normal hemoglobin levels are achieved following diagnosis and treatment. Beginning in the fourth month, a complete blood count (CBC) is performed on an outpatient basis by a GP or a specialist monitoring the patient for the underlying condition (gastroenterologist, oncologist, surgeon, obstetrician-gynecologist, urologist, nephrologist, or other specialist) once every six months. Patients at risk of developing iron deficiency are recommended to have their complete blood count and ferritin levels monitored annually.

The duration of temporary disability depends on the severity of IDA. Patients with mild IDA are generally able to work, but with severe clinical symptoms, the following average periods of temporary disability are possible: 10–12 days for mild anemia, 14–15 days for moderate anemia, and 30–35 days for severe anemia. Patients with severe IDA, due to an unfavorable course of the disease (frequent exacerbations — 5–6 times per year), the ineffectiveness of specific therapy, and the presence of severe cardiovascular and nervous system dysfunction, may be referred for medical and social assessment.

Medical Monitoring and Medical and Social Examination for Vitamin B12 Deficiency Anemia

Medical monitoring of patients with vitamin B12 deficiency anemia is carried out considering the underlying causes of vitamin B12 deficiency. CBC values are monitored by a GP or a specialist at the patient's place of residence once a month for three months after the patient's hemoglobin levels have returned to normal after diagnosis and treatment. Subsequently, CBC values are monitored every six months by the GP or specialist monitoring the patient's underlying condition (gastroenterologist, oncologist, surgeon, neurologist, or other specialist).

Serum vitamin B12 levels should be monitored annually in patients at risk of deficiency. Disability in patients with vitamin B12 deficiency anemia is also influenced by the severity of the disease and the degree of functional impairment, primarily affecting the nervous system. Patients with a mild course of the disease, not accompanied by prolonged and frequent relapses, and with initial clinical and hematological manifestations are able to work.

The ability to work of patients with moderate anemia is determined by the severity of vestibulocerebellar, autonomic-vascular, and polyneuritic pain syndromes, mild to moderate motor impairment of the lower extremities (paresis), and stage I–II heart failure. The average period of temporary disability for moderate anemia is 30–40 days, with employment options determined by a medical commission.

In severe B12-deficiency anemia, the expected period of temporary disability may be 45–60 days, with possible referral to a medical and social assessment (disability groups III–II).

Medical Monitoring and Medical and Social Examination within the Folate Deficiency Anemia

Medical monitoring of patients with folic acid deficiency (FAD) is also conducted considering the causes of folic acid deficiency (underlying illness, dietary factors). CBC values are monitored by a general practitioner, internist, or other specialist in the patient's community once a month for three months after normal hemoglobin levels are achieved following diagnosis and treatment. Subsequently, CBC values are monitored by the general practitioner or specialist monitoring the patient with the condition that caused the FAD (gastroenterologist, oncologist, surgeon, neurologist, or other specialist) every six months for five years.

Serum folate levels are monitored annually in patients at risk for deficiency and in elderly patients. If the cause of folic acid deficiency cannot be corrected, lifelong medical monitoring is required.

Patients with FAD are generally able to work, but limitations may arise due to exacerbation of the underlying disease.

SELF-ASSESSMENT OF TOPIC ACQUISITION

Cases

Case No. 1

Patient P., 60, consulted a primary care physician complaining of increasing weakness, lethargy, dizziness, palpitations (not only when walking but also at rest), numbness and tingling in her fingers, and shortness of breath with minimal physical activity over the past several months. She considered herself ill for the past six months, when she first began noticing increasing fatigue disproportionate to physical activity. Subsequently, she noted difficulty inserting a needle due to discomfort in her fingertips. About 15 years ago, she underwent gastrectomy with vagotomy for frequent exacerbations of a duodenal ulcer with prolonged bleeding. She felt well for the first few years after the surgery. Clinical examination revealed an increase in hemoglobin levels to normal (preoperatively, her hemoglobin levels were consistently below normal). On examination, the patient's condition is satisfactory. Build is normosthenic, nutrition is normal. Height is 165 cm, weight is 62 kg. The skin is pale, with a slight icteric tint and areas of vitiligo-like hypopigmentation. There is no icterus of the sclera and soft palate. The tongue is not coated, the papillae are smoothed out. Peripheral lymph nodes are not palpable. Breathing is vesicular, there are no wheezing. Respiratory rate is 18 beats per minute. Heart sounds are muffled, a slight systolic murmur is heard at the apex, which increases in the upright position and with minor physical activity. The rhythm is regular. Heart rate is 96 beats per minute. Blood pressure is 115/70 mmHg. The abdomen is slightly distended, soft, painless on palpation. The liver does not protrude from under the costal margin. Liver dimensions according to Kurlov are 9 × 8 × 7 cm. The spleen is not palpable. Stool is normal. Percussion is negative on both sides. Urine flow is normal. There is no peripheral edema. Superficial sensitivity on the palmar surface of the fingers is decreased. Muscle strength is normal. There is no paresis. Finger tremor. Unsteadiness when walking.

A complete blood count (CBC) was performed: Hb — 88 g/L; erythrocytes — 2.4×10^{12}/L; leukocytes — 6.8×10^{9}/L, white blood cell count is normal; ESR — 28 mm/h.

Questions:

1. Presumptive diagnosis.
2. Examination plan.
3. Treatment plan.
4. Treatment measures.

Case No. 2

Patient N., 52, was admitted to the neurology department of a city hospital by ambulance on a stretcher. According to the patient, he had been unable to

walk or even get out of bed for the past few days due to severe weakness and «uncontrollability of his legs». His medical history revealed that approximately six months earlier, after the death of his wife, he went to stay with relatives in the village, where he drank at least half a liter of vodka daily, which helped him avoid dwelling on the «misfortune that had befallen him». About a month before hospitalization, he noted hand tremors, moderate pain in his arms and legs, including decreased pain sensitivity, leading to frequent burns and cuts, as well as coldness and numbness in his arms and legs. He then developed strange sensations while walking: according to the patient, it felt like he was walking «on cotton wool». His relatives brought him to the city and called an ambulance, which took him to the hospital with a presumptive diagnosis of «paraparesis of unknown origin». The patient, a 48-year-old retired test pilot, reported previously drinking alcohol «in moderation». He has no chronic internal diseases and has undergone annual medical examinations. He is a nonsmoker.

On examination, the patient's condition is moderate. He is of normosthenic build and well-nourished. His height is 175 cm and his weight is 92 kg. His face is puffy. The skin is pale, with a distinct lemon-yellow tint, with areas of hyperpigmentation. The visible mucous membranes are pale. The tongue is crimson, and the papillae are smoothed out. Peripheral lymph nodes are not palpable. Breath sounds are weakened, vesicular, and there are no wheezing. Percussion sounds are clear and ringing over the entire surface of the lungs. Respiratory rate is 16 beats/min. Heart sounds are muffled, in the left lateral position, a distinct systolic murmur is heard at the apex of the heart without conduction. The rhythm is regular. Heart rate is 112 beats per minute. Blood pressure is 140/85 mmHg. The abdomen is enlarged due to excess subcutaneous fat deposition, soft, painless on palpation. The indurated edge of the liver protrudes from under the costal arch by 3 cm. Liver dimensions according to Kurlov are 11 × 9 × 9 cm. The edge of the spleen is palpable. The patient has been bothered by constipation for the past week. Percussion symptom is negative on both sides. Urine flow is normal. Swelling of the calves. In the neurological status: muscular hypotonia of the upper and lower extremities, decreased tendon reflexes, pathological Babinski and Oppenheim reflexes. Superficial and deep sensation in the distal upper and lower extremities is decreased. Moderate hearing loss, a sharp decrease in smell, and taste disturbance are noted. The patient is markedly lethargic and taciturn. He responds slowly to questions, speaks in monosyllables, but is oriented to time and place.

Biological analysis: hemoglobin — 60 g/L, erythrocytes — 1.6×10^{12}/L, macrocytosis, leukocytes — 6.8×10^{9}/L, band cells — 4 %, segmented cells — 72 %, lymphocytes — 18 %, monocytes — 3 %, eosinophils — 3 %, platelets — 235×10^{3}/L, ESR — 52 mm/h. Blood biochemistry: glucose — 6.2 mmol/L, cholesterol — 5.5 mmol/L, creatinine — 0.086 mmol/L, total protein — 58 g/L, ALT — 84 IU/L, AST — 62 IU/L, GGT — 140 IU/L.

Questions:

1. Prospective diagnosis.
2. Examination plan.
3. Treatment strategy.
4. Treatment measures.

Case No. 3

Patient S., 43, complains of weakness, fatigue, dizziness, tinnitus, increased heart rate at rest and during physical exertion, brittle nails and hair, and taste disturbances.

Three years ago, she was diagnosed with uterine fibroids accompanied by profuse menorrhagia.

Objectively: She is in satisfactory condition. She has a normosthenic build, dry skin, decreased turgor, pale skin and conjunctiva, and wheezing at the corners of the mouth. Her breathing is vesicular, without wheezing, and her respiratory rate is 19 beats/min. The rhythm is regular, with muffled tones. Auscultation reveals a soft systolic murmur over all points. Heart rate is 84 beats/min, and blood pressure is 110/70 mmHg. The abdomen is soft and painless. The liver is at the costal margin, not enlarged, and painless. The spleen is not enlarged. The stool is formed, without pathological impurities, once a day. Diuresis is maintained, urination is not impaired. Peripheral lymph nodes are not enlarged, there is no edema.

Complete blood count: leukocytes — 5.2×10^9/L, erythrocytes — 4.8×10^{12}/L, Hb — 10^5 g/L, color index (CL) — 0.65, MCH — 25 pg, MCV — 75, RDV — 15.5, reticulocytes — 2 %; platelets — 210×10^9/L, ESR — 28 mm/h. Urinalysis: unremarkable.

Questions:

1. Presumptive Diagnosis.
2. Examination Plan.
3. Treatment Tactics.
4. Therapeutic Measures.

Case No. 4

A 42-year-old patient works in a factory and complains of frequent loose stools, sometimes mixed with blood, pus, and mucus. He had been ill for about five years when constipation and abdominal pain developed. Subsequently, his stools became more frequent, up to 2-4 times a day, semi-formed, sometimes with a small amount of blood, and the pain intensified. He did not seek medical attention. He noted a real deterioration in his condition about six months ago, when his stools became more frequent, up to 6-8 times a day. In addition to blood, mucus and pus began to appear in his stool. He also complains of general weakness and a low-grade fever in the evenings. He has lost 5 kg over the past year.

Objectively: his condition is moderate. Axillary temperature is 36.8 °C. The skin is pale and dry. Visible mucous membranes are normal. Breathing in the lungs is vesicular, without wheezing. Respiratory rate is 20 beats per minute. Heart sounds are rhythmic and clear. Heart rate is 90 beats per minute. Blood pressure is 110/70 mmHg. The abdomen is enlarged, soft on palpation, and painful along the colon. Urination is normal. Stool is loose, 6-8 times per day, mixed with blood and mucus. Complete blood count: Hb — 98 g/L, WBC — 10.5, band form — 6 %, segmental leukocyte — 78 %, eosinophilic leucocyte — 1 %, MON — 1 %, LYM — 14 %, platelets — 190. ESR — 35 mm/h. Urinalysis: unremarkable.

Questions:

1. Proposed diagnosis.
2. Examination plan.
3. Treatment plan.
4. Treatment measures.

Tests

1. List the main hematological indicators of iron deficiency anemia according to their sensitivity and specificity (diagnostic significance): 1) low color index, 2) decreased mean corpuscular hemoglobin (MCH), 3) increased serum iron levels, 4) decreased serum iron levels, 5) decreased reticulocyte count, 6) decreased serum ferritin levels:

a) 1, 3, 4, 5;
b) 6, 2, 4, 1;
c) 3, 4, 2, 1;
d) 2, 6, 5, 3.

2. Anemia is:

a) a symptom of a number of diseases;
b) a group of symptoms with a common pathogenesis;
c) a group of diseases;
d) a clinical hematological syndrome.

3. Macrocytosis is observed in:

a) alcoholism;
b) B12-deficiency anemia;
c) liver cirrhosis;
d) iron malabsorption;
e) some hemolytic anemias.

4. Microcytosis is observed in:

a) folic acid deficiency anemia;
b) B12-deficiency anemia;
c) anemia of chronic disease;
d) iron malabsorption;
e) some hemolytic anemias.

5. List the main hematological indicators of B12-deficiency anemia according to their sensitivity and specificity (diagnostic significance): 1) increased color index, 2) increased vitamin B12 content in the blood, 3) macrocytosis (increased mean corpuscular volume) and megalocytosis, 4) increased hemoglobin content in a single erythrocyte (MCH), 5) increased reticulocyte content, 6) the presence of nuclear debris in erythrocytes:

a) 2, 3, 4, 1;
b) 6, 2, 4, 1;
c) 3, 4, 2, 1;
d) 2, 6, 5, 3.

Correct answers for cases

Case No. 1

1. Preliminary diagnosis: anemic syndrome, likely moderate B12-deficiency anemia.

2. Additional examination: complete blood count, urinalysis, blood biochemistry, fecal occult blood test, determination of vitamin B12 and folic acid levels, EGDS, ECG.

3. Hospitalization is not required.

4. After diagnosis verification, prescribe cyanocobalamin 500 mcg/day for 30 days until hemoglobin and/or vitamin B12 levels are normalized, then transfer the patient to maintenance therapy. Parenteral administration of cyanocobalamin intramuscularly or intravenously at 500-1000 mcg once a week for 2 months, then twice a month for 2 months (maintenance therapy).

Case No. 2

1. Preliminary diagnosis: anemic syndrome, likely severe B12 deficiency anemia.

2. Hospitalization.

3. Additional examination: complete blood count, urinalysis, blood chemistry panel, fecal occult blood immunoassay, vitamin B12 and folic acid levels, EGDS, ECG, neurological examination, abdominal ultrasound.

4. After diagnosis verification, prescribe cyanocobalamin 500 mcg/day for 30 days until hemoglobin and/or vitamin B12 levels are normalized, then switch to maintenance therapy. Parenteral administration of cyanocobalamin intramuscularly or intravenously at 500–1000 mcg once a week for 2 months, then twice a month for 2 months (maintenance therapy).

Case No. 3

1. Preliminary diagnosis: anemic syndrome, likely mild iron deficiency anemia.

2. Additional examination: complete blood count, biochemical blood test, fecal occult blood immunoassay, EGDS, ECG, gynecological examination.

3. Hospitalization not required.

4. Diet: beef, fish, organ meats, eggs, cereals (oatmeal, buckwheat), beans, peas, grains (wheat, rye, oats, barley), vegetables (apples, peaches, raisins, prunes), parsley, sorrel, various berries, porcini mushrooms, cocoa, chocolate, honey, etc. are recommended. Outpatient drug treatment options for patients with IDA include: oral iron supplementation at a dose of up to 200 mg/day, calculated as elemental iron, for 4–6 weeks until hemoglobin levels are normalized, followed by continued administration at a dose of up to 100 mg/day, calculated as elemental iron, for 2–3 months until ferritin levels reach at least 40 μg/L.

Case No. 4

1. Preliminary diagnosis: anemic syndrome, likely anemia of chronic disease due to ulcerative colitis.

2. Additional testing: complete blood count, blood chemistry, stool occult blood and calprotectin testing, EGDS, colonoscopy, ECG.

3. After additional testing, decide on hospitalization.

4. Basic therapy for ulcerative colitis.

Correct answers for tests: 1 — b; **2** — d; **3** — a, b, c, d; **4** — c, d, e; **5** — a.

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ДИФФЕРЕНЦИАЛЬНАЯ ДИАГНОСТИКА АНЕМИЧЕСКОГО СИНДРОМА. АМБУЛАТОРНЫЕ АСПЕКТЫ ДИАГНОСТИКИ И ЛЕЧЕНИЯ АНЕМИЙ, ОБУСЛОВЛЕННЫХ ДЕФИЦИТОМ ЖЕЛЕЗА, ВИТАМИНОВ B12 И ФОЛИЕВОЙ КИСЛОТЫ

DIFFERENTIAL DIAGNOSIS OF ANEMIC SYNDROME. OUTPATIENT ASPECTS OF DIAGNOSIS AND TREATMENT OF ANEMIAS CAUSED BY IRON, VITAMIN B12, AND FOLIC ACID DEFICIENCY

Учебно-методическое пособие

На английском языке

Ответственная за выпуск Е. В. Рылатко
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Компьютерная вёрстка А. В. Янушкевич

Подписано в печать 01.04.26. Формат 60×84/16. Бумага писчая «Снегурочка».
Ризография. Гарнитура «Times».
Усл. печ. л. 1,86. Уч.-изд. л. 1,55. Тираж 90 экз. Заказ 170.
Издатель и полиграфическое исполнение: учреждение образования
«Белорусский государственный медицинский университет».
Свидетельство о государственной регистрации издателя, изготовителя,
распространителя печатных изданий № 1/187 от 24.11.2023.
Ул. Ленинградская, 6, 220006, Минск.