Ministry of Health of Ukraine
Zaporizhzhya State Medical University

Syvolap V.D., Nazarenko O.V.

DIAGNOSTICS AND TREATMENT OF ANEMIA IN THE ELDERLY

Training manual

Zaporizhzhya 2019

УДК 616.155.194-07-08-053.9 (075.8)
ББК 54.101/.102
С 95

Training manual is recommended for by Central Methodical Council of Zaporizhzhya State Medical University (protocol № 10 , from 23 May 2019)

Reviewers:

S.Y. Docenko, MD, PhD, Head of Department of Internal Diseases-3 of Zaporizhzhya State Medical University.

V.V. Syvolap, MD, PhD, Head of Department of Propedeutics of Internal Diseases with the Course of Patients' Care of Zaporizhzhya State Medical University

Authors:
Syvolap V.D. -Head of Department of Internal Diseases-1, MD, PhD
Nazarenko O.V. –Assistant of Department of Internal Diseases-1, PhD

С 95 Syvolap V.D. Diagnostics and treatment of anemia in the elderly/ V.D. Syvolap, O.V.Nazarenko– Zaporizhzhya: ZSMU, 2019. – 87 P.

The training manual contains materials on the method of educational organization in accordance with the requirements of the program of the discipline "Internal Medicine", the Content module "Diagnostics and treatment of diseases in the elderly." The clinical materials presented in the manual for practical exercises and independent work of students meet the modern requirements of national and international guidelines for patients with anemia. The training manual will help to improveacquiring of theoretical knowledge and practical skills by students duringstudying of anemia and curation of elderly patients.

УДК 616.155.194-07-08-053.9 (075.8)

Abbreviations

MCV	Mean volume of erythrocytes
AChD	Anemia of chronic diseases
WHO	World Health Organization
IDA	Iron deficiency anemia
IHD	Ischemic heart disease
EGDS	Esophagogastroduodenoscopy
MDS	Myelodysplastic syndrome
NSAIDs	Nonsteroidal anti-inflammatory drugs
CKD	Chronic kidney disease
CRF	Chronic renal failure
CHF	Congestive heart failure

CONTENT

INTRODUCTION

The feasibility of preparing a training publication is due to the need to make changes to the organization of the educational process in accordance with the requirements of the new program of the discipline "Internal Medicine" approved by the Ministry of Health of Ukraine. The main component of these changes in the program is addition of Content module 5 (Etiology, pathogenesis and clinical manifestations of internal diseases in the elderly). The program of the discipline provides for increasing the requirements for students to master theoretical knowledge, acquire the skills of physical examination of elderly patients, interpret the results of laboratory and instrumental studies, master the methods of differential diagnostics and substantiate the diagnosis, prevention and treatment of patients with hematological diseases, especially anemia, the acquisition of knowledge on medical ethics and deontology in curating elderly patients.

ACTUALITY

According to numerous studies in the world, about 40% people suffer from anemia, and its frequency depends on age, sex, comorbidities, etc. A variety of causes provoking the development of anemic syndrome in the elderly, comorbid conditions and diseases significantly impede early diagnosis of anemia. The prevalence of anemia begins to increase significantly in people over 50, reaching 11.0% in men and 10.2% in women under the age of 65, and after 85 years the frequency rises to 20% (Guralnik JM, 2004).

Anemia is more common in women, than in older men. Concomitant chronic kidney disease, inflammatory processes, cancer significantly increase risk of anemia. Timely detection and treatment of anemia in almost 80% of cases leads to the successful correction of the violations. The significant prevalence, duration, and economic costs indicate the great medical and social significance of anemia in the elderly and its relevance and need for a deep study of the problem of anemia in these patients.

Educational purposes:

- timely diagnosis of anemia in elderly patients;
- identification of the main etiological factor of anemia in elderly patients;
- selection of research methods and interpretation of their results in the diagnosis of anemic syndrome in elderly patients;
- rational pharmacotherapy of anemic syndrome taking into account features of the action of antianemic drugs in the elderly;
- • improving the quality of life of older people with anemic syndrome.

A list of basic terms and characteristics that student must study

Student must know:

• features of metabolism in the elderly;

• features of the clinical course of anemia in the elderly;

• etiology and pathogenesis of various clinical forms of anemia (iron deficiency, B12-deficient, folate deficiency, hemolytic, hypoplastic, posthemorrhagic, anemia of chronic disease)

• modern classification of anemia;

• research methods used to diagnose anemia, taking into account their sensitivity and informativeness;

• features of pharmacokinetics of drugs in the elderly and senile age.

Student must acquire the skills:

- To reveal the main clinical symptoms of anemia in elderly patients, taking into account comorbid pathology;
- To draw up a survey plan for elderly patients with anemia;
- To interpret the results of laboratory and instrumental studies;
- to conduct differential diagnostics of diseases involving anemia syndrome in patients of elderly and senile age;
- to evaluate indications and prescribe treatment of anemia, taking into account the peculiarities of pharmacotherapy in the elderly.

TOPIC CONTENT

Anemia in the elderly

An integral indicator of the effective development of medical care for the population of the planet is a progressive increase in life expectancy, which currently averages 64 years in the world with variations from 56 (in certain countries of Africa and Asia) to 80 years (in Japan). If this figure in the middle of the twentieth century was less than 50 years, then by 2025, according to the scientific and statistical forecast, it will increase to 73 years. One of the main tasks of WHO is to preserve the health and improve the quality of life in the elderly (over 60 years) and study the most common diseases with the aim of timely treatment and prevention.

Aging is the subject of rigorous scientific research aimed at expanding knowledge about the molecular and cellular basis of life and disease. The common signs of the aging process are established — genome instability, epigenetic alterations, impaired proteostasis and nutrient recognition, mitochondrial dysfunction, cell aging, depletion of the stem cell pool, and changes in the intercellular interaction (J.A. Knight, 2005).

Reducing the regenerative potential of tissues is one of the most obvious characteristics of aging. With age, hemopoiesis decreases, which leads to a decrease in the production of adaptive immune cells - immune aging, is associated with a high risk of developing anemia and myeloid malignancies (Shaw et al., 2010). Studies conducted on old mice revealed a decrease in the activity of the cell cycle of hematopoietic stem cells — older cells had fewer cell divisions than the younger ones (Rossi et al., 2007). Reduced mitosis correlated with the accumulation of DNA damage and with overexpression of cell cycle inhibitor proteins, such as p16INK4a (Janzen et al., 2006).

The incidence in the elderly and senile age is characterized by polymorbidity, the accumulation of diseases of internal organs, among which anemia occupies a prominent place.

Special attention of specialists is caused by the peculiarity of anemic syndrome in elderly patients, which, by its clinical manifestations, effects on comorbidities and treatment approaches, is fundamentally different from well-studied and clearly classified anemias in young and mature patients.

Most often, anemia in the elderly is not an independent nosological form, but a consequence of chronic inflammatory, neoplastic, endocrine diseases, that is, anemia of a chronic disease. The prevalence of anemia in the elderly and senile age varies from 2.9 to 61% in men and from 3.3 to 41% in women, while in young and mature age it is more common in women (R. Carmel, 2001). In hospitalized elderly patients, its frequency reaches 36–80% (in outpatient patients, 5–14%). With age, this indicator significantly increases from 25% in 65-74-year-olds to 43% - in old age (P. Duggan., 2003). However, anemia is not the prerogative of the elderly, it is a consequence of the accumulation of diseases that contribute to its development. Moreover, the efficiency and quality of blood formation (including erythropoiesis) in the elderly do not deteriorate, the possibility of reparation and effective regulation remains when the pathological influence of associated diseases is turned off (M. Dugas, 2004).

In most cases (75%), anemia in the elderly is first detected during hospitalization for various somatic diseases, and the anemic syndrome itself is the cause of hospitalization much less frequently (9%).

Anemic syndrome in the elderly is most often a manifestation of various diseases of the internal organs, especially oncological diseases typical of old age, and intestinal diverticulosis (A. Marengoni et al, 2011). Infectious-inflammatory processes, erosive and ulcerative lesions of the gastrointestinal tract do not have strict age characteristics, but in patients of elderly and old age there is an increased risk of complications leading to the development of anemia.

Table 1. Etiological factors of the development of in the elderly (according to population studies)

Etiologyof anemia	**Prevalence**	
	Joosten and coauthors*	**Ania and coauthors ****
Chronic diseases	35	17
Unknown reasons	17	36
Iron deficiency	15	15
Post-hemorrhagic	7	7
Renal failure, endocrine diseases and liver disease	6,5	8
Myelodysplasia or acute leukemia	5,5	-
Chronic leukemia or	5,5	-

lymphoma		
Vitamin B12 or folate deficiency	5,5	-
Other blood disorders	3	17

References: * - discharged from the hospital, ** - the population of Olmsted County, USA.

On the one hand the symptoms of anemia is determined by non-specific clinical manifestations of the anemic condition (shortness of breath, dizziness, etc.), and on the other hand the clinical course of anemia depends on the disease that caused it (NA Andreichev, 2014).

The development of anemia in elderly patients is accompanied by a significant deterioration in the quality of life (decreased mental and physical activity, rapid fatigue, depressed mood), aggravates the course of the existing pathology and poses a threat of premature death. Thus, 63 patients aged 70 to 90 years were observed and the 5-year survival rate in the group of patients without anemia was 67%, and in the group with a low level of Hb - 48% (L.I. Dvoretsky, 2011).

The risk of death was 1.5 times higher in the group with Hb level <120 g/l in1002 disabled women over 65, than in Hb level 130 g/l. In 2280 patients with chronic heart failure (G. Fonarow et al., 2002) anemia was observed in 48% of them; the mortality ratio in this group and in patients without anemia was 4:1, with 1% decrease in hematocrit accompanied by an increase in the risk of death by 2%.

The development of anemia in the elderly is associated with impaired cognitive functions - a decrease in intelligence, memory, and concentration. Greek scientists report decrease of cognitive function (S. Argyniadon et al., 2001) in 55.6% older men with anemia and in 34.4% without it, in older women the corresponding figure was 47.5 and 40.1 %

Population surveys in elderly and senile patients (V. Drozdov, 2014) demonstrated the dependence of the prognosis of the disease on hemoglobin level. A connection has been established between tachycardia, increased cardiac output, low vascular resistance, and low hemoglobin levels (less than 70-80 g/l). In addition, control studies did not reveal an improvement in the state of patients with iron deficiency anemia as a result of treatment if the level of hemoglobin in the blood before the start of iron supplementation was above 80 g/l.

Anemia in the elderly has certain features; its knowledge is very important for timely diagnosis and adequate treatment:

• Often anemia is the result of the combined effects of many factors (iron deficiency, vitamin B12, folic acid, etc.).

• Non-specific manifestations of anemia in the elderly may be masked by the symptoms of the underlying disease, which can lead to medical errors in the management of such patients. For example, it`s dyspnea in patients with heart failure and respiratory failure, dizziness in patients with vascular brain pathology etc. Renal failure is important etiological factor for anemia in patients of any age. Despite the fact that the kidney function stably decreases with age, these changes are usually not accompanied by the development of significant anemic syndrome in patients without kidney pathology.

• The presence of anemic syndrome is associated with clinical manifestations of cardiovascular diseases (angina pectoris, heart failure) and central nervous systems (encephalopathy), which are most common in the elderly.

• The etiology of anemia in the elderly is associated with the presence of chronic inflammatory processes (infectious and non-infectious), malignant tumors, nutritional deficiency more often than in young people.

• The development of anemia is more likely to result in impaired quality of life than in young and middle age, when patients are not burdened with multiple comorbidities.

• Treatment of anemia in elderly patients requires a comprehensive approach, including the treatment of the underlying disease, pathogenetic and symptomatic treatment.

The mechanisms of development and the causes of anemia are very diverse, so in each case, the doctor should be focused on identifying the disease underlying this hematological syndrome.

When doctor conducts differential diagnosis in patients with anemia, it is rational to search for the causes of the anemic syndrome in accordance with the various pathogenetic variants of this disease.

The WHO defines anemia as hemoglobin below 13 g/dL in men over 15 years, below 12 g/dL in non-pregnant women over 15 years, and below 11 g/dL in pregnant women.

Classification of anemia

There are two main classifications of anemia:

- the pathogenetic and etiological classification, based on the cause of the anemia;
- the morphological classification based on the characteristics of the red cell

These two classifications are complimentary to each other, as the clinical investigation of a patient with anemia involves two distinct steps:

- determination of the morphological type of anemia;
- determination of the cause of the anemia.

Classification of anemia by etiology and pathogenesis (L. Idelson, 1979)

I. Anemia caused by blood loss.

1. Acute post-hemorrhagic anemia.

2. Chronic post-hemorrhagic anemia.

II. Anemia due to impaired blood formation.

1. Anemias due to impaired hemoglobin formation

a) anemia due to iron deficiency

b) anemia due to iron redistribution (with infection and inflammation)

c) anemia caused by impaired synthesis or utilization of porphyrins;

d) anemia due to impaired synthesis of heme and globin.

2. Anemia caused by impaired synthesis of DNA or RNA (megaloblastic anemia).

3. Anemia caused by the violation of the process of separation of red blood cells

4. Anemia caused by inhibition of bone marrow cell proliferation.

5. Anemia due to replacement of the hematopoietic bone marrow by the cancer.

6. Anemia caused by impaired production of erythropoietin or the appearance of inhibitors to it:

a) anemia due to reduced oxygen need (hypothyroidism and other endocrine pathology, fasting)

b) anemia due to increased erythropoietin destruction (red cells aplasia).

III. Anemia associated with increased destruction of red blood cells.

1. Hereditary hemolytic anemia:

a) caused by a violation of the structure of the membrane of erythrocytes;

b) caused by a violation of the activity of erythrocyte enzymes;

c) caused by a violation of the structure or synthesis of hemoglobin (thalassemia, sickle cell anemia).

2. Acquired hemolytic anemia:

a) caused by the action of antibodies (immune)

b) caused by changes in the structure of the erythrocyte membrane due to somatic mutation (disease Marchiafawa-Mikkeli)

c) due to mechanical damage to the erythrocyte membrane (marching hemoglobinuria, in patients with prosthetic heart valves, hemangiomas, DIC, etc.);

d) due to chemical damage of red blood cells

e) due to deficiency of vitamins (B12, folate)

e) caused by the destruction of red blood cells by parasites (malaria, toxoplasmosis).

Morphological Classification.

An alternative classification of anemia is based on the morphology of the red cells, usually their size and staining characteristics.

Red cell indices

MCV (mean corpuscular volume)

The average volume of RBC (fl) =Hct × 10/ RBC count (m/μL) **NR= 80-96 fl.**

MCH (mean corpuscular hemoglobin)

The average content of Hb in average RBC. It is directly proportional to the amount of Hb and RBC size.

MCH =Hb/RBC count (m/μL)*10 (pg). **Normal range= 27-32 pg**.

MCHC (mean corpuscular hemoglobin concentration)

Express the average concentration of hemoglobin per unit volume of RBC. It defined as the ratio of the weight of hemoglobin to volume of RBC.

MCHC=Hb (g/dl)/Hct (%)× 100 (%). **NR= 32-36%.**

Red cells may be normal in size (normocytic), large (macrocytic), or small (microcytic). They stain pink with the stains used in hematology, but there is a central area of pallor which does not exceed 1/3 the diameter of the cell. Cells stained in this way are normochromic. If the central area of pallor is greater than 1/3 the diameter of the cell it is described as hypochromic.

On this basis the anemia may be classified as

1) microcytic (MCV is < 80 fl).

- IDA.
- Thalassemia (non thalassemic conditions associated with microcytosis).
- Anemia chronic disorders (ACD) (rheumatoid arthritis, Hodgkin's lymphoma, chronic infection, neoplasia).
- Sideroblastic anemia (hereditary, lead poisoning).

2) normocytic (MCV is 80-100 fl).

- Nutritional anemia (iron deficiency, cobalamin, folate).
- Anemia of renal insufficiency.
- Hemolytic anemia.
- Red cell intrinsic causes: membranopathy, enzymopathy, hemoglobinopathy.
- Red cell extrinsic causes: immune-mediated, microangiopathic, associated with infection, chemical agent (spider venoms), metabolic.
- ACD.
- Primary bone marrow disorder.
- Causes that are intrinsic to hematopoietic stem cells: bone marrow aplasia (idiopathic, PNH, Fanconi syndrome), pure red cell aplasia (acquired, congenital, Diamond-Blackfan syndrome), myelodysplastic syndrome.
- Extrinsic causes: drugs, toxins, radiation, viruses, immune-mediated, bone marrow infiltration (metastatic and lymphoma).

3) macrocytic (MCV >100 fL).

- Megaloblastic anaemia (nutritional:vitamin B12 and folate deficiency).
- Drugs (hydroxyurea, zidovudine, methotrexate).
- Drug-induced hemolytic anemia.
- Dyserythropoiesis, myelodysplastic syndrome, clonal hematologic disorder.
- Hereditary hematologic disorders.
- Excess alcohol intake, liver disease, smoking.
- Hypothyroidism, Waldenström's macroglobulinemia.
- Copper deficiency, bone marrow aplasia, erythroblastopenic anemia.

- Down syndrome.
- Chronic obstructive pulmonary disease.

Classification of anemia by severity:

- ✓ mild (Hb 130/120-110 g/l)
- ✓ moderate (Hb 109-80 g/l);
- ✓ severe (Hb less than 80 g/l).

Reticulocytes are larger than mature red cells and contain portions of polyribosomal RNA material. Supravital stains of peripheral blood detect these reticulated cells, and their number permits an assessment of the marrow's response to the peripheral anemia. The reticulocyte count provides an easy means of implicating either the marrow or the periphery as the source of the anemia. This differentiation dictates the further investigative work up by narrowing the focus to the bone marrow in reticulocytopenic states but to peripheral loss/or hemolytic abnormalities when reticulocytosis is present. The normal count is as follows: adults and children - 0.2-2.0%.

Peripheral reticulocytosis is considered as an indicator of the functional state of the bone marrow.

- ✓ Anemia + High reticulocyte count = Hyperegenerative anemia.
- ✓ Anemia + Low reticulocyte count = Hyporegenerative anemia.

Diagnosis of anemia is based on combination of traditional clinical, morphological, laboratory, biological and instrumental methods of examination. Traditional clinical investigational methods and simple laboratory tests, as the most accessible in the diagnosis of anemia, in no way lost their importance, despite the importance of all other modern investigational methods, especially in the elderly and senile.

Patient's recollections. Typical complaints in the elderly are weakness, dizziness, headache, impaired vision and hearing, flickering flies before the eyes, loss of memory. If these symptoms appear suddenly or significantly worsen, the doctor should pay attention to this and make a differential diagnosis of the anemic syndrome. Presence of many comorbid diseases in the elderly is the serious diagnostic issue. It is very important to record the dynamic changes in complaints, which are typical clinical manifestations of comorbidities, primarily IHD. When patients have changes in the typical clinical course of

angina pectoris, chronic heart failure or their clinical manifestations increase it may be caused by the development of anemic syndrome.

Typical symptoms of cardiac pathology - shortness of breath, palpitations, heart pain and edema of legs arethe most characteristic for anemia. Itleads tothe difficulties to take diagnose, especially in the elderly (LB Lazebnik, 2001). The first stage of the diagnostic search is diagnosis of anemia of unknown origin. In addition to typical complaints of anemia, regardless of their genesis, there are subjective symptoms - complaints and blood test data that are specific to anemia.These depend on its etiology. are Clinical manifestations of sideropenic syndrome are quite characteristic for IDA. B-12 deficiency anemia may be accompanied by symptoms of funicular myelosis.

When doctor collects anamnesis, important data is the presence in the past of gastric or duodenal ulcers, nasal, hemorrhoidal bleeding, or other bleeding symptoms;also presence of liver disease, alcohol abuse. Physicians should pay special attention to medicines that the elderly often use without control. For example, anemia may appear due to long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs). There are frequent drugs in the treatment of chronic pain syndrome (especially in patients with joints pathology) and they have ulcerogenic effect on the gastric mucosa and can lead to bleeding. The risk of gastrointestinal bleeding highly increases with the contemporaneous intake of NSAIDs and aspirin as an antiplatelet drug in patients with coronary artery disease.

Complaints of gait disturbance are often observed in elderly and senile patients (they say that they walks on a fragile floor). In combination with complaints of burning sensation in the tongue, a change in its color to crimson with smooth papillae and the presence of diarrhea, these symptoms may be manifestations of B-12 deficiency anemia. The deterioration of the general condition of the patient after an infection in combination with the appearance of dark urine may indicate the development of autoimmune hemolytic anemia with incomplete thermal antibodies. Autoimmune hemolytic anemia with complete thermal antibodies is characterized by typical clinical manifestations of anemic syndrome that occur after cooling or in the cold season.

Anemia is often complication of hypothyroidism and chronic renal failure. If doctor detect enlarged peripheral lymph nodes at objective examination of patient it may indicate

the presence of cancer and, as a consequence, the development of anemia of chronic disease. Also, lymphadenopathy is characteristic for chronic lymphocytic leukemia, which most often develops in people after 50-60 years and leads to anemia after 3-5 years from the onset of the disease as a result of leukemic infiltration of the bone marrow.

IRON DEFICIENCY ANEMIA

Iron deficiency anemia (IDA) is the most common anemia in patients. It`s up to 90% in the structure of all diagnosed anemias. Identification of IDA in the elderly is difficult due to polymorbide conditions, so careful identification of non-specific symptoms (Vorobiev PA, 2001) is quite important. It allows the doctor to suspect anemic syndrome in patients on time.

Most of the body's iron (it is 2.6 g with 3-4 g) is transported as part of hemoglobin, and undergoes repeated recycling when the red blood cells crack up. One gram of iron is deposited in the liver and 0.47 g in myoglobin and cytochromes. A small amount (3 mg) is transported to the blood plasma in a form associated with transferrin. About 1 mg of iron per day is excreted from the body of men and women; the body of women during menstruation additionally loses an average of another 1 mg of iron per day.

Food iron enters the body in heme (animal products) and non-heme (cereals and vegetables) form. Iron in heme form (deposited in hemoglobin and myoglobin) is better absorbed than iron in non-heme form. Iron in a non-heme form is absorbed by cells from the intestinal lumen with the participation of specific transporters (bivalent metal transporters located on the apical membranes of intestinal enterocytes) and enters the circulating blood, where it binds to transferrin. Erythroblast transferrin receptors absorb iron-transferrin complexes.Iron is incorporated into the hemoglobin composition as a result of the endocytosis process.

Iron absorption is activated under conditions of iron deficiency and activation of erythropoiesis and decreases during inflammatory processes under conditions of iron overload. The process of iron homeostasis is indirectly regulated by hepcidin, which blocks the release of iron from enterocytes and macrophages. Iron body stores are regulated by iron absorption. Iron in a non-heme form is better absorbed in the form of ferrous iron (Fe^{2+}). The formation of ferric iron (Fe^{3+}) occurs under the influence of gastric

acids, ascorbic acid, supplied with food; reductases in the intestinal lumen also contribute to absorption. The absorption of iron in the non-heme form is suppressed with the simultaneous supply of phytates (contained in grain products and legumes), tannin (contained in tea) and calcium. Simultaneous consumption of foods that serve as a source of iron in a non-heme form with ascorbic acid improves iron absorption. With the standard diet is absorbed less than 20% of the available iron. If people adhere to a vegetarian diet this number is even lower.

The development of IDA consists of three stages - from the depletion of iron reserves to the development of iron deficiency anemia.

With the depletion of iron stores, iron depot decreases, but the amount of circulating and functional iron may be normal. Patients with low iron levels don't have the necessary supply of it in the body for mobilization if the organism needs additional iron. On the background of iron deficiency reserves of erythropoiesis are depleted. Further the level of iron, which is transferred in the blood serum, decreases. The amount of iron absorbed from the intestine is not enough to compensate the loss rate and provide the necessary requirements for the functioning of the organism. At this stage iron deficiency leads to a restriction in the production of red blood cells and increase in the concentration of red blood cell protoporphyrin. Iron deficiency anemia is the most severe form of iron deficiency. There is a depletion of iron reserves, a decrease in transport and functional iron levels, which leads to a decrease in hemoglobin levels in addition to low serum ferritin concentrations and low erythrocyte protoporphyrin concentrations.

Symptoms of IDA depend on the severity of clinical manifestations of anemic and sideropenic syndromes.

With a lack of iron in the body anemia does not develop immediately. Initially there is period of latent iron deficiency with signs of a decrease in iron stores in the body without visible symptoms of anemia. Anemia leads to the development of hemic hypoxia of internal organs and tissues. In the elderly patients it can aggravate the clinical course of existing chronic hypoxia of another genesis (most often against the background of IHD).

The main complaints of the patients are general weakness, fatigue, dizziness, syncopal states, shortness of breath, irritability, tearfulness, pale skin and mucous membranes, a tendency to lower blood pressure, tachycardia.

Iron deficiency is characterized by the development of sideropenic syndrome: skin, nails, hair changes are associated with tissue iron deficiency. It is accompanied by decreased activity of many enzymes that include iron (cytochrome oxidase, peroxidase, succinate dehydrogenase, etc.). Characteristic signs are taste perversion (pica chlorotica) and olfactory smell; muscular weakness, dry skin, thinning, brittleness and transverse banding of nails, koilonichia, angular stomatitis, glossitis, as well as atrophic changes of the esophageal mucosa (sideropenic dysphagia - Plummer-Vinson`s symptom), gastric and intestinal mucosa (atrophic gastritis, enteritis).

As a rule, etiological factor is chronic blood loss from the gastrointestinal tract; less often - insufficient intake of iron from food. The loss of every milliliter of blood (at a hemoglobin level of 150 g/l) results in a loss of about 0.5 mg of iron. Bleeding from the gastrointestinal tract is the most common cause of IDA in women and older men. Such blood loss is often asymptomatic, it cannot be excluded only on the basis of negative fecal occult blood analysis. Therefore, the identification of IDA in this category of patients requires the full examination of the gastrointestinal tract, primarily to exclude tumor neoplasms.

Etiology of gastrointestinal bleeding

- ✓ Esophagitis
- ✓ Varicose esophageal veins
- ✓ Peptic ulcer
- ✓ Use of NSAIDs
- ✓ Gastric cancer
- ✓ Inflammatory bowel disease
- ✓ Angiodysplasia
- ✓ Colon cancer
- ✓ Benign intestinal polyps

Pathology of the upper gastrointestinal tract is the cause of 40-50% of IDA in the elderly. It is also necessary to study the lower parts of the gastrointestinal tract, since in 10-15% of patients both pathologies are present simultaneously. Examination of the patient with IDA doctor should begin with an esophagogastroduodenoscopy. Detected

esophagitis, erosion or ulcers are not considered as the ultimate cause of development of IDA until the lower part of the gastrointestinal tract will has been examined.

If positive results of serological examination for celiac disease were obtained or the examination was not performed small intestinal material (biopsy) should be collected for further histological examination during endoscopy.

The colonoscopy has advantages, since this method allows you to identify angiodysplasia and conduct a biopsy of the affected area. However, double-contrast barium irrigoscopy is an alternative method, with or without rectoromanoscopy, especially if the resources for a colonoscopy are limited or lacking.

If the patient has anemia dependence on blood transfusions, angiodysplasia may be a likely cause of the development of the anemic syndrome, which requires an enteroscopy. The examination of the small intestine in such cases it is advisable to combine with the implementation of capsule video endoscopy, the diagnostic accuracy of it is 40-55%. The small intestine X-ray or radioisotope scanning is primarily indicated for patients who have the clinical symptoms of Crohn's disease.

Impaired iron absorption can be caused by a pathology of the intestinal mucosa (most often celiac disease), a violation of the secretion of hydrochloric acid (including due to the intake of proton pump inhibitors), as well as when the patient has bypass gastrointestinal anastomosis. Colonization of Helicobacter Pylori can cause deterioration in the absorption of iron or increases its loss; as a result iron deficiency can develop. According to some clinical studies, H. Pylori eradication promotes regression of anemia. The "gold" standard for diagnostics of Helicobacter pylori infection in the body is the respiratory urea test (13C or 14C) or fecal test (determinationof Hp antigen in the feces which based on the monoclonal antibodies). When this infection wasdetected patients should be prescribed eradication therapy. Latest treatment recommendationsare reflected in the fifth edition of the Maastricht Consensus Report.

The fecal occult blood test should not be included in the examination plan of patient with IDA, since the method is insensitive and nonspecific and will not help the doctor in determining the etiology of anemia.

It is recommended to conduct urine analysis to detect hematuria in all patients with IDA. According to statistics approximately 1% of patients with IDA havemalignant renal

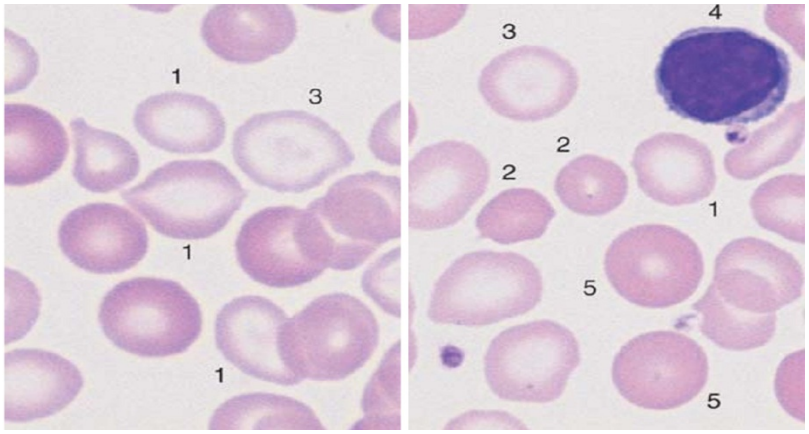
formation. Also, anemia is detected in about a third of patients with renal cell carcinoma. It is associated with hematuria and the deposition of hemosiderin in the tumor. If the patients have hematuria a renal ultrasound examination must be recommended. If it is necessaryintravenous urography and computed tomography can be used.

One of the causes of iron deficiency anemia in women is abnormal uterine bleeding. According to the National Consensus for the management of patients with abnormal uterine bleeding (Association of Gynecologists and Endocrinologists in Ukraine - 2015), elderly patients rarely visit a doctor with this complaint. Therefore, general practitionersshould pay special attention to this issue during the collection of anamnesis.

When iron deficiency is supposed, it is necessary to determine the indicators of iron metabolism in the body and correlate these results with the corresponding indices of the red blood cells.

Complete blood count. Characteristic changes are low hemoglobin level, decreased mean volume of erythrocytes(MCV), an average hemoglobin content in average RBC (MCH) and an average hemoglobin concentration in the erythrocyte (MCHC).

A blood smear can confirm the presence of microcytic hypochromic erythrocytes with characteristic elongated cells. However, microcytic, hypochromic indices can also occur in hemoglobinopathy. In addition, in patients with mild iron deficiency, MCV may remain within normal limits.



Picture 1. Iron-deficiency anemia. The erythrocyte morphology at iron deficiency anemia: ring-shaped erythrocytes (1), microcytes (2) target-like erythrocytes (3), lymphocyte (4) for size comparison. Normal red blood cells (5) after blood transfusion.

The serum iron level (normal valuesare 8.1-31.3 mmol/l for men and 5.4-31.3 mmol/l for women) and the level of transferrin saturation with iron (in the norm - 20-50%) decrease as a rule. Also the total iron-binding capacity of blood serum increases (normal value - 39.4-75.2 μmol/l). However, doctor should take into consideration that theserum iron level varies significantly during the day and decreases both with iron deficiency and with inflammatory processes. Therefore, this indicator is not a reliable marker for the diagnosis of iron deficiency.

A highly specific and informative test for the diagnosis of IDA is the serum ferritin level. It allows us to estimate the iron reserves in the body. The ferritin level has already reduced at the latent stage of IDA, when hemoglobin level and RBC arenormal still. The serum ferritin level<15 mg/l indicates a deficiency of iron in the tissues. If its level is more than 100 mg/l, the diagnosis of IDA can be excluded.

Ferritin also increases with inflammatory and infectious diseases, liver disease and malignant tumors because it is an acute-phase reagent protein. As a result, a false interpretation of elevated ferritin level is possible in patients with iron deficiency with thesepathology. In the elderly with inflammatory processes, iron deficiency is possible at a ferritin level of 60-100 mg/l. Identifying markers such as C-reactive protein level helps identify the presence of an inflammatory process.

Functional iron deficiency is formed under conditions when it cannot be mobilized for erythropoiesis despitethe adequate iron reserves in the body. It is associated with elevated hepcidin level. This violation is often observed in patients with terminal chronic renal failure. The response to erythropoietic effects can be optimized when ferritin content is more than 200 mg/l. Functional iron deficiency can contribute to the development of anemia in patients with inflammatory processes, such as rheumatoid arthritis. The percentage of hypochromic erythrocytes and hemoglobin concentration in reticulocytes (determined by some automated hemoanalyzers) are used to assess the state of iron in patients who use erythropoietic drugs.There are useful indicators to diagnose functional iron deficiency.

If ferritin level is from 15 to 100 mg/l the diagnosis of IDA is doubtful and the level of transferrin receptors should be determined (normal valuesare 2-9 mg/l). Transferrin receptors are transmembrane glycoproteins that bind to circulating transferrin carrying one

or two iron atoms. Thanks to these receptors, transferrin with iron is transported to the cytoplasm, where iron is released, and the protein returns to the cell surface and enters the blood. A progressive decrease in iron stores is manifested by a decrease in ferritin serum level, and a decrease in the content of functional iron in the tissues - by an increase in the level of receptors for transferrin. The level of this indicator does not depend on the inflammatory syndrome, infectious or malignant disease. The level of transferrin receptors increases even before the appearance of changes in the complete blood count in patients with IDA.

Table 2. Laboratory tests available for the diagnosis of iron deficiency and their sensitivity and specificity

Parameter	Normal Range*	Absolute Iron Depletion Without Anemia	Absolute ID With Anemia	Functional ID Without or With Anemia	Sensitivity, %†	Specificity, %†
Bone marrow iron stores	Normal	Absent from both erythroid progenitors and reticuloendothelial cells	Absent from both erythroid progenitors and reticuloendothelial cells	Low in erythroid progenitors, normal in reticuloendothelial cells	Gold standard	
Hemoglobin, g/dL	M: 13.5–17.5; F: 12.0–15.5	N	↓/↓↓	N/↓	Poor	Poor
Mean red cell volume, fL	M: 81–95; F: 82–98	N/↓	↓/↓↓	N/↓	Poor	88.3
Ferritin, µg/L	M: 24–336; F: 11–307	≈20	<15–30	N/↑	35–48	75–100
Serum iron, µg/dL‡	M: 50–150; F: 35–145	↓	↓	↓	Poor	Poor
Total iron binding capacity, µg/dL, or transferrin, mg/dL	250–400; 200–360	N	↑	N/↓	Poor	Poor
TSAT, %‡	≈15–50	≈30	<15	N/↓	59–88	63–78
sTfR, mg/L§‖	1.8–4.6	↑	↑↑	↓	70–81	59–71
sTfR:log(ferritin) ratio‖	≤1.03[66]	↑	↑↑	↑	81	83
Hepcidin, ng/mL‖[67]	M: 29–254; F: 17–286	N	↓	↑	50–92.5	85–90
ZPP, µmol ZPP/mol heme‖[68]	<70	↑	↑	↑	38	87
Hypochromic RBC, %	<2.5	N/↑	↑	N/↑	64–78	77–78
CHr, pg	≈28–35	N/↓	↓	N/↓	53–78	53–100

CHr indicates reticulocyte hemoglobin content; F, female; ID, iron deficiency; M, male; MCV, mean red cell volume; N, normal; NA, not available; RBC, red blood cells; RES, reticuloendothelial cell; sTfR, soluble transferrin receptor; TIBC, total iron binding capacity; TSAT, transferrin saturation; and ZPP, red cell zinc protoporphyrin.

*The normal ranges for various parameters may vary in individual laboratories.

†Data from von Haehling and colleagues[65] or as otherwise referenced.

‡Grote Beverborg and colleagues[69] reported that the sensitivity and specificity (as single parameters) of TSAT were 94% and 84%, respectively, and for serum iron were 94% and 88%, respectively, for absolute or functional ID, confirmed by bone marrow examination in patients with heart failure undergoing coronary artery bypass grafting.

§Jankowska and colleagues[70] reported that the sensitivity and specificity of sTfR were 67% and 97%, respectively, for ID confirmed by bone marrow examination in patients with coronary artery disease.

‖These tests may not be routinely available in clinical laboratories.

Trial treatment with iron drugs

Trial treatment with iron drugs is as diagnostic and as therapeutic method. If the patient knows that he has hemoglobinopathy it is necessary to determine the serum ferritin level first of all.In other cases microcytic or normocytic anemia should be considered as iron deficiencyanemia, until the contrary is proven. From the point of view of economic and time costs, evaluation of the results of trial treatment with iron drugs is an effective method. An increase in hemoglobin level after 2 weeks confirms iron deficiency. If the status of hemoglobinopathy is unknown, then, while the examination (screening) is being performed, it is advisable to start treatment with iron drugs. A compulsory condition is to control results effectively. If there is no increase in hemoglobin in the second week of treatment, other causes of anemia should be considered, such as vitamin B12 deficiency or folic acid deficiency.

Diet therapy

Increasing iron intake with food is not enough to treat iron deficiency anemia. For this it is necessary to use iron drugs in large doses. Nevertheless, an increase in the supply of iron from food and the optimization of its absorption by minimizing its suppressing factors, as well as enhancing the factors favorable for absorption, is useful as a means of preventing recurrence of iron deficiency in elderly patients.

To ensure an adequate supply of iron by changing the diet should take into account traditional methods of cooking and eating habits. Since the iron content is low in diets based on cereals and potatoes, adding legumes to the diet can slightly increase the iron content. However, the bioavailability of these sources of non-heme iron is low. Thus, to ensure the consumption of the recommended amount of iron and zinc with such a traditional diet is impossible, it is necessary to include meat, poultry or fish.

When you add a small amount (50 g) of meat, poultry or fish into the diet it increases the total intake of iron, as well as the amount of biologically available iron. Accepting ascorbic acid together with the products rich by iron significantly improves its absorption.

There is a critical balance between activators and iron absorption inhibitors. To ensure the bioavailability of iron, an essential prerequisite is the reduction in the consumption of iron absorption inhibitors and an increase in the intake of suction activators at each meal. The nutritional status can be greatly improved by educating

patients on the right methods of cooking, which minimize the use of iron absorption inhibitors. It is also important to recommend a minimum heat treatment of vegetables rich in vitamin C, folates and other water-soluble and heat-sensitive vitamins. It is useful to increase the consumption of sprouted grains, fermented grain products, grain products to be heat-treated, meat, fruits and vegetables rich in ascorbic acid, as well as consumption of tea, coffee, chocolate or herbal tea not at the same time as other products.

Iron therapy

Treatment of the main cause of anemia promotes the cessation of further loss of iron. Treatment of an underlying cause should prevent further ironloss, but all patients with IDA should have iron supplementation both to correct anemia and replenish body stores.

The average dose is 200 mg of ferrous sulfate twice a day. Patients who have symptoms of intolerance to iron preparations should reduce the daily dose of iron sulfate. Also, this group of patients may be prescribed other iron salts (ferrous fumarate, ferrous gluconate) or recommend dosage forms of iron in the form of a suspension. The recommended daily dose of iron for oral administration in adults is 100-200 mg of elemental iron per day and can be divided into 2-3 doses.

In patients with mild or moderate IDA who have gastric disorders when taking iron preparations in a standard daily dose and rapid increase in hemoglobin levels, it is advisable to prescribe iron supplements containing 30-60 mg of elemental iron or use a method of periodic dosing (for example, one day or one once a week).

Oral iron should becontinued for 3 months after the hemoglobinlevel has beencorrected so that stores are replenished. The reticulocytosis is usually observed in 72 hours after initiation of iron therapy, and the hemoglobin level increases by an average of 20 g/l every three weeks.

Ascorbic acid (250-500 mg twice daily with the iron preparation may enhance iron absorption, but there are no data forits effectiveness in the treatment of IDA

Patients who have an absolute intolerance to oral iron drugs or lack an adequate response in the background of their use iron parenteral preparations are indicated. Also, refusal to use the oral form of iron preparations is advisable in patients with impaired absorption in the intestine (for example, due to the inflammatory process in the intestine); with constant loss of iron (progressive blood loss), which exceeds the ability to absorb; in

patients with chronic kidney disease who need rapid recovery of iron stores and treatment with erythropoietin.

There arethree parenteral preparations available, two of which can onlybe administered intravenously (iron sucrose (Venofer) and ferriccarboxymaltose (Ferinject)), and one that can be given eitherintravenously or by deep gluteal intramuscular injection (iron(III) hydroxide dextran (Cosmofer)), although this can bepainful and requires several injections. A comparison of intravenousiron compounds is shown in table 2. The principal advantageof ferric carboxymaltose, a recent addition to intravenous therapy.

Table 3.Intravenous iron preparations available for clinical use in the elderly

Intravenous iron preparation	Maximum single dose	Duration of infusion
Iron dextran* (Cosmofer)	20 mg/kg	6 h
Iron sucrose (Venofer)	200 mg	10 min
	500 mg	4 h
Ferric carboxymaltose (Ferinject)	1000 mg	15 min

Red blood cell transfusion in patients with IDA is associated with adverse effects, including hypervolemia in elderly and senile patients (it is observed in about 1% of patients), as well as a number of immunological and infectious threats. This method should be used only if it is necessary to provide instant, targeted assistance to patients with severe anemia - at a hemoglobin level of <70 g/l. Based on clinical observations and taking into account risk factors, a hematocrit of about 15% (hemoglobin concentration 50-45 g / l) is taken as a critical threshold value for the absolute indication for red blood cell transfusion as replacement therapy.

At higher hemoglobin levels (<100 g/l), red blood cell transfusion can be prescribed to patients with severe anemic symptoms or to patients with severe anemia if they have:

• cardio-pulmonary symptoms: tachycardia, arterial hypotension of unknown etiology, shortness of breath;

• ECG changes occurring for the first time: ST segment depression, T wave inversion, rhythm disturbances, signs of violation of myocardial contractility;

• General indicators of oxygen transport decline: an increase in total oxygen extraction> 50%; decrease in oxygen consumption> 10% of the original value; reduced oxygen saturation of mixed venous blood <50%; oxygen voltage drop in mixed peripheral venous blood <32 mm Hg; reduction of central venous oxygen saturation by <60%; lactic acidosis (lactate> 2 mmol/l + acidosis).

When hemoglobin level is more than 70 g/l, further red blood cell transfusion is considered impractical and it is necessary to continue treatment with iron preparations.

Also, blood transfusion can be prescribed to patients with IDA and acute bleeding that cannot be stopped.

After restoring normal hemoglobin levels and red indices they should be monitored every three months during a year. At the end of the second year, patients are given complete blood test. If patients have a repeated low hemoglobin level or red indices, oral iron supplements should be reappointed.

ANEMIA OF CHRONIC DISEASE

Among anemic syndromes in geriatric practice, 35-50% are anemias with redistribution of iron, the so-called anemias of chronic diseases, although anemic syndrome also occurs in acute inflammations, especially in the presence of a purulent process in internal organs (apostematic nephritis, lung abscess, etc.). The development of anemia is observed in various inflammatory diseases of both infectious and non-infectious genesis. There are different pathogenetic mechanisms of the anemic syndrome in these situations. However, the main mechanism is redistribution of iron into the cells of the macrophage system against the background of inflammatory (infectious and non-infectious) or malignant processes.

Table4.Causes of anemia of chronic disease

Diseases	Examples
Acute infections	Bacterial, fungal, viral
Chronicinfections	Tuberculosis, endocarditis, urinary tract infections, coccidioidomycosis and other chronic fungal infections
Non-infectiouschronicinflammatory diseases	Osteoarthritis, rheumatoid polyarthritis, rheumatic polymyalgia, acute and chronic hepatitis
Malignantdiseases	Metastatic carcinoma, hematologic oncology
Acute conditions	Surgery, severe injury
Otherdiseases	Diabetes mellitus, congestive heart failure, malnutrition, bedsores

In chronic diseases, iron metabolism is disturbed due to the activation of immune-competent cells, iron deficiency occurs due to its accumulation in tissue macrophages. However, a decrease in the content of serum iron in patients with anemia during AHD does not limit the entry of iron into the bone marrow, since the need for it is reduced due to inhibition of erythropoiesis. An important role in the development of anemia in chronic diseases is played by activated macrophages that inhibit the growth of erythroid progenitors through the production of cytokines, the expression of which is induced by various factors (bacterial endotoxin, interleukins, tumor antigens, circulating immune complexes).

Synthesis of hemoglobin is not disturbed; with the result that anemia of chronic diseasehas a normochromic and normocytic character, which creates additional difficulties in the interpretation of a complete blood count, especially in the elderly. Due to the extreme prevalence of iron deficiency in elderly patients, there is an absolute deficiency of iron and, in some cases, anemia can be hypochromic in nature, but the degree of hypochromia is small.

Some authors believe (G. Weiss, 2005) that the fact of hemolysis and a decrease in the life span of red blood cells in the elderly in various chronic diseases, tumors is beyond doubt and its contribution to the formation of anemia is obvious. Hemolysis has great importance in the formation of anemic syndrome and in patients with chronic alcoholism.

Determining the etiology of anemia has the great importance for the tactics of further treatment, since the unjustified use of iron preparations can lead to its accumulation in the

tissues (siderosis). It is proved that it is advisable to refrain from treating anemia until the cause of its development has been established. It must be remembered that the successful treatment of the underlying disease naturally leads to a decrease in the degree of anemia, and in some cases to its elimination.

Anemias of redistribution, especially in older people, are characterized by a protracted course, depending on the focus of the lesion and the activity of the process, there is also a refractoriness to treatment by hemostimulating agents. This suggests that in their complex pathogenesis there are common mechanisms that give these anemias a large part of the universal features with a variety of reasons causing them.

According to various sources in rheumatoid arthritis a significant hemoglobin reduction occurs in 63-100% cases (H. Papadaki, 2002); in chronic diffuse liver diseases - in 16.7-96%; in chronic renal failure - in 30-46.8% of patients.50% elderly patients with diabetes mellitus have anemic syndrome (J. E. Shaw, 2010). It is associated with decreased life duration of erythrocytes in hyperglycemia,entering to the bloodstream a large number of deformed and hemolyzed erythrocytes, violations of nutrients in the small intestine, including iron, vitamin B12, folic acid. Morphological changes of erythrocytes are observed in both types of diabetes.

According to clinical studies, it was proved that one in five patients with type 1 or type 2 diabetes have manifestations of anemia, which leads to an increase in the incidence of diabetic micro- and macroangiopathies (D. K. Singh, 2009).According to clinical studies, approximately 7–8% of patients with diabetes have low Hb level <110 g/l. In most cases anemia remains unrecognized and untreateduntil chronic kidney disease or other critical conditions develop. Further studies showed that 75% of patients had a functional deficiency of erythropoietin, especially when they have renal dysfunction.The clinical manifestations of anemia were diagnosed in 50% of patients with CKD (A. Angelousi, 2015). At the same time, 70% of patients with anemia without renal impairment had a low erythropoietin level. When it happens the vicious circle closes - the deficiency of erythropoietin aggravates the manifestations of anemia in diabetes mellitus. It has been proven that the severity of anemia correlates with the stage of diabetic nephropathy, increases the risk of progression of cardiovascular disease and stroke; Hb level is a reliable prognostic factor of survival to the start of dialysis therapy in patients with chronic renal

failure (U. Mehdi, 2009).COPD is traditionally regarded as one of the most important causes of polycythemia, but recent studies (J.P. Wrobel, 2012) have shown that anemia is also often observed in patients with COPD. The prevalence of anemia in patients with COPD is about 29%; this syndrome develops significantly more often in the earlier stages of COPD in women than in men. Most patients have normocytic and hypochromic anemia without changing of the reticulocytes number. The presence of anemia significantly worsens the condition of patients, especially in women. They hadmore severe shortness of breath whereas men with the same degree of bronchial obstruction. Also, there was significant decrease in exercise tolerance and an increase in the frequency of hospitalizations in patients with COPD and anemia (Dvoretsky L.I, 2012).

The main cause of the development of anemia in patients with chronic renal failure is a decrease in the synthesis of erythrocytogen erythrocyte growth hormone in peritubular cells (D. VanWyck et al., 2007) of the proximal nephron in shriveled kidneys. As a result, plasma erythropoietin levels become relatively low. The inverse linear relationship between plasma erythropoietin level and hemoglobin concentration is absent in renal pathology, as a result the synthesis of erythropoietin does not increase in proportion to the severity of anemia. It leads to the development of ineffective erythropoiesis, which is accompanied with intraosseous cerebral hemolysis and a reduction in the average lifespan of erythrocytes. Also, platelet dysfunction, which causes bleeding, has a definite effect as risk factor for anemia. Other etiological factors of anemia include the effect of uremic toxins on red blood cells, reduced iron levels due to inadequate absorption in the intestines and hemodialysis blood loss, removal of folic acid during hemodialysis.

In chronic kidney disease anemia is normocytic and normochromic more often. When iron deficiency developsanemia becomes hypochromic. In patients with chronic renal failure and anemia, a decrease of hemoglobin level is only 1 g/l increases mortality by almost 20%. It is associated with cardiovascular and infectious complications and significantly reduces the quality of life of these patients (S. Brugnara, 2011). Thus timely correction of anemia in patients with chronic kidney disease is extremely important. Pharmacological correction of erythropoietin deficiency in chronic renal failure provides adequate stimulation of the bone marrow and stops ineffective erythropoiesis. Erythropoietin stimulates the growth of stem erythroid precursors - colony-forming units

of erythropoiesis. Unfortunately, therapy often begins late - when an average hemoglobin level is 90 g/l. Anemia therapyinvolves administration of erythropoietin 2-3 times a week, given the length of the half-life of this drug. According to the meta-analysis (W. Horl. et al, 2003) there was no significant difference between the administration of erythropoietin in hemodialysis patients with one, two or three times a week. Subcutaneous administration of erythropoietin is recommended both for patients with anemia in the predialysis stages of chronic renal failure, as well as for patients on programmed hemodialysis or for patients undergoing kidney transplantation. At the same time, patients on programmed hemodialysis can receive erythropoietin either intravenously (100 IU/kg/week) or subcutaneously (60 IU/kg /unit).

Many elderly patients suffer from chronic heart failure. More often anemia develops in patients with history of heart failure is more than 7 years (Dzyak GV, 2013). Anemia in patients with chronic heart failurehas various causes. The main of them is iron deficiency. Also, risk factors for anemia are long-term use of ACE inhibitors, chronic kidney disease (chronic pyelonephritis, diabetic neuropathy) and gastrointestinal tract pathology, a decrease of renal GFR less than 90 ml/min by 1.73 m2.

According to clinical studies, the frequency of anemia in patients with CHF ranges from 10% to 55% (Dzyak GV, AM Vasilenko, 2013). The prevalence of anemia in patients with CHF 60-75 years averages 10-20% and it is a predictor of poor prognosis. In patients with severe CHF and anemic syndrome mortality during the year reaches 50% (Voronkov LG, 2010).

Anemia affects the contractile function of the myocardium, peripheral microcirculation. It contributes to the overstressing of the neuro-humoral systems and reduces renal blood flow. It leads to deterioration in the clinical course of CHF, increasedrecurrent heart failure hospitalizations and cardiovascular mortality in patients (Korkushko AV, 2010).

The main causes of anemic syndrome in congestive heart failure are:

1. Iron deficiency due to its deficiency in the diet.

2. Violation of iron absorption in the intestine with its adequate use due to edema of the mucous membrane.

3. Reducing the release of iron from the depot as a result of stagnation and abnormal liver function.

4. Prolonged use of ACE inhibitorsas complex CHF therapy.

5. Prolonged use of acetylsalicylic acid (other antiplatelet agents), anticoagulants, which leads to microbleeding.

6. Reduced erythropoietin synthesis in the kidney is cardiorenal anemic syndrome.

This concept includes combination of CHF, anemia and kidney dysfunction. According to the studies (D.S. Silveberg, 2006), the prevalence of cardiorenal anemic syndrome ranges from 10 to 70% in patients with CHF. According to different clinical studies there is a direct relationship between the severity of CHF, impaired renal function and the synthesis of erythropoietin. In patients with chronic kidney disease anemia is also associated with a reduction in the erythrocyte life expectancy, platelet dysfunction (increased bleeding), and exposure to erythrocytes of uremic toxins.

7. The cytokine mechanism consists in the redistribution of iron and the occurrence of erythropoietin resistance due to the pro-inflammatory action of interleukin 1 cytokines, interleukin 6, hepcidin, and tumor necrosis factor.

With a lack of available iron from the bone marrow reticulocytes enter the blood with a low content of hemoglobin. In turn, an adequate amount of available iron stimulates erythropoiesis and reduces the need for erythropoietin. As described above, the cause of the decrease in serum iron in patients with CHF is the true iron deficiency due to venous stasis in the gastrointestinal tract and the processes of maldigestion and malabsorption, and iron loss in patients who used acetylsalicylic acid. On the other hand, iron deficiency due to its redistribution associated with cytokine-induced anemia of chronic disease is the important pathogenetic mechanism in CHF.

AChD is normochromic normocytic anemia with an average red blood cell volume (MCV) within the normal range (80-100 fl) in typical cases, although sometimes there is a microcytosis (MCV <80 fl). The bone marrow response to AChD is inadequate, so the reticulocyte synthesis index is significantly below 2. The reticulocyte count, serum iron level and transferrin saturation are lowered, and ferritin as an unspecific marker of inflammation is elevated (may be normal). Sometimes, to confirm the diagnosis, it is necessary to perform a morphological study of the bone marrow (bone marrow

biopsy).The most specific test for the differential diagnosis of iron deficiency anemia and anemia of chronic disease is the determination of ferritin level. Ifitis more than 100 mg/ml it excludes IDA, and an indicator less than 15 mg/ml confirms the presence of iron deficiency. In patients with chronic inflammatory diseases the ratio of serum transferrin receptors to serum ferritin levels is usually less than 50 whereas at iron deficiency - more than 50.

Table5. Differential diagnostics IDA andAChD

Laboratory test	**IDA**	**AChD**
Serum iron	↓	↓
Total iron binding capacity	↑	↓
Transferrin saturation	↓	↓
Ferritin level	↓	N or ↑

The results of clinical studies have demonstrated a positive effect in the use of iron preparations for the treatment of anemia in patients with CHF.

The rational use of erythropoietin in combination with iron preparations in the treatment of anemic syndrome contributes to a more rapid compensation of CHF, improves the systolic function of the left ventricle (D.M. Mancini, 2012).

The RED-HF study had demonstrated that hemoglobin targets during treatment with erythropoietin should not exceed 150 g/l, because it increasedrisk of thromboembolic complications and strokes in elderly patients with CHF and anemia (JJ McMurray, 2009).

Some authors (B. Langstrom, P. Beris, 1999, G. Perewusnyk 2002) had reportedthat intravenous iron preparations were more effective compared with oral iron in patients with CHF. There are several forms of intravenous iron preparations: iron sucrose, iron gluconate, iron dextrin, iron carboxymaltozate, iron (III) hydroxide-sucrose complex.

Idiopathic normocytic-normochromic anemia

Despite a thorough examination (including a bone marrow biopsy)the etiology of low hemoglobin level is not possible to establish in 14-36% of anemic elderly patients. Clinical symptoms are absent in these patients and their quality of life remains satisfactory. Therefore, they do not need therapy and the prognosis is favorable in this case.

MACROCYTIC ANEMIA

A deficiency of vitamin B12 and folic acid occurs in 5-15% of gerontological patients, causing, as a rule, the development of macrocytic anemia. Sometimes MCV can be normal, therefore, the deficiency of these vitamins should be excluded in patients with unknown normocytic anemia.

Cyanocobalamin (vitamin B12) is a cofactor of the methyltransferase catalytic reaction. It is the resynthesis of methionine and the regeneration of 5-methyltetrahydrofolate into tetrahydrofolate and 5,10-methylenetetrahydrofolate at the same time. When folic acid and (or) cyanocobalamin are deficient, the process of incorporation of uridine into the DNA of developing hematopoietic cells and the formation of thymidine are disturbed, which leads to DNA fragmentation (blocking its synthesis and disruption of mitosis). At the same time, megaloblastosis develops, large forms of leukocytes and platelets accumulate, their early intraosseous cerebral destruction and shortening of circulating blood cells lifetime. As a result, hematopoiesis becomes ineffective and anemia develops, often combined with thrombocytopenia and leukopenia.

In addition, cyanocobalamin is a coenzyme in the reaction of converting methylmalonyl-CoA to succinyl-CoA. This reaction is necessary for the metabolism of myelin in the nervous system. In connection with vitamin B12deficiency leads to nervous system disorders in patients with megaloblastic anemia.

Cyanocobalamin is found in foods of animal origin - liver, kidneys, eggs, milk. Its reserves in the body of an adult (mainly in the liver) are large - about 5 mg, and if you consider that the daily loss of vitamin is 5 μg, then the complete depletion of reserves in the absence of income (violation of absorption, with a vegetarian diet) occurs only after 3 years. In the stomach, vitamin B12 is associated (against the background of the acidic reaction of the environment) with the intrinsic factor of Castle (gastromucoprotein) produced by the parietal cells of the stomach, or with other binding proteins, R-factors, which are present in saliva and gastric juice.

These complexes protect cyanocobalamin from destruction during transportation through the gastrointestinal tract. In the small intestine with an alkaline pH value, under the influence of pancreatic protein proteinases, cyanocobalamin is cleaved from R-proteins and connected to an internal factor. In the ileum, the intrinsic factor complex and cyanocobalamin binds to specific receptors on the surface of epithelial cells, and with the

help of special plasma proteins, transcobalamin cyanocobalamin is released and transported to the tissues.

B12-DEFICIENCY ANEMIA

As a result of vitamin B12 deficiency and folic acid, DNA synthesis is disturbed in hematopoietic cells, an ineffective megaloblastic erythropoiesis develops (normally only in the fetus) with the production of unstable megalocytes and macrocytes. B12-deficiency anemia is a common pathogenetic variant of the anemic syndrome in elderly patients, especially in combination with diabetes mellitus and thyroid diseases.

According to clinical studies data there is a probable link between the incidence of B-12-deficiency anemia and age. Prevalence of B-12 deficiency anemia is 0.1% in the general population and 1% in the elderly in Northern Europe (Sweden, Norway, UK). P. J. Stover(2016) reported thatprevalence of undiagnosed B12-deficiency anemia in people over 60 years old is about 19% in the United States according to morphological blood tests, serum vitamin B12 levelassessment and antibodies to the intrinsic factor of Castle.

Table6. The main etiological factors of B12-deficiency in elderly patients

Pathophysiological mechanism	***Etiological factors***
Insufficientfoodintake	Chronic alcoholism Chronic malnutrition Strict vegetarian diet
Disorders of absorption	Atrophic gastritis (associated with Helicobacter pylori or autoimmune) After stomach resection Excessive reproduction of bacterial flora in the small intestine Malabsorption syndrome Crohn's disease Chronic pancreatitis
Metabolic disorders	Medicines Transcobalamin II deficiency

	B12 analogues antivitamin
Decrease of body stores of vitamin B12	Severe liver diseases
Druginteractions	
Malabsorption	Metformin, antibiotics, difenin, colchicine, paraamosalicilic acid, cholestyramine
Malabsorption of foods containing vitamin B12, inactivation of metabolism	Vitamin C, nitric oxide, proton pump inhibitors, H2 receptor antagonists

Hematological, neurological and psychiatric manifestations of the disease can occur simultaneously, sequentially or independently of each other.

Symptoms of anemia syndrome depend on the severity of anemia, and are manifested by general weakness, increased fatigue, shortness of breath, feeling of palpitations, low blood pressure.

In 25-30% of patients with B12-deficient anemia, clinical manifestations of Glont Günther-Müller may be observed - complaints of pain, burning sensation in the tongue, taste disturbance. On examination, the tongue has a crimson color, there are areas of inflammation, aphthae, atrophy, and flattened nipples - the so-called "lacquered" tongue.

In 10-12% of patients with severe B12-deficient anemia, neurological disorders are observed, which are manifestations of funicular myelosis, a dystrophic lesion of the lateral and posterior cords (funiculitis) of the spinal cord. Patients complain of paresthesia - a feeling of numbness, tingling, goose bumps in the upper and lower extremities, sometimes the symptoms spread to the anterior surface of the abdominal wall and chest. Then join the violation of deep sensitivity, sensitive ataxia and weakness in the legs, accompanied by a violation of the gait of the patient. Typical forms are characterized by a combination of sensitive ataxia and paraplegia (atactic paraplegia). Paresis of the lower limbs may be spastic or lethargic. Tendon jerks are at first elevated, but as the disease progresses, they decrease and disappear. The combination of pyramidal symptoms with flaccid paresis of the legs is a characteristic feature of funicular myelosis. Senso-motor disorders of the extremities may be accompanied by dysfunction of the pelvic organs (delay or

incontinence of urine and feces). Often patients complain of reduced vision, weakness, drowsiness, depression and apathy, headache, tinnitus, dizziness, memory loss.

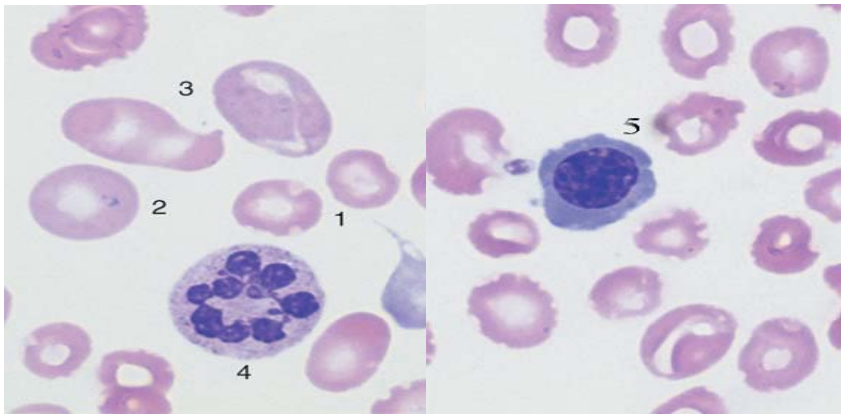
When examining patients revealed pale skin and mucous membranes, there may be jaundice, moderate hepatosplenomegaly. The development of jaundice is due to an increase in the content of indirect bilirubin as a result of the accelerated death of erythrocriocytosis in the bone marrow and increased destruction of large red blood cells (macrocytes) in the spleen.

In patients with severe thrombocytopenia, manifestations of the hemorrhagic syndrome may occur - hemorrhages on the skin and mucous membranes (ecchymosis and petechiae), external and internal bleeding.

When conducting endoscopy and morphological studies of the gastric mucosa in most patients revealed signs of atrophic gastritis.

The main diagnostic criteria for B12-deficiency anemia are changes in the complete blood count:

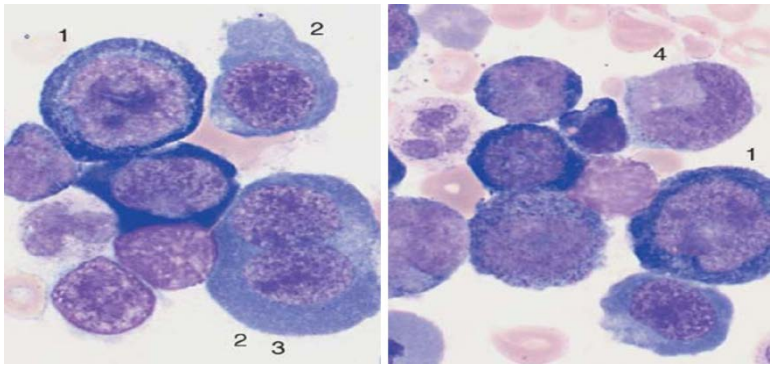
- macrocytic anemia (MCV> 100 fl).
- megaloblasts, megalocytes;
- erythrocytes with residues of nuclei (Jolly`s bodies, Kebot`s rings)
- hypersegmentation of neutrophil nuclei;
- leukopenia (neutropenia)
- thrombocytopenia.



Pic. 2. B12 deficiency anemia. Significant anisocytosis. Normal erythrocyte (1), macrocyte (2), megalocyte (3), hypersegmented neutrophil (six or more segments), polychromatophilic erythroblast.

If the serum vitamin B12 level (normally is 162-835 pmol / l) does not exceed one third of the normal the serum level of methylmalonic acid and homocysteine is should be estimated to confirm the diagnosis. If these concentrations are normal vitamin B12 deficiency is should be excluded. An increased level of methylmalonic acid confirms the presence of vitamin B12 deficiency.Whenhomocysteine levelincrease additional examination is necessary to eliminate other causes of its growth.

A reliable diagnostic method to make final diagnosis of B12-deficiency anemia is the traditional investigation of hematopoiesis - bone marrow biopsy. Anemia is characterized by the formation of the megaloblastic type of blood formation - the chromatin of the nuclei of the red cells (erythroblasts, normoblasts) has a characteristic view resembling red caviar.



Pic. 3. Bone marrow at B12 deficiency anemia. Moderate (1) or pronounced (2) hypersegmentation of nuclei, in some cases, there are dual-core cells (3). Giant granulocytes and metamyelocytes (4).

The investigation should be carried out before treatment, since even a single injection of vitamin B12 masks the megaloblastic nature of erythrocaryocytes and makes it difficult to diagnose. Another additional diagnostic criterion is the presence of a reticulocyte crisis in patients: an increase in the number of reticulocytes after 5-10 days of treatment with vitamin B12 (on average on the 7th day) of normal or lowered levels due to the revival of normoblastic hematopoiesis and release of young red blood cells into the blood.

Treatment

When diagnosis of B12-deficient anemia has confirmed prolonged treatment with vitamin B12 (cyanocobalamin, hydroxycobalamin) is indicated. The drug is administered intramuscularly at daily dose of 500 mcg.In patients with severe anemia and clinical manifestations of funicular myelosis thedaily dose increases to 1000 mcg/day. The

treatment lasts until the hemoglobin level is normalized, then supportive therapy is prescribed: within 2 weeks - injections every other day, then 2-4 weeks - 1-2 times a week. After half a year, they switch to supporting replacement therapy in the form of injections of vitamin B12 at a dose of 500 μg 1 time per week. Lack of maintenance therapy can lead to relapse of the disease. If necessary, treatment of the underlying disease (enteritis, deworming) should be carried out. The use of folic acid in patients with B-12-deficient anemia is not indicated, as it may worsen the existing neurological symptoms. Appointment of iron supplements may be appropriate with simultaneous iron deficiency, which is often found in older people. In addition, on the background of treatment with vitamin B12 and the activation of normoblastic hematopoiesis, there may be an increased need for iron, and therefore the administration of iron supplements is also advisable. Erythrocyte transfusions are indicated only in patients with severe heart failure.

FOLATE DEFICIENCY ANEMIA

Folic acid is quietly important for the formation and maturation of erythrocytes. Folate stores, half of which are in the liver, in the body of an adult are 5-10 mg. The daily requirement for folic acid is 20-50 μg. Folate deficiency leads to a decrease in the rate of DNA synthesis, resulting in the deterioration of cell proliferation, impaired erythro, granulo-and thrombopoiesis. The result is a shortened red cell cycle and the development of anemia.

Folic acid absorption occurs in the duodenal and proximal areas of the small intestine, where folic acid is metabolized by dihydrofolate reductase to 5-methyltetrahydrofolate, which is transported in blood plasma bound to proteins, a specific folate carrier protein, also albumin and transferrin. Folic acid compounds play an important role in DNA synthesis as single carbon donors in the conversion of deoxyuridine to deoxythymidine.

The vast majority of folates are transported to the liver, where they accumulate in the form of glutamate, or are activated by cofactors and are included in the metabolism. Folates are also transported to the bone marrow, since they significantly affect cell proliferation processes. The accumulation of folate in cells is a vitamin B12-dependent process. Cobalamin deficiency is accompanied by blockade of folate metabolism at the

stage of methyltetrahydrofolate formation. A small amount of folate - up to 10 mg/day is excreted in the urine.

A common cause of folate deficiency in elderly patients is malnutrition - a low content of fresh vegetables and fruits in the daily diet. A large amount of folate is found in liver, lettuce, tomatoes, meat, beans, asparagus, and yeast.

Increased use of folic acid is noted in patients with myeloproliferative processes, exfoliative dermatitis (psoriasis). Long-term medication, such as anticonvulsants (difenin, phenobarbital) or anti-TB drugs (isoniazid) leads to the destruction of folic acid in the body. Also, the development of folic-deficiency anemia is observed in patients using cytotoxic drugs (methotrexate, aminopterin), which are antimetabolites of folic acid.

Hematologic manifestations of folic deficiency anemia are similar to vitamin B12 deficiency, but neurological symptoms are not characteristic. Many elderly patients have normocytic anemia. Serum folic acid level (normally 7-28.1 nmol / l) may be erroneously normal after a meal, therefore the concentration of folate in erythrocytes (normal - 422-1464 nmol / l) more specifically reflects the stores of this vitamin in tissues. If the result reaches the lower border of the norm, the level of homocysteine should be determined - in 90% of cases with a folate deficiency, its level increases. The level of methylmalonic acid is usually normal.

Folic acid deficiency is compensated by its intake (by mouth at a dose of 5 mg three times a day for 1-2 months). In order to prevent relapse, such courses are held twice a year (their duration can be reduced to 1 month).

Myelodysplastic syndrome

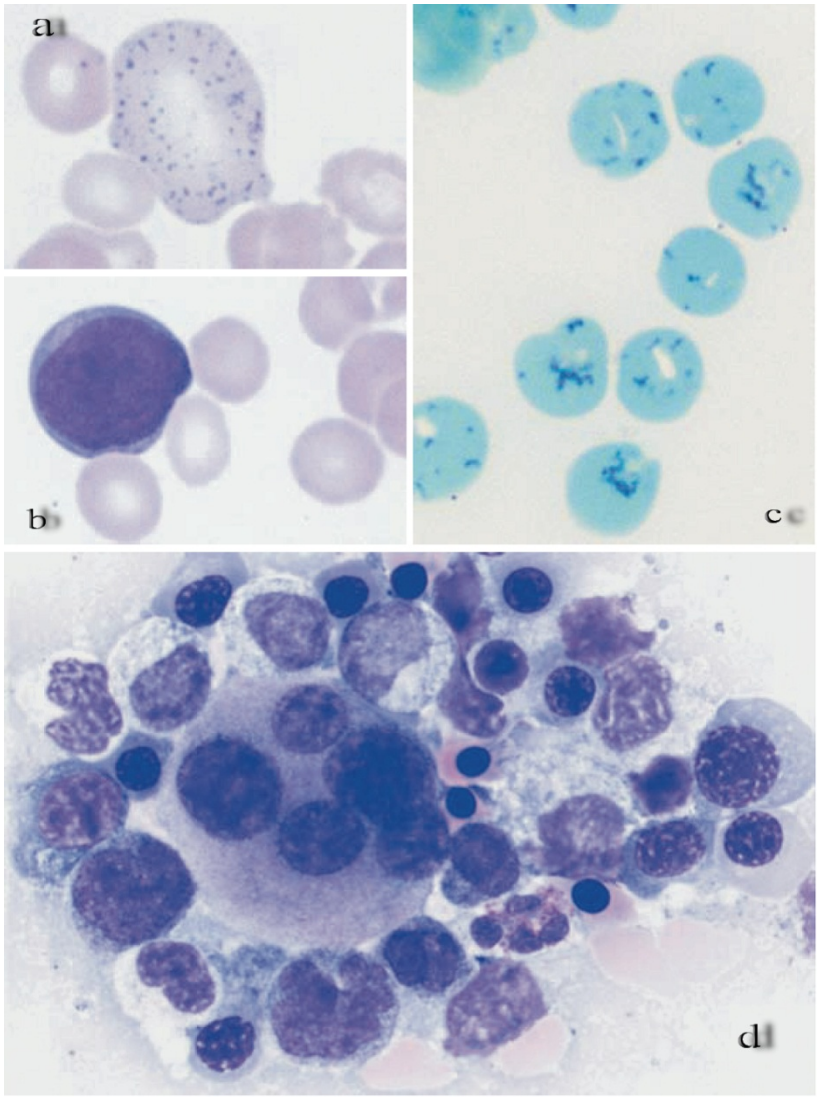
Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematopoietic stem cell diseases characterized by ineffective multiline hematopoiesis due to an increase in the number of apoptotic cells that die. The main clinical syndrome is cytopenia(s), which manifests itself in the form of various combinations of anemia, neutropenia and thrombocytopenia. There is risk of transformation of the disease to acute myeloid leukemia.

In the general population, the incidence of MDS is 5 cases per 100 thousand population, and in patients after 70 years, the incidence of the disease increases to 22-45 cases per 100 thousand population and continues to increase in elderly patients. Bone marrow biopsy is

required to confirm the diagnosis. This disease is characterized by the presence of chronic cytopenia, bone marrow hyperplasia and morphological pathology of progenitor cells in the bone marrow.

Table7. WHO 2008 classification of myelodysplastic syndromes

Nosological form	Changesinperipheralblood	Changes in the bone marrow
Refractory cytopenia with unilineage dysplasia	Unicytopeniaorbicytopenia No or rare blasts (<1%)	Unilineage dysplasia: ≥10% of cells in one myeloid lineage <5% blasts <15% erythroid precursors are ring sideroblasts
Refractory anemia Refractory neutropenia Refractory thrombocytopenia		
Refractory anemia with ring sideroblasts		
Refractory cytopenia with multilineage dysplasia		
Refractory anemia with excess blasts-1	Cytopenia(s) <5% blasts No Auer rods <1×10^9/L monocytes	Unilineage or multilineage dysplasia 5%–9% blasts No Auer rods
Refractory anemia with excess blasts-2	Cytopenia(s) 5%–19% blasts Auer rods ± <1×10^9/L monocytes	Unilineage or multilineage dysplasia 10%–19% blasts Auer rods ±
Myelodysplastic syndrome – unclassified	Cytopenias <1% blasts	Unequivocal dysplasia in less than 10% of cells in one or more myeloid cell lines when accompanied by cytogenetic abnormality considered as presumptive evidence for diagnosis of MDS <5% blasts
MDS associated with isolated del (5q)	Anemia Usually normal or increased platelet count No or rare blasts (<1%)	Normal to increased megakaryocytes with hypolobated nuclei <5% blasts Isolated del (5q) cytogenetic abnormality No Auer rods



Pic.4. Myelodysplastic syndrome a) Significant basophilic granularity in the cytoplasm of macrocytes. b) Myeloblasts with hyperchromic red blood cells. c) A significant count of reticulocytes is a sign of hemolysis (in this case with the absence of pyruvate kinase activity). d) Bone marrow with MDS (refractory anemia with an excess of blasts).

In the hypoplastic (hypoproliferative) variant of MDS, as well as in the treatment of patients with aplastic anemia, immunosuppressive therapy is used (cyclosporine, antimonocytic immunoglobulin). The main indications for its use is the confirmation of bone marrow hypoplasia. Also in the treatment regimens of elderly and senile patients DNA methyltransferase inhibitors 5-azacytidine and 2-deoxy-5 azacytidine (decitabine) are used.

When patients have severe comorbidities or they are older 75 years small doses of cytarabine are prescribed.

Patients with severe anemia (Hb <60 g/l) or manifestations of anemic syndrome (tachycardia, dyspnea, angina pectoris, syncopal states, ST segment depression) are indicated blood transfusion of the red blood cell.

The use of erythropoietin is effective only in 15-30% of patients with MDS and is carried out only after determining the erythropoietin serum level.

The only radical treatment for MDS is allogeneic hematopoietic blood stem cell transplantation (C. Cutler, 2004). However, in the elderly the use of this method of treatment may not be possible due to the absence of an HLA-compatible donor and severe concomitant pathology. In addition, carrying out allogeneic stem cell transplantation in patients over 70 is associated with high mortality due to the development of toxic and infectious complications, graft rejection, and the development of graft versus host disease.

SITUATIONAL TASKS

1. The patient is 67 years old, complains of general weakness, shortness of breath and palpitations with minimal exertion, edema of the lower extremities. The condition slowly deteriorated over six months. Objectively: the skin is pale, icteric. Tongue - crimson, smooth, with cracks. Above the lungs hard breathing, in the lower lobes a small amount of moist rales. RR - 26/min, HR - 100 / min, BP 100/70 mm Hg. The heart activity is rhythmic, systolic murmur above the apex and in the 5 point. The liver is enlarged by 4 cm, painless on palpation. Swelling of the shins, foots. ECG: sinus rhythm, total right bundle branch block, negative T wave in V4-V6 leads. Complete blood count: Er. -2.0 *10*12/l, Hb- 73 g/l, MCV -110 fL, L-2.3*10*9*/l, platelets 80*10*9/l, ESR is 43 mm/ , megalocytes 1-2, Jolly`s bodies. MCH 34 pl. Total bilirubin - 42 μmol/l, direct - 6,4 μmol/l, thymol test - 6 U, AsAT - 2.1 mmol/l * h, ALT - 2.7 mmol/l*h. Creatinine 78 μmol/l. Serum iron - 17 μmol/l, ferritin level -50 ng/ml, serum B12 level - 80 pg/l, serum folic acid level - 20 ng/ml.

Tasks:

1. Make a diagnostic search.
2. Make a plan of examination, determine the required additional research.
3. Formulate a clinical diagnosis and list the main diagnostic criteria.
4. Administer treatment and justify it.

The main clinical syndromes are heart failure (shortness of breath, edema of the lower extremities, moist rales over the lungs) and jaundice (yellow skin, hyperbilirubinemia). The cause of the development of heart failure can be a violation of the coronary circulation (coronary artery disease, myocarditis, valvular heart disease). It requires an echocardiography, coronary angiography. Jaundice can be a manifestation of viral hepatitis, therefore, it is necessary to assess the serological markers of viruses hepatitis B and C.

Also, the patient has severe hyperchromic anemia, which is confirmed by complete blood test data. Clinical symptoms can be regarded as manifestations of hemic hypoxia and anemic cardiomyopathy. The diagnosis of B12 deficiency anemia can be set on the basis of the macrocytic nature of anemia, the presence of megalobalasts in the blood, hepatomegaly and jaundice (due to the accelerated hemolysis of red blood cells), low

serum vitamin B12 level. To reveal the causes of anemic syndrome, it is necessary to assign an EGDS with biopsy. It helps to exclude the pathology of the stomach and duodenum. Alsoparasitic examination stool is required (diphyllobotriosis). Additionally, it is necessary to determine the serum levels of methylmalonic acid and homocysteine.

The patient hassuppression of all three hemopoietic sprouts, therefore it is necessary to exclude the presence of hypo-, aplastic anemia and conduct the bone marrow examination.

Clinical diagnosis: severe B12 deficiency anemia. Anemic cardiomyopathy. Congestive heart failure II B, functional class IV.

Adequate therapy includes cyanocobalamin at dailydose of 1000 mcg. It must last until hemoglobin will has normalized. Then maintenance therapy - cyanocobalamin at weekly dose of 500 mcg should be recommended.

2. A 67-year-old patient went to the doctor with complaints of heart pain, increased blood pressure to 220/120 mm Hg, headache, palpitation, shortness of breath, general weakness, nausea, dry mouth, and skin itch. She periodically noted swelling around the eyes, protein and red blood cells were detected in urine tests in the past, near 10 years ago.She was treated at the therapist but shedoes not remember the diagnosis. She haven't visited doctor during last 5 years. In last year she noticed headaches, dizziness. increased blood pressure to 180/110 mm Hg. Also she had heartbeat, shortness of breath at walking. She hadused enalapril herself and itseffect was insignificant during last 6 months. She hadincreased blood pressure constantly (180-200/100-110 mm Hg). She notednausea, episodic diarrhea, swelling of the face and lower extremities month ago. She has beenheart pain, skin itch and shortness of breath during 2 weeks. Objective examination: the skin is pale, dry, with traces of scratching, swelling of the face and legs, and anterior abdominal wall. Breath is hard, weakened in the lower lobes, rales are absent. RR - 26/min. BP-220/120 mmHg. The left border of the heart is shifted 1.5 cm outwards from the left medioclavicular line. There are muffled heart sounds, irregular rhythm (5-7 extrasystoles per minute); I tone is weakened over the tip, accent II tone over the aorta. A pericardial friction rub is heard. The tongue is dry, the abdomen is soft, painless. The liver is not enlarged, painless. The Pasternacky`s symptom is negative on both sides. Complete blood count: Er. -2,6×10^{12}/l, Hb- 72 g/l,

MCV --86 fL, L-5,7*10*9*/l, platelets 80*10*9/l, eosinophils - 2%, band cells - 3%, segments - 68%, lymphocytes - 25%, monocytes - 2%, ESR is 40 mm/h. MCH 30 pl. Urine test: yellow color, pH is neutral, specific gravity 1005, protein 3.8 g/l, leukocytes 2-4, erythrocytes 10-12, grainy cylinders 3-4, waxy cylinders -2-3 in sight.

Total bilirubin - 18 μmol/l, AsAT - 0,43 mmol/l * h, ALT - 0,45 mmol/l*h.Glucose - 3,8 μmol/l. Cholesterol - 7,5 μmol/l, creatinine 760 μmol/l, urea - 38,2μmol/l. Potassium level - 5,5μmol/l, sodium – 128μmol/l.

ECG: sinus rhythm, irregular, 106 beats per minute, single ventricular extrasystoles, the electrical axis is shifted to the left, signs of left ventricular hypertrophy. Ultrasound of the kidneys: the right kidney is 80 × 36 mm, mobile, contours are even, indistinct, the thickness of the parenchyma is 11 mm; the left kidney is 84 × 44 mm, the contours are even, indistinct, the thickness of the parenchyma is 9 mm. The parenchyma of both kidneys is “heterogeneous”, with hyperechoic inclusions. Concrementsare not found.

Tasks:

1. Make a diagnostic search.
2. Make a plan of examination, determine the required additional research.
3. Formulate a clinical diagnosis and list the main diagnostic criteria.
4. Administer treatment and justify it.

The patient has chronic renal failure, as evidenced by a combination of urinary, nephrotic syndromes, arterial hypertension, symmetric nephrosclerosis, the presence of dyspepsia, skin itching, pericardial friction rub, increased serum creatinine and serum urea level.

The patient is recommended to determine the GFR (according to the MDRD formula), the assesment of daily proteinuria, proteinogram, lipidogram, blood CBS, renal biopsy to clarify the form of glomerulonephritis and to exclude amyloidosis.Echocardiography helps to confirm pericarditis, evaluation of diastolic and systolic functions of the heart. Also patient is needed chest X-ray to exclude lung diseases.

Femalehas severe normochromic anemia according to complete blood count data. Considering the pathology of the kidneys, chronic renal failure is the main cause of the anemic syndrome. To determine the tactics of treatment in a patient, it is necessary to estimate the serum erythropoietin and serum ferritin levels.

Clinical diagnosis: Chronic kidney disease V. Chronic glomerulonephritis, mixed form, active phase. Uremic pericarditis. Symptomatic renoparenchymal arterial hypertension, stage II, grade 3, risk 4. Ventricular extrasystole. Secondary severe anemia.

The main tactic of management is the therapy of chronic renal failure. Correction of azotemia, electrolyte disturbances is should be made. The need for program hemodialysis is considered. Loop diuretics, calcium channel blockers are recommended as antihypertensive drugs.

For the treatment of anemia, subcutaneous administration of erythropoietin is appropriate (60 IU/kg/ week). If iron deficiency is diagnosed, it is necessary to prescribe iron preparations intravenously.

TESTS FOR FINAL CONTROL

1. A 30-year-old patient complains of general weakness, sweating, fever, the appearance of dense lesions on the neck to the right, up to 4 cm in size. Pale, lymph nodes are dense, painless, not soldered to the skin and with each other. The liver is not enlarged. Spleen + 2 cm, painless. Blood test: Er.-3.2*10*12/ l, Hb-95g/l, CI-0.9, L-12.5*10*9/l, e-8%, band-10%, segm.-64% , lymph.-8%, mon. 10%. ESR 40 mm/hour. Platelets 380*10*9/l. What research is needed to establish a final diagnosis?

A. Bone marrow examination

B. Abdominal ultrasound examination

C. Biopsy of the cervical lymph nodes

D. Biopsy of the spleen.

E. Chest CT scan

2. Which of the following changes in laboratory parameters is characteristic of B12-deficiency anemia?

A. Reduced color index

B. Positive sucrose sample

C. Reduced osmotic resistance of erythrocytes

D. Increased serum iron level

E. Megaloblastic type of hemopoesis

3. What symptom does not correspond to the diagnosis of iron deficiency anemia?

A. Hypochromia of erythrocytes

B. Microcytosis

C. Aniso-, poikilocytosis

D. Color index 0.7

E. Hypersegmentation of neutrophil nuclei

4. A patient of 50 years old complains of weakness, fatigue, brittle nails, hair loss. He had peptic duodenal ulcer 5 years ago. EGDS - scarring deformation of the duodenal bulb. Blood test: Er-3,6x10*12/l, Hb 90 g/l, CI-0.7, serum iron-8.7 μmol/l. What is mechanism of anemia in this case?

A. Disruption of iron transport

B. Insufficient iron intake

C. Increased iron need

D. Increased iron loss

E. Iron malabsorption

5. A 50-year-old patient complains of severe weakness, dizziness, and spots on the skin. A month ago he had a sore throat andusedantibiotics himself. Objectively: the general state is severe, the skin and mucous membranes are pale. There are blue and brown spots of different sizeon the face and body. At palpation - the stomach is painless, the liver + 1.5 cm below the right costal arch. Complete blood count: erythrocytes - 1.2x10*12/l, Hb - 50 g/l, CI 0.70, platelets - 2x10*9/l, aniso-, poikilocytosis. ESR - 55 mm hour. What is the diagnosis?

A. Acute post-hemorrhagic anemia

B. Thrombocytopenic purpura

C. Hemorrhagic vasculitis, abdominal form

D. Hemophilia

E. Multiply myeloma

6. A woman complains of severe weakness, fever, sore throat, multiple bruises on the skin. These symptoms occurred one week ago. She had tonsillitis in last month. Objectively: temperature - 38.9, RR - 24 per min., HR- 110/ in., BP-100/65 mm Hg. Pale skin, multiple petechial rash on the extremities, enlarged lymph nodes. Blood test: Hb-80g/l, Er.-2,2x10 ^12/l; Leikocytes-3,5x10 ^ 9 / l; blast cells - 62%; eos. -2%; band -3%; segm-19%; lymph.-13%; mon.1%; Platelets 35.0x10 ^ 9/l. ESR - 47 mm / hour. What research is needed to clarify the diagnosis?

A. Lymph node biopsy

B. Coagulogram, proteinogram

C. Bone marrow examination, titer of antiplatelet antibodies

D. Assesment of serum ferritin

E. Karyotyping

7. A patient of 72 years old was admitted to the clinic with complaints of chest pain, lumbarpain and general weakness. Objectively: the skin and visible mucous membranes are pale. Pulse-110 per min., BP-110/60 mm Hg. At auscultation - systolic murmur over the apex of the heart. An enlarged liver is palpated, its lower edge is 2 cm below the costal

arch. Blood test: er-3,5x10 ^12/l, Hb-90 g/l, CI-0,8; Leikocytes-9x10^ 9 / l, Platelets - 120x10^ 9/l, ESR-70 mm / h; plasma cells are found in blood smears. There is 25%of plasmocytes in the bone marrow. Serum protein - 106 g/l. Proteinuria - 1.65 g/l . Chest X-ray andscull X-ray- focal destruction of flat bones up to 0.5 cm in size. What is the most likely diagnosis?

A. Chronic myeloid leukemia

B. Metastatic to the bones of the skull, chest

C. Multiply myeloma

D. Lymphogranulomatosis

E. Acute leukemia

8. The patient was admitted to the hospital with complaints of fatigue, heaviness in the left hypochondrium. Objectively: the skin is pale, peripheral lymph nodes are not palpable. The liver is not enlarged. The spleen – on 5 sm below costal arch. The body temperature is 37-37.2 C. Complete blood count: Hb-106 g/l; Er. - 3.05*10^ 12/l; CI-0.9; Leikocytes-125 *10^9/l; basoph. 6%; eos. 9%; promyelocytes 1%; myelocytes 24%; metamyelocytes-12%; band-16%; segm.-16%; lymph-7%; platelets- 355*10^ 9/l; ESR 10 mm/hour. Myelogram: blasts -3%; immature granulocytes-50%; mature (band cells and segment cells) -35%; erythroblasts 12%; large number ofmegakaryocytes. The Philadelphia chromosome was found in the bone marrow cells. What disease can we suppose?

A. Lymphogranulomatosis

B. Chronic myeloid leukemia

C. Acute myeloid leukemia

D. Multiply myeloma

E. Chronic lymphocytic leukemia

9. Which of the following laboratory parameters allows makingdiagnose autoimmune hemolytic anemia?

A. Determination of osmotic resistance of erythrocytes

B. Erythrocyte autohemolysis test

C. Sucrose test

D. Coombs`test

E. Reticulocytosis

10. What anemia is characteristic by microspherocytosis?

A. Addison-Birmeranemia

B. Minkowski-Chauffard disease

C. Thalassemia

D. Fanconianemia

E. Marcifera-Michelianemia

11. A 24-year-old patient has intensive headache, general weakness, dizziness, bleeding (nasal bleeding, hemorrhages on the skin and mucous membranes) during the last two months. Lymph nodes, liver and spleen are not enlarged. Blood test: Hb-50 g/l, Er-1.6x10* 12/l, CI-1.0, Leikocytes-2.0x10*9/ l, band 1%, segm.-35%, eos. 1%, bas. 1 %, lymph.-10%, mon. 4%, platelets - 30x10*9/l. What is the probable diagnosis?

A. Aplastic anemia

B. B12-deficiency anemia

C. Iron deficiency anemia

D. Acute leukemia

E. Hemolytic anemia

12. A 72-year-old man complaints of severe general weakness, poor appetite, weight loss, jointpain, and heaviness in the right hypochondrium. Complete blood count: Er-3,4x10^12/l, Hb-102 g/l, CI-0.9; platelets - 240x10^9/l, Leikocytes-138x10^9/l, blasts 1%, promyelocytes-2%, myelocytes-13%, younger-12%, band-16%, segments-31%, basophils-3%, eosinophils-8%, l 9%, mon. 9%, ESR-30 mm/hour. What is the diagnosis?

A. Leukemoid reaction

B. Chronic lymphocytic leukemia

C. Chronic myeloid leukemia

D. Acute leukemia

E. Erythremia

13. The patient of 67 years complains of general weakness, dizziness, shortness of breath. Objectively: the skin is pale, the eyesare subicteric. Heart sounds are weak, systolic murmur at the apex. HR - 110/min. The tongue is red, smooth. Blood test: Er. - 2.7x10*12 / l, Hb- 100 g/l, CI - 1.4; L - 4.2x10* 9/l; Jolly bodies, poikilocytosis, ESR - 20 mm/hour,

total bilirubin - 28 μmol/l. EGDS: atrophic gastritis. What drug doadminister this patient?

A. Cyanocobalamin

B. Actiferin

C. Vitamin B 1

D. Folic acid

E. Prednisone

14. In a 42-year-old woman with uterine fibromyoma and menorrhagia, anemia was detected: Hb - 80 g/l, hypochromia and erythrocyte microcytosis. The most likely diagnosis is:

A. Sickle cell anemia

B. B 12 deficiency anemia

C. Iron deficiency anemia

D. Aplastic anemia

E. Hereditary spherocytosis

15. For which of the listed diseases are the following hematological indicators characterized: anemia, leukopenia, an increased number of plasma cells in the bone marrow?

A. Chronic myeloid leukemia.

B. Chronic lymphocytic leukemia.

C. Acute leukemia.

D. Lymphogranulomatosis.

E. Multiply myeloma.

16. A 64-year-old woman during the last 2 months had shortness of breath, palpitation, and dull heart painat walking. BP - 90/60 mm Hg, heart rate - 88/min. Blood test - Er. - 3.2x10*12/l, Hb - 90 g/l, CI - 0.87. Leukocytes - 6.8x10*9/l. ECG - T waves inversion in V1-V3. Heart ultrasound: left ventricular hypertrophy. What is the most likely cause of cardialgia?

A. New onset angina pectoris

B. Anemic heart

C. Thyrotoxic heart

D. IHD: stable angina, FC III

E. Postmenopausal cardiomyopathy

17. A female complaints of bruising, hemorrhagic rash on the body and mucous membranes, and nasal bleedings. These symptoms occurred 10 days ago after ARVI. Blood test: Er-3,4x10^12/l, Hb-94 g/l, CI-1.0; platelets - 20x10^9/l, Leukocytes-12x10^9/l, eosinophils-3%, band-2%, segm.-68%, lymph. 29%, mon. 8%, ESR-25 mm/hour. The Duke bleeding - 8 min, retraction of the blood clot - in 72 hours. Which medication would be the most appropriate?

A. Ascorbic acid

B. Vitamin B12

C. Heparin

D. Platelet mass

E. Prednisolone

18. A woman complaints of general weakness, fatigue, fever up to 37.5^{o}C. Objective examination - icteric sclera, enlarged liver. Blood test: Er-2.5x10 ^ 12, Hb-90g/l, CI-1.1; Leukocytes2,5x10^ 9/l; platelets.-152x10^9, reticulocytes-0.6%. Total bilirubin-38 μmol/l, indirect bilirubin-30 μmol/l. Myelogram - megaloblastic type of blood formation. What is the most likely diagnosis?

A. Iron deficiency anemia

B. Congenital hemolytic anemia

C. B 12 deficiency anemia

D. Folic acid deficiency anemia

E. Acquired hemolytic anemia

19. Which anemia is characterized by splenomegaly?

A. Markiapha-Micheli

B. Post-hemorrhagic

C. Aplastic

D. Iron deficiency

E. Minkowski-Chauffard

20. A 64-year-old patient was hospitalized with renal colic. He complains of back pain, frequent urination, weakness, dizziness. Objectively: the skin is pale, the pulse is 92/min,

BP is 90/50 mm Hg, systolic murmur at the apex of the heart. Blood test: Hb-80g/l, Er.-3.1 * 10^12/l, Platelets - 50*10^9/l; Leukocytes- 8 * 10^9/l. Urine test: L-6-8, red blood cells cover the entire field of view. Protein – 0.5 g/l. What is the most likely diagnosis for this patient?

A. Acute glomerulonephritis

B. Thrombocytopenic purpura, renal bleeding

C. Chronic pyelonephritis

D. Chronic glomerulonephritis

21. Which of the following research methods is the most informative to establish the diagnosis of multiple myeloma?

A. Electrophoresis of serum proteins.

B. Bone X-ray

C. Bone marrow examination

D. Assessment of serum calcium.

E. Urine test

22. Patient with B12-deficient anemia and clinical manifestations of the funicular myelosis is needed the daily dose of cyanocobalamin:

A. 2000 mcg

B. 1000 mcg

C. 100 μg

D. 400 μg

E. 200 μg

23. The patient has pain in the tubular bones which appeared after a sore throat. Objectively: generalized enlargement of the lymph nodes, hepatosplenomegaly. Blood test: red blood cells - 3.0*10*12/l, hemoglobin -80 g/l, leukocytes - 18*10*9/l, blasts - 54%, lymphocytes - 46%, platelets - 50 * 10^9 / l, ESR - 65 mm/hour. What is the diagnosis?

A. Acute leukemia.

B. Chronic myeloid leukemia

C. Multiply myeloma

D. Chronic lymphocytic leukemia

E. Aplastic anemia

24. Complete blood count: Er. 1.3*10*12 l, Hb 58g/l, CI 1.3, megaloblasts 2/100, reticulocytes 0.2%, leukocytes 2.8*10*9/l, eos 2%, band 8%, segm. 45%, lymph. 40%, mon. 5%, platelets 70*10*9/l, ESR 30 mm/h, anisocytosis, poikilocytosis, macrocytosis.Make a diagnosis.

A. Aplastic anemia.

B. Hemolytic anemia.

C. Iron deficiency anemia

D. B - 12-deficiency anemia

E. Agranulocytosis.

25. The patient is 43 years old, complains of weakness, sore throat at swallowing, fever up to 39°C. Objectively: pale skin, solitary bruises on the hips. Necrotic changes in the tonsils. Sternalgia. The liver is not enlarged. The spleen protrudes on 3 sm below left hypochondrium. Blood test: Er. 2.0x10*12/l, Hb-70 g/l, platelets- 40x10*9/l, leukocytes - 28.8x10 * 9/l, blasts 60%, band 1%, segm- 10% , lymph 29%. ESR - 60 mm / hour. Your diagnosis is:

A. Acute leukemia

B. Thrombocytopenic purpura

C. Hypoplastic anemia

D. Chronic lymphocytic leukemia

E. Chronic small leukemia

26. A woman notes general and muscular weakness, shortness of breath, dizziness, brittle hair and nails, the desire to eat chalk. She has uterine fibroids. Blood test: Er. 2.8 T/l, hemoglobin 80 g/l, color index 0.78, anisocytosis, poikilocytosis, serum iron - 10 μmol/l. What is the most likely diagnosis?

A. Autoimmune-hemolytic anemia

B. Hypoplastic anemia

C. Iron deficiency anemia

D. B12 - deficiency anemia

E. Aplastic anemia

27. What disorders are not typical for hypoplastic anemia?

A. Ulcerative - necrotic processes.

B. Low red blood cells and hemoglobin

C. Thrombocytopenia

D. Increased leukocytes

E. Antibodies to red blood cells, leukocytes, thrombocytes.

28. Complete blood count: Er. 3.5 *10*12/l, Hb 110 g/l, leukocytes 130*10*9/l, basophils 5%, eos. 9%, promyelocytes 2%, myelocytes 22%, metamyelocytes 21%, band 10%, segm. 17%, lymphocytes 9%, monocytes 5%, platelets 38*10*9/l, ESR 20 mm/h.Make a diagnosis:

A. Chronic lymphocytic leukemia.

B. Chronic myeloid leukemia

C. Lymphogranulomatosis

D. Acute myeloid Leukemia.

E. Acute lymphocytic leukemia

29. What is the indicator of peripheral blood to assess the regenerative capacity of the bone marrow?

A. Erythrocytes

B. Megakaryocytes

C. Reticulocytes

D. Leukocytes

E. Erythroblasts

30. The patient complains of severe pain in the lower back, ribs, fever, weakness. For a long time was under the supervision of a neurologist about severe radicular syndrome. He had compression fracture L1-L2 one year ago. Objectively: t-37.1, BP 140/85 mm Hg,HR-80/min. Palpation marked tenderness along the ribs and spine. Liver +2 cm, spleen is not enlarged. There is no edema. Blood test: Hb-70g/l, Er. -2.2x10 ^12/l; Leukocytes-3,5x10 ^/l; eos-2%; band -5%; segm-55%; lymph-34%; Mon.4%; Platelets-35.0x10^ 9/l; ESR -67 mm/hour. These changes are more typical for?

A. Lymphoid proliferation

B. Myelofibrosis

C. Plasma cell proliferation

D. Depression of blood formation

E. Myeloid proliferation

31. A 67-year-old female was admitted to the hematology department with complaints of pain in the lumbar region, in the right hypochondrium, and severe general weakness. She had the flu a week ago. Examination: the skin is pale and yellow, the liver 1 cm protrudes from the edge of the costal arch, sensitive. Blood test: Er.-1,7x10^12/l, Hb-64 g/ , CI-0.9; Leuc. 12.0 x10^9/l; reticulocytes-8%. Total bilirubin-38 μmol/l, indirect bilirubin-30 μmol/l. The direct Coombs` test is positive. What is the diagnosis?

A. Sideroachristic anemia

B. Addison-Birmer`s disease

C. Acquired immune hemolytic anemia

D. Marchiafava–Micheli syndrome.

E. Congenital hemolytic anemia

32. A woman notes general and muscular weakness, shortness of breath, dizziness, brittle hair and nails, the desire to eat chalk. She has uterine fibroids. Blood test: erythrocytes 2.8 *10*12/l, hemoglobin 105 g/l, color index 0.8, anisocytosis. What additional research will help to verify the diagnosis?

A. Serum iron

B. Coagulogram

C. Serum Vitamin B12

D. Serum ferritin

E. Osmotic resistance of erythrocytes

33. A 56-year-old woman complains of general weakness, increased brittle nails, and hair loss. Objectively: pulse 94/min, blood pressure 110/70 mm Hg. Skin is pale. Blood test: Hb 90 g/l, Er. - 3.5 x 10*12/l, CI - 0.7, ESR - 20 mm/hour. Serum iron - 8.7 μmol/l, feritin - 9 ng/ml. What is therapy is the most appointment for this patient?

A. Vitamin B12 i/m

B. Iron per os

C. Hemotransfusion

D. Folate acid

E. Iron transfusion

34. Which of these changes in peripheral blood is characteristic for B 12-folate deficiency anemia?

A. Thrombocytosis

B. High color index

C. Eosinophilia

D. Reticulocytosis

E. Leukocytosis

35. A severe general weakness and jaundice are appeared in a patient with chronic lymphocytic leukemia. Blood test: Er-2.1*10*12/l; Hb - 65g/l, color index-1.0; reticulocytes - 5%. Total bilirubin - 80.3 μmol/l, indirect - 65.3 μmol/l. What is the leading pathogenesis of anemia?

A. Folic acid deficiency

B. Autoimmune hemolysis

C. Violation of porphyrin metabolism

D. Inhibition of the erythroid branch of hemopoiesis

E. Erythropoietin deficiency

36. Pathogenetic therapy of megaloblastic anemia is:

A. Iron preparations

B. Vitamin B1

C. Splenectomy

D. Corticosteroids

E. Vitamin B12

37. What changes are the most characteristic of multiple myeloma?

A. Hyperproteinmia with M-gradient

B. Hypocalciemia

C. Hyperproteinemia

D. Hypoalbuminemia

E. Hyperkalemia

38. A 62-year-old patient complains of weakness, shortness of breath, a burning sensation in the tongue, numbness in the extremities. Objectively: pallor, pasty crus. Pulse - 140 per min., blood pressure - 130/80 mm Hg. Heart tones are weakened, with systolic murmur at

the apex. Tongue is like raspberry, "varnished." The liver is + 2 cm, the spleen is + 1 cm. Blood test: Er - 2.0x10^12/l, Hb - 60 g/l, L - 2.5x10*9/l, eos - 1%, band -5%, segm. - 57%, lymph. - 36%, mon. - 1%, ESR - 62 mm/h, megaloblasts, Cabot rings, Jolly bodies. What is the most likely diagnosis?

A. B12-folate deficiency anemia

B. Hemolytic anemia

C. Sideroachristic anemia

D. Aplastic anemia

E. Iron deficiency anemia

39. 65-year-old patient noted oliguria after taking sulbactam. Objectively: jaundice,pale skin, spleen is enlarged. Blood test: Er.-2,2x10 *12/l, Hb 60 g/l, CI 0.62, L-14x10 *9/l, reticulocytes 24%. Indirect bilirubin 35 μmol/l. Urine and feces have dark color, high stercobilin level in urea. What is the most likely diagnosis for this patient?

A. Toxic hepatitis

B. Obstructive jaundice

C. Hemolytic anemia

D. Aplastic anemia

E. Acute leukemia

40. Blood test: er-3.4x10 *12/l, Hb-94 g/l, CI-1.0; Leucocytes 12x10 * 9/l, platelets-20x x10 *9/l, eos.-3%, band-2%, segm.-68%, lymph. 29%, mon. 8%, ESR-25 mm/h, anisocytosis. The duration of bleeding by Duke is 8 minutes, plasma recalcification time is 80 sec, PTI - 84%, the blood clot retraction took place after 72 hours.What is the most likely diagnosis?

A. Werlhoff's Disease

B. Willebrand Disease

C. Hypoplastic anemia

D. Schönlein-Henoch disease

E. Hemophilia

41. Jolly bodies are typical for anemia:

A. Iron deficiency anemia

B. Aplastic anemia.

C. B - 12-deficiency anemia

D. Hemolytic anemia.

E. Sickle cell anemia

42. Blood test: Er. 2.8*10*12/l, Hb 80 g/l, CI 0.8, reticulocytes 20%. Leukocytes 7.5 * 10 * 9/l, eos 2%, band 4%, segm. 54%, lymph. 37%, mon. 3%, platelets 200*10*9/l, ESR 15 mm / h, microsphereocytes. What is preliminary diagnosis?

A. Minkowski-Chauffard disease

B. Acute post-hemorrhagic anemia

C. Folic deficiency anemia

D. B - 12 deficiency anemia

E. Iron deficiency anemia

43. A 60-year-old woman at the last year had weakness, dizziness, fatigue. Recently shortness of breath, paresthesia have been occurred. The skin and mucous membranes are pale and icteric. Nipples tongue smoothed. Liver, spleen - at the edge of the costal arch. Blood test: hemoglobin -70 g/l; red blood cells -1.7 x 10*12/l, CI - 1.2; macrocytes. The administration of which drug is pathogenetically justified:

A. Ascorbic acid

B. Vitamin B1

C. Vitamin B12

D. Vitamin B6

E. Iron preparations

44. Female 52 years old. The skin is pale, with numerous petechiae and ecchymosis. Peripheral lymph nodes are not enlarged. HR-110/min, BP 110/70 mm Hg. There is systolic murmur at heart auscultation. The abdomen is soft, painless, the liver and spleen are not palpated. Blood test: Er.-2.5 *10*12/l, Hb-70 g/l, CI-0.7, leucocytes-6.4 * 10*9/l, band neutrophils - 3%, segmented -67%, lymphocytes-25%, monocytes-5%, platelets 15.0 *10*9/l, ESR - 30 mm/hour. Myelogram: megakaryocytes are not surrounded by platelets. What pathogenetic treatment is indicated for this patient?

A. Iron preparations

B. Platelet transfusion

C. Cyclophosphamide

D. Prednisolone

E. Cryoprecipitate

45. Which of these laboratory indicators is the most characteristic of hemolytic anemia?

A. Reticulocytosis

B. Low erythropoietin level

C. Hyperthrombocytosis

D. Bleeding

E. Increased serum transferrin

46. Which study is the most informative for the diagnosis of hypoplastic anemia?

A. Complete blood count

B. Bone marrow examination

C. Osmotic resistance of erythrocytes

D. Desferal test

E. Coomb's Test

47. The patient, 68 years old, was hospitalized with severe anemia. After examination atrophy of the papillae of the tongue surface, sclera jaundice, symmetrical paresthesias, gait disturbance, atrophic gastritis with achlorhydria, splenomegaly and macrocytosis were revealed. What research should start to clarify the genesis of anemia?

A. Serum Vitamin B12

B. Bone marrow examination

C. Serumferritin

D. Osmotic resistance of erythrocytes

E. Serum iron

48. What laboratory index is the most characteristic of hemolytic anemia?

A. Increased serum transferrin

B. Reticulocytosis

C. Low erythropoietin level

D. Hypertrombocytosis

E. Bleeding

49. Blood test: Er. 1.3*10^12/l, Hb 58g/l, CI 1.3, megaloblasts 2:100, reticulocytes 0.2%, leukocytes 2.8*10*9/l, E 2%, B 8%, S 45% , L 40%, M 5%, platelets 70*10*9/l, ESR 30 mm / h, anisocytosis, poikilocytosis, macrocytosis. Make a diagnosis:

A. Iron deficiency anemia

B. B - 12-deficiency anemia

C. Aplastic anemia.

D. Hemolytic anemia.

E. Agranulocytosis.

50. What disorders are not characteristic of hypoplastic anemia?

A. Reducing the number of red blood cells and blood hemoglobin levels

B. Thrombocytopenia

C. Lukocytosis

D. Ulcerative - necrotic processes

E. Antibodies to red RBC, WBC, platelets.

51. Blood test: Er. 2.8*10*12/l, Hb 80 g/l, CI 0.8, reticulocyte 20%. Leukocytes 7.5*10*9/l, eos. 2%, band. 4%, segm. 54%, L 37%, M 3%, platelets 200*10*9/l, ESR 15 mm / h, microsphereocytes. What is preliminary diagnosis?

A. B - 12 deficiency anemia

B. Folate deficiency anemia

C. Minkowski-Chauffard disease

D. Iron deficiency anemia

E. Acute post-hemorrhagic anemia

52. A 42-year-old woman with uterine fibroids and menorrhagia has anemia: Er. 2.74*10*12/l,Hb - 80 g/l, hypochromia and microcytosis. What is the most likely diagnosis?

A. B 12 deficiency anemia

B. Sickle cell anemia

C. Aplastic anemia

D. Hereditary spherocytosis

E. Iron deficiency anemia

53. What symptom does not correspond to the diagnosis of iron deficiency anemia?

A. Color index 0.7

B. Hypochromia of erythrocytes

C. Microcytosis

D. Aniso-poikilocytosis

E. Hypersegmentation of neutrophil nuclei

54. When anemia is observed microspherocytosis?

A. Fanconi

B. Marcifera-Micheli

C. Addison-Birmer

D. Minkowski-Chauffard

E. Thalassemia

55. Jolly bodies are typical for anemia:

A. B - 12 deficiency anemia

B. Aplastic anemia

C. Sickle cell anemia

D. Iron deficiency anemia

E. Acute post-hemorrhagic anemia

56. A woman notes general and muscular weakness, shortness of breath, dizziness, brittle hair and nails, the desire to eat chalk. She has uterine fibroids. Blood test: erythrocytes 2.8 *10*12/l, hemoglobin 105 g/l, color index 0.8, anisocytosis. What additional research will help to verify the diagnosis?

A. Serum Vitamin B12

B. Serum iron

C. Osmotic resistance of erythrocytes

D. Coagulogram

E. Serum ferritin

57. The patient, 68 years old, was hospitalized with severe anemia. At examination: atrophy of the papillae of the tongue surface, sclera jaundice, symmetrical paresthesias, gait disturbance, atrophic gastritis with achlorhydria, splenomegaly and macrocytosis were revealed. What research should be undertaken to clarify the genesis of anemia?

A. Serum Vitamin B12

B. Bone marrow examination

C. Osmotic resistance of erythrocytes

D. Serum iron

E. Serumferritin

58. A 73-year-old patient complains about a feeling of heaviness in the left hypochondrium. Objectively - hypersplenomegaly. Blood test: Er - 3.1x10*12/l, Hb - 104 g/l, L - 126 x 10*9/l, promyelocytes - 3%, myelocytes - 5%, young - 9%, band - 17 % segm - 48%, eos - 7%, basoph.. - 3%, lymph. - 8%, platelets - 580x10*9/l, ESR - 24 mm/hour. What disease can you think about?

A. Acute myeloid leukemia

B. Chronic myeloid leukemia

C. Chronic lymphocytic leukemia

D. Hemolytic anemia

E. Aplastic anemia

59. A 60-year-old patient complains of weakness, sweating, weight loss, and dull pain in the left hypochondrium. Objectively: the skin is pale, moist. Lymph nodes are not enlarged. The liver +3 cm, the lower spleen border - at the level of the navel, painless, dense. Blood test: Er. - 3,0x10*12/*l, Hb - 100 g/l, Leucocytes. - 96.0x10*9/l, myeloblasts - 2%, promyelocytes - 4%, metamyelocytes - 8%, band - 12%, segment. - 52%, eosin. - 5%, basoph. - 5%, lymph. - 12%, platelets - 200.0 × 10*9/l. ESR - 56 mm/hour. What is your diagnosis?

A. Acute myeloid leukemia

B. Leukemoid reaction of myeloid type

C. Chronic myeloid leukemia

D. Chronic lymphocytic leukemia

E. Multiply myeloma

60. A 56-year-old patient complains of nasal, gingival, uterine bleeding, weakness, shortness of breath. Objectively: the skin is pale, there are bruises on the front surface of the thighs, and the stomach. Systolic murmur at the apex of the heart, heart rate - 98/min, blood pressure - 100/70 mm Hg. The liver and spleen are not enlarged. Blood test: er. - 2.8 x 10*12/l, Hb - 76 g/l, CI-0.81, Leuc. - 9.2×10*9/l, platelets - 32 × 10*9/l, ESR - 22

mm/hour. Duration of bleeding 18 min. The indications for splenectomy for this disease are:

a) lack of effect of glucocorticoids

b) incomplete effect of hormones within 1-2 months of therapy

c) incomplete effect of hormones during 3-4 months of therapy

d) debut of the disease with severe bleeding, hemorrhage

e) lack of effect of local hemostatic agents

A. a, b

B. a, c

C. d, e

D. b, c

E. a, d

61. B 12-deficiency anemia can occur against the background of all states except for:

A. Pregnancy

B. Chronic gastritis with secretory insufficiency

C. Gastric cancer

D. Gastric resection

E. Malabsorption syndrome

62. The causes of folic-deficiency anemia can be everything except for:

A. taking anticonvulsants

B. vegetarianism

C. alcohol abuse

D. RBC hemolysis

E. severe liver disease

63. Treatment of folate-deficiency anemia is carried out by prescribing:

A. folic acid orally

B. Vitamin B12

C. Vitamin B12 and folic acid

D. combination of vitamins C, B12 and folic acid

E. Special diet

64. When a patient has megaloblastic anemia of unspecified origin you should prescribethis drug for initialtherapy

A. Vitamin B12

B. Prednisolone

C. Vitamins B6 and B1

D. Folic acid

E. Iron preparations

65. What is not typical for B12-deficiency anemia:

A. the presence of symptoms of funicular myelosis in patients

B. megaloblastic type of blood formation

C. hyperchromic anemia

D. hypochromic anemia

E. decreased white blood cell count

66. The erythrocyte sedimentation rate is affected by all factors except for:

A. proteins of the acute phase

B. increased concentration of immunoglobulins

C. hypoalbuminemia

D. pregnancy

E. anemia

67. After the administration of vitamin B12 in patients with B12-deficiency anemia, reticulocytosis is expected in:

A. 12-14 days

B. 2-3 days

C. 4-5 days

D. 16-18 days

E. in a month

68. All statements about the causes of iron deficiency anemia are correct, except for:

A. frequent repeated bleeding

B. impaired iron absorption

C. increased iron loss (lactation, pregnancy)

D. deficiency of intrinsic factor

E. vegetarianism

69. What changes in peripheral blood are characteristic for iron deficiency anemia?

A. Hypochromic, microcytic

B. Hyperchromic, macrocytic

C. Normochromic, macrocytic

D. Hyperchromic microcytic

E. Hypochromic macrocytic

70. The myelogram in the patient with B12-deficient anemia is characterized by:

A. megaloblastic type of blood formation.

B. normoblastic type of blood formation with erythroid germ irritation.

C. the bone marrow is devastated

D. changed the picture of the bone marrow

E. myeloblastic hematopoiesis

71. A 68-year-old patient complains of weakness, sweating, and weight loss of 10 kg over 2 years. There areenlarged liver, spleen and all groups of lymph nodes. Blood test: HB - 85 g/l, Er -3.0 x 10*12/l, Leucocytes 135.0 x10*9/l, band - 3%, lymph. - 96%, mon. - 1%, ESR - 28 mm/hour. Total bilirubin 45 μmol/l, direct - 11 μmol/l. Serum iron - 28 mmol/l, ferritin level - 46 ng/ml, Coombs` test is positive. The required research method to confirm the diagnosis is:

A. Complete blood count

B. Bone marrow examination

C. Determination of osmotic resistance of erythrocytes

D. Lymph node

E. Spleenbiopsy

72. What disease corresponds to this blood test: Hb - 90 g/l, Er. - 4.5*10^12/l, CI-0.72, l. - 4.5*10^9/l, band. - 3%, segm. - 57%, eos. - 1%, mon. - 9%, reticulocytes - 12%, lymph. - 30%, platelets - 180 * 10^9/l, ESR - 15 mm/hour.

A. B 12 deficiency anemia

B. Chronic myeloid leukemia

C. Iron deficiency anemia

D. Hemolytic anemia

73. A 68-year-old patient complains of weakness, sweating, and weight loss of 10 kg over 2 years. There areenlarged liver, spleen and all groups of lymph nodes. Blood test: HB - 85 g/l, Er -3.0 x 10*12/l, Leucocytes 135.0 x10*9/l, band - 3%, lymph. - 96%, mon. - 1%, ESR - 28 mm/hour. Total bilirubin 45 μmol/l, direct - 11 μmol/l. Serum iron - 28 mmol/l, ferritin level - 46 ng/ml, Coombs` test is positive. What is the cause of the severe clinical patient state?

A. Blast crisis

B. Gastrointestinal bleeding

C. Autoimmune hemolysis

D. Acute hepatitis

E. Agranulocytosis

74. Blood test: Hb - 60 g/ , Er. - 1.8 * 10^12/l, CI-1.11, platelets 60 * 10^9/l, leucocytes- 2.0*10^9/l, eos. - 3%, mon. -7%, lymph. - 46%, band.- 4%, segm. - 30%, anisonitosis, poikilocytosis, ESR - 15 mm/ hour. Total bilirubin 40 μmol/l, direct - 12 μmol/l. What is the most probable disease?

A. Hypoplastic anemia

B. Hemolytic anemia

C. B 12 - deficiency anemia

D. Cancer metastases in the bone marrow

E. Iron deficiency anemia

75. Blood test: Hb - 60 g/l, Er. - 2.0*10^12/l, CI - 1.0, reticulocytes - 1%, platelets - 30 * 10^9/l, leucocytes - 1.8 *10^9/l, band. - 1%, segm. - 14%, eos. - 3%, mon.- 5%, basoph.- 1%, lymph. - 76%, ESR - 15 mm/h, anisocytosis, poikilocytosis. Total bilirubin - 18 μmol/l, spleen and lymph nodes are not enlarged. What is the most likely pathological process?

A. B 12 deficiency anemia

B. Iron deficiency anemia

C. Aplastic anemia

D. Acute leukemia

E. Systemic lupus erythematosus

76. Blood test: Hb - 150 g/l, Er. - 5.0*10^12/l, CI - 1.0. Leucocytes - 1.0 * 10 ^ 9/l, band. 1%, segm. - 2%, eos. 3%, basoph. - 1%, mon. - 6%, lymph. - 84%, plasmatic calls - 3%, platelets 180 *10^9/l, ESR - 50 mm/h.What is the most likely pathology?

A. Leukemoid reaction

B. Chronic lymphocytic leukemia

C. Aplastic anemia

D. Systemic lupus erythematosus

E. Agranulocytosis

77. 68-year-old patient complains of weakness, sweating, and weight loss of 10 kg over 2 years. There areenlarged liver, spleen and all groups of lymph nodes. Blood test: HB - 85 g/l, Er -3.0 x 10*12/l, Leucocytes 135.0 x10*9/l, band - 3%, lymph. - 96%, mon. - 1%, ESR - 28 mm/hour. Total bilirubin 45 μmol/l, direct - 11 μmol/l. Serum iron - 28 mmol/l, ferritin level - 46 ng/ml, Coombs` test is positive.What is your diagnosis?

A. Acute leukemia

B. Chronic lymphocytic leukemia

C. B-12 deficiency anemia

D. Chronic myeloid leukemia

E. Autoimmune hemolytic anemia

78. A 72-year-old patient complains of general weakness, dizziness, shortness of breath, pain, a feeling of heaviness in the epigastrium after eating. Objectively: icteric skin, palpation - epigastric pain, moderate hepato-, splenomegaly. Blood test: Er. 2.5x10*12/l, Hb - 88 g/l, reticulocytes - 0.2%. CI 1,1. Leucocytes- 3,2 × 10*9/l, eos- 2, band. - 2, segm. 68, lymph. 24, mon. - 4. Platelets-150×10*9/l. ESR 22 mm/hour. Total bilirubin - 42 mmol/ , indirect 33 mmol/l. Prescribe treatment:

A. Tardiferon

B. Cyanocobalamin

C. Hemotransfusion

D. Pantoprazole

E. Prednisolone

79. Most often MDS develops as a result of:

A. Vitamin B12 deficiency

B. Disruption of erythropoietin production

C. Impaired function of polypotent stem cell

D. Development of autoimmune anti-erythrocyte antibodies

E. Folic acid deficiency

80. A 66-year-old patient complains of weakness, sweating, and weight loss of 10 kg over 2 years. There areenlarged liver, spleen and all groups of lymph nodes. Blood test: Hb - 85 g/l, Er -3.0 x 10*12/l, Leucocytes 135.0 x10*9/l, band - 3%, lymph. - 96%, mon. - 1%, ESR - 28 mm/hour. Total bilirubin 45 μmol/l, direct - 11 μmol/l. Serum iron - 28 mmol/l, Coombs` test is positive. What is required test to confirm the diagnosis?

A. Assessmentof osmotic resistance of erythrocytes

B. Bone marrow examination

C. Liver biopsy

D. Lymph node biopsy

E. Assessment of anti-erythrocyte antibodies

Standards of answers

1	C	21	C	41	C	61	A
2	E	22	B	42	A	62	D
3	E	23	A	43	C	63	A
4	D	24	D	44	D	64	A
5	B	25	A	45	A	65	D
6	C	26	C	46	B	66	D
7	C	27	D	47	A	67	C
8	C	28	B	48	B	68	D
9	D	29	C	49	B	69	A
10	B	30	C	50	C	70	A
11	A	31	C	51	C	71	C
12	C	32	D	52	E	72	D
13	A	33	B	53	E	73	C
14	C	34	B	54	D	74	C
15	E	35	D	55	A	75	C
16	B	36	E	56	E	76	B
17	E	37	A	57	A	77	B
18	C	38	A	58	B	78	B
19	E	39	C	59	C	79	C
20	B	40	A	60	E	80	B

Annex1

Basic laboratory parameters in healthy adults

A complete blood count

Red blood cells (RBC), 10 cells12 steps per liter of blood (10*12/l, tera/litr) men women	 4,4 – 5,0 3,8 – 4,5
Hemoglobin (HBG, Hb), gramsper liter of blood (g/l) men women	 130 – 160 120 – 140
Hematocrit (HCT),% men women	 39 – 49 35 – 45
Color index (ЦП)	0,8 – 1,0
Mean corpuscular volume(MCV), femtolitr (fl)	80 – 100
Mean cell hemoglobin (MCH), picogram (pg)	26 – 34
Mean corpuscular hemoglobin concentration (MCHC), grams per deciliter (g/dl)	3,0 – 37,0
AnisocytosisRBC (RDW),%	11,5 – 14,5
Reticulocytes (RET) % ‰	 0,2 – 1,2 2,0 – 12,0
Leucocytes (WBC), 10 cells 9 steps per liter of blood (10*9/l, giga/liter)	4,0 – 9,0
Basophyles (BASO),%	0 – 1
Basophyles(BASO),10*9/л (абсол. значения)	0 – 0,065
Eosiniphyles (EO),%	0,5 – 5
Eosiniphyles(EO),10*9/л	0,02 – 0,3
Neutophyles (NEUT),% Myelocytes,% Young,% Band cells,% Absolute values,10*9/ l Segment cells,% Absolute values,10*9/l	47 – 72 0 0 1 – 6 0,04 – 0,3 47 – 67 2,0 – 5,5
Lymphocytes (LYM),%	19 – 37
Lymphocytes(LYM),10*9/л	1,2 – 3,0
Monocytes (MON),%	3 – 11
Monocytes(MON),10*9/л	0,09 – 0,6
Platelets (PLT),10*9/л	180,0 – 320,0
Mean plateletsvolume (MPV), flormcm^3	7 – 10
Anisocytosisplatelets(PDW),%	15 – 17
Trombocrit (PCT),%	0,1 – 0,4
Erythrocyte sedimentation rate (ESR), mm/hour	

men women	1 – 10 2 -15

The cellular composition of the bone marrow of an adult

(by V.V.Sokolov andI.A. Gribova)

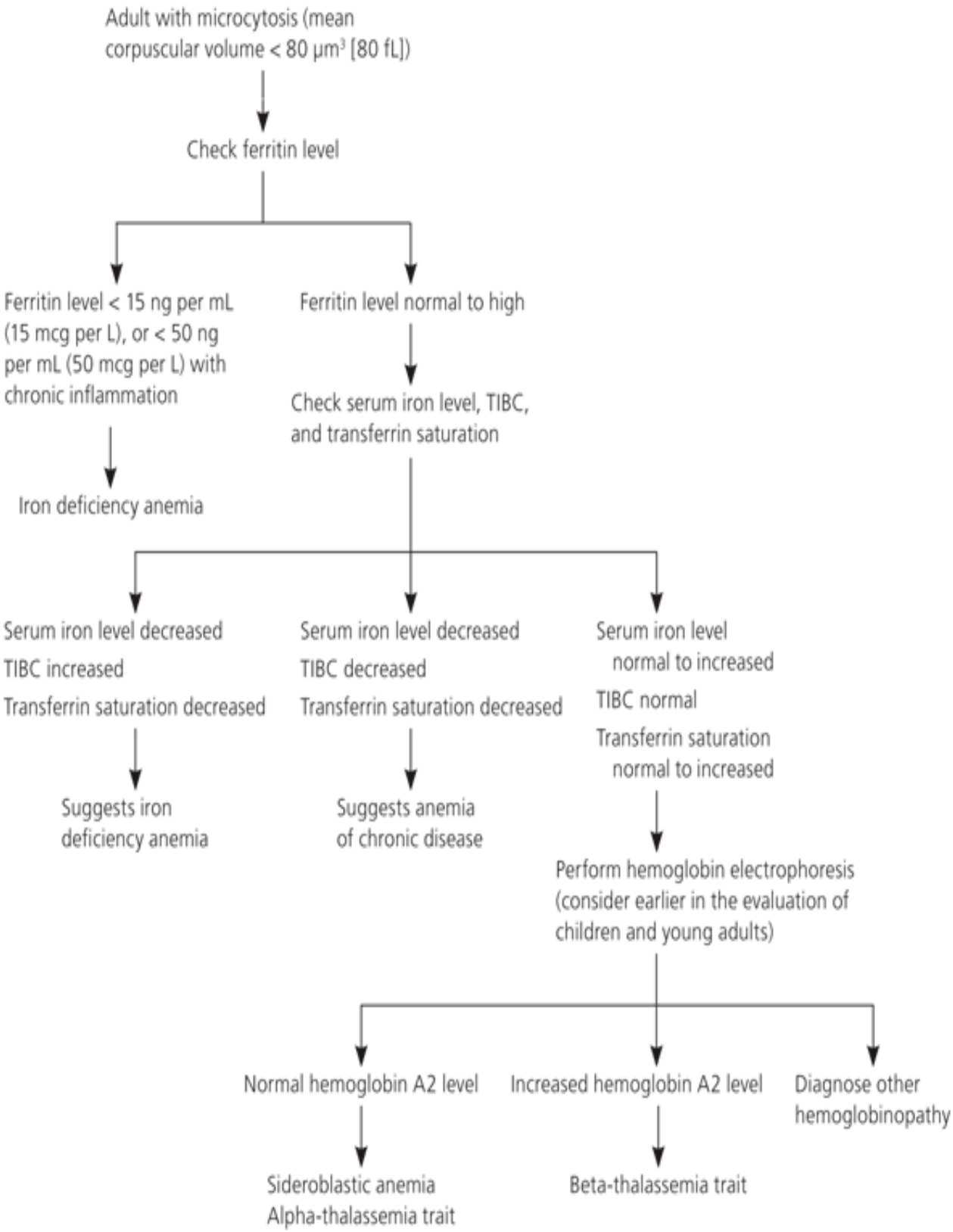
Bone marrow cells	Mean value	Normal borders (%)
Undifferentiated blasts	0,6	0,1–1,1
Myeloblasts	1,0	0,2–1,7
All neutrophil elements	60,8	52,7–68,9
Promyelocytes	2,5	1,0–4,1
Myelocytes	9,6	6,9–12,2
Metamyelocytes	11,5	8,0–14,9
Bandcells	18,2	12,8–23,7
Segmentcells	18,6	13,1–24,1
Eosinophils of all generations	3,2	0,5–5,8
Basophils	0,2	0–0,5
Erythroblasts	0,6	0,2–1,1
Pronormoblasts	0,6	0,1–1,2
Normoblasts:		
Basophilic	3,0	1,4–4,6
Polychromatophilic	12,9	8,9–16,9
Oxyphilic	3,2	0,8–5,6
All erythroid elements	20,5	14,5–26,5
Lymphocytes	9,0	4,3–13,7
Monocytes	1,9	0,7–3,1
Plasma cells	0,9	0,1–1,8
Reticular cells	0,9	0,1–1,6
The number of megakaryocytes (cells/μl)		50-150
Leucoblasts-erythroblastsratio	3,3	2,1–4,5
Erythronormoblastmaturationindex	0,8	0,7–0,9
Bone marrow index of neutrophils	0,7	0,5–0,9
The number of myelokaryocytes (thousand/μl)	118,4	41,6-195,0

Vascular-platelet hemostasis

Research methods	Norma
Rumppel-Leede-Konchalovsky`scuff test	Lessthan 10 pethechiain 5 sm
Duke`s method	less 4 min
Ivy`s method	less 8 min
Plateletsnumber	180-320 x 10^9/l
Blood clot retraction	40-95%
Platelets retention	20-55%
Plateletsaggregation	10-60 sec
Bloodclottingtime	5-10 min
Activatedplasmarecalcificationtime	60-120 sec, With caolin - 50-70 sec
Activations of partial thromboplastin time (APTT)	35-50 sec
Prothrombin time	12-18 sec
Thrombin time	15-18
Autocoagulation test (ACT)	
Plasma fibrinogen level	2-4 g/l

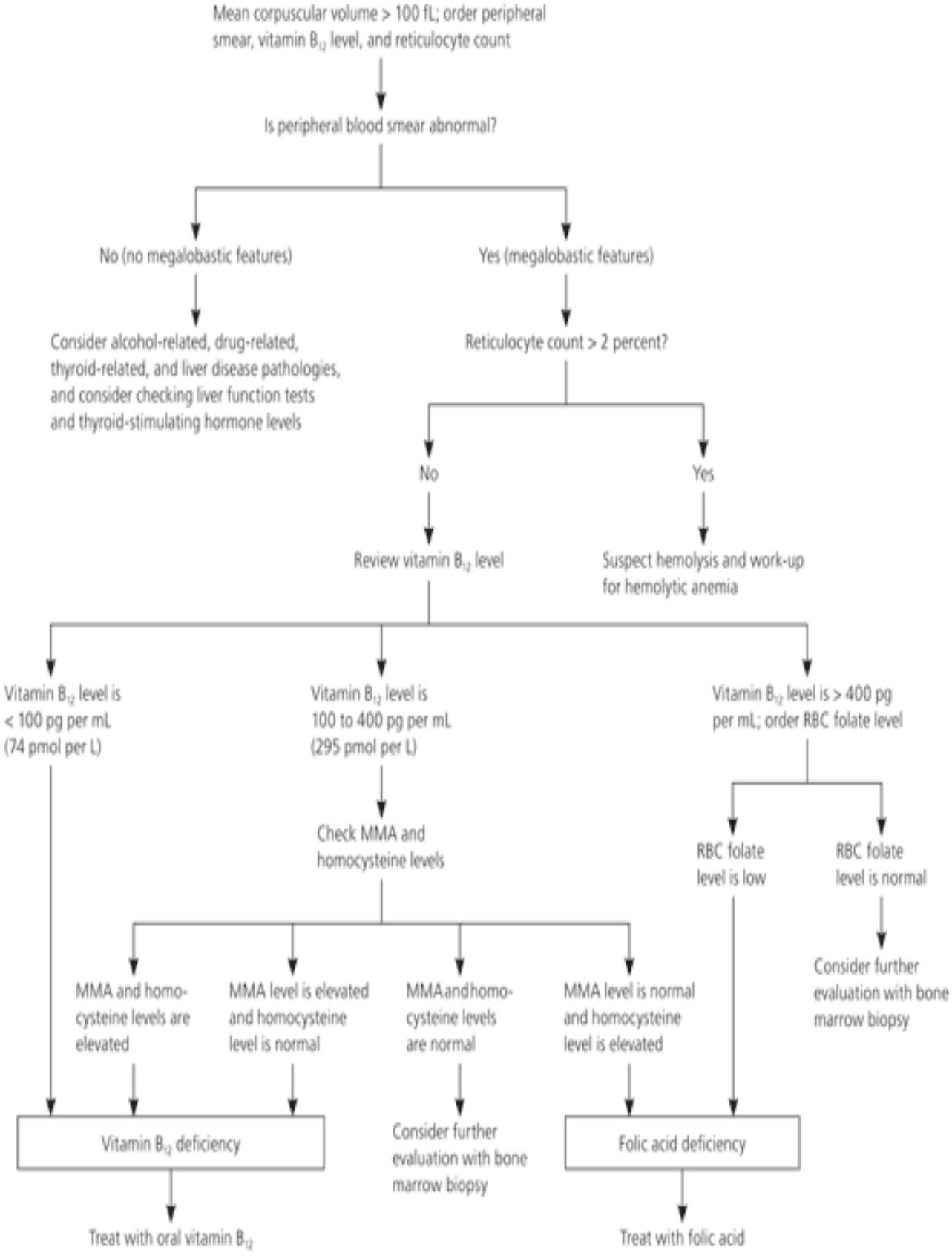
Annex 2

Algorithm for evaluation of microcytic anemia



Annex 3

Algorithm for evaluation of macrocytic anemia



Annex 4

BLOOD GROUP TYPING
ABO blood typingwith cross method

I. Determination of antigens A and B with immune polyclonal serum or monoclonal reagents.

Blood typing should be carried out with two series of anti-A and anti-B reagents, or one series of each reagent, if anti-AB reagent is also used, which is an additional control of the correctness of determining the ABO blood group with anti-A and anti-B reagents.

The determination should be carried out in the room with good lighting at a temperature of 15-25°C. The whole blood, washed red blood cells, red blood cells in plasma, serum or physiological solution are used for the determination.

Procedure:

1. Marking sections on the tablet, writing the names of the reagent.
2. Application of 1 large drop (about 0.1 ml) of each reagent: anti-A, anti-B and anti-AB.
3. Apply 1 small drop (about 0.03 ml) of the test blood (erythrocytes) next to each reagent.
4. Mix separately with a glass rod each drop of blood (red blood cells) with the appropriate reagent.
5. You need to shake the record a little. Despite the fact that when using standard reagents, a clear agglutination occurs already in the first seconds, the results of the reaction are taken into account 3 minutes after the end of mixing, so as not to miss the weak form of antigens.
6. Fixing the results of the reaction after determining.

II. Determination of agglutinin anti-A and anti-B in the serum with standard red blood cells.

Erythrocytes from donors of groups A and B should be used as standard erythrocytes. Erythrocytes are stored in a refrigerator for no more than a week. In a special preservative, the shelf life of red blood cells can be increased. Erythrocytes from one pre-typed donor can be used (for each group), or a mixture of erythrocytes from 2-3 donors (for each group).

Procedure:

1. Preparation of 5% suspension in physiological solution once washed in physiological solution standard erythrocytes.
2. Transfer to 2 labeled tubes of 2 drops of the serum (plasma) under investigation.
3. Addition of 1 drop of 5% suspension of erythrocytes of group A to tube A and drops of erythrocytes of group B to test tubes B, thorough mixing and incubation at room temperature for 5 minutes.
4. Centrifuge the tubes at 2000 rpm for 30 seconds (it is recommended that the optimum time and centrifugation rate be selected so that the sediment is easily separated from the bottom of the tube).
5. Swing the tube to separate the sediment of red blood cells from the bottom of the tube.
6. Determine the presence of agglutinates by looking at the tube into the light.
7. Fixing the results of the reaction after determining.

III. Interpretation of results and determination of blood group

The result of the reaction of red blood cells with reagents			The result of the reaction of serum with standard red blood cells		Blood belongs to the group
anti-A	anti-B	anti-AB	A	B	
-	-	-	+	+	0(I)
+	-	+	-	+	A(II)
-	+	+	+	-	B(III)
+	+	+	-	-	AB(IV)

* A plus sign (+) indicates the presence of agglutination, a minus sign (-) - no agglutination.

Annex 5

Formulation of the diagnosis of anemia

When formulating the diagnosis should be indicated:

1. Etiology of anemia (for example, iron deficiency). When etiology of anemia is unknown it`s required description. It should be included morphogical changes of erythrocytes. In this case anemia referred to as "unspecified" and requires further referral of the patient to hematologist.

2. Causeof anemia (for example,alimentary or posthemorragic). If blood loss is indicated in the diagnosis, then information about its source is given (if detected) or its most likely source is given (questionable), which provides for further examination of the patient.

3. Severity of anemia.

4. Complications, which are consequence of anemia.

Examples of the formulation of the diagnosis:

- Iron deficiency anemiadue to gastro-intestinal bleeding, severe, complicated by hypoxic cardiomyopathy.
- Iron deficiency anemia due to frequent hemorroidal bleeding, moderate.
- Chronicatrophicpangastrititiswithintestinal metaplasia, B12- deficiency anemia, severe.
- B12-folate deficiency anemia, severe. Funicular myelosis.
- Primaryaplasticanemia with the defeat of the three sprouts blood, chronic course, mild.
- Acuteposthemorragic anemia, grade 3, severe.

Reference

1. Harrison's Principles of Internal Medicine by Longo et al.: Volumes 1 and 2, 20th Edition, 2018, 4012 p.
2. Hematology basic principles and practice. Elsevier; 7 edition, 2017, 2374p.
3. Guidelines for the management of iron deficiency anaemia / Andrew F Goddard, Martin W James, Alistair S McIntyre, Brian B Scott onbehalf of the British Society of Gastroenterology //Gut. – 2011, Vol.60. – P.1309-1316.

4. Guidelines for the management of iron deficiency anaemia. British Society of Gastroenterology. Goddard AF, James MW, McIntyre AS, Scott BB. et al. // Gut. – 2011. –S. 60. – P. 1309-1316.

5. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative. Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Official journal of the international society of nephrology – Vol 2, issue 4. 2012 – 64p.

6. Chronic kidney disease: managing anaemia. NICE guidelines. 2015. [E-resources]. - https://www.nice.org.uk/guidance/ng8
7. Management of anemia: acomprehensive guide for clinicians by R. Provenzano (editor), Edgar V. Lerma (editor). -Springer; 1st ed., 2017, 256p.
8. Inder S. Anand. Anemia and iron deficiency in heart failure / Inder S. Anand, Pankaj Gupta // Circulation. – 2018. – Vol. 138. – P.80–98.
9. Guidelines for the diagnosis and management of adult aplastic anemia. Sally B. Killick Writing Group Chair et al. // British Journal of Haematology. – 2016. – Vol. 172, Issue 2. – P. 187–207.
10. Goodnough L. Evaluation and management of anemia in the elderly / L. Goodnough, S. L. Schrier // Am J Hematol. – 2014. – Vol. 89(1). – P. 88–96.
11. Stauder R. Anemia in the elderly: clinical implications and new therapeutic concepts / R. Stauder, S. Thein // Haematologica. -. 2014. – Vol. 99(7). – P. 1127–1130.
12. Douglas L. Smith, M.D. Anemia in the elderly //Am Fam Physician. -. -2000. – Vol.62(7). – P. 1565-1572

List of recommended literature

A. Main literature

1. Hematology basic principles and practice. Elsevier; 7 edition, 2017, 2374p.
2. Clinical hematology and fundamentals of hemostasisby Denise M. Harmening PhD MLS(ASCP) CLS(NCA). F.A. Davis Company; 5 edition. 2008, 768p.

B. Additionalliterature

1. Peyrin-Biroulet L, et al. Guidelines on the diagnosis and treatment of iron deficiency anemia //Am J Clin Nutr. 2015. – Vol.102 . – P.1585-94.
2. Camaschella C. Iron deficiency anemia // N Engl J Med. 2015;3721832-43.
3. Guideline for thelaboratory diagnosis of functional iron deficiency /Thomas D, Hinchliffe R, Briggs C, Macdougall I, Littlewood T, Cavill I, et al. // Br J Haematol. – 2013. – Vol. 161(5). – P. 639-48.
4. Johnson-Wimbley T. Diagnosis and management of iron deficiency anemia in the 21st century / T. Johnson-Wimbley, D. Graham // Therapeutic Advances in Gastroenterology. – 2011. – Vol. 4(3): P. 177-84.