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**SAMARKAND STATE MEDICAL UNIVERSITY**

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# PHYSIOLOGY AND PATHOPHYSIOLOGY OF THE BLOOD SYSTEM

*For students of medical universities*

*textbook*

Educational manual of the Academic Council of Samarkand State Medical University

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*This textbook is recommended for medical universities, and is presented from the perspective of the analysis of the physiology and pathophysiological processes of the blood system in the human body. The textbook is designed to coordinate the teaching process, taking into account the participation of the attending physician in the analysis of the activity of the blood-forming system in normal and disease states. In particular, some methods and information for examining anatomical, physiological and pathophysiological processes that can be carried out directly in the human body are included. Along with modern methods, this textbook also includes non-traditional classical anatomical and physiological processes in a schematic form. This will help students to thoroughly master the pathophysiological laws of the organism, its organs, systems and the cellular level.*

The textbook was approved at a meeting of the Scientific Council of Samarkand State Medical University and recommended for publication.

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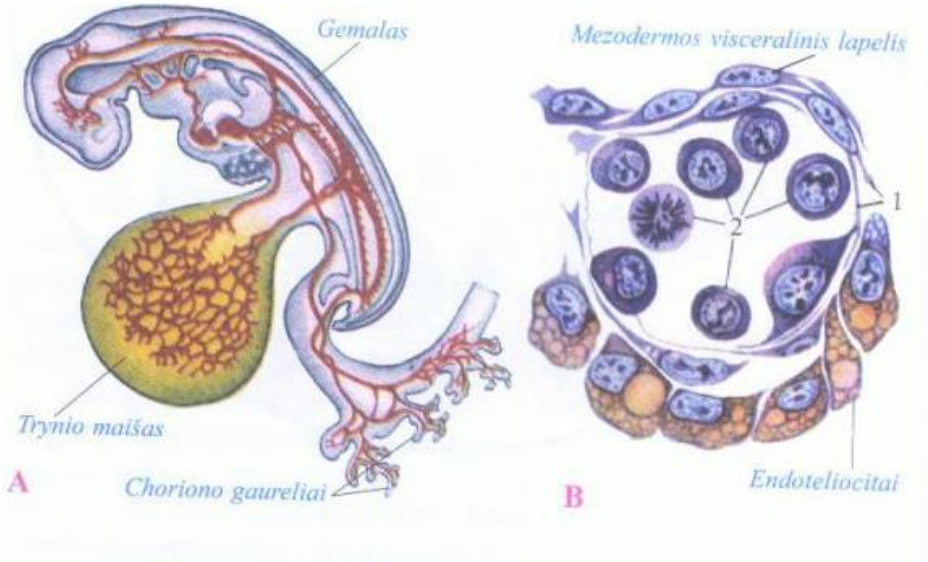
# CHAPTER I
# PHYSIOLOGY OF THE BLOOD SYSTEM

## 1. BLOOD FORMATION IN THE FETAL MATERNITY AND BLOOD PROPERTIES IN CHILDREN

Blood formation in the fetus begins very early. There are several stages of blood formation in the prenatal period. The first stage of the system is considered to be the 19th day and is localized strictly outside the embryo in the structure of the yolk sac . By the 6th week, the yolk sac reaches a diameter of 5 mm. The developing mesodermal layer consists of free mesenchymal cells, blood cells and vascular cells. Here are the most primitive blood cells in the plasma , which from this period acquire the ability to migrate to other "territories". At the stage of the yolk sac, the main blood cell is erythrocyte but at this stage primitive megakaryocytes, similar to granular leukocytes, may appear. After the 10th week, foci of blood formation in the yolk sac are not detected, they gradually move to the liver and spleen. This change begins at week 6 but reaches its peak at week 10-12. Hematopoietic foci are found in the liver outside the vessels and in the endoderm as clusters of mainly undifferentiated blasts.




Mesoblastic blood formation in the yolk sac wall and chorion

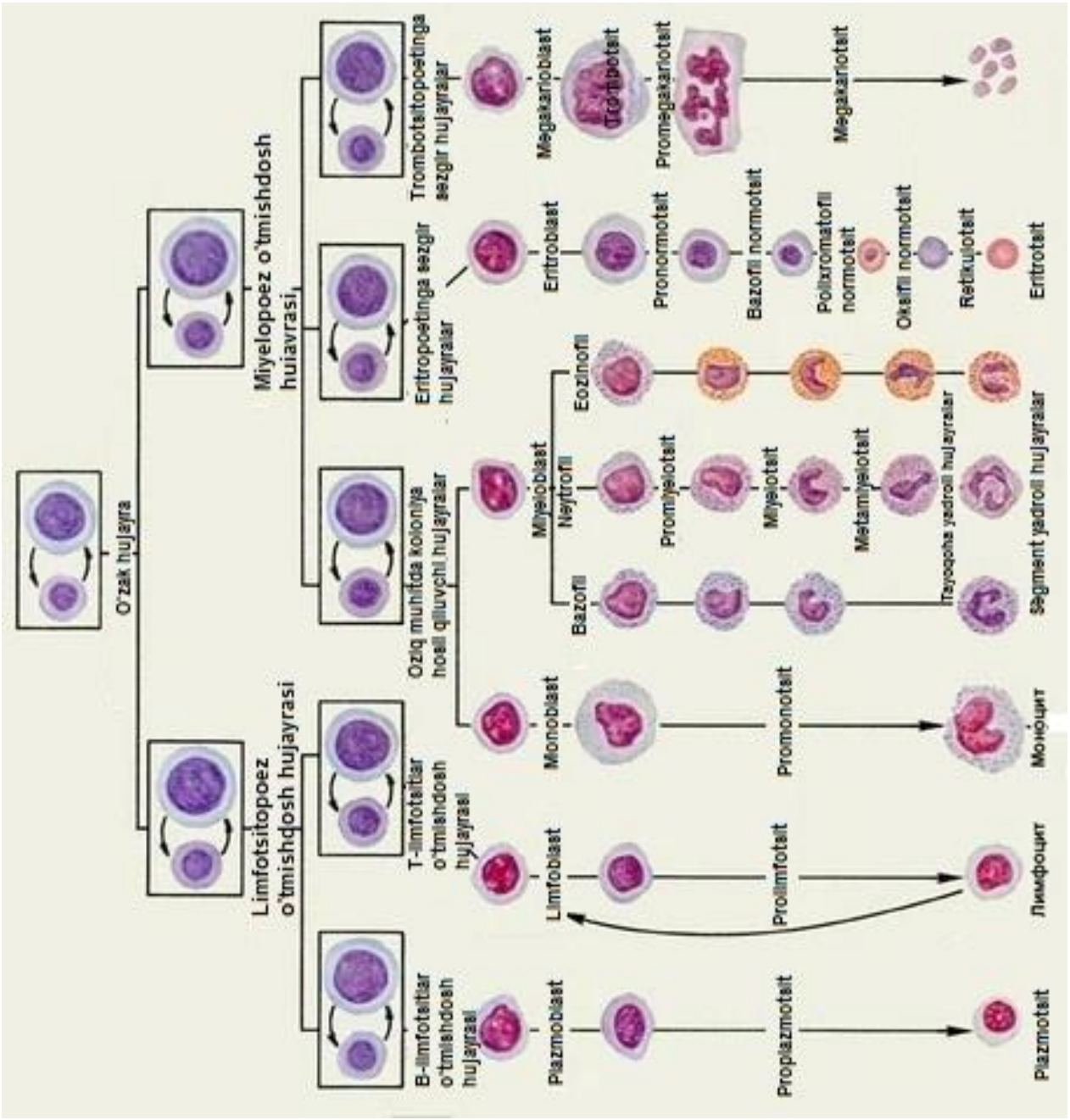
At the 2nd month of pregnancy, along with megaloblasts and megalocytes, megakaryocytes, macrophages and granulocytes can be detected in the blood . Only a month later, the intensity of blood formation in the spleen reaches a maximum and disappears in this organ by about the

5th month. Starting from the 3rd month of intrauterine development, blood formation begins in the spleen and stops by the 5th month of development of the internal organs. Lymphopoiesis occurs at the 2nd month. At 50-60 days, lymphocytes appear in the blood, thymus, spleen, lymph nodes, tonsils, and grouped lymphatic follicles (Peyer's patches). Monocytic blood cells appear at 18-20 days of gestation.

**Bone marrow** is formed at the end of the 3rd month of embryonic development due to mesenchymal perivascular elements that penetrate the bone marrow cavity together with blood vessels from the periosteum. From the 4th month, bone marrow hematopoiesis begins, which remains the main one from the end of intrauterine development and throughout the postnatal period. In the prenatal period, bone marrow is red. With fetal age, its volume increases by 2.5 times (for example, at the 9th week, the volume of bone marrow is 16 ml, and at birth it is 43 ml). In newborns, the weight of bone marrow is approximately 1.4% of body weight (about 40 g). The mass of bone marrow increases by age, reaching the 3000 g on average in adults. During prenatal development, all bones contain red bone marrow and are surrounded by endosteum in the bone cavity. Only after pregnancy ,fat cells begin to form in the bone marrow. During growth, the ratio of red and yellow bone marrow changes. With age, the mass of various blood cells in the bone marrow also increases.

**Weight of bone marrow isolated growth cells**

| **Cells** | **Cell weight , g** | |
|---|---|---|
| | **Newborns - 1 month old** | **in adults** |
| Erythrocytes | 10.0 | 100 |
| Leukocytes: | | |
| Granulocytes | 36.0 | 900 |
| Lymphocytes | 7.5 | 100 |
| Other cells (monocytes, plasma cells, eosinophils, basophils, platelets) | 11.7 | 200 |




**Blood formation scheme**

Fetal blood cells increase in the number of red blood cells, hemoglobin content and leukocytes. If in the first half of intrauterine development (up to 6 months) a large number of immature elements (erythroblasts, myeloblasts, pro and myelocytes) are found in the blood, the following months the peripheral blood of the fetus contains mainly mature elements.

The composition of hemoglobin also changes. Initially (9-12 weeks), primitive hemoglobin (Hb R ) is present in megaloblasts, which is replaced by fetal hemoglobin ( HbF) . It becomes the main form in the prenatal period. From the 3rd week of gestation , the synthesis of adult hemoglobin (HbA) begins, the intensity of formation increases with the age of the fetus. However, at the time of birth, fetal hemoglobin and HbA account for approximately 60% of the total hemoglobin in peripheral blood erythrocytes. The important physiological feature of primitive and fetal hemoglobins is their high affinity for oxygen , which is of great importance for oxygenation of the fetus during the intrauterine period, while oxygenation of fetal blood in the placenta is lower than that of the blood after birth due to respiration through the lungs . In fact , if the oxygen saturation of arterial blood in adults is 100 and 30 % , in the fetus it is only 30 and 15 % . If the partial pressure of oxygen is less than 27 % for the saturation of Hb with oxygen in adults , then in a child with HbF, a partial pressure of oxygen less than 16 % is sufficient.

In the period of erythropoiesis in the fetus , several erythroblast precursors are identified - early erythroid barrier-forming cells (BFU - E), mature or late ( BFU - E) and erythroid colony - forming cells (CFU - E). The first two stages have a high proliferative potential and are almost completely independent of the regulatory influence of erythropoietin . With increasing gestational age , colony - forming cells significantly predominate over barrier-forming cells. The synthesis of gamma chains of globin, and therefore the synthesis of hemoglobin F or A , depends on the predominance of one or another precursor of erythropoiesis . According to the programs of human ontogenesis, the transition to HbA synthesis should occur after 40 weeks of gestation. This is clearly confirmed by the timing of postnatal transformation of hemoglobinopoiesis in children born at full term.

In the fetus, erythropoietin is poorly correlated with the level of blood oxygenation, and its site of synthesis is mainly the liver.

The iron saturation of the fetus is carried out transplacentally . Iron administered to mother, is detected in the fetal circulation after 40 minutes and accumulates in its tissues after 6 hours . The transfer of iron increases with the weight of the fetus and the duration of pregnancy . When a pregnant woman is well- nourished, about 75 mg/kg of iron can accumulate in the fetal tissues, of which only 25 mg is stored in the main depot - the liver.

Bone marrow hematopoiesis develops the ability to differentiate granulocytes and macrophages, reaching high intensity, and stromal cells exert a leading influence on these processes . Some of the factors that determine the direction of granulocyte cell differentiation are common to other cells hematopoiesis .

In the bone marrow , there is a significant predominance of myeloid elements over erythropoiesis precursors, but this predominance increases further towards the end of pregnancy. Several " amplifiers " activate myelopoiesis , including inflammatory interleukins ( IL-1) and cytokines that initiate the process of labor .

**Key factors for the growth and differentiation of leukocytes, erythroid elements, and macrophages**

| Growth factor | Molecular mass , kD | Location on the chromosome | Target cells for the factor |
|---|---|---|---|
| Erythropoietin | 30–39 | 7q11–22 | Colony -forming unit of erythroblasts , embryonic follicle-forming unit |
| stimulate colony growth : | | | |
| Granulocytes | 18–22 | 17q11.2–21 | Granulocytes , macrophages , neutrophils KHB |
| Granulocytes and macrophages | 18–30 | 5q23–31 | Mixed group BPH, granulocytes and macrophages , monocytes, neutrophils BPH |
| Macrophages | 45–70 | 5q1 | macrophages KHB , macrophages |
| Stem cell factor | 36 | 12 | Mixed group BPH, granulocytes and macrophages BPH, |

| Growth factor | Molecular mass , kD | Location on the chromosome | Target cells for the factor |
|---|---|---|---|
| | | | erythroblasts , blister - forming unit , plasma cells |

The absolute number of leukocytes in the umbilical cord blood is up to 10 9 / l .The mononuclear fraction of leukocytes in the umbilical cord blood is approximately 44% in full-term infants and up to 63% in premature infants . The granulocyte fraction is 44% in full-term infants and 37% in premature infants.

Differentiation in the direction of myelopoiesis is the appearance of precursor cells of myeloid blood formation. Then a succession of bipolar cells is observed . Among them are granulomono-, granuloerythro-, erythromegakaryopoiesis precursors . Afterwards, unipotent cells are formed - granulocyto - , eosin o -, basophilopoiesis and mast cells, erythropoiesis, megakaryocytopoiesis. In the final stages, all lines of bone marrow hematopoiesis, morphologically differentiated in the myelogram, appear, intermediate and mature cells.

All phagocytes of the body are derived from hematopoietic cells and are descendants of monocytes, which are not from reticuloendothelial cells and endothelium (reticuloendothelial system ), as previously thought . Currently , the rate of maturation of various cells during the process of hematopoiesis has been studied.

**The rate of cell proliferation during blood formation**

| Blood-forming line and cell | Cell maturation duration , hours |
|---|---|
| Erythropoiesis: | |
| Proerythroblasts | 24 |
| basophilic normocytes | 11.3 |
| polychromatophilic normocytes | 24.0 |
| oxyphilic normocytes | 15.5–16.0 |
| Granulocytopoiesis: | |
| Myeloblasts | 9–32 |
| Promyelocytes | 24–78 |
| Myelocytes | 37–126 |
| Metamyelocytes | 89–108 |
| rod-shaped nucleus | 24–96 |
| segment core | 12–120 |
| Thrombocytopoiesis: | |
| Megakaryocytes | 10–25 milk |

In the first days after birth, the composition of peripheral blood changes significantly. Immediately after birth, the red blood of newborns is characterized by a large amount of hemoglobin and erythrocytes. The hemoglobin content is on average 210 g / l ( range 180-240 g / l) and erythrocytes $6 \times 10^{12}$ / l ( range $7.2 \times 10^{12}$ / l - $5.38 \times 10^{12}$ / l) . A few hours later, due to placental transfusion and hemoconcentration, erythrocytes and hemoglobin levels increase in the 1st day of life, hemoglobin decreases by the end of the 2nd day (maximum by the 10th day of life), erythrocytes decrease (in the 5th-7th day).

The red blood of newborns differs from the blood of older children not only quantitatively, but also qualitatively. The blood of newborns is characterized by anisocytosis and macrocytosis, which are observed for 5-7 days, consequently in the first days of life the diameter of erythrocytes is much larger than in the later period. The average diameter of an erythrocyte - 7.5 microns - is approximately twice the diameter of the smallest capillaries (about 3 microns). In the blood of newborns there are a lot of young, immature erythrocytes, which indicate the activity of the erythropoiesis process. In the first hours of life, the number of reticulocytes, which are the precursors of erythrocytes, varies from 0.8-1.3 to 4.2%. However , the degree of reticulocytosis increases maximally in the first 24-48 hours, and then rapidly decreases between the 5th and 7th days of life,

reaching minimal levels. In the blood of infants, it is normal to have nucleated erythrocytes ,in addition, form of young erythrocytes, and normocytes and erythroblasts are often found. They are found in large numbers in the first few days of life and are then found as single cells in the blood. The high number of erythrocytes in the peripheral blood in the first days of life, an increase in hemoglobin content, and a large number of immature forms of erythrocytes indicate intense erythropoiesis in response to the lack of oxygen to the fetus during intrauterine development and childbirth.

At birth, erythropoiesis in children is $4\times10^{12}$ /l per day, which is 5 times more than in children older than 1 year and adults. After birth, in connection with the establishment of external respiration, hypoxia alternates with hyperoxia. This leads to a decrease in the production of erythropoietin, and accordingly, erythropoiesis slows down, and the amount of erythrocytes and hemoglobin begins to decrease. Hemodilution also contributes to this due to the rapid increase in body weight and length. In addition, erythrocytes produced in utero have a short life span and are more prone to hemolysis. This is due to the presence of fetal hemoglobin, a low content of unsaturated fatty acids in the erythrocyte membrane, as well as tocopherol deficiency, which, often occurs against the background of increased peroxidation activity. The average lifespan of erythrocytes in newborns in the first days of life is 12 days, which is 5-6 times less than the average lifespan of erythrocytes in children older than one year and adults.

There are also differences in the number of leukocytes. In the first days of life after birth, up to the 5th day of life, the number of leukocytes in the peripheral blood exceeds $18 \times 10^{9}$ /l - $20 \times 10^{9}$ /l, neutrophils make up 60-70% of white blood cells. The leukocyte formula is shifted to the left due to a high content of rod-shaped nuclei and a small number of metamyelocytes (Young). One or two myelocytes can also be detected.

The leukocyte formula undergoes significant changes, which is reflected in a decrease in the number of neutrophils and an race in the number of lymphocytes. On the 5th day of life, they equalize to 40-44% in the white blood cell formula ( the so-called first crossover ). Later, against the background of a decrease in the number of neutrophils (about 30%), an increase in the number of lymphocytes is observed (up to 55-60% on the 10th day) . The shift of the formula to the left gradually disappears. At the same time, myelocytes completely disappear from the blood, the number of metamyelocytes is up to 1 % , and the number of rod-shaped cells is only 3 %. The following weeks, months and years in children maintain a number

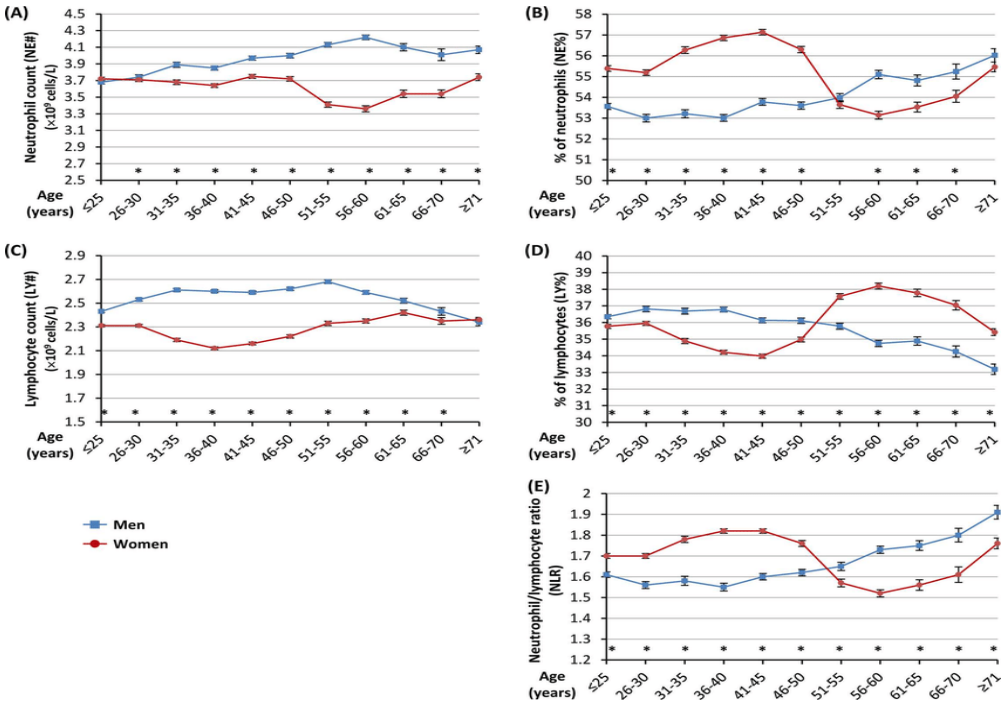
of features of blood formation , and the balance of formation , development of blood cells and their consumption and destruction determines the composition of the peripheral blood of children of different ages.

**Healthy child's hemogram**

| Children's Age | Erythrocyte, (million 1 mm $^3$) | Hb, g/l | Leukocytes, thousand 1 mm $^3$ | Leukocyte formula, % | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | neutrophil | lymphocyte | monocyte | eosinophil | basophil |
| 2–4 weeks | 5.31 | 170.0 | 10.25 | 26.0 | 58.0 | 12.0 | 3.0 | 0.5 |
| 1–2 months | 4.49 | 142.8 | 12.1 | 25.25 | 61.25 | 10.3 | 2.5 | 0.5 |
| 2–3 » | 4.41 | 132.6 | 12.4 | 23.5 | 62.5 | 10.5 | 2.5 | 0.5 |
| 3–4 » | 4.26 | 129.2 | 11.89 | 27.5 | 59.0 | 10.0 | 2.5 | 0.5 |
| 4–5 » | 4.45 | 129.2 | 11.7 | 27.5 | 57.75 | 11.0 | 2.5 | 0.5 |
| 5–6 » | 4.55 | 132.6 | 10.9 | 27.0 | 58.5 | 10.5 | 3.0 | 0.5 |
| 6–7 » | 4.22 | 129.2 | 10.9 | 25.0 | 60.75 | 10.5 | 3.0 | 0.25 |
| 7–8 » | 4.56 | 130.9 | 11.58 | 26.0 | 60.0 | 11.0 | 2.0 | 0.5 |
| 8–9 » | 4.58 | 127.5 | 11.8 | 25.0 | 62.0 | 10.0 | 2.0 | 0.5 |
| 9–10 » | 4.79 | 134.3 | 12.3 | 26.5 | 61.5 | 9.0 | 2.0 | 0.5 |
| 10–11 » | 4.69 | 125.8 | 13.2 | 31.5 | 57.0 | 9.0 | 1.5 | 0.25 |
| 11 months – 1 year | 4.67 | 129.2 | 10.5 | 32.0 | 54.5 | 11.5 | 1.5 | 0.5 |
| 1–2 Years | 4.82 | 127.5 | 10.8 | 34.5 | 50.0 | 11.5 | 2.5 | 0.5 |
| 2–3 » | 4.76 | 132.6 | 11.0 | 36.5 | 51.5 | 10.0 | 1.5 | 0.5 |
| 3–4 » | 4.83 | 129.2 | 9.9 | 38.0 | 49.0 | 10.5 | 2.0 | 0.5 |
| 4–5 Years | 4.89 | 136.0 | 10.2 | 45.5 | 44.5 | 9.0 | 1.0 | 0.5 |
| 5–6 » | 5.08 | 139.4 | 8.9 | 43.5 | 46.0 | 10.0 | 0.5 | 0.25 |
| 6–7 » | 4.89 | 136.0 | 10.6 | 46.5 | 42.0 | 9.5 | 1.5 | 0.5 |
| 7–8 » | 5.1 | 132.6 | 9.98 | 44.5 | 45.0 | 9.0 | 1.0 | 0.5 |
| 8–9 » | 4.84 | 137.7 | 9.88 | 49.5 | 39.5 | 8.5 | 2.0 | 0.5 |
| 9–10 » | 4.9 | 136.0 | 8.6 | 51.5 | 38.5 | 8.0 | 2.0 | 0.25 |

| Children's Age | Erythrocyte, (million 1 mm $^3$ ) | Hb, g/l | Leukocytes, thousand 1 mm $^3$ | Leukocyte formula, % | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | neutrophil | lymphocyte | monocyte | eosinophil | basophil |
| 10–11 » | 4.91 | 144.5 | 8.2 | 50.0 | 36.0 | 9.5 | 2.5 | 0.5 |
| 11–12 » | 4.83 | 141.1 | 7.9 | 52.5 | 36.0 | 9.0 | 2.0 | 0.5 |
| 12–13 » | 5.12 | 132.4 | 8.1 | 53.5 | 35.0 | 8.5 | 2.5 | 0.5 |
| 13–14 » | 5.02 | 144.5 | 8.3 | 56.5 | 32.0 | 8.5 | 2.5 | 0.5 |
| 14–15 » | 4.98 | 146.2 | 7.65 | 60.5 | 28.0 | 9.0 | 2.0 | 0.5 |

In the process of child growth, the leukocyte formula undergoes the greatest changes, and among the formed elements, changes in the number of neutrophils and lymphocytes are especially significant. After a year, the number of neutrophils increases again, and the number of lymphocytes gradually decreases. At 4-5 years of age, the leukocyte formula again intersects, the number of neutrophils and lymphocytes becomes equal again . Later, an increase in the number of neutrophils is observed with a decrease in the number of lymphocytes. From the age of 12, the leukocyte formula does not differ from that of adults.




Change in the ratio of neutrophils and lymphocytes

Along with the relative composition of cells included in the concept of "leukocyte formula", their absolute content in the blood is also of interest. The absolute number of neutrophils is highest in newborns. In the first year of life, their number is minimal, and then increases again, exceeding $4 \times 10^9$ /l in peripheral blood. In the period from about 5 to 12 years, the proportion of blood neutrophils increases by 2% annually. During the first 5 years, the absolute number of lymphocytes is $5 \times 10^9$ /l and above, and after 5 years their number gradually decreases and by the age of 12 does not exceed $3 \times 10^9$ /l.

Similar to lymphocytes, changes occur in monocytes. Perhaps such similarity of changes in the absolute number of lymphocytes and monocytes is explained by the commonality of their functional properties, which play a role in immunity. The absolute number of eosinophils and basophils practically does not change during the development of children.

**Absolute number of white blood cells in children , thousand per 1 mm $^3$**

| Age | Eosinophil | Basophil | Neutrophil | Lymphocyte | Monocyte |
|---|---|---|---|---|---|
| At birth | 0.15–0.7 | 0–0.100 | 12.0–14.0 | 5.0 | 1.8 |
| 1st year | 0.150–0.250 | 0–0.100 | 2.5–3.0 | 5.0–6.0 | 0.6–0.9 |
| 1–3 Years | 0.150–0.250 | 0–0.100 | 3.5–4.0 | 5.0–5.6 | 1.0–1.1 |
| 3–7 Years | 0.150–0.250 | 0–0.100 | 3.7–4.8 | 4.0–5.0 | 0.9–1.0 |
| 7–12 » | 0.150–0.250 | 0–0.075 | 4.0–4.5 | 3.0–3.5 | 0.7–0.9 |
| Age over 12 | 0.150–0.250 | 0–0.075 | 4.2–4.7 | 2.1–2.8 | 0.6–0.7 |

## 2. ERYTHROCYTE SYSTEM

The blood of an infant is characterized by a low content of hemoglobin and erythrocytes compared to the blood of older children and newborns. The hemoglobin content decreases sharply in the first months of life, in most cases by 2-3 months it decreases to 116-130 g/l, and sometimes even to 108 g/l. This is a kind of crisis period of life and development. In fact, this is a real pathological condition - anemia. This state of erythropoiesis is not enough to increase body weight and dilate blood vessels. At the same time, the peculiarity of this so-called "physiological"

anemia is that it is constantly associated with the process of growth and development. Tissue hypoxia stimulates the formation of mechanisms that control erythropoiesis. Hypoxia enhances the production of erythropoietin. Subsequently, with an increase in the production of erythropoietin , the number of reticulocytes increases first, and then erythrocytes and hemoglobin are restored. By the middle of the first year of life, the number of erythrocytes exceeds $4 \times 10^9$ -$4.5 \times 10^9$ , and the hemoglobin content reaches 110-120 g/l and is quantitatively less different from that of adults. In the first two months of life, anisocytosis and polychromatophilia occur. In the first year of life, the number of reticulocytes is slightly higher and averages 5-6%, and after a year their number decreases (by 1%). There is data explaining the occurrence of transient reticulocytosis with the development of iron and copper deficiency in the diet of children 5-6 months of age. With the expansion of the diet, correction and introduction of fortified complementary foods, blood formation is normalized.

Most erythrocytes have a diameter of 7-8 microns. At the same time, the diameter of erythrocytes varies between 4.75-9.5 microns. The ratio of the number of erythrocytes of different diameters is graphically expressed in the form of an erythrocyte cytometric curve (Lyapunov-Pray s- Jones curve ) . The height of this line in the 1st week of life is 8 , 5-9 mm, then the number of erythrocytes dicreases slightly and by 3 months averages 7 , 5-7 m . In older children , the average size of erythrocytes is 7.2 mm. An erythrocyte with a diameter of more than 7 , 7 mm is a macrocyte. It is very important to determine the thickness of the erythrocyte, which can be calculated by the following formula:

$$T = V/S$$

where T is the thickness, V is the volume, S is the area of the base.

The erythrocyte count is determined by the ratio of erythrocytes to plasma, known as hematocrit. In the neonatal period, the erythrocyte count is slightly higher than in other periods of childhood . Their average size sometimes reaches 113 $mm^3$ , up to 6 months the erythrocyte count is on average 77 $\mu m^3$ , then it increases slightly - to 87 $\mu m^3$ and remains at that level until puberty .

The area of the erythrocyte base (S) is calculated by the following formula:

$$S = k/r$$

where k is a constant, equal to 3.14; r is half the average diameter of erythrocytes.

The average thickness of an erythrocyte is 1.9-2.1 microns. The ratio of diameter to thickness (D/ Q ) is normally 3.4-3.9 ; if the D/ Q level is less

than 3.4, there is a tendency to spherocytosis , and if it is more than 3.9 , there is a tendency to planocytosis . Microcytosis with spherocytosis is characteristic of congenital hemolytic anemia; on the contrary, macroplanocytosis is often observed in liver diseases and in some forms of acquired hemolytic anemia. The resistance of erythrocytes is determined by their resistance to hypotonic solutions of sodium chloride of various concentrations. At minimum resistance , the first signs of hemolysis are observed. Usually, it is 0.44-0.48% sodium chloride solution. At maximum resistance , complete hemolysis is observed. Usually, it is 0.32-0.36% of sodium chloride solution.

A functional-morphological concept of "erythron" includes the system of erythropoiesis precursor cells in the bone marrow , reticulocytes and blood erythrocytes . In adults , the total volume of erythron is approximately 2000-3500 ml, weighing 260 g, the number of erythrocytes reaches 25 trillion, every second 10 million erythrocytes are broken down in the reticuloendothelial tissue and the same number are released into the bloodstream from blood-forming organs and reserve depots .

Over one year of age , the daily intensity of erythropoiesis is $55 \times 10^{12}$/l - $80 \times 10^{12}$/l , in children over one year of age and adults, the average daily loss of erythrocytes is 1.43% of the total number ; 1% is destroyed due to accidental causes and 0.43% due to aging. These figures indicate the rate of erythrocyte renewal. The life span of an erythrocyte determined by radiological methods in children over one year of age and adults is 80-120 days.

## 3. GRANULOCYTE SYSTEM

In an adult , the number of granulocytes is $2 \times 10^{10}$ cells. Of this amount, only 1% of granulocytes are in the peripheral blood, 1% in small vessels, and the remaining 98% are in the bone marrow and tissues. The life span of granulocytes is from 4 to 16 days, an average of 14 days, including 5-6 days of maturation , 1 day - circulating in the peripheral blood and 6-7 days in the tissues. As a result, three periods of granulocyte life are distinguished : bone marrow, peripheral blood , tissue. The granulocyte reserve in the bone marrow is divided into 2 groups . The first is the mitotic, dividing part . It includes myeloblasts, promyelocytes, myelocytes. The second group is the maturing , non-dividing part . Metamyelocytes , rod-shaped and segmented neutrophils are included. The last group of cells is constantly renewed due to the entry of cells from the mitotic division . The

weekly portion constitutes the bone marrow granulocyte reserve . Usually, it changes every 6 days. The number of granulocytes in the bone marrow reserve is 20-70 times greater than the number of granulocytes circulating in the blood. Normally, despite the constant migration of neutrophils into the tissues, their number in the bloodstream remains constant as a result of the release of white blood cells from the bone marrow granulocyte reserve. The weekly portion is also the main reserve of granulocytes used as needed (infection, aseptic inflammation, the effect of pyrogens , etc.).

Some neutrophils circulate in the blood in suspension, while others are located near the wall . Blood cells in the circulation and near the wall constantly interact with each other . The life span of neutrophils in the peripheral blood is short and ranges from 2 to 30 hours . Then they are deposited in the small capillaries of various organs, such as the lungs, liver, spleen. Depending on the needs of the body, the deposited neutrophils easily pass into the peripheral blood or are redistributed to the small capillaries of other organs and tissues. From the capillary network, neutrophils migrate to the tissues, where their main functions (phagocytosis, trophic, immunological and allergic processes, etc.) are manifested. Recirculation of granulocytes has not been proven.

During the growth of a child, the leukocyte formula undergoes the greatest changes, and among the formed elements, changes in the number of neutrophils and lymphocytes are of significant importance.

## 4. LYMPHOD SYSTEM

The lymphoid system consists of the thymus gland, spleen, lymph nodes, and circulating lymphocytes. In addition, there are connections with lymphoid cells in various areas of the body, especially the tonsils, laryngeal granules, and lymphatic follicles (Peyer's patches).

Thymus is an important organ of lymphatic system. Experimental thymectomy in the fetus, a delay in the formation and development of other lymphatic organs was observed . The thymus gland develops in utero at the 6th week of development - earlier than other derivatives of the lymphoid system. In an embryo 40-50 mm long , the cortex and medulla can be distinguished, and at 11-12 weeks thymic corpuscles (Gassal's corpuscles ) appear in the medulla. Thymocytes begin to form by the 7th-8th week and by the 14th week are mainly located in the cortical layer of the thymus gland . Subsequently, the mass of the thymus gland increases rapidly, its growth continues until the postnatal period . At 6-12 years of age , the

thymus gland reaches its maximum mass . In subsequent years, a gradual involution of the thymus gland is observed with a decrease in the parenchyma , an increase in adipose and connective tissue .

The **spleen** first appears in the 10 mm (approximately 5-week -old ) embryo as a collection of mesenchymal cells in the dorsal mesentery of the stomach , near the pancreatic duct . During prenatal development, especially in the second half of pregnancy , the spleen increases in mass. However, after birth, the spleen does not fully develop : the trabeculae and capsules are poorly developed . At the same time, the lymphatic follicles are well developed and occupy most of the organ . In children, the weight of the spleen increases with age . Although the weight of the spleen increases with age, the ratio of the spleen to body weight remains constant in childhood, making up 0.25-0.3%. The size of the spleen also increases with age. The functions of the spleen are not sufficiently studied. It is known that this is the main site of destruction of aging platelets and erythrocytes , active phagocytosis occurs . The role of the spleen in immunity remains largely unclear . Clinical observations of children whose spleens were removed for any reason at an early age indicate a predisposition to frequent diseases, especially infectious diseases, and these diseases differ in their severity . It is assumed that the synthesis of immunoglobulins and antibodies observed in the lymph nodes also partially occurs in the splenic pulp .

**Lymph nodes are formed** in utero from the 2nd month of development and are initially formed in the cervical , pulmonary , retroperitoneal and iliac regions . Later, other groups of lymph nodes develop. At the 5th month, the capsule of the lymph nodes develops. However, their final formation (follicles, sinuses, stroma) continues in the postnatal period . In the luminal centers of the follicles, there are V-lymphocytes, and in the paracortical zone, there are T-lymphocytes. After birth, in connection with antigen stimulation, the terminal centers of the lymphoid follicles significantly expand. In the first year of life, due to the poorly developed capsule and trabeculae, as well as the relatively well -developed subcutaneous fat layer , palpation of peripheral lymph nodes is somewhat difficult . Their maximum number is reached by the age of 10 . An adult has up to 460 lymph nodes, their mass is equal to 1% of body weight (500-1000 g). Lymph nodes perform a barrier function. Bacteria, foreign bodies, etc. entering the lymph flow are trapped in the lymph node sinuses and are captured by macrophages . In children, in the first two years of life, the barrier function of the lymph nodes is low , therefore, at this age

, the spread of infection is often observed (sepsis, meningitis, development of generalized forms of tuberculosis, etc.).

clusters of lymphatic tissue in the gastrointestinal tract appear in the appendix and small intestine ( more in the ileum) at 3-4 months of fetal development . From the 4th month, groups of lymphatic follicles appear. Their number and mass in the small intestine gradually increase, but by the time of birth , both their number and mass are reduced . The average number of lymphatic follicles in the small intestine in newborns is 100, in children 1-12 months - 160, in 1-5 years - 161, in 10-15 years - 239-340 and in adults - 195 .

The gastrointestinal tract, as well as other organs in direct contact with the environment (respiratory system), play an important role in the lymphatic system not only in the synthesis of serum immunoglobulins (it is assumed that the intestinal lymphatic system , especially the group of lymph follicles, participates in the formation of B -lymphocytes, similar to the sac of Fabricius in birds ), but also in local immunity. The latter protects the body from the invasion of infectious agents . In humans, the gastrointestinal tract contains lymphoid tissues containing about 50 g of immunoglobulins , which produce 3 g of IgA per day. The insufficient development of the lymphoid apparatus of the digestive system before birth affects the rapid susceptibility of children in the first year of life to intestinal infections and early enteral allergization of the body .

*Lymphocytes* . Adults contain an average of 1.5 kg of lymphocytes , of which 3 g are located in the blood , 100 g in lymphoid tissue , 70 g in the bone marrow , and approximately 1300 g in all other tissues and organs except the central nervous system . The total number of lymphoid cell clones ( descendants of a single stem cell ) can reach $10^7$ . The number of cells in each clone is up to $10^5$ . The life span of lymphocytes is usually 100 to 300 days ; as an exception , very short-lived lymphocytes can live for 3 to 4 days, and very long-lived ones can live for more than 1.5 years. The mitotic activity of lymphocytes is lower than that of other leukocytes. Lymphocytes in the blood can be replaced by recirculation from the tissues within 4-12 days . The kinetics of lymphocytes usually repeats the kinetics of neutrophils , but lymphocytes have a different recirculation from neutrophils. With age , a gradual decrease in the number of lymphocytes in the peripheral blood of children is observed. The total mass of lymphocytes and their distribution in the body have age-dependent characteristics.

**Total lymphocyte count and distribution by age**

| Age | Total mass, g | % of body weight | Red bone marrow | Divorce, lymph nodes, etc. | Blood | Outside the blood-forming organs |
|---|---|---|---|---|---|---|
| 1 month | 150 | 3.75 | 4.9 | 16.3 | 0.3 | 78.4 |
| 3 » | 365 | 6.4 | 4.7 | 15.8 | 0.3 | 79.2 |
| 6 » | 650 | 8.6 | 3.1 | 11.6 | 0.2 | 85.1 |
| 9 » | 650 | 7.3 | 3.1 | 11.6 | 0.2 | 85.1 |
| 12 » | 650 | 6.5 | 3.1 | 11.6 | 0.2 | 85.1 |
| 6 years old | 650 | 3.2 | 3.1 | 11.6 | 0.2 | 85.1 |
| 8 » | 700 | 2.9 | 3.2 | 11.1 | 0.2 | 85.5 |
| 10 » | 900 | 2.8 | 4.3 | 9.4 | 0.2 | 86.1 |
| 15 » | 1250 | 2.3 | 5.9 | 7.5 | 0.2 | 86.4 |
| Adults | 1400 | 2.1 | 7.1 | 7.2 | 0.2 | 84.9 |

observed , especially in the first year of life (2.5 times for 3 months, 4.3 times for 6 months) . After 6 months, their number remains relatively stable until 8 years, and then increases again. This dynamics of the total mass of lymphocytes follows certain patterns in relation to body mass. Up to 6 months after birth , lymphocytes increase per 1 kg of body weight. Then they do not increase, but decrease to the same level as in adults - 4 times . In young children, a large number of lymphocytes are present in the lymph nodes, which reflects the general trend in the development of the lymphoid system due to antigen stimulation , which is especially noticeable in the first days, weeks and months . The increase in the number of lymphocytes is reflected in their ratio and absolute composition in the peripheral blood , which is determined in the first 5 years of life , especially in the first year of life . After the 5th day of life, the number of lymphocytes increases by 1.5% per month for the first half of life, and by 1% for the second half of the year . At the same rate, but to a lesser extent, the number of neutrophils changes . Subsequently, in the first 5 years , the number of lymphocytes decreases by 4% per year.

## 5. THROMBOCYTOPOSIS

Blood platelets or thrombocytes (Bitsoceros platelets ) - round , oval or spherical formations with an average diameter of 2-3 mm , play an important role in the mechanism of blood clotting. Blood platelets are formed from megakaryocytes by the detachment of particles from protoplasm . 3000-4000 platelets are formed from one megakaryocyte.

Human platelets are not cells in the full sense of the word, since they do not have a nucleus, but they have many of the properties of a cell: mobility, antigen and enzyme activity , intensive metabolism. The number of platelets in peripheral blood is relatively stable and ranges from $150 \times 10^9$ /l to $300 \times 10^9$ /l. The stability of the number of platelets in the blood is ensured by balancing the processes of their destruction in the bone marrow megakaryocyte apparatus and the reticuloendothelial system with their formation in the organs of the reticuloendothelial system . The life span of platelets is 8-11 days. The thrombocytopenia is on average $100 \times 10^9$ /l of platelets.

## 6. FEATURES OF THE BLOOD COAGULATION SYSTEM

The blood coagulation system is one of the physiological systems that maintains blood in a liquid state due to the dynamic balance of coagulation and anticoagulation factors . It is formed during development in the womb , and this system does not reach the level of maturity typical of adults at the time of birth .

There are three main directions in the process of hemostasis: blood vessels, plasma and platelets. The morphological development of the vascular part of hemostasis is completed by the time of birth. However, due to the lack of argyrophilic skeletons of the vessels , the fragility and permeability of the capillaries are high , as well as the decreased contractile function of the precapillary walls . The last two features may be mechanisms that maintain the high level of metabolism characteristic of children in the first days of life. By the end of the neonatal period , the mechanical resistance of the vessels reaches the characteristics of older children and adults.

The plasma part of hemostasis consists of various blood coagulation factors , which have the following properties at birth . At birth, the level of proaxellerin (factor V), antihemophilic globulin A (factor VIII), and fibrin stabilizing factor (XIII) in the blood is no different from that of adults . At the same time, in the first hours and days of life , the activity of vitamin K-

dependent factors is relatively low. This is characteristic of prothrombin (factor II), proconvertin ( factor VII), antihemophilic globulin (factor IX), Stuart-Prawer factor ( factor X ) and contact factors ( factors XI and XII) . The low activity of these factors is especially pronounced on the third day of life . Then, due to the entry of sufficient vitamin K into the body and the activation of the protein-producing function of hepatocytes , their amount begins to increase . The number of platelets at birth is almost the same as that of adults , but their functional activity ( the ability to aggregate under the influence of adenosine diphosphate and collagen ) is lower, which is explained by the specific features of platelet metabolism during this period .

anticoagulant system in children has not been sufficiently studied . It is known that in newborns , heparin levels are high during the first 10 days of life . Tissue and plasma antithromboplastins , antithrombin III activity, antiactivators of factors X and XI, antithrombin activity are low . At birth , the fibrinolytic activity of the blood is high, which decreases to adult levels within a few days . The level of plasminogen in infants is significantly lower , and reaches adult levels only by 3-6 months .

Thus, in newborns, almost all coagulation factors have reduced or low activity compared to adults. Reduced activity is a physiological phenomenon that protects against the release of tissue thromboplastin into the blood as a result of tissue damage during birth and the occurrence of thrombosis in children. By the end of the first year of life , the indicators of blood coagulation and anticoagulant systems approach those of adults . Although blood coagulation indicators in children older than one year have individual differences , they are characterized by certain constancy . The large differences observed in children in the pre- and pubertal periods can be explained by the significant hormonal changes observed during this period. Other indicators in children ( blood clotting time , bleeding time , plasma recalcification time, plasma heparin tolerance ) do not differ from those in adults . Only the prothrombin index and time , thrombin time are reduced and slowed down in infants.

**newborns and the time it takes for them to reach adult levels**

| Factors | Amount of factors | | |
|---|---|---|---|
| | At birth | In children over 1 year of age and adults | Normalization period |
| I (fibrinogen), g/l | 1.5–2.0 | 2.5–3.0 | After 2–4 days |
| II (prothrombin), % | 24–65 | 100 | After 10 days |
| V (proaccellerin), % | 70–170 | 75–100 | until birth |
| VII (proconvertin), % | 20–50 | 75–100 | After 2–12 months |
| VIII (antihemophilic globulin A), % | 70–150 | 50–150 | until birth |
| IX (antihemophilic globulin V), % | 15–60 | 50–150 | After 3–9 months |
| X (Stewart–Prawer factor ), % | 20–55 | 100 | After 2–12 months |
| XI (Rosenthal factor ), % | 15–70 | 100 | After 1–2 months |
| XII (Hageman factor ), % | 22–55 | 100 | After 9–14 months |
| XIII (fibrin stabilizer ), % | 100 | 100 | until birth |
| Anticoagulants and the fibrinolytic system | | | |
| Antithrombin II, % | 60–80 | 75–125 | After 10 days |
| Antithrombin III, % | 55–75 | 70–125 | After 3–6 months |
| Heparin, s | 7 | 4–5 | After 10 -30 days |
| Plasminogen, % | 20–45 | 100 | After 3–6 months |
| Fibrinolysin, % | 20–45 | 85–115 | After 2–3 months |

# CHAPTER I.
# PATHOPHYSIOLOGY OF THE BLOOD SYSTEM

The blood system includes blood circulating in the blood vessels, blood-forming organs, which are formed and supplied with blood formed elements, and organs, where blood formed elements are absorbed. Due to their close interrelationship, the pathological process usually never occurs in a strictly limited isolated case. The pathological process may involve mainly the damage of the blood-forming organs or only the blood, but in any case the whole system reacts as a whole.

Depending on the part of the blood system where the pathological process is located, one of its functions is impaired to a greater extent. For example, when erythrocytes are damaged, the respiratory function of the blood is mainly impaired (transport of oxygen and $SO_2$), while in the pathology of leukocytes, its protective function, and changes in the system involved in blood coagulation, lead to a violation of its ability to clot. When the pathological process progresses to other organs and tissues, secondary changes occur in it due to the functional characteristics of the blood system. One of such changes is the reaction of the blood to hypoxia (hypoxic erythrocytosis), in which compensation occurs by increasing the transport function of the blood. Or, in response to infection, the protective function of leukocytes increases, due to leukocytosis. There may also be changes aimed at maintaining circulating blood in a liquid state.

The nature of the pathological process of the blood system, its etiology and pathogenesis depend on the following functional, morphological and regulatory features of this system.

1. High mitotic activity of the hematopoietic tissue, its excessive damage by mutagenic factors (ionizing radiation, viruses, chemical mutagens, cytostatics, lack of plastic materials, iron, cyanocobalamin, folic acid, proteins), leads to leukemia, the development of deficiency anemia, leukopenia, thrombocytopenia, the formation of mutant valves of lymphocytes.

2. Proliferation and differentiation of hematopoietic stem cells (the differentiation of which is genetically determined by the metabolism and structure of the cells leads to genome changes and disruption of genetic regulation , which are the causes of diseases of the blood system), for example, leukemia, hereditary neutropenia, hemolytic anemia, etc.

3. The formation of blood cells is regulated by erythroleukocytes and thrombocytopenia, and their deficiency (lack) leads to pathological changes in the blood.

4. Pathogenic factors (bacteria, viruses, endogenous and exogenous chemicals) enter the blood and lyse blood cells (for example, the breakdown of erythrocytes leads to hemolytic anemia) and change their antigenic structure, causing secondary cytolysis due to autoimmune reactions.

5. Damage to blood vessels leads to blood loss, which results in a decrease in the total volume of blood and disruption of all its functions.

## 1. CHANGES IN TOTAL BLOOD VOLUME

The total blood volume is one of the most important indicators of hemodynamics. Its constancy is controlled by complex control systems: nervous and humoral mechanisms. The normal amount of blood is 6-8% of body weight.

In various pathological processes, the total blood volume changes and, in comparison with the norm (normovolemia), its decrease (hypovolemia) and increase occur. In such cases, simple, polycythemic, oligocythemic hypo- and hypervolemia are distinguished depending on the ratio of blood plasma to formed elements. The ratio of blood cells to plasma is assessed by its hematocrit. This represents the amount of erythrocytes in the total blood volume. Normally, it is equal to 45/55.

### Hypovolemia

**Simple hypovolemia** (a decrease in blood volume without a change in hematocrit) occurs immediately after acute blood loss and persists until the interstitial fluid is released into the blood.

**Oligocythemic hypovolemia** (reduced blood volume, mainly due to a decrease in the number of erythrocytes in the blood).

In Addison-Biermer anemia and during acute blood loss, the ingress of tissue fluid into the vascular bed may occur due to the inability to compensate for the volume of blood, especially its components.

**Polycythemic hypovolemia** (a relatively high number of red blood cells per unit volume of blood, due to a decrease in blood volume) occurs when the body is dehydrated (diarrhea, vomiting, heavy sweating, hyperventilation ), or in shock (due to fluid leaking into the interstitial spaces due to increased permeability of the vascular walls).

### Hypervolemia

**Simple hypervolemia** (an increase in blood volume when the ratio of erythrocytes to plasma is maintained at a normal level) occurs when a large amount of blood is transfused. However, over time, the liquid part of the blood leaves the vascular bed, while the erythrocytes remain in the vessels, causing their thickening. Simple hypervolemia also occurs during intense physical exertion. It is generally associated with the release of blood from the depot into the bloodstream.

**Oligocythemic hypervolemia.** – an increase in blood volume due to plasma, which occurs due to the accumulation of water in the body due to kidney disease, as well as when fluids are used instead of blood are injected. It can be modeled in experimental animals. For this, an isotonic solution of sodium chloride is injected into the animal's vein.

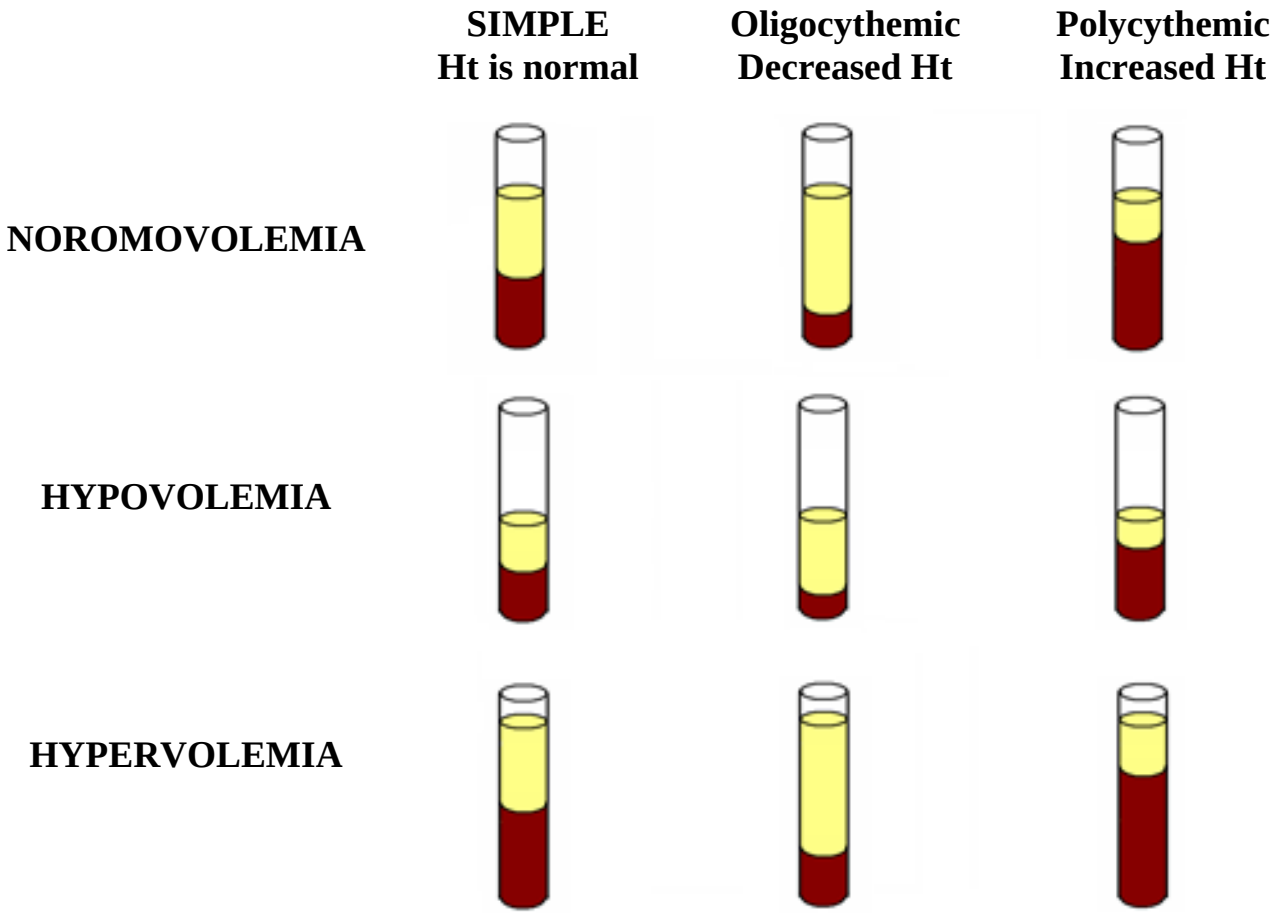
**Polycythemic hypervolemia** is an increase in blood volume due to an increase in the number of red blood cells. This condition occurs when atmospheric pressure drops, as well as in diseases associated with insufficient oxygen demand (heart defects, pulmonary emphysema), and is considered a compensatory state.

However, the occurrence of polycythemic hypervolemia in erythremia is a consequence of the proliferation of erythrocyte-forming tumor cells in the bone marrow.

## Normovolemia

Blood pathology can also occur due to a change in the ratio of blood cells to plasma without changing its total volume. Two types of such changes are known, one of which is oligocythemic and the other is polycythemic normovolemia. **Oligocythemic normovolemia** occurs in anemia caused by blood loss (the total blood volume is normalized as a result of the transfer of tissue fluid into the vascular bed, and the number of erythrocytes is not yet fully restored), when erythrocyte hemolysis is severe, and hemopoiesis is impaired.

**Polycythemic normovolemia** is observed when a patient is given a small amount of red blood cells.


SIMPLE
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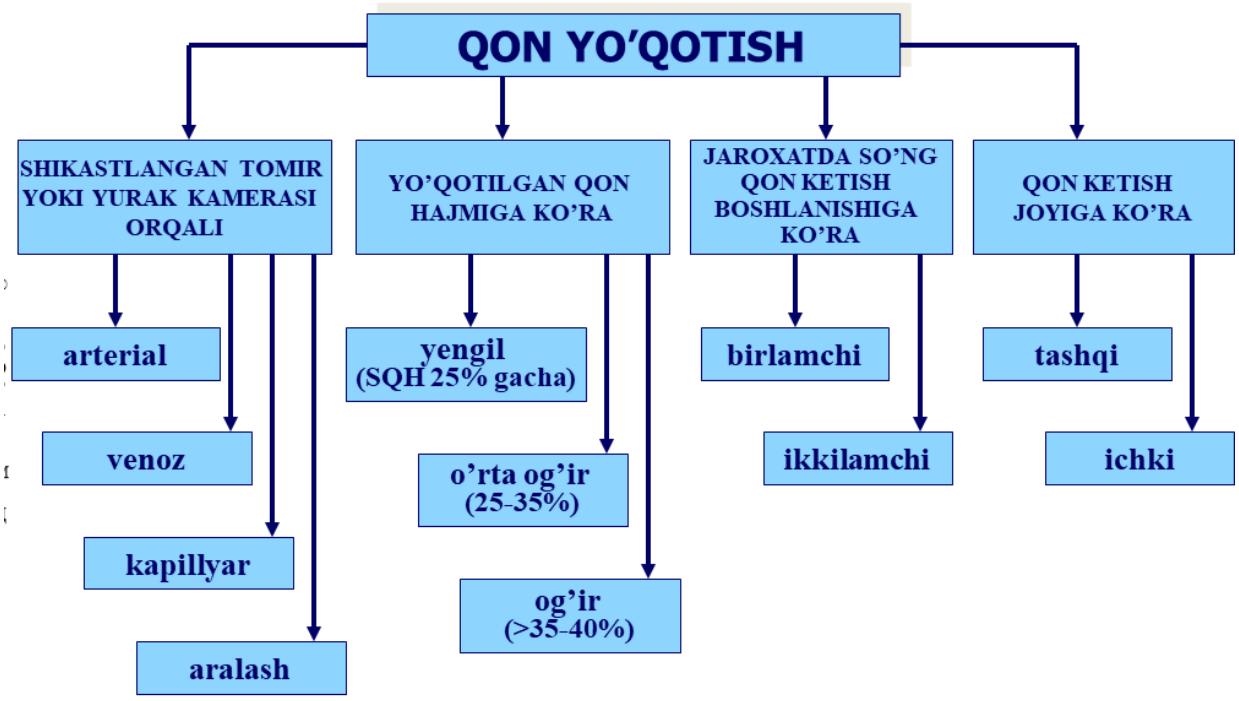
Oligocythemic
Decreased Ht
Polycythemic
Increased Ht
NOROMOVOLEMIA
HYPOVOLEMIA
HYPERVOLEMIA


QON YO'QOTISH
SHIKASTLANGAN TOMIR YOKI YURAK KAMERASI ORQALI
YO'QOTILGAN QON HAJMIGA KO'RA
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QON KETISH JOYIGA KO'RA
arterial
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og'ir (>35-40%)
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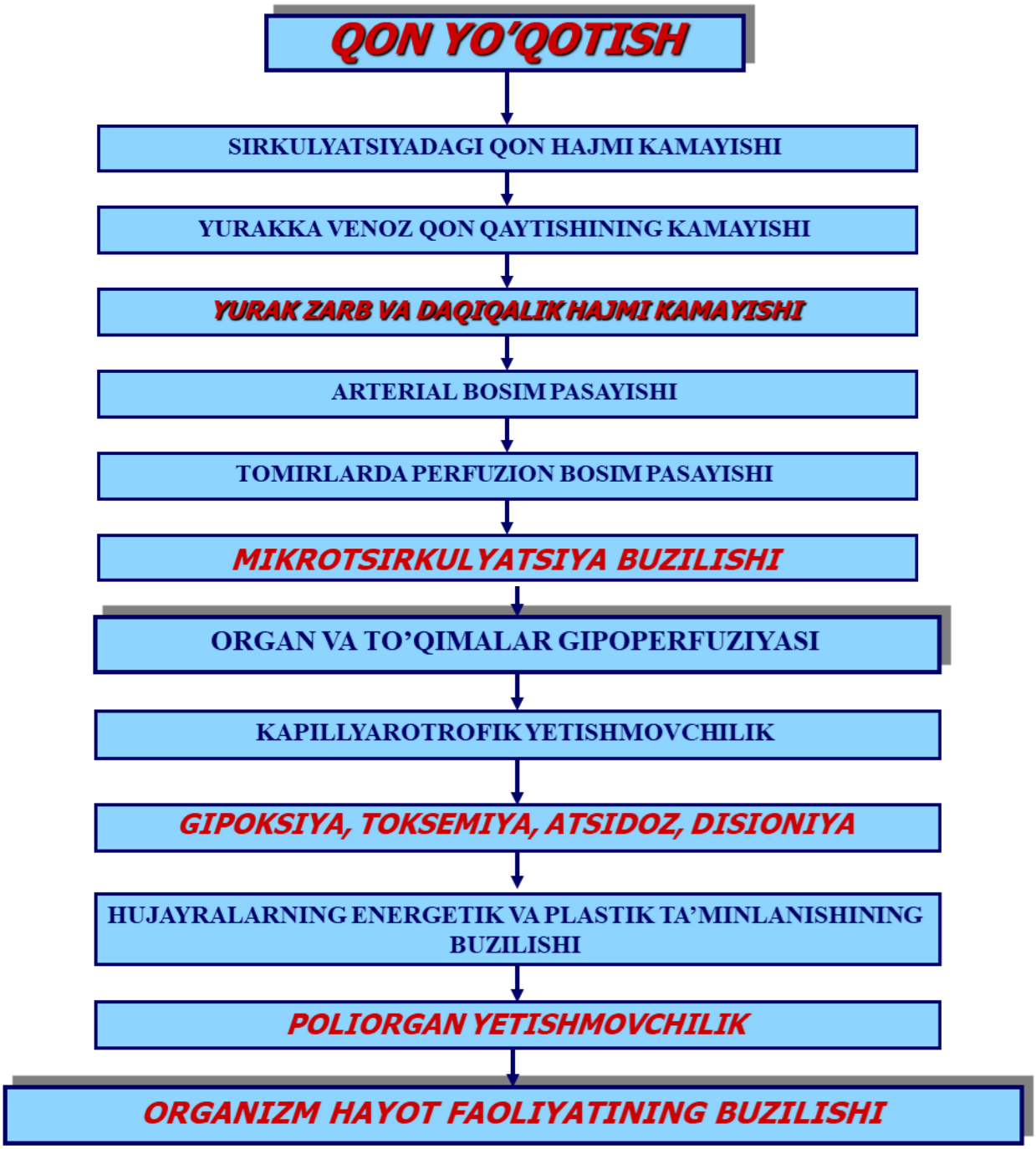
# POSTGEMORRAGIK HOLATLARNING ASOSIY PATOGENETIK ZVENOLARI



## 2. PATHOLOGICAL CHANGES IN ERYTHROCYTES

Changes in the quantity of erythrocytes and their qualitative deterioration lead to changes in the respiratory function of the blood.

Changes in the number of erythrocytes can occur due to a violation of the ratio of their production to their destruction, loss of erythrocytes as a result of impaired vascular integrity, and redistribution of erythrocytes in the vascular bed.

Changes in the number of erythrocytes per unit volume of blood manifest themselves in the form of their increase (erythrocytosis) and decrease (anemia).

Qualitative changes in erythrocytes occur due to impaired maturation in the bone marrow.

In addition, as a result of increased permeability of the bone marrow barrier, the passage of immature cells with low hemoglobin (physiological regeneration cells) into the blood increases. Qualitative changes in erythrocytes occur due to the transformation of erythroblastic hematopoiesis to the megaloblastic type. At this time, megaloblasts and megalocytes (pathological regeneration cells) appear in the bone marrow and blood. In addition, qualitative changes in erythrocytes occur due to hereditary and acquired metabolic disorders, the composition and structure of erythrocytes, including (violation of hemoglobin synthesis due to decreased hemoglobin formation or as a result of the synthesis of abnormal hemoglobins) leading to the appearance of degenerative forms of erythrocytes in the blood.

The number of erythrocytes in the peripheral blood is determined by the state of balance between their formation and destruction. Since erythropoiesis is associated with neurohormonal and humoral regulation, changes in this regulation can cause pathological changes in the number and quality of erythrocytes. For example, when the brain of animals is decorticated and the sympathetic ganglia of the upper neck are tightened, the number of erythrocytes increases in patients with a tumor of the posterior fossa of the head. Cutting the sciatic nerve of animals inhibits erythropoiesis, while tickling the cut end of the nerve enhances erythropoiesis in the bone marrow of the operated leg of the animal.

In patients with pituitary cachexia, a decrease in pituitary function, as well as hypophysectomy in animals, is manifested by a decrease in the number of erythrocytes and their hypochromia. Hyperfunction caused by a tumor of the anterior pituitary gland (acromegaly, Itsenko-Cushing's syndrome) leads to an increase in the number of erythrocytes in the blood.

Changes in the number of erythrocytes are also observed in hyper- and hypofunction of the thyroid gland, in cases of changes in the function of the adrenal glands. In experimental animals, a decrease in erythropoiesis is observed with thyroid and adrenalectomy, and in humans with myxedema and Addison's disease. An increase in the number of erythrocytes occurs in thyrotoxicosis. Large doses of estrogen hormones inhibit erythropoiesis, since they disrupt iron storage. Androgen metabolites have a stimulating effect on erythropoiesis. Changes in the number of erythrocytes, in addition to disturbances in neurohormonal regulation, also depend on the amount of special factors in the body. Such factors of erythropoiesis include cyanocobalamin, folic acid, iron, cobalt, copper, manganese, etc. In addition, there are special humoral stimulators of erythropoiesis - erythropoietins. The number of erythrocytes in the blood depends on their effect on the bone marrow.

The erythropoietic properties of blood plasma were first discovered by Carnot and Deglandre (1960). They were able to observe that the serum of previously bled rabbits increased erythropoiesis when they injected it into healthy rabbits.

The nature of erythropoietins is still not fully understood. It is known that the epithelioid cells of the supraglomerular apparatus of the kidney (SUGA) are very sensitive to changes in the oxygen content in the blood and tissues. In renal hypoxia, erythropoietins are produced in these cells and released into the blood, where they bind to plasma globulins and travel through the bloodstream to affect the bone marrow.

There are two fractions of them: the heat-stable fraction of erythropoietin, and the bone heat-intolerant fraction.

In erythrocytes, it stimulates the synthesis of hemoglobin and the saturation of erythrocytes with hemoglobin.

Hormones of the thyroid, pituitary and adrenal glands (thyroxine, corticotropin, glucocorticoids) increase tissue oxygen consumption and thereby create oxygen deficiency in the tissues, which allows us to assume that one of the erythropoiesis-stimulating effects of these hormones is associated with their indirect, additional effect on the formation of renal erythropoietins. However, hyperoxia inhibits the erythropoietic function of the kidneys. Erythrocyte destruction occurs after the expiration of their physiological life , or as a result of the influence of pathological factors on them. The formation of erythrocytes (erythropoiesis) and their destruction (erythrodiaresis) are a single process, providing a certain amount of erythrocytes in the norm and pathology.

## Morphological characteristics of erythrocytes

The morphological characteristics of erythrocytes are examined in stained blood smears. At the same time, attention is paid to changes in the size, shape, color intensity of red blood cells, and the presence of pathological inclusions in them.

The normal size (diameter) of red blood cells is 7-8 microns. The following types of pathological changes occur in the size of red blood cells:

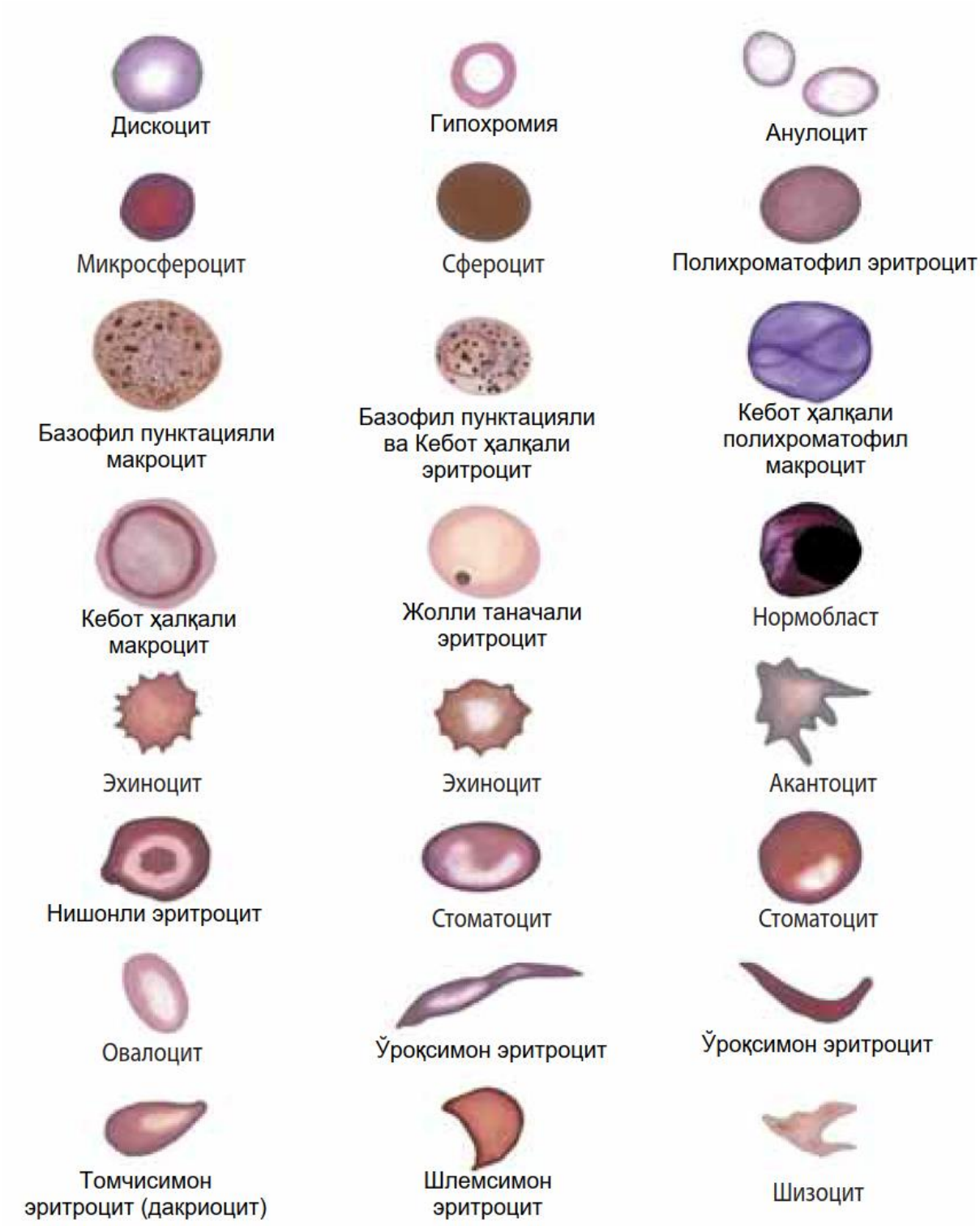
- microcytosis - a predominance of microcytes in the blood with a diameter of less than 6 microns;
- macrocytosis - a predominance of macrocytes with a diameter of more than 8.5-9 microns in the blood;
- megalocytosis - a condition in which red blood cells predominate in the blood - megalocytes with a size larger than 12 microns;
- Anisocytosis is a condition in which red blood cells of different sizes are found in the blood. In healthy people, physiological anisocytosis can be noted, since "Young" red blood cells (up to 15%) have a slightly larger diameter (8.0-9.5 μm) than "old" (5.7-7.0 μm). With physiological anisocytosis, the proportion of cells that differ in size from normal is k am (+). The condition indicated by two plus signs (++) corresponds to the presence of 50% of changed cells, the marked condition (+++) indicates that more than 50% of red blood cells are changed.

A normal mature erythrocyte in circulation is a discoid with two concave sides, and on a smear it appears as a round cell with a white center. Determining the presence of pathological forms of red blood cells is especially important in the diagnosis of hereditary defects.

The most common erythrocytes have the following shape changes:

- codot t cell – a flat erythrocyte with a black dot in the center ( target- shaped erythrocytes) and a colored periphery; found in hemolytic anemia, especially thalassemia ;
- leptocyte – a flat cell with a dark periphery in the form of a ring (annulocyte) in iron deficiency anemia;
- acanthocyte (leaf-shaped cell or spore-shaped cell) – a spheroid erythrocyte consisting of 5-10 outgrowths of various sizes, located at different distances from each other; found in α-, betalipoproteinemia, severe liver diseases, hereditary pyruvate kinase deficiency, lipid metabolism disorders, heparin therapy;

- drepanocyte (sickle-shaped erythrocyte) contains anomalous hemoglobin S, which forms crystals (tactoids) under hypoxic conditions, stretching and tearing the membrane, turning the erythrocyte (8 μm in diameter) into a strip sometimes up to 50 μm long;
- stomatocyte - has an elongated (mouth-shaped) central luminal zone; found in hereditary stomatocytosis, neoplasms, alcoholism, cirrhosis and obstructive liver disease, cardiovascular pathologies, after transfusion, and when taking certain medications;
- elliptocyte – an elliptical-shaped erythrocyte with a bipolar arrangement of hemoglobin;
- spherocyte – spherical erythrocyte without a central lumen . Typically, spherocytes are distinguished as normal ( normocyte ) or small in size (microspherocyte, diameter 4-6 μm); found in hereditary spherocytosis ;
- keratocytes, schizocytes – erythrocytes that have undergone fragmentation ;
- occurs in G-6-FDG y deficiency, hemoglobin instability ;
- echinocyte (hedgehog cell, pineal cell, berry cell, dentate cell) resembles a sea urchin in shape, has 10-30 barriers of the same size, evenly distributed on the surface of erythrocytes; occurs in uremia, transfusion of blood containing old red blood cells, stomach cancer, peptic ulcer complicated by bleeding, hypophosphatemia, hypomagnesemia, hereditary deficiency of pyruvate kinase, phosphoglycerate kinase. Often found as an artifact;
- dacryocytes (drop-shaped tear-like cells); observed in myelofibrosis, myeloid metaplasia, myelophthisic anemia, thalassemia, severe iron deficiency, toxic hepatitis;
- Poikilocytosis is a condition in which there is no specific pattern of changes in the shape of red blood cells, with erythrocytes of various shapes being observed.




The intensity and nature of the staining of erythrocytes depends on their saturation with hemoglobin, as well as the presence of abnormally altered chemical structures. Normal mature red blood cells are normochromic, that is, they have a uniform pink color with light in the center.

*Hypochromia* is observed with a decrease in the amount of hemoglobin in erythrocytes, they are less intensely stained and have a wide

central area. *Hyperchromia* is observed with an increase in the amount of hemoglobin in erythrocytes, they are more red stained and do not have a central glow. *Anisochromia* is the appearance of red blood cells with different color intensities in smears . Reticulocytes with basophilic substance in their cytoplasm are polychromatophilic stained and are called *polychromatophils* .

Normal red blood cells do not contain colored inclusions, so the appearance of any particles in mature red blood cells should be considered a pathology:

- Howell-Jolly bodies – remnants of nucleoplasm (nucleus); small round purple-red inclusions 1-2 microns in size. Detected in severe hemolysis, after splenectomy, in megaloblastic anemia ;
- Kebot rings (Kebot) – remnants of the nucleolemma (nuclear envelope) of an erythrokaryocyte, in the form of eight red rings, found in megaloblastic anemia;
- basophilic granulation of erythrocytes - blue-violet or blue granules of various sizes, often located on the edge of the erythrocyte or normoblast, are aggregated basophilic substances (remnants of ribosomes); occurs in lead or heavy metal poisoning, thalassemia, alcohol poisoning, cytotoxic effects of drugs, severe anemia;
- siderosis (iron-storing) granules - intracellular iron (hemosiderin, ferritin) associated with mitochondria, not included in hemoglobin, stained blue with Berlin blue;
- Pappenheim's corpuscles are small granules that appear as pale purple bodies in erythrocytes and are detected in normal smear staining .
- Heins-Ehrlich bodies – small round purple-red inclusions (single or multiple) 1-2 microns in size formed from denatured hemoglobin; Usually, the formation of single Heins bodies is observed in erythrocytes; in pathology, their number in red blood cells increases (4-5 or more), which can be observed in poisoning with certain drugs (sulfanilamides) and toxins (phenylhydrazine, nitrobenzene, aniline, pyridine, toluenediamine), etc.

## 3. INCREASED NUMBER OF RED BLOOD CELLS IN THE BLOOD

in the number of erythrocytes in the blood above the norm (4-5, 5x10 $^{6}$ – 1 μl) is called erythrocytosis and is often a secondary process, resulting from other diseases. Erythrocytosis can be absolute, in which case there is a reactive increase in erythropoiesis.

There is also a relative type of erythrocytosis, which occurs due to blood thickening.

absolute erythrocytosis is a lack of oxygen in the body. This condition occurs in residents of high-altitude regions, climbers, and patients with chronic diseases of the lungs and cardiovascular system. At this time, the amount of erythrocytes increases as a result of the stimulating effect of erythropoietin on the red part of the bone marrow . Similarly , absolute erythrocytosis also occurs in tumors of the erythropoietin-producing part of the kidney.

The causes of relative erythrocytosis , the change in which occurs when the transient etiological factor ceases to act , return the number of erythrocytes and the amount of hemoglobin to normal. This feature fundamentally distinguishes erythrocytosis from erythremia .

Erythremia is characterized by a blastocystic proliferation of myeloid tissue. In the bone marrow , an increase in the red marrow is observed. At this time , erythrocytosis is accompanied by pancytosis. The number of erythrocytes in 1 μl of blood reaches 6-7 , even $10x10^{6}$ , while the hemoglobin content in the normal state is 167 g / l, at this time it reaches 180-200 g / l. In this pathological process, the color index of the blood is low, since the formation of erythrocytes is accelerated, but they are not yet saturated with hemoglobin . The volume of circulating blood increases, and in parallel with this, the hematocrit index also increases. (polycythemic hypervolemia) Blood viscosity increases, as a result of which blood movement slows down, which sharply complicates the work of the heart. Blood pressure rises, the heart works harder, and left ventricular hypertrophy occurs. There is hyperemia of the mucous membranes of the skin, which is associated with organ congestion and metaplasia of myeloid tissue. Due to thrombocytosis and slow blood flow , numerous thrombi are formed , and at the same time , the use of fibrinogen for thrombus formation is reduced , which leads to fibrinogen deficiency and increased vascular permeability , leading to bleeding.

## 4. ANEMIA

Anemia is a decrease in the number of erythrocytes and hemoglobin per unit volume of blood , as well as qualitative changes in their composition and morphology . Qualitative changes are characterized by the appearance of pathologically shaped erythrocytes in the peripheral blood. It is divided into the following groups:

1. Physiological regeneration cells - cells that appear in the peripheral blood as a result of increased erythropoiesis due to the release of erythrocyte breakdown products into the bone marrow, hypoxia , and the stimulating effects of erythropoiesis. These include reticulocytes (revealed when supravital staining), polychromatophilic erythrocytes, normoblasts, and erythroblasts.

2. Pathological regeneration cells. These include cells that appear in the peripheral blood as a result of a change in the erythroblastic type of blood formation to the megaloblastic type - megaloblasts, megalocytes, erythrocytes with Cabot and Jolly bodies.

3. Degeneratively shaped erythrocytes - these include anisocytes, poikilocytes, hypochromic and hyperchromic erythrocytes, erythrocytes with basophilic granules. The detection of such pathologically shaped erythrocytes in the blood indicates the loss of the bone marrow's ability to produce full-fledged erythrocytes (or the destruction of erythrocytes in the blood).

## Classification of anemias

1. Etiopathogenetic classification of anemia

I. Anemia caused by blood loss (posthemorrhagic anemia):
- acute posthemorrhagic anemia;
- chronic posthemorrhagic anemia.

II. Anemia due to impaired hemoglobin formation or erythropoiesis:
- Iron deficiency anemia;
- iron redistribution anemia (iron utilization disorder);
- iron-deficiency (sideroanthesic) anemia (impaired synthesis and utilization of porphyrins);
- megaloblastic anemia (impaired DNA and RNA synthesis), including B12 and folate deficiency anemia;
- hypoproliferative anemia;
- anemia associated with bone marrow failure, including hypoplastic (aplastic) anemia, refractory anemia in myelodysplastic syndrome;
- metaplastic anemia, including anemia caused by hemoblastoses, anemia caused by cancer metastases to the bone marrow;
- dyserythropoietic anemia.

III. Anemia caused by increased breakdown of red blood cells in the body (hemolytic):

- hereditary, including Minkowski-Shoffar, sickle cell anemia, hemoglobinosis, thalassemia;
- acquired, including autoimmune, paroxysmal nocturnal hemoglobinuria, drug, traumatic and microangiopathic, due to poisoning with hemolytic poisons and bacterial toxins.

IV. Mixed anemia (polydeficiency) caused by a combined deficiency of various hematopoietic factors and the influence of a number of pathological mechanisms (hemolysis, metaplasia, autoimmune processes, blood loss, sepsis, etc.).

## 2. Morphological classification of anemia

I. Microcytic anemia (MCV < 80 fL, erythrocyte diameter < 6.5 μm).
II. Normocytic anemia (MCV 81-99 fL, erythrocyte diameter 7.2-7.5 μm).
III. Macrocytic anemia (MCV > 100 fL; erythrocyte diameter > 8 μm).

## 3. Classification of anemia by color index

I. Hypochrome (RK< 0.8, MCH < 27 pg, MCHC < 30 g/dl).
II. Normochrome (RK <0.85-1.05, MCH 27-35 pg, MCHC <31-36 g/dl).
III. Hyperchromia (RK - 1.05 or more, MCH more than 35 pg, MCHC more than 36 g / dl).

## 4. Classification of anemia according to regeneration and compensation

I. Regenerative anemia - reticulocyte count is normal
II. Hyperregenerative anemia (reticulocyte count > 2%).
III. Hyporegenerative anemia (reticulocyte count < 1%).
IV. Aregenerative anemia (reticulocytes less than 0.2%).

## 5. Classification of anemia by severity

I. Mild degree (hemoglobin concentration 119-90 g/l, erythrocyte count 3.5-3.0 × 1012 / l);
II. Moderate level (hemoglobin concentration 89-70 g / l, erythrocyte count 2.9-2.5 × 1012 / l);
III. Severe degree (hemoglobin concentration less than 70 g / l, erythrocyte count <2.5 × 1012 / l).

# 5. POSTHEMORRHAGIC ANEMIAS

Posthemorrhagic anemias can be acute and chronic. Acute posthemorrhagic anemias occur as a result of a single, rapid and large amount of blood loss. Their main causes are injuries to large vessels and damage to internal organs. When blood loss occurs, a number of compensatory mechanisms appear, aimed at reducing the total volume of circulating blood, lowering blood pressure, and reducing hypoxia of organs and tissues. Adaptive reactions occur gradually and can be conditionally divided into 3 periods:

1. The reflex period occurs within hours after blood loss and is characterized by spasm of peripheral vessels, redistribution of blood to vital organs, tachycardia, increased minute blood volume, squeezing of blood from depots, rapid and deep breathing, etc. However, hematological changes do not occur during this period, since with a decrease in the total volume of blood, changes in the number of erythrocytes and hemoglobin per unit volume do not have time to occur.

2. The hydremic period - 24-48 hours after blood loss, a decrease in the number of erythrocytes and hemoglobin per unit volume of blood occurs, as another compensatory mechanism aimed at restoring the total volume of circulating blood appears. Tissue fluid moves into the veins. This mechanism is facilitated by increased production of hormones that increase the osmotic pressure of the blood, reduced diuresis and increased thirst. The color index does not change during this period, since hemoglobin and erythrocytes decrease at the same time.

3. Bone marrow compensatory period - since acute posthemorrhagic anemias are regenerative anemias, this period is characterized by increased erythropoiesis . 4-5 days after blood loss, a large number of physiological regeneration cells appear in the peripheral blood: reticulocytes, polychromatophilic erythrocytes, normoblasts of various generations, and even erythroblasts. Blood formation is of the normoblastic type. The color index of the blood is hypochromic, since the hemoglobinization of erythrocytes lags behind their formation. All blood parameters are gradually restored, but it should be noted that the recovery period depends on the general condition of the body, the amount of blood loss and the rate of loss, the person's gender, age, reactivity, the development of compensatory reactions, and a number of other factors. Hunger, infectious diseases, frostbite, overheating, deep anesthesia, etc. increase sensitivity to blood loss.

Children's bodies are especially sensitive to blood loss, the younger the child, the more severe the consequences of blood loss for him. This is explained by the fact that in nursing children, especially infants, the protective-adaptive mechanisms are not fully formed, and immediate compensatory mechanisms, such as vasospasm (narrowing of blood vessels), tachycardia, blood redistribution, etc., are not yet well developed. Also , this period is characterized by the incomplete maturation of the blood coagulation system, and therefore its role in stopping bleeding is small.

Usually, a single loss of 20% of circulating blood in a healthy adult is not life-threatening. A loss of 25-30% of blood is life-threatening, and a single loss of 50% of blood is fatal. When blood is lost , the pressure of the circulating blood decreases. A decrease in blood pressure below 60 mm Hg leads to collapse, impaired blood circulation in the central nervous system, heart, and other vital organs, hypoxia occurs in them , and death occurs due to paralysis of the respiratory center.

Acute blood loss in newborns is associated with placental injury, rupture of the umbilical vessels, and hemorrhages resulting from injuries during childbirth . Perinatal infections, hereditary hemorrhagic diatheses , and blood loss from the umbilical cord and organs occur. It should be remembered that blood loss in children is more severe than in adults. In infants, a loss of 10-15% of circulating blood causes symptoms of shock, while in adults, a loss of 10% of blood is compensated for on its own . In older children, a loss of 30-40% of circulating blood leads to severe shock, and a single loss of 50% of circulating blood ends in death. However, a slow loss of 50% of circulating blood is not life-threatening.

Treatment of acute blood loss begins with stopping the bleeding and restoring the normal volume of the blood by blood transfusion and blood replacement fluids . Along with transfusion, drugs that improve heart function, glucose-salt solutions , and drugs that strengthen the walls of blood vessels are prescribed.

Chronic posthemorrhagic anemias occur as a result of repeated, small blood losses (menstruation, metrorrhagia, gastrointestinal ulcer disease, hemorrhoidal and other blood losses). These anemias are mainly associated with iron deficiency and therefore are analyzed as a group of iron deficiency anemias. In children , chronic posthemorrhagic anemias are less common than in adults. It should be noted that despite the fact that the child's body has a much larger blood volume , due to compensatory mechanisms, it adapts to such anemias more easily than to acute posthemorrhagic anemias.

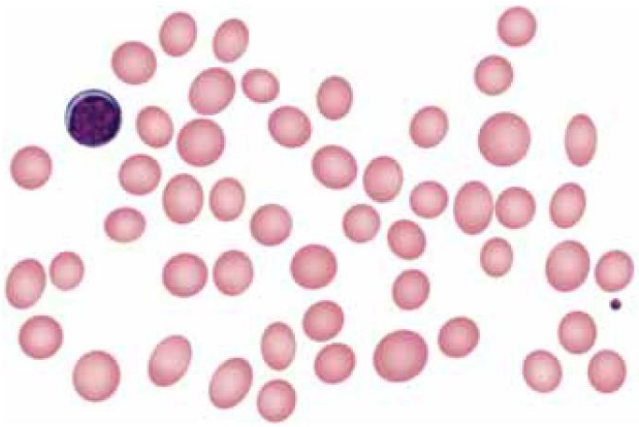
# 6. ANEMIAS ASSOCIATED WITH INCREASED BLOOD BREAKDOWN (HEMOLYTIC)

In a healthy organism, the existence of a dynamic balance between erythropoiesis (the formation of erythrocytes) and erythrodieresis (the breakdown of erythrocytes) ensures a constant number of erythrocytes in the peripheral blood. Anemias occur when the breakdown (hemolysis) of erythrocytes exceeds their formation and release into the blood. Hemolytic anemias are hereditary and acquired will be.

Hereditary hemolytic anemias are characterized by premature destruction of erythrocytes (normally erythrocytes live 100-120 days), a shortened lifespan, due to a hereditary defect. Hemolysis often occurs intracellularly. Hereditary hemolytic anemias may be associated with pathology of the erythrocyte membrane (hereditary membranopathies) or with a deficiency of erythrocyte enzymes (hereditary enzymeopathies), as well as hereditary changes in the structure and synthesis of hemoglobin (hereditary hemoglobinopathies) or with hemoglobinoses.

## HEREDITARY membranopathies

Anemias are characterized by abnormalities in the protein and lipid components of the erythrocyte membrane , which leads to a change in the shape of erythrocytes and their premature hemolysis. A striking example of this group of anemias is hereditary microspherocytosis (Minkowski-Shoffar disease ).



Minkowski–Schoffar disease (microspherocytosis, ×1000)

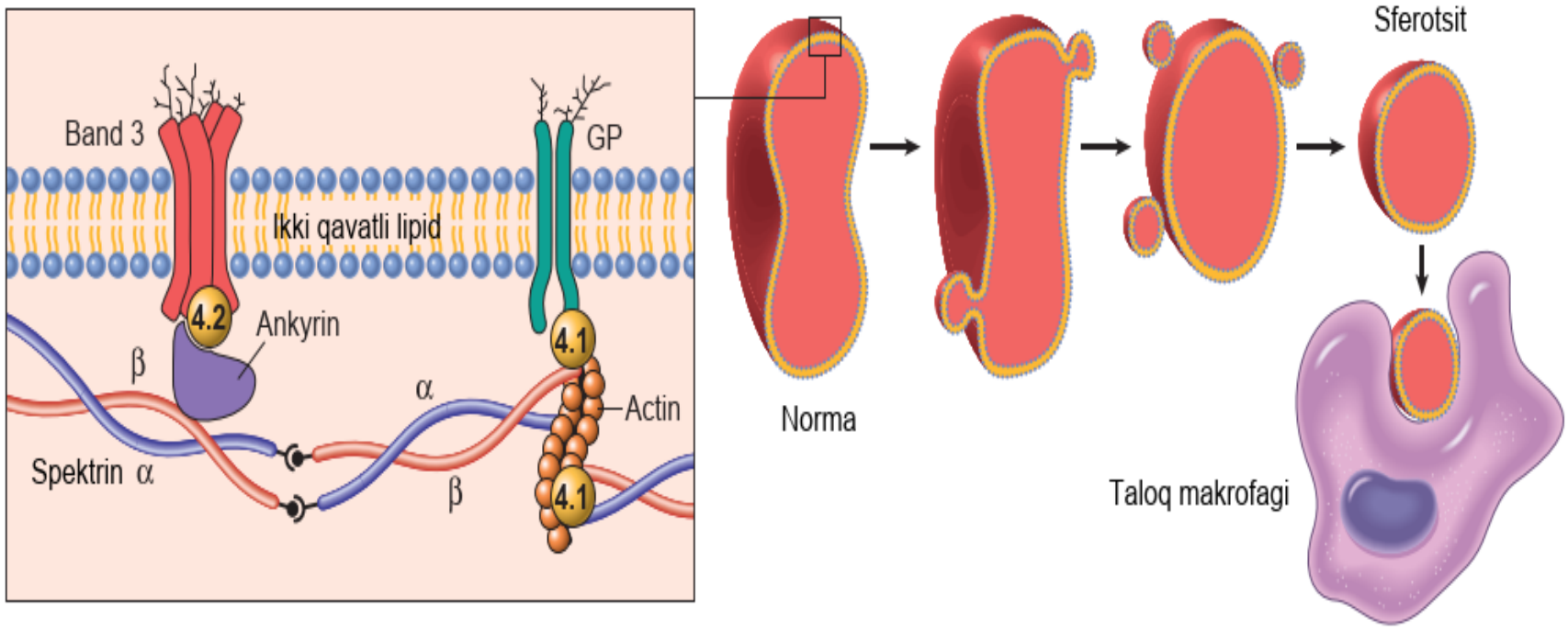
The disease is based on a genetic defect in the protein that makes up the erythrocyte membrane, which allows the membrane to become more permeable to sodium ions and water, as a result of which the erythrocytes swell and turn into microspherocytes. At the same time, the glycolysis process in the membranes is activated and the rate of phospholipid metabolism increases. The elasticity of microspherocytes is lost, they are trapped in the spleen and are rapidly destroyed in this organ. Inverse (unconjugated) bilirubin accumulates in the blood, causing jaundice. The life span of microspherocytes is shortened and can be only 8-14 days. Hereditary microspherocytosis can occur in young children (in the infant and neonatal periods) and is characterized by severe jaundice.

Treatment of the disease is mainly carried out in two ways:

I) Conservative treatment, which is mainly against bilirubin intoxication The goal is to restore hemodynamic and metabolic changes to normal. In severe anemia, hemotransfusion, especially red blood cell transfusion, is appropriate.

2 *)* Splenectomy, which is the only radical treatment.

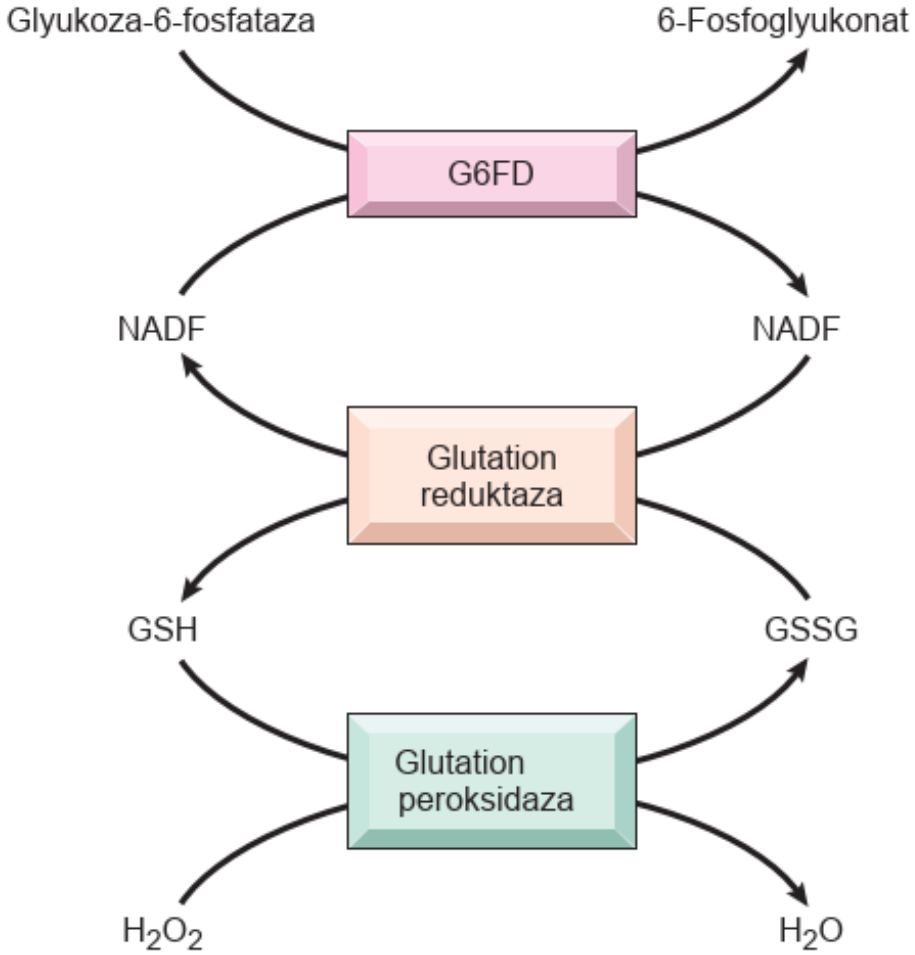
Hereditary defect (defect) of erythrocytes. Instead of being destroyed, the spleen, which retains (filters) them, stops functioning, and as a result, defective erythrocytes circulate in the peripheral blood for a much longer period of time.




**Qizil hujayra membranasi skeletining irsiy sferotsitozdagi roli. Chap panelda asosiy qizil hujayra membranasi skelet oqsillarining normal tashkil etilishi ko'rsatilgan. a-spektrin, b-spektrin, ankirin, diapazon 4.2 yoki diapazoni 3 ni o'z ichiga olgan turli mutatsiyalar, bu qizil hujayralar o'rtasidagi o'zaro ta'sirni susaytiradi. Natijada yuzaga keladigan o‘zgarishlarga moslashish uchun sirt maydoni hajmga nisbatda bu hujayralar sharsimon shaklni qabul qiladilar. Sferotsitar hujayralar normal hujayralarga qaraganda kamroq deformatsiyalanadi va shuning uchun taloqdagi tuzoqqa tushib qoladilar.**

## Hereditary enzymopathies

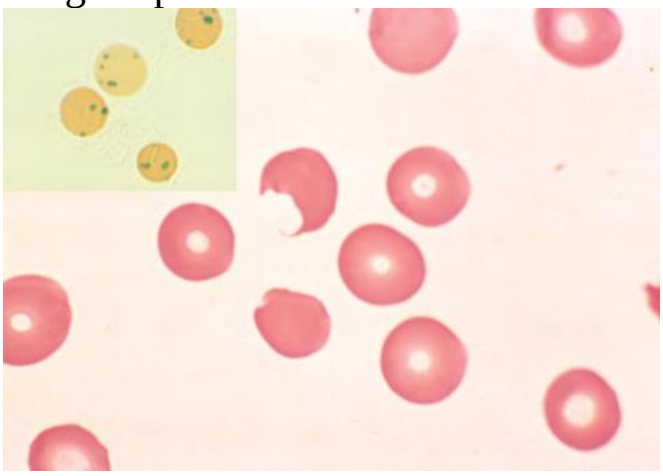
Group B disease can manifest at any age. The basis of the disease is a chronic hemolytic process caused by a hereditary anomaly of enzymes . The best studied of these anemias is the enzymopathy associated with a deficiency of the enzyme glucose-6-phosphate dehydrogenase. This anemia occurs in the territories of CENTRAL Asia and the Transcaucasus. In these areas, malaria was previously widespread, and people with enzymopathies did not develop malaria. Deficiency of G-6-FDG leads to a decrease in reduced glutathione in erythrocytes and a decrease in the strength of erythrocytes under the influence of various oxidizing agents , antimalarial drugs, PASK, phtivazide, eating horse beans or smelling their pollen when they bloom).




**Glyukoza-6-fosfat-degidrogenazaning (G6FD) oksidlovchi shikastlanishdan himoyalanishdagi roli. H2O2 ning, potensial oksidlovchining utilizatsiyasi qaytarilgan glutatyon (GSH) adekvatligiga bog‘liq, ta’sir natijasida hosil bo‘ladigan shakli kamayishi nikotinamid adenin dinukleotid (NADF). NADPH ning sintezi G6FD, GSSG - oksidlangan glutation faoliyatiga bog'liq.**

Clinically , this type of hemolytic anemia can manifest itself both in children and in adults. The disease is based on a chronic hemolytic process,

and its manifestations include anemia of varying degrees of regenerative-degenerative type, bright reticulocytosis, increased unconjugated bilirubin in the blood, and an enlarged spleen.



Enzymopathy associated with deficiency of the enzyme glucose-6-phosphate dehydrogenase

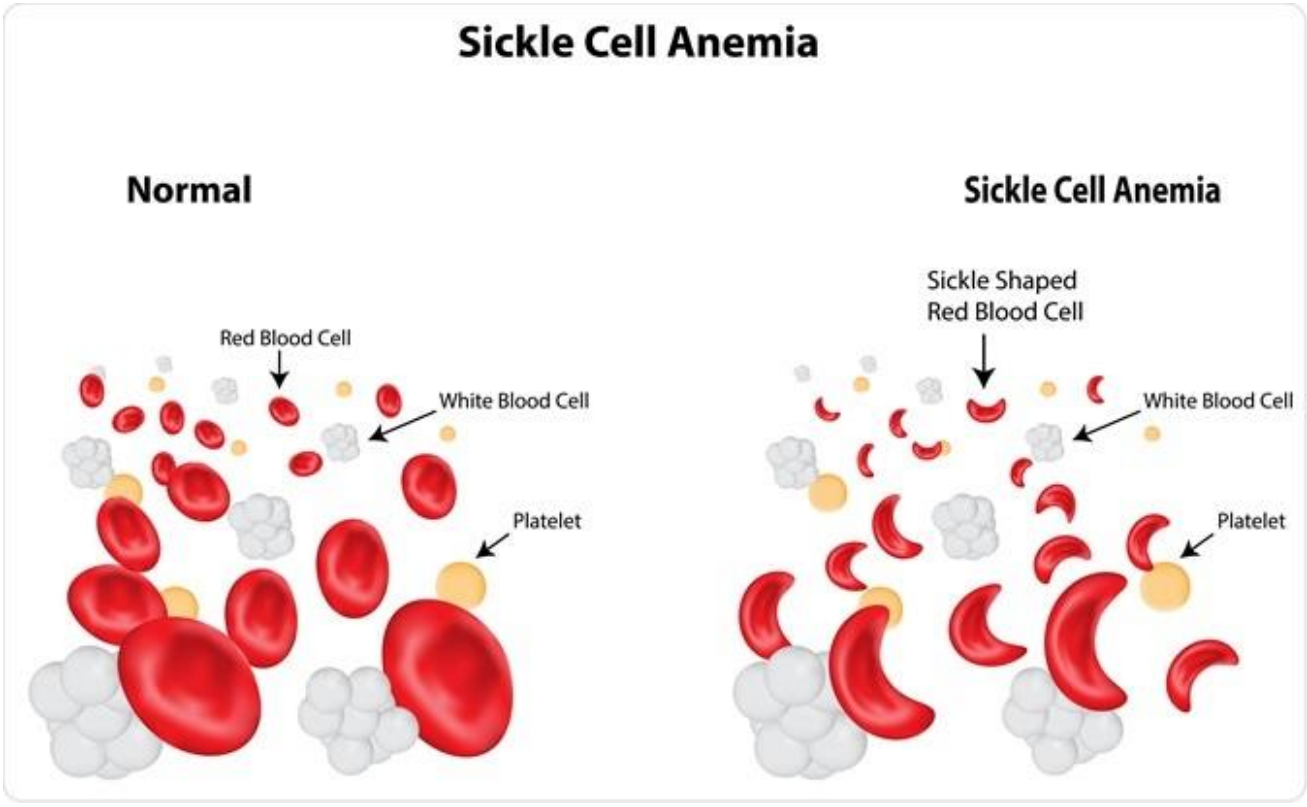
In the treatment of these anemias, it is important to identify the factor that causes hemolysis . If anemia is common in children, it is advisable to familiarize parents with the primary agents that cause anemia.

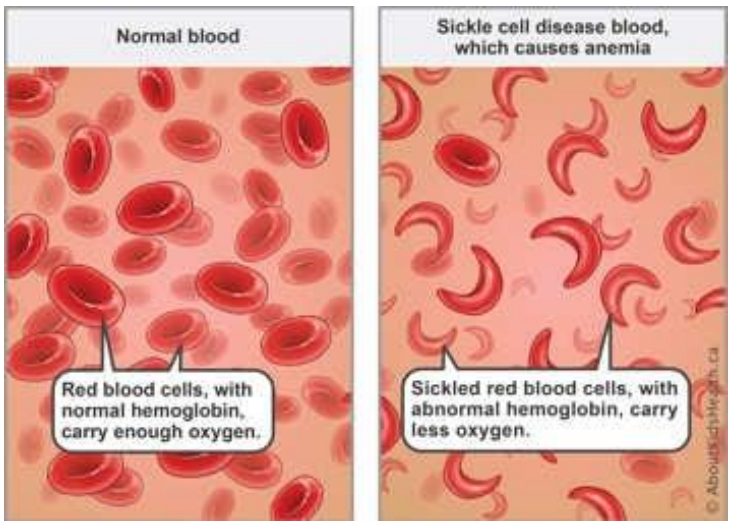
## Hereditary hemoglobinopathies

, differing in their physicochemical properties and amino acid composition . Of these, 3 types are normal (normal) hemoglobins. These are called primitive hemoglobin (NvR), fetal hemoglobin (NvG'), and adult hemoglobin (NvA).

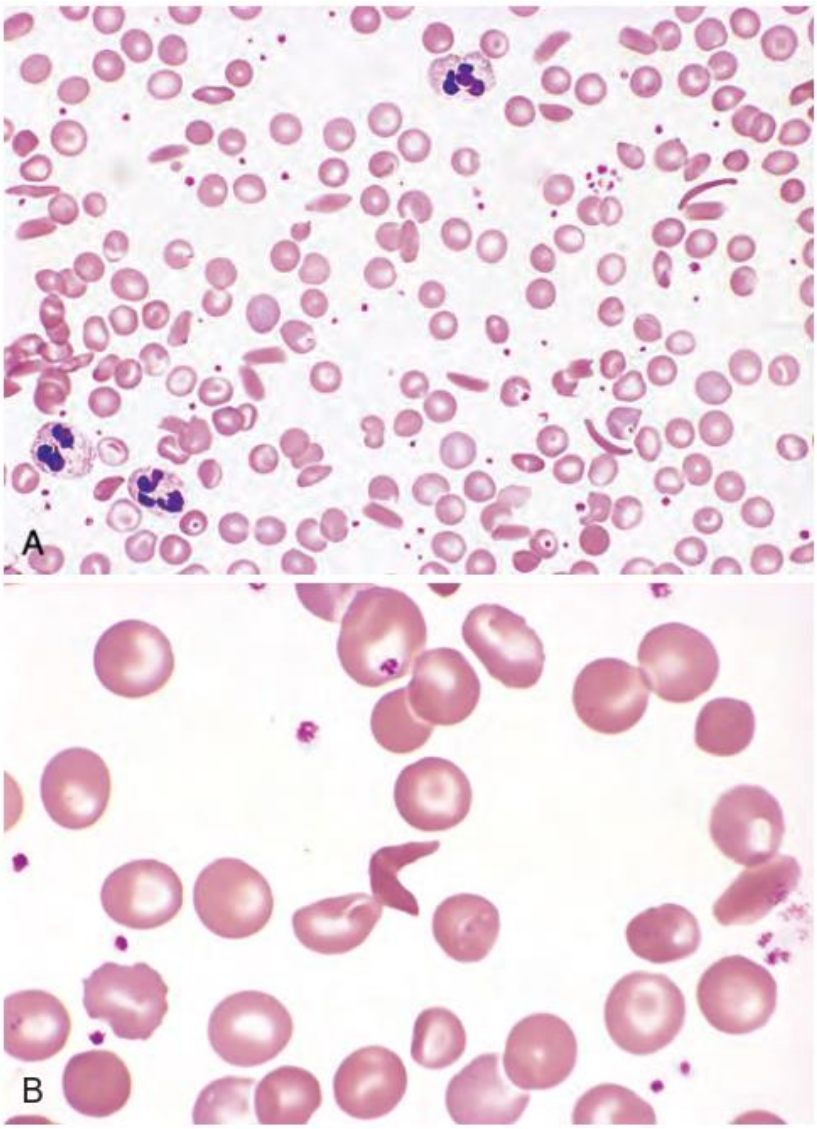
According to modern ideas , the occurrence of hemoglobinoses ( hemoglobinopathies ) is due to mutations in structural and regulatory genes that control the synthesis of polypeptides , which leads to the formation of hemoglobin with an abnormal structure. The most common and best studied of the hemoglobinoses are sickle cell anemia and thalassemia.

Sickle cell anemia is caused by the substitution of glutamic acid for valine in the β -chain of hemoglobin , resulting in the formation of NvS. A decrease in the partial pressure of oxygen in the environment causes the characteristic feature of the disease, namely a change in the shape of erythrocytes (sickle-shaped erythrocytes ). The disease occurs only in homozygotes (NvS), while heterozygotes (NvA *)* are practically healthy.



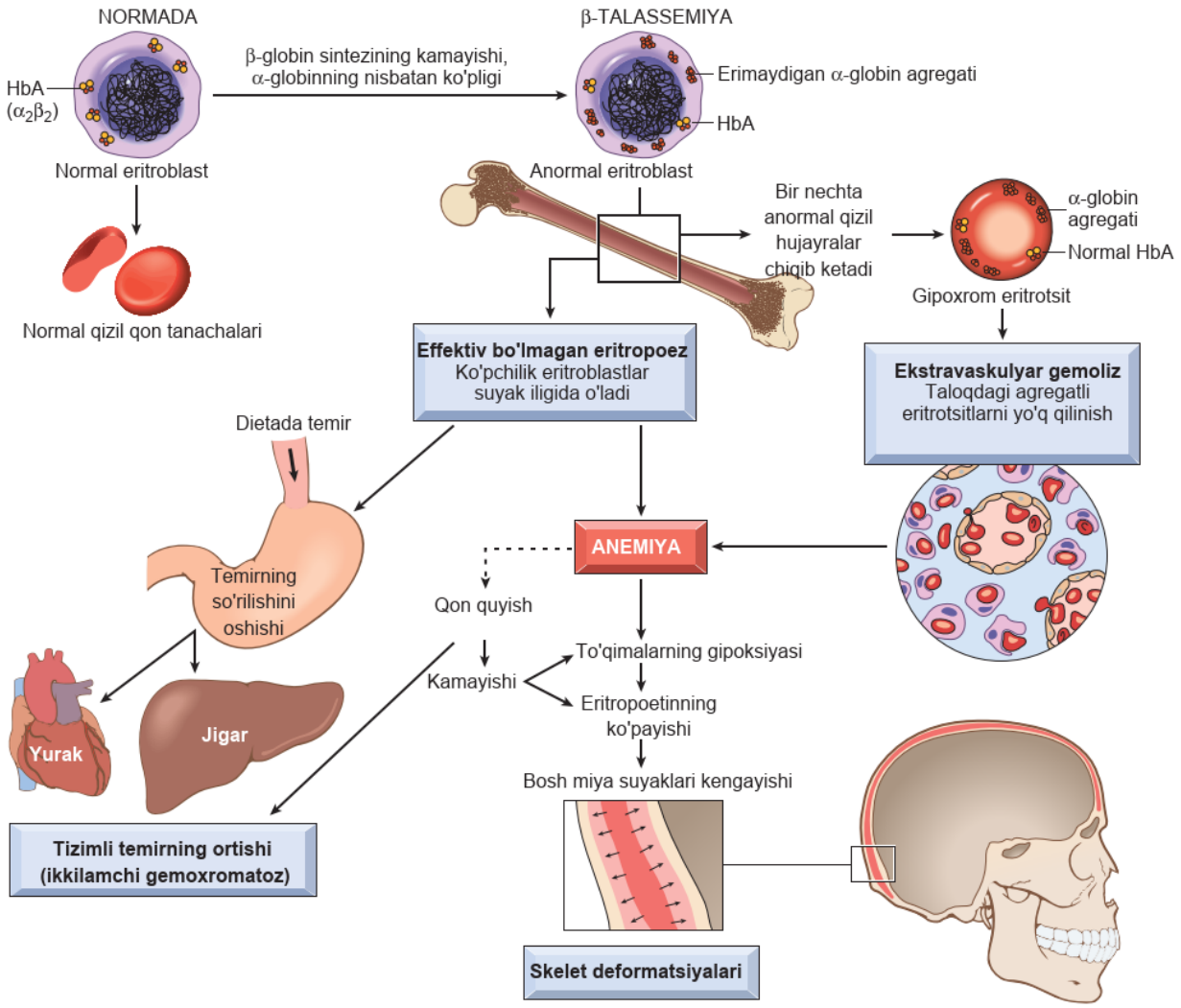

The disease has various symptoms, mainly progressive hemolytic anemia, sometimes accompanied by abdominal pain due to the development of splenic infarction . This symptom occurs due to the blockage of the vessels of the spleen by sickle-shaped erythrocytes.



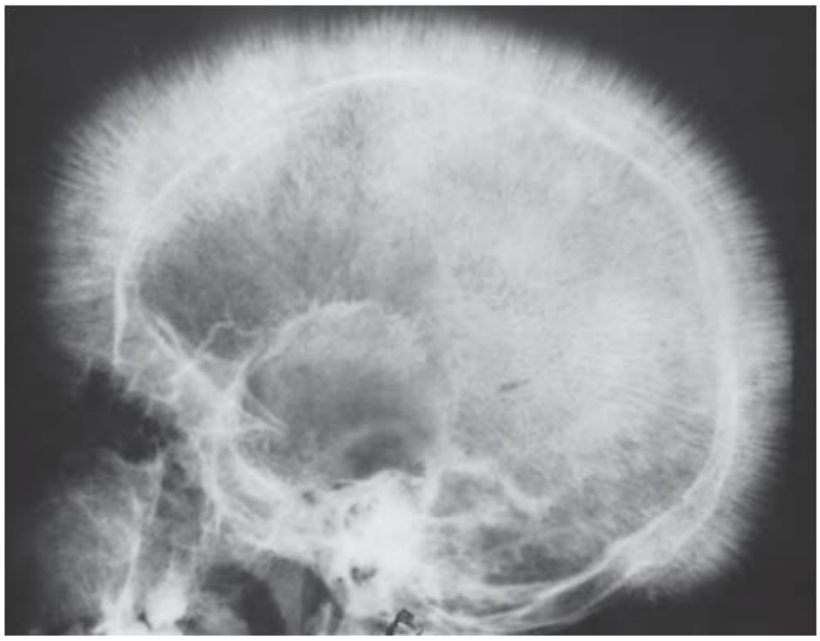
Blood smear in sickle cell anemia

## Thalassemia syndrome

Thalassemia syndromes are a heterogeneous group of disorders caused by an imbalance in globin chain synthesis due to inherited mutations that impair the synthesis of either the α-globin or β-globin chains that make up adult hemoglobin, HbA (α2β2), leading to anemia, tissue hypoxia, and red blood cell hemolysis. The two α chains in HbA are encoded by the same pair of α-globin genes on chromosome 16, while the two β chains are encoded by a single β-globin gene on chromosome 11. , whereas α-thalassemia results from a deficiency in the synthesis of α chains. The hematological consequences of decreased synthesis of one globin chain are not only due to hemoglobin deficiency, but also due to a relative excess of the other globin chain, especially in β-thalassemia (described below).




**b-talassemiyaning asosiy patogenezi. E'tibor bering, kasallikning o'ziga xos belgisi bo'lgan juftlashtirilmagan a-globin zanjirlarining agregatlari muntazam ravishda bo'yalgan holda ko'rinmaydi. Qon quyish ikki jihati bo'lib, kamqonlik va uning asoratlarini kamaytiradi, ammo temir bilan haddan tashqari yuklanishga olib keladi.**



Skeletal deformities in thalassemia

## Increased immune hemolytic anemias

Immune anemias are associated with damage and destruction (hemolysis) of erythrocytes by the action of antibodies. Several groups of immune hemolytic anemias are distinguished. These are hetero-, iso-, trans-, and a u toimmune anemias. In heteroimmune hemolytic anemias, the antigenic properties of human erythrocytes change under the influence of drugs, viruses, and microbes, and antibodies are formed against their own erythrocytes. Transimmune hemolytic anemia occurs as a result of the transfer of antibodies from a mother suffering from autoimmune hemolytic anemia to the fetus. If the erythrocytes of the mother and fetus have a common antigen, then antibodies are formed against them in the mother's body and hemolytic anemia occurs in the child. Autoimmune hemolytic anemia is characterized by the accumulation of antibodies in the blood of a person against the unchanged antigen of his own erythrocytes. In isoimmune hemolytic anemias, antibodies enter the child's body from outside and cause hemolysis. For example, during a blood transfusion according to the AVO system , the destruction of donor erythrocytes may be due to the action of the recipient's antibodies, or a similar situation is observed in hemolytic disease of the newborn.

## Hemolytic disease of infants

Hemolytic disease of the newborn is a serious disease of infancy and is associated with the presence of a strong antigen called Rhesus factor on the erythrocytes of the fetus. Rhesus factor in the erythrocytes of the fetus begins to pass from the mother to the blood of the fetus during the 3RD MONTH OF FETAL DEVELOPMENT and can lead to the formation of specific anti-Rhesus antibodies in it.

The pathogenesis of hemolytic disease of the newborn is as follows. During the pregnancy of a Rh-negative woman with a Rh-positive embryo, Rh incompatibility (incompatibility) occurs between the mother and the child. The mother's body is immunized and begins to produce anti - Rh antibodies, which pass through the placenta into the fetal blood and cause its erythrocytes to agglutinate and then hemolyze. Various lesions of the placenta facilitate the transfer of Rh antibodies to the fetus. It should be noted that immune incompatibility often occurs in repeated pregnancies, since the mother's body is sensitized during previous pregnancies. Repeated transfusions of blood to women without taking into account the Rh factor also contribute to the development of hemolytic disease to a certain extent. In hemolytic disease , in addition to the hypoxia associated with hemolysis

of erythrocytes , a violation of bilirubin metabolism is also of great importance, and the condition of the baby (the severity of the disease) is largely dependent on the level of reverse bilirubinemia in his blood. Unconjugated bilirubin has a number of toxic properties: it is an inhibitor of respiratory enzymes and, therefore, reduces tissue respiration, which is why it is called a tissue poison. This bilirubin is soluble in lipoids, due to which it causes severe damage to tissues rich in fatty compounds, such as the brain, liver, and adrenal glands.

of infants can be caused not only by Rh incompatibility, but also by incompatibility of factors of the AVO system of blood or other antigenic factors.

The most effective treatment is to quickly remove antibodies and unconjugated bilirubin from the baby's body. To achieve this goal , a blood transfusion is performed to replace the baby's blood.

One of the achievements of modern medicine in the prevention (prophylaxis) of hemolytic anemia due to Rh incompatibility is the method of immunoprophylaxis . According to this method , it is recommended to administer anti-D immunoglobulin to a Rh-negative woman when she gives birth to a Rh-positive child.

**Acquired (non-immune ) hemolytic anemia**

Acquired hemolytic anemias occur as a result of exposure to toxic substances on erythrocytes , or their damage due to mechanical or other factors. In all these cases, erythrocytes undergo hemolysis, that is, the structure of the erythrocyte membrane changes, the process occurs mainly in the vascular bed. Severe hemolysis of erythrocytes leads to anemia, impaired respiratory function of the blood and hypoxia. The amount of hemoglobin in the blood increases (hemoglobinemia), and when its level exceeds 20.9 mmol / l, hemoglobinuria (excretion of hemoglobin in the urine) occurs.

**In hemolytic anemias of blood landscape**

The degree of decrease in erythrocytes and hemoglobin depends on the rate of hemolysis. In the blood smear, physiologically regenerated cells and degeneratively changed erythrocytes (anisocytosis, poikilocytosis, segmented, fragmented) are revealed.

In the blood of patients with hereditary hemolytic anemia, microspherocytes (in Minkowski-Shoffar disease), sickle-shaped erythrocytes (in S-hemoglobinopathy), and target-shaped erythrocytes (in thalassemia) are observed. Activation of regenerative processes is expressed

in the appearance of reticulocytes, polychromatophilic erythrocytes, and erythrocytes with fewer nuclei in the blood. This is especially evident after a hemolytic crisis. Hemolytic anemias are normoblastic according to blood formation, and normo- or hypo-, and sometimes even hyperchromic (due to the adsorption of hemoglobin to erythrocytes) according to the color index. In all hemolytic anemias, symptoms such as yellowing of the skin and mucous membranes, very yellow blood serum, darkening of the color of urine (due to an increase in the amount of urobilin), darkening of the color of feces (feces), and hemoglobinuria are observed.

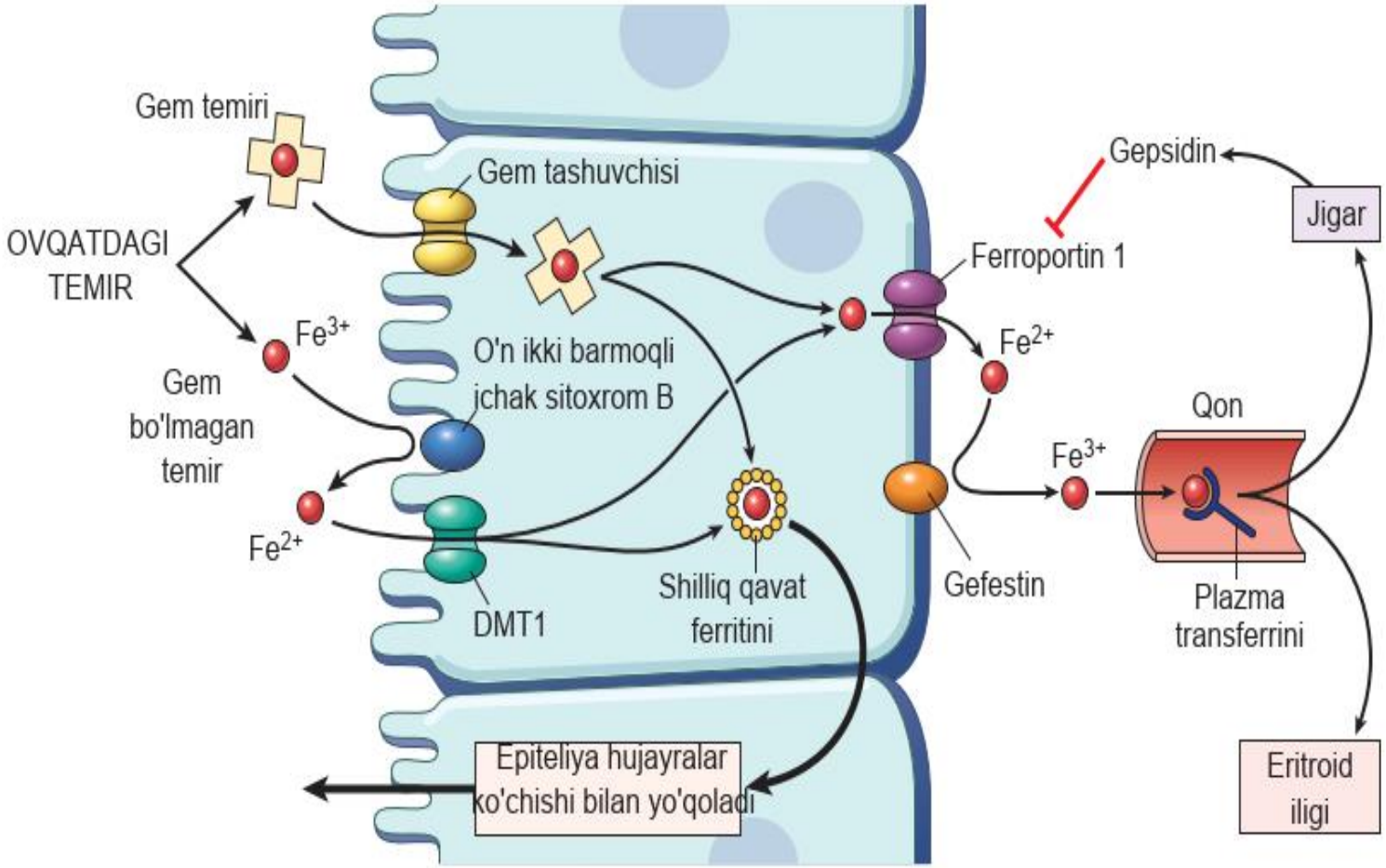
## 7. DEVELOPING ANEMIAS DUE TO IMPAIRED BLOOD FORMATION (DEFICIENCY ANEMIAS)

This group of anemias includes anemias that occur due to a deficiency of factors necessary for normal erythropoiesis: iron, vitamin B12 , folate, and protein.

### Anemias due to iron deficiency

These anemias are very common pathologies among children and adults. Among children, it occurs from 10% to 70%, especially among children and adolescents under 2 years of age. Iron is a component of various proteins in the body, especially hemoglobin. The iron-binding part of hemoglobin is heme. This form is a strong compound formed by iron with a porphyrin ring, which is not only present in hemoglobin, but also in myoglobin, cytochrome, catalase, etc. Iron is a component of enzymes and proteins (ferritin and transferrin) in non-heme form.

of iron in the fetus begins in the early stages of pregnancy and is carried out from the mother's body through the placenta. The maximum accumulation of iron in the fetus occurs in the last period of development in the mother's womb. After birth , the child receives iron with food, and its absorption occurs mainly in the duodenum and upper part of the small intestine. Only 10% of all iron in food is absorbed . However , heme iron contained in meat products is absorbed more easily than Fe contained in plants. For the absorption of non-heme iron, the presence of hydrochloric acid in the gastric juice is necessary, since it converts iron from $Fe^{3}$ to $Fe^{2}$.




**Temirning so'rilishini regulyatsiyasi. O'n ikki barmoqli ichak epitelial hujayrasi gem va gem bo'lmagan temirni o'zlashtirishi tasvirlangan.**

this way , its absorption is facilitated. The absorption process of heme iron depends on the alkaline reaction in the duodenum. There, iron is absorbed in the porphyrin structure and is released from porphyrin only on the intestinal mucosa , turning into an ionized form . The transfer of iron to the blood plasma is carried out by enzymatic reactions, and in the blood its transportable form - transferrin is formed. Transferrin delivers not only exogenous iron, but also endogenous iron (formed during the breakdown of erythrocytes) to the bone marrow and other organ depots. The body's iron reserves consist of hemoglobin iron, ferritin and hemosiderin contained in the liver, spleen, muscles, bone marrow, iron bound to transferrin, myoglobin, iron in iron-binding enzymes and biocatalysts.

Iron is excreted from the body through feces, urine, sweat, and natural blood loss.

From the above, it can be seen that iron deficiency anemia develops according to the following mechanisms:

1) The main cause of iron deficiency anemia in children is insufficient dietary iron, especially in young children who are formula-fed.

It is known that the absorption of iron in foods prepared based on cow's milk is 2-3 times less than the absorption of iron in mother's milk .

2) Iron deficiency anemia occurs in premature or large-birth-weight children under the age of two. This anemia also occurs in children born from multiple pregnancies, because iron deficiency in the mother during pregnancy, mainly due to toxicosis, hypoxia, mineral losses, prevents the accumulation of iron in the fetus.

3) Increased iron requirements occur during pregnancy, lactation (in nursing mothers), sepsis, accelerated growth, and in patients who have undergone surgery, leading to anemia.

4) In cases of enteritis, gastroenteritis, enterocolitis, duodenitis, celiac disease, cystic fibrosis, exudative diathesis, intestinal reactions, etc., the absorption of iron in the gastrointestinal tract is impaired.

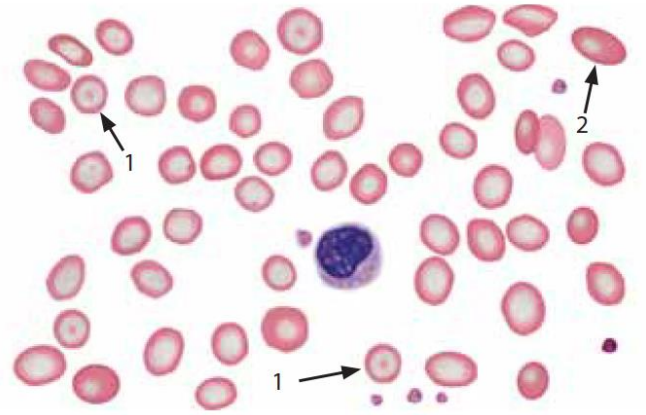
5) In hypo- and anacidic conditions, hypovitaminosis, the ionization of iron is impaired. Ascorbic acid, on the other hand , ensures the stability of divalent iron (trivalent iron is not absorbed by the body).

6) Iron is lost from the body in large quantities during chronic bleeding, puberty in girls (during the development of sexual function), intense physical exertion, hot climates , and work in high-temperature factories.

7) When the liver is damaged, iron storage is impaired because hepatocytes absorb and accumulate iron from the blood serum.

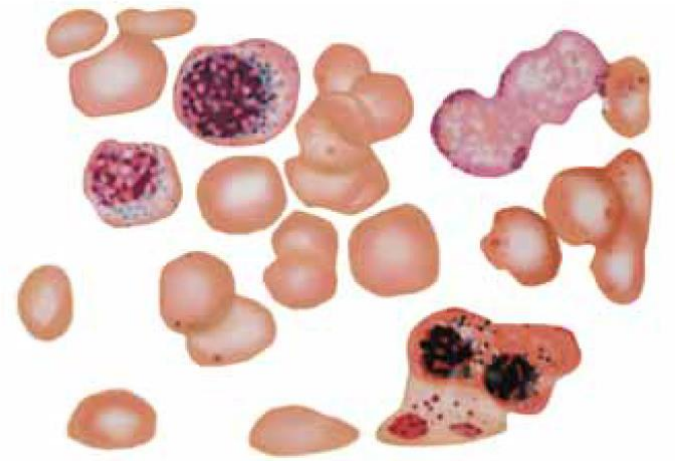
8) Due to the lack of enzymes in the erythroblasts of the bone marrow, iron absorption is impaired. In this case, the amount of iron in the blood serum is normal, or even increased. In all other iron deficiency anemias, a decrease in the amount of iron in the blood plasma (sideropenia) is observed. Therefore, prescribing iron drugs to such patients does not have a beneficial effect. In iron deficiency anemias caused by other causes, iron drugs have a very good effect.

Iron deficiency reduces the efficiency of erythropoiesis ; hemoglobin synthesis in erythroblasts is impaired. Insufficient hemoglobinization of red blood cells leads to impaired maturation of erythrocytes and their release into the bloodstream. In addition, erythrocytes undergo hemolysis in the bone marrow.




Peripheral blood picture in iron deficiency anemia , ×1000. Hypochromia and microcytosis, stellate (1) erythrocytes , ovalocytes ( 2)

In this anemia, the color index is hypochromic, 0.6-0.5 or even less, since the amount of hemoglobin in them is much less than the number of erythrocytes. Blood formation is normoblastic (in the bone marrow). Blood morphology is characterized by Yorkin hypochromia of erythrocytes. Poikilocytosis, anisocytosis, especially microcytosis are found among erythrocytes, that is, degenerative pathological forms of erythrocytes predominate. An increase in the number of reticulocytes among erythrocytes is an indicator of successful treatment of a patient with iron deficiency anemia.



Bone marrow . Ring-shaped sideroblasts , ×1000

It turns out that iron deficiency also occurs in the tissues of people with this anemia. Symptoms of the condition include brittle nails, hair loss, and atrophic processes in the gastric mucosa. Atrophic gastritis causes impaired iron absorption, which further aggravates anemia.

## Vitamin B12 and folate deficiency anemias

These anemias occur due to a deficiency of the necessary factors that ensure normal erythropoiesis, due to which blood formation changes from normoblastic to megaloblastic type.

Vitamin B $_{12}$ (extrinsic factor of Castle) was first isolated from raw liver in 1948. Vitamin B $_{12}$ , which comes with food (meat, eggs, liver, etc.) , combines with gastro-mucoproteins (intrinsic factor of Castle) contained in gastric juice, forming a protein-cyanocobalamin complex. In this case, vitamin B 12 is protected from the harmful microbes in the upper intestine and is easily absorbed through the intestinal wall. The main place of absorption of vitamin B $_{12}$ is the lower ileum, where it is stored in the liver. In the liver, vitamin B $_{12}$ acts on folic acid, converting it into tetrahydrofolate acid, which is involved in the synthesis of nucleic acids and the process of cell division.

Vitamin B12 and folate deficiency lead to impaired synthesis of nucleic acids, which is manifested by impaired cell division and an increase in cell size. First of all , rapidly dividing blood cells and cells of the gastrointestinal tract are damaged. The rate of amino acid metabolism in these cells is extremely fast . As a result of impaired mitotic processes in hematopoietic tissues, an increase in blood cells is observed. These include megalocytes, megaloblasts (erythropoiesis), extremely large polysegmented

neutrophils (myelopoiesis), and extremely large megakaryocytes (thrombocytopoiesis), which belong to the hematopoietic triad.

the gastrointestinal tract is manifested by atrophic inflammation of their mucous membranes. This leads to glossitis (a red, smooth condition of the tongue), enteritis, colitis, etc.

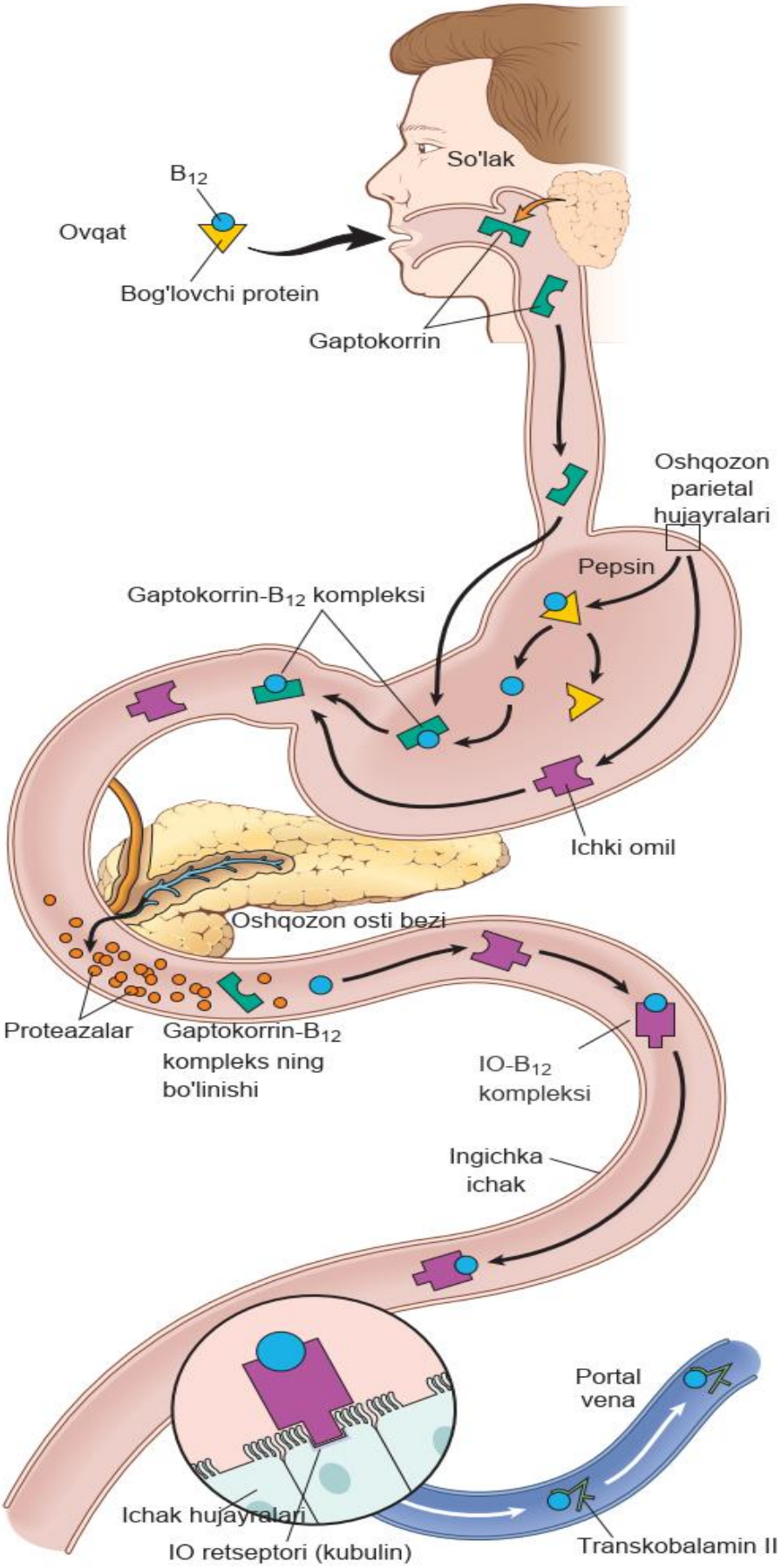
In addition to hematological and gastroenterological symptoms, neurological changes also occur, as a degenerative lesion called funicular myelosis occurs in the posterior columns of the spinal cord .

vitamin $_{B12}$ and folate deficiency anemia are:

1. Vitamin B12 $_{malabsorption}$ . This condition occurs due to a dysfunction of the gastromucoprotein-producing cells of the stomach. The decreased function of these cells is a result of the action of autoantibodies on them. This condition is mainly observed in Addison-Biermer's disease (pernicious anemia). Gastromucoprotein deficiency can also occur 2-8 years after total and subtotal gastric reactions.

2. Deficiency of vitamin $_{B12}$ and folic acid is caused by impaired absorption in the small intestine. This condition is observed in intestinal resection, its damage by tumors, diverticula, sprue, celiac disease (congenital epitheliopathy of the small intestine ). Among these diseases , invasion of the small intestine by a wide tapeworm occupies a special place, since this parasite is a predator of vitamin B12 $_{and}$ robs the human host of the vitamin. However, the location of the worm below the ileum does not lead to anemia.

3. Anemia often occurs in pregnant women. This is because the replacement of embryonic blood loss with normoblastic type in the fetus requires an increased need for erythropoietic substances.



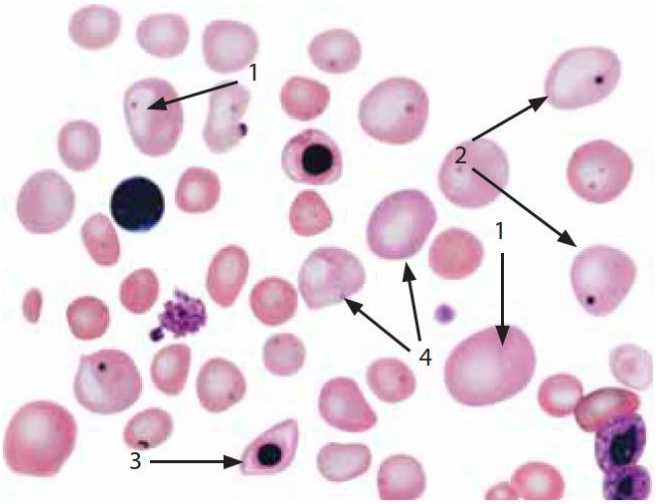

**Vitamin B12 singishining sxematik tasviri**

4. Liver damage such as hepatitis and cirrhosis can cause anemia. This occurs due to impaired storage of vitamin B12 and folate in the liver and changes in folate metabolism.

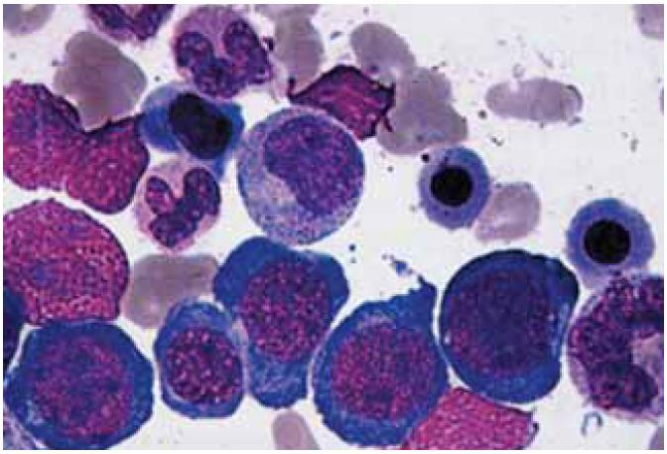
5. The main cause of anemia in children is exogenous vitamin B12 deficiency , which is associated with feeding infants with dried milk mixtures or goat's milk.

6. Finally, in some cases, anemia may occur due to the inability of the bone marrow to absorb vitamin B12 and folic acid. This condition is mainly due to a hereditary defect in the enzymes involved in the conversion of folic acid to its coenzyme form.

**Blood appearance.** The main symptom of this anemia is a decrease in the number of *red* blood cells.




Peripheral blood picture in B12 deficiency anemia: 1 — macro- and megalocytes; 2 — Jolly bodies in erythrocytes; 3 — normoblasts ; 4 — polychromatophil erythrocytes

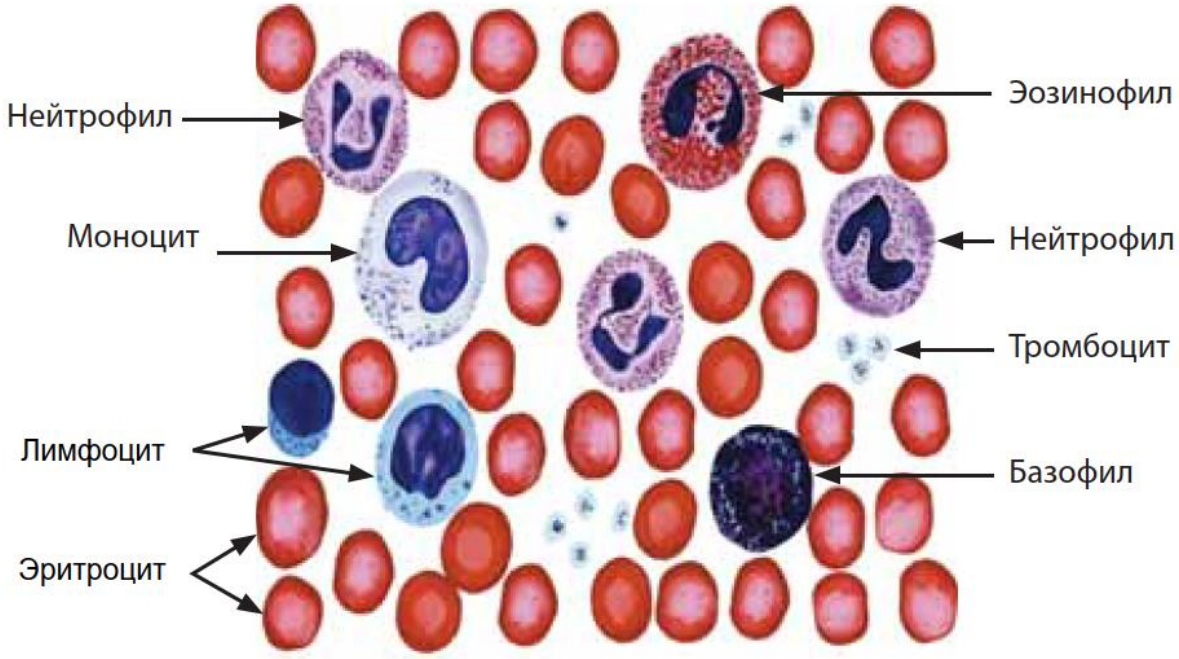


Myelogram in megaloblastic anemia

These are associated with a decrease in the proliferation and maturation of erythrocytes from precursor cells, the hematopoiesis changes from a normoblastic (bone marrow) type to a megaloblastic type, the efficiency of erythropoiesis decreases, the life span of erythrocytes is shortened. In the peripheral blood, along with pathological regenerative cells (megalocytes, megaloblasts), degenerative cells are also clearly visible. The maturation of megaloblasts into megalocytes is impaired.

## 8. LEUKOCYTE SYSTEM DISORDERS

Pathological changes in leukocytes, their formation in the blood-forming organs, are also manifested by quantitative and qualitative changes in leukocytes in the blood. These changes can be due to primary damage to cells of the granulocyte, lymphocyte and monocytic lines, such changes can occur during the periods of formation and maturation of leukocytes under the influence of various causal factors. Also, their destruction occurs in the blood-forming organs and in the blood vessels. Secondary changes in leukocytes are a response of the body to pathological processes occurring in the organs, tissues, and systems of the body, often as a protective reaction.




The main link in the pathogenesis of leukocyte pathology is a change in the reactivity of the body, including immunological and allergic reactivity. This is due to the functional properties of leukocytes. They participate in the processes of phagocytosis, antibody formation, inactivation of biologically active substances (histamine, serotonin,

bradykinin). Pathological changes are accompanied by local microcirculatory changes with trophic disorders in these areas. It should be noted here that one of the functions of leukocytes is to provide regenerating tissues with nutrients and cell division stimulants. Granulocytes, being carriers of vasoactive substances (basophils, eosinophils), participate in the development of vascular changes.

### Changes in leukocytes in quantity and quality

Quantitative and qualitative changes in blood leukocytes are manifested in the form of leukocytosis, leukopenia, as well as changes in the ratio of mature and immature leukocytes, and degenerative changes in leukocytes.

## 9. LEUKOCYTOSIS

An increase in the total number of leukocytes in 1 μl of blood is called leukocytosis.

Leukocytosis is a transient reaction of the body, often reflecting various physiological states of the body, or is mainly a sign of pathological conditions in the body, as a result of which the leukocytes in the blood return to normal.

Physiological and pathological leukocytes are distinguished.

1. Physiological leukocytosis is observed in various pathological conditions of the body. For example, leukocytosis occurs due to emotional, mental, excitement, physical stress (emotional or myogenic leukocytosis). There are also leukocytosis observed when moving from a horizontal to a vertical position (static leukocytosis), when eating food (alimentary leukocytosis). Also, leukocytosis is observed in pregnant women and newborns (the number of leukocytes in 1 μl of blood reaches 15,000).

2. Pathological leukocytosis is associated with various pathological processes in the body, they are observed in various infectious, bacterial and non-bacterial inflammatory diseases (infectious-septic leukocytosis). Leukocytosis also occurs in endogenous and exogenous intoxications (toxic leukocytosis), hypoxia, in patients with malignant tumors, in endocrine gland pathologies, as a result of impaired neurohumoral regulation of leukopoiesis . A further increase in the number of leukocytes (more than 20,000 per 1 μl of blood) is called hyperleukocytosis. Usually in such a case, immature neutrophils, lymphocytes and monocytes are observed in the peripheral blood . Since the picture of the blood resembles that of leukemia

, this condition is called a leukemia - like reaction. The ability of leukocyte cells to mature is sharply reduced in leukemia - like reactions. In this case, changes in the blood-forming organs, as well as in the blood, resemble those of leukemia, but they differ from leukemia in etiology (often the etiological factor is known) and pathogenesis (reactive hyperplasia of leukopoietic tissue). Leukemic reactions are temporary (short-term), reversible, and never develop into a tumor. ( See Leukemic reactions)

## Pathogenesis of leukocytosis

1. In the mechanism of physiological leukocytosis, the redistribution of leukocytes in the vascular bed is also of decisive importance (distributive leukocytosis). However, during prolonged strenuous exercise, the release of leukocytes from the bone marrow into the blood is accelerated.

Redistribution is the main feature of leukocytosis. Its short duration, after the cessation of the action of the provoking factor, the number of leukocytes returns to normal. In such leukocytosis, the ratio of leukocytes in the leukocyte formula is normal. Toxic granulocytosis is not observed in the cells. Physiological leukocytosis of pregnant women is associated, on the one hand, with the redistribution of blood, and on the other hand, with an increase in the formation of neutrophils among leukocytes. It is suspected that this is associated with profound endocrine changes in the body of a pregnant woman. 1 The mechanism of development of physiological leukocytosis in the body of young children is quite complex.

2. The mechanism of development of pathological leukocytosis is associated with increased leukopoiesis , increased leukocyte formation and accelerated release into the blood.

Increased leukopoiesis is manifested by an increase in the proliferative activity of leukopoietic tissue. This is a short-term reactive state of the tissue, as a result of which a large number of normal leukocytes are formed. It can also occur in the form of tumor-like hyperplasia, during which the appearance of leukocytes that have undergone pathological changes increases. In turn, this is what determines the reactive enhancement of leukopoiesis, the preservation of the ability of leukocytes to differentiate and the passage of immature cells. Reactive enhancement of leukopoiesis , which occurs under the influence of infectious factors, antigen-antibody complexes, and some chemical factors, may be associated with an increase in the production of humoral stimulants of leukopoiesis - leukopoietins (neutrophil, lymphocyto, monocytopoietins) and a decrease in the production of inhibitors of these factors . At this time, the proliferation of

leukopoietin-sensitive cells in the bone marrow is noted , as well as their acceleration of differentiation into mature cells. Which cells of the leukocyte lineage undergo hyperplasia depends on the etiological factor, resulting in an increase in the total number of leukocytes and an increase in the number of individual types of leukocytes.

Based on this, leukocytes are classified into neutrophilia, eosinophilia, basophilia, lymphocytosis, and monocytosis. In addition, absolute and relative types of leukocytes are also distinguished.

If the absolute number of leukocytes in the blood increases, such leukocytosis is considered absolute, which is the norm or is due to an increase in the production of leukocytes that have undergone pathological changes, including tumor cells, cells of the leukopoietic stem, or due to an increased transfer of leukocytes stored in the bone marrow into the blood vessels.

Relative leukocytosis is observed due to the redistribution of leukocytes closer to the vessel wall, when adrenaline is injected, during emotional stress, shock, collapse, as well as in the blood vessels of tissues located close to the focus of inflammation ( phlegmon , abscess, appendicitis).

Leukocytosis, which occurs as a result of reactive hyperplasia of leukopoietic tissue, is usually accompanied by an increase in the functional activity of leukocytes, which leads to an increase in the body's protective reactions.

phagocytes in parallel . Eosinophil leukocytosis, due to the antihistamine function of these cells, has a compensatory role in allergic reactions.

Blood picture. In leukocytosis, an increase in the total number of leukocytes is accompanied by a change in the leukocyte formula (calculated from 200 cells counted in a stained blood smear, the leukocyte formula is the percentage of individual leukocytes). The absolute or relative nature of these changes is determined by counting the absolute number of granulo- , agranulocytes in 1 μl of blood. The total number of leukocytes in 1 μl (or 1 liter) of blood and the leukocyte formula are calculated. Leukocytosis, especially neutrophilic leukocytosis, is often accompanied by the appearance of immature cells in the blood (shift of the nuclei to the left). Regenerative changes in leukocytes are also observed.

## Neutrophilic leukocytosis (neutrophilia, neutrophilia)

Neutrophilic leukocytosis is most often observed in infections that cause purulent inflammation (staphylococcus, streptococcus, meningococcus). It is also observed in aseptic inflammation, myocardial infarction, acute blood loss, acute hemolysis of blood, intoxications caused by exogenous and endogenous causes, and malignant tumors. The mechanism of the occurrence of neutrophilic leukocytosis is diverse. Such leukocytosis is often associated with increased production of neutrophils in the bone marrow and increased release into the blood. Endotoxins of streptococcus and staphylococcus mainly increase the production of neutrophilpoietins. They, in turn, cause hyperplasia of granulocytic cells in the bone marrow, acceleration of differentiation, maturation and release of granulocytopoiesis precursors from the bone marrow depot into the blood. It is necessary to take into account the shift of the nuclei of endogenous intoxications with the products of tissue breakdown (acute hemolysis, hypoxia, myocardial infarction, malignant tumors) to the left or right. This is explained by the fact that immature cells (myelocytes, metamyelocytes, neutrophils with a rod nucleus) are located on the left side of the Arnett and Schilling formula, while mature cells with segmented nuclei are located on the right side of the table. An increase in the number of immature neutrophils in the blood is manifested by a shift of the nuclei to the left, or by a shift of the nuclei of neutrophils located between them, as well as an increase in the number of segments of the nucleus (5-6 segments). With a shift to the right, the loss of young cells can also be observed. The following types of nuclear shift are distinguished:

1. Regenerative shift of nuclei to the left is an indicator of reactive activity of granulocytopoiesis, in which case, in conditions of moderate leukocytosis, the leukocytes contain rod-shaped nuclei, metamyelocytes, and even a small number of myelocytes.

2. Hyperregenerative shift of nuclei to the left - reflects excessive hyperplasia of the leukopoietic tissue of the bone marrow: impaired cell maturation, and a sharp rejuvenation of leukocytes (neutrophils) in the blood. At this time, the number of rod-shaped nuclei and metomyelocytes in the blood increases sharply, myelocytes increase, and even promyelocytes appear. Leukocytes may increase, or remain unchanged, or even decrease. This is a consequence of the first activation of the myeloid tissue, and then its significant weakening.

Hyperregenerative shift is observed in severe infectious diseases and purulent septic processes.

3. Degenerative shift to the left indicates a deep violation of leukopoiesis, its severe weakening. At this time, on the basis of general leukopenia, an increase in rod-shaped nuclei is revealed in the leukogram, but degenerative changes are detected in their cytoplasm and nuclei, segmented nuclei are reduced, and metomyelocytes are not revealed.

4. In the case of regenerative-degenerative left shift, there is an increased production of pathologically altered leukocytes in the bone marrow and a violation of their maturation. In this case, leukocytosis is noted, and in the blood smear, an increase in the number of rod-shaped nuclei, metomyocytes , myelocytes, and signs of degeneration are observed.

Right shift of nuclei. – is characterized by the appearance of hypersegmented neutrophils in the blood with a decrease in the number of rod-shaped nuclei. The right shift of nuclei occurs with leukopenia and indicates a severe weakening of granulopoiesis, for example, this condition occurs in radiation sickness, vitamin $B_{12}$ deficiency anemia. In neutrophilic leukocytosis, a change in the nuclear index is also noted (the nuclear index is calculated as the ratio of all unsegmented neutrophils to segmented nuclei :

$$\frac{M + M.M. + T.Ya}{C.Ya} =$$

is calculated. Normally, the nuclear index is 0.06-0.08. In a positive course of the disease (active increase in granulocytopoiesis ) The nuclear index does not exceed 0.25-0.4, which is most often observed in the case of regenerative shift of neutrophil nuclei to the left. In the case of hyperregenerative shift of nuclei, the index reaches 1.0-2.0.

## Eosinophilic leukocytosis (eosinophilia)

Eosinophilic leukocytosis is of important diagnostic importance. It is observed in allergic reactions and diseases , such as anaphylaxis, urticaria, Quincke's edema, bronchial asthma, hay fever , etc.

This is probably due to the participation of eosinophils in the inactivation of histamine. Eosinophilia, along with neutrophilic leukocytosis, is observed in rubella, rheumatism, and nodular psoriatic arthritis .

The pathogenesis of eosinophil leukocytosis in allergic reactions is associated with an increase in their production in the bone marrow and their accelerated release into the bloodstream. The basis of such changes is the ability of lymphocytes, after stimulation with an antigen, to secrete eosinophilic cytopoiesis stimulants. These substances allow the precursor cells (primary cells) of eosinophils to mature into eosinophilic granulocytes.

In addition, other biologically active substances released during antigen-antibody reactions also stimulate the release of eosinophils from the bone marrow into the blood.

Eosinophil leukocytosis is also typical for parasitic invasions, parasitic diseases, and myeloid leukemia. In trichinosis, echinococcosis (liver), ascariasis, etc., the number of eosinophils can reach 30% or more (hypereosinophilia).

Eosinophilia is also observed in hypofunction of the adrenal cortex, that is, with a decrease in the production of glucocorticoids (an increase in glucocorticoids, on the contrary, leads to eosinophilia, since these hormones facilitate the lysis of eosinophils). A slight eosinophilia is also observed during the recovery period from some infectious diseases.

## Basal leukocytosis (basophilia)

An increase in basophils is a relatively rare hematological symptom. It occurs in systemic blood diseases: chronic myelogenous leukemia, polycytopenia, erythremia, hemorrhagic diathesis, as well as in allergic reactions (as a target cell).

## Lymphocytosis – lymphocytic leukocytosis

Lymphocytosis, an absolute and relative increase in the number of lymphocytes, is a condition generally characteristic of early childhood.

Absolute lymphocytosis is an increase in the percentage of lymphocytes and the number of lymphocytes in 1 μl of blood (more than 3000). This symptom is observed in chronic infectious diseases

(tuberculosis, syphilis, brucellosis , etc.), infectious mononucleosis, a disease called infectious leukocytosis, lymphosarcoma and lymphocytic leukemia. Lymphocytosis is also observed in some acute infectious diseases: whooping cough, viral hepatitis, as well as in endocrine diseases - hyperthyroidism, acromegaly, etc.

If the total number of leukocytes decreases and the absolute number of lymphocytes is close to normal, but due to a decrease in other leukocytes (for example, a decrease in neutrophils), an increase in the percentage of lymphocytes is observed in the leukocyte formula, this condition is called relative lymphocytosis. Relative lymphocytosis is observed in infectious diseases accompanied by leukopenia due to a slowdown in granulocytopoiesis (influenza, dysentery).

The mechanisms of lymphocytosis and hyperplasia of leukocyte cells in the blood are still unclear. It is assumed that under the influence of some viruses (pertussis, viral hepatitis) and microorganisms (tuberculosis, syphilis, brucellosis pathogens), the formation of humoral substances that stimulate leukocytopoiesis is impaired, and the formation of special inhibitors of lymphocyte proliferation - chelons - in lymphocytes is also reduced.

**Monocytosis – monocytic leukocytosis**

An increase in the number of monocytes is observed in some acute infectious and viral diseases (rash, chickenpox, rubella). Long-term monocytosis is observed in some chronic processes and protozoal diseases (septic endocarditis, malaria, infectious mononucleosis, tuberculosis, leishmaniasis), as well as in individuals with agranulocytosis and chronic monocytic leukemia.

The occurrence of monocytosis in the above-mentioned diseases is due to the increased monocytopoiesis in the tissues of the blood-forming organs under the influence of monocytopoietins. The formation of monocytopoietins is stimulated by viruses, microorganisms, and protozoa. (Table 1)

**1- Table**

## Changes in leukocyte formula in norm and pathology.

| No. | Body condition | The number of leukocytes in 1 µl of blood | Basophils | Eosinophils | Neutrophils | | | | Lymphocytes | Monocytes | Nuclear shift index | Changes in leukogram |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | myelocytes | metamyelocytes | Rod-shaped cells | Segmented nuclei | | | | |
| **1.** | Rate (%) | 100 | 0 - 1 | 2 - 4 | - | - | 3 - 5 | 51 - 67 | 21 - 35 | 4 - 8 | 0.06 – 0.08 | No scrolling. |
| | absolute number | 4500 - 8000 | 0 – 80 | 100 - 250 | - | - | 180 - 400 | 3000 - 5500 | 1800 - 2500 | 200 - 600 | | |
| **2.** | Appendicitis Or pneumonia | -- | -- | 2 | -- | 5 | 15 | 65 | 10 | 3 | 0, 31 | Neutrophilic leukocytosis, regenerative shift of nuclei to the left. Relative lymphopenia |
| | | 15000 | -- | 300 | -- | 750 | 2250 | 9750 | 1500 | 450 | | |
| **3.** | Sepsis | 25000 | -- | -- | 5 | 18 | 29 | 28 | 18 | 2 | 1, 8 | Neutrophilic leukocytosis, hyperregenerative left shift of nuclei. Aneosinophilia, monocytopenia. |
| | | | -- | -- | 1250 | 4500 | 7250 | 7000 | 4500 | 500 | | |
| **4.** | Internal sweating | 3800 | -- | -- | -- | -- | 20 | 25 | 50 | 5 | 0.8 | Leukopenia, neutropenia, degenerative shift of neutrophil nuclei to the left (rod- |
| | | | -- | - | - | - | 760 | 950 | 1900 | 190 | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | nucleated). Aneosinophilia. Relative lymphocytosis. |
| **5.** | Vit. $B_{12}$ – folate deficiency anemia (Addison-Biermer anemia) | 2500 | -- | -- | -- | -- | -- | 45 | 50 | 5 | | Leukopenia, neutropenia, nuclear shift to the right. Relative lymphocytosis. Aneosinophilia |
| | | | -- | -- | -- | -- | -- | 1125 | 1250 | 125 | | |

# 10. LEUKOPENIAS

in the total number of leukocytes in 1 μl of blood below 4000. Leukopenia is characterized by a uniform decrease in the number of leukocyte types or a decrease in one of the individual types of leukocytes ( neutrophils , eosinophils, lymphocytes, monocytes). Leukopenia can be absolute or relative.

## Etiology of leukopenia

Leukopenia occurs when the body is exposed to an infectious agent (influenza, measles, rubella virus, enteritis toxin), under the influence of drugs (sulfanilamides, barbiturates, cytostatics, some antibiotics, antithyroid drugs, etc.), under the influence of ionizing radiation, a number of chemicals (benzene, arsenic, DDT, etc.), when eating food from grains that have spent the winter in the field, with genetic defects in the formation and differentiation of leukocytes (neutrophils), under stress, anophylactic and hemotransfusion shock. In addition, leukopenia is also a legitimate symptom of many diseases of the blood system, for example, this condition is observed in vitamin $B_{12}$ (folate acid) deficiency and hypoplastic anemia. Hepatolienal syndrome with an increase in the spleen (splenomegaly) is observed in many diseases, which also lead to leukopenia. A large group of leukopenia of unknown etiology is distinguished.

## Pathogenesis of leukopenia

The pathogenesis of leukopenia is diverse and depends on the causative factors. The following mechanisms underlie the occurrence of leukopenia:

1. Slowing of leukopoiesis.
2. Increased breakdown of leukocytes in the blood and blood-forming organs.
3. Redistribution of leukocytes in the vascular bed.
4. Separation of leukocytes from the body.

Leukopoiesis inhibition is caused by a violation of the neuro-humoral control of leukocyte formation (decreased leukopoietin production), a lack of plastic factors necessary for leukopoiesis (protein starvation, lack of cyanocobalamin and folic acid in the body). Leukopoiesis inhibition occurs due to hereditary or acquired damage to the stroma cells of granulocytes and agranulocytes during the differentiation of stem cells,

which normally determines the direction of myelo-lymphocytopoiesis , or generalized damage to leukopoietic tissue. Such a decrease in leukopoiesis occurs in hereditary neutropenia, under the influence of ionizing radiation, under the influence of tumor metastases (displacing normal cells that produce leukocytes), drug allergies, and severe destruction of leukopoietic cells in the blood-forming organs. The decrease in leukopoiesis, in some cases, involves all or most of the leukocyte lineages. For example, during the acute phase of radiation sickness, the destruction of hematopoietic stem cells occurs under the influence of ionizing radiation. In autoallergy caused by prolonged use of amidopyrine, immune agranulocytosis occurs, mainly affecting the granulocyte lineage.

Leukopenia resulting from the intense destruction of leukocytes. Leukocytes can be destroyed by antileukocyte antibodies. Antileukocyte isoantibodies can occur in some patients after blood transfusion (especially leukomas), which can lead to leukopenia with repeated blood transfusions. Antileukocyte antibodies often appear under the influence of certain drugs, in particular drugs with allergic or hapten properties (amidopyrine, phenacytin, sulfonamides, etc.). With repeated use of such drugs, they combine with specific antibodies and are adsorbed to leukocytes. Such leukocytes undergo agglutination and destruction (immune agranulocytosis). In autoimmune diseases, severe destruction of leukocytes is noted in the blood and bone marrow. Similarly, changes in the physical and chemical properties of leukocytes and their membrane permeability also lead to their lysis.

The mechanism of leukopenia resulting from leukocyte redistribution is that in this case the ratio of the total number of leukocytes circulating in the blood to the leukocytes that have approached the vessel wall changes, such a situation is observed in anaphylactic, hematotransfusion shocks, and leukocytes accumulate in the dilated capillaries of the lungs, liver, and intestines. Redistributive leukopenia is a temporary condition.

In some cases, leukopenia also occurs due to the excessive release of leukocytes from the body (for example, in purulent exudates, purulent endometritis, cholecystoangiocholitis, etc.).

In leukopenia, the body's reactivity is weakened. The protective functions of leukocytes are reduced to a point of complete cessation, leading to severe disorders of immunological reactivity, agranulocytosis. A sharp decrease in granulocytes in the blood is accompanied by myelotoxic (damage to the bone marrow) and immunological destruction of granulocyte cells under the influence of anti-leukocyte antibodies.

Agranulocytosis (aleksiya) is a sharp decrease in the number of myeloid leukocytes in the blood or their complete absence and is of great importance in pathology among true leukopenias.

The following forms of agranulocytosis are distinguished:

1. Immune agranulocytosis (death of leukocytes under the influence of anti-leukocyte antibodies), this condition occurs in collagenoses, infections, and when taking certain medications.

2. The type that occurs due to allergic causes.

3. Radiation-induced myelopoiesis disorder.

4. Myelotoxic (decreased myelopoiesis in the bone marrow due to exposure to chemicals, such as benzene, or physical factors) agranulocytosis includes these.

## Features of leukopenia in children

In addition to leukocytosis, leukopenia is sometimes observed in children, which reflects the deficiency of these reactions, which is considered a bad sign from a prognostic point of view. In premature and hypotrophic children, a leukopenic reaction is especially observed to infectious agents. The number of leukocytes in children varies depending on age, therefore, a decrease in the number of leukocytes by more than 30% from the average age norm should be considered leukopenia. Congenital types of leukopenia may be genetically linked or may be associated with the incompatibility of the antigens of the mother and fetus leukocytes, the intake of various medications by the pregnant woman, the presence of occupational hazards, the effects of ionizing radiation, etc. Neutropenia in children and infants is very well studied and has different names. The term agranulocytosis is used to emphasize the severity of the acute symptom complex. At the same time, the terms neutropenia, “granulocytopenia” and “leukopenia” reflect only one change in the blood. In children, neutropenia caused by the effects of drugs (analgin, pyrimenal , indomethacin, phenacytin, diazepam, sulfonamides, antithyroid drugs, antiepileptic drugs, levomecetin, ampicillin, etc.) and hereditary types of neutropenia (genetic agranulocytosis) are distinguished. Among leukopenias, lymphopenia, which occurs due to a decrease in lymphocytes, is less common, the cause of which is immunodeficiency diseases associated with the thymus.

Leukopenia in children is acute, subacute and chronic. In acute, subacute leukopenia, a decrease in the number of neutrophils per 1 μl of

blood (agranulocytosis) to 750 - 500 creates the opportunity for the development of generalized infections with adverse consequences.

Chronic types of leukopenia are constant and fluctuating. Among the leukopenias of children, according to IA Kassirsky, it is necessary to distinguish a type of physiological leukopenia. Such leukopenia is associated with the redistribution of leukocytes in the body. In such leukopenia, blood formation occurs normally in the bone marrow, and no changes are detected in the functional properties of leukocytes, leukocytopoiesis reserves do not change, and there is no need for treatment.

## 11. DEGENERATIVE CHANGES OF LEUKOCYTES IN THE BLOOD

Degenerative changes in leukocytes are manifested by anisocytosis, their wrinkling and even microformation, vacuoles in the cytoplasm of leukocytes, toxic granulation, Knyazkov-Dele granules (basophilic cytoplasmic nodules), large azurophilic granulation, loss of their own granules, pyknosis or swelling of the nuclei, hypo- and hypersegmentation of the nuclei, mismatch of the degree of maturation of the nuclei and cytoplasm, karyoregression, cytolysis, etc. Degenerative changes are most often observed in neutrophilic granulocytes and monocytes. Their occurrence is associated with the formation of leukocytes with impaired metabolism, which leads to structural anomalies (in leukemias, hereditary enzymopathies). Other causes include damage to blood-forming organs and blood leukocytes from the effects of various pathogenic factors (bacteria, viruses, antibodies, ionizing radiation, leukocytolytic serums, etc.).

## 12. CHANGES IN THE LEUKOCYTE FORMULA IN CHILDREN'S DISEASES

At different ages of childhood, in various conditions and diseases, not only the total number of leukocytes in the peripheral blood changes, but also the percentage ratio of individual cells. In infants, an increase in the total number of leukocytes is observed, and this is physiological leukocytosis. Sometimes the number of leukocytes in 1 μl of blood can be 15 thousand or even more. The leukocyte formula of children's blood changes depending on age. In newborns, the ratio of neutrophils to

lymphocytes is similar to that of older people, that is, neutrophils are 65%, lymphocytes are 25%. In the following days, the percentage of neutrophils decreases, and the number of lymphocytes increases rapidly, and by 3-7 days after birth they become equal, this is called the first leukocyte cross-section. In the following days, the number of lymphocytes continues to increase (by the end of the 2nd week they reach 55%). Neutrophils continue to decrease (in 12-15-day-old infants they are 26-29%), by the end of the 1st year, lymphocytes reach a maximum of 65%, and neutrophils decrease to a minimum of 25%. In the following years, the number of lymphocytes gradually decreases. Neutrophils, on the contrary, increase. When the child reaches 3-5 years, sometimes at 7 years, a second crossover occurs. The age of occurrence of this crossover in children depends on their individual constitutional characteristics. In later years, the percentage of neutrophils increases and reaches the norm in adolescence at 12-14 years.

A characteristic feature of the hematopoietic system of children is that the system is very unstable to various external and internal harmful influences. In early childhood, the leukopoietic system has a high reactivity. Therefore, leukocytosis can occur under the influence of physiological and pathological factors, for example, leukocytosis is observed during fear, pain, deep breathing, coughing, physical exertion, screaming, etc. Strong stimuli lead to a sharp increase in the number of leukocytes in the peripheral blood, a pronounced regenerative shift of neutrophil nuclei. These features of the hematopoietic organs of children often contribute to the development of leuko-like reactions (see the section on leuko-like reactions). The hematopoietic organs of children have a very high regenerative capacity, that is, young cells are quickly created instead of dead cells. Severe infectious diseases in early childhood are accompanied by individual characteristics in the reaction of the hematopoietic system. In some cases, children experience very pronounced neutrophilic leukocytosis and regenerative shift of their nuclei (in purulent, septic and inflammatory diseases, mumps, sepsis, osteomyelitis, tetanus, smallpox, jaundice and other pathological processes).

Moderate neutrophil, eosinophil, leukocytosis (leukocyte count reaches 15-18 thousand) is observed in children with rubella, rheumatism, acute allergic, some forms of pulmonary tuberculosis and other diseases. In whooping cough, infectious mononucleosis, rickettsiosis, miliary tuberculosis intoxication, congenital syphilis, brucellosis, dysentery, chickenpox, infectious hepatitis, leukocytosis is accompanied by a

simultaneous increase in lymphocytes and monocytes, even with a lymphoid-leukomyoid picture of the blood (the number of leukocytes in 1 μl of blood reaches 50 thousand and the number of lymphocytes in them increases).

In children, an increase in eosinophils to 20-30% is observed in helminthic invasions (ascariasis, trichinellosis, epistrichosis, fascioliasis, etc.). Eosinophilia to a lesser extent occurs in the invasion of hookworms, broad tapeworms, echinococcus, etc. Usually, eosinophilia in children occurs in allergic diseases, reactions, reactions to vaccines, food (especially when artificially feeding, infants, when drinking cow's or goat's milk), as well as in allergic diathesis, urticaria, angioedema, bronchial asthma and other diseases (nodular periarthritis, eosinophilic granuloma), etc.

## 13. LEUKEMA

A systemic disease of the blood-forming tissue that has a tumorous nature is called leukemia.

tumor proliferation of immature cells of the hematopoietic system . These are cells of the 2nd, 3rd, and 4th classes of hematopoiesis. In leukemias , the phenomena of hyperplasia and metaplasia of the hematopoietic tissue are irreversible. Since the process of cell proliferation exceeds the process of their differentiation (differentiation), a large number of immature, pathologically changed (anaplastic) cells are released into the blood. Tumor leukemia cells metastasize. Therefore, leukemia is considered a systemic lesion of the hematopoietic tissue.

the disease progresses, leukemic infiltrates form in organs other than the blood-forming organs: the liver, spleen, kidneys, skin, and other organs and tissues.

Depending on the type of proliferating tissue and its cellular composition, leukemias are divided into myelogenous leukemia, lymphogenous leukemia, reticulosis, erythromyelosis, and megakaryoblastosis.

Depending on the basis of tumor development and the loss of the ability of leukemia cells to differentiate, acute and chronic leukemias are distinguished. The basis of the tumor of acute leukemias is formed by undifferentiated blast cells of grades 2-3-4 of hematopoiesis, which have lost their ability to differentiate. These include acute myeloblastic , lymphoblastic , monoblastic , megakaryoblastic leukemias , and

erythromyeloses. If the basis of the tumor is formed by grade 2 and 3 cells, that is, morphologically unidentified cells , then we are talking about acute undifferentiated leukemia.

The basis of the tumor of chronic forms of leukemia is formed by mature and mature cells. These include chronic myelo- , lympho- , mono- , megakaryocyte leukemias and chronic erythromyelosis. The less differentiated the cell that becomes a tumor (malignant) , the more acute and malignant the disease will be. Acute leukemias begin suddenly in healthy people , since the onset of the disease is asymptomatic. The patient's condition gradually worsens. After the onset of the disease, it ends with death within a few months , even a month. In chronic leukemias, exacerbations of the disease alternate with remissions (alleviation of the disease). With the help of treatment, it is possible to extend the remission period to 1-2 years. Depending on the form of leukemia and the success of treatment, the life expectancy of patients is 2-10 years or even longer.

In leukemia, the total number of leukocytes increases significantly and can reach 200-500,000 or even 1 million in 1 mm $^3$ of blood. This form of leukemia is called leukemic leukemia. In addition, leukemias are further divided into subleukemic , aleukemic, with an average increase in the total number of leukocytes, and leukopenic leukopenia, i.e., with a decrease in the total number of leukocytes. Leukopenia forms of leukemia often develop in chronic forms of the disease. Leukemic and leukopenic leukemias are observed in acute leukemias.

## Etiology of leukemia

The etiology of leukemia has not yet been definitively determined. Several factors have been implicated in the development of leukemia: oncogenic viruses, ionizing radiation, chemical carcinogens, and genetic abnormalities.

The role of oncogenic viruses was established by inducing leukemia by injecting a cell-free filtrate of leukemia cells from animals with leukemia into healthy animals (chickens). The viral nature of leukemias has been proven in cases of sudden leukemias in birds, cats, mice, large mammals, monkeys, and other animals. The viruses belong to the group of S-type RNA-containing viruses. Viruses are transmitted from one organism to another through feces, urine, nasal and throat secretions, and finally from mother to offspring (visceral lymphoma in chickens). In humans, the viral origin of lymphoid tissue tumors has been established in Burkitt's lymphoma (a DNA-containing virus), but direct transmission of

leukemia from person to person has not been proven. No leukemia has been observed in children who have been breastfed by mothers with leukemia, or when blood from donors with leukemia is transfused into healthy people.

The role of ionizing radiation in the development of leukemia in animals has been experimentally proven. This factor is also of great importance in humans. It is known that among the inhabitants of the cities of Hiroshima and Nagasaki, which experienced the atomic bombings of 1945, the number of people with leukemia is high. There is evidence of an increase in the number of people with leukemia in patients treated with X-rays, radioactive isotopes, as well as in children irradiated before birth.

occur as a result of exposure to chemical carcinogens . For example, occupational exposure to chemicals ( benzene ) or treatment with mutagenic drugs ( cytostatic immunosuppressants, butadione, chloramphenicol ) . Leukemia and other tumors can occur as a result of administration of carcinogens to animals . Benzene extracts of tissues of leukemia patients , as well as products such as tryptophan , tyrosine , and indole, can also cause leukemia in animals . Such substances have the property of causing mutations in hematopoietic cells of mice and in human embryonic cells . Genetic features of hematopoiesis are of great importance in the etiology of leukemia . It is known that ethnic groups with a high incidence of leukemia , the presence of a dominant or recessive inheritance of the disease from generation to generation ( familial chronic lymphocytic leukemia ) , as well as the concordance of the form , clinic and hematological picture of leukemia in 1/3 of twins originating from one cell. The same increased incidence of leukemia is observed in patients with chromosomal anomalies ( Down , Shershevsky - Turner and Klinefelter syndromes ) and in patients with immune system defects.

h /, known as the Philadelphia chromosome , has been revealed in people with chronic myeloid leukemia. In the experiment, genetically pure strains of mice were created that were highly susceptible to leukemia and almost immune to it.

In the mechanism of leukemia, gene mutations or epigenome changes that control the processes of proliferation and maturation of hematopoietic cells of classes 2 and 3 play an important role. In the bone marrow, a clone of tumor cells with unlimited growth potential but very low differentiation ( relatively benign , monoclonal phase) appears. The rapid growth of leukemia cells leads to their spread throughout the blood system (metastasize). As the process progresses, new cells are mutated due to the

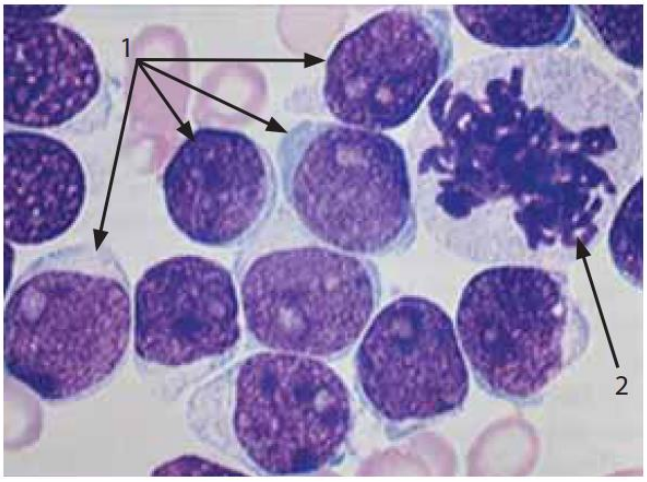
continuation of the etiological effect and spontaneously, resulting in the formation of new leukemia clones. This is the polyclonal phase of leukemia development , the most malignant phase , characterized by tumor progression of cells, and these cells lose their morphological and cytochemical differentiation.

In the blood and blood-forming organs, a large number of degeneratively transformed blast cells appear , which spread beyond the blood-forming system and form leukemic infiltrates (accumulations of leukemic cells) in various organs. The most resistant clone of cells to the effects of drugs , radiation , hormones and chemicals makes up the majority. Violation of hemopoiesis leads to anemia, hemorrhagic thrombocytopenia and the development of hemorrhagic syndrome , as a result of which secondary infections are activated.

As a result of weakening immunological control, forbidden clones of cells appear , which produce antibodies against the body's own tissues , resulting in the development of autoimmune processes.

In leukemia, the blood picture reflects the changes described above.

acute leukemias, blast cells predominate. The disruption of cell differentiation and maturation is characterized by the absence of intermediate forms in the transition of blast cells to mature cells , that is, mature granulocytes , lymphocytes, and monocytes are rare in the blood , a condition called the " leukemic gap . "

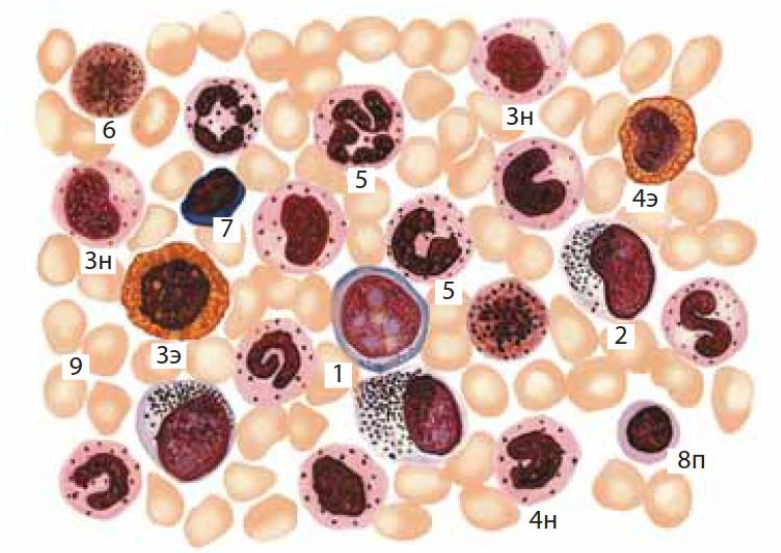



Acute myeloblastic leukemia (M0). Peripheral blood : 1 — blasts ; 2 — mitosis, ×1000

**In chronic myeloid leukemia,** the number of granular cells in the blood - segmented nuclei , rod-shaped nuclei , metamyelocytes , as well as younger , immature cells of this series - myelocytes , and occasionally

even myeloblasts - increases. The number of eosinophils and basophils in the blood also increases.

In the terminal phase of chronic myeloid leukemia, a blast crisis is observed , during which the number of myeloblasts and undifferentiated blast cells in the blood increases sharply. Chronic lymphocytic leukemia is characterized by a sharp increase in lymphocytes in the blood. Lymphocytes make up 80-96% of all leukocytes in the blood. Most of these lymphocytes are mature cells, but prolymphocytes and lymphoblasts are also found. The most common type of β-lymphocyte leukemia is leukemia.




Peripheral blood picture in chronic myeloid leukemia: 1 — myeloblast; 2 — promyelocyte; 3n — neutrophilic myelocyte; 3e — eosinophilic myelocyte; 4n — neutrophilic metamyelocyte; 4e — eosinophilic metamyelocyte; 5 — neutrophil; 6-basophil; 7 — lymphocyte; 8p — polychromatophilic proerythrocyte; 9 — erythrocyte

Other hematopoietic cells in the bone marrow are almost completely destroyed and replaced by lymphocytes. Patients develop anemia and thrombocytopenia.

Blast crisis occurs in only 3-4 cases of this type of leukemia. Leukemia in children is one of the most severe and relatively common diseases of the blood-forming organs.

Acute forms of leukemia are most common in children aged 2 to 4 years. After that, acute leukemias are also observed among adolescents aged 12-14 years. Sometimes acute leukemia affects very young infants at the age of one month , one week , or even the day after birth. The clinical course of leukemia in children is polymorphic.

Acute lymphocytic leukemia is the most common form of leukemia in preschool children, accounting for 75% of leukemia cases in children of this age. Acute myeloid leukemia in children accounts for 5% of all leukemias , although it is rare.

The incidence of acute myeloid leukemia in school-age children is increasing, reaching 35%, and leukemia accounts for 50%. According to the combined data of Hungarian scientists, the ratio of individual forms of leukemia in children is as follows.

1. Acute lymphoid leukemia – 70% of cases
2. Acute myeloid leukemia – 26% of cases
3. Myelo-monocytic leukemia - in 2 % of cases
4. Chronic myeloid leukemia – 2% of cases
5. Chronic lymphocytic leukemia – 0% of cases

According to various scientists, half or 1/3 of all malignant tumors in children are leukemia. Boys are 5 times more likely to develop acute lymphocytic leukemia than myeloid leukemia. Girls are 2 times more likely to develop acute lymphocytic leukemia than myeloid leukemia.

The diagnosis of acute leukemia in children is often difficult and can sometimes be made only after histochemical examination, since this method is able to distinguish between blast cells of the lymphoid and myeloid lineages (differentiation).

In young children, acute leukemias often have a leukemic and subleukemic appearance, while chronic myeloid leukemia has a leukemic appearance.

**Chronic lymphocytic leukemia**

This form of leukemia belongs to the chronic lymphoproliferative diseases and is considered an incurable pathology for older people. There are 5 stages of the development of chronic lymphocytic leukemia (CLL):

• Stage 0 is characterized only by lymphocytosis of more than 15 × 109/l (if by chance a patient is diagnosed with SLL at this stage, he or she can live for more than 14 years);

• Stage 1 - lymphadenopathy is added to lymphocytosis (from this point on, life expectancy may be about 8 years);

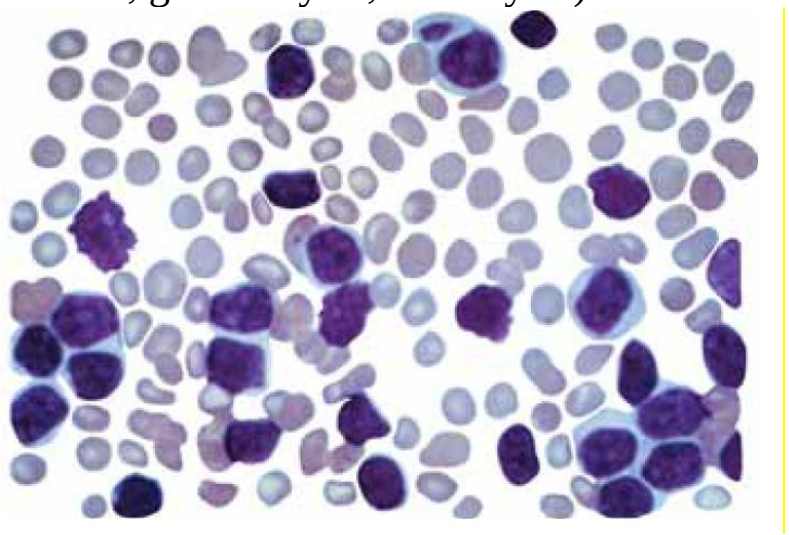
• Stage 2 - splenomegaly appears (life expectancy may be about 6 years);

• Stage 3 – anemia develops;

• Stage 4 - thrombocytopenia occurs (the patient's life expectancy does not exceed 19 months).

In the final stage of the disease, the total number of leukocytes in the blood in most cases is about 50-100 × 109 / l (exceptions are possible). 60-80% of peripheral blood cells are represented by mature (often atypical) lymphocytes, with a small number of prolymphocytes. CD markers disappear.

Blood smears contain characteristic Botkin-Gumprecht bodies (shadows) - these are lymphoblasts (remnants of their nuclei) smeared on a glass slide during the preparation of the smear. Other blood cells (erythrocytes, platelets, granulocytes, monocytes) are rare.



Peripheral blood picture in chronic lymphocytic leukemia

Lymphoid cells in the bone marrow significantly exceed 10% (metaplasia). Characterized by a significant enlargement of the lymph nodes, spleen, and the presence of leukemic infiltrates in other organs. In 50% of cases, patients with SLL die from infection due to a sharp decrease in immunity: there are many lymphocytes in the blood, but they are functionally incomplete and do not differentiate into plasma cells (i.e., antibody synthesis is impaired) and do not provide auxiliary functions and mechanisms of cellular immunity.

There is a deficiency of granulocytes and monocytes due to bone marrow metaplasia. In some patients, against the background of tumor development, "forbidden clones" of lymphocytes may appear, which cause severe autoimmune diseases, including autoimmune hemolytic anemia and thrombocytopenia (the cause of death may be massive hemolysis or bleeding).

## 14. CHANGES IN PHYSICAL AND CHEMICAL PROPERTIES OF BLOOD

The physicochemical properties of blood (specific gravity , surface tension , osmotic pressure , electrical conductivity , acid-base balance , clotting ability) undergo various changes in pathological conditions. Their study is of practical importance.

of blood (normally 1.050-1.060) The composition of blood depends on the amount of erythrocytes , proteins , and minerals. Normally, the specific gravity of blood plasma is 1.025-1.034 , and the specific gravity of erythrocytes reaches 1.090. This indicator increases in pathological processes associated with water loss and blood thickening. Blood dilution causes a decrease in its specific gravity.

Blood viscosity. If the viscosity of water is taken as 1 , then the viscosity of blood plasma is 1. 7-2. 2 , and that of the blood itself is 4. 5-5. This indicator depends on the amount of proteins , colloids , and formed elements in the blood. When the amount of $SO_2$ in the blood increases (hypercapnia), erythrocytes swell , their membrane surface increases , frictional force increases , and at the same time, oxygen and sugar are released from erythrocytes into the plasma. This leads to an increase in blood viscosity. The viscosity of venous blood is higher than that of arterial blood. This is due to the excess of $SO_2$ in venous blood . Polycythemia and hyperproteinemia (especially with an increase in the amount of fibrinogen in the blood) cause an increase in blood viscosity. In cases of hydremia , anemia, and hypoproteinemia, a decrease in blood viscosity is observed.

Surface tension of blood. The surface tension of blood is normally 57-58 dyn/cm. When bile acids are released into the blood (in mechanical and parenchymal jaundice) , in uremia , asphyxia and other diseases, the surface tension of the blood decreases. In pathological conditions such as hypoproteinemia and hydremia, its surface tension increases.

Osmotic pressure of blood. The osmotic pressure of a liquid depends on the concentration of ions and molecules in the solution. The osmotic pressure of a healthy person's blood ranges from 7. 6 to 8. 1. At this time, the total amount of ions and molecules in the blood is equal to 300 milliosmoles / liter. An increase in the osmotic pressure of the blood is called hyperosmia , and a decrease is called hypoosmia. Sodium ions play a significant role in changing the osmotic pressure of the blood. If the sodium content in the blood is more than 150 mEq / l., hyperosmia occurs , and if it is less than 135 mEq / l., hypoosmia occurs. When the body loses water sharply , when excessive salt is consumed in food, or when the

excretion of sodium chloride from the body is impaired, the osmotic pressure of the blood increases. In cases of severe hyperosmia, cells are dehydrated , and tissue proteins are rapidly broken down. As a result of a decrease in the osmotic pressure in the blood and intercellular fluids, a large amount of water enters the cells , resulting in swelling of the cells , edema. Edema of brain cells is especially dangerous in this regard. A decrease in the osmotic pressure of blood plasma leads to hemolysis of erythrocytes.

When erythrocytes are kept in a hypertonic solution , part of the water in their cytoplasm is released into the external environment, as a result of which the erythrocytes become wrinkled. When erythrocytes are kept in hypotonic solutions , a rapid influx of water into their cytoplasm is observed. In such cases , the volume of erythrocytes increases. It is known that normal human erythrocytes can increase their volume by 46 times , and rabbit erythrocytes by 37 times. The continued entry of such excess water into the cytoplasm leads to the rupture of the erythrocyte membranes and the release of hemoglobin into the external environment (hemolysis occurs).

The ability of erythrocytes to maintain their integrity in hypotonic solutions is called their resistance to osmotic pressure. The concentration of a hypotonic solution that causes hemolysis of a relatively large proportion of erythrocytes in the blood is called the minimum resistance , and the concentration of the solution that causes the disintegration of all erythrocytes in the blood is called the maximum resistance. The minimum resistance of the blood of healthy people is 0.44-0.46 l to a sodium chloride solution , and the maximum resistance to this solution is 0.28-0.32 l. The resistance of erythrocytes to osmotic pressure depends on their maturation , shape, and plasma composition. The ratio of the thickness of erythrocytes to their diameter is called the sphericity. The sphericity of normal erythrocytes is 0.27-0.28. The sphericity of erythrocytes in a person with hereditary spherocytosis is greater than normal. At this time, erythrocytes have a spherical shape. They have low resistance to osmotic pressure. Therefore, hereditary spherocytosis is accompanied by hemolytic anemia. In diseases accompanied by hypercapnia, the osmotic resistance of erythrocytes decreases. Because when the amount of SO2 in the blood increases, erythrocytes swell. In conditions of hypercholesterolemia, the osmotic resistance of erythrocytes increases. The reason for this is that cholesterol is deposited on the erythrocyte membrane and strengthens it.

The erythrocyte sedimentation rate (ESR) in healthy men is 3-9 mm/h , while in patients it is 7-12 mm/h. An increase in the erythrocyte sedimentation rate (ESR) is observed in infectious inflammatory diseases , malignant tumors , collagenoses , nephroses, and pathological processes accompanied by tissue destruction. An increase in ESR during inflammatory diseases is associated with a change in the amount of proteins (albumin , globulin , fibrinogen) in the blood . Under normal conditions, the membranes of erythrocytes have a negative charge , so they repel each other. Large dispersed proteins with a low ionic charge (globulin , especially fibrinogen) accumulate on the surface of erythrocytes , reducing their ionic charge. As a result, erythrocytes easily approach each other and quickly settle. Other factors also affect the sedimentation rate of erythrocytes. For example , an increase in the amount of cholesterol in the blood also increases the ECHT , while lecithin, on the contrary, reduces it. In diseases accompanied by increased blood viscosity and a decrease in the number of erythrocytes (hydremia , anemia), ECHT increases. Increased viscosity and an increase in the number of erythrocytes (dehydration , erythremia) lead to a decrease in ECHT. In hypercapnia, due to the large amount of water entering the erythrocytes, their specific gravity decreases. In this case, ECHT slows down. When the osmotic pressure of the blood plasma increases , erythrocytes sink faster. In this case, erythrocytes lose water , their volume decreases , and their specific gravity increases.

## 15. BLOOD HEMOSTASIS SYSTEM AND ITS PATHOLOGY

The body's defense response to stop bleeding from damaged blood vessels consists of a complex set of physiological and biochemical processes. In this process, blood vessels , blood cells (especially platelets) and components of the coagulation system are involved in a interconnected manner. Taking into account the specific properties of individual components involved in stopping bleeding, two mechanisms are distinguished in stopping bleeding:

1 ) vascular platelet mechanism ;

2 ) blood clotting.

Hemostasis is a response reaction that restores blood flow to damaged vessels by vascular-platelet mechanisms and the involvement of platelets in this reaction. This mechanism is also called " microcirculatory hemostasis " . The vessels of the microcirculatory system participate in these processes , the small blood vessels in the damaged tissues narrow

under the influence of biologically active substances. However, the narrowing of the vessels is not enough to completely stop the flow of blood, and platelets are involved in the process. Shortly after the injury occurs, platelets begin to adhere to the damaged areas of the vessel wall (adhesion). At the same time, platelet aggregation occurs (sticking together). Aggregates of platelets precipitate on the agglutinated platelets , as a result of which a platelet plug forms in the damaged part of the vessel.

Platelets aggregate under the influence of their own and ADF released from damaged tissues. Adrenaline , serotonin and thrombin have a stimulating effect on the aggregation process. Platelet factors that accelerate blood clotting are released from the aggregated platelets. The most important of them is platelet factor 3 (thromboplastic factor).

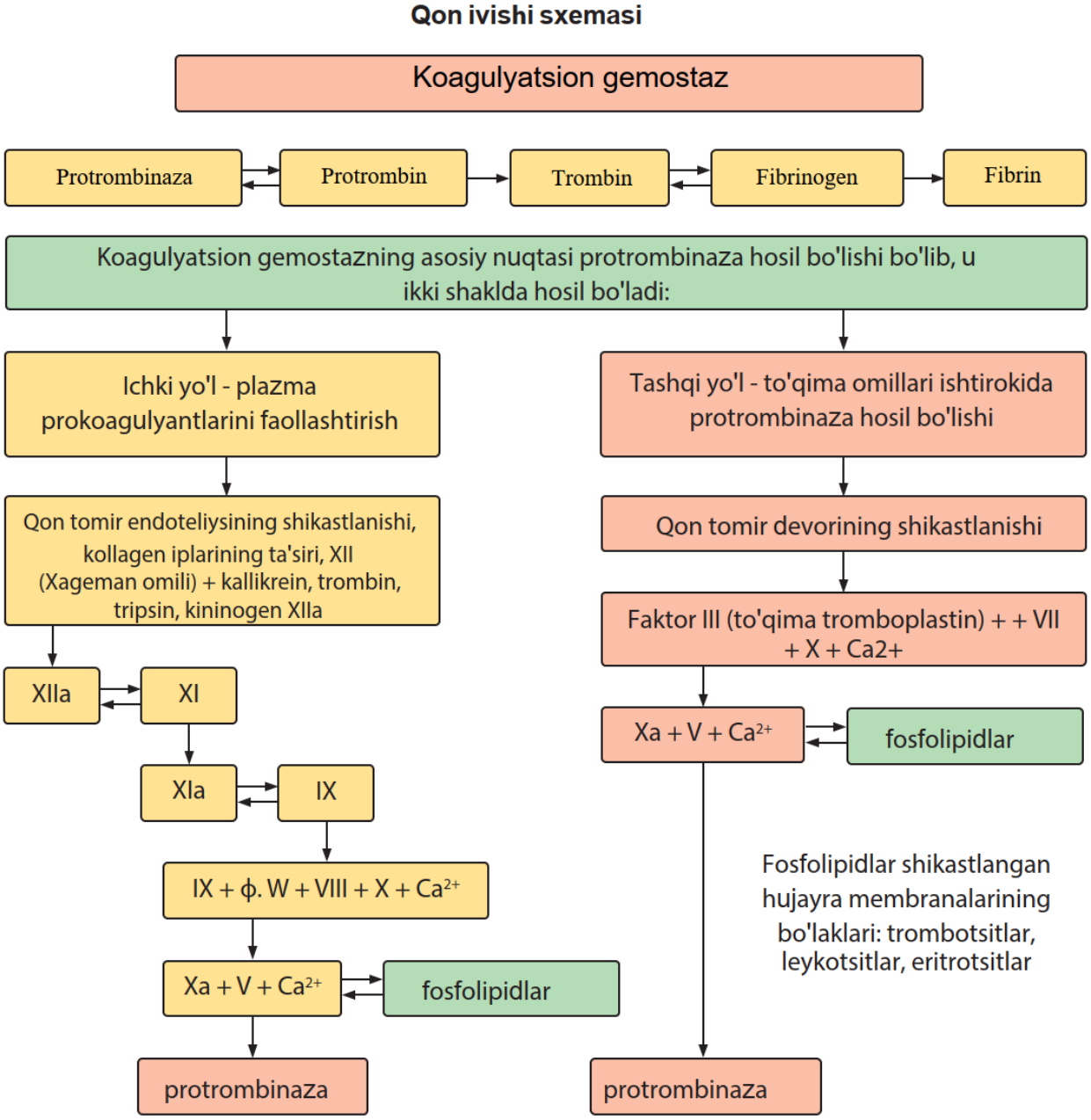
Physiologically active substances in platelets normally provide the strength of the vascular wall. It follows that a sharp decrease in the number of platelets (violation of their aggregation and adhesion properties) leads to increased vascular permeability , sometimes to small hemorrhages on the surface (petechiae).

There is a close relationship between the vascular-platelet mechanisms of hemostasis and the blood coagulation system. Blood clotting is the second main mechanism of hemostasis. When large vessels are damaged, vascular-platelet reactions are no longer sufficient to stop the flow of blood. In such conditions, blood coagulation (clotting) and the closure of the damaged vessel with a thrombus are of great importance. A thrombus is formed as a result of the activity of the blood coagulation system. The body has a blood coagulation system and a system that prevents blood from clotting, which is opposite to it. The anticoagulant system prevents blood from clotting inside the vessels.

Blood clotting is an enzymatic autocatalytic reaction consisting of 3 stages. This process begins with the conversion of fibrinogen in plasma to fibrin. Currently, there are 13 plasma factors involved in the blood clotting process. They are named by Roman numerals. In addition, there is a special name for clotting factors (procoagulants). Normally, there are more procoagulants in the blood than are necessary for clotting. However, they are in an inactive form, and the body's physiological anticoagulant system prevents their activation.

The first stage of the blood clotting process is the formation of active thromboplastin. According to the source of its formation, two types of thromboplastin are distinguished : tissue and plasma thromboplastin. The active form of tissue thromboplastin is formed by the action of plasma

factor 3 (SA ions , factors VI and X) on substances released into the blood from damaged tissues.



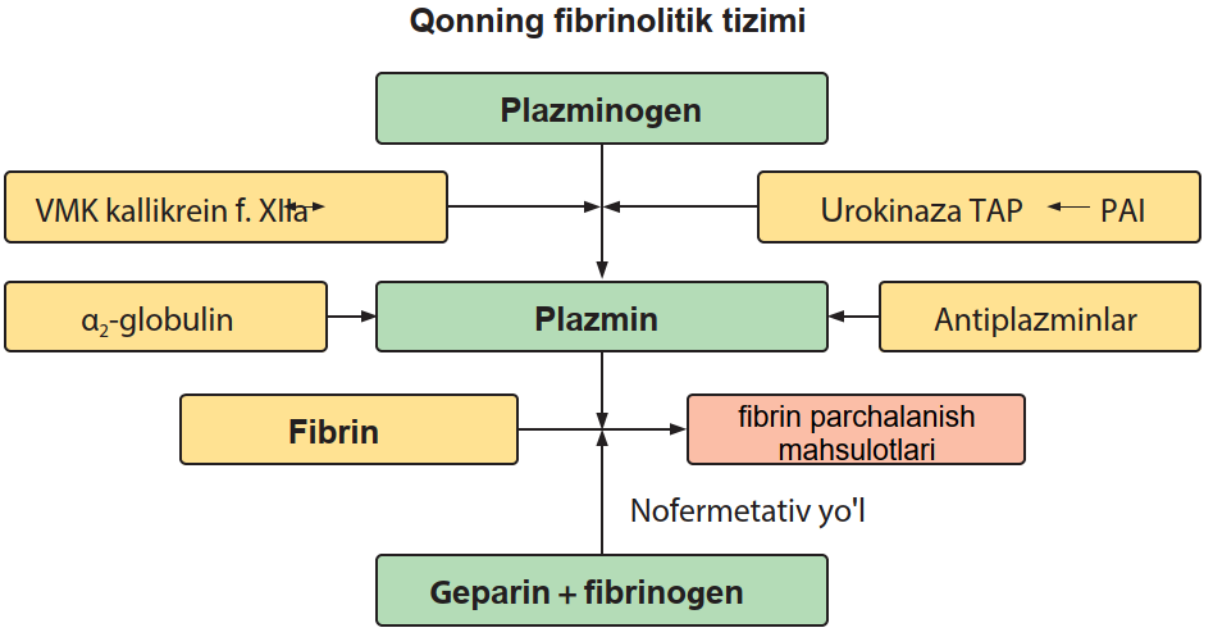

In the initial phase of plasma thromboplastin formation, coagulation factor X II is activated. Plasma thromboplastin is formed as a result of the interaction of activated contact factor with plasma factor 6 ( factors XI, IX, V III , X, V and Ca++ ions) and platelet factor 3. Tissue thromboplastin causes blood to clot in 60-70 seconds. Activation of plasma thromboplastin and blood clotting last for 5-8 minutes.

In the second phase of coagulation, prothrombin is converted to thrombin. This process occurs under the influence of activated

thromboplastin and Ca+ ions. However, activation of prothrombin can occur through an autocatalytic pathway.

of coagulation is the conversion of fibrinogen dissolved in plasma into fibrin. Under the action of thrombin, small molecular peptides (peptides A and B) are released from the fibrinogen molecule , resulting in the formation of fibrin monomers. They polymerize under the influence of fibrin stabilizing factor ( factor XIII ) , turning into fibrin threads. Then a certain amount of blood serum is released from the thrombus , the volume of the clot decreases , and its retraction occurs. Factor 6 of platelets ( retrocoenzyme ) participates in this process.

Fibrin formed in the damaged areas of the vessels, after fulfilling its hemostatic function, is rapidly degraded. This process is called fibrinolysis. In the blood plasma, there is an enzyme called fibrinolysin, which hydrolytically degrades fibrin. It is inactive. This protein, called profibrinolysin, is converted to fibrinolysin under the influence of special activators.




Biologically active substances - anticoagulants - also participate in preventing blood from clotting in the vessels. The main ones are heparin , antithrombin , antithrombaplastins. Heparin is synthesized in mast cells . It has a slowing effect at all stages of coagulation . There are 6 types of antithrombins. Antithrombaplastins prevent the formation of active thromboplastin. Under physiological conditions, blood clotting and the activity of its anticoagulation systems are in a state of dynamic equilibrium. Their mutual balance is controlled by neuroendocrine mechanisms. Sometimes the ability of blood to clot decreases and a

tendency to bleed occurs in the body , while accelerated clotting, on the contrary, creates conditions for the formation of thrombosis . In addition, disruption of the vascular-platelet mechanisms of the hemostasis system also causes a tendency to bleed in the body.

Hemostasis disorders are also caused by hereditary and acquired defects of the vessels. One of the hereditary diseases of the vessels that predispose to bleeding is hemorrhagic telangiectasia. This disease is transmitted from generation to generation in an autosomal dominant manner. In childhood, the disease is latent. Later, dilated areas appear in the small vessels (venules , capillaries) of the skin and mucous membranes, which are easily damaged. The most striking symptom of the disease is nosebleeds. Also, bleeding can occur from the digestive system , lungs , and urinary tract.

infectious and toxic factors (influenza , angina , rubella , food poisoning) , drugs (quinine , barbiturates , antibiotics) also lead to a violation of the permeability of the vascular wall and the vascular mechanisms of the hemostasis system , resulting in the appearance of hemorrhagic spots on the skin and mucous membranes.

Slowing of blood clotting leads to increased bleeding and the development of hemorrhagic symptom complex. In this case, the blood begins to flow spontaneously or bleeding occurs after a minor injury. Decreased blood clotting ability is often caused by hereditary deficiency (deficiency) of plasma and tissue coagulation factors.

first phase of blood coagulation is caused by the absence of antihemophilic factors in the body ; namely, factor VII ( hemophilia A) , factor IX (Christmas factor) (hemophilia V) , and the plasma thromboplastin precursor factor XI (hemophilia S). Types of hemophilia A , V and S differ little from each other in clinical terms, and therefore they are called hemophilia by the same name. Types of hemophilia A and V are inherited in a recessive manner, linked to the X chromosome. The second phase of blood coagulation is a violation of thrombin formation, which can be caused not only by a deficiency of procoagulants and procoagulants , but also by a decrease in the synthesis of prothrombin in the liver. It is known that, in addition to prothrombin, coagulation factors V , II, IX, X are also synthesized in the liver with the participation of vitamin K. A decrease in this vitamin has a negative effect on the synthesis of these factors. Therefore, in practical medicine, vitamin K antagonists are used to weaken the blood's ability to clot (for example, coumarin , dicoumarin, etc.). It should also be noted here that in endogenous vitamin K deficiency

(mechanical jaundice , enteritis , resection of the small intestine , diffuse liver damage), the synthesis of these coagulation factors is reduced , resulting in hemorrhagic syndrome.

Another cause of decreased blood clotting is hypoprothrombinemia in newborns. The infant's intestines lack the bacterial flora that converts provitamin K from food into real vitamin K , and there are not enough bile acids necessary for its absorption from the intestines. In addition, there is not enough vitamin K in mother's milk, all these factors combine to cause hypoprothrombinemic purpura in infants.

Disturbance of the III phase of blood coagulation , that is, the formation of fibrinogen, occurs for two reasons ;

1 ) Due to low levels of fibrinogen or its complete absence.

2 ) It may be due to increased activity of the fibrinolytic system .

Decreased fibrinogen in the blood (hypofibrinogenemia) and its complete absence (afibrinogenemia) are associated with various causes. In addition to hereditary afibrinogenemia and congenital deficiency of fibrinostabilizing factor [ factor XII ] , the amount of fibrinogen is reduced due to impaired synthesis due to liver damage. Other causes include liver cirrhosis , pulmonary tuberculosis , and metastasis of malignant tumors to the bone marrow. In some cases, fibrinogen with a changed molecular structure and physicochemical properties is also synthesized in the body. This condition is called dysfibrinogenemia. Dysfibrinogenemia occurs as a result of exposure to ionizing radiation , infectious and toxic factors. In such cases, fibrin polymerization is impaired and blood clots slowly. In addition, in cases of damage to the lungs , uterus , pancreas , thyroid gland, severe burns , and anaphylactic shock, profibrinolysis activators are released from the tissues into the blood. These are enzymatic substances (fibrinokinase and proteolytic enzymes) that convert profibrinolysin into active fibrinolysin , under the influence of which fibrinolysis increases. As a result, hemorrhages , hematomas , hematuria , and even severe bleeding occur on the skin and mucous membranes. Afibrinogenemic bleeding occurs especially often during childbirth. Fibrinogen and fibrin are also broken down by other proteases. For example , increased fibrinolysis occurs in this way during acute leukemia. A decrease in blood clotting ability may also be associated with an increase in its anticoagulant content.

This is the reason for bleeding in injuries, trauma, anaphylactic shock, exposure to ionizing radiation , pulmonary tuberculosis, etc. In addition , a decrease in blood clotting leads to thrombocytopenia. Thrombocytopenia is caused by infections , drugs , endogenous and

exogenous intoxications , exposure to ionizing radiation , changes in the blood-forming tissue with leukemia and tumor metastases.

The pathogenesis of thrombocytopenia is based on a decrease in the production of platelets from megakaryocytes of the bone marrow , or an acceleration of platelet destruction in the vessels. In addition , it is associated with a decrease in the number of platelets in the peripheral blood , or their redistribution in the body , or their consumption for the formation of large numbers of thrombi .

inhibition of platelet destruction may also be due to antiplatelet autoantibodies . One of the causes of thrombocytopenia is Werlhof's disease. The etiology of this disease has not yet been determined . In this disease, the destruction of platelets in the blood vessels is accelerated. The mechanism of its development is attributed to autoimmune reactions , deficiency of thrombocytopoietic factor, and internal factors that inhibit platelet production .

Thrombocytopenia not only leads to a violation of the first phase of blood coagulation , but also leads to a sharp change in clot retraction, as a result of which the white blood cell life is significantly prolonged .

In Werlhof's disease, a decrease in the number of platelets during bleeding leads to a decrease in the amount of serotonin (a powerful vasoconstrictor) in the blood (which is contained in platelets) , which leads to increased bleeding.

The permeability of the vascular wall increases , since the platelets in the vessels are in a state of adrift , and the amount of histamine in the blood increases. Pathology of blood coagulation can also occur as a result of qualitative changes in platelets. Such changes occur as a result of leukemia , uremia , and exposure to streptomycin. In such cases, platelets lose their ability to agglomerate and adhere. Such pathological changes are associated with a deficiency of ATP , ADF , ATP-ase , magnesium ions , pyruvate kinase, etc. in platelets.

Increased blood clotting ability leads to thrombosis. The causes of such pathology include an increase in the number of platelets , an increase in the concentration of procoagulants in the blood , a decrease in blood fibrinolytic activity , a decrease in natural anticoagulants in the blood, etc. In such cases, damage to the vascular wall, slowing down of blood flow in the vessels , local and general changes in blood flow are of great importance.

Increased blood clotting ability is not associated with an increase in the amount of prothrombin , proconvertin , fibrinogen, which are factors of

blood clotting. As it is known, the normal amounts (concentrations) of these substances exceed the amount necessary for hemostasis , and their further increase does not affect the level of blood clotting. Therefore, thrombi can form even if the amount of these substances in the blood decreases. In the formation of thrombi, qualitative changes in fibrinogen , especially a decrease in the activity of the blood fibrinolytic system, are important. This condition is observed with excessive physical exertion , when eating a lot of and very fatty foods. The intake of large amounts of fats into the body with food requires a sufficient amount of heparin, which activates lipase. However, the amount of this substance is insufficient, therefore, a favorable opportunity for blood clotting arises. A decrease in fibrinolytic activity further accelerates clotting.

In the pathogenesis of thrombosis, a change in the ratio between the coagulation and fibrinolytic systems is of great importance. In the norm, the acceleration of blood coagulation is accompanied by the activation of fibrinolysis. In pathology, however, a violation of the synchrony of the activity of these two systems often occurs . For example , in atherosclerosis , in stress conditions, the acceleration of blood coagulation occurs due to the weakening of its fibrinolytic activity and is the cause of the development of thromboembolic complications .

the production of activated thromboplastin is accelerated, most of the prothrombin present in the blood is converted to thrombin . Thrombin also accelerates the conversion of fibrinogen to fibrin, activates other coagulation factors in the blood, and causes platelet aggregation. When only a large amount of thromboplastin is released into the human vessels , most of the plasma coagulation factors are consumed , most of the fibrinogen is converted to fibrin , and platelets combine with each other to form microaggregates . In some cases , circulating microaggregates and microthrombi appear in the vessels . At the same time, as a result of a decrease in the amount of fibrinogen , the blood loses its ability to clot ( consumption - related coagulopathy ) . Such a pathological process is called disseminated intravascular coagulation. This is observed in some severe diseases, such as septic abortion, sepsis, shock, leukemia, burn disease, and others .

## 16. THROMBOCYTES AND THEIR FUNCTIONAL SIGNIFICANCE IN PATHOLOGICAL CONDITIONS

Platelets are the smallest blood elements in terms of size [d=2-4μm]. However, they also contain a variety of enzymes and other secretory products , which is why they perform a variety of functions in both normal and pathological conditions.

## Involvement of platelets in hemostasis.

The role of platelets in hemostasis is well known and has been studied in detail. They contain more than 10 hemostatic factors. Factor I accelerates the conversion of prothrombin to thrombin. Factor II accelerates the conversion of fibrinogen to fibrin. Factor III is a membrane or phospholipid factor involved in the formation of prothrombinase (platelet prothrombinase). Factor IV is an antiheparin factor , platelet fibrinogen. Other platelet factors ; antifibrinolytic factor ; activator of fibrinolysis ; provides the ability of platelet actomyosin (control of platelet movement) and blood clot retraction. ADF (the main endogenous factor of aggregation) ; serotonin (vasoconstrictor factor , aggregation stimulator) ; fibrin stabilizing factor (platelet fibrinase or transglutaminase) ; TxA2 enhances platelet adhesion and aggregation, and is also involved in the localization of the blood coagulation system and the regulation of its aggregate state.

## Anti-angiogenic function of platelets.

One of the factors maintaining hemostasis is the resistance of the vascular walls to mechanical stress . The ability of platelets to influence the resistance of the vascular walls is called the endothelial barrier function.

In healthy humans and animals, blood vessels are constantly exposed to physiological damage ( traumatization ) from minor injuries, tissue stretching , sudden changes in pressure inside the vessels, and other causes . However, disruption of the integrity of the vessels does not lead to bleeding , since rupture of the hemostatic thrombus does not occur.

Every day, 5 % of all platelets in the circulating blood are used for anti-angiogenic function. Secretory products in platelet granules and the most important enzymes of platelets are.

Vascular wall prostacyclin plays a special role in regulating the endothelial-adherent activity of platelets.

The isolation of a factor from platelets that strengthens the vascular wall or changes its permeability allows us to include these factors among the cellular regulators of hemodynamics and microcirculation. (Table 2)

**2 -Table**

| Membrane phospholipids | Fatty bodies (granules) | α-grains | Enzymes in various locations | |
|---|---|---|---|---|
| | | | **Lysosomes, peroxisomes** | **Cytoplasmic** |
| PG H2<br>PGG2<br>TxA 2<br>PF3<br><br><br><br><br>FAT<br><br><br>LT | ADF<br>ATF<br>Calcium<br>Serotonin<br><br><br><br>Catecholamines (adrenaline and nor-adrenaline)<br><br><br><br>Pyrophosphate<br>Antiplasmin | Platelet factor 4 (antiheparin)<br>β-thrombo-globulin<br>Fibrinogen<br>V-FACTOR<br>FACTOR VII<br>FibrinectinAlbumin<br>Growth factor<br>Transmission factor<br>Hemostatic factor<br>bactericidal factor<br>Thrombospondin (TSP) | Oxidoreductases.<br>Peroxidase<br>Hydrolase Chitosan phosphatase<br>DNA-ase<br>RNA-ase<br>Nonspecific esterase<br>ArylsulPhatase<br>diglyceride lipase<br>FlA2<br>FlS<br>Glycosidases<br>β-D glucuronidase<br>β-D-galactosidase<br>Proteases<br>Cathepsin DE<br>phosphohydrolases<br>Transferases | Dehydrogenases<br>Cytochrome oxidase<br>D-amino-k-thals<br>Oxidase<br>5-nucleooxidases<br>FDE-I<br>Aminopeptidase<br>ATF-ase |

## Platelets and microcirculation

Platelets respond to tissue damage both locally and at a general circulatory rate. Tissue necrosis (from which tissue thromboplastin can be released), release of ADP (released from damaged cells into the microcirculation), as well as bacteria, viruses, AG+AT complexes, endotoxin, enzymes such as trypsin, and other factors cause platelet aggregation and accelerate blood clotting.

Platelets are the most important element in the formation of thrombi in microvessels. Their participation in the mechanisms of this process is due to the results of adhesion, aggregation, interaction of platelets with the vessel wall, and disruption of the balance between blood coagulation and fibrinolysis.

Disturbances in microcirculation in organs and tissues, in particular, can lead to blood clotting within the vessels, dystrophic changes in parenchymal cells, the formation of small foci of necrosis, infarctions, and irreversible shock.

## The role of platelets in thrombus formation

Platelets do not normally affect normal endothelial cells, but after they are damaged, platelets adhere to the microfibrils and collagen of the supraendothelial basement membrane. After binding to collagen, they release from their granules, along with ADF, some potent metabolites of arachidonic acid and TxA2. These substances cause the aggregation of other platelets and form an initially unstable platelet mass that accumulates at the site of vascular injury. Changes in the platelet membrane stimulate the formation of a thrombus, which in turn increases platelet aggregation, causes the release and formation of fibrin, which in turn stabilizes the platelet mass and leads to the formation of a thrombus.

Two distinct pathological processes are observed in the veins; one is the formation of a blood clot that does not adhere to the vessel wall, which is the process of blood clotting inside the vessel mainly due to hemocoagulation changes, and the other is the process of thrombus formation inside the vessel, in which a blood clot forms and adheres to the vessel wall due to damage to the inner layers of the vessel and hemocoagulation changes in the blood. In both cases, the result of vascular occlusion can be the same.

## Platelets and atherogenesis

Platelets are the most important structures that mediate platelet adhesion, aggregation, and thrombin generation.

Platelets can provide low-density lipoprotein delivery to a slightly damaged area of the vessel and allow lipids to accumulate in the damaged area. Platelet membranes contain receptors for low-density lipoproteins. The ability of platelet receptors to bind low-density lipoproteins, then engulf them and dehydrate them intracellularly, or to deliver low-density lipoproteins unchanged to sites of atheromatous plaques has been demonstrated. Fatty acid synthesizing enzymes have been identified in extracts of human platelets. However, fatty acids are synthesized (de novo) in platelets and their chain is extended, and phospholipids are synthesized from glycerophosphate in platelets. Low-density lipoproteins activate platelets, inhibit fibrinolysis, as a result of which the anticoagulation system weakens and thrombus formation accelerates.

The participation of platelet lipoproteins in the transport and absorption of platelets in the vascular wall, the close relationship between lipoidosis and the formation of thrombus in the vascular wall, and the disruption of the interaction of platelets with the vascular wall, although

not completely explain the mechanism of atherosclerosis development and are considered the main pathogenetic factors of myocardial infarction, strokes, thrombophlebitis and other complications during atherosclerosis.

## The importance of platelets in metabolic processes

One of the important properties of platelets is their adsorption activity. These blood cells have the ability to adsorb substances of various chemical composition. In this regard, their ability to absorb and bind serotonin, adrenaline and other biogenic amines is of great importance. It turned out that the adsorption property of platelets is an indicator of their vital activity, and this indicator depends on the metabolic processes in the platelets themselves, that is, on energy consumption. It is known that platelets of vertebrates contain 0.3-7.5 μg/109 tr, serotonin, 0.09 –4 μg/. 109 tr histamine, 109.6- 6.9 μg/1011 tr dopamine. Only in rabbit platelets is it characteristic that histamine is present in an amount of 4 μg/109 tr, that is, in a very large amount.

Histamine in platelets occurs in two ways: one is exoplatelet-mediated and the other is synthesized in platelets themselves. About 10% of histamine is synthesized from histidine in platelets. Histidine decarboxylase inhibitors reduce histamine formation. Platelets actively absorb histamine from blood plasma.

It has been found that healthy older people tend to have a decreased level of enzymes involved in the metabolism of ACE and COMT.

Above, platelets adsorb various blood proteins, enzymes, hormones, and trace elements on their surface. The transport of proteins that have blood clotting (coagulation) properties is a specific ability of platelets.

Under pathological conditions, platelets adsorb abnormal proteins on their surface, for example, phosphatides in uremia.

## The involvement of platelets in inflammatory and infectious processes

It has been proven that platelets accumulate in the vessels of the focus of inflammation and that viruses participate in the digestion of bacterial AG + AT complexes. These phenomena are associated with endocytosis, as is known, even true phagocytosis is observed in viral infections. In relation to bacteria, aggregates are formed around them. Such aggregates can be phagocytosed by macrophages or, in an aggregate state, can spread through the bloodstream and participate in the development of the septic process.

Increased aggregation also occurs from the interaction of platelets with bacterial endotoxins.

During the development of the inflammatory process, platelets actively interact with complement. Platelet membranes contain receptors for SI, which are likely to play a role in the aggregation that forms immune complexes.

There is evidence that platelet membranes contain the complement fragment CIS, which is a receptor for collagen. The formation of a bond between collagen and CIS activates the protease activity of S, which in turn stimulates FlA2 (phospholipase A2). Immunofluorescence has shown that platelet membranes contain receptors for C1, C3, and C4. No receptor for S3 has been found in human platelets. It should be noted that some fractions of complement can be directly adsorbed to glycocolloidal surfaces.

healthy women with congenital deficiency of S2, platelet ADF aggregation remains normal.

Substances within platelet granules have been shown to enhance tissue damage at the site of inflammation. Factors released from platelets can be divided into the following groups based on their function in terms of their effects on inflammation and tissue damage:

Vasoactive humoral factors - serotonin, catecholamines, histamine (in experimental animals) - affect hemostasis, coagulation, and vascular permeability.

Factors that provide localization of cells are chemotoxic factors. The function of chemotactic factors is performed by proteins with cationic properties, which are similar to the cationic proteins of granulocytes, metabolites of arachidonic acid, in particular PGE2 and FAT (platelet activating factor), are also chemotoxic factors that affect neutrophils. ATF (platelet growth factor) is a chemoattractant for neutrophils and monocytes.

Factors that enhance the functional activity of cells are mitogenic factors, or TFR, and cationic proteins called FATs, which are factors that enhance the degranulation of basophils and mast cells.

Factors that reduce the functional activity of the cell, including arylsulfatases.

For any inflammation, cooperation of platelets with other cells is characteristic. The course and consequences of the inflammatory process largely depend on the accumulation and inactivation of the above-mentioned platelet factors. These substances affect permeability and

stimulate chemotoxicity, and they also stimulate the release of anaphylactic mediators from mast cells and basophils.

The above classification is very conditional, since the effects of the factors are different. For example; not only are the cationic proteins of platelets hemoattractant, but their immediate and prolonged effect on vascular permeability is a result of their enzymatic action on S5, the breakdown of which forms the anaphylotoxic product S5, which has chemotoxic activity for neutrophils.

With the active participation of platelets, proliferation processes and wound healing occur. Platelet- derived growth factor (TDF) is released from platelets at the site of injury. This factor stimulates cell proliferation and division. The same substance stimulates the migration of fibroblasts and smooth muscle cells. It is assumed that the biochemical mechanism of action of TDF is that it binds to sensitive elements on the cell surface, as a result of which a stimulus enters the cell, as a result of which phosphate groups begin to combine with tyrosine residues of the protein. Currently, the main attention is paid to the issue of the effect of phosphate on tyrosine, because this molecular mechanism is one of the bases of reparative regeneration processes (angiogenesis, vascular smooth muscle hyperplasia, endothelial regeneration) and the transformation of normal cells into carcinoma cells.

## Involvement of platelets in immune reactions

In immune and allergic reactions, platelets can act as effector cells, when they are exposed to immune factors, or they can act as regulatory cells. As effector cells, platelets are sensitive to the effects of various autoimmune, isoimmune, transimmune, and heteroimmune factors.

Their effects can lead to various forms of thrombopathies and thrombocytopenia, in which case platelets act as the primary target cells. In this case, antibodies or sensitized lymphocytes directly interact with antigenic structures on platelets that correspond to them.

Platelet dysfunction can occur not only due to the action of antiplatelet antibodies, but also due to the action of specific antibodies directed against individual structural elements of platelets - thrombosthenin, glycoproteins.

However, in addition to the direct effect of antiplatelet antibodies, platelets can also be exposed to the “nonspecific” effect of immune factors that do not directly affect antigens on the platelet membranes. Thrombocytopenia can occur due to the action of antibodies to viruses.

The mechanism of damage in this case is as follows: the virus accumulates in platelets, and the action of antibodies produced against the virus causes platelet self-destruction. This type of thrombocytopenia is characteristic of various viral infections, including OIDS (acquired immune deficiency syndrome).

It has been shown that platelet membranes can interact with immune complexes. The main effect is on the immune complex that binds to IgG. The biological significance of the binding of immune complexes to platelets is probably to remove these immune complexes from the bloodstream.

In recent years, it has been found that platelets can also participate in inflammation and immune reactions through their interaction with complement components. The complement system acts as a connecting link between the immunological system and the blood coagulation system. The generally recognized initiators of the complement activation pathway include, in descending order, IgM, IgG, IgG1, IgG2, GgA, GgO, while other initiators of the complement activation pathway (S3) include IgG, IgE, GgA, bacterial polysaccharides, inulin, and zymosan.

In recent years, studies have revealed new lipid mediators that trigger platelet aggregation and secretion in atopic reactions. Platelets serve as secondary target cells in atopic diseases. Platelets are recruited to IgE-mediated reactions in the presence of platelet-activating factor.

It is known that there are various platelet-activating factors and similar substances. Platelet-activating factors are formed during immunological (and even non-immunological) activation of basophils, mast cells, neutrophils, macrophages, and other cells by the action of phospholipase A2 on cell membrane phospholipids. Platelet-activating factors can also be formed during platelet aggregation by platelets themselves.

The interaction of platelets with platelet-activating factor causes bronchoconstriction, pulmonary hypertension, leukopenia, and anaphylaxis.

Some results are obtained from the administration of platelet-activating factor (PAF) to experimental animals, for example, its direct cardiovascular effects. Respiratory changes (bronchoconstriction, pulmonary hypertension) are associated with the effects of eicosanoids produced by platelets or by platelets.

In atopy, the release of TFO from primary target cells (basophils, mast cells) triggers platelet aggregation and secretion . However, changes

in platelet functional activity in atopy (in addition to the effect of TFO) may also be due to the effect of IgE, since platelet membranes contain a receptor with a lower sensitivity to IgE.

In atopy, the activation of platelets by TFO and IgE can be considered a biologically appropriate adaptive response. Platelets also play a role in contributing to the local homeostasis of the limiting tissue of the inflammatory focus. If the sanogenetic effect of platelets is observed in the context of a controlling physiological process, then an inadequate (incompatible) increase or decrease in these mechanisms becomes a damaging factor.

In general, platelets are involved in the primary and secondary immune response, allergy, and immune inflammation in tissues. It is assumed that platelets are involved in the presentation of antigenic materials to macrophages. Bidirectional communication between platelets and other cells provides control over cell migration and the release of mediators into the tissue environment .

Thus, the presence of various action properties in platelets allows us to consider them as an important component of maintaining immunological homeostasis. The biological control system determines the physiological or protective effects of platelets and the damaging effects associated with a sharp increase or decrease in their activity, therefore, the search for agents that regulate platelet reactions should be considered as a new direction in the pharmacotherapy of allergic diseases.

## Test tasks

Which symptom corresponds to the diagnosis of "hemophilia"?

- Slowing of blood clotting
- Afibrinogenemia
- Erythrocytopenia
- Eosinophilia
- Erythrocytosis

A 3-year-old boy has been diagnosed with hemophilia B. What blood deficiency is causing this?

- Christmas factor
- Antihemophilic globulin
- Prothrombin
- Fibrinogen
- Hageman Factor

A patient with anemia has hypersegmentation of neutrophils. Which anemia is this characteristic of?

- Pernicious
- Toxicohemolytic
- Sickle cell
- Aplastic
- Posthemorrhagic

What type of hypoxia develops in anemia?

- Hemic
- Hypoxic
- Histotoxic
- Circulator
- Respirator

The patient has been taking sulfonamides for a long time. What type of anemia is likely to occur in this case?

- Aplastic
- Metaplastic
- Dysregulator
- VitB12 deficiency

- Fe-deficient

The normal ECT for infants is
- 1-2 mm/s
- 20-22 mm/s
- 2-15 mm/s
- 4-10 mm/s
- 15-32 mm/s

Anemia that develops as a result of excessive destruction of erythrocytes
- Hemolytic
- Posthemorrhagic
- Metaplastic
- Aplastic
- Fe deficiency

What are the regenerative forms of erythrocytes?
- Reticulocytes
- Hypochromic erythrocytes
- Oxyphilic megaloblasts
- Erythrocytes with basophilic granulation
- Megalocytes

Hemophilia A is caused by a deficiency of what?
- Blood clotting factor III
- Blood clotting factor IX
- Blood clotting factor XI
- Platelets
- Fibrinogen

Hemophilia B is caused by a deficiency of what?
- Blood clotting factor IX
- Blood clotting factor III
- Blood clotting factor XI
- Platelets
- Fibrinogen

Hemophilia C is associated with a deficiency of what?

- Factor XI
- X-factor
- Factor IX
- Factor YIII
- Fibrinogen

How is hemophilia inherited?

- Recessive X-linked
- Autosomal dominant
- Autosomal recessive
- Recessive Y-chromosome-linked
- Slightly dominant

Which type of hemophilia occurs in girls?

- Does not meet
- A
- B
- C
- D

What is the probability that a man with hemophilia and a healthy woman will have a sick son?

- 100% healthy
- 100% sick
- 50% healthy
- 25% sick
- 75% sick

What cells are characteristic of the embryonic type of hematopoiesis?

- Megaloblasts
- Basophilic normocytes
- Pronormocytes
- Reticulocytes
- Eosinophilic normocytes

What type of anemia is characterized by megaloblastic hemopoiesis?

- Pernicious

- Thalassemia
- Sickle-shaped
- Iron deficiency
- Posthemorrhagic

What cells are characterized by hyperchromia?
- Megaloblasts
- Polychromatophiles
- Basophilic normocytes
- Reticulocytes
- Oxyphilic normocytes

How much blood must be lost at once (%) to trigger acute blood loss in an animal?
- 25%
- 10%
- 15%
- 50%
- 35%

What is the synonym of idiopathic thrombocytopenic purpura?
- Verlhof's disease
- Vaccination disease
- von Willebrand disease
- Erythremia
- DVS syndrome

Give an example of hereditary aplastic anemia.
- Fanconi anemia
- Addison-Biermer's disease
- Marchiafava-Micheli anemia
- Culi anemia
- Thalassemia

What type of anemia occurs when autoantibodies to clotting factor are formed?
- Pernicious
- Immunohemolytic

- Aplastic
- Toxicohemolytic
- Thalassemia

What could be the cause of subcutaneous bleeding in minor mechanical injuries?

- Thrombocytopenia
- Erythrocytopenia
- Leukocytopenia
- Lymphocytosis
- Thrombocytosis

What type of anemia develops in leukemia?

- Metaplastic
- Aplastic
- Hypoplastic
- Hemolytic
- Pernicious

Develops as a result of local intravascular coagulation

- Thrombosis
- Embolism
- TTQI (DVS) syndrome
- Sludge
- Ischemia

What cells are characteristic of Minkowski-Shoffar anemia?

- Microspherocytes
- Reticulocytes
- Stomatocytes
- Sickle cells
- Basophilic normocytes

Give an example of acquired membranopathy.

- Paroxysmal nocturnal hemoglobinuria
- Sickle cell anemia
- Sideroachrastic anemia
- Minkowski-Shoffar disease
- Thalassemia

How many stages are distinguished in the development of acute posthemorrhagic anemia?

- 3
- 2
- 4
- 5
- 6

Total blood volume depletion that develops 1-2 days after acute blood loss

- Oligocythemic normovolemia
- Polycythemic hypovolemia
- Simple hypovolemia
- Oligocythemic hypervolemia
- Polycythemic normovolemia

A patient develops oligocythemic hypovolemia 2 days after acute blood loss. What can be determined in this case?

- Decreased hematocrit
- Increased hematocrit
- K+ increase
- Increased blood viscosity
- Decreased globulins

When does reticulocytosis develop after acute blood loss?

- After 5-7 days
- After 1-2 hours
- After 1-2 days
- After 5-7 hours
- After 3-4 days

What can be the blood volume in polyuria?

- Polycythemic hypovolemia
- Oligocythemic hypervolemia
- Normal normovolemia
- Oligocythemic hypovolemia
- Simple hypovolemia

Which cells contain Pappenheim bodies?

- In sideroblasts and siderocytes
- In erythroblasts and reticulocytes
- In megaloblasts and megalocytes
- In erythrocytes and normocytes
- In normocytes and reticulocytes

In which disease can the syndrome of TTQI (DVS) develop?

- Burn
- Bronchitis
- Arthritis
- Rhinitis
- Gastritis

A sign of increased red blood cell regeneration

- Reticulocytosis
- Poikilocytosis
- Anisocytosis
- Spherocytosis
- Anisochromia

What is the mechanism of simple hypervolemia that develops during intense physical exertion?

- Bleeding from the depot
- Increased blood flow rate
- Increased stroke volume
- Increased cardiac output
- Leakage of tissue fluid into the blood

Which of the following causes can lead to DVS syndrome?

- Premature separation of the placenta
- Acute appendicitis
- Chronic pneumonia
- Tuberculous meningitis
- Chronic bronchitis

In S-Hemoglobin, glutamic acid replaces:

- Valine
- Alanine
- Cysteine
- Leucine
- Isoleucine

What is the probability that a healthy man and a woman carrying the hemophilia gene will have a sick child?

- 25% (50% sons)
- 50% of all children
- 75%
- 50% girls
- 25% (50% tuition)

What type of hemolytic anemia develops in patients with chronic lymphocytic leukemia?

- Autoimmune
- Heteroimmune
- Toxicohemolytic
- Mechanical
- Pernicious

Develops as a result of disseminated intravascular coagulation

- TTQI (DVS) syndrome
- Thrombosis
- Embolism
- Ischemia
- Sludge

What is the name of the pathological condition that occurs after external or internal blood loss (20-40%) and is characterized by microcirculatory disorders, hypoxia, and dystrophic changes in tissues?

- Hemorrhagic shock
- Anaphylactic shock
- Traumatic shock
- Cardiogenic shock
- Iron deficiency anemia

Which protein is used to transport iron to the bone marrow?

- Transferrin
- Ceruloplasmin
- Fibrinogen
- Bradykinin
- Haptoglobin

What is typical for iron deficiency anemia?

- Hypochromia
- Hyperchromia
- Normochromia
- Megalocytosis
- Spherocytosis

What is thrombocytopathy?

- Functional platelet deficiency
- Decreased platelet volume
- Decreased platelet count
- Increased platelet count
- Platelet formation disorder

What is impaired in von Willebrand factor deficiency?

- Platelet adhesion
- Platelet aggregation
- Fibrin formation
- Blood clot retraction
- Erythrocyte adhesion

What is the mechanism of funicular myelosis in vitamin B12 deficiency anemia?

- Myelin synthesis disorder
- Decreased synthesis of neurotransmitters
- Termination of axonal transport
- Decreased sensitivity of cholinergic receptors
- Decreased sensitivity of adrenergic receptors

Which enzyme is not synthesized in hemopoietic cells in Fanconi anemia?

- Endonuclease
- Ligase
- Revertase
- Polymerase
- Reverse transcriptase

What is the inheritance pattern of anemia due to glucose-6-phosphate dehydrogenase deficiency?

- X-linked, recessive
- X-linked, dominant
- Linked to the Y-chromosome, dominant
- Autosomal dominant
- Autosomal recessive

What is the platelet count in idiopathic thrombocytopenic purpura?

- Less than $180.0x10^{9}/l$
- Less than $200.0x10^{9}/l$
- More than $180.0x10^{9}/l$
- More than $250.0x10^{9}/l$
- More than $320.0x10^{9}/l$

Which blood protein component is involved in the destruction of erythrocyte membranes in immune hemolytic anemia?

- Complement
- Spectrin
- Bradykinin
- Ceruloplasmin
- Haptoglobin

In which group of anemias does Marsh hemoglobinuria occur?

- Mechanical hemolytic
- Toxic hemolytic
- Immune hemolytic
- Metaplastic
- Aplastic

In which stage of acute posthemorrhagic anemia does reticulocytosis occur?

- Bone marrow
- Reflector
- Hydramic
- In the first 1-2 days
- Does not meet

A patient developed oligocythemic hypovolemia 2 days after acute blood loss. What would be the hematocrit in this case?

- 30/70
- 45/55
- 80/20
- 55/45
- 70/30

Hemolytic toxins of staphylococci and streptococci destroy lipids of the erythrocyte membrane. Name them.

- Lecithin
- Cholesterol
- Arginine
- Sphingosine
- Hemolysin

Mechanism of vascular-platelet hemostasis

- Vasoconstriction, platelet adhesion and aggregation
- Vasodilation, platelet adhesion and aggregation
- Vasoconstriction, vasodilation, platelet adhesion
- Vasoconstriction, vasodilation, platelet aggregation
- Vasoconstriction, platelet agglutination and degranulation

A potent inhibitor of platelet aggregation

- Prostacyclin
- Bradykinin
- Endorphin
- Plasminogen
- Testosterone

Which nucleoside is not phosphorylated in vitamin B12 deficiency?

- Thymidine

- Cytosine
- Uridine
- Adenosine
- Alanine Submit

A 44-year-old patient has had bronchial asthma since childhood. Objectively: the skin is pale with a cyanotic tint, respiratory rate - 27/min, A/B - 130/70 mm Hg, heart rate - 86/min. General blood test: E - 5.9x10 12 /l, HB - 160 g/l, RK - 0.9, L - 6.1 x 10 9 /l, ECHT - 8 mm/h. The most effective manifestation of adaptation to hypoxia in such conditions

- Erythrocytosis
- Shortness of breath
- Tachycardia
- Angiospasm

The patient complains of pain in the epigastric region, vomiting after eating. Vomiting mass of "coffee grounds" color. History of peptic ulcer. Skin is pale, heart rate 110/min, blood pressure - 90/50 mm Hg, red blood cell count -. 2.8 x 10 12 /l, Hb - 70 g/l. What complications can the patient have?

- Bleeding
- Penetration
- Perforation
- Moving to Cancer

A patient is being treated in the hematology department with a diagnosis of polycythemia vera. What is the patient's total blood volume disorder?

- Polycythemic hypervolemia
- Polycythemic hypovolemia
- Oligocythemic hypervolemia
- Oligocythemic hypovolemia

A patient was admitted to the infectious diseases department with suspected food poisoning. During the day, he had diarrhea 3 times and repeated vomiting. What type of blood volume disorder develops in this case?

- Polycythemic hypovolemia

- Polycythemic hypervolemia
- Oligocythemic hypervolemia
- Oligocythemic hypovolemia

Repeated vomiting in a pregnant woman led to the development of hypovolemia as a result of significant dehydration. In this case, the main endocrine compensatory mechanism

- Aldosterone hypersecretion
- Increased adrenaline
- Increased synthesis of corticotropin
- Increased prolactin secretion

After acute blood loss, oxyphilic normocytes appeared in the patient's blood. Supravital blood staining revealed 25% reticulocytes. What type of anemia did the patient develop based on the bone marrow's ability to regenerate?

- Regenerator
- Disregenerator
- Aregenerator
- Hyporegenerator Submit

Autoimmune processes can develop as a result of the loss of which property of T-lymphocytes:

- Loss of immune control
- The ability to synthesize interferon
- Ability to emigrate
- The ability to produce antibodies
- Increased erythrocyte count

Bacterial endotoxins enhance the proliferation of which cell line of the dominant cell?

- Neutrophils
- Monocytes
- Basophils
- Eosinophils
- Erythrocytes

The number of leukocytes in the patient's blood is 167*10 $^{9}$ / l. Find the name of the disease:

- Leukemia
- Leukocytosis
- Leukopenia
- Leukemoid reaction
- Leukemic cavity

What causes leukopenia in lazy leukocyte syndrome?

- Slow release of granulocytes from the bone marrow
- Storage of leukocytes in blood depots
- Rapid breakdown of leukocytes in blood vessels
- Excessive release of leukocytes through mucous membranes
- Vascular insufficiency

A leukemoid reaction can occur in infectious mononucleosis. What type of reaction is this?

- Lymphocytic
- Promyelocytic
- Neutrophil
- Eosinophilic
- Basophilic

Itsenko-Cushing's disease is characterized by excessive secretion of adrenocorticotropic hormone. What happens as a result:

- Eosinopenia
- Monocytosis
- Lymphocytopenia
- Basophilia
- Monocytopenia

At what stage is granulocyte maturation impaired in Kostmann syndrome?

- Promyelocyte - myelocyte
- Myelocyte –metamyelocyte
- Metamyelocyte - a granulocyte with a rod nucleus
- Rod-nucleated granulocyte - segmented-nucleated granulocyte
- Metamyelocyte - segmented nuclear granulocyte

Reverse transcriptase enzyme detected in leukemia cells. What causes leukemia?

- RNA-carrying virus
- DNA-carrying virus
- X-rays
- Benzene poisoning
- Ionizing radiation

The incidence of leukemia is known to be higher in individuals with chromosomal aberrations. Which of the following diseases is this characteristic of?

- Turner syndrome
- Alder disease
- Fanconi syndrome
- Dressler syndrome
- Inflammation

What does the proliferation of nuclei, multinucleation, and vacuolization of the cytoplasm of leukemia cells indicate?

- Morphological anaplasia
- Biochemical anaplasia
- Physicochemical anaplasia
- Functional anaplasia
- Antigenic anaplasia

What type of leukocytosis is observed in leukemia?

- Absolute neoplastic
- Relative neoplastic
- Relative hemoconcentration
- Absolute hereditary
- Absolutely innate

When does neutrophilic leukocytosis occur naturally?

- Acute appendicitis
- Turner syndrome
- Down syndrome
- Ascariasis

- Bronchial asthma

Neutropenia can occur in the following cases:
- Vitamin B12 deficiency
- Acute appendicitis
- Myocardial infarction
- Tumor fragmentation
- Zatiljam

What special research methods are used to detect blast cells in acute leukemia:
- Cytochemical
- Cytogenetic
- Spectrophotometric
- Electron microscope
- Photometric

In acute monoblastic leukemia, at what stage of maturation does leukocyte differentiation stop?
- IV
- III
- II
- V
- I

Which drugs play a role in the development of acute leukemia, which is caused by mutations in blood cells?
- Levomycetin
- Acetylsalicylic acid
- Nitroglycerin
- Atropine
- Citramon

In addition to being outside the blood vessels, leukocytes are destroyed by which macrophages?
- Divorce
- Lungs
- Liver

- Stomach
- Kidney

Which of the following drugs can cause neutropenia?
- Cytostatics
- Antioxidants
- Antidepressants
- Anticoagulants
- Antispasmodics

What types of blood formation are disrupted in the bone marrow under the influence of high doses of ionizing radiation?
- All hemopoiesis
- Partial erythropoiesis
- Partial myelopoiesis
- Partial leukopoiesis
- All leukopoiesis

Leukopenia occurs in patients with purulent endometritis. What is the mechanism underlying this:
- Leukocytes are released from the body in the form of pus.
- Destruction of leukocytes in the blood
- Leukocyte lysis in the spleen
- Redistribution of leukocytes in internal organs
- Redistribution of leukocytes in the blood

Eosinophilia in allergic diseases has a protective mechanism, since eosinophils:
- Suppresses histamine production
- Increases vascular permeability
- Inhibits the formation of lymphocytes
- Slows down the synthesis of antibodies
- Slows down the synthesis of leukocytes

In patients with allergies, the number of eosinophils in the blood increases. Which substance increases the permeability of the bone marrow to eosinophils?
- Histamine

- Serotonin
- Bradykinin
- Acetylcholine
- Aspirin

Basophilia is observed:
- In hypothyroidism
- In tuberculosis
- In meningitis
- In galactosemia
- In anemia

The simultaneous increase in basophils and eosinophils (basophil-eosinophil association) is characteristic of which disease?
- Chronic myelocytic leukemia
- Chronic B-lymphocytic leukemia
- Chronic T-lymphocytic leukemia
- Acute myeloblastic leukemia
- Chronic monocytic leukemia

The patient has leukocytosis, and in the blood there are a large number of rod-shaped neutrophils, metamyelocytes, and myelocytes with signs of degeneration. What is this called?
- Regenerative-degenerative left shift
- Hyperregenerative left shift
- Degenerative left shift
- Regenerative left shift
- Regenerative right shift

The patient has symptoms of HIV infection. What cellular pathology leads to the development of an immunodeficiency state in such patients?
- T-helpers
- B-lymphocytes
- T-killers
- T-suppressors
- Lymphoblasts

When does Burkitt lymphoma occur?

- In the translocation of a segment of chromosome 8 to 14
- In inversion of a segment of chromosome 14
- 8 In the deletion of a segment of chromosome
- Translocation of chromosome segment 14 to 8
- 8 Inversion of chromosome segment 22

What blood cell count increases in the blast crisis phase of chronic myeloid leukemia?

- Myeloblasts
- Promyelocytes
- Myelocytes
- Metamyelocytes
- Leukocytes

Find the primary immunodeficiency syndrome with a high incidence of leukemia in children:

- Wiskott-Aldrich syndrome
- Phenylketonuria
- Galactosemia
- Color blindness
- Albinism

When analyzing the child's blood: the number of leukocytes -20-10 $^{9}$ /l; basophils -1%, eosinophils -16%, rod-nucleated neutrophils -3%, segmented neutrophils -60%, lymphocytes -18%, monocytes -2%. What does this data indicate?

- Eosinophilic leukocytosis
- Chronic myelocytic leukemia
- Chronic lymphocytic leukemia
- Neutrophilic leukocytosis
- Agranulocytosis

When does degenerative leftward shift occur?

- Streptococcal sepsis
- Acute appendicitis
- Viral hepatitis
- Bronchial asthma
- Liver cirrhosis

Eosinophil-basophilic leukocytosis is characteristic of which leukemia?

- Chronic myelocytic leukemia
- Acute myeloblastic leukemia
- Acute erythroblastic leukemia
- Acute monoblast leukemia
- Chronic erythromyelosis

In basophilic adenoma of the anterior pituitary gland, the production of adrenocorticotropic hormone is increased. As a result, there is an increase in:

- Eosinopenia
- Neutropenia
- Lymphocytopenia
- Basophilia
- Leukocytosis

Glycogen and acid phosphatase enzymes are markers of which leukemia:

- Lymphoblast
- Myeloblast
- Monoblast
- Erythroblast
- Normoblast

In cases of immunodeficiency, it is observed:

- Lymphocytopenia
- Eosinopenia
- Monocytopenia
- Neutropenia
- Erythropenia

Find the substance that inhibits the production of colony-stimulating factor:

- Lactoferrin
- Interferon
- Antikylon

- Histamine
- Serotonin

What is Pelger's anomaly in leukocytes?
- Genetic defect
- Consequences of benzene poisoning
- The occurrence of neoplastic transformation of the tumor
- Sign of intravascular leukocyte lysis
- Agranulocyte deficiency

The risk of developing leukemia is higher if:
- In chromosomal abnormalities
- In molecular diseases
- In iron deficiency anemia
- Lymphoid type leukemoid reaction

Where do neoplastic clones form in leukemia?
- Bone marrow
- Lymph node
- Divorce
- Duodenum
- Kidney

When is a lymphoid-type leukemoid reaction observed?
- "Transplant vs. Host" Reaction
- Immune agranulocytosis
- Complications of croupous pneumonia
- Atopic bronchial asthma
- Hypertension

It is known that hemorrhagic syndrome develops in patients with leukemia. Name its main pathogenic mechanism:
- Thrombocytopenia
- Thrombocytopathy
- Vasopathy
- Hypoproteinemia
- Anemia

The blood picture of acute leukemia is characterized by a leukemic space. Which class of intermediate cells is not found in this:

- Class V
- Class IV
- Class III
- Class I
- Class II

What is the mechanism of action of oncoproteins?

- Tyrosine phosphorylation
- Phosphorylation of tryptophan
- Oxidation of phenylalanine
- Alanine deamination
- Deamination of tryptophan

Choose a disease that occurs when a large number of leukocytes leave the body:

- Purulent endometritis
- Phlegmonous appendicitis
- Croupous pneumonia
- Chronic colitis
- Chronic gastritis

Pancytopenia is:

- Simultaneous decrease in the number of erythrocytes, leukocytes, and platelets
- Decreased granulocyte count
- Decreased red blood cell count
- Decreased number of agranulocytes
- Decreased white blood cell count

As a result of activation of the protono-oncogene, the synthesis of what increases in the cell:

- Oncoproteins
- Prostaglandins
- Glucosaminoglycans
- Lymphokines
- Lymphocytes

What is observed in decreased thyroid function (hypothyroidism)?

- Basophilia
- Eosinophilia
- Neutrophilosis
- Lymphocytosis
- Erythrocytosis

What type of anemia is characterized by neutrophil hypersegmentation?

- Pernicious anemia
- Toxic-hemolytic anemia
- Sickle cell anemia
- Aplastic anemia
- Chronic anemia

Which leukemia is characterized by a hyperregenerative shift of the leukocyte formula to the left?

- Chronic myelocytic leukemia
- Chronic lymphocytic leukemia
- Acute myeloblastic leukemia
- Acute B-lymphoblastic leukemia
- Acute leukemia

Which of the following drugs causes leukemia?

- Cytostatics
- Adrenoblockers
- Analgesics
- Antispasmodics
- Adrenomimetics

The genetic marker of chronic myeloid leukemia is the Philadelphia chromosome. What chromosome aberration is it caused by?

- Translocation of the long arm of chromosome 9 to chromosome 22
- Translocation of the chromosomal arm of chromosome 9 to chromosome 22
- Inversion of the short arm of chromosome 21
- Deletion of the short arm of chromosome 21

- 5 Chromosome deletion

What type of cells predominate in the blood in chronic myelocytic leukemia?

- Neutrophil, basophil, eosinophil
- Eosinophil, lymphocystis
- Basophil, lymphocyte, monocyte
- Monocyte, lymphocyte
- All types of leukocytes

Characteristic for viral diseases (hepatitis, measles, infectious mononucleosis):

- Lymphocytosis
- Eosinophilia
- Neutropenia
- Neutrophilosis
- Erythrocytosis

What group of diseases does Hodgkin's disease belong to?

- Lymphoid tumors
- Myeloproliferative disorders
- Myelodysplastic syndromes
- Acute lymphoid leukemia
- Chronic lymphocytic leukemia

A patient has symptoms of HIV infection. Studying the functional state of which cells can determine the cause of the development of immunodeficiency in such patients?

- T-helpers
- B-lymphocytes
- T-killers
- T-suppressors

The patient underwent a donor skin transplant. However, on day 8, the graft swelled, changed color, and on day 11, a rejection reaction began. Which cells are involved in this?

- T-lymphocytes
- Eosinophils

- Erythrocytes
- B-lymphocytes

The patient's leukocyte formula showed 40% eosinophils. What does this symptom indicate?

- Sensitization status
- Colon cancer
- Pulmonary tuberculosis
- Viral hepatitis

The patient's blood revealed leukocytosis, lymphocytosis, neutropenia, anemia, and Gumprecht cells. What disease should the doctor think about?

- Chronic lymphocytic leukemia
- Acute myeloid leukemia
- Acute lymphoblastic leukemia
- Chronic monocytic leukemia

A scheduled blood test was canceled because the patient had breakfast in the morning. What changes in blood components could occur under these circumstances?

- Leukocytosis
- Hyperproteinemia
- Erythrocytosis
- Thrombocytopenia

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