Ministry of Education and Science of Ukraine
V. N. Karazin Kharkiv National University

MORPHOFUNCTIONAL PECULIARITIES, METHODS OF EXAMINATION, SEMIOTICS OF AFFECTION BLOOD SYSTEM IN CHILDREN

Methodical recommendations
for students of 3th course of medical faculty

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CONTENTS

LIST OF ACRONYMS

IgM – Immunoglobulin M
ESR – erythrocyte sedimentation rate
Hb – Hemoglobin
RBC – red blood cells
HCT – hematocrit
MCV – mean red blood cell volume
MCH – mean red blood cell hemoglobin content
MCHC – the average concentration of hemoglobin in the red blood cell
RDW – RBC Anisocytosis
WBC – White Blood Cells
PLT – Platelets

INTRODUCTION

Propaedeutic of pediatrics is the most important discipline in the formation of the clinical thinking of a future doctor. The study of the blood system is one of the key topics in pediatrics. It is important to teach students to analyze clinical and medical history and laboratory instrumental data. 3rd course students should have a concept for studying the blood system, analyzing laboratory parameters and their interpretation.

FORMATION OF THE BLOOD SYSTEM

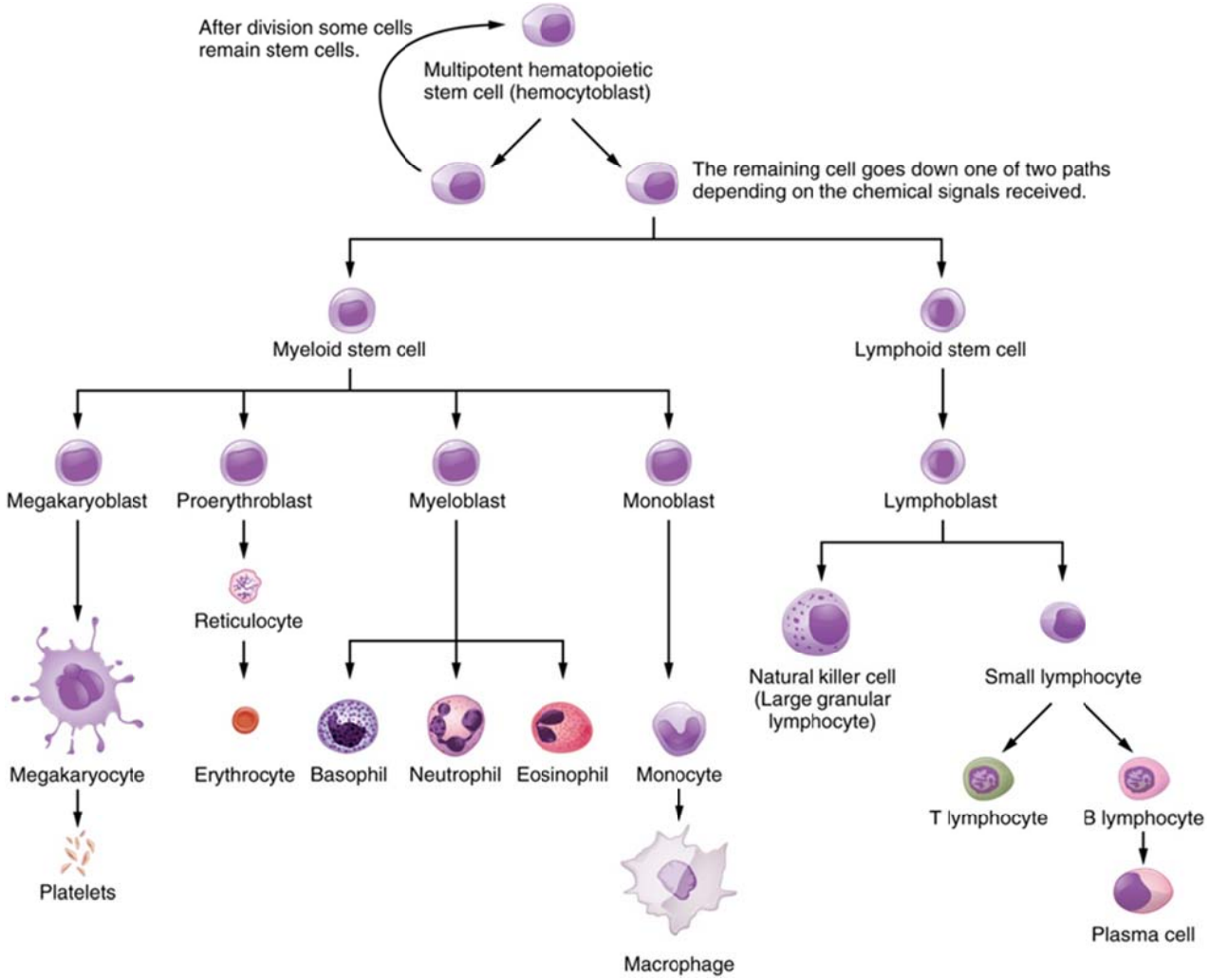

Fig. 1. Hematopoietic System of the Bone Marrow

All the cells of the immune response as well as of the blood arise by differentiation from hematopoietic stem cells.

Bone marrow hematopoietic system

All cells of the immune response, as well as blood, are formed by differentiation from hematopoietic stem cells. The formation of red blood cells in the bone marrow is stimulated by the kidney hormone erythropoietin. The development of the hematopoietic system in humans begins quite early, occurs with different intensities, with a change in the primary localization of hematopoiesis at different gestational periods. In the period of intrauterine development of the child, four stages of hematopoiesis can be distinguished topographically.

Stages of hematopoiesis:

1. mesoblastic,
2. hepatic,
3. splenic
4. bone marrow.

The mesoblastic stage of hematopoiesis occurs in the yolk sac, the stalk of the chorion at the end of the 2nd – beginning of the 3rd week of gestation. Vessels form from the peripheral cells of the yolk sac, and hematopoietic cells form from the central ones. The latter have an oval shape, large size, basophilic cytoplasm, the nucleus of a soft-mesh structure containing nucleoli. Hemoglobin gradually accumulates in these cells. In appearance, they are similar to megaloblasts, and they are called primitive erythroblasts. From the 6th week of gestation in the blood of the embryo there are cells without a nucleus – megalocytes. Although erythropoiesis is predominantly observed in the mesoblastic period of hematopoiesis, in this period it is possible to detect the progenitor cells of all hematopoietic germs, including pluripotent stem cells. Thus, during cultivation of the yolk sac of a 7–9-day gestation, monocytomacrophage, erythrocyte, megakaryocyte, granulocyte, and mixed colonies are formed. These data indicate that there are cells in the yolk sac that can differentiate in different hematopoietic directions. Starting from the 8th week of gestation, the hematopoietic islets in the yolk sac begin to regress, and megaloblasts disappear from the blood by the 12–15th week.

The hepatic stage of hematopoiesis occurs from the 5th week of gestation, and in the period of 3–6 months of gestation, the liver is the main hematopoietic organ. The liver is also the site of erythropoietin formation. First, intense erythropoiesis occurs in the liver – by the 9–10th week of gestation, up to 93.4 % of the nuclear cells are primitive erythroblasts. However, the latter are gradually replaced by secondary erythroblasts, and by the 32nd week of gestation, erythroid cells make up 40 %. In a fetal liver of 6–7 week gestation, erythrokaryocytes account for 90.3 %, while 24.6 % of them are megaloblastic elements. With an increase in gestational age (week 22–27), the number of erythroid elements decreases to 80.3 %, while megaloblastic cells make up only 1.3 %. In the period of 6–7 weeks of gestation, neutrophilic cells are also found in the liver, represented mainly by promyelocytes and myelocytes, and their content remains unchanged by the 27-week gestation period (about 1 %). The content of mature neutrophils is initially low (about 0.15 %>), but increases with increasing gestational age. In the period of 6–7 weeks of gestation, eosinophils, basophils, monocytes, macrophages and megakaryocytes are also found in the embryonic liver, the content of which, with the exception of macrophages and megakaryocytes, gradually increases by the 22–27-week gestation period. Starting from the 8–9 week period, 0.14 % of lymphocytes appear, the number of which is increasing, and by the 22–27 week gestational period they make up more than 10 %. At an 8-week gestation, up to 90 % of lymphocytes belong to pre-B cells, B-lymphocytes that carry surface IgM are detected, and then cells appear on the surface at about 11 weeks old, and IgA are also detected on their surface. By the 14-week gestation period, the percentage of cells circulating in the blood and each class of receptors is the same as in adults, but the ability of these fetal cells to synthesize and secrete immunoglobulins appears only by the 20th week.

In addition, during the period of hepatic hematopoiesis (6–27 weeks of gestation) 3–5 % of undifferentiated blasts are determined. When cloning in a semi-solid nutrient medium a suspension of hematopoietic cells obtained from a fetal liver, it was found that already in the early stages of gestation (6–7 weeks) cell aggregates are formed. The number of myeloid progenitor cells in the study of liver cell suspension of 9- and 21-week gestational periods is determined several times more than in the bone marrow of a child. In the second (21 weeks), cluster formation prevails, in aggregates, myeloblasts and promyelocytes, sometimes mature granulocytes, are mainly determined; spontaneous erythropoiesis is absent. Starting from the 18–20th week of gestation, the hematopoietic activity of the liver gradually decreases, by the time the baby is born, it ceases, and although during the first week of postnatal life certain hematopoietic elements may appear.

Hemopoiesis in the spleen occurs from the 12th week of gestation. First, granulo-, erythro- and megakaryocytopoiesis is determined in it. B-lymphocytes appear from the 15th week of gestation. At the age of 19–25 weeks of intrauterine development, 85 % of spleen cells are of lymphoid origin, lymphocytes with an intracellular IgM content appear. Hemopoiesis in the spleen reaches its maximum by the 4th month of gestation, and then decreases and ceases at the age of 6.5 months of fetal development. The reduction of the bridgehead of extramedullary hematopoiesis coincides with the appearance of the first signs of the next stage of hematopoiesis.

Bone marrow hematopoiesis occurs from about the 4th month of gestation. First, bone marrow occurs in the vertebral bodies of the fetus with a length of 95 mm. In fetuses of 11–14 weeks of gestation, the immature hematopoietic cells and red blood cells are determined in the ilium; 23–27 weeks are elements of all three sprouts of hematopoiesis at all stages of development. At the age of 13–14 weeks of fetal development, the first foci of hematopoiesis appear in the diaphysis of the humerus and femur. Among the bone marrow elements, the cells of the myeloid and megakaryocytic series are determined. At the age of 12–20 weeks of gestation in the fetus, pre-B cells prevail among the lymphoid elements. The role of bone marrow hematopoiesis increases as the skeleton develops, after 30 weeks the bone marrow is represented by all hematopoietic cells, and becomes the main source of blood cell formation. In the prenatal period, the bone marrow is red. From 32 weeks of age, all gaps in bone tissue are filled with hematopoietic tissue, that is, the volume of bone marrow is equal to the volume of hematopoietic cells. By the time a baby is born, hematopoiesis is almost completely limited to bone marrow.

So, at different stages of gestation, hematopoiesis has different organ localization, and in some periods hematopoiesis occurs simultaneously in different organs. It is believed that with a change in the overwhelming organ localization of hematopoiesis, the same stem cells do not move from one organ to another, but proliferate in a new place on another stem cell. It is believed that the

difference in the number and activity of progenitor cells at different stages of the development of the body confirms the concept of the population of bone marrow by circulating stem cells.

At different times of intrauterine development of the child in the blood, cells of different organ origin are determined. The earliest cells are erythroid. Among the latter, three generations can be distinguished – primitive, primary and definitive.

In a 6-week-old embryo, low hemoglobinized microcytes of hepatic origin prevail. Along with them, megalocytes are found, which make up about 20 % of the entire erythroid population and are probably a product of mesoblast hematopoiesis. At the 7–8th week of gestation, a normocytic, sufficiently hemoglobinized population of red blood cells appears, which is probably the second generation of hepatic hematopoiesis. In this period, megalocytes account for less than 5 %, which is associated with the regression of mesoblastic hematopoiesis. The third generation of red blood cells, occurs on the 9–10th gestational week, is characterized by a higher concentration of hemoglobin.

Hematopoiesis after birth in a child

In the first months of life, hematopoiesis occurs in the bone marrow of all bones. The bone marrow mass in a newborn is 1.4 % of its body weight and the entire bone marrow is red - the most active in hematopoiesis.

After 4 years, a gradual transformation of the red bone marrow into yellow, consisting of fat cells, is observed and the active function of hematopoiesis ceases.

During puberty (12–15 years), hematopoiesis is preserved only in the bone marrow of the flat bones, ribs, in the vertebral bodies, in the proximal ends of the shoulder, forearm and femur.

In an adult, bone marrow mass is more than 4.6 % of body weight, but red bone marrow is only half (about 50 %) of its total mass. And after 30 years, hematopoiesis occurs only in the bone marrow of the ribs, vertebral bodies and the sternum.

Functional lability of the hematopoietic system is characteristic of young children, and there is the possibility of a return to the embryonic type of hematopoiesis under the influence of any adverse factors. In this case, foci of hematopoiesis appear in the liver, spleen and lymph nodes. This is due to the fact that in young children there are no reserves for an increase in hematopoiesis, since the most active hematopoietic volume of the bone marrow is equal to the total volume of the bone marrow. In addition, under the influence of endo- and exogenous factors, the appearance of myeloid and lymphoid metaplasia in the bone marrow is possible. The latter is associated with a relatively large number in children than in adults of undifferentiated cells, which easily turn into cells of the myeloid or lymphoid series. This must be remembered when evaluating the results of a study of the blood system in sick children. In young children, a high regenerative ability of blood cells is also observed.

Blood system parameters' interpretation in children

In absolute terms, the amount of blood in children is significantly less (0.5 L) than in adults (4–6 L). But the relative amount of blood in relation to body weight in children is greater than in adults. Thus, in newborns, the weight of blood in relation to body weight is on average 14 %, in infants – 11 %, and in adults 7 %. A larger relative blood volume in children provides a higher level of metabolism in their body.

Blood viscosity at birth is higher compared to adults. But already during the first week it decreases and reaches the values of adults. Blood viscosity significantly affects the **erythrocyte sedimentation rate** (ESR). In relation to blood viscosity, ESR has an inverse relationship. In particular, in newborns, ESR is 0–2 mm / hour, in infants – 2–4 mm / hour, in older children – 4–10 mm / hour. ESR is considered accelerated if its value exceeds 14 mm / hour. **Hematocrit** (the ratio of the volume of blood cells to plasma volume) in children at birth is 55 %, that is, it is higher than in adults (40–45 %). Subsequently, the hematocrit value gradually decreases and at the end of the neonatal period is more than 42 %. In infants, the hematocrit value is 35 % and up to 15 years, this value reaches the level of an adult. A higher hematocrit in newborns is due to a high concentration of red blood cells and a large average volume of individual red blood cells.

Blood pH at the time of birth and in the first days of life is shifted to the acid side compared with adults and is in the range of 7.13–7.23, while in adults it is 7.35–7.40. During the first 3-5 days after birth, the pH reaches figures close to those in adults. Acidosis in children in the first days after birth is metabolic, it is due to the formation of under-oxidized metabolic products. It is important to emphasize that throughout the entire period of childhood, insignificant compensated acidosis (reduced value of buffer systems) remains. It gradually decreases with the growth and development of children.

Peripheral blood in healthy newborns

The number of red blood cells and hemoglobin is increased. *The number of red blood cells* at birth is 5–7 * 10^{12} in 1 liter and subsequently decreases to 4–4.5 * 10^{12} in 1 liter for 3–6 months of life. *The hemoglobin level* at the time of birth reaches 180–210 g / l. Starting from the 2nd day of a child's life, the level of hemoglobin decreases and at the end of the first month it averages 145 g / l, continuing to decrease for 6 months. and reaching minimum values (120–125 g / l) at the 7th month. In the future, the hemoglobin level gradually rises and at 15 years old is 130–140 g / l. An increased number of red blood cells and a high level of hemoglobin in children at birth are associated with hypoxia, which occurs during fetal development.

Another fundamental property worthy of discussion is the presence of a large amount of fetal hemoglobin (Hb) compared to maternal blood. In children in the first months of life, fetal hemoglobin prevails, which averages 70% and

only 30 % of "adult" hemoglobin (HLA). Starting from the first weeks of a child's life, a sharp increase in HbA synthesis occurs, while Hb synthesis decreases (by about 3 % per week) and up to 6 months of age the amount of Hb does not exceed 3 %, and HbA is 95–98 %. A feature of fetal Hb is that it has a high alkali resistance and binds oxygen quite easily, but it is very difficult to give to tissues. Therefore, the transport function of fetal Hb is insufficiently expressed. Its amount decreases only at the end of the first month of life.

Red blood cells of newborns are characterized by a higher hemoglobin content and this contributes to a higher level of color index, which may exceed 1.1, indicating red blood cell hyperchromia. For red blood cells of newborns, qualitative signs are characteristic that distinguish them from red blood cells of adults. Thus, an erythrocyte in children of the first months of life is characterized by *anisocytosis* (various sizes of erythrocytes ranging from 3 to 13 μm), *poikilocytosis* (different forms of red blood cells), *polychromatophilia* (different color of red blood cells), as well as an increased number of reticulocytes (young nucleated forms of red blood cells). The number of reticulocytes in newborns is in the range of 8–40 cells per 1000 mature red blood cells.

The average life expectancy of red blood cells in children in the neonatal period is less than in adults. In children, on the 2–3rd day of life, it is 12 days, and at the end of the first year of life – about the same as in adults, that is, an average of 120 days.

The osmotic resistance of red blood cells in children depends on age. So, in newborns, the onset of hemolysis is observed at higher concentrations of sodium chloride than in infants and adults, and the end of hemolysis, on the contrary, occurs at lower concentrations.

The number of leukocytes in peripheral blood

At birth, physiological leukocytosis is observed in children. The number of leukocytes in the peripheral blood in the first day of life is in the range of 1–33 * 10^9 in 1 liter, and then their number decreases and at the end of the first year of life is 8–9 * 10^9 in 1 liter.

An important, from a clinical point of view, feature is the *ratio of the number of neutrophils and lymphocytes* in peripheral blood throughout childhood. So, at birth in children in the peripheral blood there are 60–65 % of neutrophils and 25–30 % of lymphocytes, but already starting from the 2nd day of life, the number of neutrophils decreases and the number of lymphocytes increases. On the 4th – 5th day of life, the so-called "*first cross*" is observed, when the number of neutrophils and lymphocytes is leveled off and averages 40–45 %. At the end of the first month of life, the number of neutrophils decreases to 25–30 %, the number of lymphocytes increases to 60–65 %. This ratio is observed at the end of the first year of life, and then the number of lymphocytes decreases and the number of neutrophils increases gradually. At the age of 4–5 years,

the "*second crossroads*" occurs, that is, the leveling of the number of neutrophils and lymphocytes is again observed (on average 40–45 %). After this, the leukocyte formula gradually approaches the formula of adults. This occurs at the age of 12–14. Without knowledge of these features of the leukocyte formula, it is impossible to diagnose many diseases in children.

The number of platelets in newborns in the peripheral blood is in the range from 140 * 10^9 to 400 * 10^9 in 1 liter and averages 220 * 10^9 in 1 liter. The platelet count in children is a fairly stable value. Platelets in children are characterized by anisocytosis with the presence of giant platelet forms. Platelet aggregation is less pronounced than in adults, and therefore more time is needed to complete the aggregation process. In addition, platelets in children secrete significantly less factor 3 and serotonin than platelets in adults.

FUNCTIONS OF THE BLOOD SYSTEM

Homeostasis is a continual balancing act of the body systems to provide an internal environment that is comparable with life. The two liquid tissues of the body, the blood and lymph have separate but interrelated functions in maintaining this balance. They combine with a third system, the immune, to protect the body against pathogens that could threaten the organism's viability.

Main functions of the blood are:

1. Transportation of gases (oxygen O2) and carbon dioxide (CO2), chemical substances (hormones, nutrients, salts), and cells that defend the body.
2. Regulation of the body's fluid and electrolyte balance, acid-base balance, and body temperature.
3. Protection of the body from infection.
4. Protection of the body from loss of blood by the action of clotting.

Components of Blood shown in figure 1 are:

Erythrocytes (Red Blood Cells)

The erythrocytes (which are normally present in the millions) have the important function of transport O2 and CO2 throughout the body. The vehicle for this transportation is a protein-iron pigment called hemoglobin. The formation of RBCs in the bone marrow is stimulated by a hormone from the kidneys called erythropoietin. RBCs have a life span of approximately 120 days, after which they decompose into hemosiderin, an iron pigment resulting from hemolysis and bilirubin. The iron is stored in the liver to be recycled into new RBCs, and the bile pigments are excreted via the liver.

Abnormal RBCs can be named by their morphology, the study of shape or form. RBCs normally have a biconcave, dislike shape. (Although the center is depressed, there is not an actual hole.) Those that are shaped differently often have difficulty in carrying out their function. For example, sickle cell anemia is a hereditary condition characterized by erythrocytes (RBCs) that are abnormally

shaped. They resemble a crescent or sickle. Abnormal hemoglobin found inside these erythrocytes causes sickle-cell anemia in a number of Africans and African-Americans.

Leukocytes (White Blood Cells)

Although there are fewer leukocytes (thousands, not millions), there are different types with different functions. In general, WBCs protect the body from invasion by pathogens. The different types of cells provide this defense in a number of different ways. There are two main types of WBCs: granulocytes and agranulocytes.

Granulocytes

Named for their appearance, granulocytes also called polymorphonucleocytes have small grains within the cytoplasm and multilobed nuclei. Both names are used interchangeably.

These are three types of granulocytes, each with its own function. They are named for the type of dye that it attracts.

1. Eosinophils - are cells that absorb an acidic dye, causing them to appear reddish. An increase in eosinophils is a response to a need for their function in defending the body against allergens and parasites.

2. Neutrophils are cells that do not absorb either an acidic or basic dye and consequently are a purplish color. They are also called phagocytes because they specialize in phagocytosis and generally combat bacteria in pyogenic infections. This means that these cells are drawn to the site of a pathogenic "invasion," where they consume the enemy and remove the debris resulting from the battle.

3. Basophils are cells that absorb a basic (or alkaline) dye and stain a bluish color. Especially effective in combating parasites, they release histamine (a substance that initiates an inflammatory response) and heparin (an anticoagulant), both of which are instrumental in healing damaged tissue.

Agranulocytes

Agranulocytes are cells named for their lack of granules. The alternative name, mononuclear leucocytes, is so given because they have one nucleus. Both names are used interchangeably. Although these cells originate in the bone marrow, they mature after entering the lymphatic system.

There are two types of these WBCs:

1. Monocytes: These cells, named for their single, large nucleus, transform into macrophages, which eat pathogens and are effective against severe infections.

2. Lymphocytes: these cells are key in what is called the immune response, which involves the "recognition" of dangerous, foreign (viral) substances, and the manufacture of their neutralizers. The foreign substances are called antigens, and the neutralizers are called antibodies Laboratorial norms are represented in table 1.

Table 1

Red and white cells reference ranges

RED CELL REFERENCE RANGES

AGE	Hb (g/l)	RCC (x 10^{12}/l)	Hct (l/l)	MCV (fl)	MCH (pg)	MCHC (g/l)	RDW-SD (fl)	RDW-CV (%)
Cord blood	121 191	3.34 5.40	0.37 0.60	101 117	33.0 38.0	302 341	61.9 81.4	15.5 19.2
1-7 d	125 195	3.90 5.60	0.38 0.60	97 107	32.0 34.8	328 325	55.0 81.4	14.0 19.2
1-2 w	120 185	3.80 5.50	0.36 0.55	95 100	31.5 33.6	333 336	50.0 70.0	12.0 18.0
2w - 3m	102 130	3.38 3.94	0.30 0.38	84 98	29.0 33.8	333 355	39.9 56.6	12.6 16.0
3-6 m	100 122	3.39 4.86	0.28 0.36	68 85	22.6 29.7	331 351	34.0 42.4	12.0 14.8
6m – 2y	104 132	3.88 5.13	0.30 0.38	70 83	23.1 29.4	323 354	34.8 44.6	12.3 17.0
2-4 y	107 136	3.86 5.01	0.31 0.38	73 85	24.8 29.9	329 359	34.3 44.1	12.1 15.6
4-8 y	110 139	3.96 4.92	0.32 0.39	74 86	25.5 30.6	332 360	34.6 42.7	11.9 14.9
8-12 y	113 143	3.98 5.15	0.33 0.41	75 86	25.7 30.6	335 361	35.3 41.0	12.0 14.1

WHITE CELL REFERENCE RANGES

AGE	WCC (x10^9/l)	N (%)	L (%)	M (%)	E (%)	B (%)
Cord blood	9.6 30.4	39 73	13 47	4 15	0 7	0 2
1-7 d	7.5 21.0	20 73	30 70	4 15	0 7	0 2
1-2 w	6.8 20.0	15 60	35 75	4 15	0 7	0 2
2w - 3m	6.4 12.1	11 44	40 80	4 12	1 7	0 2
3-6 m	5.6 14.1	7 35	53 83	3 14	0 6	0 1
6m – 2y	5.4 13.6	14 55	37 79	2 12	0 6	0 1
2-4 y	4.9 12.8	24 67	28 64	2 11	0 7	0 1
4-8 y	4.7 12.3	32 71	20 59	2 10	0 8	0 1
8-12 y	4.7 12.2	37 70	22 55	2 10	1 8	0 1

AGE	N(A) x10^9/l	L(A) x10^9/l	M(A) x10^9/l	E(A) x10^9/l	B(A) x10^9/l	NRBC
Cord blood	4.4 21.0	2.5 9.1	0.6 4.1	0.0 1.3	0.0 0.4	1 24
1-7 d	1.5 15.3	2.3 14.7	0.3 1.5	0.1 1.3	0.0 0.4	
1-2 w	1.0 12.0	2.4 15.0	0.3 1.5	0.1 1.3	0.0 0.4	
2w - 3m	0.8 4.9	3.8 7.6	0.3 1.2	0.1 0.8	0.0 0.2	
3-6 m	0.5 4.4	3.4 9.8	0.2 1.1	0.0 0.7	0.0 0.1	
6m – 2y	1.1 6.0	2.7 8.9	0.2 1.1	0.0 0.6	0.0 0.1	
2-4 y	1.7 6.7	2.0 6.6	0.2 1.0	0.0 0.6	0.0 0.1	
4-8 y	1.8 7.7	1.6 5.1	0.1 1.0	0.0 0.6	0.0 0.1	
8-12 y	1.8 7.6	1.7 4.5	0.2 0.9	0.1 0.6	0.0 0.1	

Thrombocytes (Platelets)

Platelets (also known as thrombocytes) have a round or oval shape and are so named because they look like small plates. Platelets aid in the process of coagulation, the process of changing a liquid to a solid. When

blood cells escape their normal vessels, they agglutinate, or clump together, by the following process: First, they release factor X (formerly called thrombokinase), which, in the presence of calcium, reacts with the blood protein, prothrombin, to form thrombin. Thrombin then converts another blood protein, fibrinogen, to fibrin, which eventually forms a mesh like fibrin clot (blood clot), achieving hemostasis (control of blood flow; that is, stopping the bleeding).

Plasma

Plasma, the liquid portion of blood, is composed of the following:

1. Water, or H2O (90%)
2. Inorganic substances (calcium, potassium, sodium)
3. Organic substances (glucose, amino acids, fats, cholesterol, hormones)
4. Waste products (urea, uric acid, ammonia, creatinine)
5. Plasma proteins (serum albumin, serum globulin, and two clotting proteins: fibrinogen and prothrombin)

Serum is plasma minus the clotting proteins.

Serology is the branch of laboratory medicine that studies blood serum for evidence of infection by evaluating antigen-antibody reactions in vitro.

Human blood is divided into four major different types: A, B, AB, and O. The differences are due to antigens present on the surface of the blood cells. Antigens are substances that produce an immune reaction by their nature of being perceived as foreign to the body. In response, the body produces substances called antibodies that nullify or neutralize the antigens. In blood, these antigens are called agglutinogens because their presence can cause the blood to clot.

The antibody is termed an agglutinin. Type A blood has A antigen, type B has B antigen, type AB has both A and B antigens, and type O has neither A nor B antigens. If an individual with type A blood is transfused with type B blood, The A antigens will form anti-B antibodies because they perceive B blood as being foreign. According to these antigen-antibody reactions, an individual with type AB blood is a universal recipient, and an individual with type O blood is a universal donor.

Another antigen, the Rh factor, is important in pregnancy because a mismatch between the fetus and the mother can cause erythroblastosis fetalis, or hemolytic disease of the newborn. In this disorder, a mother with a negative Rh factor will develop antibodies to an RH + fetus during the first pregnancy. If another pregnancy occurs with an Rh + fetus, the antibodies will destroy the fetal blood cells.

LYMPHATIC SYSTEM AND ITS COMPONENTS

The lymphatic system is responsible for the following:
1. Cleansing the cellular environment
2. Returning proteins and tissue fluids to the blood
3. Providing a pathway for the absorption of fats into the bloodstream
4. Defending the body against disease

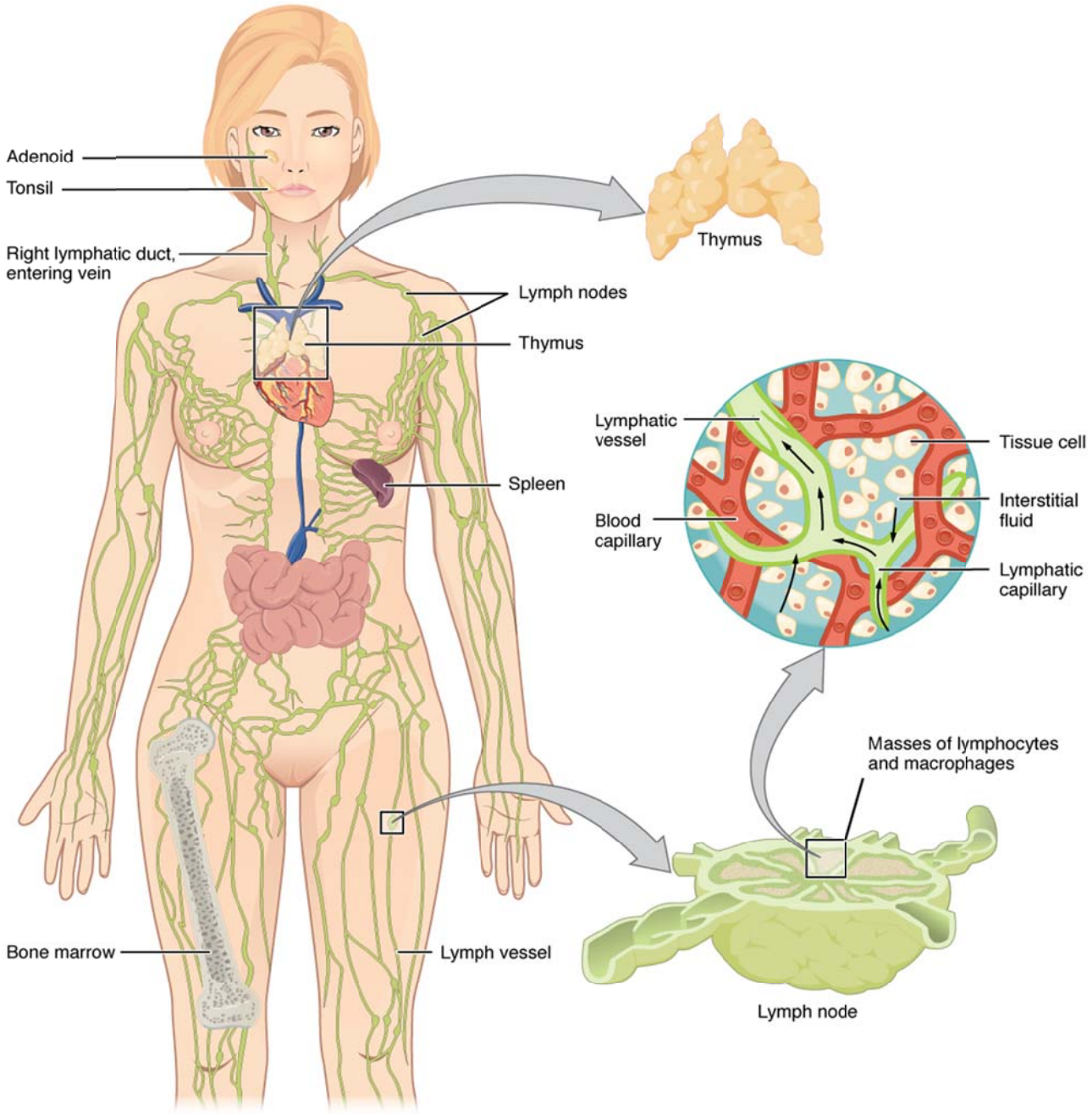

Fig. 1 Components of the lymphatic system

The lymphatic system consists of: (1) lymph (or interstitial fluid), (2) lymphatic vessels (3) lymph nodes (4) lymphatic organs (tonsils, adenoids, appendix, spleen, thymus, and areas of tissue in the intestine called Peyer's patches) , and (5) lymphoid tissue (Fig. 1).

Components of the lymphatic system are:

Lymph

Lymph is a fluid that circulates throughout the body in the lymphatic system. It forms when tissue fluids/blood plasma (mostly water, with proteins and other dissolved substances) drain into the lymphatic system. It contains a high number of lymphocytes (white cells that fight infection). Lymph that forms in the digestive system called **chyle**, this contains higher levels of fats, and looks milky white.

Lymph vessels

Walled, valved structures that carry lymph around the body

Lymph nodes

Small bean-shaped glands that produce **lymphocytes**, filter harmful substances from the tissues, and contain **macrophages**, which are cells that digest cellular debris, pathogens and other foreign substances. Major groups of lymph nodes are located in the tonsils, adenoids, armpits, neck, groin and mediastinum.

Lymphatic organs. The **thymus** is a specialized organ of the immune system located between the sternum and the heart. It is involved in the differentiation and selection of lymphocytes, which is important for the maturation of T cells (i.e., T derivatives from the thymus). The **spleen** is an organ in the upper left part of the abdomen that filters blood, utilizes "worn out" red blood cells and provides a "supply" of blood. It contains both red tissue and white lymph tissue. Different parts of the spleen specializing in different types of immune cells. **Tonsils** – are clusters of oval-shaped lymphoid tissue located on the border of the oral cavity and pharynx in the mucous membrane. The task of these formations is extremely important: tonsils are the first "filter" for microbes and viruses that penetrate from air and food. In addition, they perform hematopoietic function and are involved in the development of immunity. **Adenoids** – pathological proliferation of the nasopharyngeal (pharyngeal, third) tonsils. Nasopharyngeal (pharyngeal, III tonsils) is part of the natural childhood protection against the invasion of pathogenic microorganisms. The pharyngeal tonsil is already formed at 6 months of embryonic development. Fully pharyngeal tonsils form at the age of 2–3 years. Normally, the thickness of the formed pharyngeal tonsil is 5–7 mm, the width is 20 mm, length is 25 mm. The condition in which these sizes are increased is considered precisely as adenoid vegetation. The system of local immunity is not developed during the first 3–4 years of a person's life. The final formation of local immunity occurs only about 14 years. From the same time, the involution of the pharyngeal tonsil begins, but the functioning of the lymphoid follicles continues throughout life. It is in the pharyngeal tonsil in children that lymphocytes are produced for the mucous membrane of the nasopharynx, nose, paranasal sinuses, middle ear, and ensure the normal functioning of local immunity factors. The **appendix** is an

appendage of the cecum of about 8 cm in size, which is part of the digestive system and plays a role in the body's immune defense. To date, its functions have not been studied exactly. It is believed that it is a reservoir of beneficial intestinal microflora. Like any part of the intestine, the appendix produces intestinal juice, but in small quantities. That is why for a long time it was believed that the appendix is a "mistake of nature" and is not needed in the human body, because of which it was often removed even for no apparent reason. However, since the appendix is also part of the immune system, its removal is justified only in acute inflammation.

METHODOLOGY OF THE STUDY OF THE BLOOD SYSTEM

The methodology for examining a child with diseases of the blood forming organs includes a detailed study of the patient's complaints, medical history, general examination, examination of the lymph nodes, bone system, liver, spleen and additional laboratory data.

When collecting an anamnesis, one should pay attention to the possibility of a hereditary disease in the patient's relatives, on feeding a child, past illnesses, sanitary living conditions, etc.

A general examination of the child can be carried out after receiving anamnestic data. First of all, it is necessary to assess the position of the body, the color of the skin and mucous membranes.

The pale color of the skin and mucous membranes often indicates various diseases of the blood and blood-forming organs. However, it must be remembered that it also depends on other causes (individual anatomical and histological features of the skin, low blood pressure) and is observed in acute heart failure, kidney disease, etc.

Yellow coloration of the skin may be one of the signs of a blood disease, but it is more often observed with liver diseases, septic conditions, after taking certain medications and food products.

When examining patients with diseases of the hematopoietic system, characteristic changes in the color of the skin, mucous membranes and sclera can be detected. With a significant decrease in hemoglobin and red blood cell count, the skin and mucous membranes become pale. If *anemia* develops as a result of acute bleeding, pallor of the skin and mucous membranes occurs immediately, which can serve as a diagnostic sign of internal bleeding. In patients with Addison-Birmer anemia, pallor has a jaundice – a waxy or lemon-yellow complexion and subicteric sclera. With chlorosis, pallor has a greenish tint. Yellowness of the skin and visible mucous membranes is characteristic of congenital hemolytic disease and hemolytic anemia.

On the contrary, in some diseases and conditions (*polycythemia or erythremia*), the skin has a cherry red color, which is associated with an increase in the number of red blood cells to 6-10 * 10^{12} / l and hemoglobin to 160–180 g / l.

Examination of the oral cavity is of great diagnostic value. Inflammation zones along the edges and at the end of the tongue, often with an aphthous rash and cracks, its smooth, shiny mucous membrane are characteristic signs of Addison-Birmer anemia. On the tonsils and the mucous membrane of the oral cavity, necrotic and gangrenous lesions in acute leukemia and agranulocytosis can be noted.

In addition to diffuse changes in skin color, focal phenomena on the skin and mucous membranes in the form of intradermal or subcutaneous hemorrhages of various sizes and localizations, which can indicate diseases of the blood and blood-forming organs and can often be the only sign of a pathological process, can be observed.

The state of the lymphatic system is important for the diagnosis of diseases of the blood and blood-forming organs. For clinical research, lymph nodes are available that are localized at the surface of the body, as well as abdominal and thoracic (with a significant increase). The following groups of peripheral lymph nodes are distinguished: occipital, parotid, submandibular, chin, anteroposterior, posterior cervical, supraclavicular, subclavian, axillary, thoracic, elbow, inguinal, popliteal.

Peripheral lymph nodes are grouped in the subcutaneous tissue of various parts of the body, where they can be detected by palpation, and with a significant increase – and visually. The study of lymph nodes is carried out in the same symmetrical areas, adhering to a certain sequence: chin, submandibular, incisal carotid, parotid, occipital, posterior cervical, anterior cervical, supraclavicular, subclavian, axillary, cubital (elbow), inguinal and popliteal.

Large, from a few millimeters to 1 cm in diameter, single lymph nodes can normally be palpated in the submandibular, inguinal and, less commonly, in the axillary regions. They have a rounded shape, a dense-elastic consistency, mobile, painless. A more significant enlargement of the lymph nodes in these areas, as well as palpable lymph nodes in other parts of the body, is usually a pathological symptom.

Enlarged lymph nodes are local and generalized. Thus, an enlarged lymph node in any one area usually indicates the presence of an inflammatory process or metastatic tumor lesion in the organs (tissues) from which lymph flows into this node, or pathological changes of a similar origin in the lymph node itself. In acute inflammation of the lymph node (*lymphadenitis*), it usually has a soft-elastic consistency, sharply painful, the skin over it is often hyperemic and hot to the touch. The node can suppurate with the involvement of surrounding tissues (*periadenitis*) in the inflammatory process, and sometimes it opens with the formation of a fistula, with which pus leaves. If regional

lymphadenitis is caused by an inflammatory focus in the lower part of the limb, then on the skin it is often possible to find a narrow strip of hyperemia, going from the site of inflammation to the node, in the projection of the inflamed lymphatic vessel (*lymphangitis*).

In some diseases, the lymph nodes enlarge in certain areas. With *lymphogranulomatosis* in the onset of the disease, a marked increase and hardening of one of the groups of lymph nodes, most often in the cervical, supraclavicular or inguinal areas, is manifested. The nodes can be single or in the form of closely welded large conglomerates, but, as a rule, are not associated with the skin, are mobile, painless and do not suppurate. Enlarged lymph nodes, mainly in the occipital region, are a typical symptom of rubella, and enlargement is mainly of the posterior cervical lymph nodes, infectious mononucleosis. Chains of moderately enlarged lymph nodes in the neck are often observed in patients with chronic tonsillitis.

A moderate increase in lymph nodes in several or all palpable areas at the same time is observed in some infectious diseases (brucellosis, toxoplasmosis, listeriosis, infectious mononucleosis, AIDS), as well as in sepsis, infectious endocarditis, sarcoidosis, immunopathological diseases, etc. However, with acute leukemia, chronic myelogenous and lymphoid leukemia, the lymph nodes in most areas increase slightly. They, as a rule, are not soldered together and with the skin, have a pasty consistency, are painless, and are mobile with displacement.

Hyperplasia of the lymph nodes is observed in various pathological conditions, in particular with leukemia. Enlarged lymph nodes give reason) to think about the possible presence of a blood disease. On examination, a sharp increase in peripheral lymph nodes in the neck or in the axillary areas (leukemia, lymphogranulomatosis, tuberculosis, tularemia, infectious mononucleosis, etc.) can be detected.

In diseases accompanied by significant hyperplasia of lymphoid tissue, numerous and systemic enlargement of the lymph nodes (lymphogranulomatosis, etc.), cervical, supraclavicular, axillary, vaginal and lymph nodes of other groups are palpated. With lymphadenopathy, they have an elastic consistency, smooth, mobile, and do not grow together between themselves and surrounding tissues. With lymphogranulomatosis, the lymph nodes are very solid ("wooden consistency"), quickly grow together with each other and with tissues, acquiring the form of solid conglomerates, which can compress vital organs.

With severe forms of anemia, changes in the *cardiovascular system* are sometimes noted in the form of functional murmurs (especially in young children), which are heard over the region of the heart and on large venous vessels.

The *liver and spleen* noticeably increase with hematological diseases, it is especially often observed with various forms of acute leukemia and anemia.

Palpation of the abdominal organs often makes it possible to establish an increase in the liver and spleen. A slight increase in the spleen and its solid consistency is observed with Verlhof disease, lymphogranulomatosis, Addison-Birmer anemia. The spleen can reach large sizes (splenomegaly) with hemolytic anemia, chronic myelogenous leukemia. A solid with a smooth surface, a rounded edge of the spleen in this disease can occupy not only the left half of the abdominal cavity, but also go in the middle line to the right, go down. Significantly less spleen increases with lymphocytic leukemia. Along with an increase in the spleen, an increase in the liver is noted, which is due to leukemia by the growth of myeloid and lymphoid tissues.

Palpation is undoubtedly the main objective method for examining the spleen. The spleen is located in the left hypochondrium, laterally from the stomach, directly under the dome of the diaphragm between the IX–XI ribs so that its long axis almost coincides with the X rib or forms an acute angle with it. In connection with this placement, the spleen naturally very significantly shifts during respiratory movements.

During spleen palpation, the patient lies on the right side with the left leg bent at the knee and hip joints, and the right leg is straightened. The patient's left arm is bent at the elbow joint and lies on the chest or both arms are folded under the head. On palpation, the position, size, texture and surface condition of the spleen are evaluated. It is generally believed that a normal, enlarged spleen in children is not palpable, and if palpated, it is enlarged. This idea is true in most cases, but in young children with asthenic physique, muscle hypotension, the spleen can be palpated.

In cases of acute infectious diseases (for example, with typhoid fever) or acute stagnation of blood in the spleen (for example, due to splenic vein thrombosis), the organ retains a soft consistency.

In some chronic diseases (syphilis, malaria, etc.), as well as in blood diseases and significant stagnation, the spleen becomes hard as a result of portal hypertension.

The edge of the spleen often has a rounded shape. An exacerbation of it, characteristic of the edge of the liver with cirrhosis, as a rule, is not noted. What forms the edge of the spleen, and then with a significant increase in its size, you can feel the physiological notch (several notches) along the front edge. According to NECK °, the spleen is distinguished from the left kidney. Spleen soreness is characteristic for acute stagnation of blood in it, as well as for fresh hemorrhage. Under physiological conditions, the surface of the spleen is smooth, and with hemorrhage uneven due to scars, appears after it. Tumors in the spleen are very rarely localized.

With lesions of the blood system, in particular with leukemia, bone pain is observed, which is determined by tapping.

Study of morphological features of blood cells

For the diagnosis of diseases of the blood system, a correct assessment of the data is very important, obtained by studying the morphological features of blood cells.

In various clinical forms of anemia in the peripheral blood, the hemoglobin level decreases (below 110 g / l) and the number of red blood cells (less than 3.5 * 10^{12} / l). This is due to various reasons: insufficiency of the erythropoietic system of the child, increased decay of red blood cells in the peripheral blood and foci of their formation, decreased hematopoietic function, blood loss, and the like.

An increase in the number of red blood cells in peripheral blood is observed with congenital heart defects, true idiopathic polycythemia, and manifestations of severe dehydration.

Anisocytosis and polychromatophia indicate an active regeneration process, and poikilocytosis indicates a degeneration of red blood cells.

Erythroblastosis (nuclear forms of red blood cells) and **reticulocytosis** (an increased number of red blood cells with supravital granularity) indicate an increase in erythropoiesis processes or functional bone marrow failure, which releases immature cells into the blood; basophilic granularity of erythrocytes – about their pathological regeneration, which can be observed with malaria, lead poisoning, congenital syphilis.

The osmotic resistance of red blood cells is sometimes significantly reduced with congenital hemolytic anemia.

An increased number of leukocytes (**leukocytosis**) is observed in infectious diseases and is a kind of protective reaction of the body against the infectious process. Especially high leukocytosis is observed in children with bacterial infections, leukemoid reactions and some forms of leukemia. The number of leukocytes decreases (**leukopenia**) in severe infectious, especially viral, diseases and toxic conditions as a result of inhibition of bone marrow function due to the action of toxins. Attention should be paid to pronounced leukopenia, since it can easily go into agranulocytosis.

The assessment of determining the total number of leukocytes has a certain value only in comparison with the data of the leukocyte formula when taking into account the clinical symptoms of the disease. Qualitative changes in the morphology of leukocytes indicate the state of the blood forming organs. When evaluating the leukocyte formula, it must be remembered that in children there are significant differences between the number of neutrophils and lymphocytes depending on age.

An increase in the number of stab nuclei and the appearance of young cells (metamyelocytes and even myelocytes) are called a shift of the blood formula to the left. This is one of the signs of an infectious and inflammatory

process that occurs in the body. A shift to the left with a part expressed by neutrophilia indicates a favorable prognosis.

A decrease in the number of neutrophils (**neutropenia**) is observed with tuberculosis, anaphylactic shock, severe forms of influenza, and typhoid fever. The combination of neutropenia with leukopenia occurs in severe forms of various infections and sepsis, long-term use of sulfa drugs.

Eosinophilia can be expressed with exudative diathesis, allergic diseases, scarlet fever, helminthic invasion, lymphogranulomatosis. An increase in the number of eosinophils in acute infectious diseases is considered a favorable prognostic sign. A decrease in their number is observed in acute infectious diseases (with the exception of scarlet fever), especially with typhoid fever, measles, and sepsis. The complete disappearance of eosinophils (aneosinophilia) is an unfavorable prognostic sign.

An increase in the number of lymphocytes (**lymphocytosis**) is observed in patients with lymphatic and exudative diathesis, rubella, whooping cough, and some other infections. Lymphopenia (a decrease in the number of lymphocytes) is noted in most viral diseases, lymphogranulomatosis, miliary tuberculosis and some blood diseases. The number of monocytes often increases in patients with measles, scarlet fever, monocytic tonsillitis. Monocytopenia (a decrease in the number of monocytes) is characteristic of severe septic diseases, malignant forms of anemia.

Platelet count. Of great diagnostic importance for a number of diseases is the correct assessment of the number of platelets in the peripheral blood. Despite the rather significant fluctuations in the number of platelets in healthy children even during the day, a decrease in their number is considered a pathological phenomenon. The number of platelets decreases sharply with Werlhof's disease, pernicious and aplastic anemia moderately - with thrombosis of the splenic veins, mourning. Often there is a temporary decrease in platelet count in acute infections, brucellosis, during the febrile period with typhoid fever, measles, hemorrhagic and gangrenous forms of diphtheria, infectious jaundice, with the transition of the pathological process during the period of convalescence. Thrombocytopenia indicates increased breakdown or decreased platelet production. With a decrease in platelet count, spontaneous hemorrhagic syndrome very often develops. An increase in the number of platelets indicates a significant production of their bone marrow or delayed decay (observed during the recovery period after acute infections, with rheumatism, pneumonia), and anemia – an increased bone marrow regeneration and a favorable prognosis.

In establishing the diagnosis and prognosis, a large role is played by the **erythrocyte sedimentation rate** (ESR). It has been reliably established that although increased ESR is not a specific reaction and occurs in various

diseases and conditions, it never rises in healthy children and in compensated or completed pathological processes.

Accelerated ESR indicates only the presence of a child's disease of an inflammatory nature, but not about its form and localization of the pathological process. The dynamics of changes in ESR over the corresponding period of time indicates either attenuation or an aggravation of the process, which is very important for forecasting. In some cases, the ESR value allows you to suspect the nature of the disease. So, the ESR value in the range of 40–60 mm / h is observed with leukemia, rheumatism, diffuse connective tissue diseases, glomerulonephritis and some other diseases.

Based on the data from a blood test, it is not always possible to make a correct diagnosis and determine the prognosis of a disease. In the main hemogram, it acquires diagnostic or prognostic significance only under the condition of a parallel assessment of clinical manifestations. Especially valuable are dynamic observations of changes in the blood during the course of the disease.

For a correct assessment of the state of hematopoiesis, the study of intravital punctures of the bone marrow (myelogram), lymph nodes, and spleen is especially important.

When performing bone marrow puncture in young children, it should be remembered that its development in the sternum occurs sequentially from the sternum handle – between I and II ribs, then between II and III, etc.

QUESTIONS FOR SELF-CONTROL

1. What are the main functions of the blood system you know?
2. What are the components of the blood system?
3. What are the main functions of the lymphatic system?
4. What are the components of the lymphatic system?
5. Describe the leading stages of the formation of the blood system?
6. What are the main methods for studying the blood system you know?

TESTS

1. In. the blood of a 16 year-old man it was revealed 18% of erythrocytes of the spherical, ball-shaped, flat and thorn-like shape. Other eritrocytes were in the form of the concavo-concave disks. How is such phenomenon called?

A. Physiological anisocytosis
B. Pathological poikilocytosis
C. Physiological poikilocytosis
D. Pathological anisocytosis
E. Erytrocytosis

2. In a patient with clinical signs of immunodeficiency the number and functional activity of T and B lymphocytes are not changed. Defect with dysfunction of antigen-presentation to the immunocompetent cells was found during investigation on the molecule level. Defect of whatcells is the most probable?

A. T-lymphocytes, B-lymphocytes
B. Macrophages, monocytes
C. NK-cells
D. Fibroblasts, T-lymphocytes, B-lymphocytes
E. 0-lymphocytes

3. Problems with T cells (lymphocytes) are following diseases except

A. Chronic mucocutaneous candidiasis
B. DiGeorge syndrome
C. X-linked lymphoproliferative syndrome
D. X-linked agammaglobulinemia

4. A 12-year-old boy often suffers from virus and bacterial infections and eczematous skin lesions. Enlargement of T-lymphocytes and IgM with normal IgA and IgG was revealed on examination. What type of immune system pathology is presented in the patient?

A. Composite immunedefficiency
B. Hypoplasia of thymus
C. Bruton's hypogammaglobulinemi
D. Turner's syndrome
E. Hereditary immundeficiency of the complement system

5. A 5 year old child is ill with measles. Blood analysis revealed increase of total number of leukocytes up to 13*109/l. Leukogram: basophils – 0, eosinophils – 1, myelocytes – 0, juvenile neutrophils – 0, band neutrophils – 2, segmented neutrophils – 41, lymphocytes – 28, monocytes – 28. Name this phenomenon:

A. Lymphocytosis
B. Agranulocytosis
C. Monocytosis
D. Eosinopenia
E.Neutropenia

6. A 15 year old girl has pale skin, glossitis, gingivitis. Blood count: erythrocytes – 3,3*1012/1, hemoglobin – 70 g/1, colour index – 0,5. Examination of blood smear revealed hypochromia, microcytosis, poikilocytosis. What type of anemia is it?

A. Iron-deficient
B. B12-folic acid-delicient
C. Sickle-cell

D. Hemolytic

E. Thalassemia

7. A child who suffers from pneumonia has high body temperature. What biologically active substance plays the leading part in origin of this phenomenon?

A. Serotonin

B. Histamine

C. Bradykinin

D. Interleykin

E. Leukotrienes

8. A 3-year-old child has been admitted to a hospital because of ostealgia and body temperature rise up то 39C. Objectively: the patient is in grave condition, unable lo stand for ostealgia, there is apparent intoxication, lymph nodes are enlarged up to 1,5 cm. Liver can be palpated 3 cm below the costal margin, spleen – 2 cm below the costal margin. In blood: \RBCs – 3,0 x 10*12/L, Hb- 87 g/I, colour index – 0,9, thrombocytes – 190 x 10*9/1, WBCs – 3,2 10*9/l, eosinophils – 1 %, stab neutrophils – 1, segmented neutrophils – 9 %, lymphocytes – 87 %, monocytes – 2 %, ESR – 36 mm/h, What examination should be conducted in order to specify the diagnosis?

A. Sternal puncture

B. Lymph node biopsy

C. Computer tomography

D. Ultrasound investigation

9. Examination of a patient 14 y.o. admitted to the surgical department with symptoms of acute appendicitis revealed the following changes in the white blood cells: the total count of leukocytes is 16* 10*9 /1. Leukocyte formula: basophils – 0, eosinophils – 2 %, juvenile forms – 2 %, subnuclear – 8 %, segmentonuclear – 59%, lymphocytes – 25%, monocytes – 4 %. The described changes can be classified as:

A. Neutrophilia with hyperregenerative left shift

B. Neutrophilia with right shift

C. Neutrophilia with degenerative left shift

D. Neutrophilic leukemoid reaction

E. Neutrophilia with regenerative left shift

10. A 7- year-old girl has dropped penicillin containing eye drops. In few minutes there appeared feeling of itching, burning of the skin, lips and eyelids edema, whistling cough, decreasing of BP. What antibodies take part in the development of this allergic reaction?

A. IgD and IgG

B. IgM and IgG

C. IgA and IgM

D. IgM and IgD
E. IgG and IgE

Answers: 1 – C, 2 – D, 3 – D, 4 – A, 5 – C, 6 – A, 7 – D, 8 – B, 9 – E, 10 – E

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