A N E M İ A


HEMATOLOGY
OTHER ANALYSES
Anemia
Adenopathy
Anticoagulant Heparin
Anticoagulant Sintron
Bleeding diathesis
Nephropathy
Patient
Lithiasis
oncology
Nephritic
Nephrotic
Thrombocytopenia
Bile acids
ANEMIA

ANEMIA - CHARACTERIZED BY A DECREASE IN THE CONCENTRATION OF HEMOGLOBIN AND HEMATOCRIT PER UNIT VOLUME OF BLOOD.

main criteria:

- decreasing of hemoglobin concentration
- decreasing of hematocrit level
- decreased number of erythrocytes*

Clinical signs of Anemic sindrome:

• general weakness, loss of appetite, physical and mental fatigue, dispnea, dizziness, tinnitus, the flashing "spots" in front of the eyes

•loss of consciousness and coma in severe cases

•during the examination: pallor of the skin and mucous membranes, tachycardia, hypotension, expansion of cardiac borders

•during auscultation: weakening of heart sounds and systolic murmur

•In ECG: depression of the ST segment, flattened T wave, disturbance of heart rhythm, arrhythmias

CLINICAL LABORATORY DIAGNOSIS OF ANEMIA (C L D)

- blood analyses
- smear of peripheral blood
- blood biochemistry
- bone marrow biopsy

AUTOMATIC HEMANALYZER (BECKMAN COULTER DXH 800)

Blood Analyses

Abbreviation	Index	Norma
WBC	**White Blood Cell**	4,0-9,0x10^9/l
RBC	**Red Blood Cell**	F: 4,8±0,6x10^{12}/l M:5,4±0,8x10^{12}/l
Hb	**Hemoglobin**	F: 140± 20 g/l M: 160± 20 g/l
Hct	**Hematocrit**	F: 42 ± 5% M:47 ± 5%
MCV	**Mean Corpuscular Volume**	87 ± 5 fl
MCH	**Mean Corpuscular Hemoglobin**	29 ± 2pg
MCHC	**Mean Corpuscular Hemoglobin Concentration**	34 ± 2 %
RDW	**Red cell Distribution Width**	11,5-14,5 %
Plt	**Platelet**	180,0-320,0x10^9/l
MPV	**Mean Platelet Volume**	8-12 fl
PDW	**Platelet Distribution Width**	11,5-15,5 %

Plt	Platelets	180,0-320,0x10^9/l
MPV	Mean Platelet Volume	8-12 fl
PDW	Platelet Distribution Width	11,5-15,5 %
Pct	Trombocrit	0,15-0,50 %
LY %	Lymphocytes, %	19-37 %
LY#	Lymphocytes, #	1,20-3,00x10^9/l
MO%	Monocytes, %	3-11%
MO#	Monocytes, #	0,09-0,60x10^9/l
NE%	Neutrophils, %	48-78 %
NE#	Neutrophils, #	2,04-5,8x10^9/l
EO%	Eosinophils, %	0,5-5 %
EO#	Eosinophils, #	0,02-0,30x10^9/l
BA%	Basophils ,%	0-1 %
BA#	Basophils, #	0-0,065x10^9/l
ESR	Erythrocyte Sedimentation Rate	F: 2-15 mm/hour M: 1-10 mm/hour

According to the protocols of the WHO, regardless of age, gender, geography, the patient's hemoglobin level is less than 110 g/l, it is considered as anemia.

Hb reference level	
Male	130-160 g/l
Female	120-140 g/l

mild anemia - hemoglobin level	**↑ 90g/L**
moderate anemia - hemoglobin level	**70 - 90 g/L**
severe anemia - hemoglobin level	**↓ 70 g/L**

Erythrocyte İndexes
Differentiation of anemia depending on MCV:

MCV < 80 fl **Microcytic anemias**	**MCV 80–100 fl** **Normocytic anemias**	**MCV >100 fl** **Macrocytic anemias**
Iron deficiency anemia Thalassemia Anemia of chronic diseases Sideroblastic (sideroachrestic) anemia	Acute posthemorrhagic anemia Aplastic anemia Hemolytic anemias Anemia in chronic diseases Hereditary dyserythropoietic anemias	Megaloblastic anemia Aplastic anemia (hereditary forms) Hemolytic anemias accompanied by chronic hemolysis Myelodysplastic syndrome

Morphological types of anemia depending on MHC-MCHC

MCH reference level : 27-31pg

MCHC reference level: 30-38% (g/dl)

Hypochromic	**Normochromic**	**Hyperchromic**
MCH – < 24 pg	*MCH* – 24–34 pg	*MCH* – > 34 pg
MCHC–< 30 g/dl	*MCHC*–30–38 g/dl	*MCHC* – >38 g/dl

RDW - red blood cells distribution width

RDW reference level: 11,5 – 14,5%

The erythrocyte distribution histogram correlates numerical values such as RBC, MCV, and RDW and provides a graphical representation of them.

İn Histogram:

RBC – shown in the **area** under the distribution curve

MCV- corresponds to the **quantity** on the x-axis

RDW – corresponds to the **width of the area** under the distribution curv

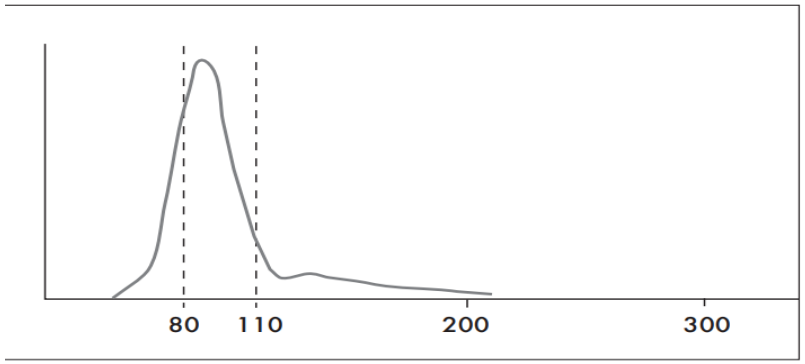


Рис. 1. Гистограмма распределения эритроцитов в норме (Hb 146, MCV 89,6, MCHC 330, RDW 12,5)

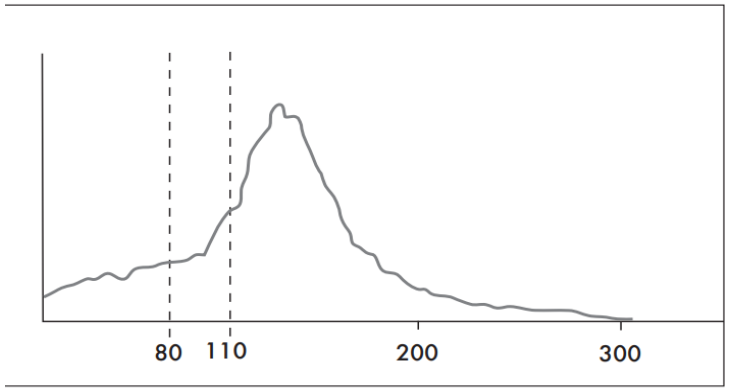


Рис. 3. Мегалобластная анемия (Hb 65, MCV 127, MCHC 324, RDW 35,7)

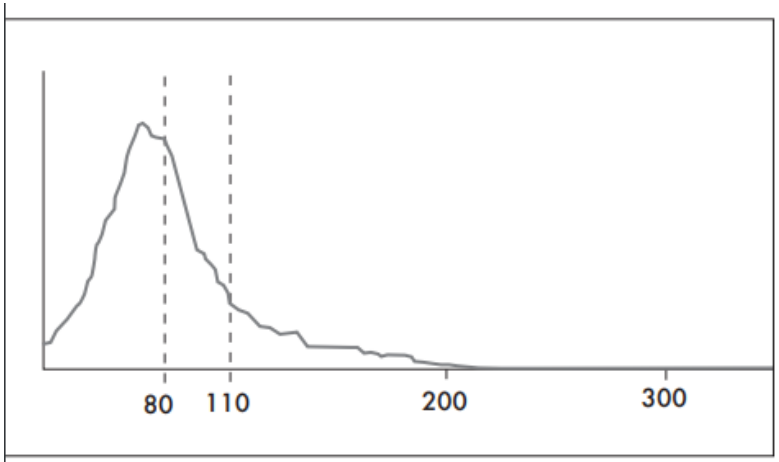


Рис. 6. ЖДА (Hb 86, MCV 65,8, MCHC 314, RDW 32,1)

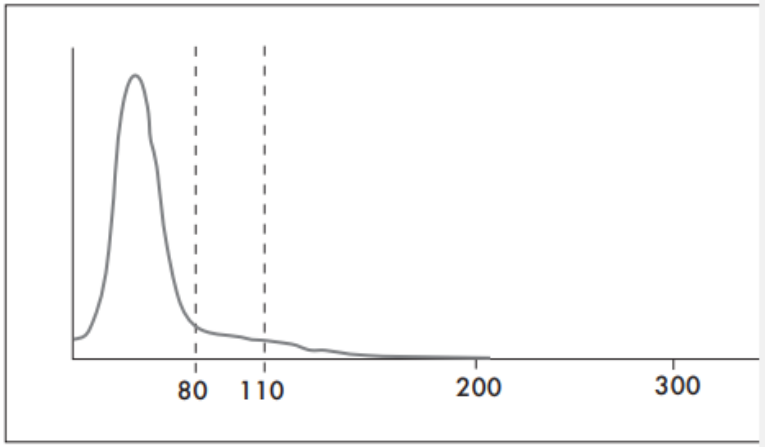


Рис. 7. β-Талассемия (Hb 86, MCV 54,6, MCHC 285, RDW 15,6)

ESR- reference level
Female 2-15 mm/hour
Male 1-10 mm/hour

ESR mm/hour		Westergren (mm/hour)
Children 17 ages		2–10
Males 17–50 ages		2–15
> 50 ages		2–20
Females 17–50 ages		2–20
> 50 ages		2–30

The main characteristics of erythrocytes in peripheral blood smear

- Size (or volume) of erythrocytes
- Shape of erythrocytes
- Color characteristic of erythrocytes
- Intracellular inclusions
- The amount of reticulocytes

In cases of doubt, a bone marrow puncture is performed and a myelogram is studied.

Erythrocyte size

diameter 6,5 - 8 µm *normocytes*
diameter < 6 µm *microcytes*
diameter > 8 µm *macrocytes*
diameter 10-12 µm *megalocytes*

Anisocytosis indicates more than 25% of micro- and macrocytes in the smear

•mild anisocytosis (+) - about 25-30% of erythrocytes differ from normal sizes (in the same or different direction);

• moderate anisocytosis (++) - approximately 30-50% of erythrocytes differ in size;

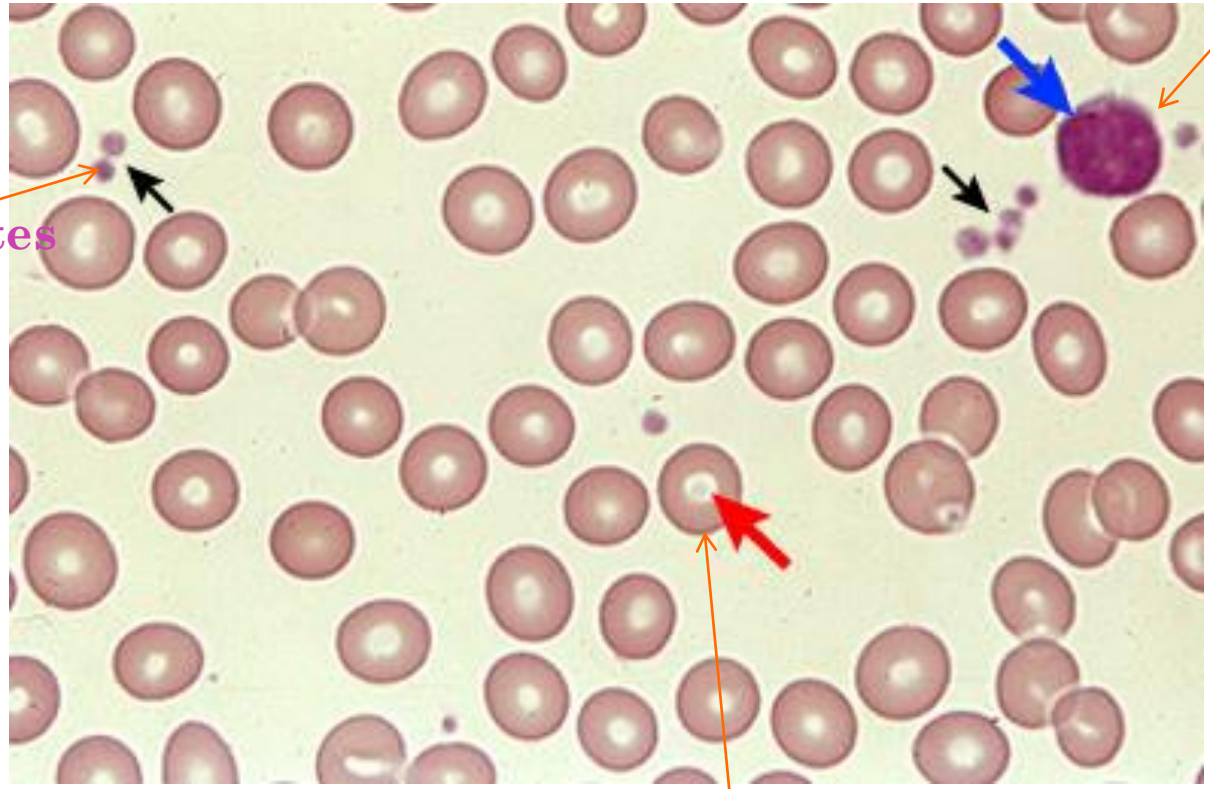
• subacute anisocytosis (+++) – approximately 50-75% of erythrocytes have changed in size;

• acute anisocytosis (++++) – almost all erythrocytes are of abnormal size.

Poikilocytosis - shape abnormality of erythrocytes, is noted when there are more than 25% of poikilocytes.

Poikilocytes	Anemia
Microspherocytes	Hereditary microspherocytosis, immune hemolytic anemias, G-6-PD enzymopathy of erythrocytes, microangiopathic hemolytic anemia
Target cells	Thalassemia, hemoglobinopathies, liver diseases, iron deficiency, post-splenectomy condition
Ovalocytes (ellipsocytes)	Hereditary ovalocytosis, megaloblastic anemia, iron deficiency, thalassemia, anemia during leukemia
Stomatocytes	Hereditary stomatocytosis - hemolytic anemia
Drepanocytes	Sickle cell anemia
Toothed erythrocytes	Uremia
Acanthocytes	Hereditary acanthocytosis (a form of hereditary hemolytic anemia), severe forms of liver diseases
Anulocytes	Hypochromic anemia
Schizocytes	DİC, uremia, hemolytic-uremic syndrome, hemolysis of erythrocytes by a mechanical and toxic factors
Droplet-like erythrocytes	Myeloproliferative diseases, myelofibrosis, thalassemia, iron deficiency, megaloblastic anemia
Bited erythrocytes	G-6-PD enzymopathy of erythrocytes

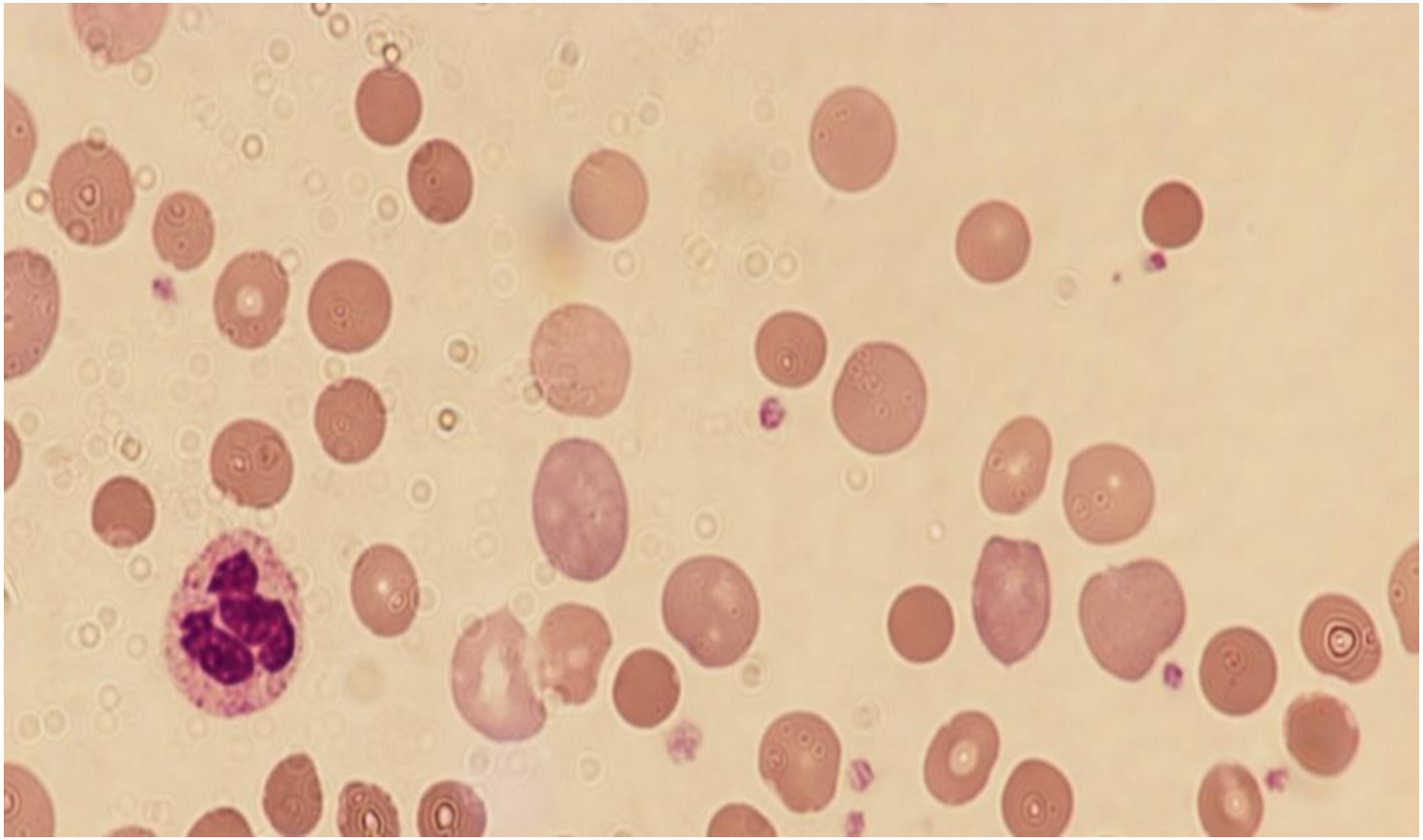
NORMAL PERIPHERAL SMEAR



the central space (pale area) is 1/3 of the total area

UPTODATE

Spherocytes, ovalocytes



Color characteristics of erythrocytes

Hypochromia-iron deficiency anemia, thalassemia, sideroblastic anemia, anemia of chronic diseases

Hyperchromia- megaloblastic anemia, spherocyitosis

Anisochromia – hereditary and aquired forms of anemia

Polychromatophilia - is more common in hereditary hemoglobinopathies

İntracellular inclusions

Jolly bodies	**Nuclear remnants are found in anemia caused by vitamin B12 and folic acid deficiency, as well as after splenectomy**
Kebot rings	Remnants of the nuclear membrane are found in B12 and folic acid deficiency anemia, polycythemia and heavy metal salt poisoning
Heinz bodies	Denatured Hb precipitates are detected during hemolytic crises in patients with hereditary deficiency of glucose-6-phosphate dehydrogenase
Basophilic granulation	Occurs during lead or heavy metal poisoning, thalassemia, alcohol intoxication, cytotoxic effect of drugs, severe anemia
Siderosis (iron granules)	An increase in their number is observed in hemolytic, sideroblastic anemia, splenectomy, lead poisoning, thalassemia

Anemias due to the regenerative capacity of the bone marrow

Hyperregenerative Reticulocytes >5-10%	**Regenerative Reticulocytes > 3%**	**Hypo-, aregenerative Reticulocytes <1%**
Acute posthemorrhagic anemia Hemolytic anemia (mainly acquired) Iron deficiency with bleeding Reticulocyte crisis during treatment of B12 and folate deficiency anemia	Iron deficiency anemia (early stage Anemia of chronic diseases (early stage) Thalassemia	Aplastic anemia Megaloblastic anemia Sideroblastic anemia Myelodysplastic syndromes

Classification of Anemia

I. ANEMIA DUE TO HEMORRHAGİA

• Acute post-hemorrhagic anemia

• Chronic posthemorrhagic anemia

II. ANEMIA DUE TO DISORDER OF ERYTHROPOESIS AND HEMOGLOBIN SYNTHESIS

A. Bone Marrow Insufficiency

•Aplastic anemia (total)

- Congenital (Fanconi anemia, Estrana-Dameshek anemia)
- Acquired (under the influence of infectious-toxic factors)

• Partial red cell aplasia

- Congenital (Blackfen-Diamond anemia)
- Acquired (Parvovirus B19 infection)

B. Pathology of Erythrocyte Maturation.

1. Anomaly of hemoglobin sintesis

• Iron deficiency anemia

• Sideroblastic (Sideroachrestic) anemia

- Congenital
- Acquired

• Anemia of chronic diseases

2. Anomaly of DNA and RNA sintesis

III. ANEMIAS ASSOCIATED WITH HEMOLYSIS OF ERYROCYTES

A. Hereditary Hemolytic Anemias

• Genetic defects of the erythrocyte membrane –membranopathies (Minkowski-Schoffard anemia, congenital ellipsocytosis (ovalocytosis), congenital stomatocytosis)

• Defects in enzyme systems of erythrocytes – enzymopathies (glucose-6-phosphate dehydrogenase deficiency)

• Structural defects of hemoglobin – hemoglobinopathies (sickle cell anemia, thalassemias)

B. Acquired Hemolytic Anemias

• Immune hemolytic anemias

- Isoimmune (incompatibility due to ABO or Rh factor
- Heteroimmune (infectious, toxic, medicinal)
- Autoimmune (associated with warm antibodies, cold agglutinins, cold hemolysins)

• **Mechanical Hemolytic Anemias**

- Thrombotic microangiopathic hemolytic anemias
- Damage to the valves of the heart and large vessels
- Hemoglobinuria during march and anemia of athletes

• **Paroxysmal nocturnal hemoglobinuria**

•**Drug-related hemolytic anemia**

• **Anemias associated with pathological activation of complement system**

• **Hemolytic anemia caused by toxins**

• **Hemolytic anemia caused by destruction of red blood cells by parasites**

• **Hypersplenism**

Acute posthemorrhagic anemia

In the first stage (1-2 days) - **thrombocytosis, leukocytosis,** and **shift to the left in the leukocytic formula** are observed.

The second stage (hemodilution) - there is no decrease in color index, because the number of RBCs and the amount of Hb decrease equally. **Normocytic and normochromic anemia** develops.

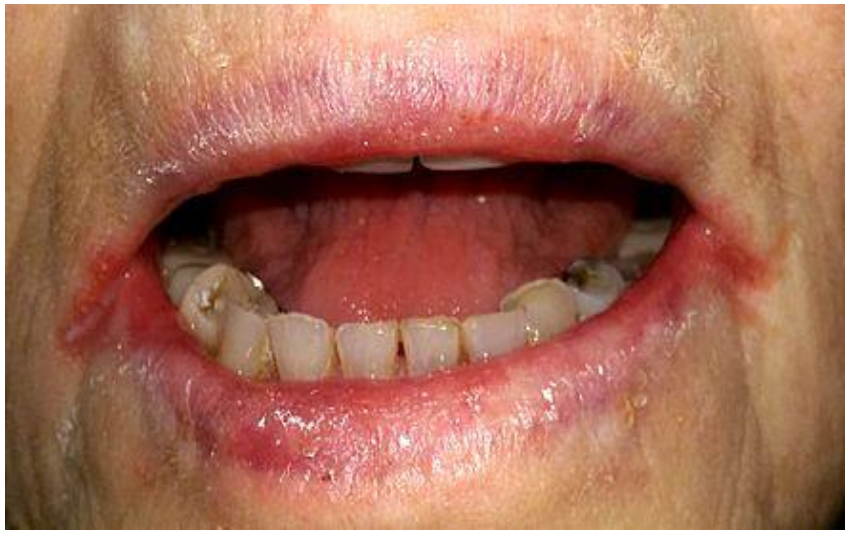
Third stage (after 3-5 days) **acute reticulocytosis** is observed. Polychromatophilic reticulocytosis and increased MCV may estimated as a hemolytic anemia which is a wrong diagnosis.

Iron Deficiency Anemia (IDA)

Causes of Iron Deficiency:

- alimentary factors
- malabsorbsion
- increased need in iron
- chronic blood loss (more frequently)

Clinical Symptoms:koilonychia, alopecia, angular gyrus, picasism, Plummer-Vinson syndrome, etc.

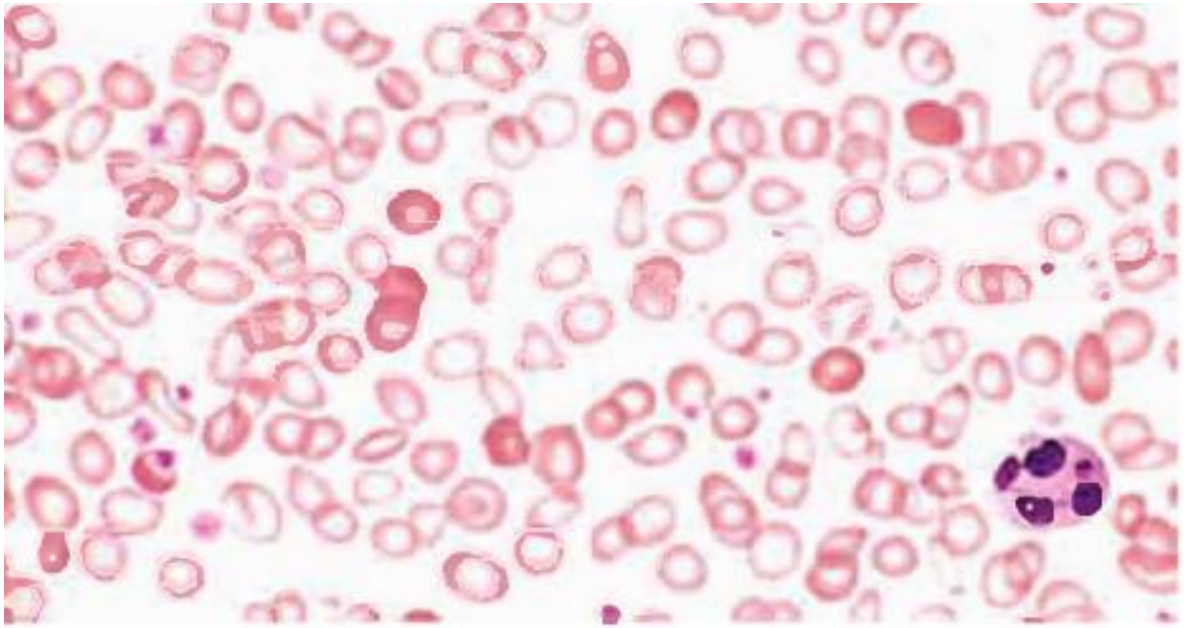


IDA

↓Iron→↓Heme→↓Hemoglobin→microcytic-hypochrom anemia

Changes in the blood:

- ✓decrease in the level of hemoglobin Hb <98 g/l
- ✓decreasing of hematocrit
- ✓moderate decreasing of erythrocytes (reduction of erythrocytes more than <2x1012/l is not characteristic of IDA)
- ✓reduction of erythrocyte indices: MCV, MCH, MCHC
- ✓microcytic-anisocytosis, increasing of RDW
- ✓reticulocytes are normal or slightly increased, their number decreases as the disease progresses (IDA is the hyporegenerative anemia)
- ✓leukocytes are normal, but there is a tendency towards leukopenia due to neutropenia (~10% of IDA)
- ✓platelets are normal, but there may be mild thrombocytosis with the development of IDA against the background of chronic blood loss
- ✓ESR is normal or increased (with a significant decrease in the number of erythrocytes)



Blood smear in IDA: hypochromia, microcytosis, annulocytes (ring-shaped), target-like erythrocytes, ovalocytes

The level of Iron in the biochemical analysis of blood

Serum Iron	1000 μg/L	The amount of iron in the blood
Serum ferritin	12-32μM/L	Reflects the level of ferritin in depots (in the liver and macrophages)
(TIBC) total iron binding capacity of serum	30-85 μM/L	It shows the amount of transferrin molecules in the blood
(LDBQ) latent iron binding capacity of serum		It is the amount of the part of transferrin that does not combine with iron
Transferrinin saturation by iron %	33%	Iron binding percentage (saturation degree) of the transferrin molecule

sTFR- soluble transferrin receptors

The amount of sTFR increases in IDA

The stages of development of İron deficiency:

1. Decreasing of iron in depots - ↓ferritin; ↑ TİBC
2. Decreasing of serum iron - ↓serum iron; ↓% saturation of transferrin
3. Bone marrow produces less, but normocytic (normocytic anemia in early stage) erythrocytes
4. Bone marrow produces less and microcytic erythtrocytes, ***microcytic, hypochrom anemia*** developes.

Decreasing of serum iron accompanies with decreasing of ***hepcidin*** sinthesis by liver.

Changes in biochemical analyses of blood in IDA :

- ✓ decreasing of serum ferritin level
- ✓ increasing of TIBC and LIBC
- ✓ decreasing of serum iron level
- ✓ decreasing of iron saturation % of transferrin
- ✓ increasing of serum sTFR level

Normalization of the serum ferritin level is the sign of successful treatment with iron preparations.

Anemia of Chronic Diseases – ACD

↓Iron Available for Hemopoiesis →↓Heme→↓Hemoqlobin→mikrositar -hipoxrom anemiya

Acute phase protein – ***hepcidin*** sinthesis increases in chronic diseases.

Hepcidin leads to:

- accumulation of iron in depots
- limitation of the transfer of iron from macrophages to erythroid cells
- inhibition of erythropoetin sintesis

Diagnostic criteria of ACD:

- ✓ decreased hemoglobin level (<80 g/l)
- ✓ increase in the level of serum ferritin, (it indicates an increase in the amount of iron in stores)
- ✓ serum iron levels are moderately reduces
- ✓ TIBC decreases, which indicates that there is no Fe-starvation in the body
- ✓ % saturation of transferrin decreases
- ✓ treatment with iron preparations is ineffective, whereas treatment with erythropoietin gives a positive result.

Sideroblastic (Sideroachrestic) Anemia

↓Protoporphirin→↓Heme→↓Hemoglobin→mikrocytic-hypochrom anemia

Due to hereditary or acquired reasons, erythroid cells can't assimilate iron needed for the synthesis of hemoglobin.

Changes in SA:

- ✓increasing of serum ferritin
- ✓significantly increasing of serum iron
- ✓ transferrin saturation % is high
- ✓ the amount of reticulocytes decreases and hyporegenerative anemia develops
- ✓along with hypochromic microcytic cells, normocytes and macrocytes are observed

The presence of normo- and macrocytes along with hypochromic-microcytic cells in the smear is a diagnostic sign of sideroblastic anemia.

Differentiation of Hypochromic Anemias

Indices	IDA	ACD	SA	Thalassemia
Serum Iron	Decreases	Decreases	Increases	Increases
TIBC	Increases	Decreases	Decreases	Decreases
Serum Ferritin	Decreases	Increases	Increases	Increases
Transferrin %	Decreases	Decreases	Increases	Increases
C-reactive protein	Normal	Increases	Normal	Normal
sTFR	Increases	Normal/Decreases	Decreases	Decreases
Erythrocyte morphology	Microcytosis	Norma/microcytosis	Dimorphism	Target cells

Megaloblastic anemias

↓VitaminB_{12}→↓FH4→↓DNA synthesis→megaloblastosis→
→ macrocytic -hyperchrom anemiya

- **Vitamin B_{12} deficiency anemia**
- **Pernicious anemia**
- **Folic acid deficiency anemia**

Vitamin B_{12} deficiency anemia

- ✓ **sharply decreasing of erythrocytes – 1,0 - 1,5x10^{12}/l**
- ✓ **MCV >100 fl**
- ✓ **MCH > 32 pg**
- ✓ **pancytopenia**
- ✓ **giant hypersegmented neutrophils**
- ✓ **decreasing of reticulocytes**
- ✓ **increased levels of homocysteine and methylmalonic acid**
- ✓ **decreasing of vitamin B_{12} level in serum**
- ✓ **glossitis**
- ✓ **neurological changes**

Pernicious Anemia *(megaloblastosis)*

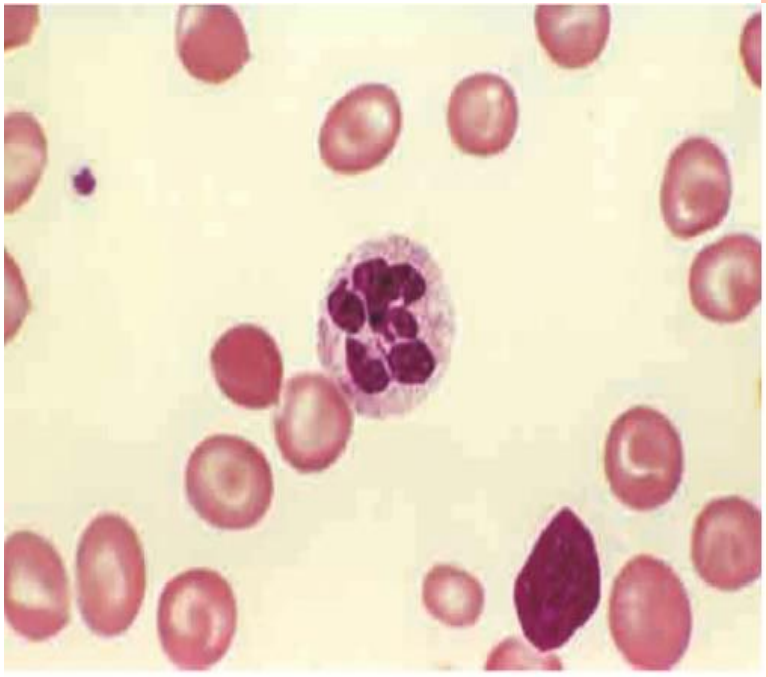
↓↓↓IF→↓vitaminB_{12}→↓FH4→↓DNAsynthesis→megaloblastosis→ macrocytic-hyperchrom anemia

- ✓ presence of antibodies against IF (intrinsic factor)
- ✓ presence of antibodies against parietal cells
- ✓moderate and severe signs of megaloblastosis
- ✓hypersegmented granulocytes on the background of leukopenia
- ✓pancytopenia
- ✓low serum vitamin B_{12} level
- ✓increasing of the homocysteine level
- ✓ increasing of the level of methylmalonic acid
- ✓glossitis
- ✓neurological changes

Folic Acid Deficiency Anemia *(megaloblastosis)*

↓FH4→↓DNAsynthesis→megaloblastosis→macrocytic-hyperchrom anemia

- ***increasing of serum homocysteine level***
- ***methylmalonate level is normal***
- ***neurological changes do not develop***



Blood smear in megaloblastic anemia

Aplastic Anemia (AA)

• genetic abnormality of stem cells (hereditary hypo-aplastic anemias)
•immunosuppression of bone marrow progenitor cells (acquired hypo- and aplastic anemias)

Hereditary forms
-Fanconi anemia (total-aplastic)
-Estren-Dameshek anemia (total-aplastic)
-Blackfen-Diamond anemia (partial-aplastic)
-Ehrlich syndrome (hypoplastic anemia)

Acquired forms
-True erythrocytic aplasia
-Parvovirus B19 infection

- ✓pancytopenia: erythro-, leuko-thrombocytopenia
- ✓hemoglobin concentration decreases to 20 - 30 g/l
- ✓the number of erythrocytes is $0.7\text{-}2.5x10^{12}/l$
- ✓persistent reticulocytopenia (reticulocytes <1%)
- ✓normochromia, macrocytosis, anisocytosis, poikilocytosis
- ✓serum iron level rises

Bone marrow biopsy is used to diff. **AA** from *aleukemic leukemia* and *MDS*
In aplastic anemia, the lack of cells in the bone marrow is very high.
During myeloid neoplasia, the bone marrow is rich in neoplastic cells.

Hemolytic Anemia

Extra/vas hemolysis	İntra/vas hemolysis
anemia, unconjugated hyper-bilirubinemia, jaundice, splenomegaly, cholelitiasis, reticulositosis	anemia, jaundice, hemoglobinemia, hemoglobinuria, hemosiderinuria, reticulositosis, ↓haptoglobin

Thalassemia (hypochrom microcytic anemia)

↓α-globin chains →↓hemoglobin→microcytic hypochromic anemia→α-thalassemia

↓β-globin chains →↓hemoglobin→microcytic hypochromic anemia→β-thalassemia

HbA or HbA_1 (ααββ) - 96%
HbA_2 (ααδδ) - ≤ 3%
HbF (ααγγ) - ≤1%(hemoglobin of fetus)

İn α-thalassemia:
HbBart-(γγγγ) in newborns
HbH (ββββ) in adults
In β-thalassemia:
HbA_2 (ααδδ) - ≥3%

α-thalassemia

"silent" thalassemia (α-thalassemia minimal)
1 α-globin gene deleted
Asymptomatic. Slight microcytosis.

α-thalassemia minor
2 α-globin genes deleted. Mild anemia with microcytosis.
Hb Electrophoresis shows HbH , HbA_2 in norma

H-Hemoglobinopathy (α-thalassemia intermedia)
3 α-globin genes deleted , severe anemia, microcytosis,
HbH (40%) damages RBC→ extra/vas. hemolysis→
→splenomeqaliya

Hydrops fetalis (α-talassemia major) 4 α-globin genes deleted,
lethal in utero. *HbBarts more than* 90% . *HbF-is absent.*

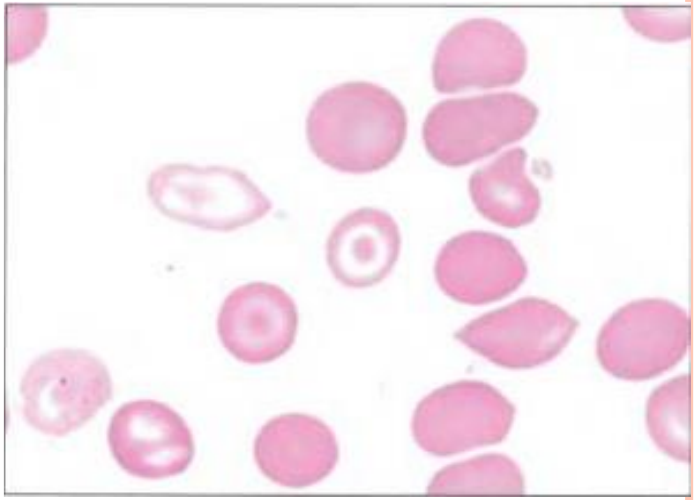
If Bart's syndrome is detected during **prenatal diagnosis** the pregnancy is terminated with the consent of the mother.

β-thalassemia

β-thalassemia minor (β/β+,β/β°) is the mildest form of the disease and usually has an asymptomatic course with an mildly increased RBC count.
Microcytosis, hypochromia target-like cells in blood smear.
Hemoglobin electrophoresis shows slightly decreased HbA, with increased HbA2 -5% (normally 2.5%) and HbF -2% (normally 1%)

β-thalassemia major (β°/β°, β+/β+ or β+/β° genotypes).
The amount of HbA2 and HbF-increases, little or no HbA

Blood smear shows target cells, microcytosis, hypochromia, sometimes nucleated erythrocytes. Ineffective erythropoiesis, reticulocytosis, splenohepatomegaly, hemasiderosis, hemochromatosis. Elevation of HbA2 and HbF is determined in hemoglobin electrophoresis. HbA is low or absent.



Prenatal diagnosis is carried out in the 16-18 weeks of pregnancy. Amniocentesis and genetic testing are performed.

Sickle Cell Anemia

Glutamic acid→Valine → HbS-$\alpha_2\beta^s{}_2$

In homozygous , more than 90% of Hb consists of HbS-$\alpha_2\beta^s{}_2$

Main manifestations:

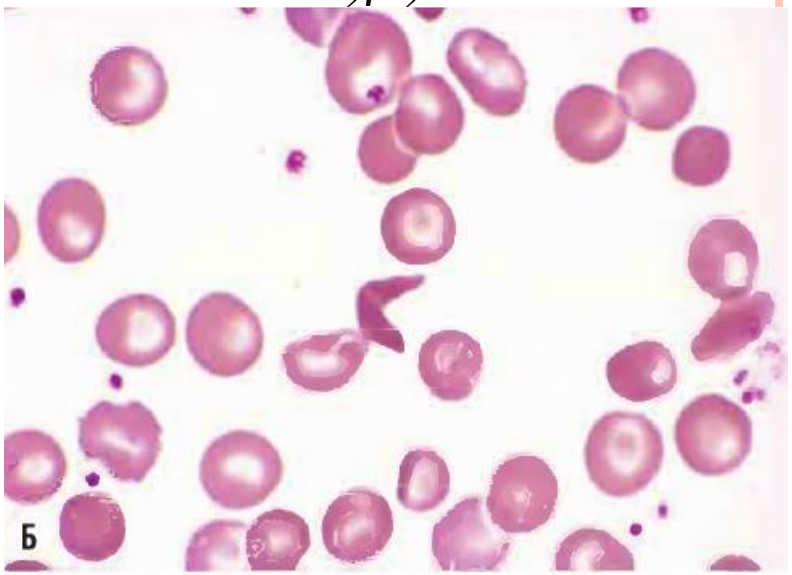
-chronic extravascular hemolysis

-occlusion of microvessels-tissue ischemia

-deformation of the bones of the skull

-splenic infarction – autosplenectomy

-pain crises, acute chest syndrome – pulmonary injury



Laboratory findings:

-Sickle-cells and target cells are detected in the blood smear.

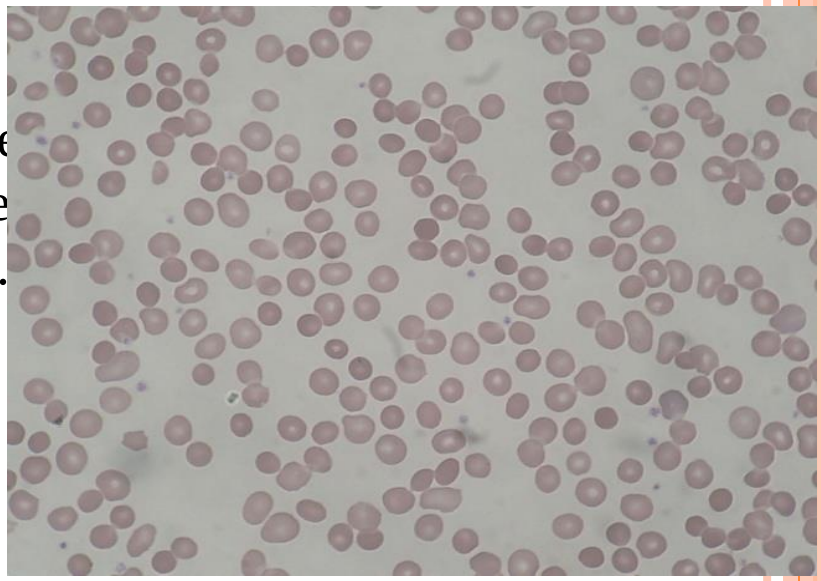
-Metabisulfite test causes sickling even in the presence of any small amount of HbS, the test is positive in both patients and carriers.

- Hb electrophoresis confirms HbS and its quantity.

- In patients (homozygotes) - 90% HbS, 8% HbF, 2% HbA2 (no HbA)

-In carriers (heterozygotes) - 55% HbA, 43% HbS, 2% HbA2

Hereditary Spherocytosis -hereditary membranopathy
(Minkowski-Shoffar disease)



Associated with mutation of membrane cytoskele
proteins as ankyrin, band3, spectrin, band 4.2 ,e
In 20-30% of cases, the disease is asymptomatic.
In moderate and severe forms occurs
with aplastic and hemolytic crises.

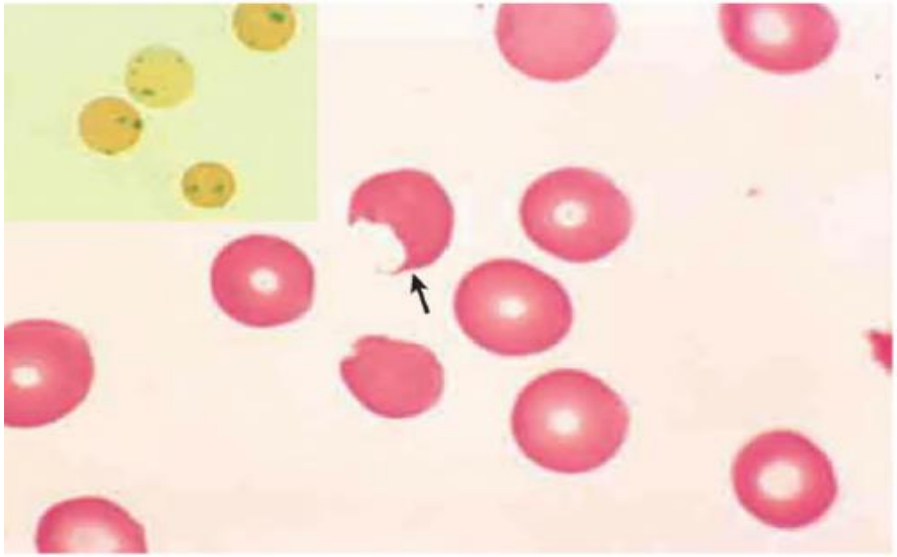
Diagnosis is based on anamnesis, hematological and laboratory tests:
-RBC decreases, MHC increases, hyperchromia is observed.
-in peripheral blood smear: spherocytosis, narrowing of central pale area, reticulocytosis are observed.
Erythroid hyperplasia of the bone marrow , splenomegaly, hemosiderosis, jaundice, cholelithiasis are characteristic.

Hemolytic anemia associated with **G-6PD deficiency**

Cases of episodic hemolysis occur due to the effect of oxidants:
- infections (viral hepatitis, pneumonia and typhus)
- drugs (antimalarials, sulfonamides)
- nutrients - horse bean (Vicia faba-favism)

Intravascular and extravascular hemolysis occurs.

Blood smear: Heinz bodies, "bitten" erythrocytes, spherocytes
Hb and RBS decrease,
Hemoglobinemia, hemoglobinuria, reticulocytosis are characteristic.
Splenomegaly, cholelithiasis are not characteristic.



Immune hemolytic anemias (İHA)

Antibody- mediated (IgG or IgM) hemolyses of the erythrocytes.

Formation of antibodies may be:

- ✓ primary – idiopathic (unknown cause)
- ✓ secondary – autoimmune cause (systemic lupus erythematosis SLE, collagenoses), chronic lymphocytic leukemia –CLL, drugs (penicillin, α-methyldopa), toxin, viral infection, etc.

Depending on etiological factor:

- ✓ isoimmune (hemolytic anemia of the newborn)
- ✓ autoimmune (idiopathic and symptomatic)
- ✓ heteroimmune (drugs , infections, ect).

Usually

IgG-mediated reactions cause extravascular

IgM-mediated reactions cause intravascular hemolysis.

Coombs tests are used for diagnosis of İHA:

Direct Coombs test confirms the presence of antibody or complement-coated RBCs. When anti-IgG/complement is added to patient RBCs, agglutination occurs .

Indirect Coombs test confirms the presence of antibodies in patient serum. Test RBCs are mixed with the patient serum; agglutination occurs if serum antibodies are present.

Hemolytic disease of the newborn (isoimmune hemolytic anemia)

Rh factor incompatibility of maternal and fetal blood

Prenatal and postnatal diagnostics are available.

In prenatal diagnosis

- antigen incompatibility of parents, previous abortions and the birth of sick children are studie
- during pregnancy, the *titer of anti-Rhesus antibodies* is determined
- in amniotic fluid bilirubin, protein, glucose, iron, Ig, etc.is determined

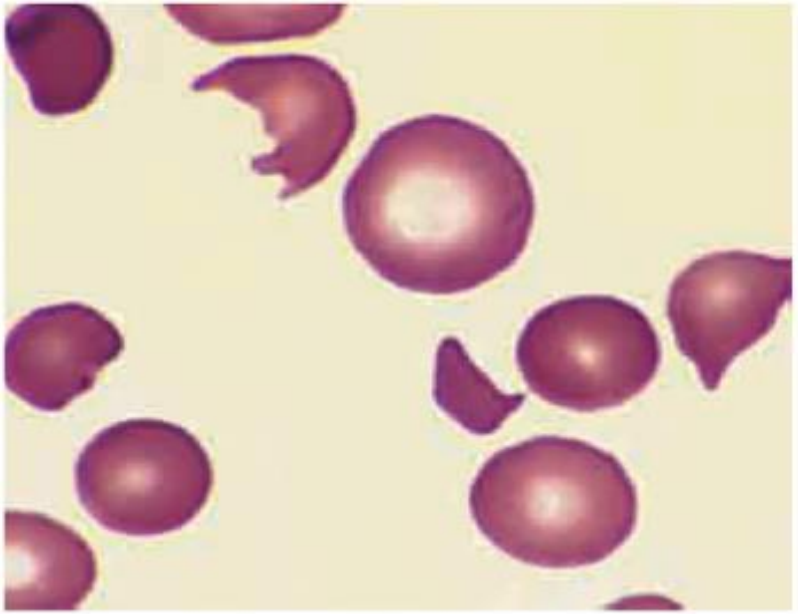
In the ultrasound examination, thickening of the placenta, edema,hepatosplenomegaly indicates hemolytic disease.

Postnatal diagnosis is based on clinical manifestations that appear after birth:

- anemia, jaundice, hepatosplenomegaly
- increasing of unconjugated bilirubin
- erythroblastosis, reticulocytosis
- positive Coombs tests are detected

Mechanical hemolysis

- ✓ artificial heart valves
- ✓ long march
- ✓ microangiopathies (DIC, TTP, HUS, SLE, tumors)



In blood smear:

severe poikilositosis – shistocytes, spiny, helmet-like, triangular-shaped erythrocytes is characteristic.

Paroxysmal nocturnal hemoglobinuria

PIGA gene acquired mutation disturbs
PIG (phosphatodyl inositol glycan) synthesis.
PIG (in norm) fixes complement-inactivating proteins on the RBC membrane.
PIG deficiency leads to inadequate activation of complement
and complement-dependent *intravascular hemolysis* occurs.

Erythrocytes with a deficiency of PIG-related proteins
detected by flow cytometry method.