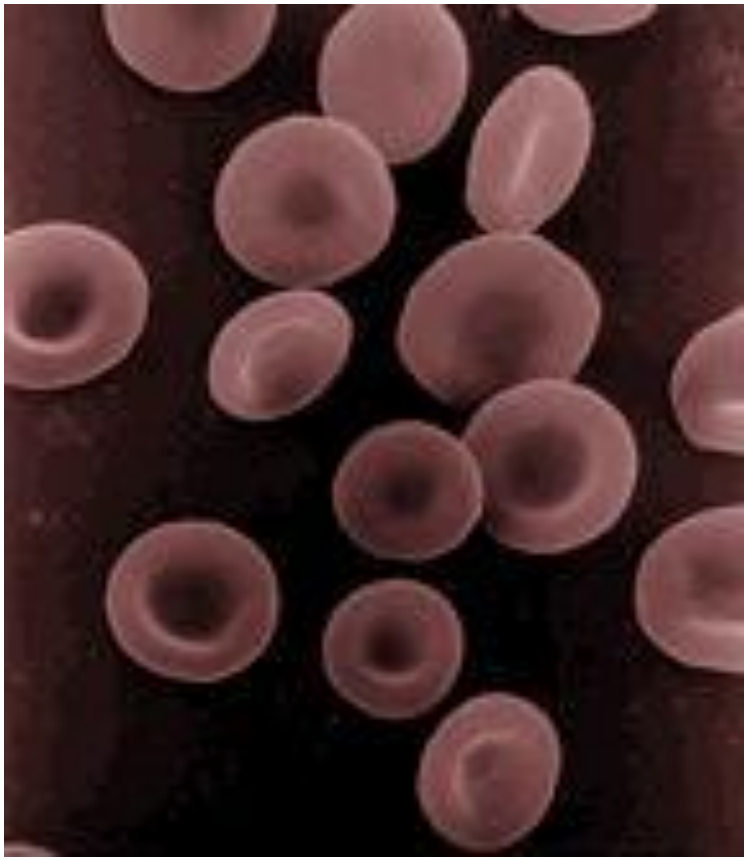
Red blood cells pathology



Lecture Plan

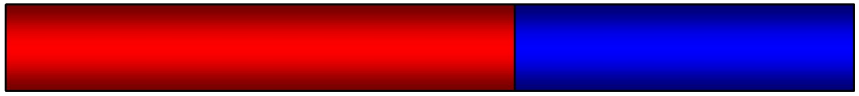
- Blood volume changes
- Anemia classifications
- Clinical features and specific signs of anemias
- Erythrocytosis (Polycytemia)

Hypervolemia

normal correlation

simple hypervolemia

transfusion of blood large doses; during intensive physical work



polycytemic hypervolemia

Vaquez' disease , hypoxia

olygocytemic hypervolemia

diseases of kidneys; disturbances of water-electrolyte balance

Hypovolemia

normal correlation

simple hypovolemia

immediately after acute blood loss

polycytemic hypovolemia

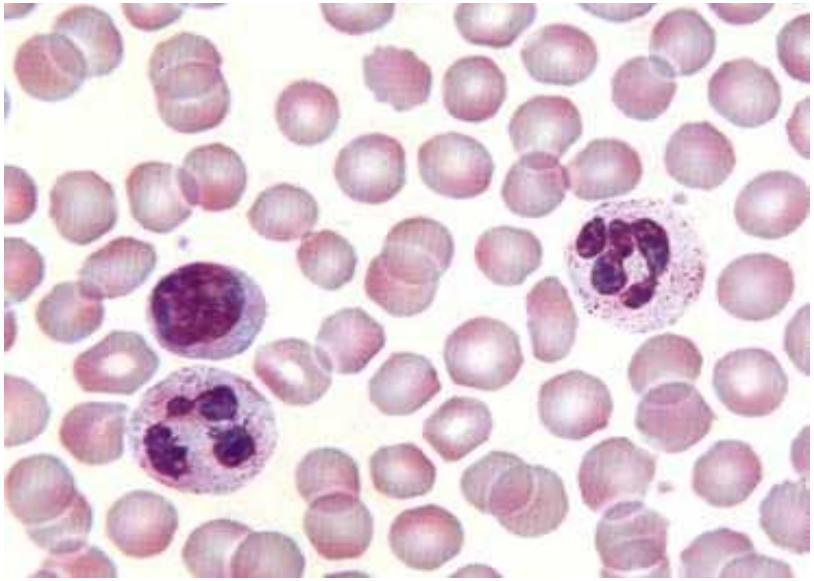
dehydration (diarrhoea, vomiting, abundant sweating, burns, overheating), shock

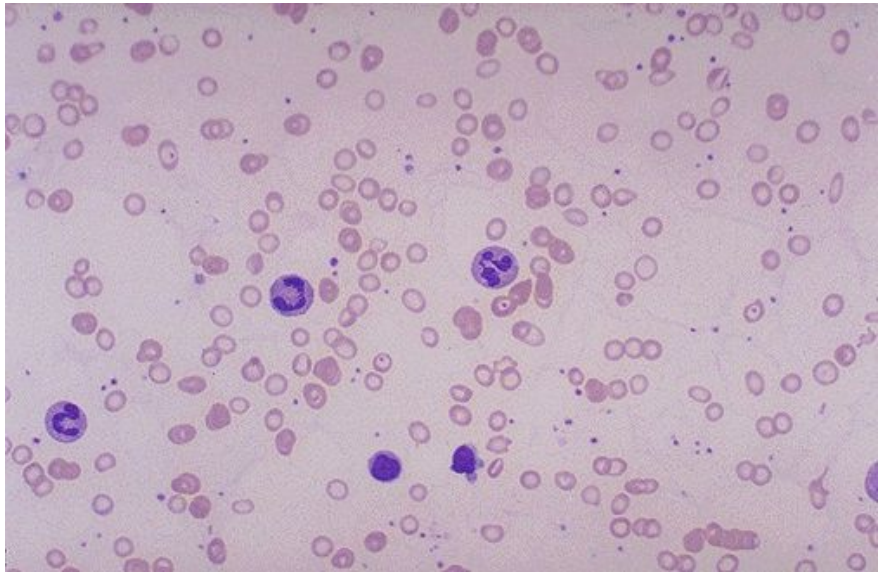
olygocytemic hypovolemia

in the second stage of acute blood loss; severe anemias

Anemia

Anemia is a lack of red blood cells and/or hemoglobin. This results in a hypoxia





Anemia classifications

Pathogenic classification.

- Posthemorrhagic (acute or chronic).
- Haemolytic - acute and chronic. Chronic haemolytic anaemias can be inherited and acquired.
- Anemias caused by disturbances of hemopoiesis:
  - deficiency of iron, proteins; vitamin B12, folic acid;
  - hypoplastic and aplastic anaemias;
  - metaplastic anaemia;
  - disregulatory anemia.

Anemia classifications

Classification due to haemoglobin content in RBC.

Normally haemoglobin content in erythrocyte is 0,8—1,05. This index is named color index (CI).

- **hyperchromic** – CI > 1,05 (B12 and pholate-deficiency)
- **hypochromic** – CI < 0,8 (iron deficiency)
- **normochromic** – CI is normal (inherited haemolytic anaemias)

Classification based on the degree of regeneration.

Normally reticulocytes constitute 0.5 to 1.5% of the RBC.

- **regenerative** - normal reticulocytes count (most of anemias)
- **hyporegenerative** - reticulocytes <0.5 (chronic posthemorrhagic)
- **non-regenerative anemia** - reticulocytes are absent (bone marrow aplasia)
- hyperregenerative - reticulocytes >1,5 (inherited hemolytic anemias)

Anemia classifications

Classification based on the on the type of RBC maturation.

- **erythroblastic** anemias
- **megaloblastic** anemias (B12 vitamin, folic acid deficiency)

Classification based on the on the size of RBC.

The size of RBC refers to **mean corpuscular volume** (MCV).

- microcytic anemia - MCV is under 80 (iron deficiency)
- normocytic - MCV (80-100) acute posthemorrhagic
- macrocytic – MCV is over 100 (B12 vitamin, folic acid deficiency)

Clinical features of anemia

- olygocythemic normovolemia (in most anemias);
- hypovolemia (acute posthemorrhagic anaemia, pernicious anaemia);
- paleness of skin and visible mucous membranes;
- decreased ability to work;
- CNS: the lowering of mental ability to work, the decline of memory, insomnia, fatigueability, dizziness, noise in ears, head aches, attacks of faintness;

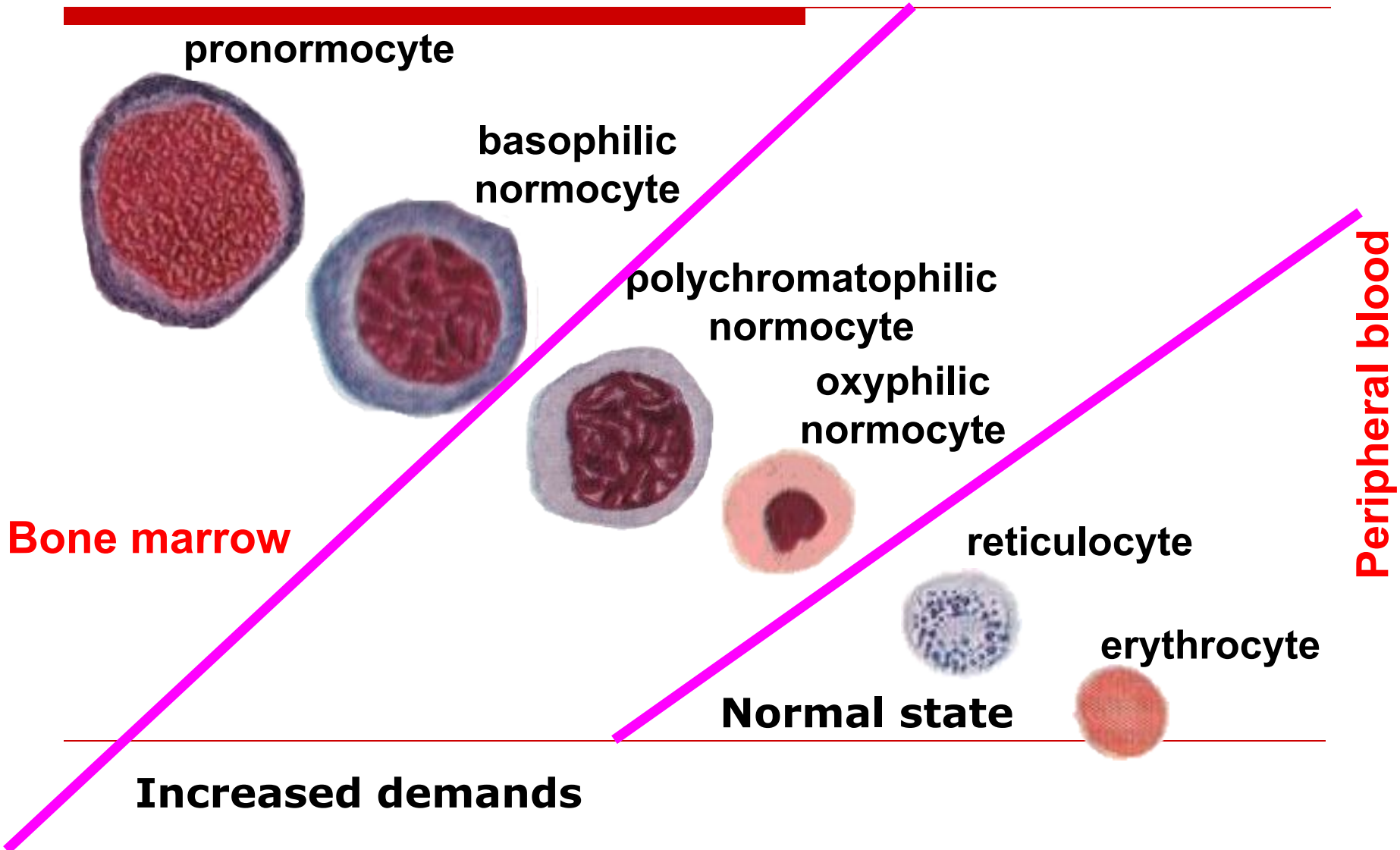
Clinical features of anemia

- Decreased function of endocrine organs (especially thyroid gland);
- GIT: anorexia, flatulence, nausea, constipation and weight loss may also occur.
- Heart and lungs: tachycardia, systolic murmur, dyspnoe in exertion. In eldery people heart failure can develop.

Specific signs of anemias

- Posthemorrhagic anaemia – signs of blood loss from different organs;
- Iron deficiency - perversion of taste, trophic disorders of skin, often gastric achylia;
- Chronic anaemia with marked hypoxia -drumstick fingers with spoon-shaped nails;
- Haemolytic anaemia – jaundice.

Regenerative forms of RBC



Degenerative forms of RBC

Poikilocytosis – abnormal variation in shape

acantocyte

target cell

ovalocyte

stomatocyte

sickle cell

Anisocytosis – abnormal variation in size

schistocyte 2-3 µ

microcyte 5-6 µ

normocyte 7-8 µ

macrocyte 8-12 µ

megalocyte >12 µ

Degenerative forms of RBC

Abnormalities in Hb content – coloring

hypochromic

normochromic

hyperchromic

RBC containing different pathological inclusions

Howell-Jolly bodies

Kebot rings

Heinz bodies

Anemia of blood loss

The main reasons of blood loss:

- blood vessels or heart walls safety loss (incision, rupture, tumor growth, aneurysm)
- increased vessels permeability (radiation sickness, leukemia, sepsis, vitamin C deficiency)
- decreased blood coagulation (coagulation factors deficiency).

Acute posthemorrhagic anemia

- 1st stage – heart rate and blood vessel tonus are increased, centralization of bloodflow, normocytic hypovolemia. First hours after blood loss.
- 2nd stage (hydremic) – increased tissue fluids outflow to blood stream, olygocytemic normovolaemia (or hypovolaemia). 1-5 day after blood loss.
- 3rd stage – activation of erythropoiesis and liver function, high reticulocyte count . 6 – 10 day after acute blood loss .

Principles of blood loss therapy

- Etiologic treatment: the increasing of blood coagulation, the reconstruction of vessel or heart walls.
- Pathogenic treatment: the transfusion of blood, native or synthetic plasma (the normalizing of blood volume), the infusion of proteins and ions.
- Symptomatic therapy: normalization of respiration, heart work, liver and kidneys function.

Chronic posthemorrhagic anaemia

- RBC number and Hb content is decreased
- Hypochromic (colour index is 0,6-0,4)
- This anaemia is hyporegenerative.
- Degenerative forms: hypochromic erythrocytes, poikilocytosis, anisocytosis with microcytes
- WBC - leukopenia, neutropenia and relative lymphocytosis
- Bone marrow: process of RBCs saturation with haemoglobin is violated, the decrease of erythroblasts maturation

Chronic posthemorrhagic anaemia

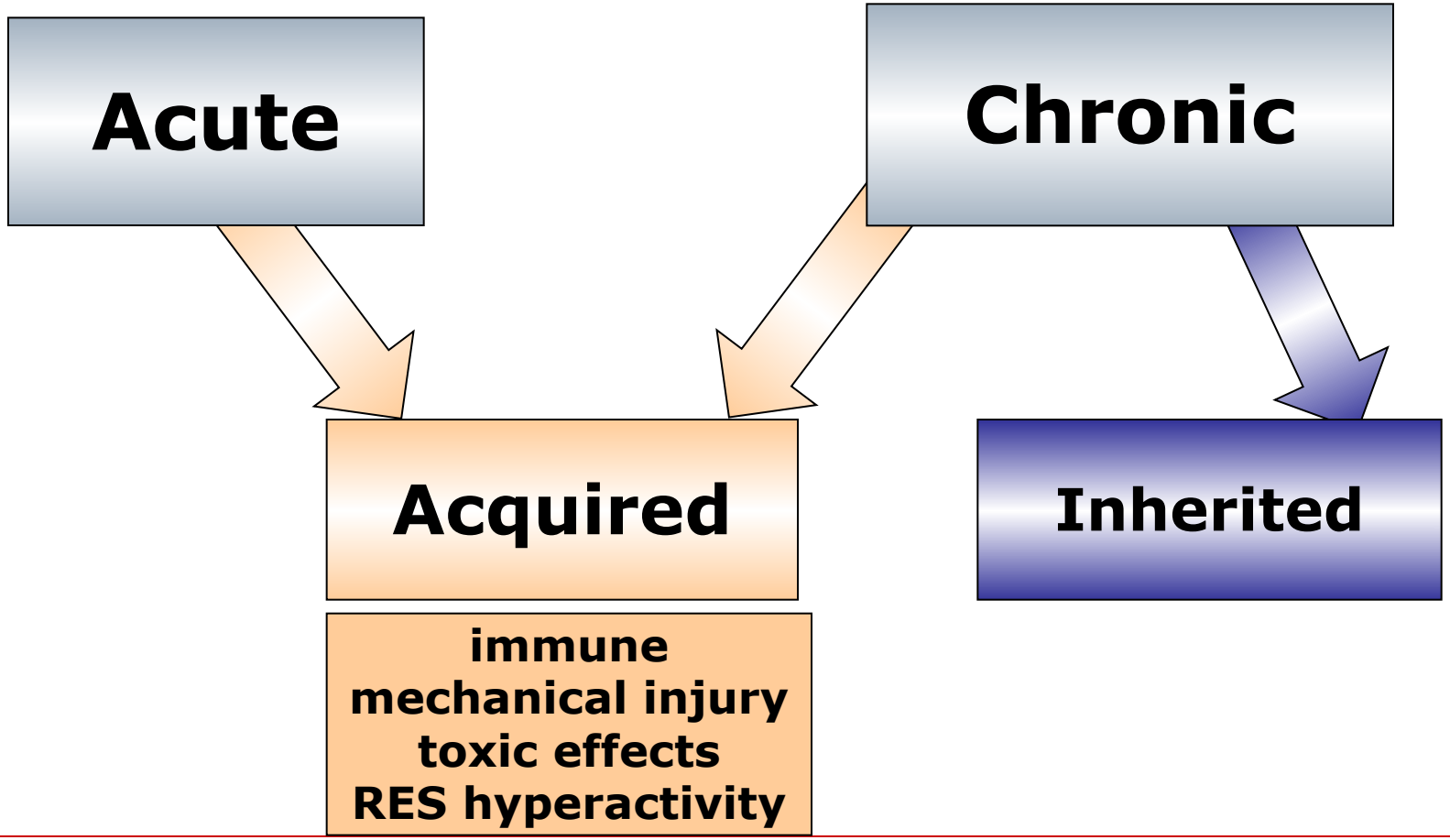
- Regeneratory stage: Hb, RBC, colour index are lower that normal. Its duration depends on the intensity of blood loss and regenerative ability of the bone marrow.
- Hyporegenerative stage: Hb and RBC lower than in 1st stage. Colour index < 0,5. Microcytes prevail. The level of serum iron is low.
- Non-regenerative stage (marrow exhaustion): Reticulocytes are absent.

Hemolytic Anemias

Types of hemolysis

- **Extravascular** (common) – occurs in phagocytic cells of the spleen, liver, and bone marrow.
- **Intravascular** (rare) – RBC undergo lysis in the circulation and release their content into plasma. Hemoglobinemia, hemoglobinuria.

Hemolytic Anemias Classification



Acquired hemolytic anemias

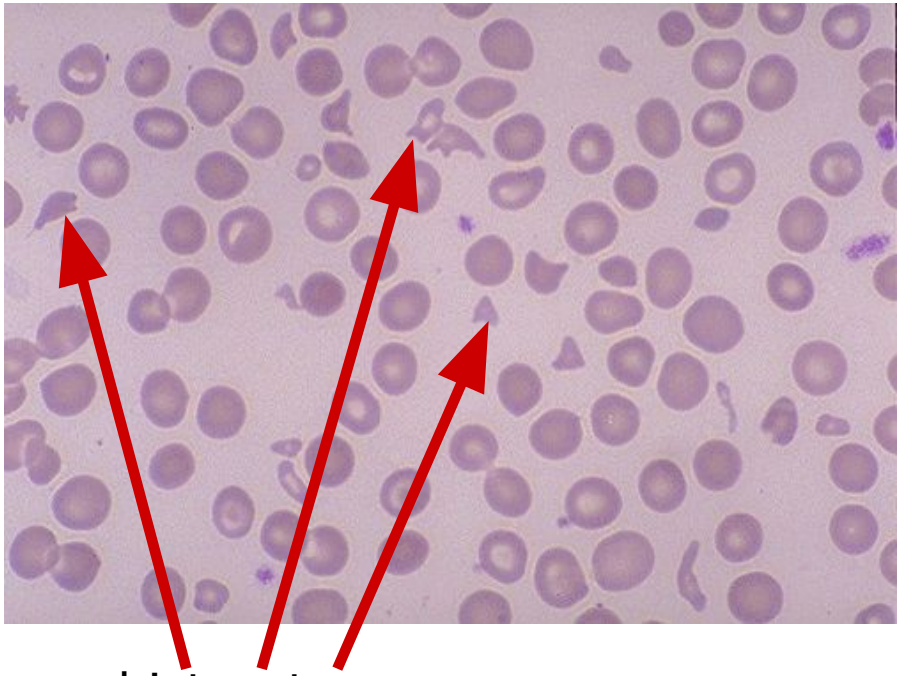
Immune abnormalities due to antibodies production:

- against own undamaged RBC (autoimmune hemolytic anemia);
- against RBC which membrane structure was changed as a result of drugs taking (sulfonamides, penicilline);
- when antibodies are acquired by blood transfusions, pregnancies and hemolytic disease of the newborns (isoimmune haemolytic anemia).

Acquired hemolytic anemias

Mechanical injury of RBC due to abnormalities of microcirculation.

- during high physical activity – prolonged marchers, joggers. March hemoglobinuria.
- patients with prosthetic cardiac valves or artificial grafts.



schistocytes

Microangiopathic hemolytic anemia

Acquired hemolytic anemias

Direct toxic effect

- Infectious agents toxic effect (α- or β-hemolytic streptococci, meningococci)
- Invasion of infectious agent and destruction of the RBC by the organism (*Plasmodium* malaria).
- Non-infectious agents – copper , lead, snakes and spiders venoms, extensive burns.

Increased reticuloendothelial activity

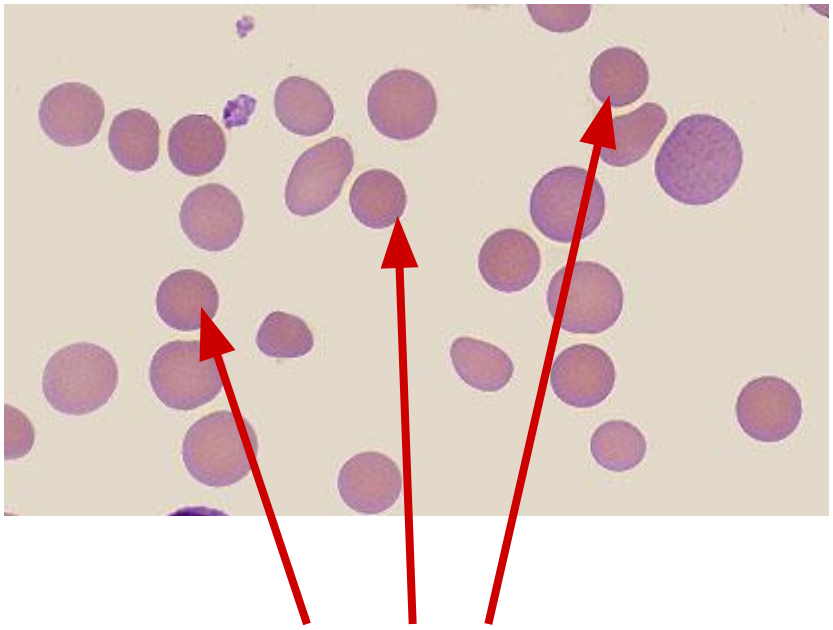
- Splenomegaly (enlargement of spleen).

Hereditary hemolytic anemias

Pathology of RBC membrane

Hereditary spherocytosis

- autosomal dominant disease
- defects in erythrocyte membrane proteins (spectrin, ankyrin) synthesis
- abnormally shaped red cells (which are typically older) are destroyed by the spleen



Spherocytes

(small, without central pallor zone)

Hereditary hemolytic anemias

Pathology of RBC enzymes

Glucose-6-phosphate dehydrogenase deficiency.

- X-linked recessive
- G6PD is necessary for glutathione synthesis, which is an antioxidant, destroying peroxides.
- Oxidative stress is possible in severe infection, some medicines (sulfonamides, primaquine (an antimalarial), glibenclamide) and certain foods.
- Oxidation and precipitation of Hb within RBC (Heinz bodies) occur in G6PD deficiency.
- **Favism –** hemolytic anemia as a result of broad beans consumption

Hereditary hemolytic anemias

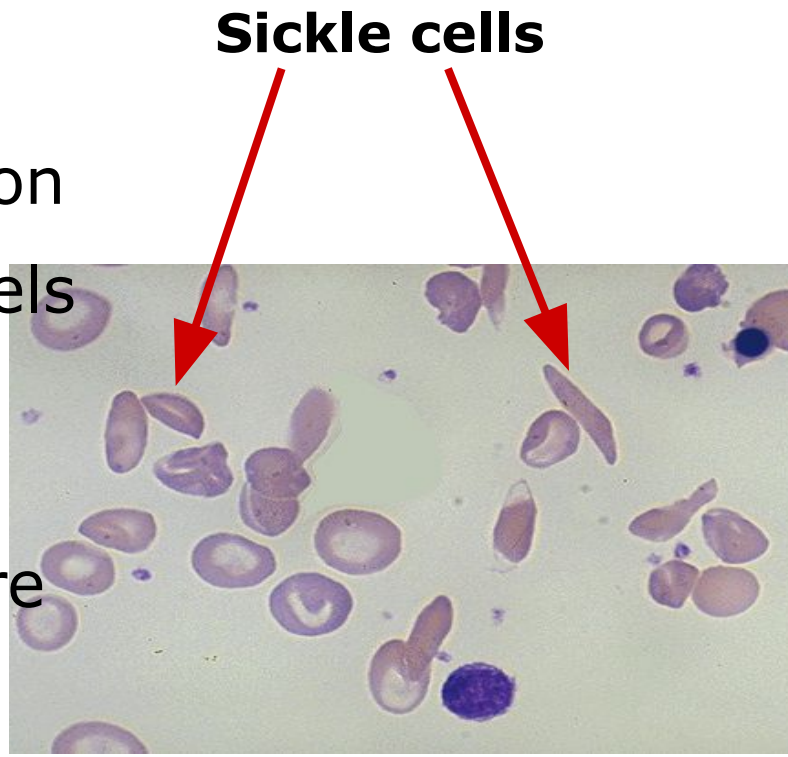
Pathology of haemoglobin

- **Sickle cell disease** is a qualitative disorder of Hb (abnormal Hb is synthesized)
- **Thalassemia** is a quantitative disorder (abnormal quantity of Hb chains)

Normally RBC contain Hb A which consist of 2 alfa and 2 beta chains (α2β2)

Sickle cells disease

- substitution of valine for glutamic acid in HbA turns it to HbS
- HbS is polymerized and RBC turn sickle cells in during deoxygenation
- RBC become stuck in blood vessels
- This causes ischemia and infarction.
- The consequences of infarction are determined by their location.

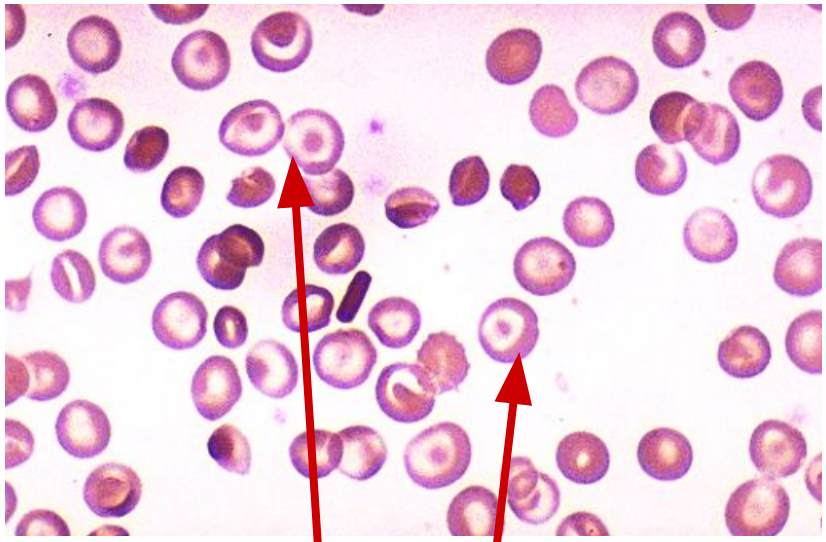


Thalassemia classification

- **α thalassemia**, the production of α globin is deficient
- **β thalassemia** the production of β globin is defective.
- The heterozygous form manifests as **thalassemia minor** - asymptomatic or mildly symptomatic.
- The homozygous form – **thalassemia major** – severe hemolytic anemia.
  - Beta thalassemia major is also known as **Cooley's Anemia**.

Thalassemia

- deficiency in the production of one globin chains type lead to excess production of other globin chains.
- Excessive globin chains are precipitated within the RBC (target-type RBC).
- Enlargement of liver and spleen, excess of tissue iron stores.



target cells

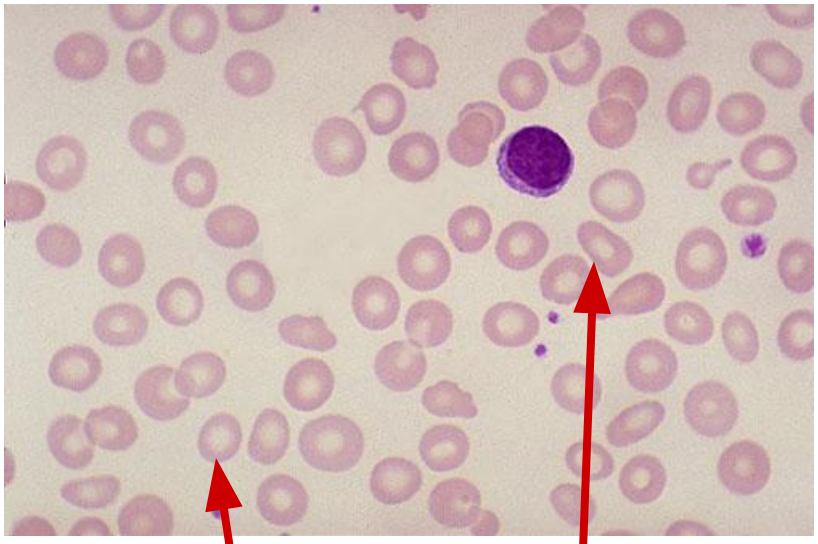
Anemias caused by disturbances of haemopoiesis

Iron deficiency reasons:

- chronic blood losses due to - excessive menstruations, other bleedings;
- increased iron requirements (pregnancy, lactation, spurts of growth in infancy, childhood and adolescence);
- inadequate dietary intake;
- insufficient absorption (achlorhydria, partial or total gastrectomy, intestinal malabsorbtion).

Anemias caused by disturbances of haemopoiesis

- nails (koilonychia or spoon-shaped nails),
- tongue (atrophic glossitis)
- mouth (angular stomatitis).
- low colour index and RBC number.
- low blood serum iron
- treatment with iron medicines.



Microcytes **poikylocytes**

Anemias caused by disturbances of haemopoiesis

Syderoblastic anemia (refractory to iron)

- defect enzymes that include iron to hemoglobin.
  - inherited
  - acquired (lead intoxication).
- Level of plasma iron is high.
- Bone marrow: erythroblasts with increased iron content are observed (syderoblasts).

Anemias caused by disturbances of haemopoiesis

Megaloblastic anaemia

- deficiency of vitamin B12 and folic acid.
- impaired DNA synthesis and abnormalities in haemopoiesis.
- cells synthesize much more RNA than normal and much less DNA.
- megaloblastic type of erythropoiesis
- leucopenia and thrombocytopenia
- megalocytes average life of 40 days.

Megaloblastic anemia

The reasons of **B12 deficiency**:

- inadequate dietary intake (strict vegetarians)
- inadequate production of intrinsic factor (pernicious anemia, congenital lack)
- malabsorption (disorders in absorption)

The reasons of **folate deficiency**:

- inadequate dietary intake (teenagers, infants, old age, alcoholics)
- malabsorption (coeliac disease, partial gastrectomy)
- excess demand (pregnancy, lactation, infancy, malignant tumors).

Vitamin B12 metabolism

combines with intrinsic factor

transport by transcobalamin

absorption

regeneration of GIT epithelium

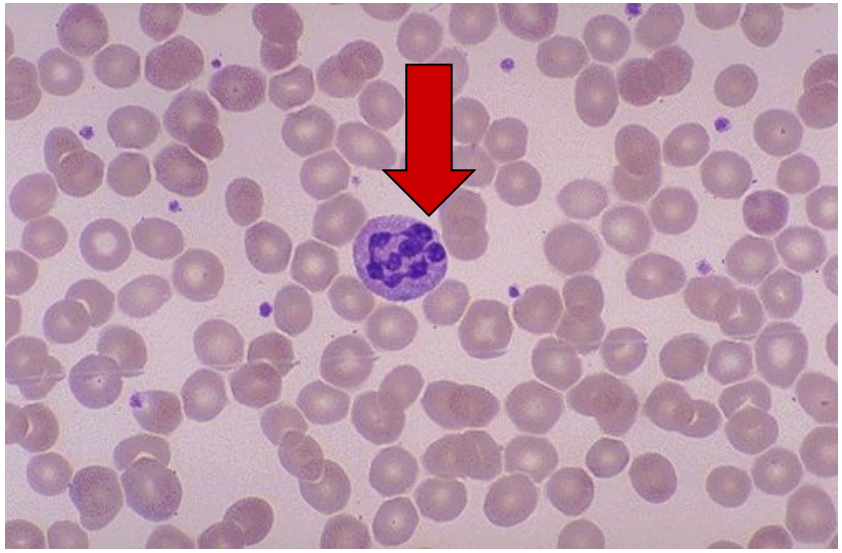
myelination of nervous fibers

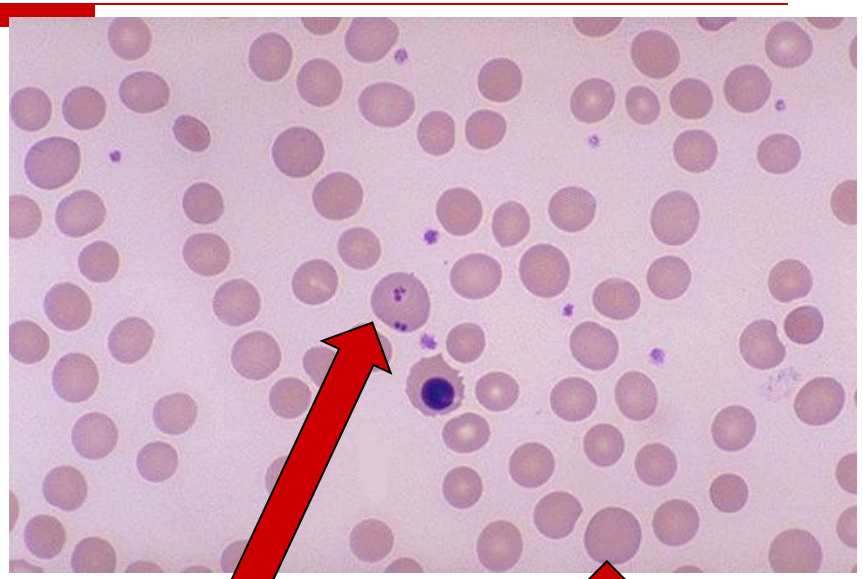
haemopoiesis

Megaloblastic anemia

hyperchromic, macrocytic, hyporegenerative

hypersegmented neutrophil





RBC with Howell Jolly bodies

Megalocyte

Megaloblastic anemia

Specific clinical features of megaloblastic anemia:

- glossitis (inflammation of the tongue; smooth, beefy, red tongue),
- mild jaundice,
- symptoms of malabsorption,
- weight loss and anorexia.
- neurological signs - numbness or tingling of the extremities and an ataxic gait (only B12 deficiency)

Pernicious anemia (Addyson anemia) develops due to autoantibodies against intrinsic factor or parietal cells which produce intrinsic factor.

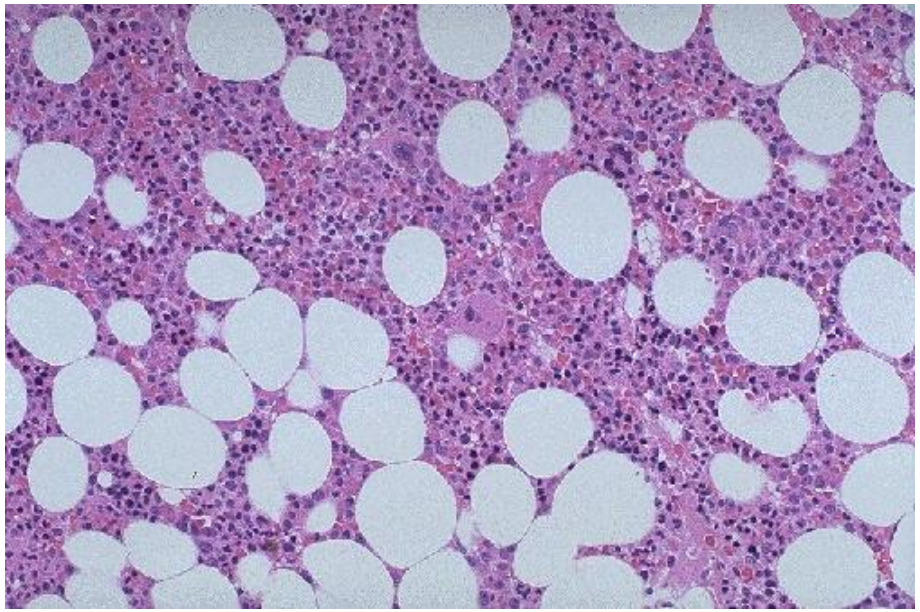
Anemias caused by disturbances of haemopoiesis

Hypoplastic and aplastic anaemias etiology:

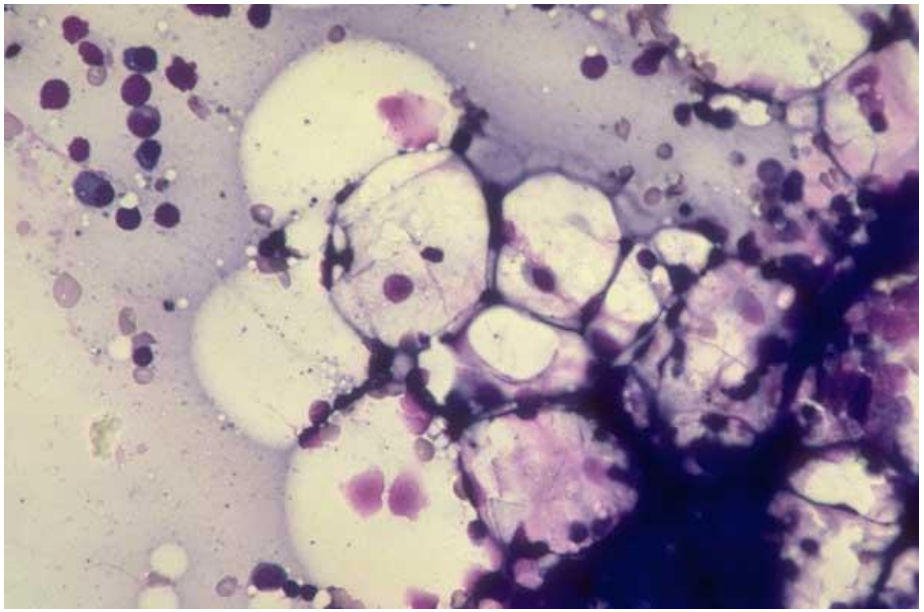
- medicines with myelotoxic effect (amidopyrine, sulfanilamides, cytostatic chemicals, antibiotics);
- autoimmune reactions in bone marrow;
- chemical substances: benzol, petrol, mercury ;
- radiant energy;
- different infections: sepsis, flu.

Anemias caused by disturbances of haemopoiesis

The picture of blood – pancytopenia – decrease of all blood cells. Regenerative forms of blood cells are absent.



normal marrow



aplastic anemia

Anemias caused by disturbances of haemopoiesis

Metaplastic anaemias etiology:

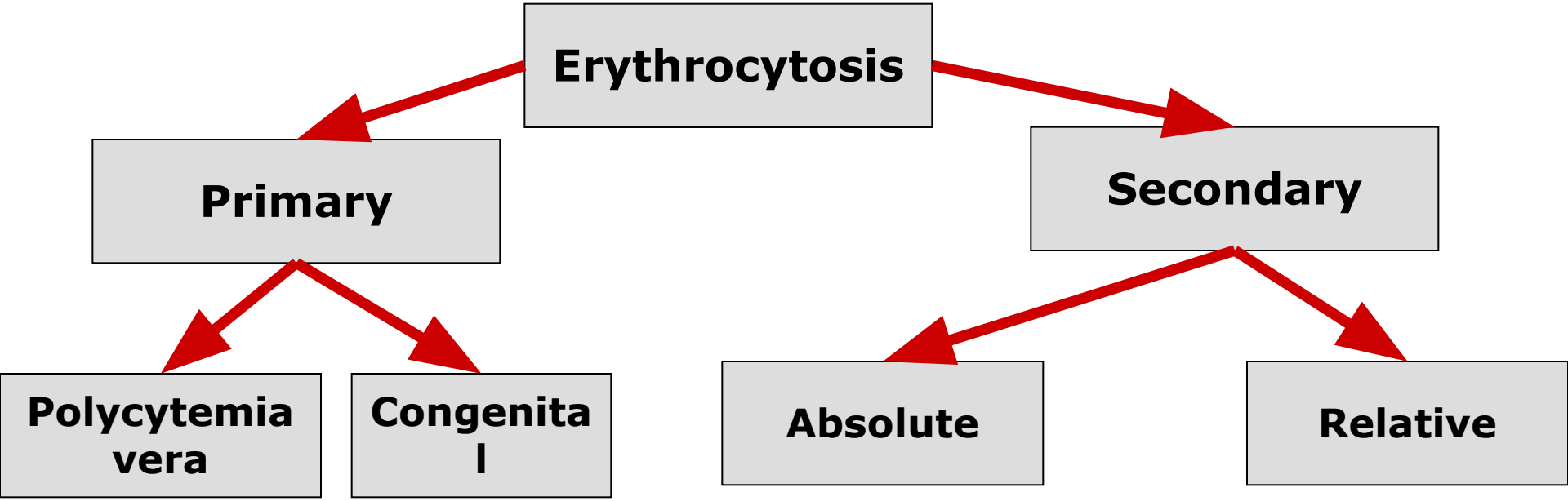
- leukemic metaplasia of bone marrow (it consists of leukemic cells only);
- cancer metastases in bones,
- diffuse osteosclerosis with obliteration of marrow cavity.

Blood picture is the same as at hypoplastic anaemias.

Disregulatory anemia – lack of erythropoietin synthesis (kidney's diseases).

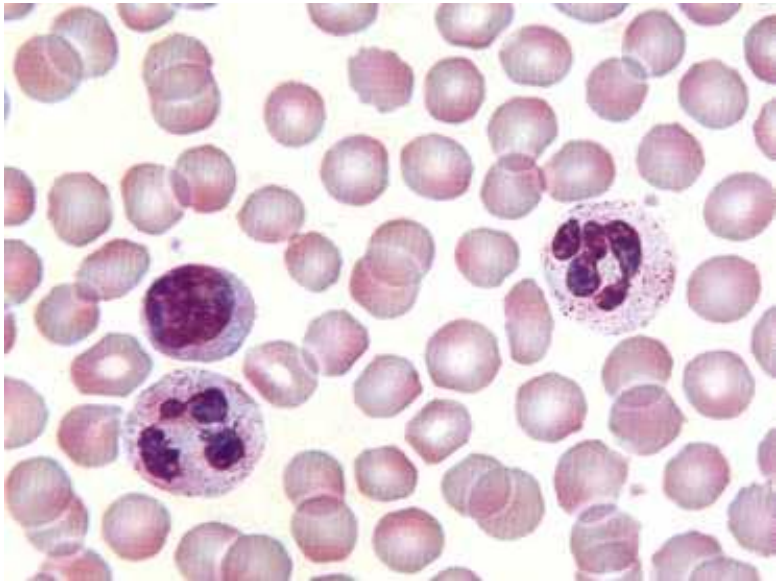
Erythrocytosis (Polycytemia)

- RBC count: more than 4,7*1012//L in women and more than 5,0*1012//L in men.

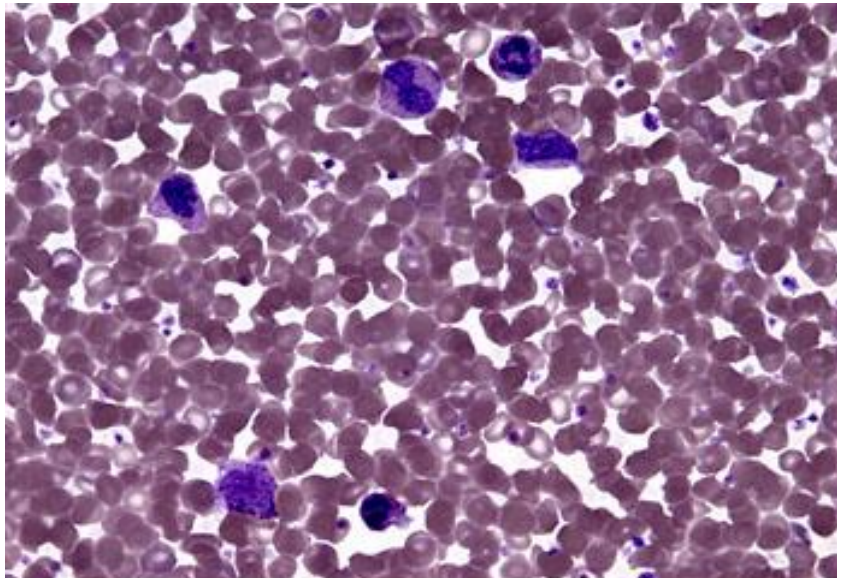


Vaquez' disease (Polycythemia vera)

Tumor induced hyperplasia of bone marrow



Normal blood smear



Polycytemia vera

Vaquez' disease (Polycythemia vera)

- Blood count:
  - increased number of RBC, reticulocytes, WBC and platelets.
- Blood volume – polycytemic hypervolemia, hematocrit is increased > 52%.
- Hb content is increased too up to 180-200 g/L. P
- Increase of blood viscosity.

Vaquez' disease (Polycythemia vera)

Clinical signs

- arterial hypertension ;
- plethora with congested mucous membranes conjunctiva and retinal veins;
- CNS disturbances (headache, dizziness, visual disturbances, paresthesias, strokelike symptoms)
- cardiovascular symptoms (myocardial ischemia, vessels thrombosis);
- enlargement of spleen and liver;
- frequent bleedings.

Secondary absolute erythrocytosis

due to increased erythropoietin production

General hypoxia:

- Chronic lung diseases;
- Carbon monoxide poisoning;
- Smoker's erythrocytosis;
- The local inhabitants of high-altitude territories.

Local renal hypoxia

- renal artery stenosis,
- final stages of renal diseases.

Tumors

- hepatocellular carcinoma, renal cell cancer

Secondary relative erythrocytosis

increased RBC number in the unit of blood volume, meanwhile erythropoiesis is not activated and absolute RBC count is normal.

- **organism dehydration** (at diarrhoea, vomiting, abundant sweating, burns, overheating)
- **blood redistribution** from blood depot to peripheral flow (stress reaction, acute hypoxia, high level of catecholamines).

Clinical signs: increased Hct, polycytemic normovolemia or hypovolemia, increased blood viscosity.