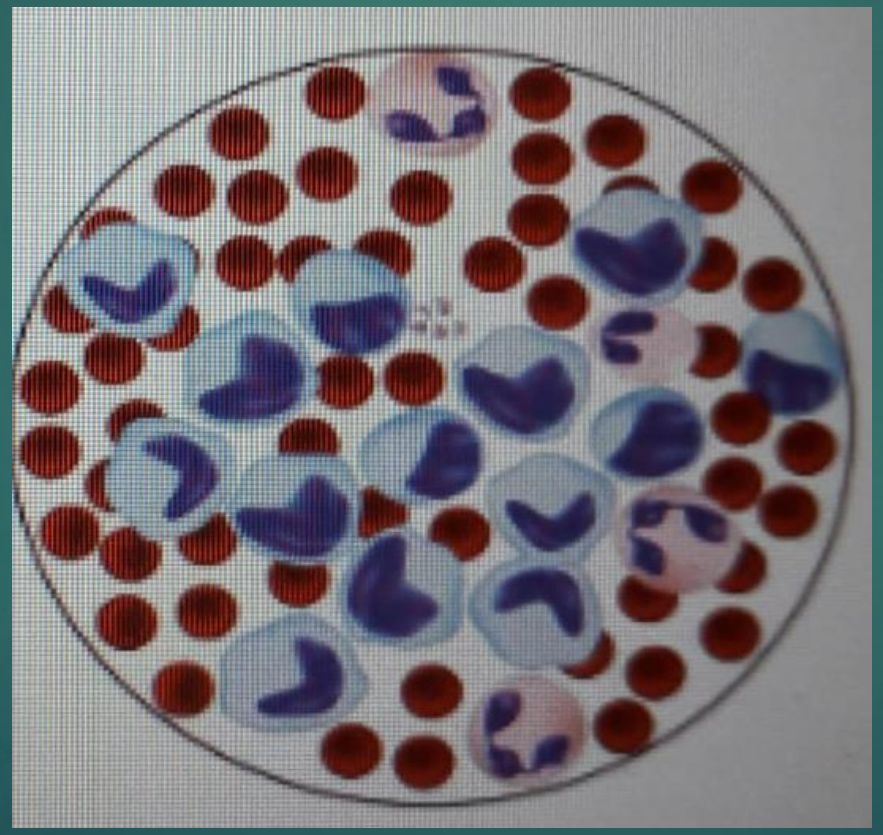
Hemoblastoses



Hemoblastoses

- Hemoblastosis is a disease of the blood system, a malignant tumor that develops from hematopoietic cells. It is the most common cause of death among diseases of the blood system.

Several laboratory diagnostic methods are used to determine hemoblastoses:

- -cytochemical reaction - reactions with myeloperoxidase, lipid, glycogen, non-specific esterase, acid-phosphatase are carried out in this method. The ability of leukemic cells to differentiate is studied.
- -immunophenotypic method – types of acute leukosis (clusters of differentiation CD) are determined
- - cytogenetic method - changes in chromosomes are studied
- - molecular- biological method - the genome of tumor cells is studied

CLASSIFICATION OF HEMOBLASTOSIS

Leukoses

Lymphoma

Acute

chronic

1. Acute myeloblastic leukoses:

-undifferentiated acute myeloid leukosis-MO

- immature (unformed) acute myeloblastic leukosis -M1

-myeloblast leukosis with some granules formed -M2

-acute promyeloblastic leukosis -M3

-acute myelomonoblastic leukosis -M4

- acute monoblastic leukosis - M5

-acute erythromyeloblastic leukosis -M6

-acute megakaryoblast leukosis -M7

2. Acute lymphoblastic leukoses:

-microlymphoblastic leukosis -L1

-leukosis with lymphoblasts of different sizes -L2

-macro - or prolymphoblast leukosis -L3

1. Chronic lymphocytic originated leukoses:

- chronic lymphocytic leukoses

- cutaneous lymphoma or Sezary's disease

-paraproteinemic leukoses

These include myeloma disease (plasmacytoma), primary macroglobulinemia (Waldenstrom disease), heavy chain disease (Franklin disease).

2. Chronic monocytic originated leukoses:

- chronic monocytic leukosis

- histiocytosis

a) Eosinophilic granuloma

b) Letterer-Siwe disease

c) Hand-Schuller-Christian's disease

3. Chronic myelocytic originated leukoses:

- chronic myeloid leukosis

- polycythemia vera (Osler- Vaquez syndrome)

- chronic megakaryocytic leukosis (idiopathic thrombocythemia)

or hemorrhagic thrombocythemia disease)

Lymphomas

According to histogenesis:

-B-cell lymphomas

- Lymphomas of T-cell origin

1. Lymphosarcoma

- nodular

-diffuse

2. Reticulosarcoma

3. Fungal sarcoma

Non-Hodgkin's lymphoma

4. Lymphogranulomatosis (Hodgkin's disease)

-local

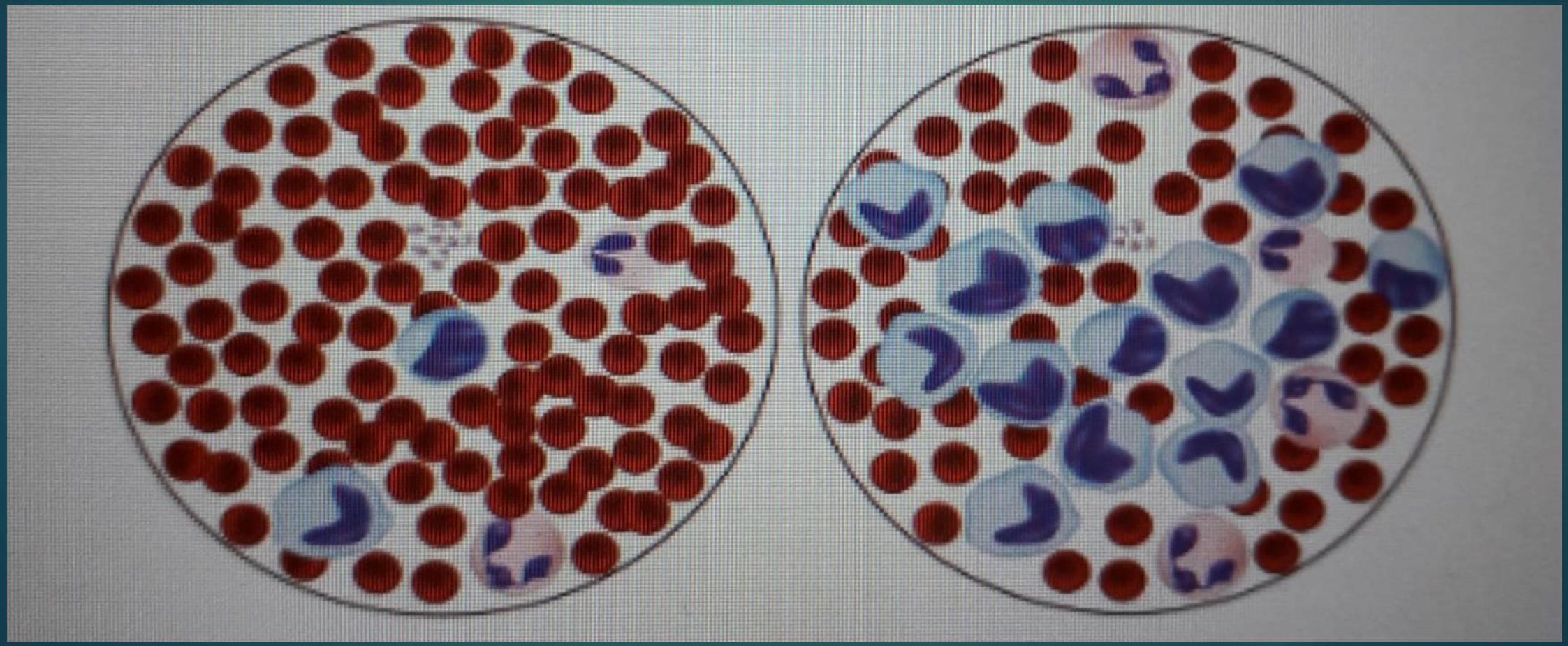
-spread

According to the total amount of leukocytes in a unit volume of blood, the following types of leukocytes are distinguished:

Leukemic leukosis - the total amount of leukocytes exceeds 30-50 $x10^9$ /l. The blast forms of leukosis cells increase.
Subleukemic leukosis - the total amount of leukocytes does not exceed $30x10^9$/l. Blast cells are the majority.
Aleukemic leukosis - the number of leukocytes is normal. Blast leukocytes are not in the peripheral blood, but atypical leukocytes, their young and blast forms are found in the bone marrow and lymph nodes.
Leukopenic leukosis - the number of leukocytes is less than normal. Blast leukocytes are found in small quantities.

Leukoses -

- develop from hematopoietic cells as a result of primary damage to the bone marrow, differ from other malignant tumors from leukocytosis, leukemoid reactions, and the proliferation of hematopoietic tissues located outside the bone marrow.



- *Unlike **other malignant tumors**, it is not possible to determine the location of the tumor during leukemia. Because the tumor cells can spread throughout the body through the blood. Leukosis cells first proliferate in the bone marrow, and then they disseminate to the peripheral blood, spleen, lymph nodes and other tissues. Lymphomas are first formed in the lymph nodes, and then they move to the blood and bone marrow. Leukoses develop only from cells belonging to the hematopoietic line, that is, from the cells described in the scheme of hemopoiesis.*

DIFFERENCE OF LEUKEMIA FROM LEUKEMOID REACTIONS

Leukemoid reactions	Leukoses
- formation of non-carcinogenic factors brings	- is caused by the effect of carcinogenic factors.
- activation of normal hemopoiesis is noted, transformation does not occur.	-normal hemopoietic cells are transformed into tumor cells.
- focal hyperplasia of normal hemopoietic cells is observed.	- widespread hyperplasia of hemopoietic tumor cells is observed.
-anemia and thrombocytopenia are not observed. Because the erythroid cells in the bone marrow are not compressed or damaged.	-anemia and thrombocytopenia are observed. Leukemic infiltrate prevents the development of erythrocytes and platelets, compresses them.
-degenerative changes occur in leukocytes (toxic granularity, Knyazkov-Dele body, pyknosis of the nucleus, cytoplasm vacuolization).	- an increase in blast cells is observed.
- the increase of leukocytes is reactive. It is observed in bacterial infectious diseases.	-blast cells do not obey the regulatory system, divide and multiply without limits, the ability to differentiate is weakened.
- does not form leukemic infiltrate in other organs.	- the leukemic infiltrate spreads to the liver, spleen, lymph nodes, lungs and other organs.

The most common types of acute leukosis:

1. **Acute myeloblastic leukosis - (M1)** - it is also called acute myeloid leukemia. It refers to bone marrow tumors that develop very quickly. Hemopoiesis originates from the myeloblast cells of the blast stage. During the development of the disease, abnormal blast cells are found in the blood.
2. **The population of myeloblast leukosis (M2**)-blast cells with some granules formed is morphologically somewhat reminiscent of myeloblasts in the blood and bone marrow. The difference is that the chromatin has a rougher structure and clearly visible nuclei, narrow cytoplasm. In a well-prepared smear, tumor cells can be distinguished from lymphoid cells. it is possible to differentiate.
3. Acute promyeloblastic leukosis (M3) - the cells show large nuclei, unclear chromatin structure, a large number of promyelocytic granules and Auer rods. Peroxidase reaction is positive.
4. Acute erythromyeloblastic leukosis (M6) - it is also called Di-Guglielmo's disease or acute erythremia. At this time, atypical myeloblasts, monoblasts and other undifferentiated blast cells are found in the bone marrow along with atypical erythroblasts.
5. Acute megakaryoblastic leukosis (M7) – originates from megakaryoblasts.
6. Acute lymphoblastic leukosis (ALL) originates from lymphoblast cells of the blast stage of hemopoiesis. The disease is called acute leukemia.

The main features of acute leukosis:

- It mostly develops in children and young people;

- in blast cells, the nucleus is very large, the chromatin has a fine mesh structure;

- "leukemic abyss" is observed, which is of great importance in establishing the diagnosis;

- clinical view - weakness, fever, tendency to bleeding, enlargement of lymph nodes, spread of leukemic infiltrate to some organs (liver, spleen, kidney, heart and other organs) is observed;

- blood analysis - hemoglobin, erythrocytes and platelets decrease, leukocytes often increase up to 80%. Blast cells predominate in the leukocyte formula. However, aleukemic leukemia is an exception. In this type of leukemia, against the background of leukopenia, anemia, thrombocytopenia, there are almost no blast cells in the peripheral blood. They are found in large quantities in the bone marrow;

- there is an increase in uric acid;

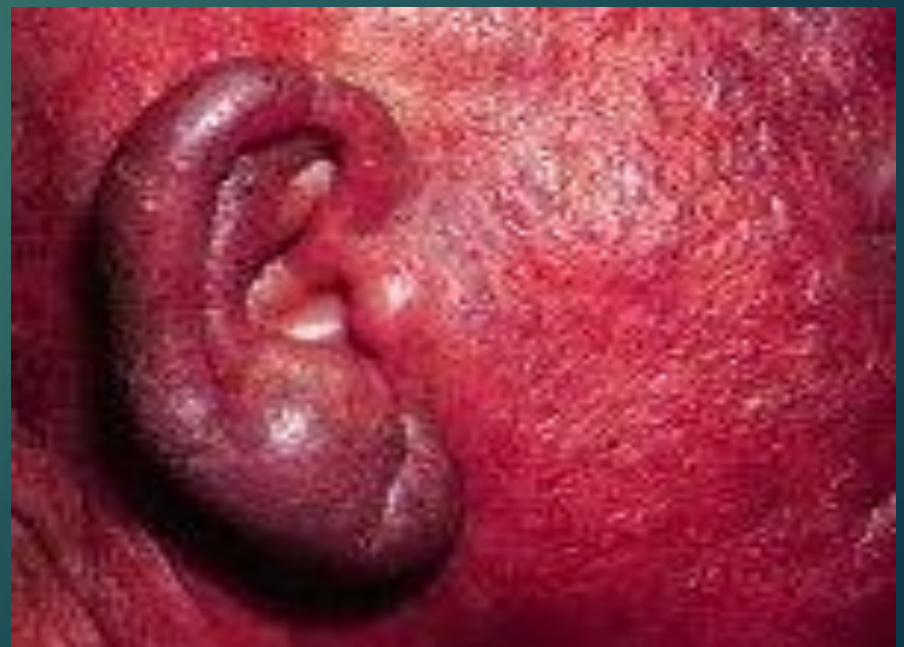
- hyperplasia, anaplasia and metaplasia are found in the bone marrow and lymphoid organs. leukemic blast cells increase, 30-90%, and erythroid, megakaryocytic and granulocytic cells decrease.

CHRONIC LEUKOSES

- ***Chronic lymphocytic leukosis.***
- ***Diagnosis of chronic lymphocytic leukosis:***
- - there is lymphocytosis in the peripheral blood;
- - lymphocytosis in the bone marrow exceeds 30%;
- - Antigens (CD19, CD23, CD5) are detected in lymphocytes of B-cell origin. The expression of CD5 confirms the presence of XLL of B-cell origin immunologically;
- - in the terminal stage - anemia, granulocytopenia, thrombocytopenia develops.
- CLL of T-cell origin is rare (3-5%). Its main features are: frequent damage to the skin with leukosis infiltrate, presence of polymorphous nuclei (bean-shaped), determination of coiled (brain-like) chromatin and detection of CD2, CD3, CD4 in lymphocytes of T-cell origin.

Cutaneous lymphoma or Sezary's disease

It is a malignant tumor of the skin. It originates from T-lymphocytes. In Sezary's disease, which damages the skin, 3 clinical signs are observed: erythroderma, lymphadenopathy, and the finding of cells with specific convoluted nuclei in the blood. The diagnosis of the disease is based on clinical signs, blood analysis and skin biopsy. In contrast to fungal mycosis, skin dyschromia is more clearly visible.



PARAPROTEINEMIC HEMOBLASTOSIS

Paraproteinemic hemoblastoses - tumors of B-cell origin - myeloma disease, Waldenstrom macroglobulinemia and heavy chain disease belong.

Myeloma disease

It refers to tumors of B-cell origin. It is also called generalized plasmacytoma, Rusty-Kahler disease. Immunoglobulins secreted during the disease differ in their structure. The disease is caused by proliferation of lymphoplasmacytic cells of tumor origin.

The disease is characterized by the accumulation of abnormal plasmatic cells in the bone marrow and the high amount of proteins in the blood. In 20% of myeloma cases, tumor cells can synthesize only the light chain of immunoglobulins. IL-6 plays a major role in the pathogenesis of myeloma. IL-6 stimulates the division of plasma cells and inhibits their apoptosis. It is believed that IL-6 causes the lysis of bone tissue and the activation of osteoclasts (macrophages that destroy osteocytes).

Myeloma diagnostic criteria:

- in the bone marrow, plasmatic cells are more than 10 - 30 %;

- paraprotein is found in the blood;

- Bence-Jones protein is determined in urine by electrophoresis;

- hypercalcemia is observed;

- kidney failure develops, the amount of creatinine in the blood increases;

- anemia is observed, hemoglobin is less than 100 g/l;

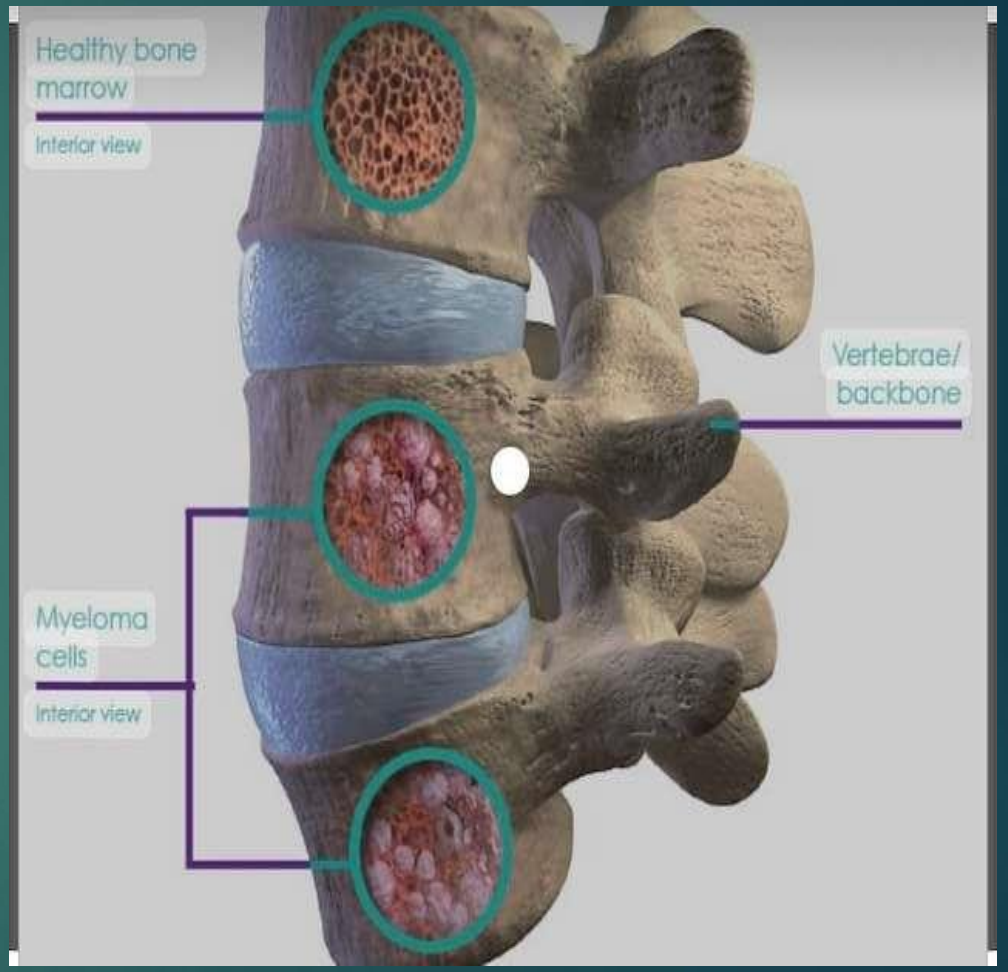
- sensitivity to infection;

- the amount of Ca in the blood increases;

- the amounts of proteins in the blood increases;

-mainly flat bones (ribs, skull bones) and vertebrae are damaged, osteolysis centers are formed.

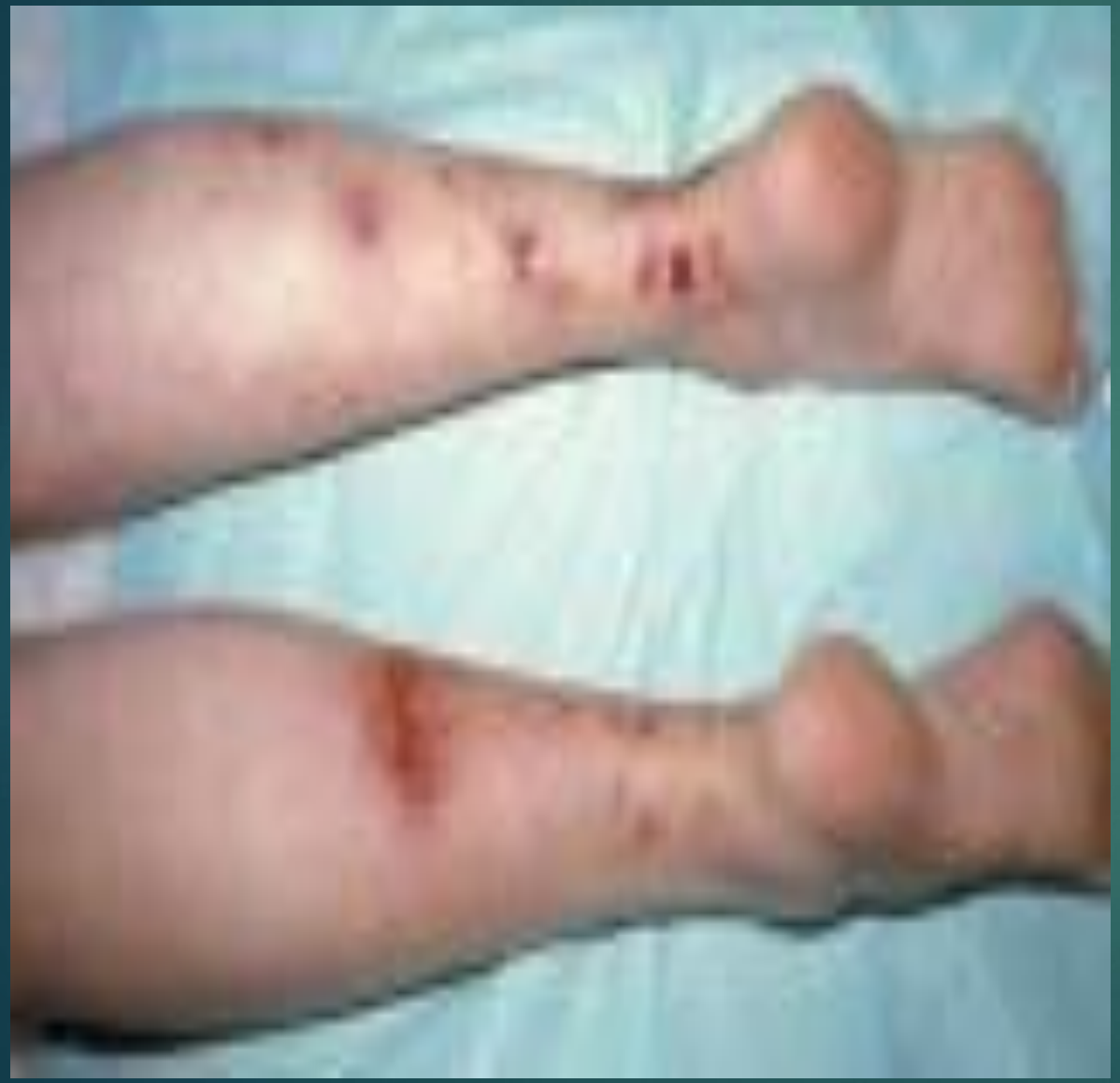
During non-tumor paraproteinemias, there are no proliferation of plasmatic cells and foci of osteolysis in the bone marrow. Bence-Jones protein is not found in the urine.

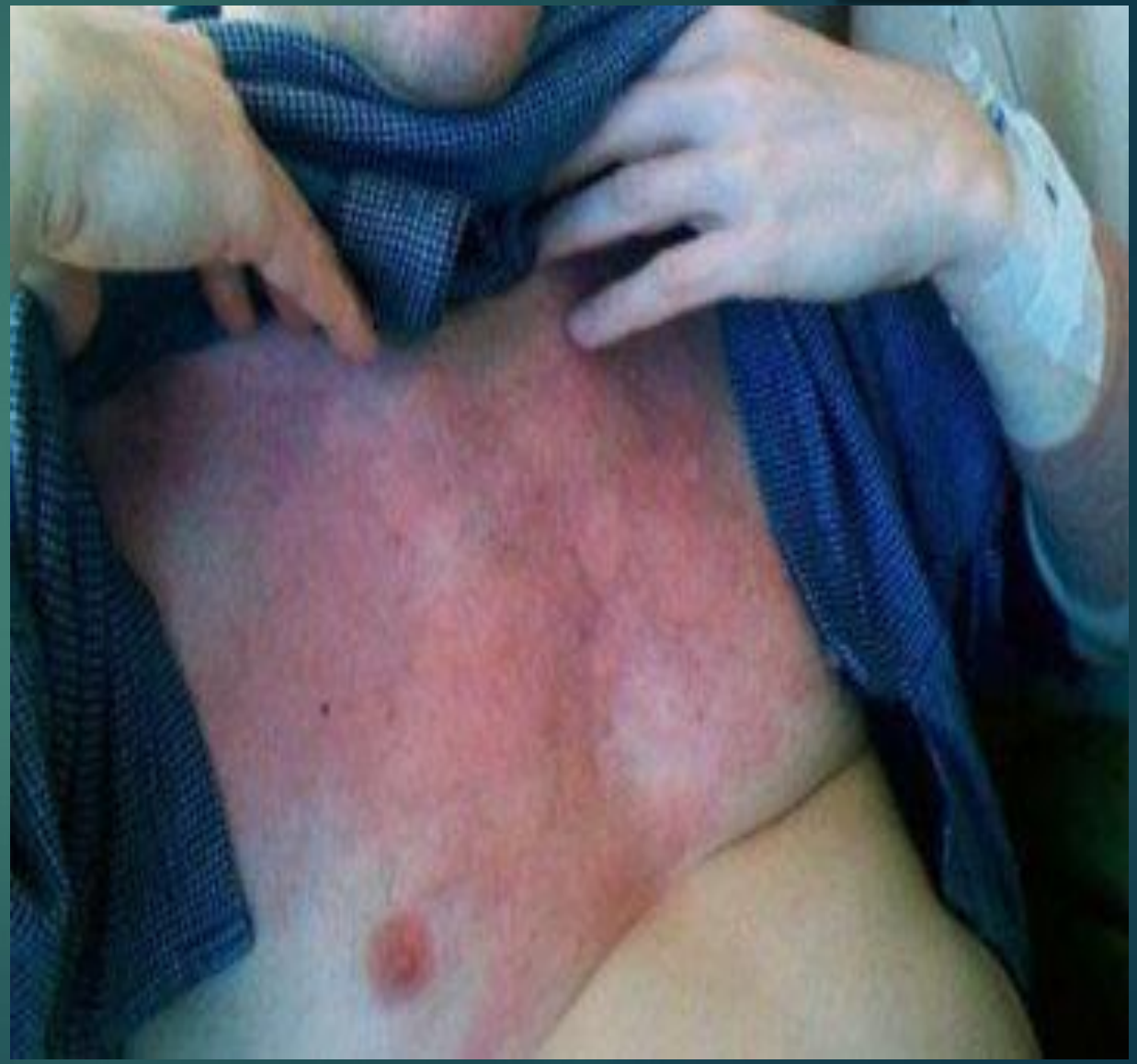


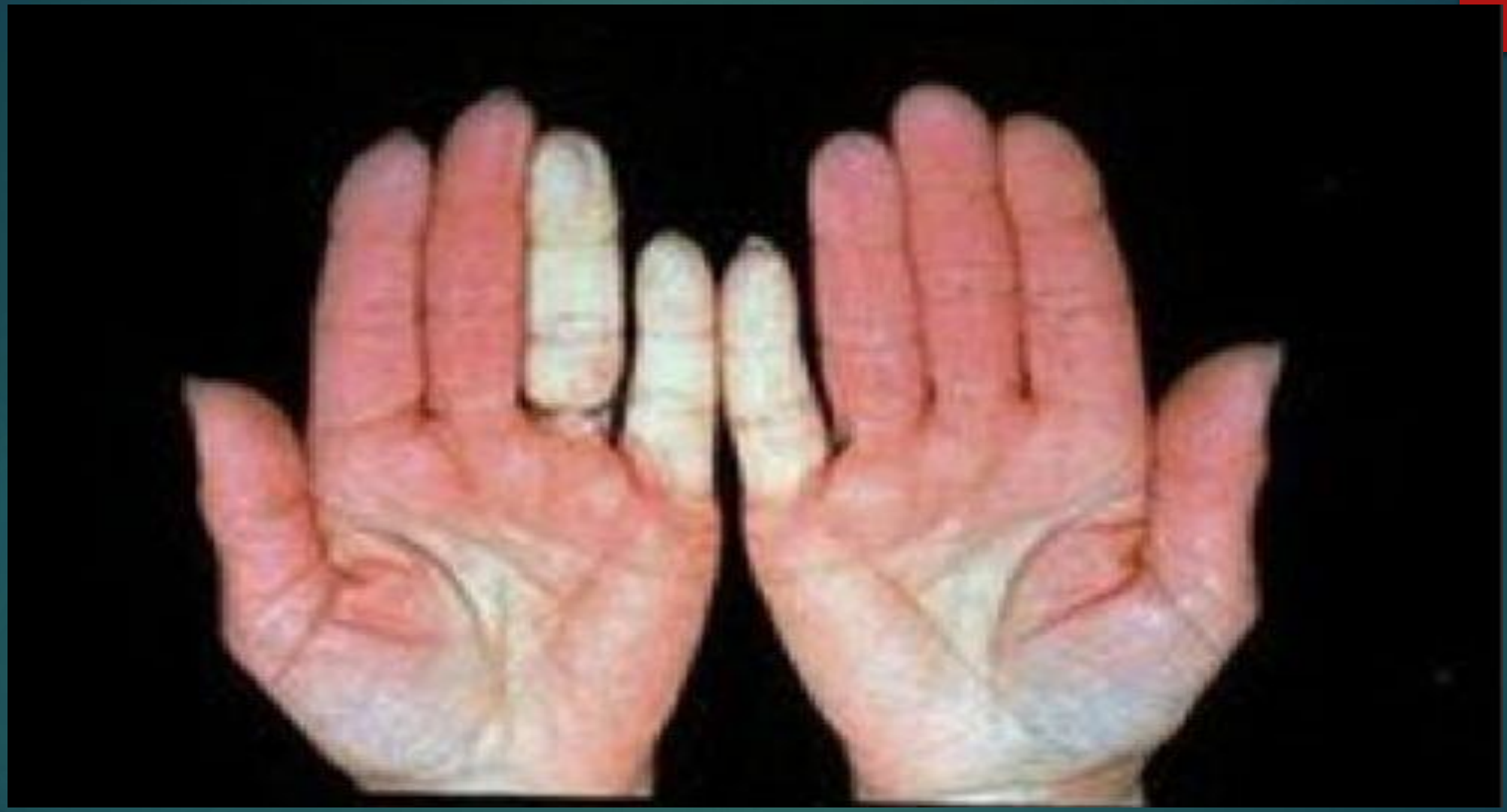
Primary macroglobulinemia

It is also called Woldenstrom disease. It refers to malignant tumors of B-cell origin. Tumor cells synthesize large amounts of pathological IgM into the blood. The thickness and viscosity of the blood increases, hepatosplenomegaly, widespread lymphadenopathy, SLAC phenomenon, anemia, increase of ESR, vascular damage, bleeding observed. Patients are prone to infection. Sometimes Bence-Jones protein is detected in the patient's urine. However, unlike myeloma, its amount is small. The diagnosis is confirmed on the basis of bone marrow examination and the increase of protein M.

Bens- Jones proteins combine with other proteins in the urine (often Tamm-Horsfall protein) to form crystalline cylinders.

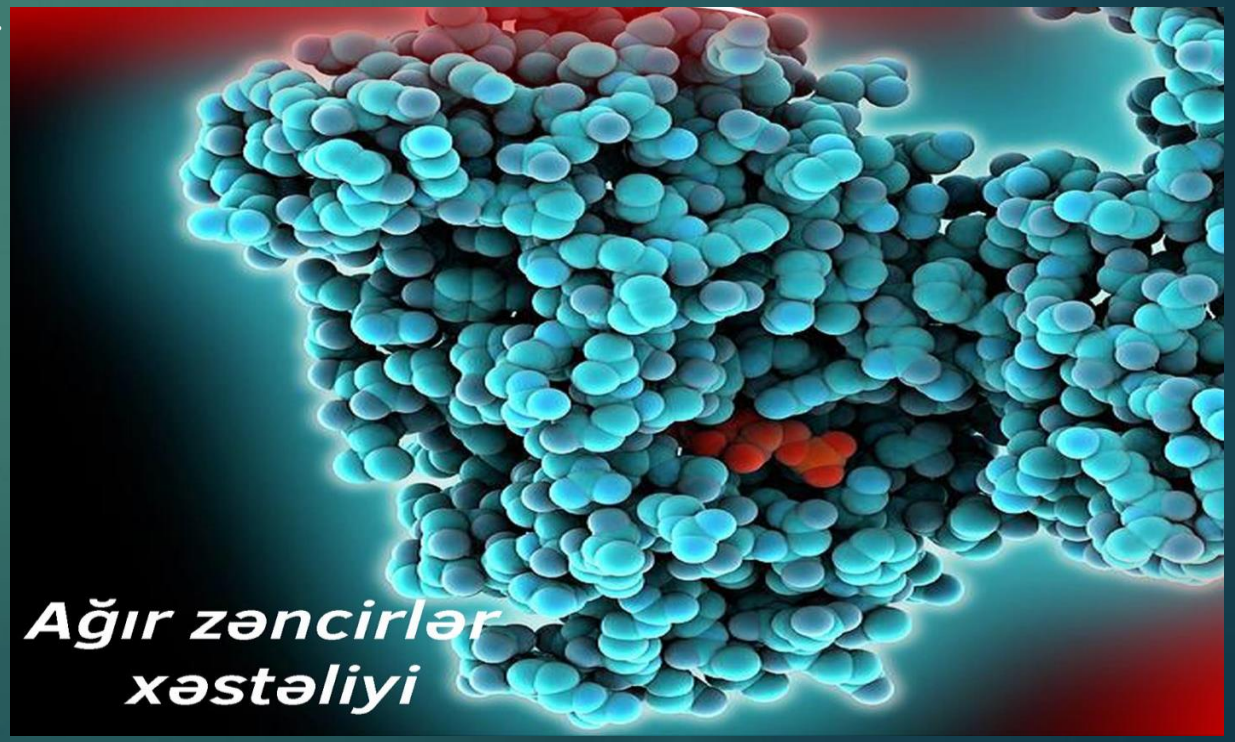






Heavy chains disease

Anemia, leukopenia, thrombocytopenia, eosinophilia, atypical lymphocytes and plasma cells are noted in the general blood analysis. The diagnosis is confirmed based on the detection of monoclonal alpha chain in blood and urine. If it is not found in the blood and urine, then a biopsy of the intestines is performed. Sometimes the abnormal protein is also found in the intestinal juice. Bence-Jones protein is not found in urine.



Chronic myelocytic leukosis:

The disease develops in 3 phases:

1. chronic phase
2. acceleration (progressive) phase
3. terminal phase (blast crisis)

The diagnostic criteria of the acceleration phase during CML refer to:

*the number of blast cells in the blood or bone marrow is up to 10-19 %;

* the number of basophils in the blood or bone marrow exceeds 20 %;

*untreated thrombocytopenia or thrombocytosis develops;

*untreated, progressive splenomegaly is observed;

*additional chromosomal abnormalities occur.

Diagnostic criteria of the terminal stage during CML refer to:

*the amount of blast cells in the blood and bone marrow exceeds 20%;

*accumulation of large blast cells is observed in trepanobioptate;

*additional abnormal chromosomes are found;

Erythremia

It is also called Vakez-Osler disease. Although it is of tumor origin, it has a benign course. The disease is asymptomatic for a long time. The role of transformation of stem cells in its etiology is noted. Mutation of tyrosine kinase occurs, replacing valine with phenylananyl. The disease originates from myelopoiesis cells. The main substrate of tumor cells is erythrocytes.

The main hematological indicators of the disease:

-increased erythrocyte mass. Erythrocytes are 6-8×1012/l and more, Hb is 180-220 g/l, color index is 0.7-0.6. Due to the increase in erythrocytes, the volume of circulating blood increases;

- increased hemoglobin concentration;

- an increase in the hematocrit index and more than 65% is observed;

- due to the regeneration of erythrocytes, the amounts of reticulocytes in the blood increases by more than 15-20%;

- due to neutrophils, the amounts of leukocytes increase by 1.5-2 times. The nuclear orientation of leukocytes tends to the left;

- the amounts of platelets increase (400-600×109/l and more);

- an increase in the thickness of the blood is noted;

- ESR decrease (1-2 mm/h), increase of uric acid is observed.

The disease is diagnosed based on the following symptoms:

- hematological and biochemical indicators change (increase of erythrocytes, Hb, leukocytes, reticulocytes, platelets);

- the patient's skin and visible mucous membranes become hyperemic;

-spleen and liver grow;

- the patient is prone to thrombosis;

- the patient's weight decreases;

- sweat secretion increases;

-genetically abnormal cells (with the exception of Philadelphia chromosomes) are found in the bone marrow;

-alkaline phosphatase increases (even in the absence of infection);

- the amount of erythropoietin is low;

- histological examination of the punctate during trypanobiopsy shows an increase in megakaryocytes.

Difference between true polycythemia and secondary absolute and relative erythrocytosis

Erytremia	Secondary absolute erythrocytosis
-tumor proliferation of myeloid cells is observed in the bone marrow; - the level of erythropoietin in blood and urine is normal or decreased; - peripheral blood has thrombocytosis, neutrophilia, monocytosis; - the color index decreases as the ratio between the rate of proliferation of erythroid cells and the synthesis of hemoglobin is broken; - abnormal cells are found in the bone marrow; -spleen and liver grow; - the patient's skin and visible mucous membranes are red.	- observed during hypoxia, kidney ischemia, cardiovascular system pathologies; - the synthesis of erythropoietin increases; - non-tumor proliferation of erythroid cells is observed in the bone marrow; - thrombocytosis and leukocytosis are not observed; -relative erythrocytosis is temporary, observed during pathological processes that cause blood clotting (continuous vomiting, severe diarrhea, etc.); - a hereditary form of erythrocytosis also develops as a result of a lack of 2,3 diphosphoglycerate in erythrocytes and a genetic defect of globin in the hemoglobin molecule. The ability of oxygen to combine with Hb increases, as a result, hypoxia develops.

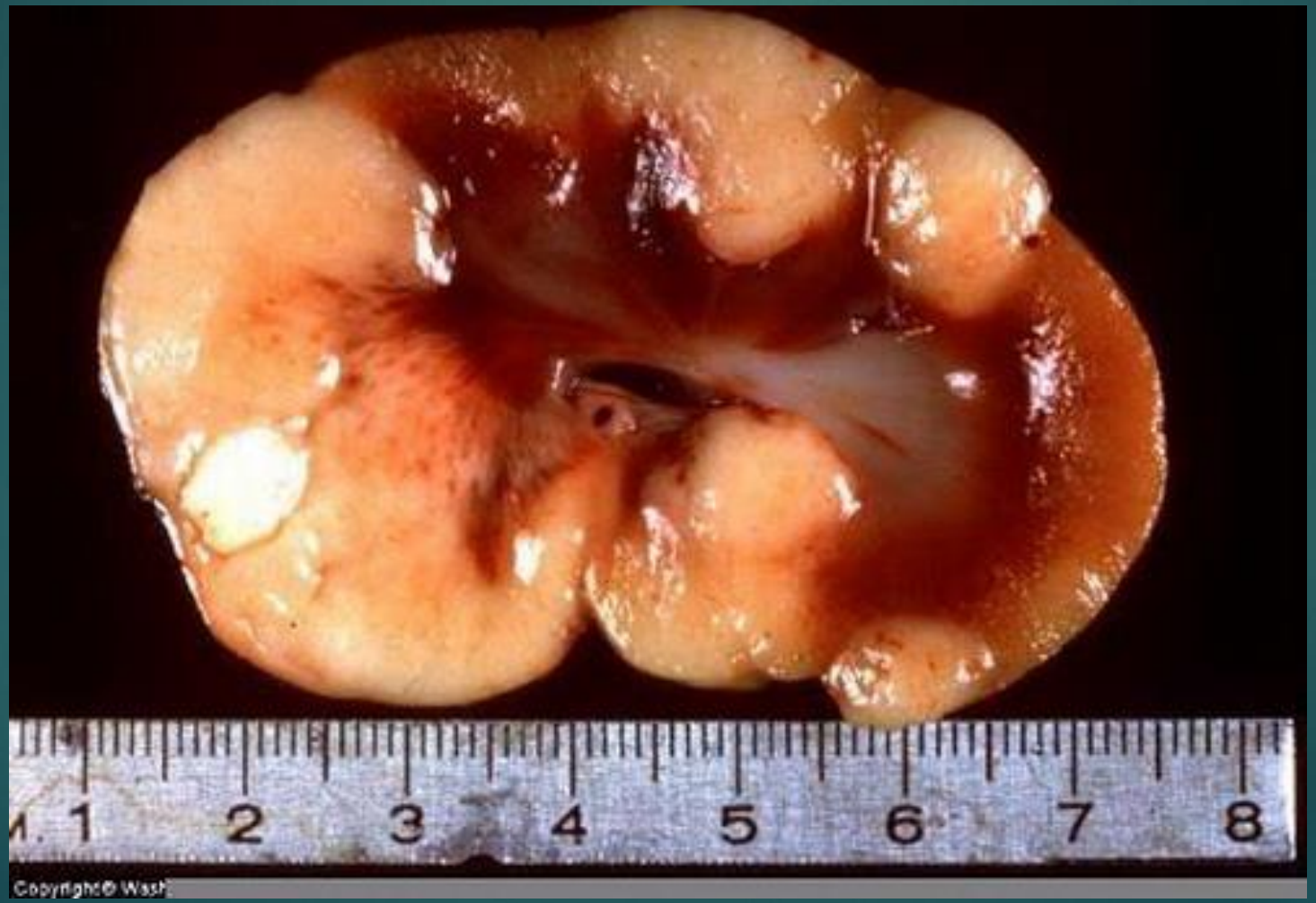
Differences between chronic myeloid leukosis and chronic lymphocytic leukosis

CML	CLL
It develops at the age of 30-40; -pioid (purulent) bone marrow is observed; - cells have 100% Ph-chromosome; -spleen grows too much, blast crisis develops; - there are leukosis infiltrates in the liver.	It develops at the age of 40-60; -bone marrow is red (raspberry); - There is no Ph-chromosome; - the spleen enlarges, hemolytic anemia, thrombocytopenia noted; - there are leukosis infiltrates along the portal tracts of the liver.

The main features of acute and chronic leukemia:

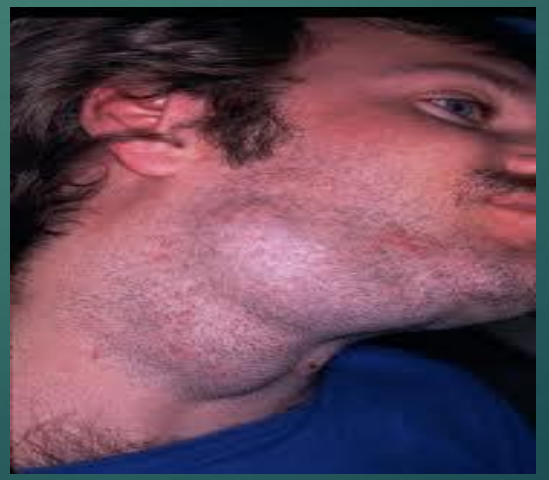
Acute	Chronic
-children and young people get sick; - "leukemic abyss" occurs; - hemorrhagic syndrome and ulcerative-necrotic processes in mucous membranes are clearly observed; -spleen, liver, lymph nodes are slightly enlarged; -tumor cells in the bone marrow and peripheral blood consist of undifferentiated or poorly differentiated blast cells; - on the basis of morphological studies, it is not possible to determine whether blast cells belong to myeloid or lymphoid cells.	middle-aged and elderly people get sick; -all cells (mature, maturing) are present. Blast cells are more than normal; - hemorrhagic syndrome and ulcerative-necrotic processes in mucous membranes are observed only when the disease is aggravated (crisis of blast cells); -spleen, liver, lymph nodes become very enlarged; - has the ability to differentiate tumor cells; - on the basis of morphological studies, it is determined which cell line the blast cell belongs to.

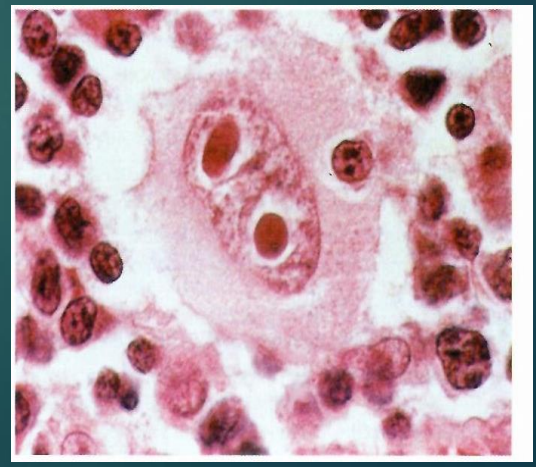
Lymphoma



Difference between Hojkin's lymphoma and non-Hojkin's lymphoma:

Hojkin's lymphoma	Non-Hojkin's lymphoma
- in 90% of cases, neck lymph nodes are damaged; - the cell population is polymorphic; - observed at young ages; - the prognosis is good in 80% of cases; -Epstein-Barr creates the virus; - Reed-Sternberg cells are found in the damaged lymph node.	- various localized lymph nodes join the process. It is not known which lymphoid tissue starts from the lymphopoietic cell; -cell population is monomorphic; - often occurs after the age of 40; - the prognosis is bad.





Prognostically unfavorable signs:

- the presence of many conglomerates (more than 5 cm in diameter) in the peripheral lymph nodes;

- damage to more than 3 lymph nodes at the same time;

- the presence of signs of intoxication and ESR exceeding 50 mm/h;

- the patient's age is over 40.