HEMATO-ONCOLOGICAL DISEASES

Learning guide
for the 4th year students

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

HEMATO-ONCOLOGICAL DISEASES

Learning guide
for the 4th year students

ГЕМАТООНКОЛОГІЧНІ ХВОРОБИ

Методичні вказівки
для проведення практичного заняття
здобувачів вищої освіти 4-го року навчання

Затверджено
Вченою радою ХНМУ.
Протокол № 5 від 23.05.2024.

Харків
ХНМУ
2024

Hemato-oncological diseases : Learning guide for the 4th year students / comp. V. Kapustnyk, O. Sadovenko, B. Shelest, O. Babycheva. Kharkiv : KhNMU, 2024. 16 p.

Compilers V. Kapustnyk
O. Sadovenko
B. Shelest
O. Babycheva

Гематоонкологічні захворювання : метод. вказ. для здобувачів вищої освіти IV-го року навчання / упоряд. В.А. Капустник, О.Л. Садовенко, Б.О. Шелест, О.О. Бабічева. Харків: ХНМУ, 2024. 16 с.

Упорядники В.А. Капустник
О.Л. Садовенко
Б.О. Шелест
О.О. Бабічева

Topic 2: «HEMATOONCOLOGICAL DISEASES. ACUTE AND CHRONIC MYELOID, LYMPHOID LEUKEMIAS AND LYMPHOMAS. ETIOLOGY. PATHOGENESIS. CLINIC. DIAGNOSIS. TREATMENT. DENTAL ASPECTS»

1. Hours. 3,5 (practical classes – 3, Independent students' activity – 0,5).

2. Importance of the topic. The incidence of hemoblastosis in various regions of the world ranges from 8–15 per 100,000 population. Leukemia ranked as the fifteenth most common diagnosed cancer. In general, the mortality rate from malignant neoplasms of hemoblastosis reaches 6 to 10 %. There is a higher incidence of hemoblastosis in men and less in women. Acute lymphoblastic leukemia is increasing in prevalence in children and young people, while acute myoblastic leukemia affects all age groups. Chronic lymphoid leukemia and myeloma are detected in people of middle and old age.

Over the past two decades, the rate of illness for hemoblastosis has decreased at a stable level, and the increase in the number of patients is explained by a thorough diagnosis and an increase in the patient's life distress.

The global incidence of leukemia is widespread, exhibiting higher prevalence and mortality rates in more developed nations, while mortality rates are elevated in developing regions.

Leukemia, a cluster of cancers originating typically in the bone marrow, leads to an excess of abnormal white blood cells known as blasts or leukemia cells. Symptoms often include bleeding, bruising, fatigue, fever, and heightened susceptibility to infections, resulting from deficient normal blood cell counts. Diagnosis commonly relies on blood tests or bone marrow biopsies.

Leukemia is most prevalent among children, with acute lymphoblastic leukemia constituting three-quarters of pediatric cases. Conversely, around 90 % of leukemia diagnoses occur in adults, with acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL) being the most prevalent types. Developed countries notably experience a higher incidence of the disease.

3. Aim of studying. The aim of this topic is to be able to mastering (improving) methods of examination of patients with hemato-oncological diseases, diagnosis of hemato-oncological diseases, treatment of hemato-oncological diseases

Specific objectives to be achieved after conducting practical classes:

Students need to know:	Students will be able to:
1) know the definition of hemato-oncological diseases;	1) use clinical terminology regarding hemato-oncological diseases;
2) etiology and pathogenesis of hemato-oncological diseases;	2) distinguish clinical syndromes in hemato-oncological diseases;
3) modern classification of hemato-oncological diseases;	3) draw up an examination plan for patients with hemato-oncological diseases;
4) clinical and laboratory syndromes of hemato-oncological diseases;	4) evaluate the results of laboratory and instrumental examination of patients with hemato-oncological diseases;

Students need to know:	Students will be able to:
5) the most frequent complications and the mechanism of their development in hemato-oncological diseases;	5) carry out differential diagnosis of hemato-oncological diseases with other diseases;
6) treatment program for patients with hemato-oncological diseases and their complications.	6) formulate a final diagnosis;
	7) draw up a treatment plan for a patient with hemato-oncological diseases;
	8) to correct emergency conditions that may occur with hemato-oncological diseases;
	9) predict the course of the disease, determine the prognosis for the life and working capacity of patients with hemato-oncological diseases.

4. Indicative syllabus.

- Definition of hemato-oncological diseases.
- Etiology of hemato-oncological diseases.
- Pathogenesis of hemato-oncological diseases.
- Pathomorphological manifistations of hemato-oncological diseases.
- Classification of hemato-oncological diseases.
- Clinical manifestation, leading syndromes of hemato-oncological diseases.
- Diagnosis of hemato-oncological diseases.
- Treatment of hemato-oncological diseases.
- Prevention, the role of the dentist.

5. Learning aids. Visual material, multimedia devices, Microsoft Power Point presentations, tables, posters. Training manuals.

Link to the discipline page in MOODLE:
https://distance.knmu.edu.ua/course/view.php?id=2858

6. Materials for practical classes.

Leukemias, also spelled leukaemias, are malignant tumors of hematopoietic tissue with primary localization in the bone marrow with subsequent dissemination to the peripheral blood, spleen, lymph nodes and other tissues. Leukemia generally begins as a cancer in the bone marrow.

Etiology. Several factors are associated with the development of leukaemia: ionizing radiation, exposure to chemicals, viral infection, genetic and hereditary factors.

Exposure to ionizing radiation is well-known cancerogenic factor. According to the findings, even low accrued doses of radiation (< 5 mGy) had an excess risk of leukemia-related mortality, suggesting that the potential threshold below which radiation is harmless should be very low. Chromosomal abnormalities occur after ionizing radiation in blast cells, which leads to the appearance of leukemia. A significant increase in myeloid leukaemia followed the atomic bombing of Japanese cities. An increase in leukaemia was observed after the use of radiotherapy and diagnostic X-rays of the fetus in pregnancy.

Leukemia can be caused by toxic exposure. These mostly involve exposure to cancer-causing agents, including different chemicals. Occupations with exposure to

benzene, pesticides and fertilizers, alkylating agents and formaldehyde are at higher risk of leukemia.

Viral infection. Particular attention is paid to the role of retroviruses in the development of leukemia. It has been established that in the genome of these viruses there are specific genes that are directly responsible for the transformation of a normal hematopoietic cell into a leukemic one. These genes are called oncogenes. The impact of a variety of infectious organisms, including the Epstein–Barr virus, herpesvirus, human immunodeficiency virus and Human T-lymphotropic virus and others are blamed in the development of leukemia. Viruses capable of transformation may integrate themselves into the genome of precursor B cells, disrupting the regulation of differentiation and proliferation. While the carcinogenic effects of fungal agents and aflatoxin are widely acknowledged, the precise mechanisms underlying this process remain unclear.

Genetic and hereditary factors play a role, although inherited forms of leukemia are uncommon. Leukemia typically does not exhibit familial patterns and is therefore not usually considered hereditary. However, certain individuals may possess genetic traits that elevate their susceptibility to the condition, although this does not guarantee its development. Occasionally, individuals may carry genetic variations not inherited from their biological parents, acquired after conception but before birth, potentially increasing their leukemia risk. Environmental and lifestyle factors, such as exposure to harmful chemicals and smoking, can also influence genetic predispositions and heighten leukemia risk. These alterations in genetic makeup occur throughout a person's lifetime and are termed acquired genetic changes.

The following inherited genetic syndromes may increase the risk of leucaemia:

- Down syndrome;
- Bloom syndrome;
- Klinefelter syndrome;
- Li-Fraumeni syndrome;
- ataxia-telangiectasia;
- neurofibromatosis;
- Fanconi anemia.

In most patients, the cause of leukemia cannot be established. The exact cause of leukemia is unknown. Different kinds of leukemia are believed to have different causes. Both inherited and environmental factors are believed to be involved.

Pathogenesis. The main role is played by the clonal theory of hemoblastosis. The mutation of the progenitor hematopoietic cell takes place under the influence of etiological factors, as a result of which DNA and the genetic apparatus are damaged. Chromosome abnormalities, which lead to changes in the cell structure, also play an important role. Such a cell is prone to hyperproliferation and loses the ability to differentiate. The first stage of leukemia formation is the formation of a clone of hematopoietic cells. In the beginning, the primary leukemic clone coexists with normal cells, and later pushes them away. Violation of apoptosis is important for the leukemia pathogen, resulting in the formation of a complex clone of cells and their metastasis.

Pathogenetic features of leukemia:

- primary tumor mutation of one cell;
- increase in tumor cells in geometric progression;

- appearance of first one, and then multiple clones of leukemic cells;
- suppression and displacement of normal hematopoietic sprouts;
- myelemia /the exit of tumor cells outside the bone marrow into the peripheral blood/;
- metastasis of leukemic cell clones from hematopoietic organs to other organs;
- gradual loss of sensitivity to cytostatics by blast cells.

Classification of leukemias. From both clinical and pathological perspectives, leukemia is categorized into various distinct groups. The primary classification is based on its distinction between acute and chronic forms:

- Acute leukemia is characterized by a rapid proliferation of immature blood cells, leading to bone marrow overcrowding and hampering the production of healthy blood cells. Urgent treatment is essential due to the swift advancement and accumulation of malignant cells, which subsequently infiltrate the bloodstream and disseminate to other organs. Acute leukemia predominantly affects children.
- Chronic leukemia entails the abnormal accumulation of relatively mature yet dysfunctional white blood cells. This progression typically spans months or years, during which these cells are produced at an elevated rate, resulting in an excess of abnormal white blood cells. While immediate treatment is imperative for acute leukemia, chronic forms are sometimes observed over time before initiating treatment to optimize therapy effectiveness. Chronic leukemia primarily afflicts older individuals but can manifest across all age groups.

Furthermore, leukemia classifications extend to the type of blood cell affected, categorizing leukemias into lymphoblastic or lymphocytic leukemias and myeloid or myelogenous leukemias:

- In lymphoblastic or lymphocytic leukemias, the cancerous change takes place in a type of marrow cell that normally goes on to form lymphocytes, which are infection-fighting immune system cells. Most lymphocytic leukemias involve a specific subtype of lymphocyte, the B cell.
- In myeloid or myelogenous leukemias, the cancerous change takes place in a type of marrow cell that normally goes on to form red blood cells, some other types of white cells, and platelets.

There are four broad types of leukemia:

- Acute lymphocytic leukemia (ALL).
- Acute myelogenous leukemia (AML).
- Chronic lymphocytic leukemia (CLL).
- Chronic myelogenous leukemia (CML).

The clinical picture of leucaemia can be different, which depends on the suppression of normal hematopoiesis.

Three stages of the course are determined:

1. Initial – can be diagnosed retrospectively.
2. The stage of the developed clinical picture.
3. Terminal stage.

Clinical manifestation. There are several variants of the initial stage of leucosis. The acute onset of the disease is observed in half of the patients and is

characterized by increase of body temperature (sometimes with presence of symptoms), intoxication, inflammatory weakness, joint pain, abdominal pain, throat pain when swallowing. The onset of the disease can look like flu, sore throat, rheumatism, acute appendicitis. Sometimes patients are mistakenly admitted to the infectious disease department.

The onset of the disease with expressed clinical manifestations is observed in 10 % cases. Usually it is characterized by profuse bleeding (bleeding gums and nosebleed). Gradually onset is manifested by general weakness, fatigue, malaise, minor hemorrhages in the form of bruises and slight enlargement of lymph nodes.

The hidden period of the course is observed in 5 % of patients, the disease is discovered occasionally (while checking of complete blood count during medical checkup or routine examination of in-patients).

The course of acute leucosis has two phases:

1. Aleukemic (without the release of blast cells into the blood).
2. Leukemic (with the release of blast cells into the blood).

The stage of the developed clinical picture includes following syndromes.

✓ Hyperplastic syndrome develops due to leukemic infiltration of soft tissues and characterized by an increase in lymph nodes, bone pain, heaviness and pain in the left and right hypochondrium, hepatosplenomegaly, development of ulcer-necrotic syndrome. Other symptoms may appear; such as headache, shortness of breath, cough, sciatica, etc. Hyperplastic syndrome includes next syndromes:

- lymphoplastic syndrome – enlargement of lymph nodes, tonsils;
- hepatolienal syndrome – enlargement of liver and spleen;
- osteoarticular syndrome – pain in bones and joints;
- ulcerative-necrotic syndrome – stomatitis, gingivitis, tonsillitis;
- neuroleucosis – focal neurological abnormalities, psychiatric desoders.

✓ Anemic syndrome: characterized by dizziness, flickering of flies before the eyes, shortness of breath during physical exertion, palpitations, noise in the head and ears – symptoms that are typical to anemia.

✓ Hemorrhagic syndrome (due to thrombocytopenia): skin hemorrhages, bleeding gums, nosebleeds, gastric, intestinal, renal, pulmonary, uterine, intracerebral hemorrhages.

✓ Tumor intoxication syndrome: is characterized by an increase in body temperature, weakness, changeability, lack of appetite, ossalgia. Such symptoms remind infectious diseases (flu, tuberculosis, sepsis, etc.).

✓ Intoxicative syndrome (due to break down of leukemic cells and cell degradation products poisoning). General weakness, tiredness, sleepiness, decreased appetite, loss of weight, nausea, vomiting, headache, fever, perspiration (particularly at night), depression.

✓ Immunodeficiency syndrome (due to significantly impaired cellular and humoral immunity related to functional inability of leucocytes): tonsilitis, pneumonia and other infections (bacterial, viral, fungal), which very often leads to the death of patients.

Acute leukemia is characterized by the development of manifestations in other organs and systems. Neuroleukemia is characterized by the development of leukemic

infiltration in the membranes and substance of the brain and spinal cord. There are several forms of neuroleukemia: meningeal, encephalic, meningoencephalic, diencephalic, polyradiculoneurotic, meningomyelic. In addition, leukemic infiltration of the brain, prostate, bladder, lesions of the gastrointestinal tract, esophagus, stomach, liver, kidneys, and heart may occur.

Changes in the mucous membrane of the oral cavity. Quite often, lesions of the mucous membrane of the oral cavity are the first signs of blood diseases (especially in the absence of obvious local causes of lesions). These symptoms should not be neglected, since timely diagnosis and complex treatment by a hematologist and dentist can prevent the development of more serious consequences on the mucous membrane (and not only on the mucous membrane of the mouth). Among the clinical manifestations hemorrhage, ulcer-necrotic lesions, hyperplasia and infiltration are common. The mucous membrane of the gums is swollen, hyperemic, and bleeds easily. Necrosis with the formation of painful ulcersin oral cavity is specific syndrome of leucaemia. Bleeding and ulcer-necrotic foci appear on the tongue and other areas of the oral cavity. Trauma provokes the appearance of elements of lesions. An ulcer in acute leukemia begins as a small area of necrosis surrounded by a bluish crown on the background of a pale mucous membrane. The process spreads quickly, and soon epithelial defects with a dirty-gray layering, distinguished by a foul rotten smell, appear near the teeth or in other areas. Painful ulcers spread along the teeth to the vestibule of the oral cavity, under the tongue, to the palate, and also to deeper tissues. Trauma, especially the extraction of a tooth, leads to heavy bleeding, and then to the formation of a deep ulcer. In acute leukemia, infiltration of the connective tissue of the gums by myeloid cells often occurs, because of this, the gums appear swollen and cover up to 2/3 of the crown of the tooth. Gum hyperplasia is also possible. An attempt to surgically cut off hyperplastic areas or infiltrates immediately causes bleeding, and later – the appearance of an ulcer. Deep tissue infiltration leads to periodontal damage and loose teeth. Histological studies reveal infiltration of the connective tissue by myeloid elements: large polygonal cells with an irregular nucleus. In chronic leukemias, the changes are less malignant. Myeloid leukemia begins slowly, imperceptibly. Later, abdominal pain, pale skin, weakness, exhaustion appear. A distinct symptom from the oral cavity is bleeding gums on the background of a bluish or pale swollen mucous membrane, which is combined with bleeding from other areas in the absence of inflammation. Ulcerations worsens the clinical picture. Lymphoid leukemia is accompanied by a significant increase in lymph nodes, as well as the formation of tumor-like nodes, or infiltrates, on the mucous membrane of the cheeks, tongue, brackets and palate. Infiltrated gums increase in size, covering the entire crown of the tooth. Ulcer-necrotic processes occur less frequently than in acute leukemias. Tooth extraction leads to heavy bleeding.

The diagnostic criteria for acute leucosis are investigation of peripheral blood and bone marrow punctate. The main criterion for acute leukemia is the presence of more than 30 % blast cells in the bone marrow (blastaemia). Their number can rise up to 80–90 % from all blood cells. In the aleukemic phase of leucaemia blasts may be absent in the blood. In such cases, the diagnosis is made based on the results of the bone marrow aspiration.

Total blood analysis usually shows:

1. Normochomic normocytic anemia.
2. Thrombocytopenia.
3. Changes of total amount white cells count (increasing or decreasing).
4. Blastemia (appearing of blast cells in bloodstream).
5. Decreasing of mature neutrophils.
6. Phenomenon of "hole".
7. Disappearing of eosinophils and basophils.
8. Increasing of ESR.

Bone marrow serves as a crucial diagnostic tool, offering material for cytological, cytogenetic, and immunological phenotyping analyses. In cases where marrow extraction proves challenging (known as dry tap), a trephine biopsy becomes necessary. Typically, the marrow exhibits hypercellularity, with leukaemic blast cells replacing normal elements to varying extents (typically exceeding 20 % of cells). The presence of Auer rods within blast cell cytoplasm signifies a myeloblastic type of leukemia. Occasionally, alongside blast cell infiltration, additional observations may include marrow fibrosis or necrosis. Myelogram data shows increased amount of blasts (up to 30 % and higher) and significant reduction of erythroid, granulocytic and megakariocytic hemopoetic lines. The main diagnostic criterion of acute leukemia is the presence of more than 30 % of blasts in the bone marrow.

Cytochemical diagnosis of acute leukemias. The type of acute leukemia is determined using a cytochemical study. A positive reaction to peroxidase indicates the presence of non-lymphoblastic leukemia, a negative one – acute lymphoblastic leukemia or acute undifferentiated leukemia. Cytochemical reactions make it possible to determine the substances involved in cellular metabolism. Evaluation of cytochemical reactions is carried out on the basis of counting 100 cells, taking into account the intensity of cytoplasmic staining according to a four-point system:

(++++) – intense color corresponds to high content;

(+++) – average;

(++) – moderate;

(+) – insignificant content of the substance in the cell.

A negative reaction is denoted as 0.

When carrying out cytochemical differentiation, the percentage of positively reacting cells and the average histochemical ratio (SHC) are determined. Diagnosis of certain forms of acute leukemia is carried out using determination of activity in blast cells of myeloperoxidase (MPO), alpha-naphthyl acetate esterase with sodium fluoride inhibitor, lipid and glycogen content (SHIK reaction).

Diagnostic criteria for chronic lymphocytic leukemia (CLL). The diagnosis is primarily based on the results of post-clinical observation of the patient and morphological analysis of peripheral blood smears. In the course of CLL, initial, advanced and terminal stages of the disease are distinguished.

The initial stage of CLL is characterized by moderate lymphadenopathy, the clinical manifestation develops slowly and imperceptibly. Complaints reveal asthenic syndrome. The disease at this stage is detected accidentally during a routine blood test, when an increase in the relative (40–50 %) and absolute number of lymphocytes

is detected with a slight leukocytosis. It should be emphasized that there are no "causeless" lymphocytes, and leukemic reactions of the lymphoid type (infectious asymptomatic lymphocytosis, lymphocytosis with whooping cough, rubella) are found only in children, infectious mononucleosis – a disease also mainly of young age – is diagnosed by the blood count. In which lymphocytes are found, which differ from the usual large size, a wide rim of cytoplasm around the nucleus and its brighter color. An increase in the absolute and relative number of lymphocytes should always alert the doctor. The majority of peripheral blood cells are represented by mature lymphocytes. Individual Botkin-Gumprecht shadows (semi-destroyed nucleus of lymphocytes with remnants of nucleoli) can also be detected. They form when a smear of blood is applied to a glass slide, when easily injured tumor lymphocytes are crushed, losing cytoplasm.

Advanced (pronounced clinical and hematological manifestations).

In this stage, asthenic complaints intensify. Characteristic lymphoproliferative syndrome: there is a generalized lesion of lymph nodes in the following sequence: first cervical, then axillary, then conglomerates of nodes appear in the mediastinum, in the abdominal cavity and inguinal areas. Lymph nodes have a pasty-elastic consistency. More often, they are painless, not welded together and with the skin, without ulcers and do not suppurate.

Characteristic hepatosplenomegalic syndrome. Changes in the lungs are manifested by frequent pneumonias and specific leukemic infiltration. The cardiovascular system, gastrointestinal tract, and genitourinary system are affected. In CLL, infiltration of the UIII pair of cranial nerves is often observed, with hearing loss, congestion, and tinnitus.

The terminal stage is characterized by exhaustion, a significant deterioration of the general condition, the development of complications, an increase in anemia (not only due to the suppression of erythropoiesis, but also due to the occurrence of cases of autoimmune hemolytic anemia), the appearance of hemorrhagic syndrome, a significant increase in lymph nodes and spleen, refractoriness to the therapy. The transition of CLL to the terminal stage is often accompanied by sarcomatous growth in the lymph node.

Such lymph nodes begin to grow rapidly, acquire a stony density, infiltrate and squeeze neighboring tissues, causing swelling and pain syndrome. Often, sarcoid growth in the lymph nodes is accompanied by an increase in temperature. Sometimes such nodes are located in the subcutaneous tissue of the face, trunk, limbs, under the mucous membrane in the oral cavity, nose, and the vessels that develop in them give them the appearance of hemorrhages. One of the manifestations of the terminal stage of the disease can be severe renal failure as a result of infiltration of the parenchyma of the organ by tumor cells. Herpetic infection is a serious, often fatal complication.

In the clinical picture 2 syndromes are distinguished:

1. lymphoproliferative, caused by lymphadenopathy, splenomegaly and lymphoid proliferation of the bone marrow:

a) general symptoms caused by intoxication, the growth of leukemic cells in the bone marrow, spleen (itching, fever, sweating, pain in the bones, spleen and liver);

b) hepato- and splenomegaly;

c) leukemic infiltrates in the skin (leukemias);

d) symptoms are associated with an increase in regional lymph nodes (mediastinal, mesenteric);

e) characteristic changes in bone marrow and peripheral blood.

2. Syndrome of complications:

a) purulent-inflammatory;

b) autoimmune (autoimmune hemolytic anemia, autoimmune thrombocytopenia).

Direct causes of death of patients with CLL are most often intercurrent infection, severe anemia, hemorrhages in vital organs and intoxication.

Diagnosis of CLL. Leukocytosis with absolute lymphocytosis in the blood

More than 30 % of lymphocytes in the bone marrow punctate with diffuse lymphoid hyperplasia in the bone marrow trepanation. Enlargement of the lymph nodes and spleen is an optional symptom of CLL, but when these organs are involved in the process, a diffuse proliferation of lymphocytes is observed. An additional diagnostic feature is Huprecht's shadow in a blood smear.

The treatment of leukemia includes pathogenetic therapy and symptomatic therapy.

- Treatment regimen.
- Cytostatic therapy.
- Detoxification therapy.
- Prevention of blast crisis syndrome.
- Immunotherapy.
- Bone marrow transplantation.
- Treatment of infectious complications.
- Treatment of anemia.
- Treatment of hemorrhagic syndrome.
- Treatment of cytostatic disease.

The treatment regimen involves admission to the specialize hematology department, where the diagnosis is verified and complex inpatient treatment is carried out. It is important that patients should be in an aseptic ward to prevent infectious complications.

Pathogenetic therapy. The aim of treatment is to destroy the leukaemic clone of cells without destroying the residual normal stem cell. Chemotherapy should contain different stages:

A. Remission induction – at the first attack of acute leukemia and relapses, various combinations of drugs are prescribed for 4–6 days. In this phase, the mass of the tumour cells are destroyed by combination chemotherapy. The patient has a period of severe bone marrow hypoplasia, requiring intensive medical support and inpatient care.

B. Consolidation (consolidation) of remission – 2–3 courses of treatment with those drugs that caused remission. If remission has been achieved by induction therapy, residual disease is attacked by therapy during the consolidation phase. It contains a number of courses of chemotherapy. Despite therapy being carried out, some patients have poor results which causes stem cell transplant.

C. Anti-relapse therapy (remission maintenance therapy) is carried out during the entire period of remission. It contains repeating cycle of drug administration. This may last up to 3 years if relapse does not occur and is usually given on an outpatient basis.

Induction of remission in acute lymphocytic leukemia:

- Vincristine (0,1 % 1 ml) by 2 ml (2 mg) daily i/v.
- Prednisolone (0,005 g) by 60 mg/m^2 daily per os.
- L-asparaginase (10000 IU) by 6000 IU/m^2 daily i/v.
- Rubomycin 50mg/m^2 daily i/v.

Supporting therapy:

- Mercaptopurine 60 mg/m^2 daily per os.
- Methotrexate 20 mg/m^2 1 time in a week per os.

Induction of remission in acute myeloid leukemia «7+3»:

- Cytarabine (1000 mg in a vial) 100 mg/m^2 2 times in a day i/v.
- Rubomycin 45 mg/m^2 daily i/v.

Supporting therapy:

- Cytarabine (1000 mg in a vial) 100 mg/m^2 2 times in a day i/v.
- Cyclophosphamide (1000 mg in a vial) 1000 mg/m^2 in a day i/v.

Degree of effect	Clinical status	Hemogram	Myelogram
Complete clinical and hematological remission	Normalization (at least 1 month)	Normal data	Presence of blast cells no more than 5 %
Incomplete clinical and hematological remission	Normalization	Normal data	Presence of blast cells no more than 25 %
Clinical and hematological improvement	Significant improvement (more than 50 %)	Hb ≥ 90 g/l; mature granulocytes ≥ 2 x 10^9/l; platelets ≥ 50 x 10^9/l	
No effect	Progression of leukemia or worse results than with clinical and hematological improvement		

The role of the dentist in the treatment of leucaemia. First of all, it is sanitation of the oral cavity. It provides full treatment and removal of crushed teeth, dental plaque, treatment of periodontal diseases or existing lesions of the oral mucosa. In addition, replacement of poorly supplied fillings, prostheses, metal prostheses made of different metals, etc. is carried out. Such sanitation allows you to eliminate many factors that injure or irritate the mucous membrane of the mouth. It also significantly reduces the amount of microflora in the oral cavity, which can also be the cause of inflammation. Elimination of foci of infectious processes from the body during sanitation of the oral cavity significantly reduces the possibility of sensitization of the body, allergic reactions and diseases of internal organs. Timely treatment during remediation of dystrophic inflammatory diseases of the periodontium and inflammatory lesions of the oral mucosa is a reliable method of prevention, because mucosal lesions that "trigger" and then support the activity of systemic lesions of the body, diseases of internal organs, and blood are much less likely to occur in a sanitized oral cavity primarily due to its high functional load.

Prognosis. Survival of patients with acute leukaemia without treatment is about 5 weeks. This period can be extended to a number of months with supportive treatment. Patients who achieve remission with specific therapy have a better

prognosis. Around 80 % of adult patients under 60 years of age with leucaemia achive remission. Remission rates are lower for older patients. However, the relapse rate continues to be high.

7. Practical skills:

- carry out a clinical examination of hemato-oncological diseases;
- draw up a plan for examination of hemato-oncological diseases;
- identify the main syndromes of the patient's disease on the basis of complaints, anamnesis, objective examination data;
- analyze the results of laboratory and instrumental investigations;
- formulate a clinical diagnosis according to the classification;
- carry out a differential diagnosis of hemato-oncological diseases;
- draw up a treatment plan for hemato-oncological diseases according to treatment standards.

8. Questions for control of knowledge.

1. Definition of hemoblastosis.
2. The main clinical symptoms of hemoblastosis.
3. Methods of diagnosis of hemoblastosis.
4. Complication of hemoblastosis.
5. Principles of hemoblastosis treatment.
6. Lifestyle with hemoblastosis.
7. Prevention of hemoblastosis.

9. Tests for self-assessment of knowledge.

1. Which of the following factors doesn't cause leukemia?

A. Frequent operative interventions.
B. Ionizing radiation.
C. Retroviral infection.
D. Genetic defects and chromosomal abnormalities.
E. Chemicals.

2. Which of the following symptoms of leukemia is not included in the hyperplastic syndrome?

A. Increase in lymph nodes.
B. Neuroleukosis.
C. Paleness of the skin.
D. Appearance of leukemia.
E. Hepatosplenomegaly.

3. Which of the following are specific indicators for blast crisis?

A. The number of blasts in the peripheral blood or in the bone marrow >30 %.
B. The presence of intermediate forms of formed elements in the peripheral blood.
C. There are no blasts in the peripheral blood.
D. The number of blasts in the bone marrow is <5%.
E. Agranulocytosis.

4. Which of the following is the phenomenon of "leukemic failure"?

A. The presence of blast cells, intermediate cells and differentiated cells in the peripheral blood.

B. The presence of intermediate cells and differentiated cells in the peripheral blood, in the absence of blast cells.

C. The presence of blast cells and differentiated cells in the peripheral blood, in the absence of intermediate cells.

D. The presence of blast cells and intermediate cells in the peripheral blood, in the absence of differentiated cells.

E. The presence of differentiated cells in the peripheral blood, in the absence of intermediate and blast cells.

5. Which of the following causes the intoxication syndrome in leukemia?

A. Intradermal hemorrhages.
B. An increase in the liver and spleen.
C. The development of kidney failure.
D. A decrease in the number of erythrocytes.
E. Increased decay of leukemic cells.

6. A 20-year-old patient underwent a course of polychemotherapy for acute lymphoblastic leukemia. which of the following morphological pattern of blood can indicate the onset of complete clinical and hematological remission?

A. Content of blast cells up to 15 %.
B. Content of blast cells up to 1 %.
C. Content of blast cells up to 10 %.
D. Content of blast cells up to 5 %.
E. Absence of blast cells.

7. A 42-year-old man complains of weakness, palpitations, nosebleeds, and hemorrhages on the skin. The condition progressively worsens over the course of a month. On examination, the condition is serious, there are petechial and spotty hemorrhages on the skin of the limbs and torso, the lymph nodes are not palpable, pulse is 116/min, the liver is +2 cm, the spleen is not palpable. In the blood: severe pancytopenia. Which of the following can be suspected first?

A. Hemorrhagic vasculitis.
B. Posthemorrhagic anemia.
C. Hypoplastic anemia.
D. Hemolytic anemia.
E. Acute leukemia.

8. The most likely cause of anemia in a patient with leukemia is which of the following:

A. Violation of porphyrin metabolism.
B. Myelofibrosis.
C. Folic acid deficiency.
D. Autoimmune hemolysis.
E. Suppression and displacement of normal hematopoietic tissue.

9. Which of the following is neuroleukemia?

A. Infiltration of leukemic cells of the nervous system.
B. Development of solid tumors such as sarcomas.
C. Enlarged mediastinal lymph nodes.
D. Appearance of likemides.
E. Terminal stage of myeloid leukemia.

10. Which of the following is ossalgia?

A. Sore throat.
B. Neutrophilia.
C. Pain in the joints.
D. Bone pain.
E. Erythrocytosis.

11. Which of the following changes in the hemogram are characteristic of chronic lymphocytic leukemia?

A. Increased content of lymphocytes in peripheral blood.
B. An increase in the content of leukocytes in peripheral blood.
C. Decrease in the number of peripheral blood monocytes.
D. Neutrophil leukocytosis.
E. Lymphopenia.

12. Which of the following are Humprecht's shadows?

A. Altered erythrocytes.
B. Destroyed monocytes.
C. Half-destroyed lymphocytes.
D. Half-destroyed nuclei of lymphocytes.
E. Nuclei of erythrocytes.

13. Which of the following diseases is characterized by the presence of the "Philadelphia chromosome"?

A. Chronic lymphocytic leukemia.
B. Chronic myeloleukosis.
C. B12-folate deficiency anemia.
D. Infectious mononucleosis.
E. Myeloma disease.

14. Which of the following conditions is most characteristic of chronic lymphocytic leukemia in the initial stage of the disease?

A. Anemia.
B. Lymphadenopathy.
C. An increase in the size of the liver.
D. Splenomegaly.
E. Thrombocytopenia.

15. Which of the following are leukemias?

A. Skin infiltration by leukemic cells
B. Abscesses
C. Cells of leucolysis
D. Rheumatic nodules
E. Xanthomas

Answers:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
A	*C*	*A*	*D*	*E*	*D*	*E*	*E*	*A*	*D*	*A*	*D*	*B*	*B*	*A*

10. References and recommended reading

1. Внутрішня медицина: підручник / К.О. Бобкович, Є.І. Дзись, В.М. Жебель та ін.; під. ред. М.С. Расін. Вінниця: Нова Книга, 2015. 328 с.

2. Harrison's Principles of Internal Medicine: 19th Edition. 262e Chemical Terrorism / Charles G. Hurst, Jonathan Newmar, James A. Romano, Jr.: 2015 by McGraw-Hill Education.

Навчальне видання

ГЕМАТООНКОЛОГІЧНІ ХВОРОБИ

Методичні вказівки
для проведення практичного заняття
здобувачів вищої освіти 4-го року навчання

Упорядники Капустник Валерій Андрійович
Садовенко Ольга Леонідівна
Шелест Борис Олексійович
Бабічева Олександра Олександрівна

Відповідальний за випуск О.Л. Садовенко

Комп'ютерний набір О.Л. Садовенко
Комп’ютерна верстка М.Ю. Орлова

Формат А5. Ум. друк. арк. 1,0. Зам. № 24-34382.

Редакційно-видавничий відділ
ХНМУ, пр. Науки, 4, м. Харків, 61022
izdatknmurio@gmail.com
vid.redact@knmu.edu.ua

Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготівників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.