

**MINISTRY OF HEALTHCARE OF UKRAINE
HSEEU "Ukrainian Medical Stomatological Academy"**

"Approved"

at the meeting of internal
medicine №1 department

Head of Department

Prof. Skrypnyk I.M.

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**GUIDELINES
FOR STUDENTS
INDEPENDENT WORK
IN THE PRACTICAL CLASSES PREPARING**

<i>Academic discipline</i>	Internal medicine
<i>Module</i>	Basics of Internal Medicine
<i>Content module</i>	Fundamentals of diagnostics, treatment and prevention of hematological diseases
<i>Study subject</i>	Acute leukemias
<i>Course</i>	IV
<i>Faculty</i>	Of foreign students training

The subject of the lesson: Acute Leukaemias

Educational goal:

The student must know:

1. Aetiology and pathogenesis of Acute Leukaemias.
2. Clinical symptoms of Acute Leukaemias.
3. Modern classification of Acute Leukaemias.
4. Methods of diagnostics of Acute Leukaemias.
5. Methods of treatment of Acute Leukaemias.

The student must be able:

1. To choose the symptoms of Acute Leukaemias from the history data.
2. In examination of the patient to choose the symptoms of Acute Leukaemias.
3. To make the scheme of investigation for the determination Acute Leukaemias.
4. To define the cause and the severity of Acute Leukaemias.
5. To assess the haemologic study results.
6. To determinate the treatment of patients with Acute Leukaemias depending on the types and degree of the disease. To estimate the efficacy of the therapy.
8. To prescribe the proper treatment for the patient with Acute Leukaemias.

The main problems of the lesson:

1. Pathogenesis of Acute Leukaemias.
2. Clinical symptoms of Acute Leukaemias.
3. Modern classification of Acute Leukaemias.
4. Methods of diagnostics of Acute Leukaemias.
5. Differential diagnosis of Myeloid and Lymphoid Acute Leukemias.
5. Treatment of Acute Leukaemias.

The aim: The students must be able to diagnose Acute Leukaemias, determine the types, severity, and prescribe the proper treatment.

Topicality: The incidence of leukaemia of all types in the population is approximately 10/100 000 per annum, of which just under half are acute leukaemia. Males are affected more frequently than females, the ratio being about 3:2 in acute leukaemia, 2:1 in chronic lymphocytic leukaemia and 1.3:1 in chronic myeloid leukaemia.

CONTENTS OF THE TRAINING MATERIALS Leukaemias are malignant disorders of the haematopoietic stem cell compartment, characteristically associated with increased numbers of white cells in the bone marrow and/or peripheral blood.

The cause of the leukaemia is unknown in the majority of patients. Factors, which are associated with the development of leukaemia: Ionising radiation, Cytotoxic drugs, Exposure to benzene in industry, Genetic, Immunological.

Leukemias were originally termed acute or chronic based on life expectancy but now are classified according to cellular maturity.

Leukaemias are traditionally classified into four main groups:

- acute lymphoblastic leukaemia (ALL)
- acute myeloid leukaemia (AML)
- chronic lymphocytic leukaemia (CLL)
- chronic myeloid leukaemia (CML).

In acute leukaemia there is proliferation of primitive stem cells leading to an accumulation of blasts, predominantly in the bone marrow, which causes bone marrow failure. In chronic leukaemia the malignant clone is able to differentiate, resulting in an accumulation of more mature cells.

Acute leukemias are malignant disorders of the haematopoietic stem cell with increase of proliferation and accumulation of predominantly immature, poorly differentiated cells (usually blast forms).

Acute leukemia occurs when a hematopoietic stem cell undergoes malignant transformation into a primitive, undifferentiated cell with abnormal longevity.

Symptoms have usually been present for only days to weeks before diagnosis. The most common:

Anemia - pallor, fatigue, tachycardia, chest pain

Infection as a result of granulocytopenia - fever, malaise, weight loss

Bleeding: petechiae, easy bruising, epistaxis, bleeding gums, or menstrual irregularity. Hematuria and GI bleeding are uncommon.

Bone marrow and periosteal infiltration may cause bone and joint pain, especially in children with ALL.

Initial CNS involvement or leukemic meningitis (manifesting as headaches, vomiting, irritability, cranial nerve palsies, seizures, and papilledema) is uncommon.

Extramedullary infiltration by leukemic cells may cause lymphadenopathy, splenomegaly, hepatomegaly, and leukemia cutis (a raised, nonpruritic rash).

Diagnosis - CBC and peripheral smear - pancytopenia and peripheral blasts, Blast cells in the peripheral smear may approach 90%, unless the WBC count is markedly decreased; Blast cells in the bone marrow are 20 - 95%.

Histochemical studies, cytogenetics, immunophenotyping, and molecular biology studies - Specific B-cell, T-cell, and myeloid-antigen monoclonal antibodies, together with flow cytometry, are very helpful in classifying ALL vs AML, which is critical for treatment.

Management of Leukaemias - The aim of treatment of Leukaemias is to destroy the leukaemic clone of cells without destroying the residual normal stem cell compartment from which repopulation of the haematopoietic tissues will occur.

There are three phases: Remission induction; Remission consolidation; Remission maintenance.

Although basic principles in treating ALL and AML are similar, the drug regimens differ. The complex nature of patients' clinical situations and the available treatment protocols necessitate an experienced team. Whenever possible, patients should be treated at specialized medical centers, particularly during critical phases (remission induction).

Specific therapy (Chemotherapy) - is generally aggressive, has a number of side effects, and may not be appropriate for the very elderly or patients with other serious disorders.

DRUGS COMMONLY USED IN THE TREATMENT OF ACUTE LEUKAEMIA

Phase	ALL	AML
Induction	Vincristine (i.v.)	Daunorubicin (i.v.)
	Prednisolone (oral)	Cytarabine (i.v.)
	L-asparaginase (i.m.)	Etoposide (i.v. and oral)
	Daunorubicin (i.v.)	
	Methotrexate (intrathecal)	
Consolidation	Daunorubicin (i.v.)	Cytarabine (i.v.)
	Cytarabine (i.v.)	Amsacrine (i.v.)
	Etoposide (i.v.)	Mitoxantrone (i.v.)
	Methotrexate (i.v.)	
Maintenance	Prednisolone (oral)	
	Vincristine (i.v.)	
	Mercaptopurine (oral)	
	Methotrexate (oral)	

Disease which relapses during treatment or soon after the end of treatment carries a poor prognosis and is difficult to treat. The longer after the end of treatment that relapse occurs, the more likely it is that further treatment will be effective.

Supportive therapy

Anaemia is treated with packed RBC transfusions (red cell concentrate infusions) to maintain Hb above 100 g/l.

Bleeding - Transfusions of platelets, RBCs, and granulocytes are administered as needed in patients with bleeding, anemia, and neutropenia, respectively.

Infection - Fever ($> 38^{\circ}\text{C}$) lasting over 1 hour in a neutropenic patient (absolute neutrophil count $< 1.0 \times 10^9/\text{l}$) indicates possible septicaemia. Granulocyte transfusions may help neutropenic patients with gram-negative or other serious sepsis but have no proven benefit as prophylaxis. Parenteral broad-spectrum antibiotic therapy is essential.

Metabolic problems Continuous monitoring of renal, hepatic and haemostatic function is necessary, together with fluid balance monitoring. Renal toxicity occurs with some antibiotics and antifungal agents. Cellular breakdown during induction therapy increases uric acid production, which may cause renal failure. Allopurinol and intravenous hydration are given to try to prevent this, along with close monitoring of biochemistry.

Psychological support

Tests for the determining of basis knowledge

Tests of the 2 level.

1. The most common symptoms of Acute leukemias are:

- A. fever, malaise, weight loss
 - B. petechiae, easy bruising, epistaxis,
 - C. pallor, fatigue, tachycardia
 - D. all of above
2. Symptoms of bone marrow failure in patients with Acute leukemias include all, except:
- A. bone pain
 - B. multiple ecchymoses
 - C. fatigue
 - D. fever
3. Leukostasis is:
- A. leukemic gap
 - B. palpable lymphadenopathy
 - C. respiratory distress and altered mental status due to markedly elevated WBC counts
 - D. gingivitis due to neutropenia with swollen gums

Recommended literature for students:

A. Main:

1. Davidson's Principles and practice of medicine (21st revised ed.) / by Colledge N.R., Walker B.R., and Ralston S.H., eds. – Churchill Livingstone, 2010. – 1376 p.
2. Harrison's Principles of Internal Medicine, 19th Edition / by Longo D.L., Kasper D.L., Jameson J.L. et al. (eds.). – McGraw-Hill Professional, 2015. – 4012 p.
3. The Merck Manual of Diagnosis and Therapy (nineteenth Edition)/ Robert Berkow, Andrew J. Fletcher and others. – published by Merck Research Laboratories, 2011.

B. Additional:

1. H.Loffler, J.Rastetter, T.Haferlach. 6th edition. Atlas of clinical hematology. Springer Berlin Heidelberg New York, 2006, - 429 p.

Composed by

as. Lymanets T.V.