The subject of the lesson: Acute Leukaemias

Educational goal:
The student must know:
1. Etiology and pathogenesis of Acute Leukaemias.
2. Clinical symptoms 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.
5. Differential diagnosis of Myeloid and Lymphoid Acute Leukemias.
1. 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.
Acute myeloid leukemia (AML) is a neoplastic disease characterized by infiltration of the blood, bone marrow, and other tissues by proliferative, clonal undifferentiated cells of the hematopoietic system. The main diagnostic criteria is the presence blast cells more than 20% in the bone marrow. To differentiate myeloblasts immunophenotype and cytochemistry are used.

**Classification.** French-American-British (FAB) classification:

<table>
<thead>
<tr>
<th>FAB classification of acute myeloblastic leukaemia</th>
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<tbody>
<tr>
<td><strong>M0</strong> Acute myeloblastic leukaemia with minimal differentiation</td>
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<tr>
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**M0** Acute myeloblastic leukaemia with minimal differentiation

**M1** Acute myeloblastic leukaemia without maturation

**M2** Acute myeloblastic leukaemia with maturation

**M3** Promyelocytic leukaemia

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*Photo courtesy of: Acute myeloid leukemia pathophysiology, 2012*
**Physical Findings.** Fever, splenomegaly, hepatomegaly, lymphadenopathy, sternal tenderness, and evidence of infection and hemorrhage are often found at diagnosis. Significant gastrointestinal bleeding, intrapulmonary hemorrhage, or intracranial hemorrhage occurs most often in APL. Bleeding associated with coagulopathy may also occur in monocytic AML and with extreme degrees of leukocytosis or thrombocytopenia in other morphologic subtypes. Retinal hemorrhages
are detected in 15% of patients. Infiltration of the gingivae, skin, soft tissues, or meninges with leukemic blasts at diagnosis is characteristic of the monocytic subtypes and those with 11q23 chromosomal abnormalities.

Gingivitis in patient with AML M5.    Unexplained bruising

Hemorrhagic syndrome: petechias

**Hematologic Findings** Anemia is usually present at diagnosis and can be severe. The degree varies considerably, irrespective of other hematologic findings, splenomegaly, or duration of symptoms. The anemia is usually normocytic normochromic. Decreased erythropoiesis often results in a reduced reticulocyte count, and red blood cell (RBC) survival is decreased by accelerated destruction.
The median presenting leukocyte count is about 15,000/μL. Between 25 and 40% of patients have counts <5000/μL, and 20% have counts >100,000/μL. Fewer than 5% have no detectable leukemic cells in the blood. The morphology of the malignant cell varies in different subsets. In AML, the cytoplasm often contains primary (nonspecific) granules, and the nucleus shows fine, lacy chromatin with one or more nucleoli characteristic of immature cells. Abnormal rod-shaped granules called Auer rods are not uniformly present, but when they are, myeloid lineage is virtually certain. Poor neutrophil function may be noted functionally by impaired phagocytosis and migration and morphologically by abnormal lobulation and deficient granulation.

Platelet counts <100,000/μL are found at diagnosis in ~75% of patients, and about 25% have counts <25,000/μL. Both morphologic and functional platelet abnormalities can be observed, including large and bizarre shapes with abnormal granulation and inability of platelets to aggregate or adhere normally to one another.

Treatment of the newly diagnosed patient with AML is usually divided into two phases. The initial goal is to induce complete remission.

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. The most commonly used remission induction regimens consist of combination chemotherapy with cytarabine and an anthracycline (e.g., daunorubicin, idarubicin, mitoxantrone). “7+3” regimen: cytarabine standard dose (100–200 mg/m²) administered as a continuous intravenous infusion for 7 days and daunorubicin (60–90 mg/m²) or idarubicin (12 mg/m²) intravenously on days 1, 2, and 3.

Anaemia is treated with packed RBC transfusions (red cell concentrate infusions) to maintain Hb above 100 g/l. Bleeding – transfusions of platelets are administered.

Infection – fever (> 38°C) lasting over 1 hour in a neutropenic patient (absolute neutrophil count < 1.0×10⁹/l) indicates febrile neutropenia. Parenteral broad-spectrum antibiotic therapy is essential.

Psychological support.

Acute lymphoid leukemias (ALLs) are predominantly cancers of children and young adults. The L3 or Burkitt’s leukemia occurring in children in developing countries seems to be associated with infection by the Epstein-Barr virus (EBV) in infancy. However, the explanation for the etiology of more common subtypes of ALL is much less certain. Childhood ALL occurs more often in higher socioeconomic subgroups. Children with trisomy 21 (Down’s syndrome) have an increased risk for childhood ALL. The main diagnostic criteria is the presence blast cells more than 20% in the bone marrow. To differentiate lymphoblasts immunophenotype and cytochemistry are used.

Classification. French-American-British (FAB) classification (see the next page):
Clinically cannot be differentiated from AML.

**Treatment** also consists of induction and postremission management (remission consolidation and maintenance). Hoelzer-based protocols are used. Induction of remission: prednisolone 60 mg/m² orally during 28 days, vincristine 2 mg/day IV on the 1, 8, 15, 22 days, daunorubicine 45 mg/m²/day IV infusion on the 1, 8, 15, 22 days, L-asparaginase 5000 U/m²/day IV infusion every other day since 15th till 28th days. Additionally, for CNS (central nervous system) injury prophylaxis methotrexate 15 mg intrathecal on the 1st day.

**Tests for the determining of basis knowledge**

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. “7+3” chemotherapy regimen for treatment of AML consists of:
A. cytarabine + idarubicine
B. imatinib
C. vincristine + prednisolone
D. cyanocobalamin + folic acid

**Recommended literature for students:**


