

## CLINICAL-LABORATORY DIAGNOSTICS OF ACUTE LEUKEMIAS

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Acute leukemias are characterized by a common feature of immature cells, such as blasts or undifferentiated cells, as the substrate. The types of acute leukemias are named after the simple plurals of the cells of origin of myeloblasts, erythroblasts, lymphoblasts, and others. Acute leukemias with undifferentiated blast cells that cannot be identified morphologically are called undifferentiated acute leukemias.

The classification of acute leukemias is based on morphological information of blast cells, cytokine properties (1, 2 tables), cytogenetic and molecular genetic research, and immunophenotypic information (3, 4 tables).

Table 1. Limfoblasts of cytochemical character

Research	Result
Myeloperoxidase	negative
Sudanese black (lipids)	Negative
PAS reaction (with glycosaminoglycan Schiff reactant)	positive, large grain
$\alpha$ -naphthyl esterase	Negative
Chloroatsetate esterase	Negative

Table 2. Cytochemical description of small species of acute myeloid leukemia according to Franco-American-British classification (English FAB)

Acute mieloblast	Myeloperoxidase	Sudan Black	Nonspecific esterase
M0	negative	negative	negative
M1	Positive	Positive	negative
M2	Positive	Positive	negative
M3	Positive	Positive	negative
M4	Positive	Positive	Positive
M5	negative	negative	Positive
M6	negative	negative	negative
M7	negative	negative	negative

Table 3. By immunological characteristics of leukemia

Immunophenotypic classification of the European group

Immunological small group	Immunophenotype properties
Acute lymphoblast leukemia from B-cell predecessors	CD19 <sup>+</sup> , va/or CD79a <sup>+</sup> , va/or CD22 <sup>+</sup>
B-I (pro-B)	No antigen for differentiating B-cells(HLA-DR, TdT, CD34)
B-II (common B)	CD10 <sup>+</sup>

B-III(pre-B)	cyIgm <sup>+</sup>
B-IV(mature b)	cyIg or sIgk <sup>+</sup> , or λ <sup>+</sup> , or sIgM <sup>+</sup>
Acute lymphoblastic leukemia from T-cell predecessors	Cytoplasmic or Superficial CD3 <sup>+</sup>
TI(pro-T)	CD7 <sup>+</sup>
T-II( pro-T)	CD2 <sup>+</sup> ,va/or CD5 <sup>+</sup> ,and/or CD8 <sup>+</sup>
T III(cortical T)	CD1a <sup>+</sup>
T-IV(mature T)	TCR α/β +, TCR γ/δ+

Table 4. Phenotypical properties of acute myeloblastic leukemia subtypes.  
Franco-American-British Classification (English. FAB)

Acute myeloleycosis small group	Common phenotype	Features
M0 D.F. document edited	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD34 <sup>+</sup> , CD117 <sup>+</sup> , CD7 <sup>-/+</sup> , TdT <sup>-/+</sup>	Blast - 90%, low-value blast population; SS and FS, CD2 can be expressed as lymphoid markers, D4, CD7, CD10
M1	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD34 <sup>+</sup> (weaker than M0), CD117 <sup>+</sup> , CD7 <sup>-/+</sup> , TdT <sup>-/+</sup> , CD15 <sup>-/+</sup>	Blasts - 90%
M2	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD117 <sup>+</sup> , CD34 <sup>+</sup> , TdT <sup>-/+</sup> , CD15 <sup>+</sup> , CD65 <sup>-/+</sup> , CD11b <sup>+// -</sup>	Blasts- 90%, with possible weakening CD19 expression
M3	MPO <sup>+</sup> , HLA-DR-, CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD34 <sup>-/+</sup> , CD117 <sup>-/+</sup> , CD15 <sup>+</sup> , CD2 <sup>-/+</sup>	Characterized by blasts High Side Propasian Values (except for CD2 <sup>+</sup> HLA-DR <sup>-</sup> )
M4	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD117 <sup>-/+</sup> , CD15 <sup>+</sup> , CD14 <sup>-/+</sup> , CD34 <sup>-/+</sup> , CD38 <sup>+</sup> , CD4 <sup>-/+</sup> , CD11b <sup>-/+</sup> , CD64 <sup>+</sup>	CD2 expression correlates With option M4E0
M5	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD117 <sup>-/+</sup> , CD15 <sup>+</sup> , CD14 <sup>-/+</sup> , CD36 <sup>+</sup> , CD11b <sup>-/+</sup> , CD11c, CD4 <sup>-/+</sup>	Large blasts, possible expression of CD56
M6	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD117 <sup>-/+</sup> , CD34 <sup>-/+</sup> , CD38 <sup>+</sup> , CD71 <sup>+</sup> , CD235 <sup>+</sup> (glycoforin LEKIN)	There is often CD7 expression
M7	MPO <sup>+</sup> , HLA-DR <sup>+</sup> , CD13 <sup>+</sup> , CD33 <sup>+</sup> , CD117 <sup>-/+</sup> , CD34 <sup>-/+</sup> , CD38 <sup>+</sup> , CD61 <sup>+</sup> , HLA-DR <sup>-/+</sup> , CD41 <sup>+</sup> , CD42b <sup>+</sup>	Platelet adhesion blasts can disrupt research results

#### Classification of acute lymphoblastic leukemia.

In the cell proliferation process, acute lymphoblastic leukemia has the following types (cytogenetic small groups):

- t (9; 22) (q34; q11); BCR / ABL;

- t (v; 11q23); MLL reformation;
- t (1; 19) (q23; p13); E2A / PBX1;
- t (12; 21) (q23; p13); ETV / CBF-a.

Acute lymphoblastic leukemia / Burkitt lymphoma (M3 according to the Franco-American-British classification).

Risk factors are used to determine the treatment strategy for acute lymphoblastic leukemia.

The following are risk factors:

leukocytosis over  $30 \times 10^9 / l$  for acute lymphoblastic leukemia

$100 \times 10^9 / l$  for B type and T type;

T (4; 11) / MLL presence;

$\geq 3$  - chromosome aberrations;

hypodiploidy (less than 46 chromosomes);

immunophenotypic variants B-I, T-I, T-IV;

absence of remission after the first phase of induction (if there are no regressions on day 21 of treatment);

neutoleukemia.

If at least one symptom is present, the patient is considered high-risk, otherwise standard-risk. If there is no remission in the patient after the first phase of induction, regardless of other signs, the patient is assigned to the high-risk group.

Morphological classification of acute myeloid leukemia:

M0. Acute undifferentiated myeloid leukemia.

M1. Acute myeloid leukemia that has not yet matured.

M2. Acute myeloid leukemia that has matured.

M3. Acute promyelocytic leukemia.

M3 (low variant). Granulocytic acute promyelocytic leukemia.

M4. Acute myelomonocytic leukemia.

M4. Acute myelomonocytic leukemia with eosinophilia.

M5. Acute monocytic leukemia.

M5a. Acute monoblastic leukemia.

M5b. Acute promonocytic-monocytic leukemia.

M6. Acute erythroblastic leukemia.

M7. Acute megakaryoblastic leukemia.

The WHO classification divides all acute myeloid leukemias into cytogenetic and molecular genetic characteristics, and precisely these characteristics form clinical and pathological groups.

Acute myeloid leukemia with stable translocations (AML).

● AML with t (8; 21) (q22; q22) translocation; RUNX1-RUNX1T1.

● AML with inv (16) (p13.1q22) ort (16;16) (p13.1; q22) translocation; CBFB-MYH11.

- AML with t (9;11) (p22; q23) translocation; MLLT3-MLL.
  - AML with t (6;11) (q27; q23) translocation; MLLT4-MLL.
  - AML with t (11;19) (q23; p13.3) translocation; MLL-MLLT1.
  - AML with t (11;19) (q23; p13.1) translocation; MLL-ELL.
  - AML with inv (3) (q21q26.2) or t (3;3) (q21; q26.2) translocation; RPN1-EVI1.
  - AML with t (1;22) (p13; q13) translocation (megakaryoblastic); RBM15-MKL1.
  - AML with NPM1 mutation; AML with CEBPA mutation (alkylating agents, topoisomerase II inhibitors, ionizing radiation).
- AML that does not respond to the above measures.
- AML with minimal differentiation.
  - AML with differentiation markers.
  - Acute myelomonocytic leukemia.
  - Acute monoblastic or monocytic leukemia.
  - Acute erythroid leukemia.
  - Acute megakaryoblastic leukemia.
  - Acute basophilic leukemia.
  - Acute panmyelosis with myelofibrosis.
  - Myeloid sarcoma.
  - Myeloid tumors associated with Down syndrome.
  - Acute leukemia of unknown etiology.
  - Acute undifferentiated leukemia.
  - Mixed phenotype acute leukemia and t (9; 22) (q34; q11.2); BCR-ABL1.
  - Mixed phenotype acute leukemia and t (v; 11q23); MLL reformation.
  - Mixed phenotype acute leukemia, B / myeloid.
  - Mixed phenotype acute leukemia, T / myeloid.

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