Diyala University – collage of medicine

Hematology -5th stage

Lec 9

ACUTE LEUKEMIA CLASSIFICATION

DR.ZAHRAA NAJAH

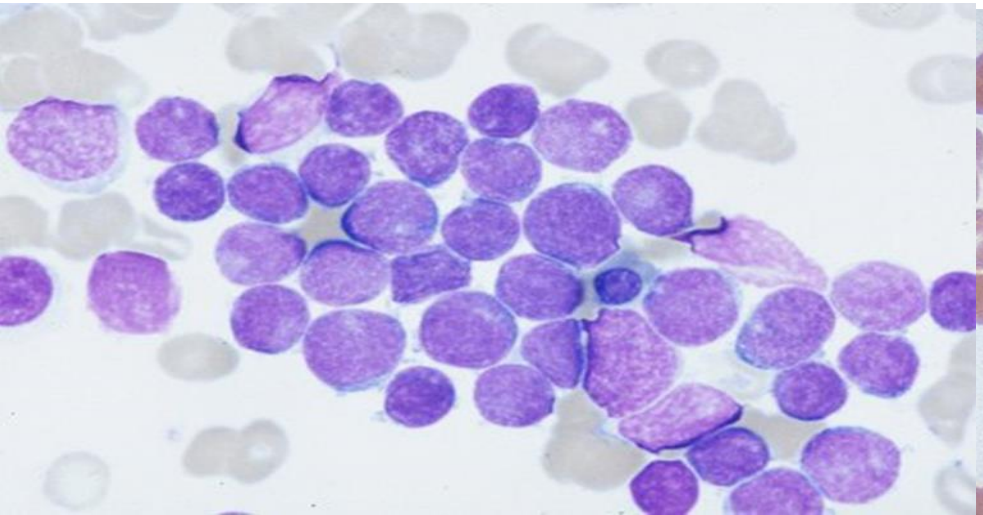
CLASSIFICATION is based on:

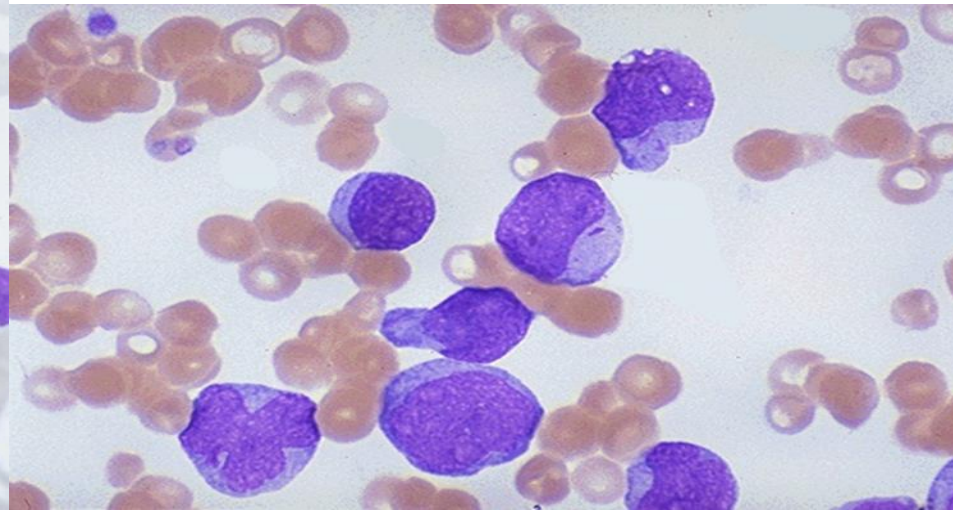
1. **Morphology of blasts.**
2. **Cytochemistry: SBB, PAS, MPO, …etc.**
3. **Immunophenotyping (by flowcytometry)**
4. **Genetic analysis includes : Cytogenetic techniques and Molecular genetic techniques**

- **(FAB)** classification is based mainly on morphology of the blasts, and on use of special stains (cytochemistry) and limited use of monoclonal markers in special situations (immunophenotyping).

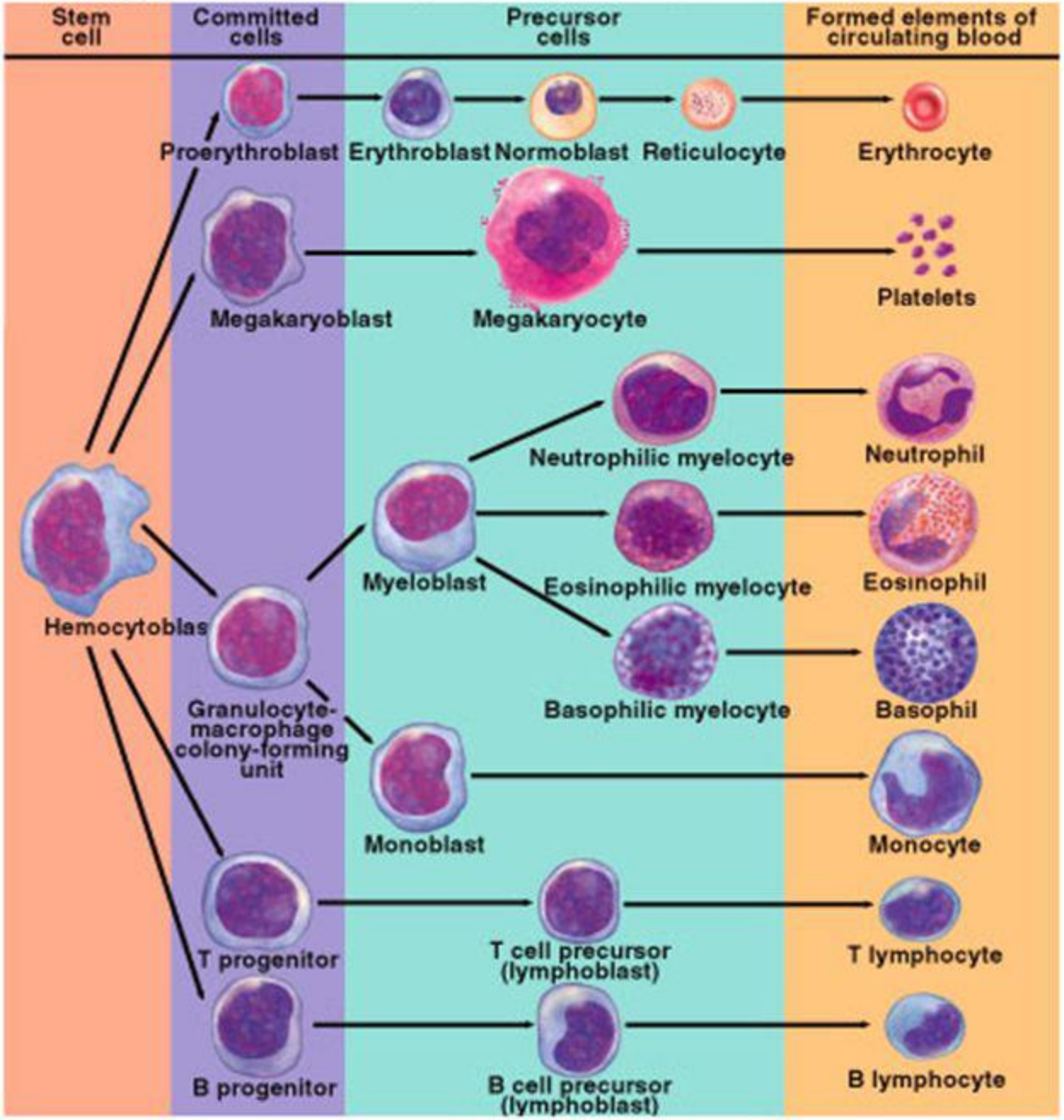
Differentiated AML from ALL

- **ALL(Lymphoblast)**
  - **Blast size** :small
  - **Cytoplasm**: Scant
  - **Chromatin**: Dense
  - **Nucleoli** :Indistinct
  - **Auer-rods**: Never present
- **AML (Myeloblast**
  - Large
  - Moderate
  - Fine, Lacy
  - Prominent
  - Present in 50%





Hemopoiesis



Acute myeloid leukemia

- four times more common than acute lymphoblastic leukemia (ALL) in adults.
- In children, the proportions are reversed, the lymphoblastic variety being more common.
- Considerable heterogeneity between cases, with respect to morphology, immunological phenotype, associated cytogenetic and molecular abnormalities and other.

- **Specific manifestation :**
  - Gum hypertrophy more common in certain subtypes of AML (monocytic AML M4 & M5)
  - Hepatosplenomegaly
  - Skins deposit
  - Lymphadenopathy
  - Renal damage
  - DIC : Disseminated intravascular coagulation, usually accompanied by skin and mucosal hemorrhage due to consumption of platelets and clotting factors, is a frequent presenting feature of acute promyelocytic leukemia

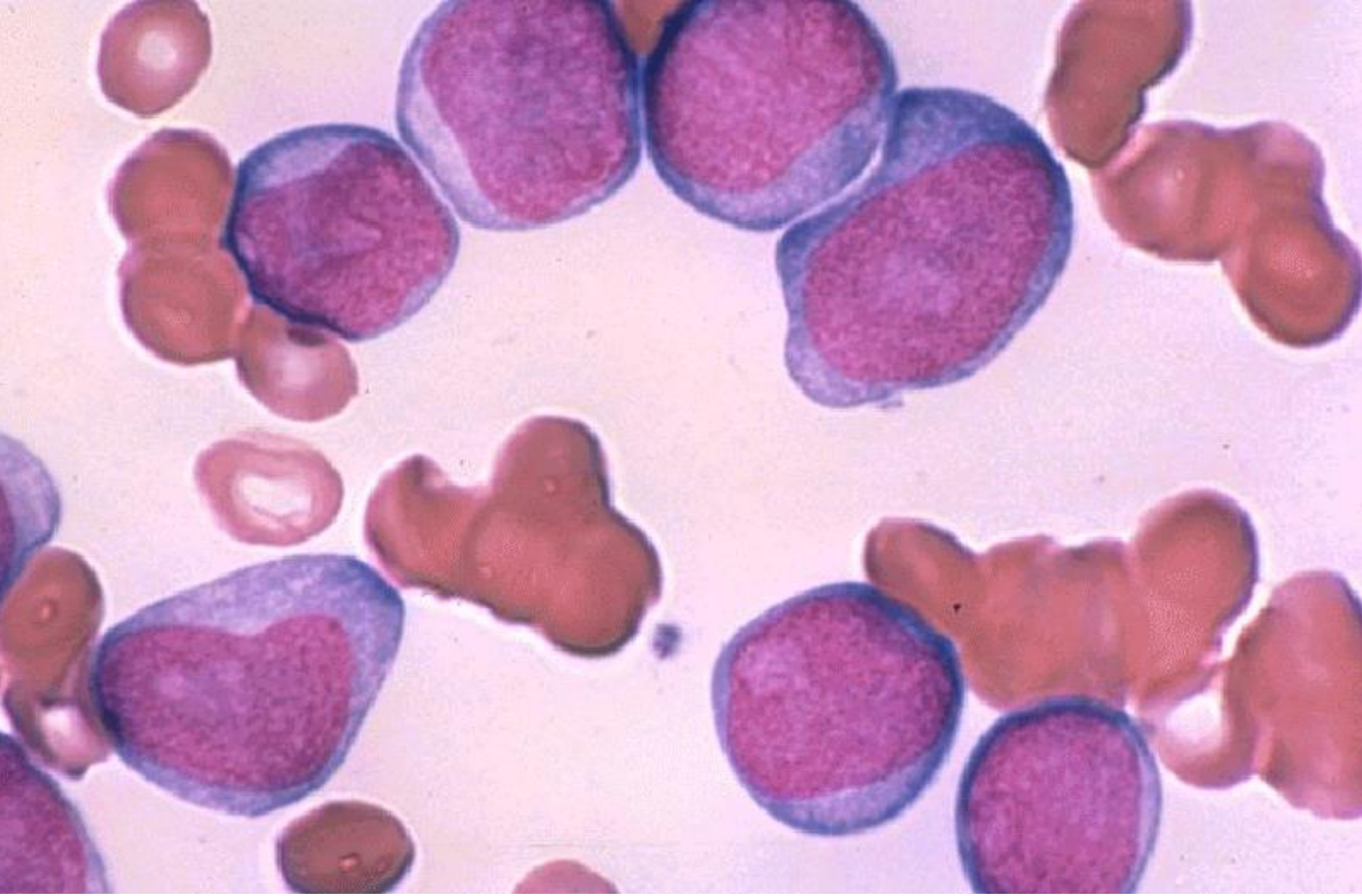
WHO Classification of AML

Acute myeloid leukemia (AML) and related neoplasms

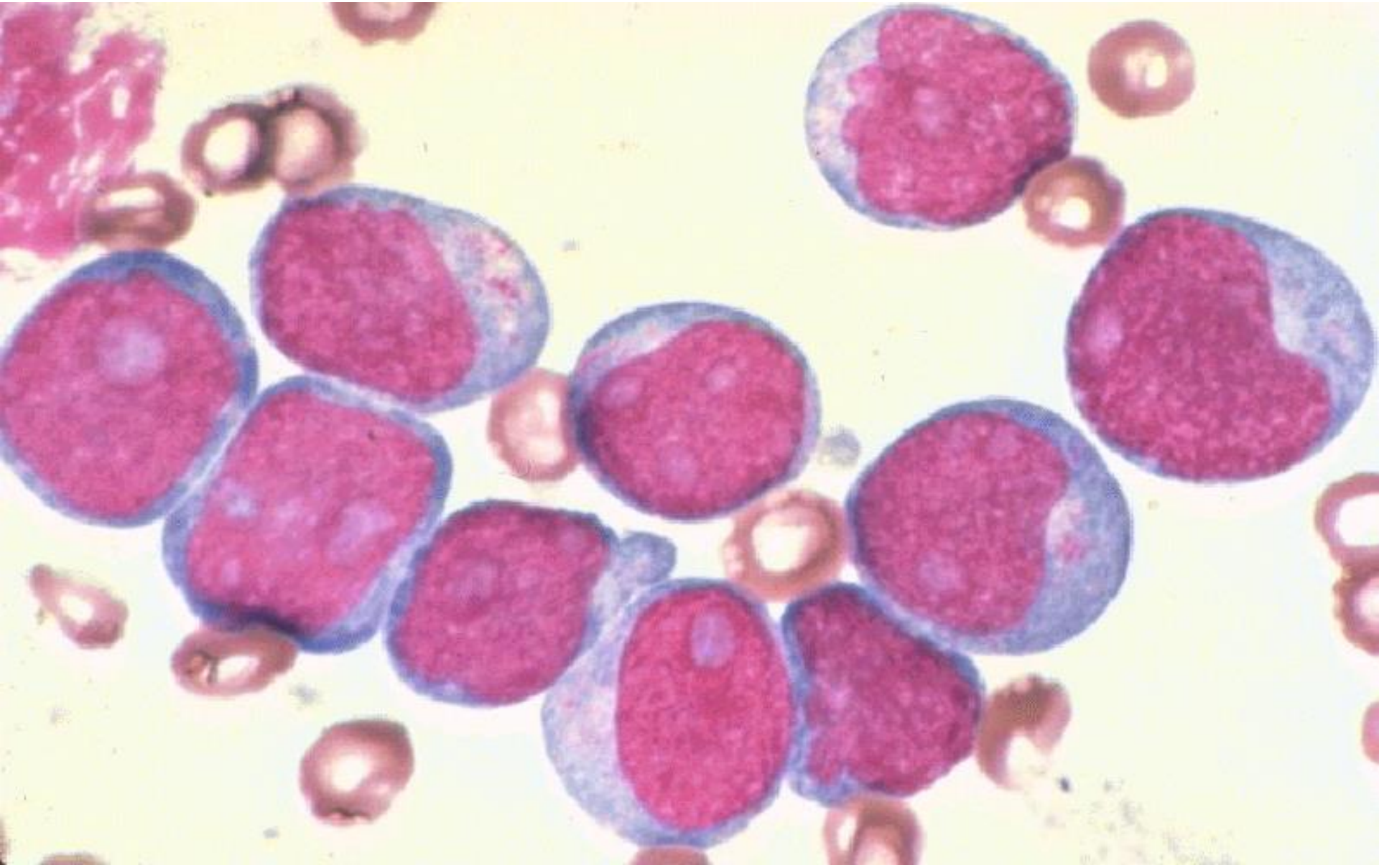
- AML with recurrent genetic abnormalities
  - AML with t(8;21)(q22;q22.1);*RUNX1-RUNX1T1*
  - AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22);*CBFB-MYH11*
  - APL with *PML-RARA*
  - AML with t(9;11)(p21.3;q23.3);*MLLT3-KMT2A*
  - AML with t(6;9)(p23;q34.1);*DEK-NUP214*
  - AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*
  - AML (megakaryoblastic) with t(1;22)(p13.3;q13.3);*RBM15-MKL1*
  - *Provisional entity: AML with BCR-ABL1*
  - AML with mutated *NPM1*
  - AML with biallelic mutations of *CEBPA*
  - *Provisional entity: AML with mutated RUNX1*
- AML with myelodysplasia-related changes
- Therapy-related myeloid neoplasms
- AML, NOS
  - AML with minimal differentiation
  - AML without maturation
  - AML with maturation
  - Acute myelomonocytic leukemia
  - Acute monoblastic/monocytic leukemia
  - Pure erythroid leukemia
  - Acute megakaryoblastic leukemia
  - Acute basophilic leukemia
  - Acute panmyelosis with myelofibrosis

French-American-British (FAB) classification of AML

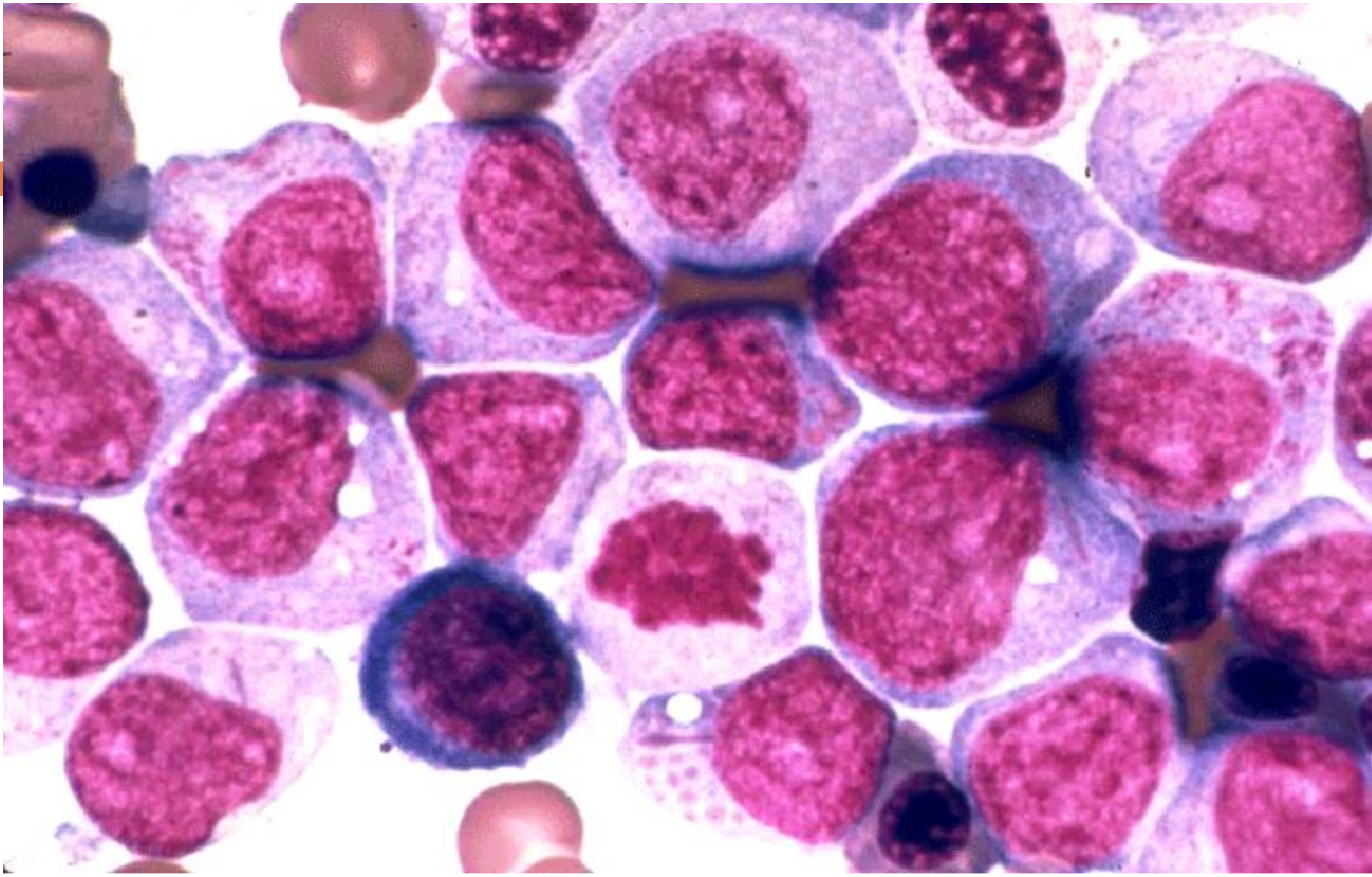
		Cytogenetics
M0	undifferentiated	
M1	Without maturation	
M2	With maturation	t(8; 21)
M3	Acute promyelocytic	t(15; 17)
M4	acute Myelomonocytic leukemia	inv(16)
M5	acute monoblastic (M5a) or monocytic (M5b) leukemia	
M6	acute leukemia with at least 50% erythroblasts in the bone marrow	
M7	Megakaryoblastic	



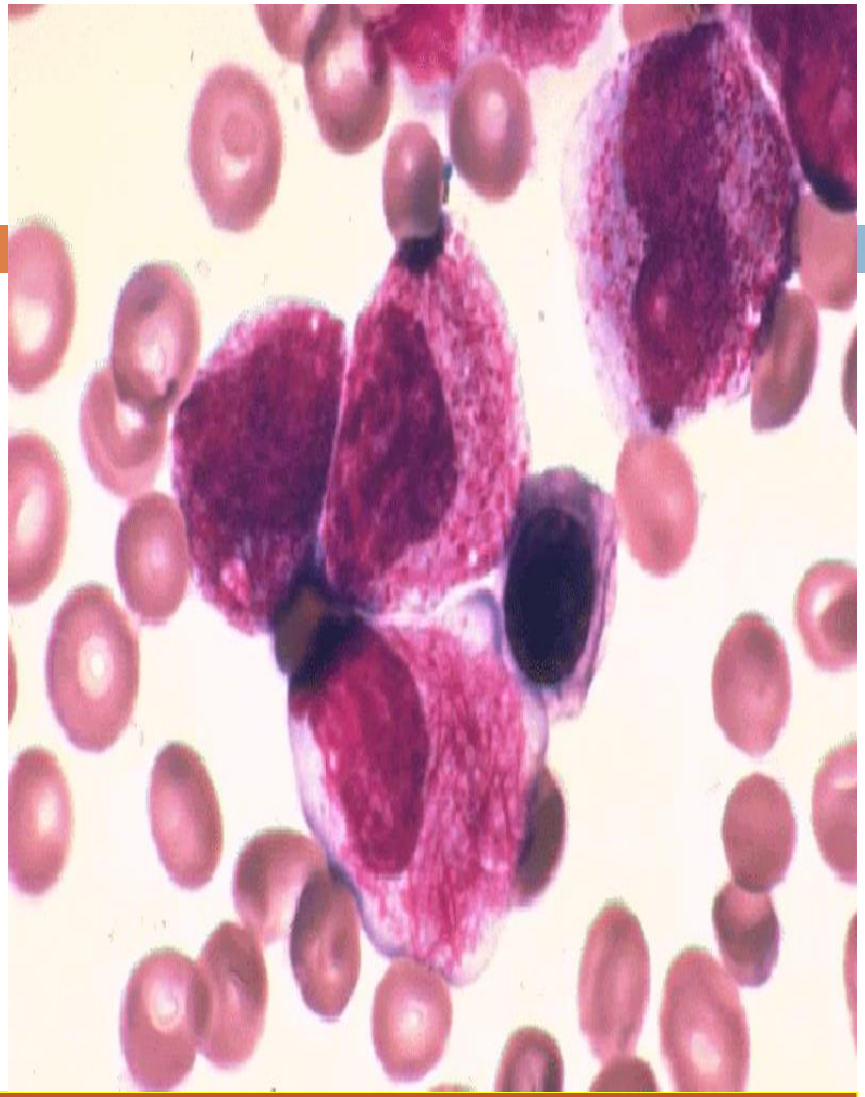
AML M0: with minimal evidence of differentiation



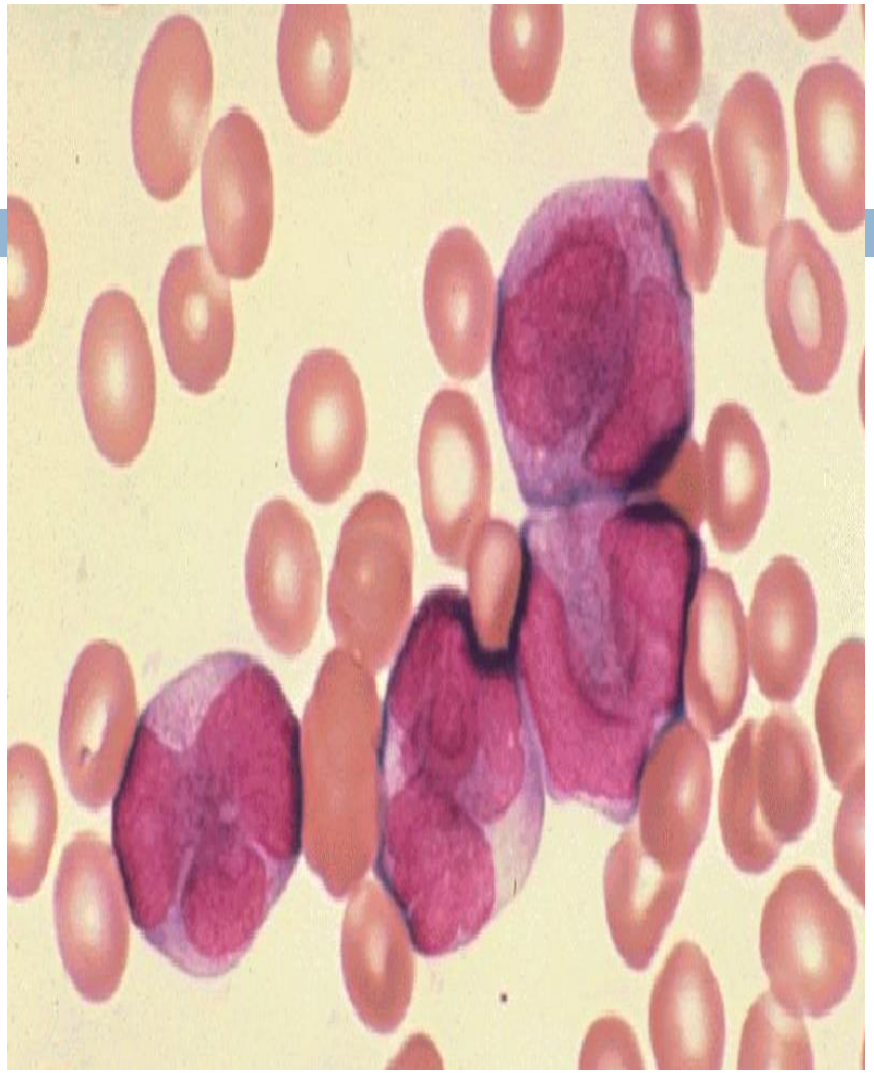
AML M1: without maturation



AML M2: with maturation



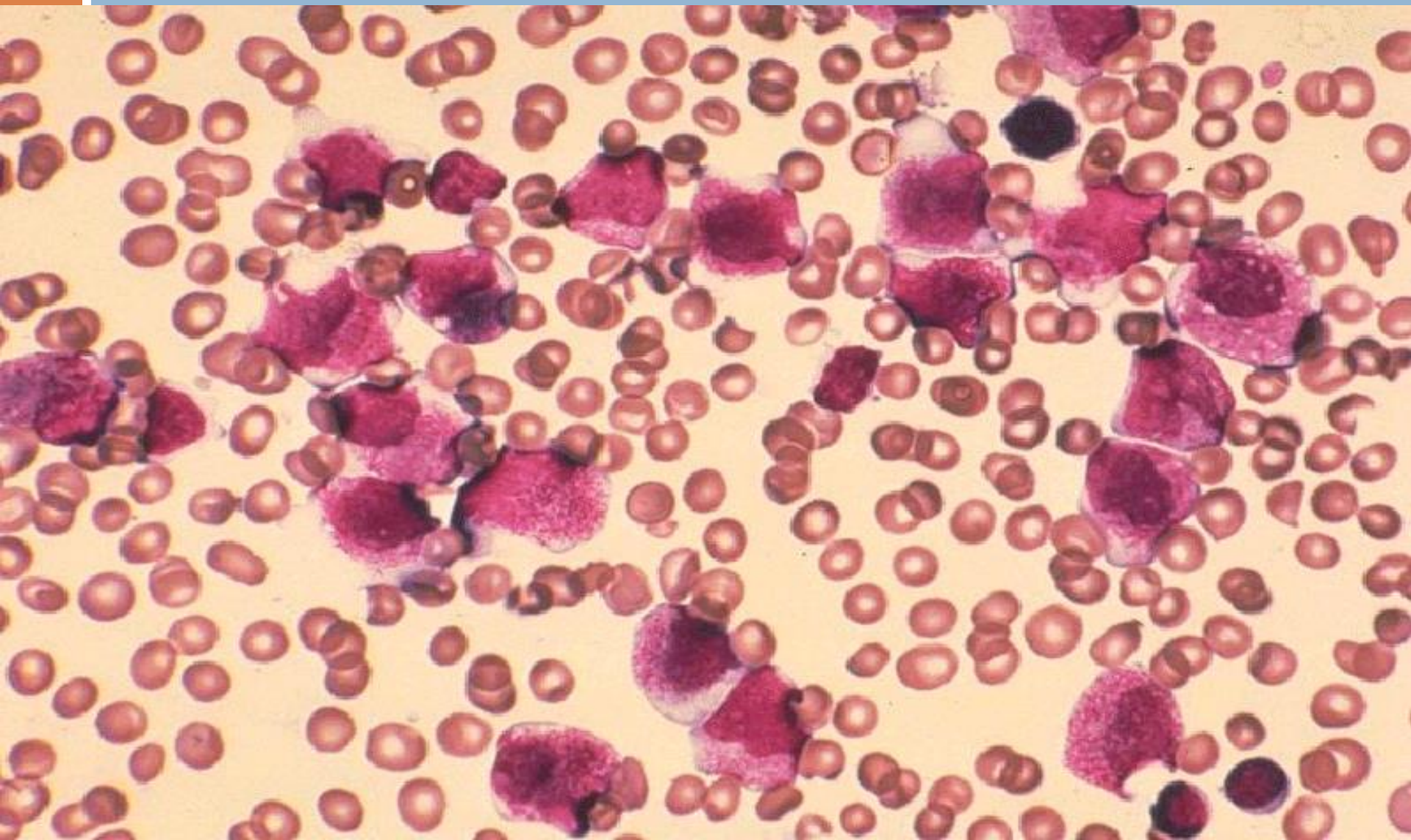
Classical M3 hypergranular

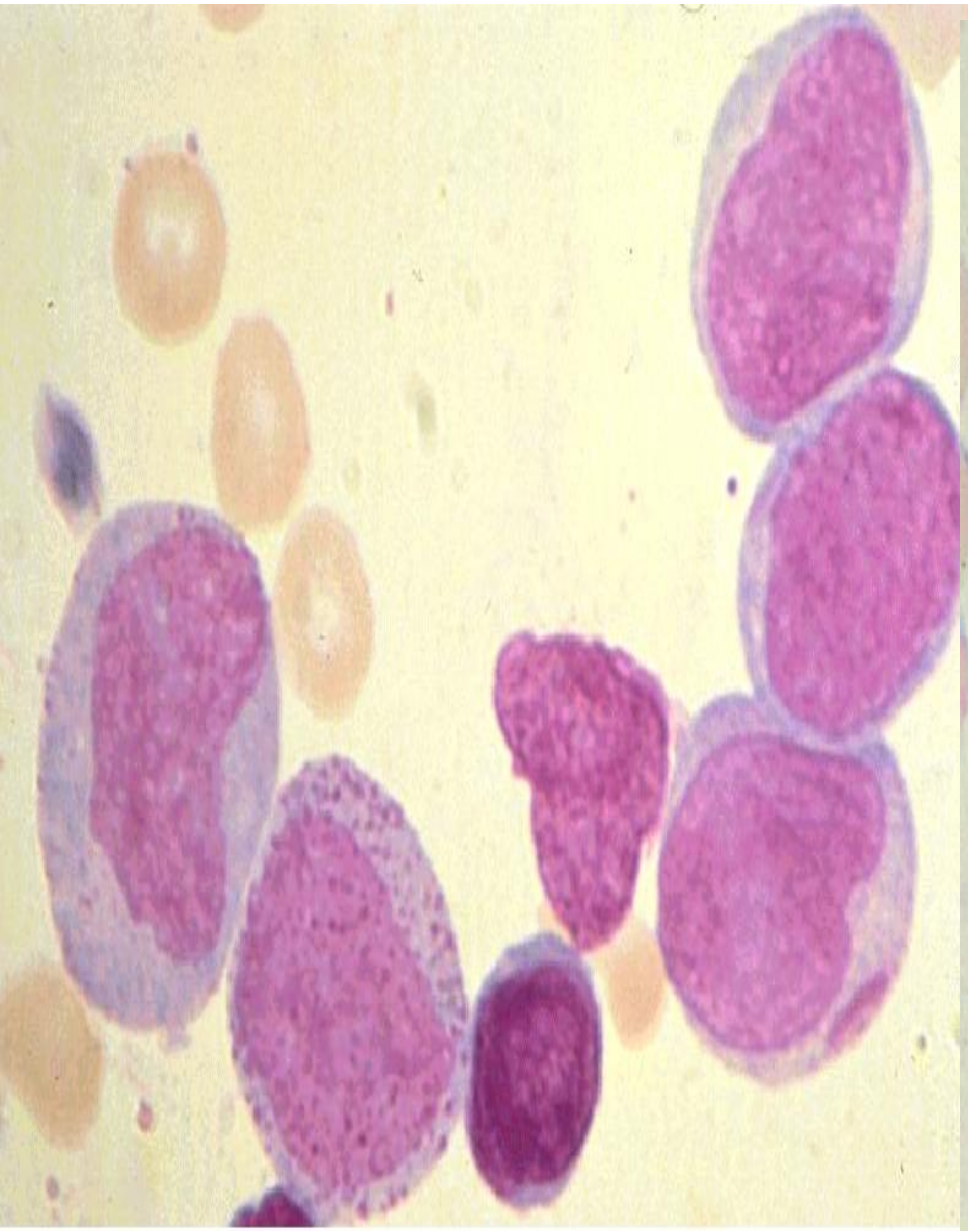


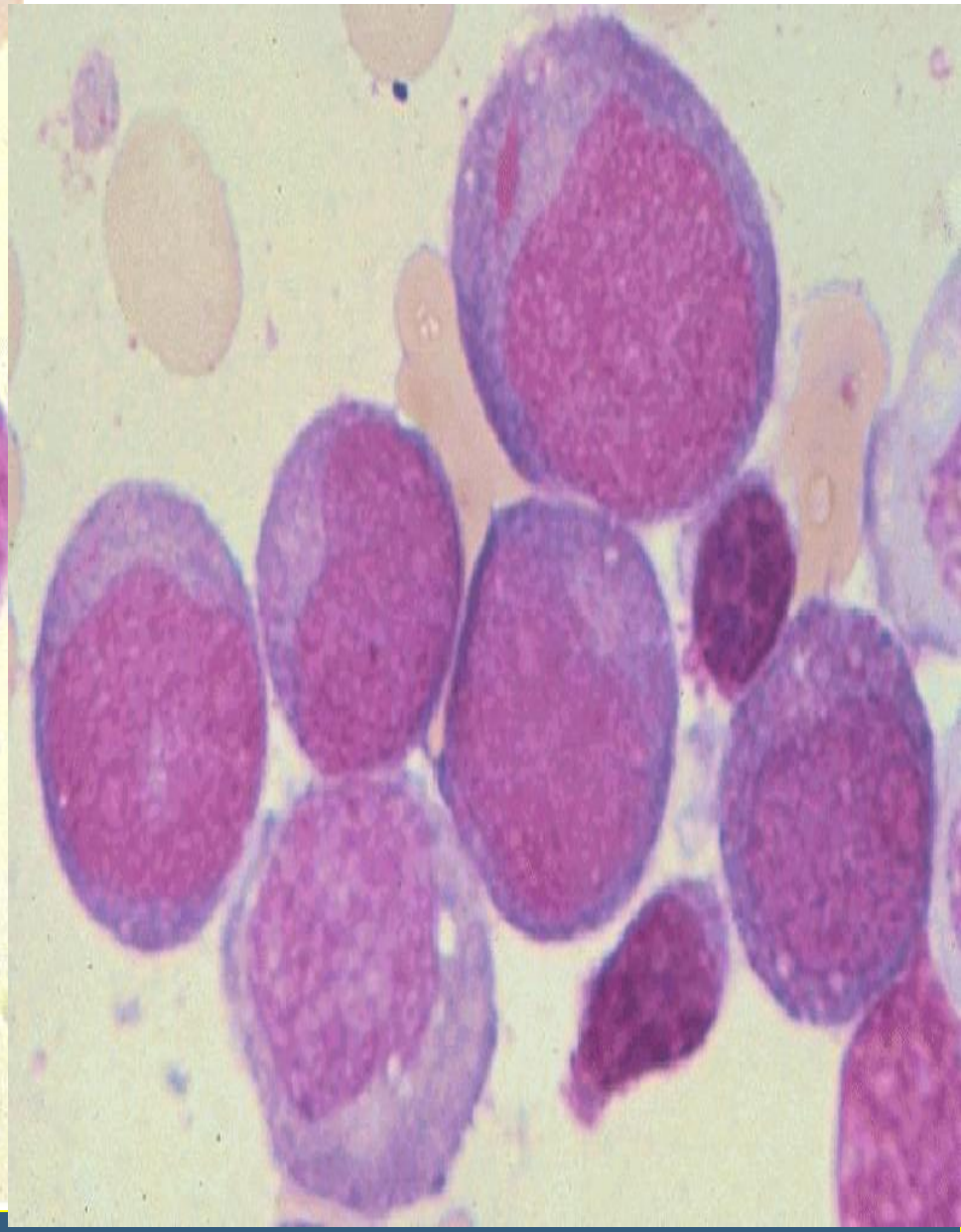
M3 variant hypogranular

AML M3: Acute Promyelocytic Leukemia

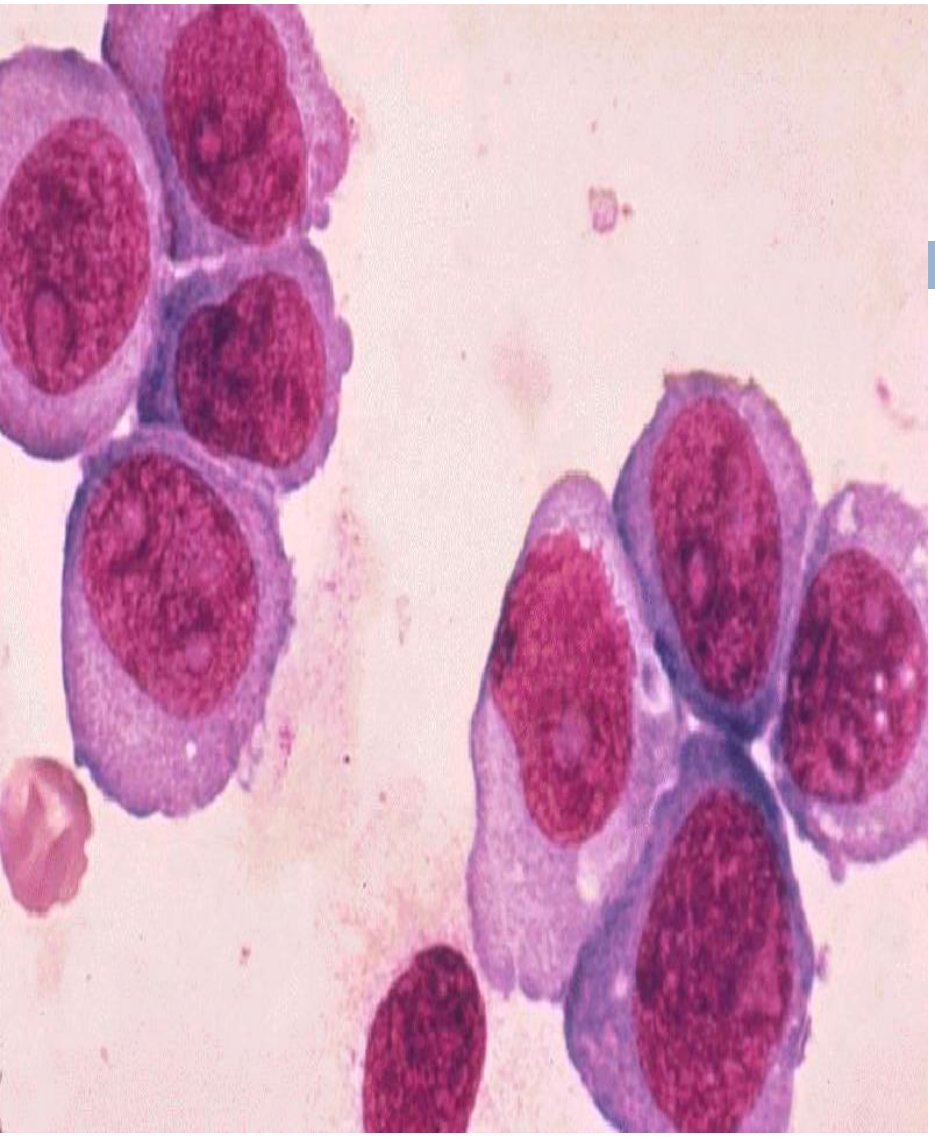
AML M3 (Classical)



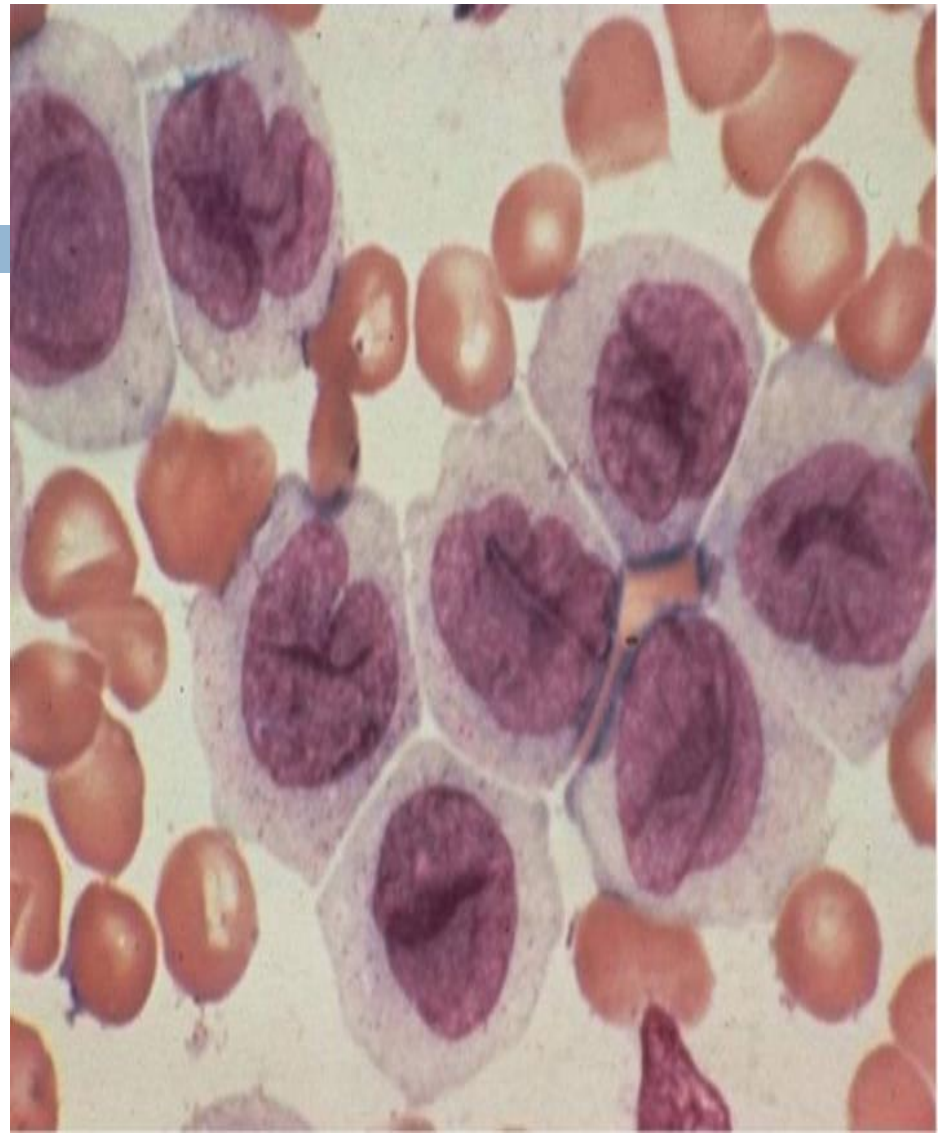




AML M4: acute myelomonocytic leukemia

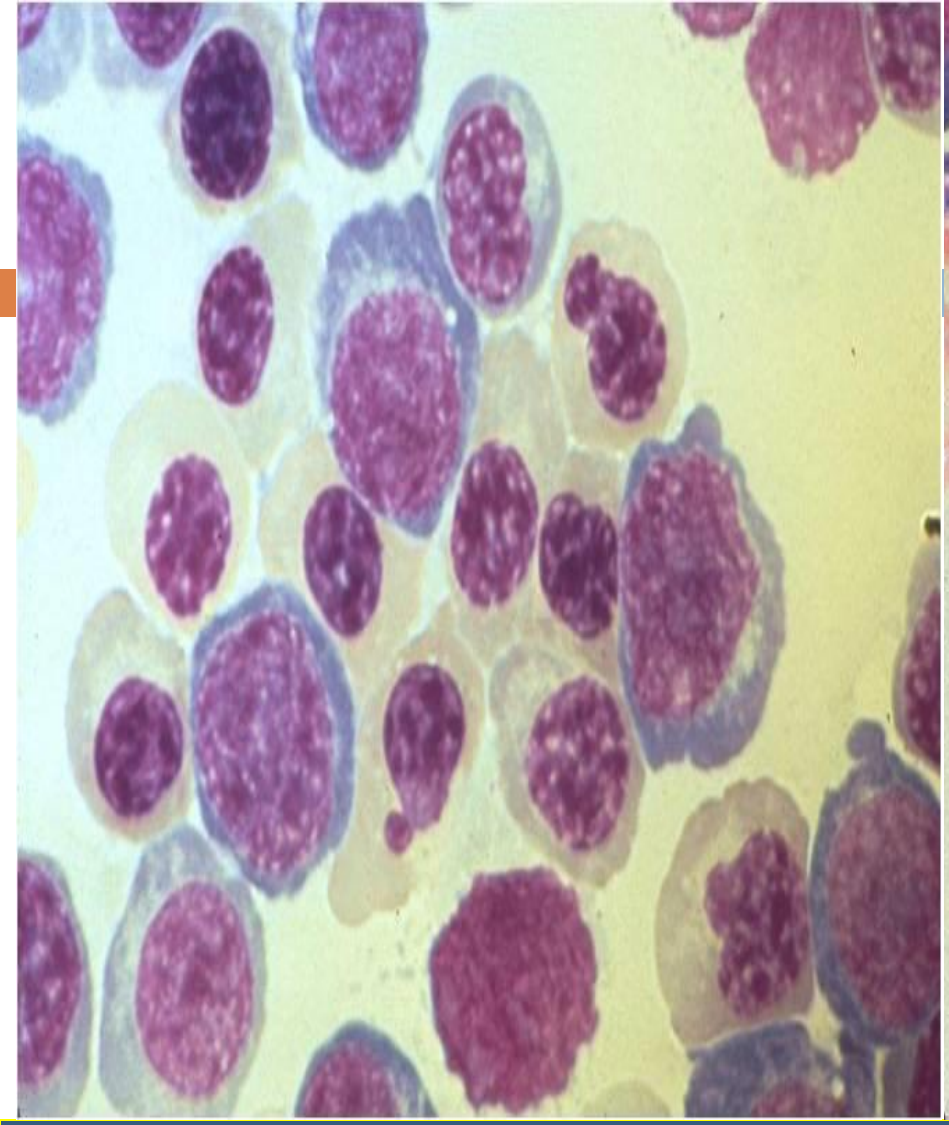


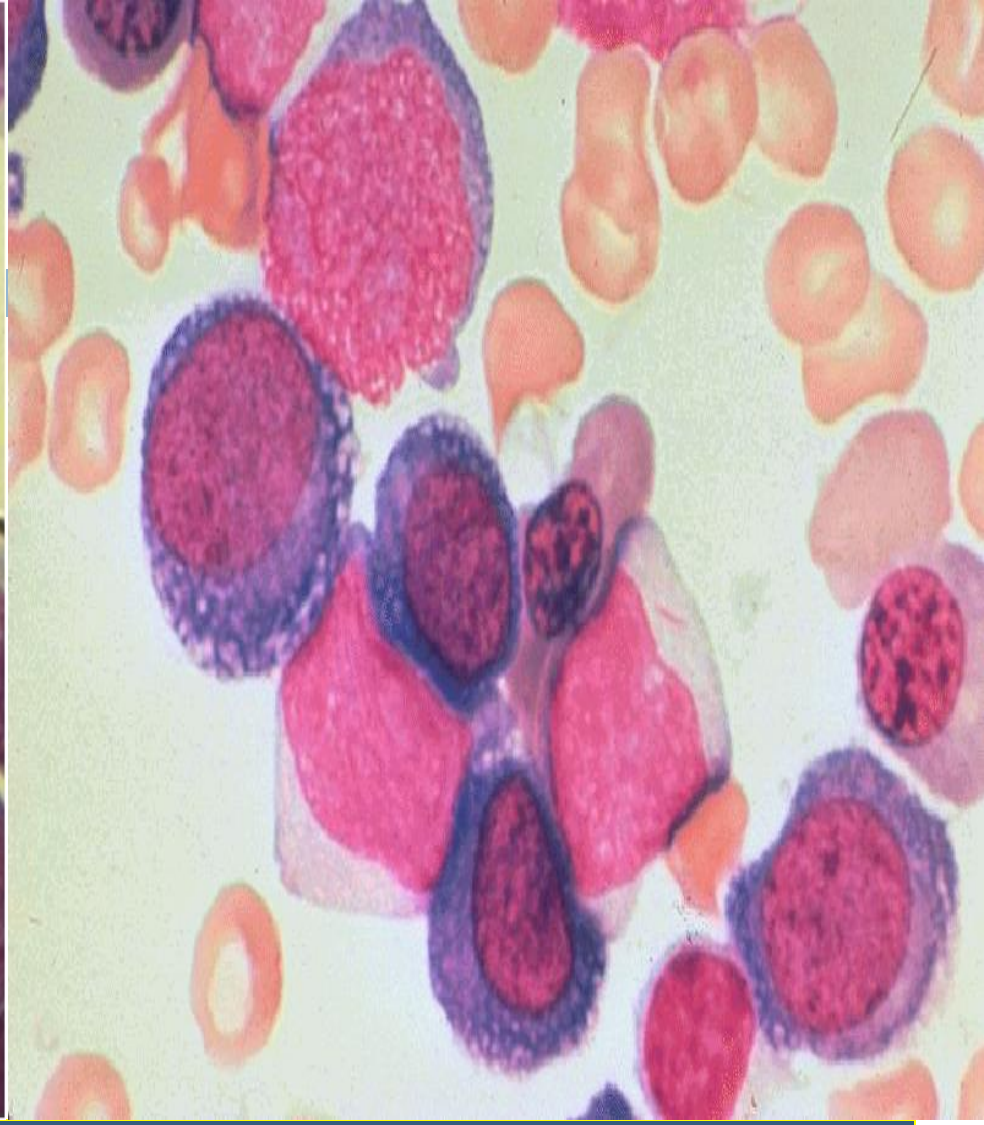
AML M5a



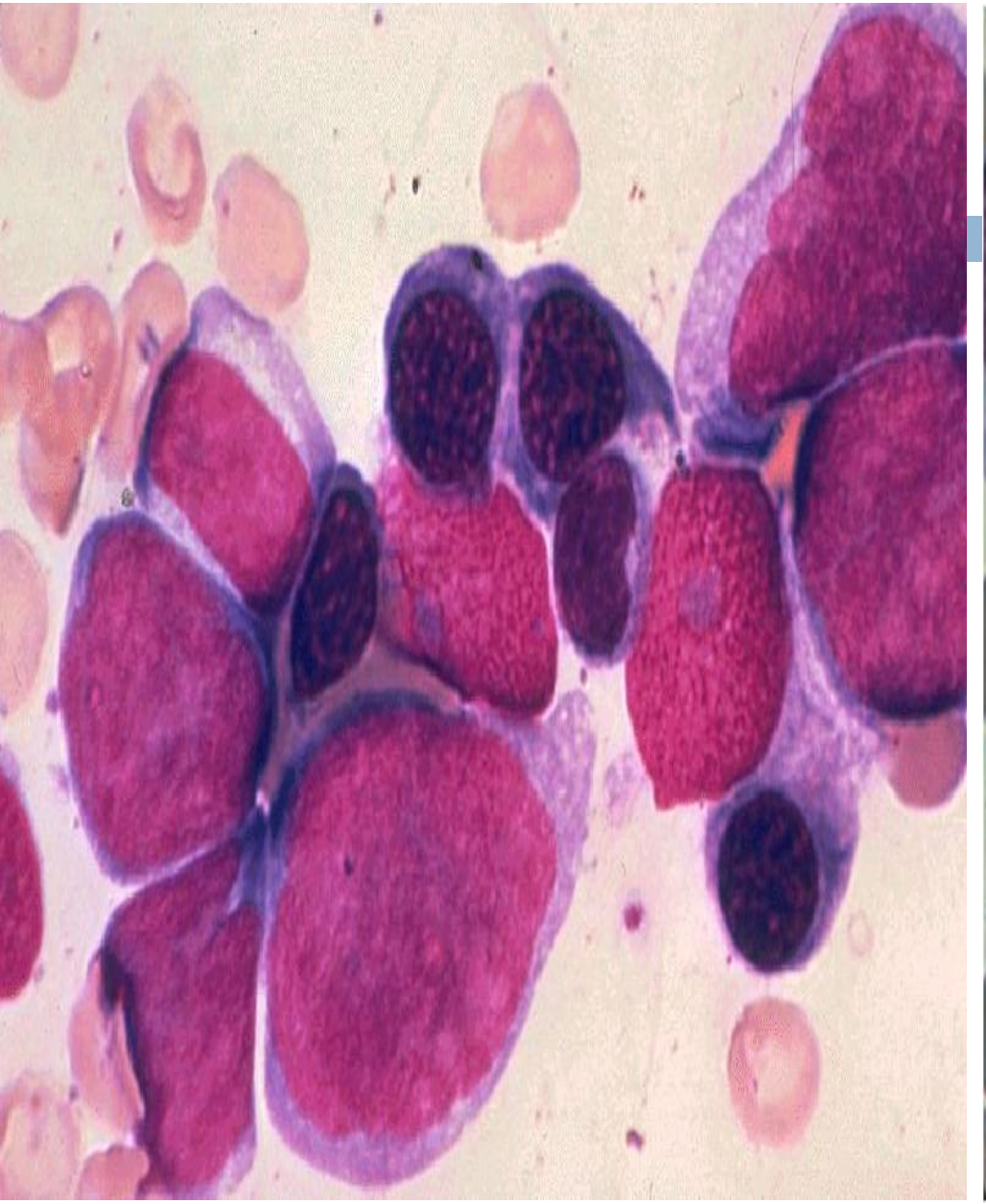
AML M5b

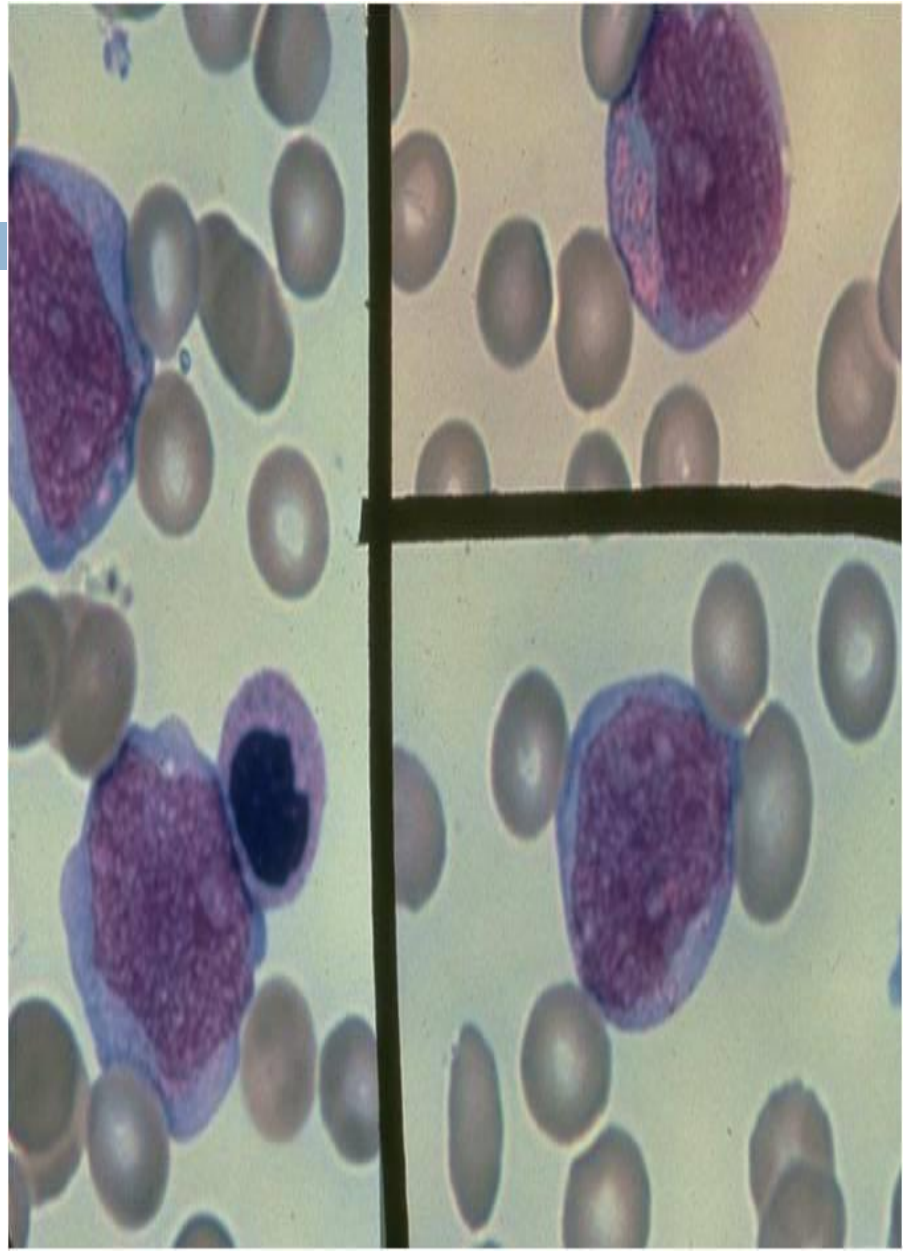
AML M5: acute monoblastic/ monocytic leukemia





AML M6: Acute erythroleukemia





AML M7: Acute megakaryoblastic leukemia

ALL

- Acute lymphoblastic leukemia represents **a clonal proliferation** of immature lymphocyte precursors. The cells may be B-cell precursors (~80 to 85% of cases) or T-cell precursors (~15 to 20% of cases)
- ALL is the **most common malignancy in childhood** and represents ~85% of childhood acute leukemia. ALL also occurs in adults but is uncommon (~15% of adult acute leukemia).
- The highest incidence of ALL is **between 1 and 5 years** of age. There is a slight male predominance.
- There is a marked increase in risk of ALL in children with **trisomy 21 (Down syndrome**) and following exposure to ionizing radiation.

- **Specific manifestation** with Acute lymphoblastic leukemia :
  - ✓ bone pain, arthritis
  - ✓ lymphadenopathy
  - ✓ hepatosplenomegaly
  - ✓ mediastinal mass
  - ✓ testicular swelling
  - ✓ meningeal syndrome

2016 WHO classification of ALL

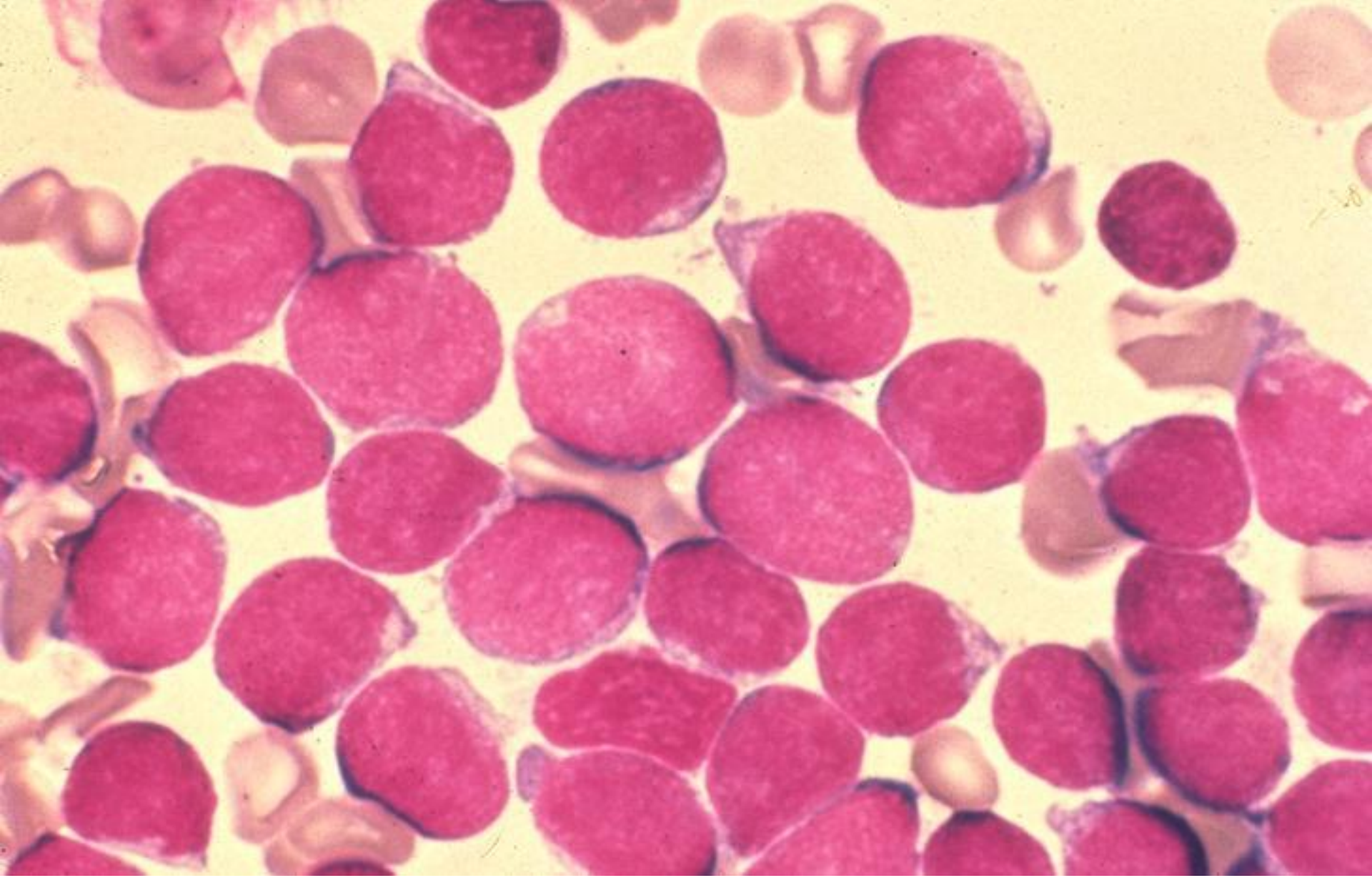
B-lymphoblastic leukemia/lymphoma
B-lymphoblastic leukemia/lymphoma, NOS
B-lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities
B-lymphoblastic leukemia/lymphoma with t(9;22)(q34.1;q11.2);*BCR-ABL1*
B-lymphoblastic leukemia/lymphoma with t(v;11q23.3);*KMT2A* rearranged
B-lymphoblastic leukemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
B-lymphoblastic leukemia/lymphoma with hyperdiploidy
B-lymphoblastic leukemia/lymphoma with hypodiploidy
B-lymphoblastic leukemia/lymphoma with t(5;14)(q31.1;q32.3) *IL3-IGH*
B-lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3);*TCF3-PBX1*
Provisional entity: B-lymphoblastic leukemia/lymphoma, BCR-ABL1–like
Provisional entity: B-lymphoblastic leukemia/lymphoma with iAMP21
T-lymphoblastic leukemia/lymphoma
Provisional entity: Early T-cell precursor lymphoblastic leukemia
Provisional entity: Natural killer (NK) cell lymphoblastic leukemia/lymphoma

1. WHO classification

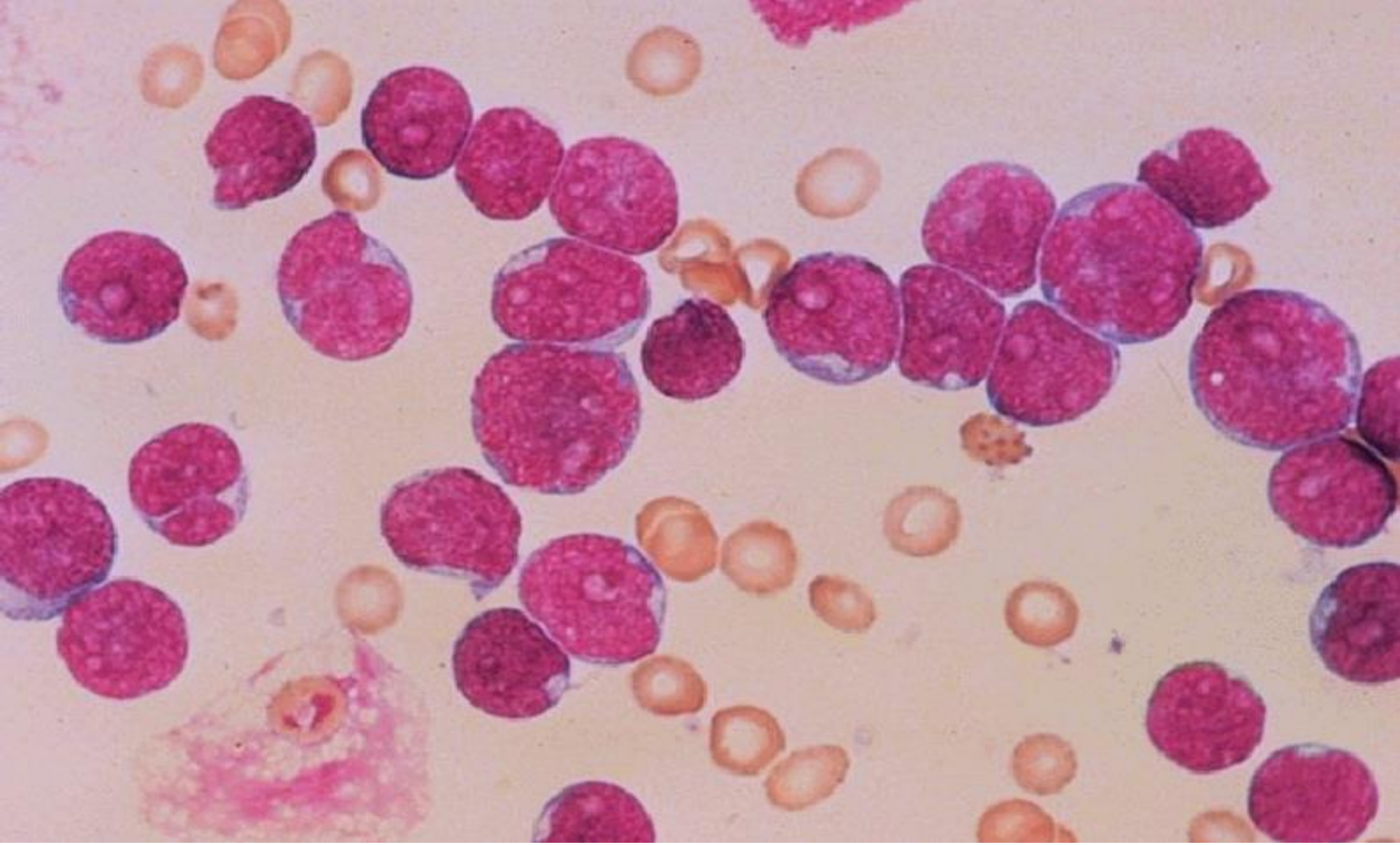
French-American-British (FAB) classification of ALL

L1	blast cells small, uniform high nuclear to cytoplasmic ratio
L2	blast cells larger, heterogeneous; lower nuclear to cytoplasmic ratio
L3	vacuolated blasts, basophilic cytoplasm (usually B-ALL)

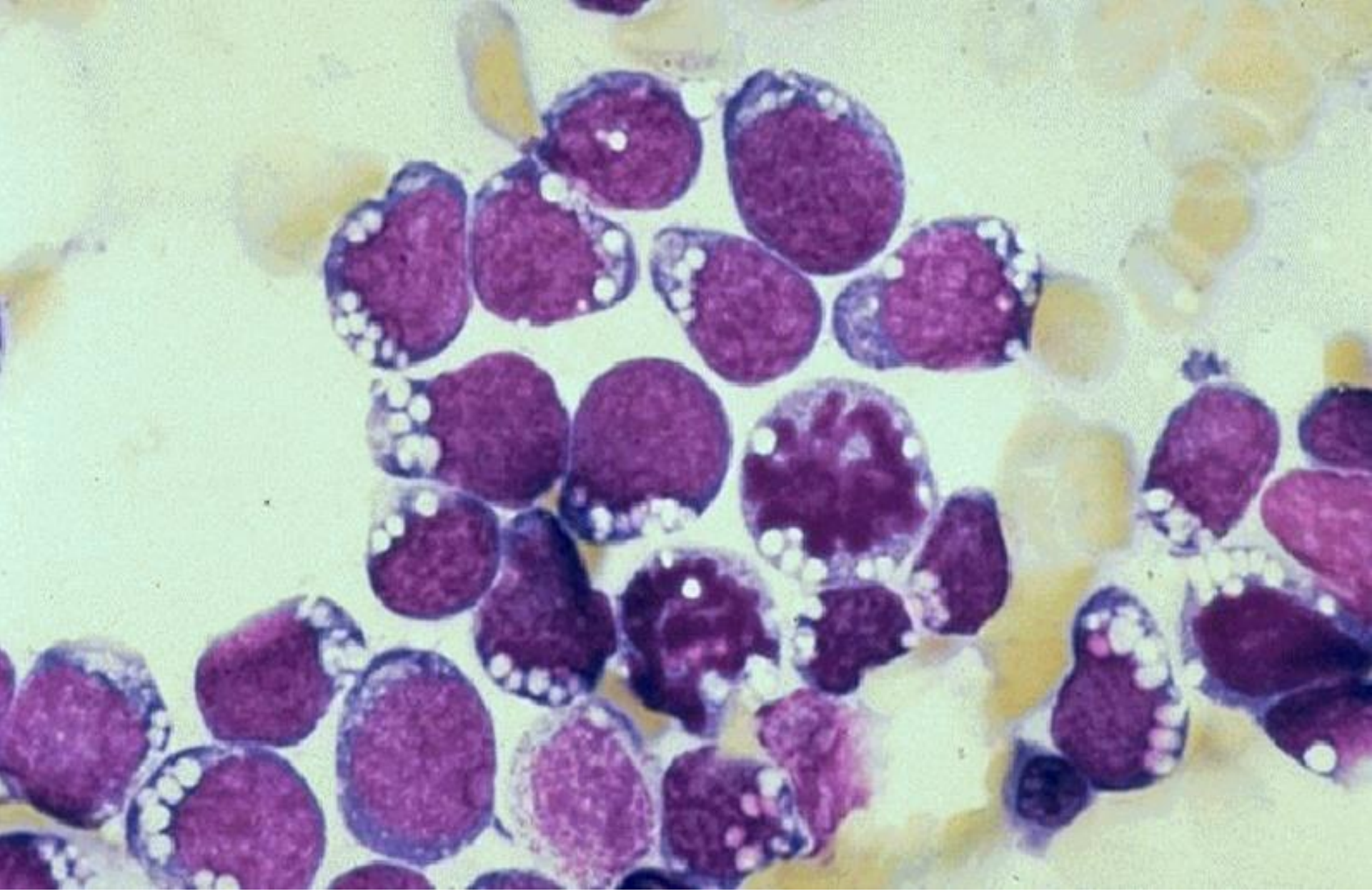
- The FAB classification based strictly on morphology. The L3 type consists of mature B cells (not precursors) and corresponds to blood involvement by Burkitt's lymphoma.



ALL L1 subtype: monomorphic blasts, majority small, high N/C ratio, scanty cytoplasm, small or inconspicuous nucleoli



ALL-L2 subtype: heterogeneous blasts, variable sizes & N/C ratios, with more prominent nucleoli & nuclear membrane irregularities



ALL-L3 subtype: monomorphic large blasts with prominent nucleoli strongly basophilic vacuolated cytoplasm

Management

1. Central venous catheter inserted to :

- facilitate blood product
- adm. of chemotherapy and antibiotics
- frequent blood sampling

2. Blood support :-

- **platelet con.** for bleeding episodes or if the platelet count is <10x109/l with fever .
- **fresh frozen plasma** if the coagulation screen results are abnormal **.**
- **packed red cell** for severe anemia (caution : if white cell count is extremely high).

Management

3. Cytotoxic drugs (Chemotherapy).
4. Bone marrow transplantation
5. Prevention and control infection
   - barrier nursed
   - Intravenous antimicrobial agents if there is a fever or sign of infection
4. Physiological and social support

Cytotoxic drugs (Chemotherapy)

- The aim of giving these drugs is to induce what is called complete remission (cytotoxic drugs cause damage to the capacity of cells for reproduction)
- Lines of cytotoxic treatment:
  - Remission induction
  - Consolidation
  - CNS prophylaxis with ALL
  - Maintenance 2-3 years to prevent the relapse usually to ALL.
  - ATRA for AML-M3.

Treatment of acute leukemia

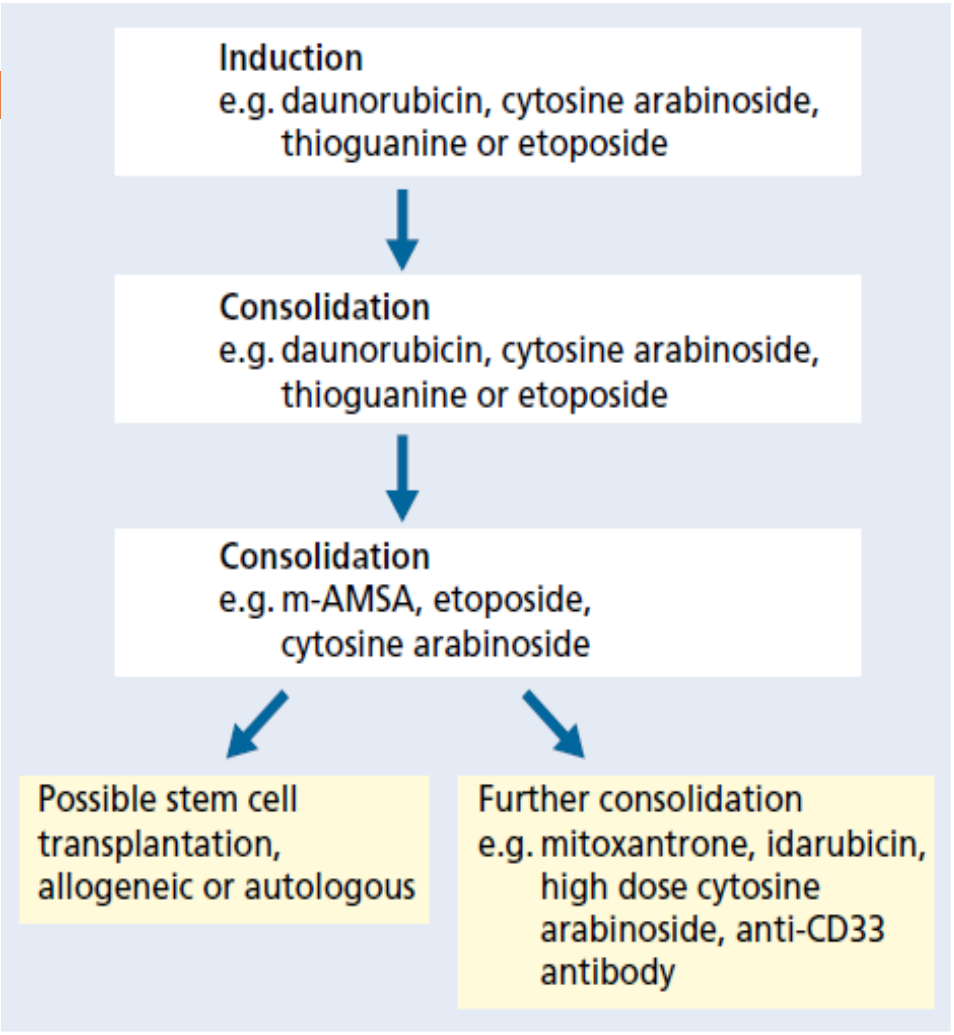
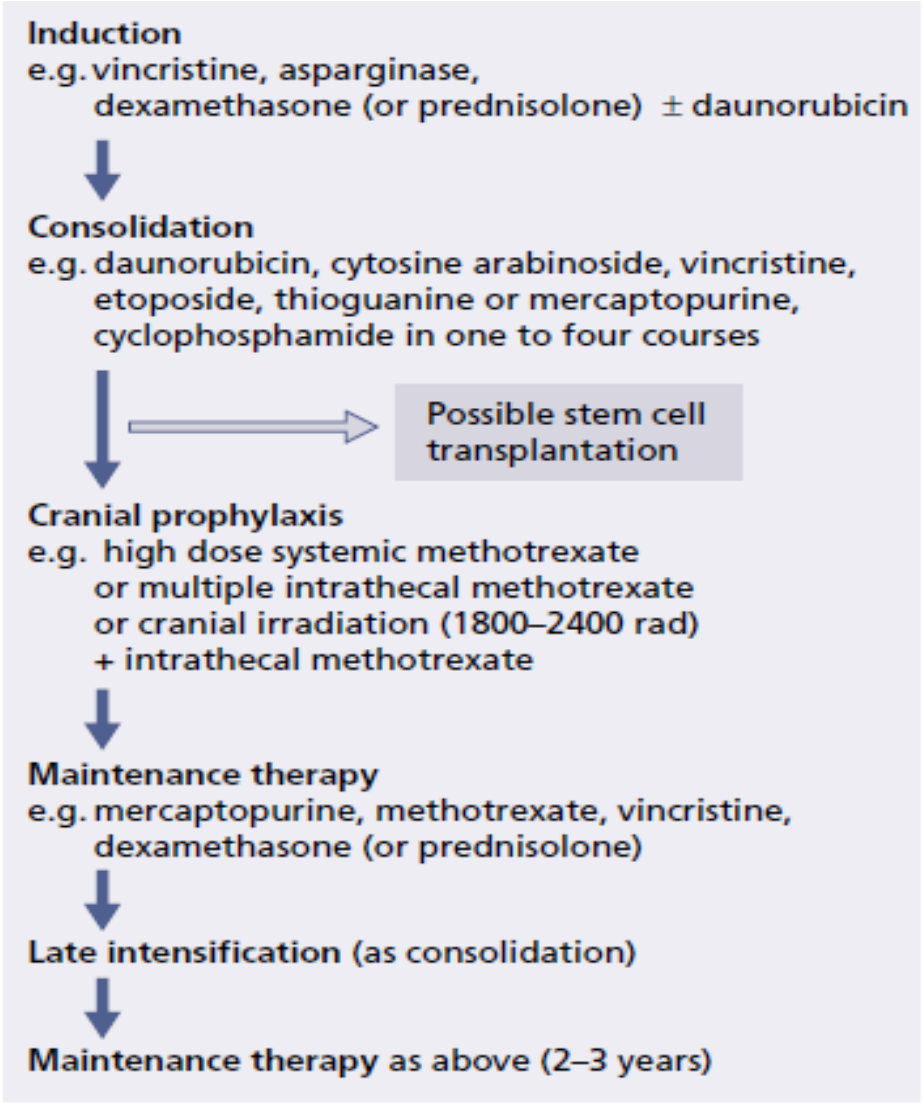


Figure 13.9 Acute myeloid leukaemia: flow chart illustrating typical treatment regimen.



(a)

Figure 17.6 Acute lymphoblastic leukaemia (ALL)

Outcome in adult acute leukemia

Disease/risk	Risk factors	survival
Acute myeloid leukaemia		
Good risk	Promyelocytic leukaemia t(15;17) t(8;21) inv 16 or t(16;16)	76%
Poor risk	Cytogenetic abnormalities −5, −7, del 5q, abn(3q), complex (> 5)	21%
Intermediate risk	AML with none of the above	48%
Acute lymphoblastic leukaemia		
Poor risk	Philadelphia chromosome High white count > 100×10^9/L Abnormal short arm of chromosome 11 t(1;19)	20%
Standard	ALL with none of the above	37%


Thank you!