

ACUTE LEUKEMIA

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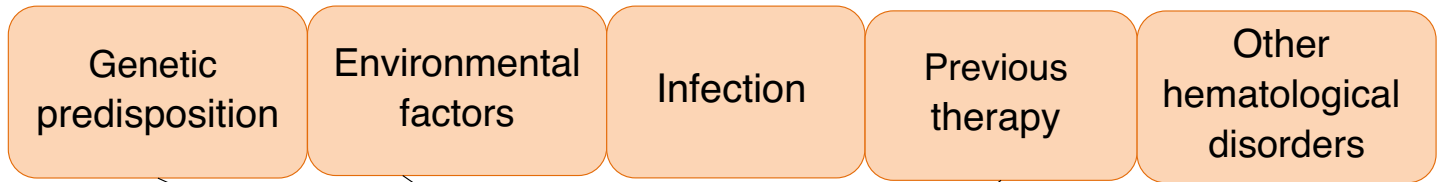
ACUTE LEUKEMIA

- ❖ Aggressive malignant hematopoietic disorders
- ❖ Accumulation of abnormal blasts (Immature precursors of WBC)
in bone marrow and blood leading to:
 - 1- Bone marrow failure (anemia ,neutropenia & thrombocytopenia)
 - 2- Organ infiltration (hepatosplenomegy ,lymphadenopathy)

HISTORY

- Means “white blood” in Greek.
- Named by pathologist Virchow in 1845.
- Classified by FAB classification systems in 1976.
- Reclassified by World Health Organization in 2001 & 2008.

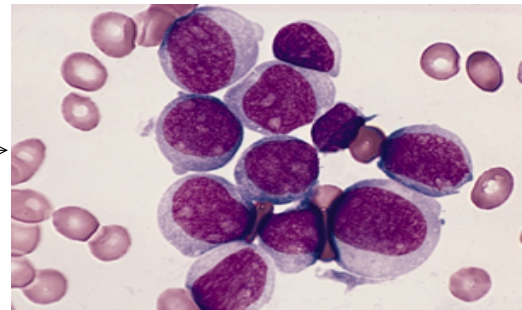
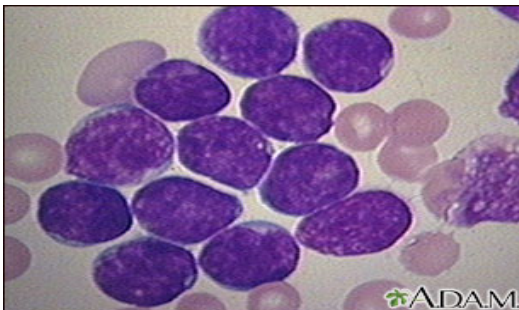
PATHOGENESIS



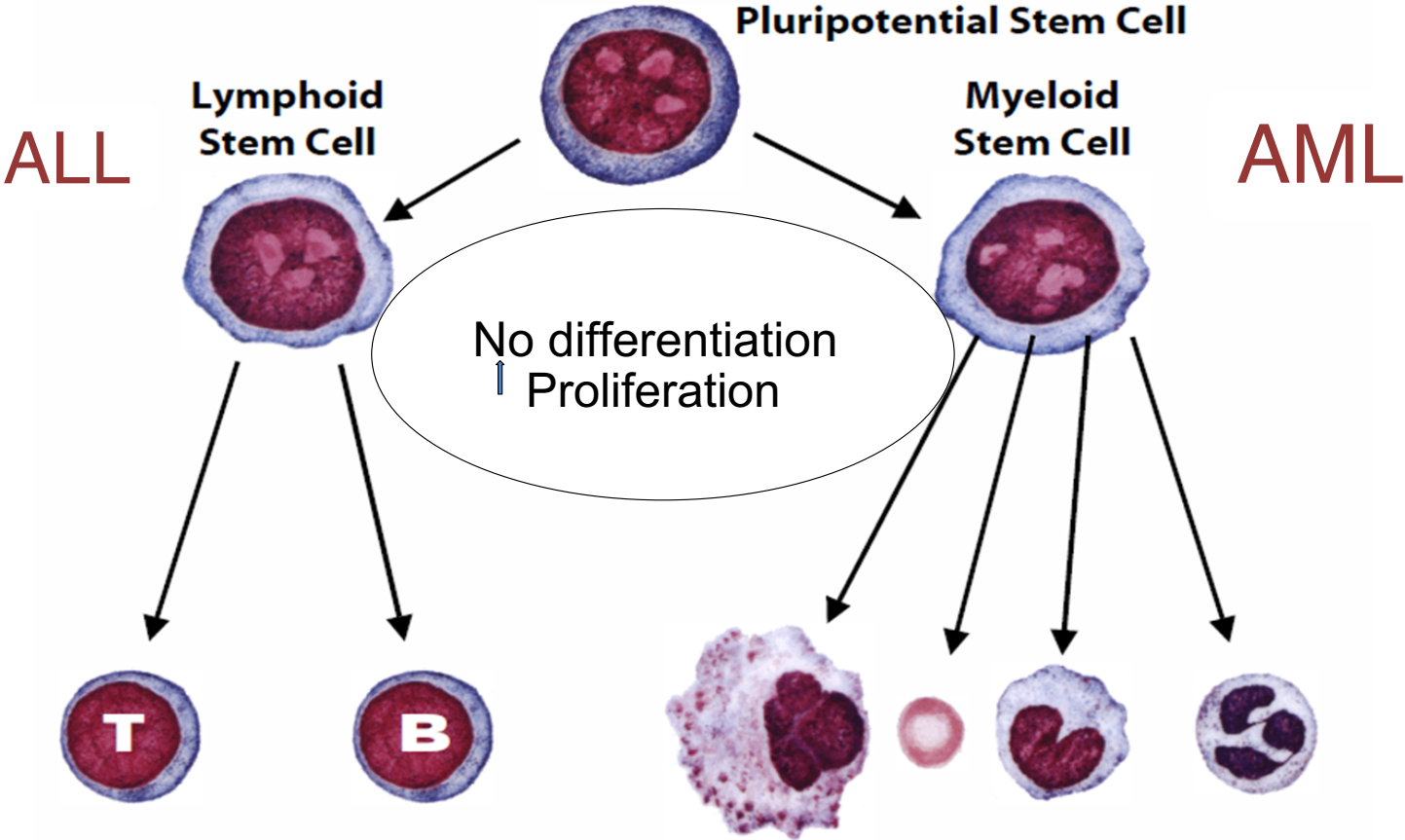
Unknown Mechanism

Genetic alteration in the immature precursors

Block of differentiation ,Enhanced proliferation & Decreased apoptosis



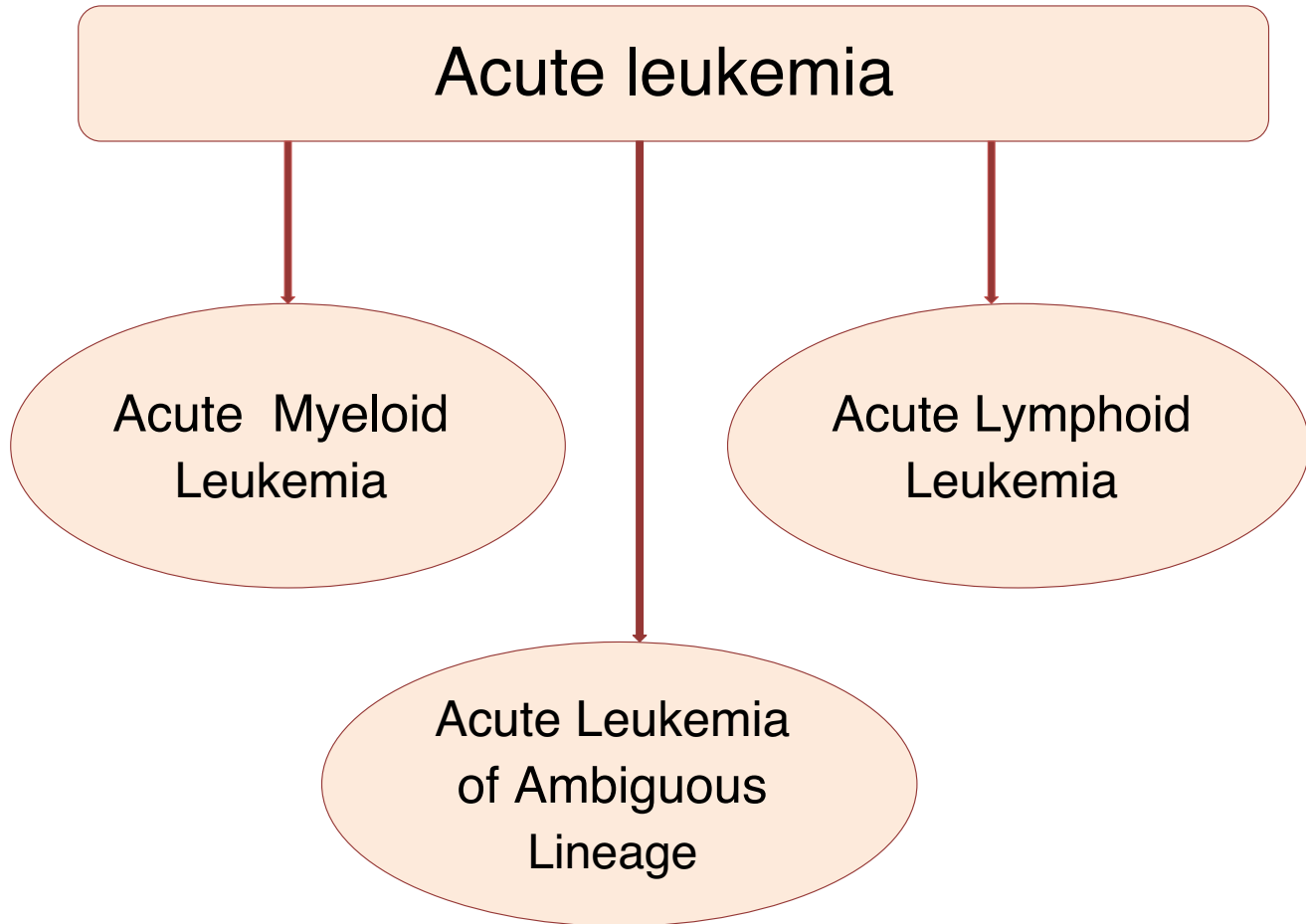
PATHOGENESIS



EPIDEMIOLOGY

- AL represent about 8% of neoplastic disease & cause about 4% of malignancy related deaths !
- AML has an incidence of 2 – 3 per 100 000 per year in children, rising to 15 per 100 000 in adults.
- ALL has an incidence of 30 per million & represent about 76% of childhood leukemia .

GENERAL CLASSIFICATION

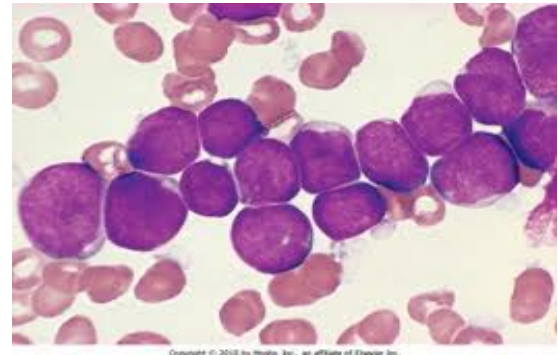
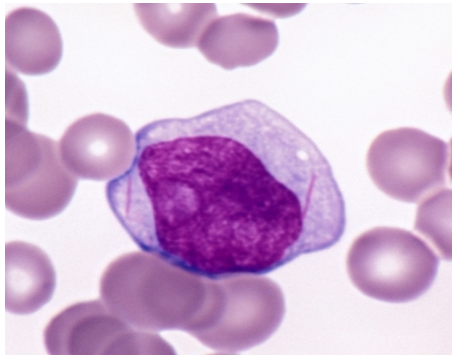


BASIS OF CLASSIFICATION

1. Clinical history (Previous therapy)
2. Morphology
3. Flow cytometry
4. Chromosomal Karyotyping
5. Molecular study

1- Light microscopy (blood smear, bone marrow aspirate & biopsy)

- Blast count : it should be $>20\%$ out of the total cells
- Blast morphology :



Myeloblast:

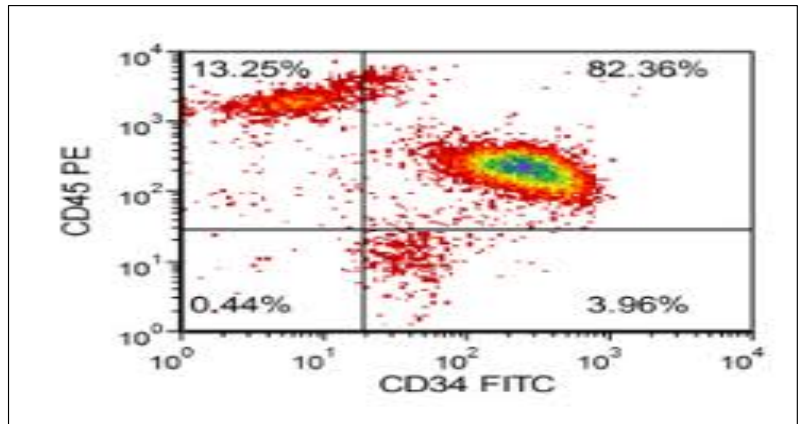
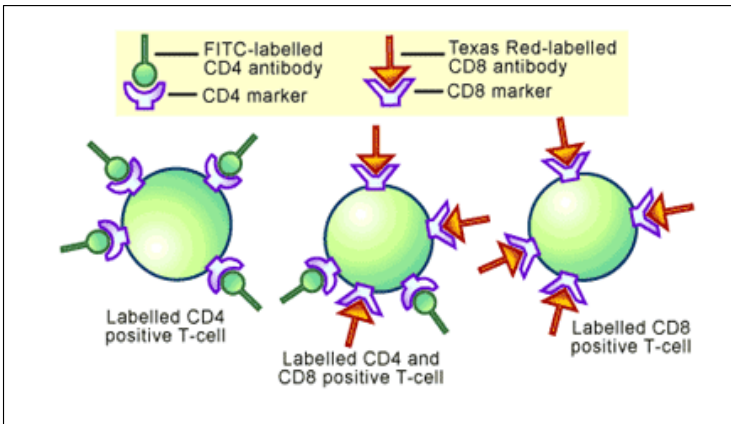
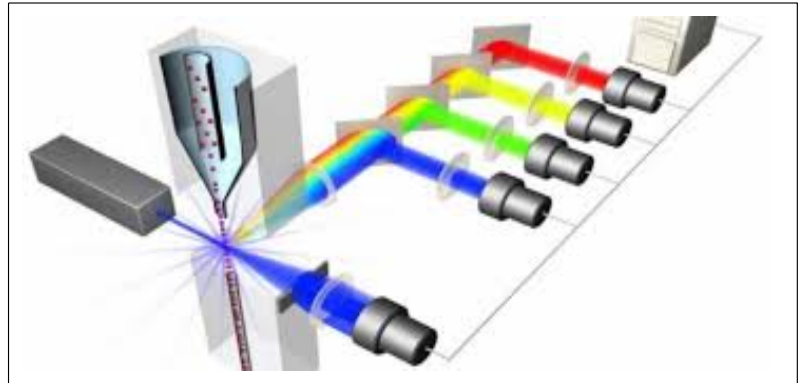
- Size: medium-Large
 - Nucleus: round, oval or irregular
 - Nucleolus: prominent
 - Cytoplasm: abundant, granular
- Auer rods is characteristic

Lymphoblast:

- Size: small- medium
 - Nucleus: round
 - Nucleolus: not prominent
 - Cytoplasm: scanty ,agranular
- may be vacuolated

2-Flow cytometry:

Laser based technology allows for cells counting & detection of their surface & cytoplasmic markers by suspending them in a stream of fluid followed by analysis through electronic system.



BASIS OF CLASSIFICATION

Stem Cell Markers: (CD34& TDT)

Myeloid

MPO

CD13

CD33

CD14

CD64

CD41

CD235a

B-Lymphoid

CD10

CD19

CD22

CD79a

T-Lymphoid

CD3

CD4

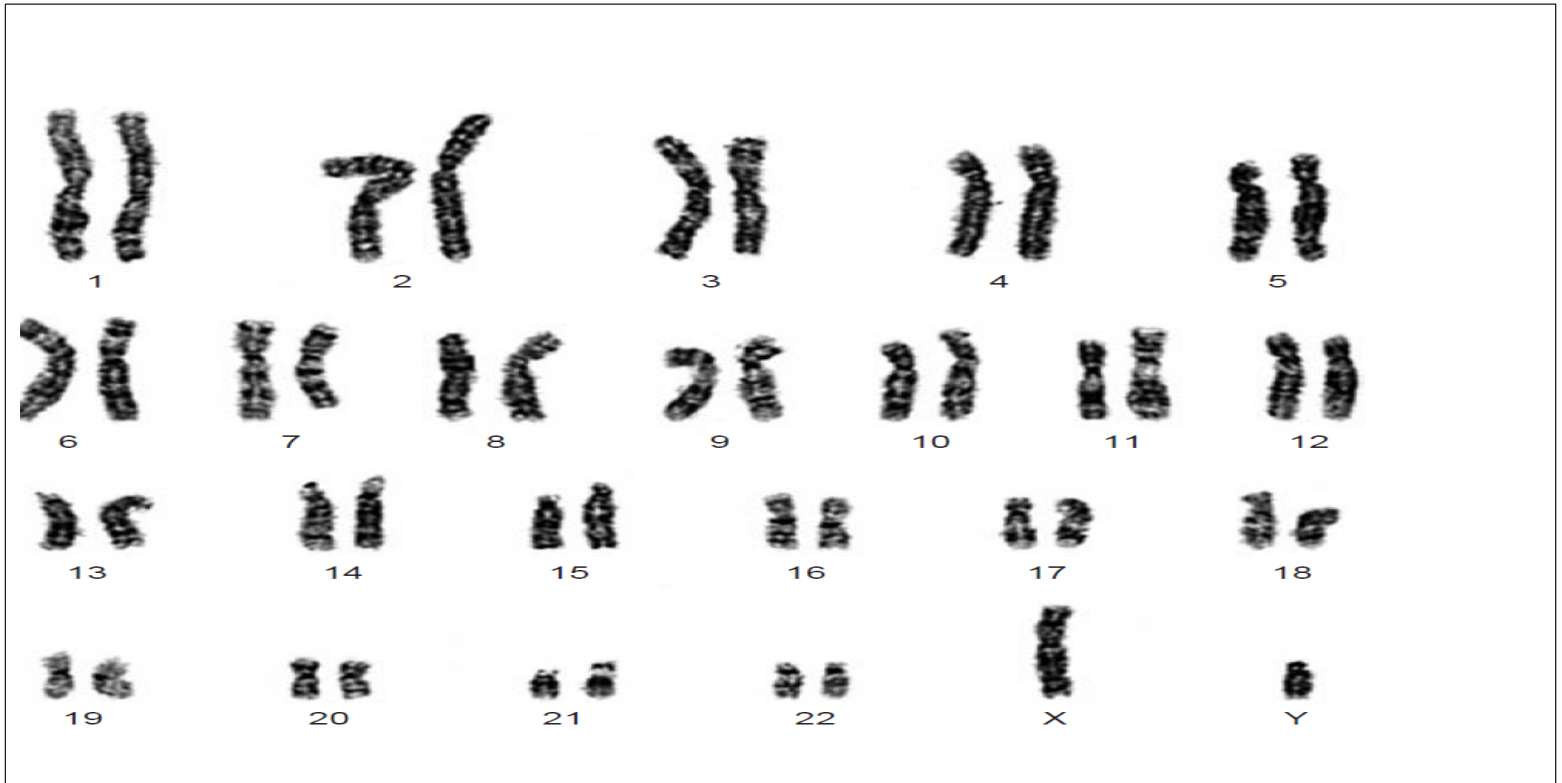
CD5

CD7

CD8

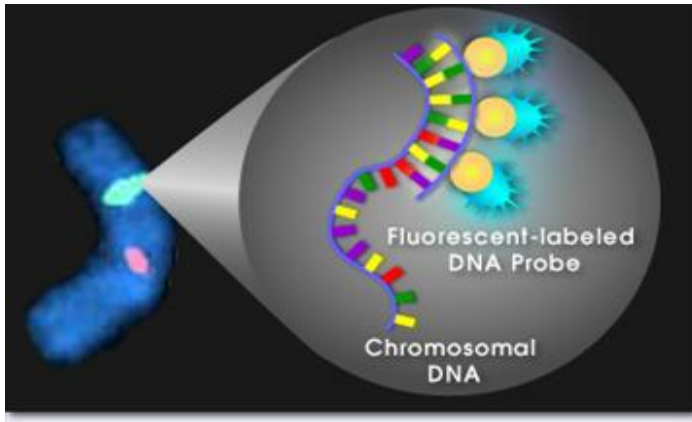
3-Chromosomal Karyotype

Set of the chromosomes from one cell during metaphase to study the numerical(deletion & trisomy) and structural (translocation & inversion) abnormality

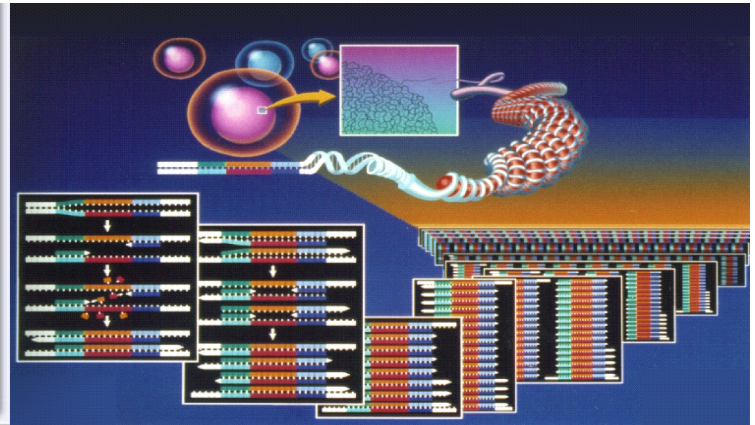


4- Molecular studies:

Several techniques used to detect and localize the presence or absence of specific DNA sequences on chromosomes



Fluorescent In-Situ Hybridization (
FISH)



Polymerase Chain Reaction
(PCR)

RECURRENT GENETIC ABNORMALITIES

AML

Molecular	Karyotype
AML1-ETO	t (8;21)
CBFB-MYH11	t (16;16) or inv(16)
PML-RARA	t (15;17)
MLLT1-MLL	t (9;11)

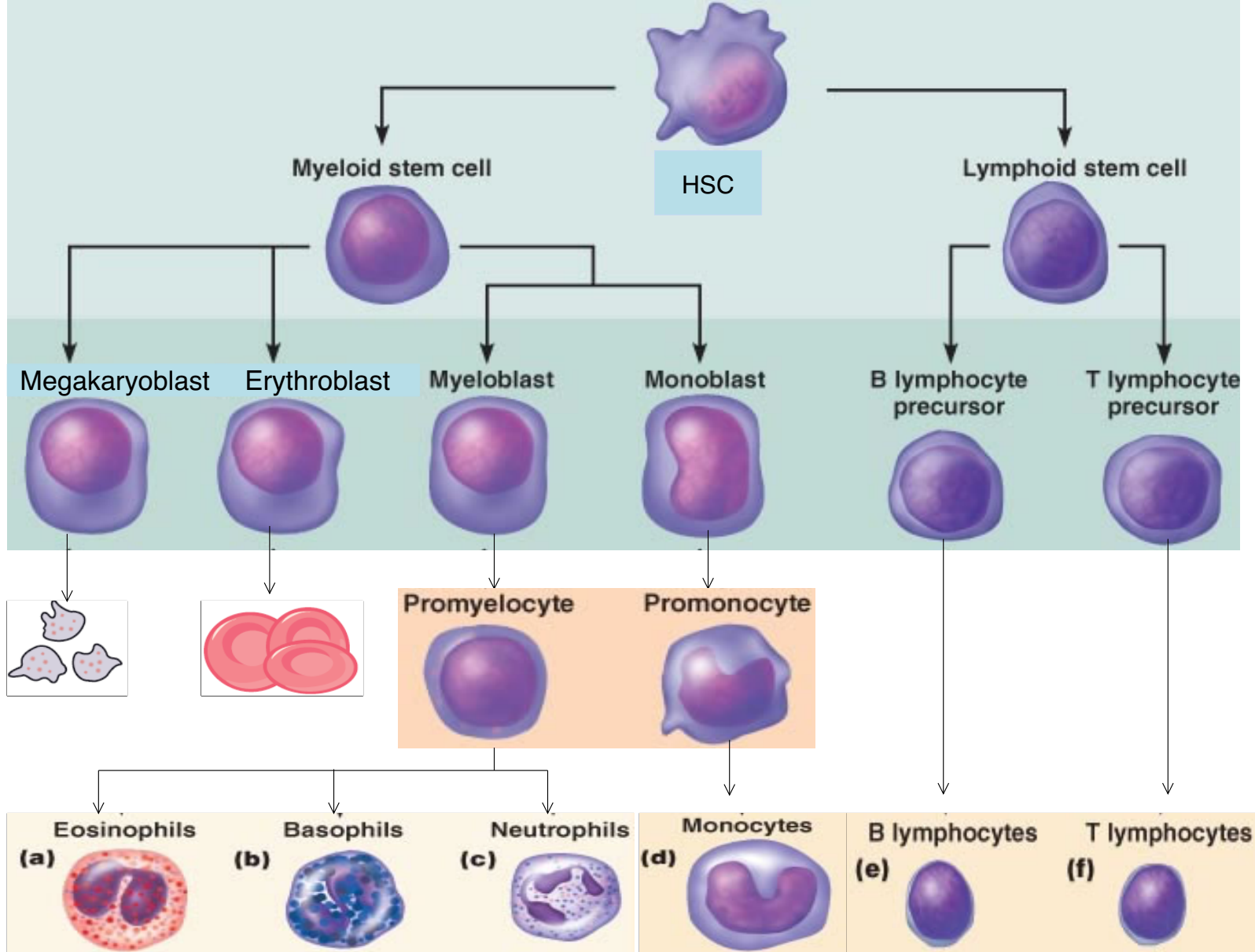
ALL

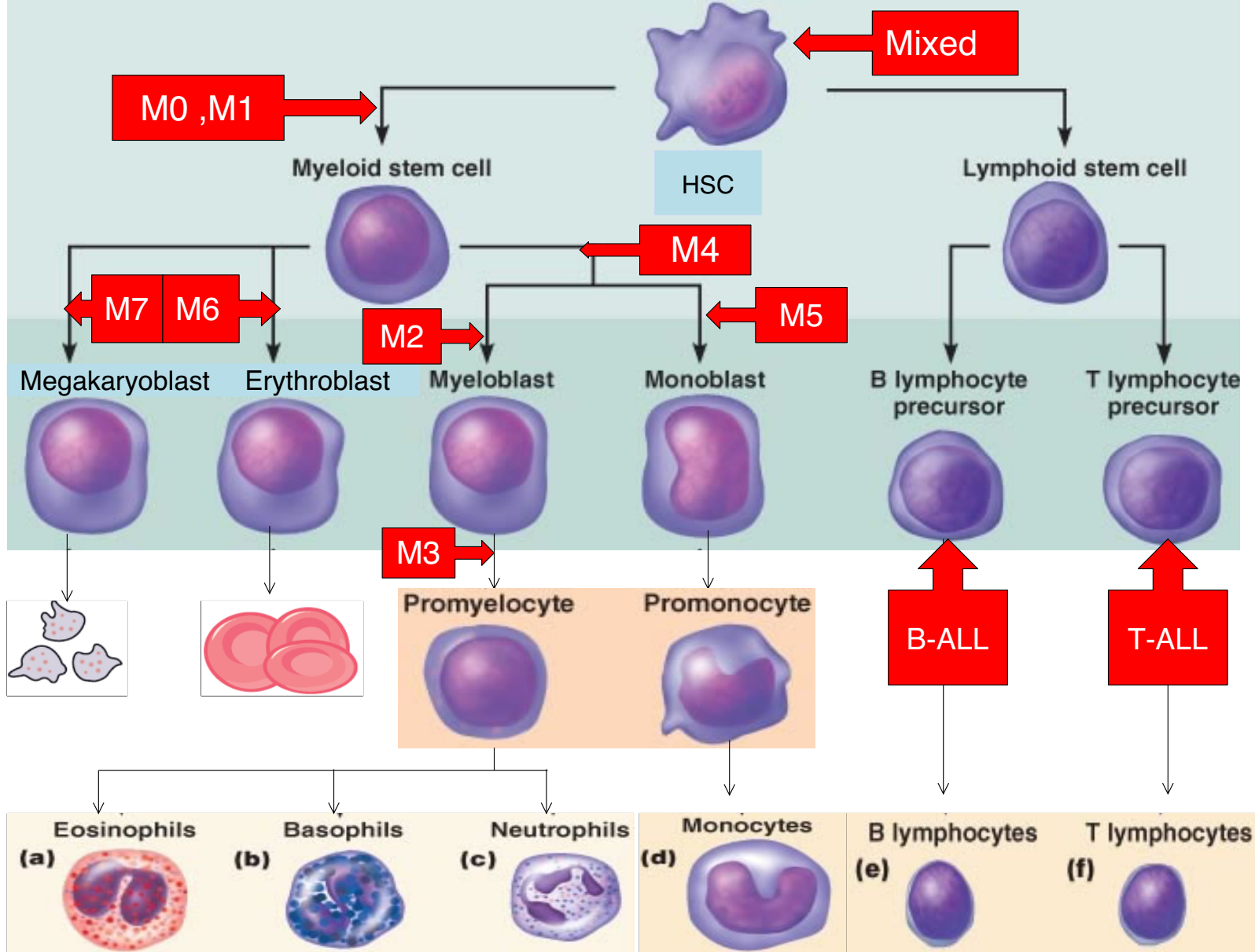
Molecular	Karyotype
BCR-ABL1	t (9;22)
AF4-MLL	t (4;11)
ETV6-RUNX1	t (12;21)
IL3-IGH	t (5;14)

**ACUTE MYELOID
LEUKEMIA (AML)**

ACUTE MYELOID LEUKEMIA (AML)

- Group of hematopoietic neoplasms caused by proliferation of malignant myeloid blasts in bone marrow and blood.
- The blast $\geq 20\%$ or t(8;21) t (16;16) or t(15;17).
- More in Adults (do occur in infants!)
- Worse than ALL





FAB CLASSIFICATION

- Based on morphology & flow cytometry

Subtype	Features	Genetics in WHO	Notes
M0	Minimal differentiation		
M1	Without maturation		
M2	With maturation	t(8;21)	
M3	Promyelocytic	t(15;17)	DIC
M4	Granulocytic and monocytic	t or inv(16;16)	Gum hypertrophy
M5	Monoblastic (M5a) Monocytic (M5b)	t(9;11)	
M6	Erythroid		CD235a
M7	Megakaryocytic		CD41
M8	Basophilic		

AML CLASSIFICATION (WHO)

AML with recurrent genetic abnormalities

- 1- t(8;21)
 - 2- t(16;16)
 - 3- t(15;17)
- Prognosis:
Good

Myelodysplasia related AML

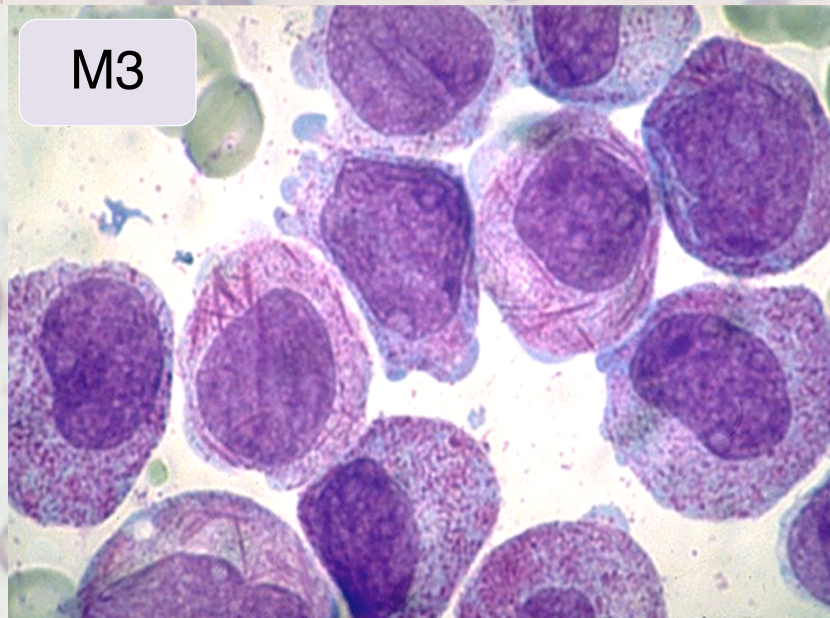
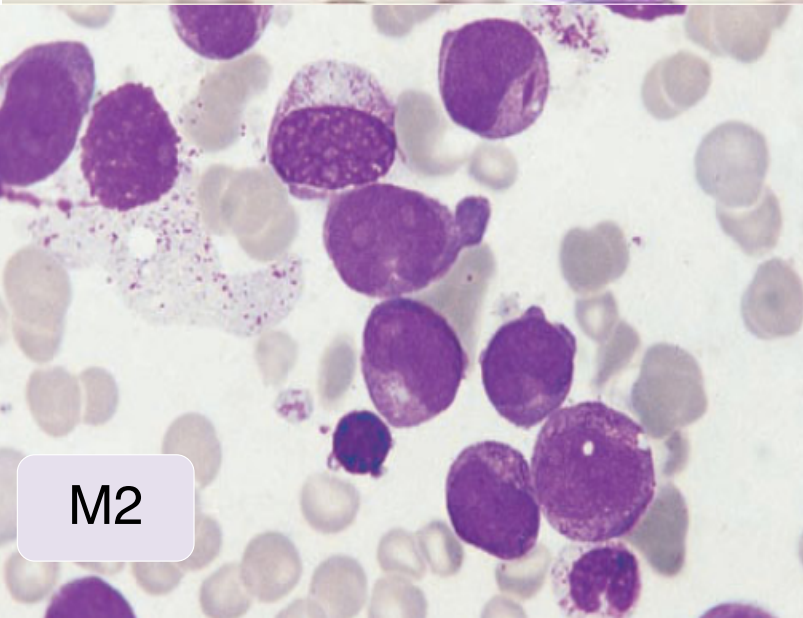
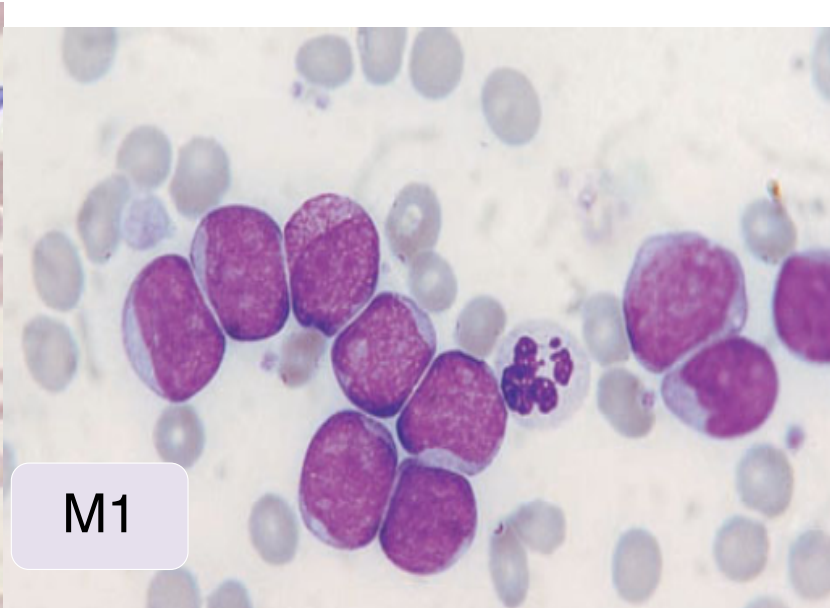
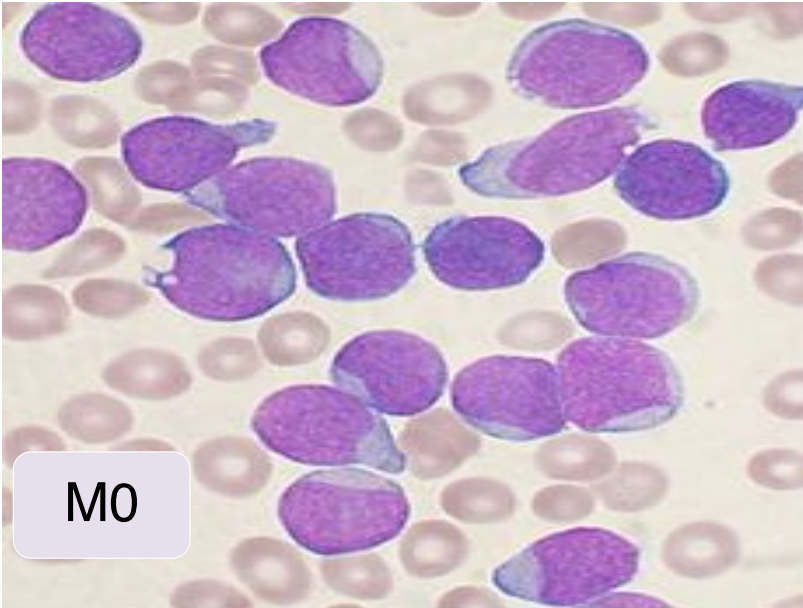
- Blasts \geq 20%
 - Significant dysplasia
- Prognosis:
poor

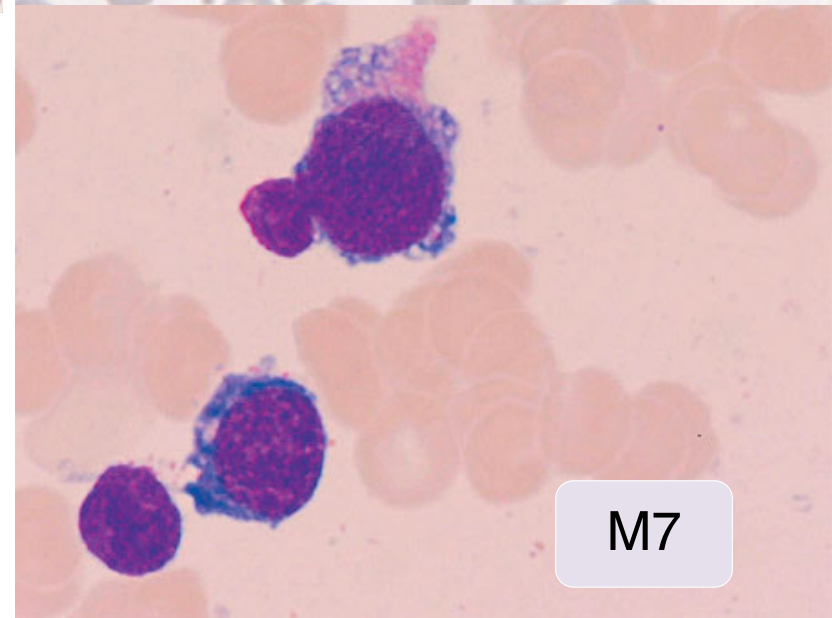
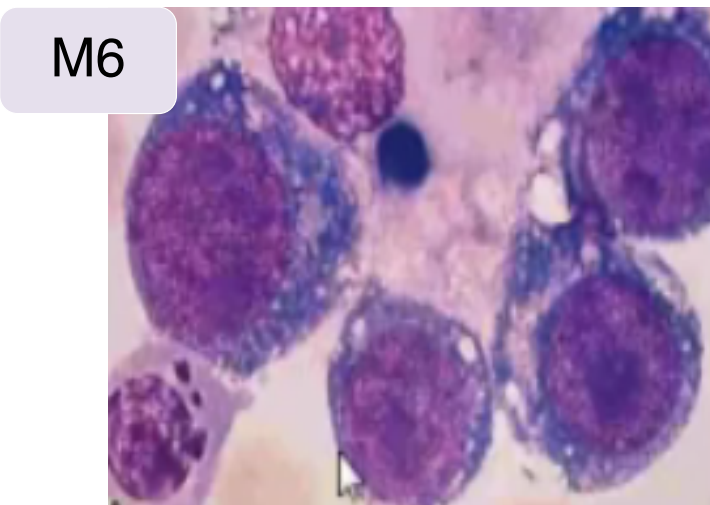
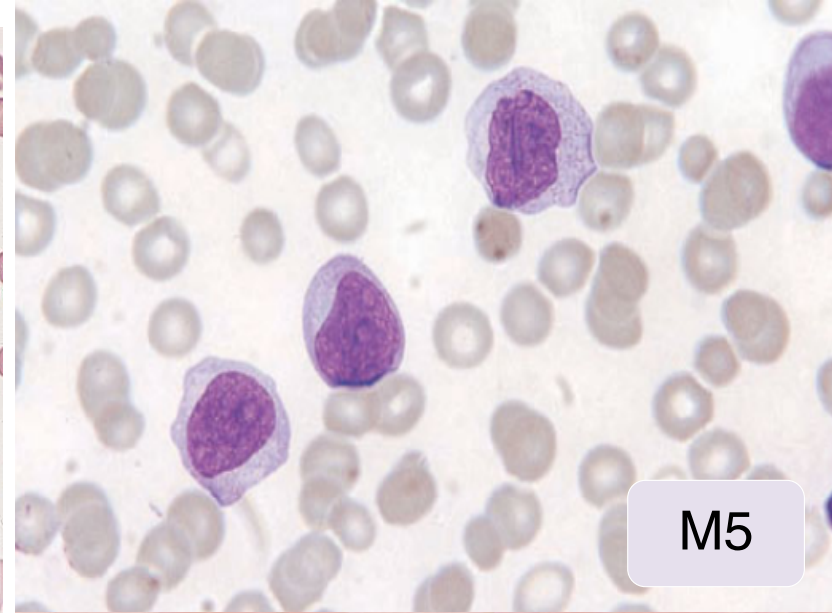
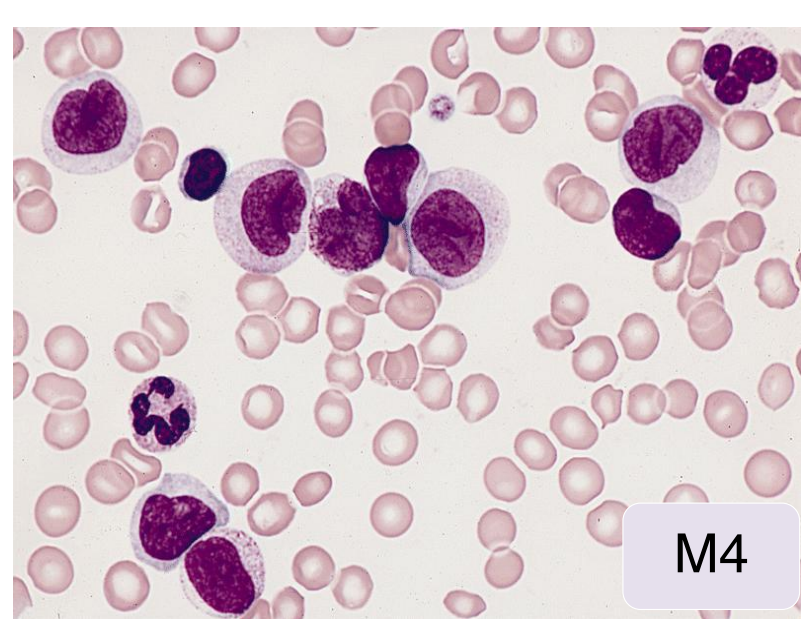
Therapy related AML

- Blasts \geq 20%
 - Previous chemotherapy
- Prognosis:
poor

AML, not otherwise specified (FAB)

- Blasts \geq 20%
 - Genetic: N
 - No dysplasia
- Prognosis:
Standard





CLINICAL FEATURES OF AML

1-Pancytopenia:

- WBC infection (fever ,septic shock)
- Hb anemia (fatigue , headache , pallor ,SOB....)
- platelets bleeding (bruises , epistaxis ,menorrhagia...)

Acute onset

2-Organ infiltration:

- Hepatosplenomegally.
- Lymphadenopathy (rare)
- Myeloid sarcoma
- Gum hypertrophy
- CNS disease

More with Acute Monoblastic Leukemia

CLINICAL FEATURES OF AML

3-Leucostasis (increased blood viscosity)

4-Disseminated Intravascular Coagulation (DIC):

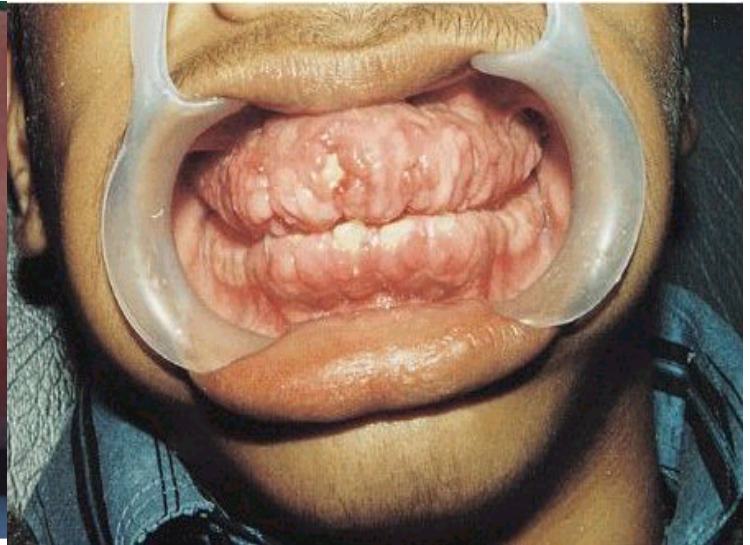
Widespread activation of coagulation system leading to intravascular fibrin deposition & consumption of platelet and coagulation factors which can be manifested as bleeding (85%) or thrombosis (15%)

More with Acute Promyelocytic leukemia (M3)

CLINICAL FEATURES OF AML



Myeloid sarcoma

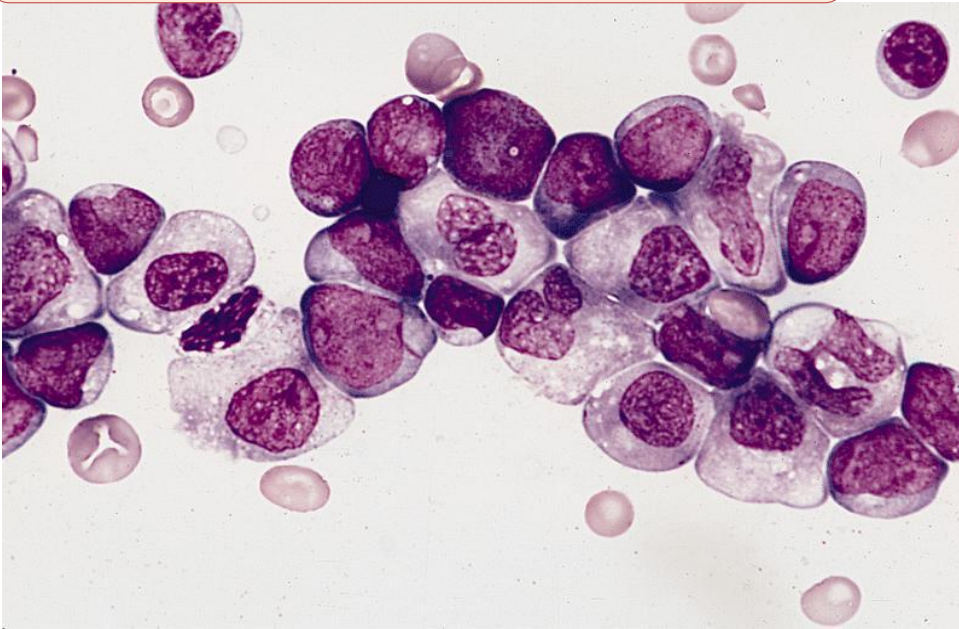


Gum hypertrophy

CASE STUDY

- 65 years old male presented to ER with fatigue ,fever and nose bleeding for 2 weeks.
- O/E : moderate hepatosplenomegaly & multiple bruises.
- CBC : WBC :40 x10⁹/L HB: 7g/dL PLT: 51 x10⁹/L

Blood smear & bone marrow:



?

Flow cytometry :

The blast are positive for CD34 ,CD13,CD33,CD117 and MPO

They are negative for CD3,CD10,CD19&CD79a

AML with maturation (M2) (FAB)

Karyotype :

t(8;21)(q22;q22)



The final diagnosis: AML with t(8;21)

(WHO)

PROGNOSIS AND TREATMENT

Better prognosis:

- Genetics: t(8;21), inv(16;16) or t(15;17)
- Age: < 60 years
- Primary better than secondary

Treatment

- Chemotherapy:
 - ❑ AML: M0-M8 but not M3 (same protocol)
 - ❑ AML: M3 (ATRA or arsenic)
- Stem cell transplantation

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

- ❑ Acute leukemia characterized by proliferation of malignant lymphoid blasts in bone marrow and blood.
- ❑ B and T cells
- ❑ More common in Children
- ❑ Better than AML

CLINICAL FEATURES OF ALL

1-Pancytopenia:

↓WBC ↓ infection (fever ,septic shock)

↓Hb ↓ anemia (fatigue , headache , pallor ,SOB....)

↓platelets ↓bleeding (bruises , epistaxis ,menorrhagia...)

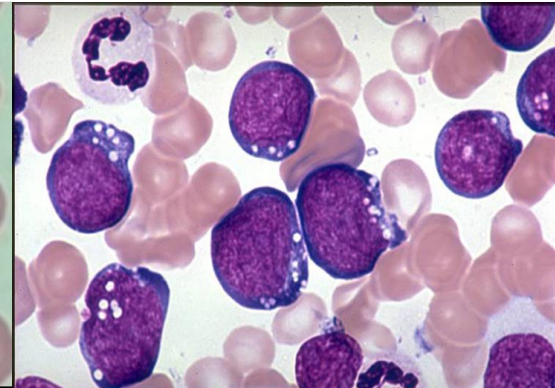
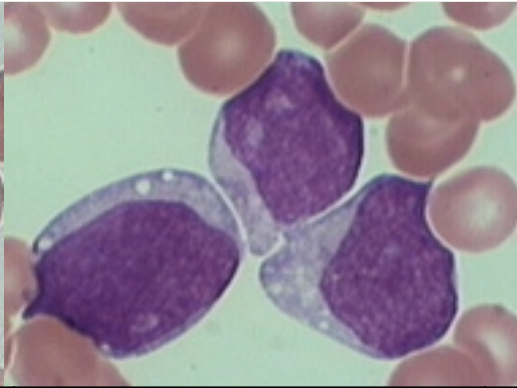
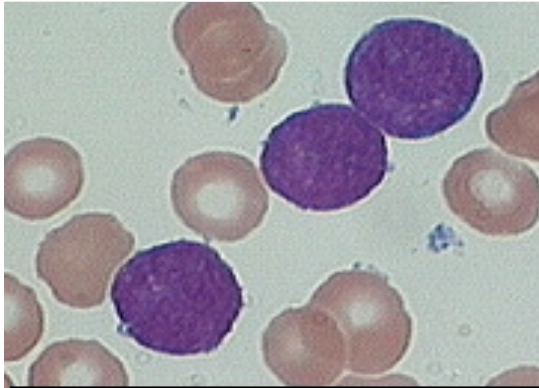
Acute onset

2-Organ infiltration:

- Lymphadenopathy (very common)
- Hepatosplenomegally.
- testicles involvement
- CNS disease
- Mediastina

Characteristic for T-ALL

MORPHOLOGICAL SUBTYPES (FAB)



L3 Burkitt's	L2	L1	
Homogenous	Heterogeneous	Homogenous	Morphology
Small	Variable	Small	Size
Vacuolated	More	Little	Cytoplasm
Prominent	Prominent	Not prominent	Nucleoli
t(8;14) cmyc	Variable	Variable	Genetics

IMMUNOPHENOTYPIC SUBTYPES (WHO)

	B cell	T cell
Markers	CD19,CD10,CD79a	CD3
Percentage	80%	20%
Age	Younger	Older
Clinical	-----	Mediastinal mass CNS relapse
WBC count	Less	Higher
Prognosis	Better	Worse
Genetics	t(9;22),t(4;11),t(12;21)	-----

L3 (Burkitt's) represents
mature lymphoid neoplasm
so it is a type of lymphoma
not Acute lymphoblastic
leukaemia

B-ALL

Precursor B cell	Mature B cell
CD34& TDT	
	Surface Immunoglobulin
CD10	
Common B-ALL	
CD19,CD20 &CD79a	
B- ALL	Burkitt's

T-ALL

Precursor T- cell	Mature T- cell
cCD3	
	sCD3
- VE (CD4&CD8)	
+VE (CD4&CD8)	CD4 only
	CD8 only
CD2,CD5&CD7	
T-ALL	T- Cell Lymphoma

PROGNOSIS AND TREATMENT

Worse	Better	
<2 - >10 yrs	2 - 10 yrs	Age
M	F	Gender
High	Low	WBC count
T cell	B cell	Cell type
Others	Common	B-ALL phenotype
Hypodiploidy t(9;22)	Hyperdiploidy t(12;21)	B-ALL genetics
Yes	No	CNS involvement

Treatment:

- ❑ Chemotherapy (high cure rate)
- ❑ Stem cell transplantation

REMEMBER !

- ❓ Acute leukaemia is a fatal neoplastic condition
- ❓ 20% or more blasts = Acute leukaemia
- ❓ Diagnosis requires special investigations
- ❓ Auer rods = AML
- ❓ AML M3 = DIC & target therapy
- ❓ Gum hypertrophy = mostly M4 or M5,
- ❓ Mediastinal = T-ALL

REMEMBER !

- ❓ Subtypes of AML (M0-M8) + cytogenetic abnormalities
- ❓ Subtypes of ALL (T or B cell)
- ❓ Main lineages markers are MPO, CD19 and CD3
- ❓ Stem cell markers are CD34, TDT
- ❓ FAB classification based mainly on morphology
- ❓ WHO classification focused more on genetics

Thank you !!!