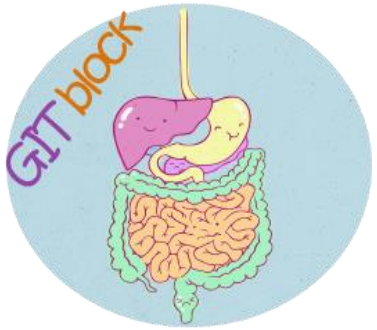


L6&7 Acute leukaemia

Color coding

- important
- Extra info
- Notes from lecturer

دعاء قبل المذاكرة :

(اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا عامرة بذكرك و قلوبنا بخشيتك، أنك على كل شيئا قدير و حسبنا الله نعم الوكيل)

DON'T FORGET to check our editing file : haematology edit

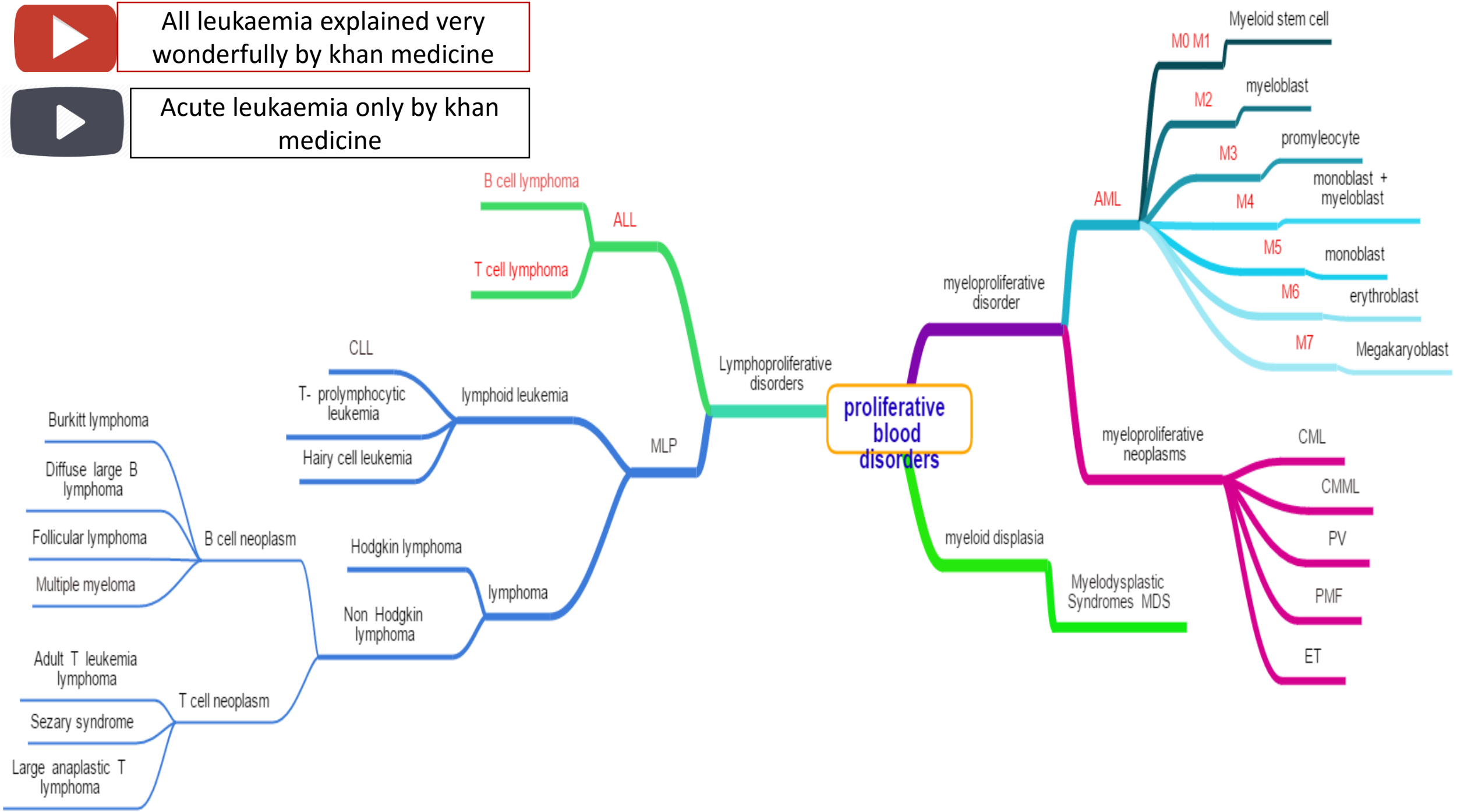
Please don't hesitate to contact us on:Haematology434@gmail.com

	Male	Female
Hemoglobin(g/dL)	13.5-17.5	11.5-15.5
Hematocrit (PCV) (%)	40-52	36-48
Red Cell Count ($\times 10^{12}$)	4.5-6.5	3.9-5.6
Mean Cell Volume (MCV) (fL)	80-95	
Mean Cell Hemoglobin (MCH) (pg)	30-35	
MCHC %	31 - 37	
Platelet count	140-450x10^3/L	
NORMAL PLATELET SIZE MPV	7.2-11.1 fl	
NORMAL PLATELET DIAMETER	1-2.5 µ	
WBC	4000-11,000 /L	
Segmented (neutrophils)	1.8-7.8	
Eos	0-0.45	
Baso	0-0.20	
Lymphs	1.0-4.8	
Monos	0-0.80	

A Good Doctor Knows CBC

All leukaemia explained very wonderfully by khan medicine

Acute leukaemia only by khan medicine



Acute leukemia is a fatal neoplastic condition

- Aggressive malignant hematopoietic disorders
- Accumulation of abnormal blasts *(Immature precursors of WBC) in bone marrow and blood leading to:

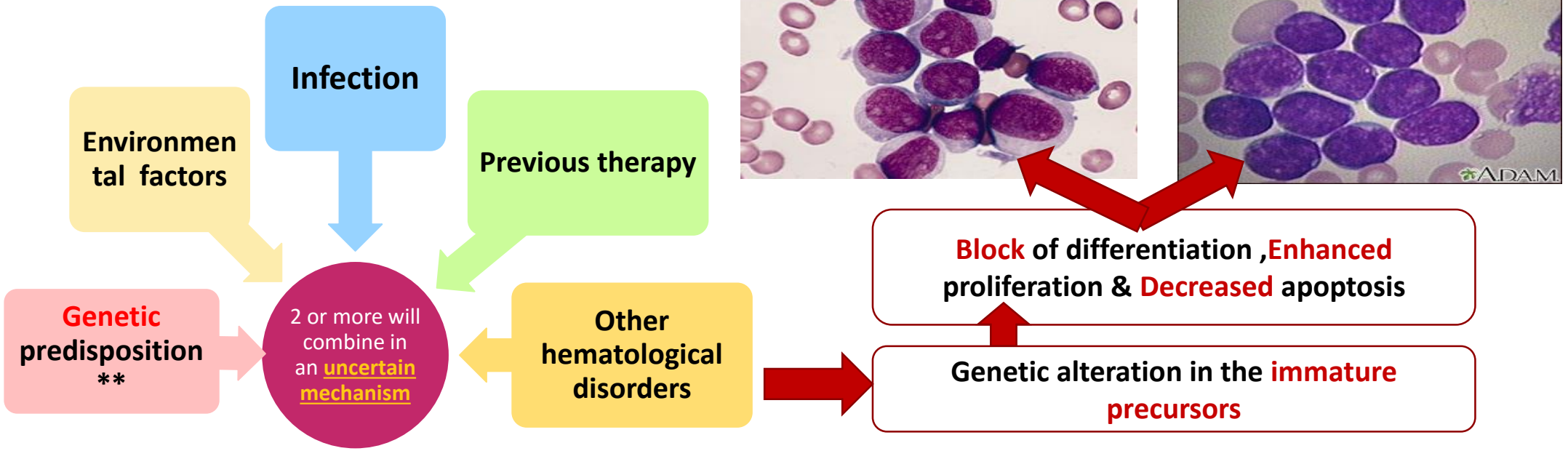
1. Bone marrow failure (anemia ,neutropenia & thrombocytopenia)
2. Organ infiltration (hepatosplenomegy ,lymphadenopathy)

*The main difference between Chronic and Acute leukemia is the presence of blasts in the peripheral blood, which happens, only in Acute Leukemia

HISTORY

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

Pathogenesis

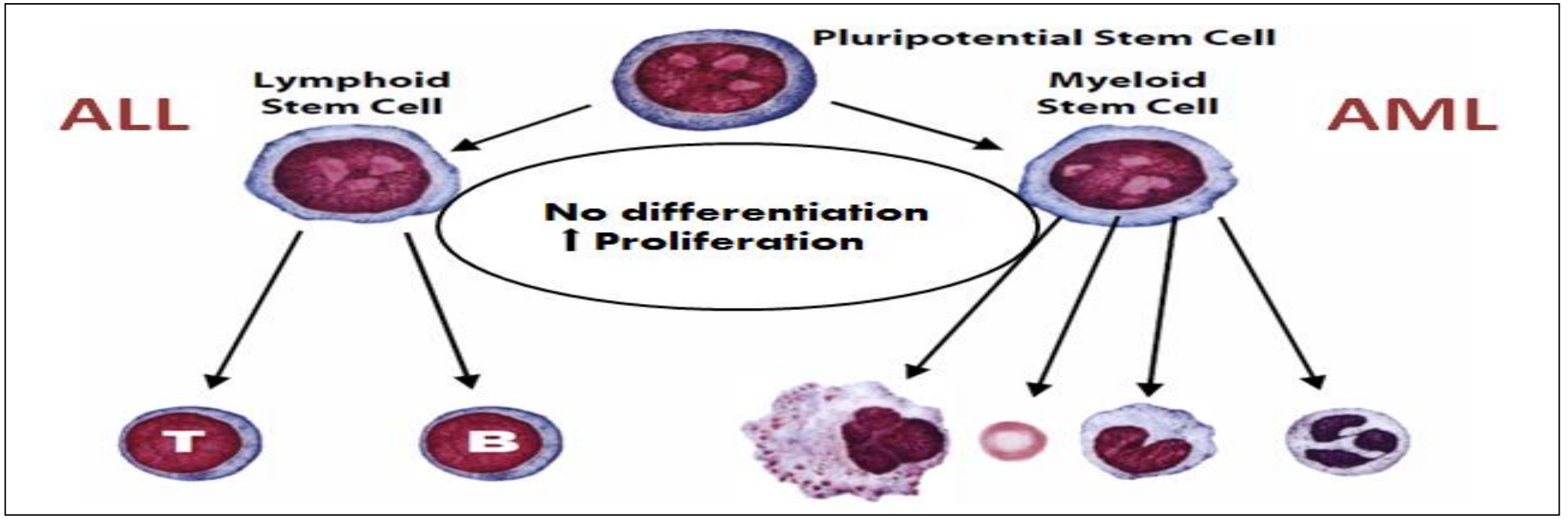


Acute Myeloid Leukemia AML

Acute Lymphoid Leukemia ALL

Most important factor, **BUT can't trigger the disease on its own.

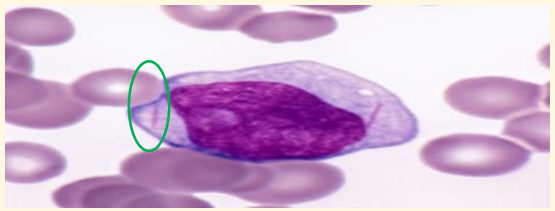
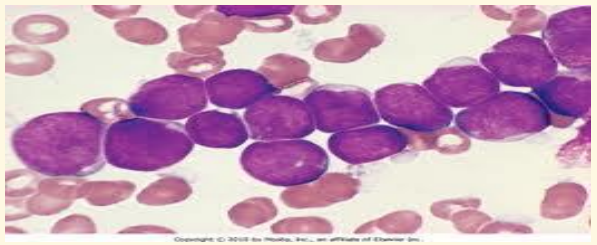
Pathogenesis



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 .

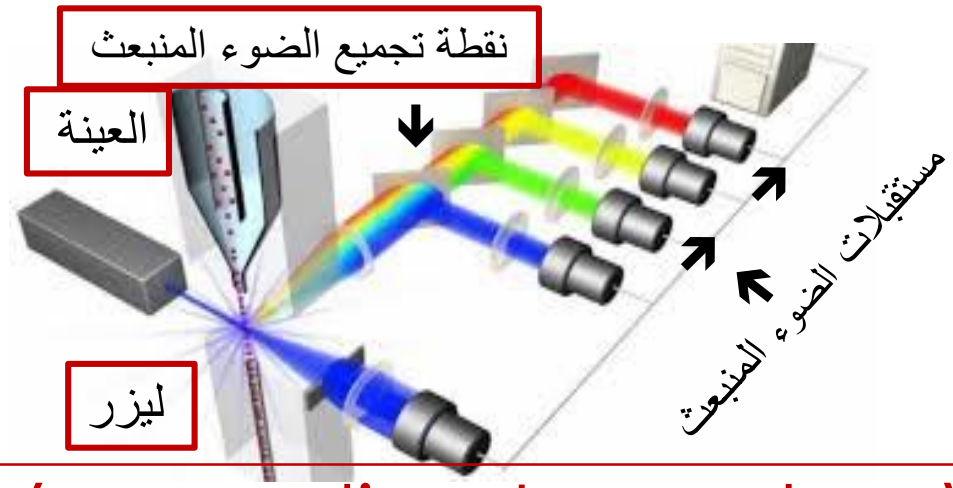
Acute Leukemia Classification

1.General Classification	2.Basic Classification	
❖ **Acute Myeloid Leukemia** ❖ **Acute Lymphoid Leukemia** ❖ **Acute Leukemia of Ambiguous Lineage** It's either doesn't belong to AML and ALL, **or** mix of the two.. *Will be explained in the next slides.. **Cytoplasmic inclusions , composed of fused lysosomes produce harmful substance that gives the symptoms	**It was categorized according to the following:** 1. **Clinical history** (Previous therapy),ex. After treating his lung cancer with chemotherapy➔ he developed leukemia.. **2.Morphology, In the light microscope..** **3. Flow cytometry*** **4. Chromosomal Karyotyping *** **5. Molecular study ***	
	According to **2.morphology** ,it's classified as:	
	a. Myeloblast:	**b. Lymphoblast:**
	-Size: medium-Large -Nucleous: round, oval or irregular -Nucleolus: prominent -Cytoplasm: abundant, granular **Auer rods is characteristic** ** عصيات 	-Size: small- medium -Nucleous: round -Nucleolus: not prominent -Cytoplasm: scanty ,agranular and may be vacuolated 

2- Flow Cytometry

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

Curious about how this works?!
يمررون عينة من الخلايا من خلال ليزر بعدها الخلايا بتبعث أشعة بألوان معينة، وحتى markersوعلى حسب االضوء الكمبيوتر يحلل صحة الخلايا، عددها وال phenotypingال!



Basis of Classification (according to markers)

Stem Cell Markers: (CD34& TDT)

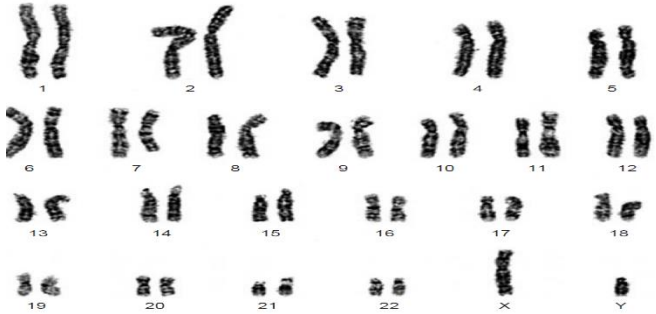
- **Myeloid**: MPO, CD13, CD33, CD14, CD64, CD41, CD235a
- **B-Lymphoid**: CD10, CD19, CD22, CD79a
- **T-Lymphoid**: CD3, CD4, CD5, CD7, CD8

Main lineages markers are
- **MPO for (AML)**
- **CD19 for (B -ALL)**
- **CD3 for (T- ALL)**

CD: Cluster of Differentiation: are a group of special molecules on the surface of the cells in our body.

3-Chromosomal Karyotype

- Set of the chromosomes from one cell during metaphase to study the numerical(deletion and trisomy) and structural (translation andinversion) abnormality

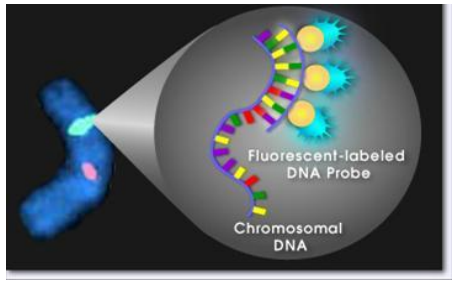


AML	**t (8;21)**
	t (16;16) or inv(16)
	t (15;17)
	t (9;11)
ALL	**t (9;22)**
	t (4;11)
	t (12;21)
	t (5;14)

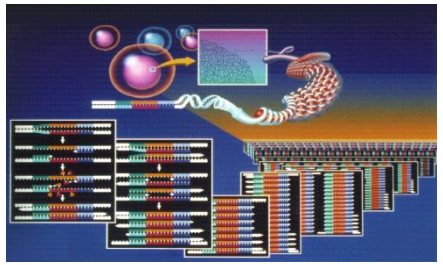
Translocations in Leukemia

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)

AML	**AML1-ETO**
	CBFB-MYH11
	PML-RARA
	MLLT1-MLL
ALL	**BCR-ABL1**
	AF4-MLL
	ETV6-RUNX1
	IL3-IGH

Molecular findings in Leukemia

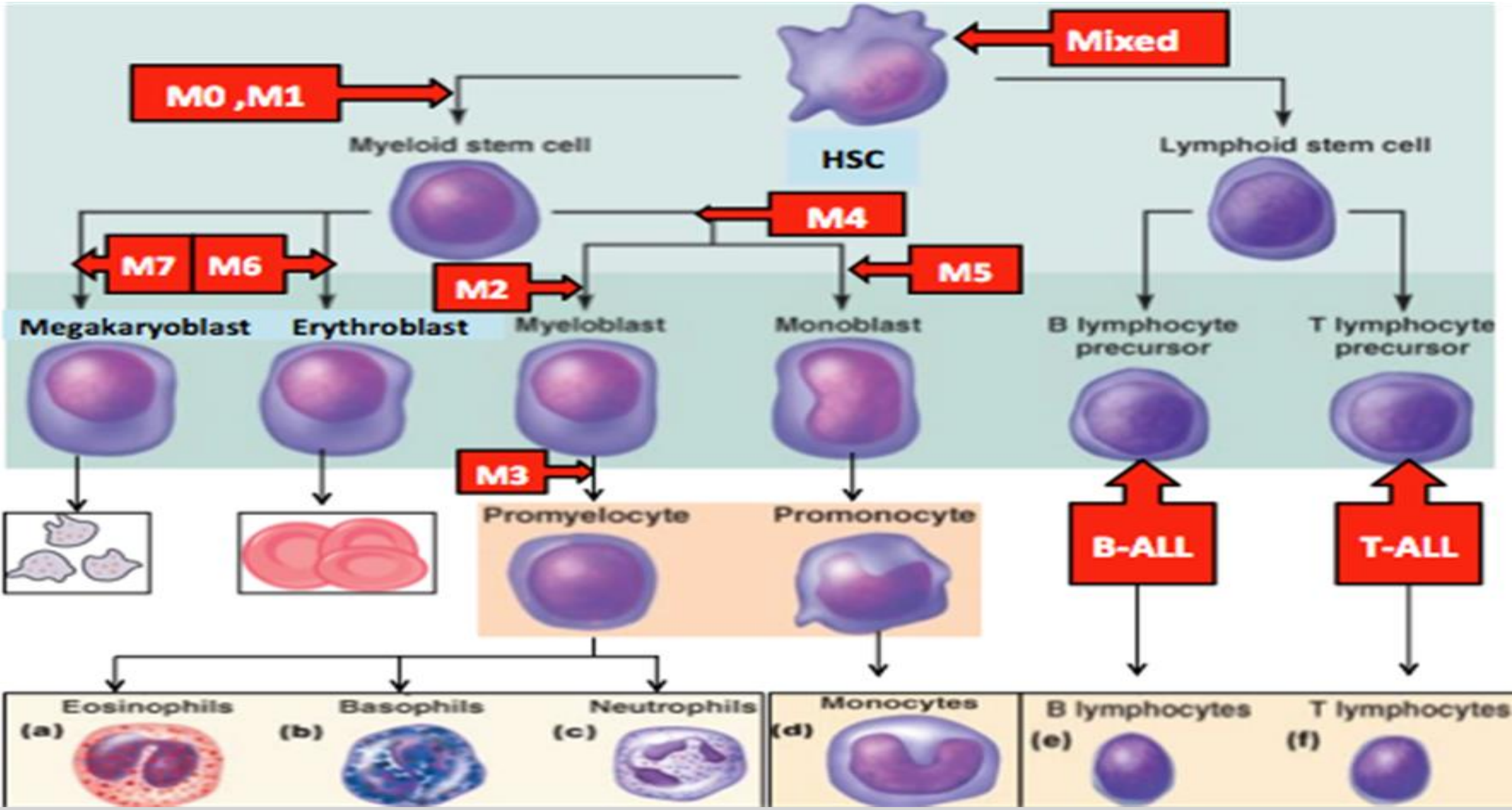
Acute Myeloid Leukemia

- Group of hematopoietic neoplasms caused by proliferation of malignant myeloid blasts in bone marrow and blood.
- Basis of diagnosis: The blast ≥20%

t(8;21) t (16;16) or t(15;17).

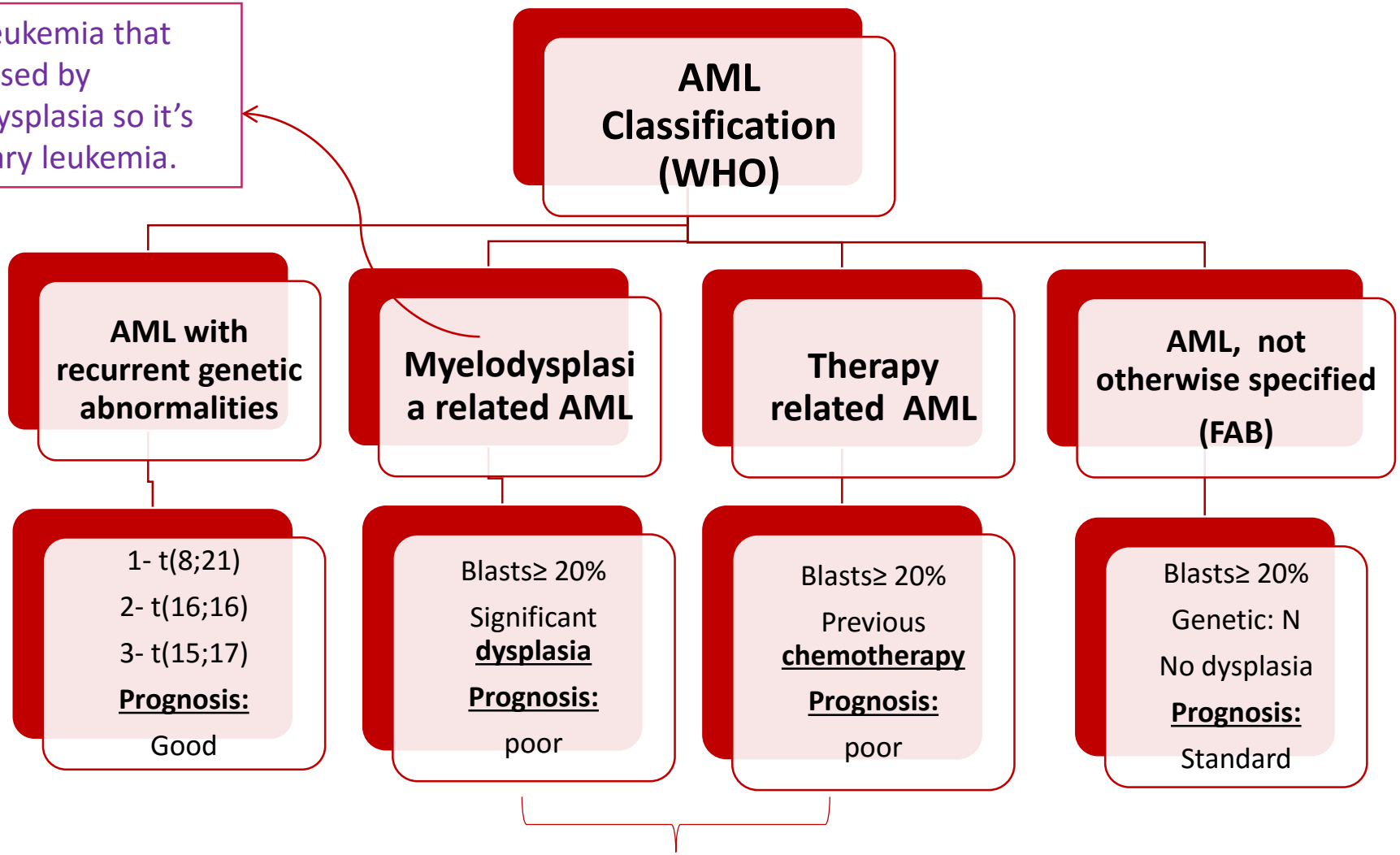
- More in Adults (do occur in infants!)
- Worse than ALL

Subtype	Features	Genetics in WHO	Notes
Mo	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		
M7	Megakaryocytic		
M8	Basophilic		


Mixed
M0 ,M1
Myeloid stem cell
HSC
Lymphoid stem cell
M4
M7
M6
M2
M5
Megakaryoblast
Erythroblast
Myeloblast
Monoblast
B lymphocyte precursor
T lymphocyte precursor
M3
Promyelocyte
Promonocyte
B-ALL
T-ALL
Eosinophils
(a)
Basophils
(b)
Neutrophils
(c)
Monocytes
(d)
B lymphocytes
(e)
T lymphocytes
(f)

AML Classification (WHO) WHO classification focused more on genetics

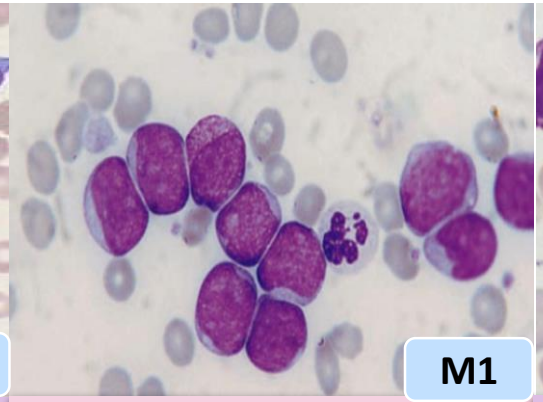
- Acute leukemia that was caused by Myelodysplasia so it's secondary leukemia.



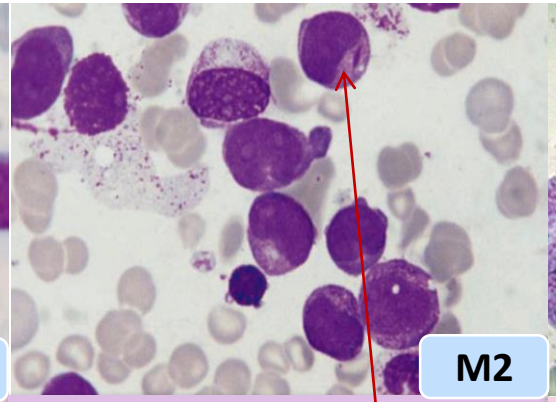
***Any leukemia that was caused by a known cause is called secondary leukemia and it has more poor prognosis than primary leukemia (Ex; Genetic).

FAB classification of AML: based mainly on morphology

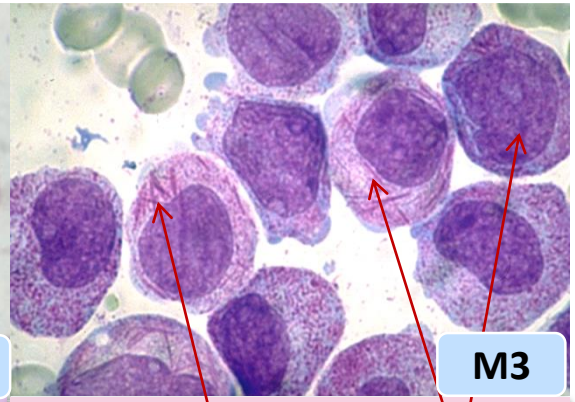
Minimal Defferentiation, No Maturation (Large blasts)



Begining of maturation, No Auer rods

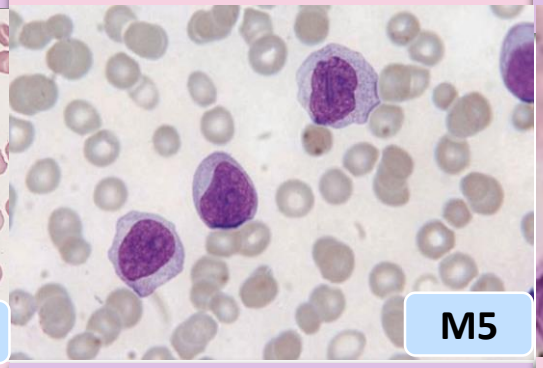


There is maturation, myeloblast, little presence of Auer rods.

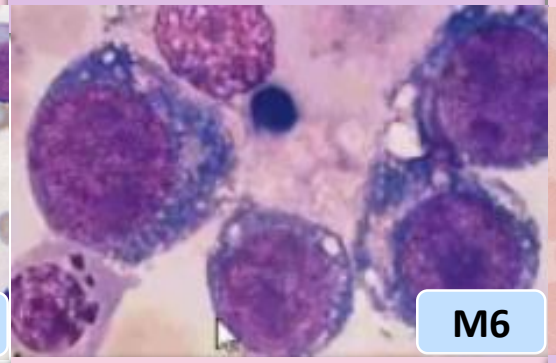


Presence of promyelocyte, and Auer rods

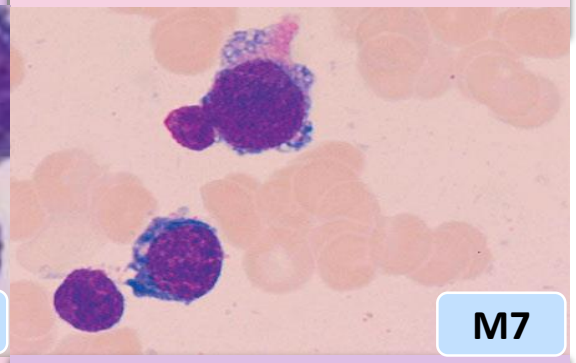
Myelocytic and Monocytic



Monoblasts and Monocyte



Precursors of erythrocyte.



Megakaryocyte.

Also M8 in basophils which have been recently discovered

All are known with **cytogenetic abnormalities**

Clinical features of AML

1-Pancytopenia: (Acute onset)

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

Most come with epistaxis and menorrhagia.

2-Organ infiltration:

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

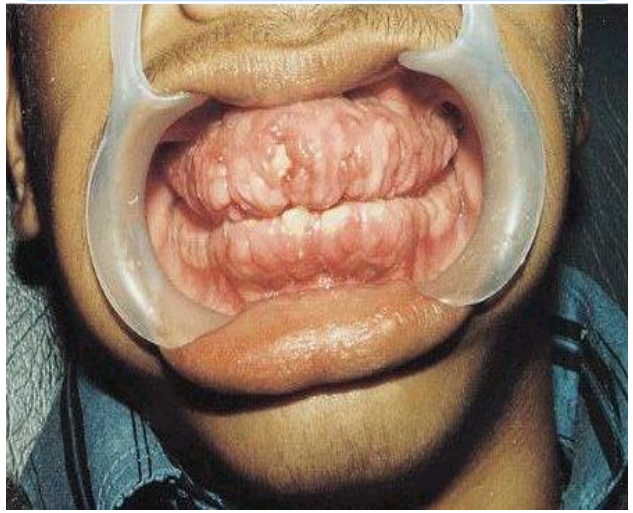
} More with Acute Monoblastic Leukemia

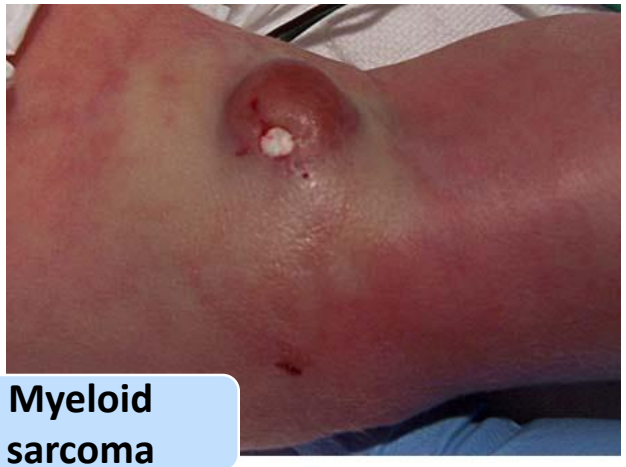
3-Leucostasis (increased blood viscosity)

4-Disseminated Intravascular Coagulation (DIC): (More with Acute Promyelocytic leukemia (M3).

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%)

Gum Hypertrophy
(To the extent u cant even see the teeth) with M4 and M5





Myeloid sarcoma

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 x10^9/L HB: 7g/dL PLT: 51 x10^9/L

➢ High WBC (Normal Total leukocytes: 4.00-11.0 x 10 ^{9}/L.)

➢ Low HB (Normal HB for male is 13.5-15.5 g/dL)

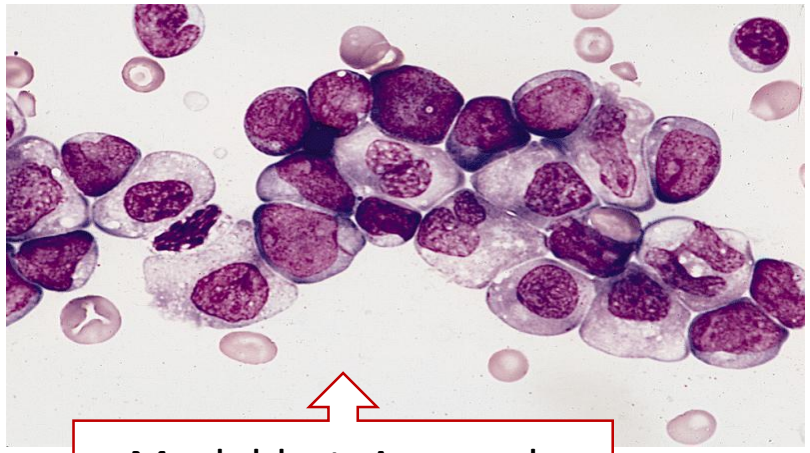
➢ Low PLT (Normal PLT is 150-350 x10^9/L)

Flow cytometry :

The blast are positive for CD34 ,CD13,CD33,CD117 and MPO (CD34 indicate stem cell marker, the rest indicate Myeloid marker)

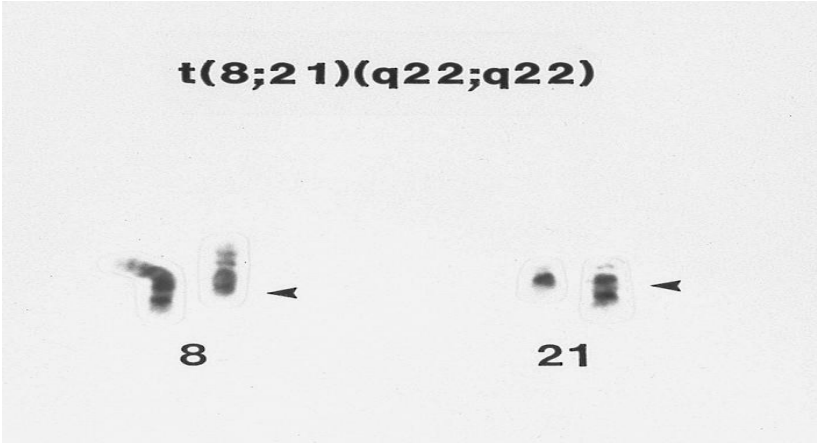
They are negative for CD3,CD10,CD19&CD79a (No T or B lymphocyte)

1)Blood smear & bone marrow:



AML with maturation (M2) (FAB)

2)Karyotype :



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

These cases are only to apply knowledge

Case Study 2 (male slides)

56 years old female presented to ER with fatigue ,fever and nose bleeding for 2 weeks.

- O/E : moderate hepatosplenomegaly & multiple bruises.
- CBC : WBC :40 $x10^9/L$, HB: 7g/dL , PLT: 51 $x10^9/L$

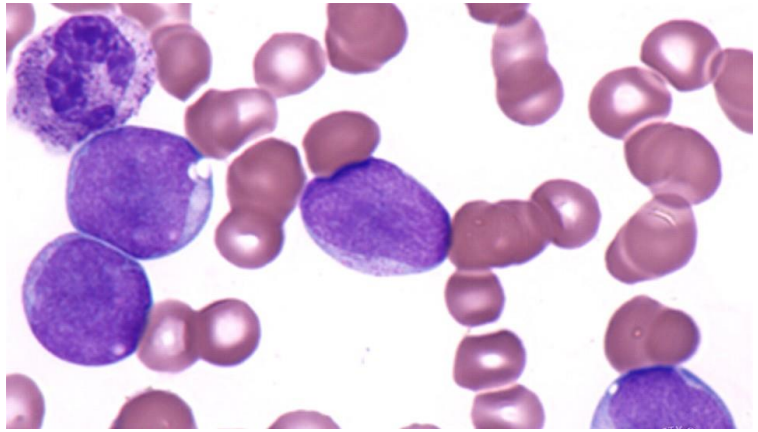
Flow cytometry :

There are 2 population of blasts :

1- (40%): CD34 ,CD13,CD33,CD117 and MPO

2- (20%): CD 34, CD14, CD 64

Blood smear & bone marrow:



Diagnosis :

Acute myelomoncytic leukemia (M4)(FAB)

These cases are only to apply knowledge

Prognosis and treatment

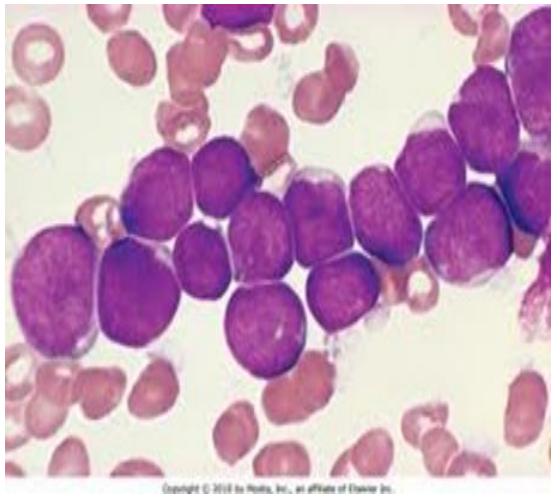
Better prognosis:

- 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) >>> important
- Stem cell transplantation best treatment

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

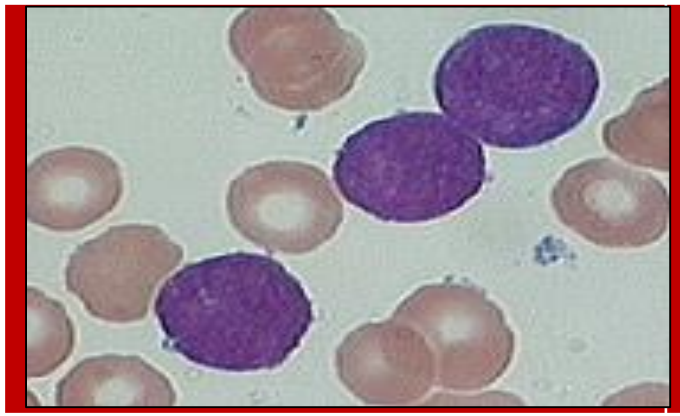
1-Pancytopenia:

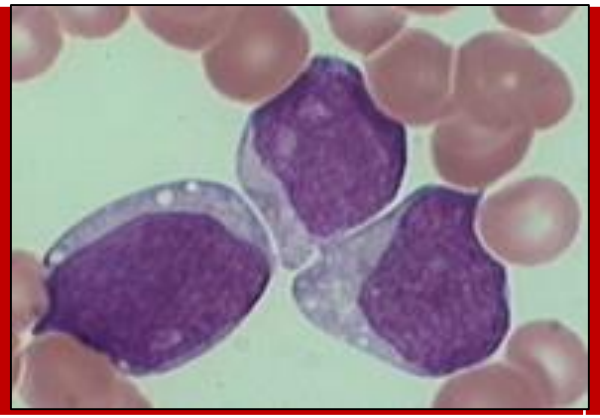
- ↓WBC→ infection
- ↓Hb →anemia
- ↓platelets →bleeding

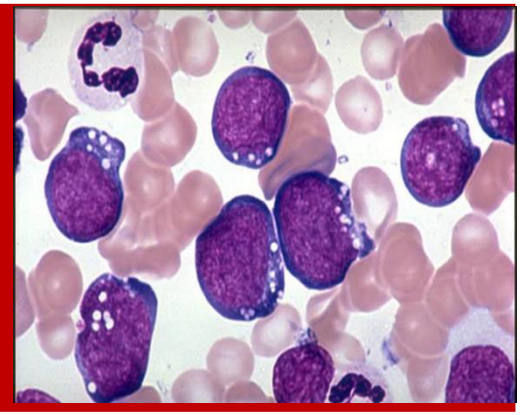
2-Organ infiltration:

- Lymphadenopathy (very common)
- Hepatosplenomegally.
- testicles involvement
- CNS disease
- Mediastinal mass common in T ALL

Morphological subtypes (FAB)





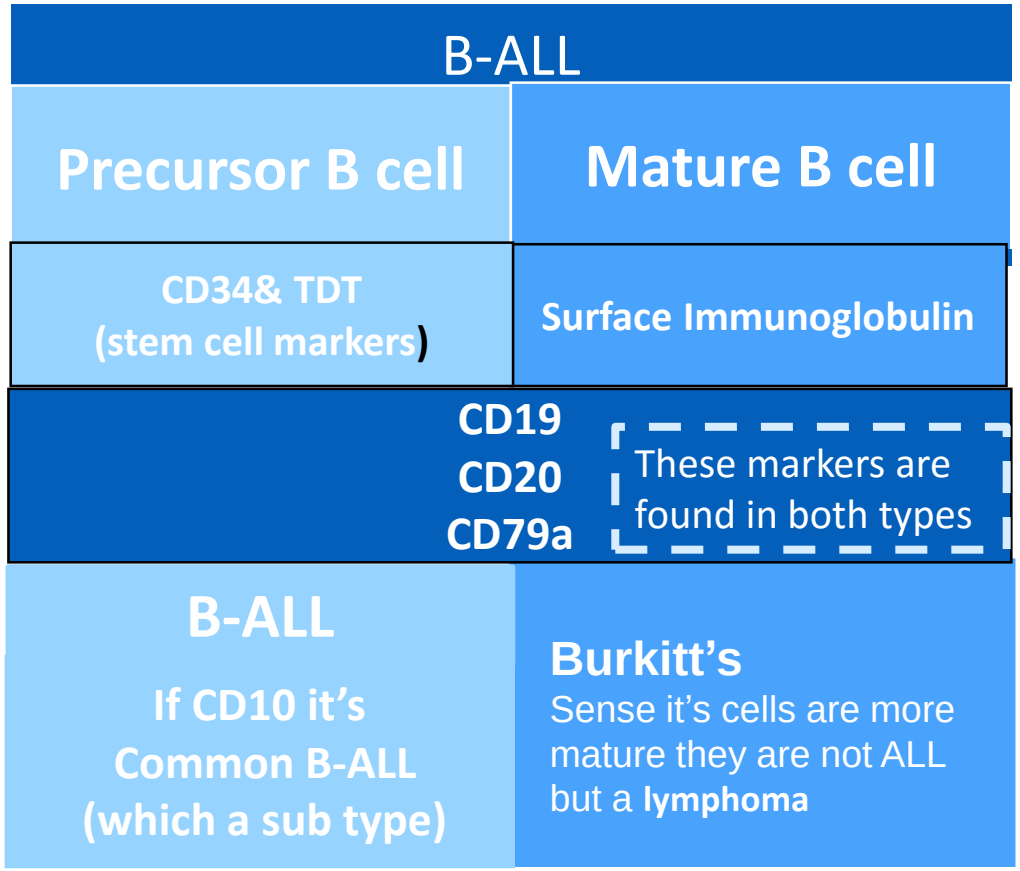


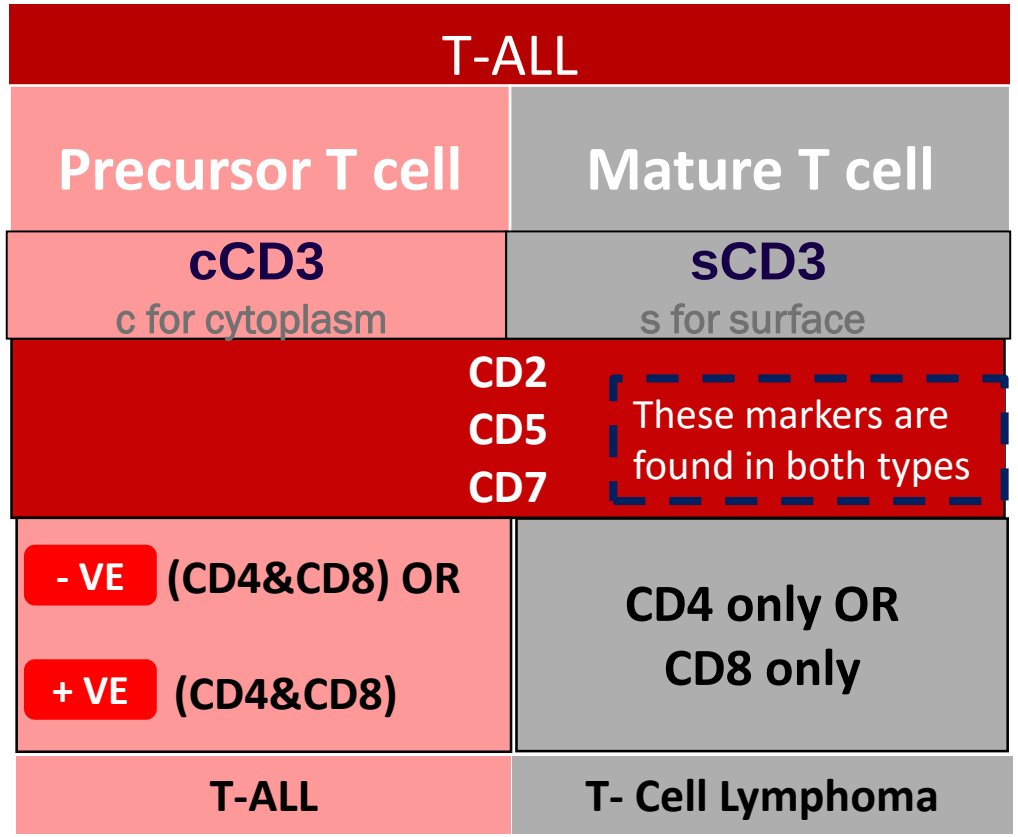
	L1	L2	L3 **Burkitt's**
Morphology	**Homogenous**	**Heterogeneous**	**Homogenous**
Size	**Small**	**Variable**	**Small**
Cytoplasm	**Little**	**More**	**Vaculated**
Nucleoli	**Not prominent**	**prominent**	**prominent**
Genetics	**Variable**	**Variable**	**t(8;14) cmyc**

Immunophenotypic Subtypes (WHO)

	B cell	T cell
Markers	CD10, CD19, CD79a	CD3
Percentage	80%	20%
Age	Younger	Older
Clinical	……	Mediastinal mass presence of enlarged thymus in the mediastinal CNS disease
WBC count	less	higher
Prognosis	Better	Worse
Genetics	t(9,22), t(4,11), t(12,21)	

B-ALL & T-ALL classification FAB





Prognosis &treatment of ALL

	Better	Worse
Age	2 - 10 yrs	<2 - >10 yrs
Gender	Female	Male
WBC count	Low	High
Cell type	B cell	T cell
B-ALL phenotype	Common (CD10)	Others
B-ALL genetics	Hyperdiploidy t(12;21) Hyperdiploidy is when chromosome in cells is more than 55	Hypodiploidy t(9;22) Hypodiplodidy is when chromosomes less than 44
CNS involvement	No	Yes

Treatment : of all ALL

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

Q1 Which one of the following is true regarding leukemia:

A. ALL is more common in adults
B. ALL is more common in children
C. ALL is worse than AML
D. AML is more common in children

Q2 Which one of the following chromosomal karyotypes is associated with Gum Hypertrophy:

A. t (12-21)
B. t(8-21)
C. t(9-22)
D. t-inv(16-16)

Q3 Which one of the following is not a characteristic of ALL under LM:

A. agranular cytoplasm
B. Round nucleus
C. Auer rods
D. Non

Q4) A 34 year old male has come to the ER with a very painful wound with bone involvement.The CBC results showed sever pancytopenia. A flow cytometry were applied and the results were as follow:

CD34: + , MPO: +

The Doctor has then diagnosed him with Acute Myeloid Leukemia. Which one of the following types is most probably is:

A. M4
B. M5
C. M3
D. M7

Q5 Which one of the following best describes flow cytometry:

A. It is used to detect the specific DNA sequences.
B. It is used to study the structural and numerical abnormality of a chromosome
C. It is used to detect certain morphologic changes
D. It is used in cellular studies through cytoplasmic markers.

Q6 FAB classification is based on more than one:

A. Clinical history
B. Morphology
C. Molecular studies
D. Flow cytometry

Q7 Which of the following is true regarding ALL:

A. B-ALL has worse prognosis than T-ALL
B. Burkitt's is a type of ALL
C. Is better in prognosis than AML
D. All

1– B
2 – D
3 – C
4 - C
5- D
6 –B &D
7- C

Q1) A 60 yrs old male came to the ER after fainting on examination he appeared very pale also in diagnosis her we found he has fever and blurred vision CBC was made showed decrease in his, RBC ,platelets ,and Hb . A blood smear film was done which showed promyelocyte with red lines ,. A genetic study was done which showed a t(15,17)

what is your diagnosis ? Acute Myeloid Leukemia AML M3

what are these red lines called ? auer rods

how to treat him? ATRA or arsenic

Q2) A 4 yrs old boy came with an enlargement in both his liver and spleen bone pain , fever. a CBC was done which showed as decrease in his WBC , RBC ,Hb ,and platletes . Blood film showed a Lymphoblast and a bone aspirate was done which showed a lot of Lymphoblast an flow cytometer showed the marker cCD3 , CD 5 ,CD7 ,CD2 ? What is your diagnosis

Acute Lymphoblastic Leukemia (ALL)

Q3) 10 year old male presented to ER after fainting the clinical examination showed enlargement in his gums, fever , he was pale. A CBC showed decrease in his RBCs, platletes ,Hb and WBCs A blood smear film showed Myelocytic and Monocytic blasts

What is your diagnosis Acute Myeloid Leukemia AML M4

Thank you for checking our work

Now you can check a lecture out :D

Done by :

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Nada alamri

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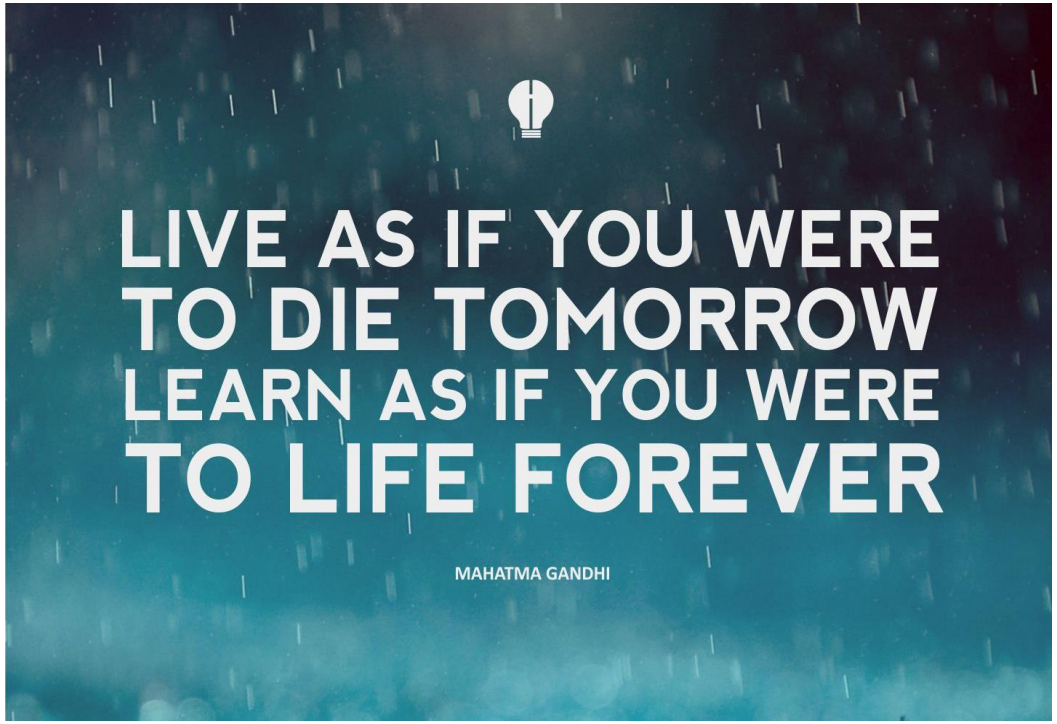

دعاء بعد المذاكرة :

(اللهم اني أستودعتك ما قرأت وما حفظت وما تعلمت، فرده لي عند حاجتي اليه أنك على كل شيء قدير، وحسبنا الله ونعم الوكيل)