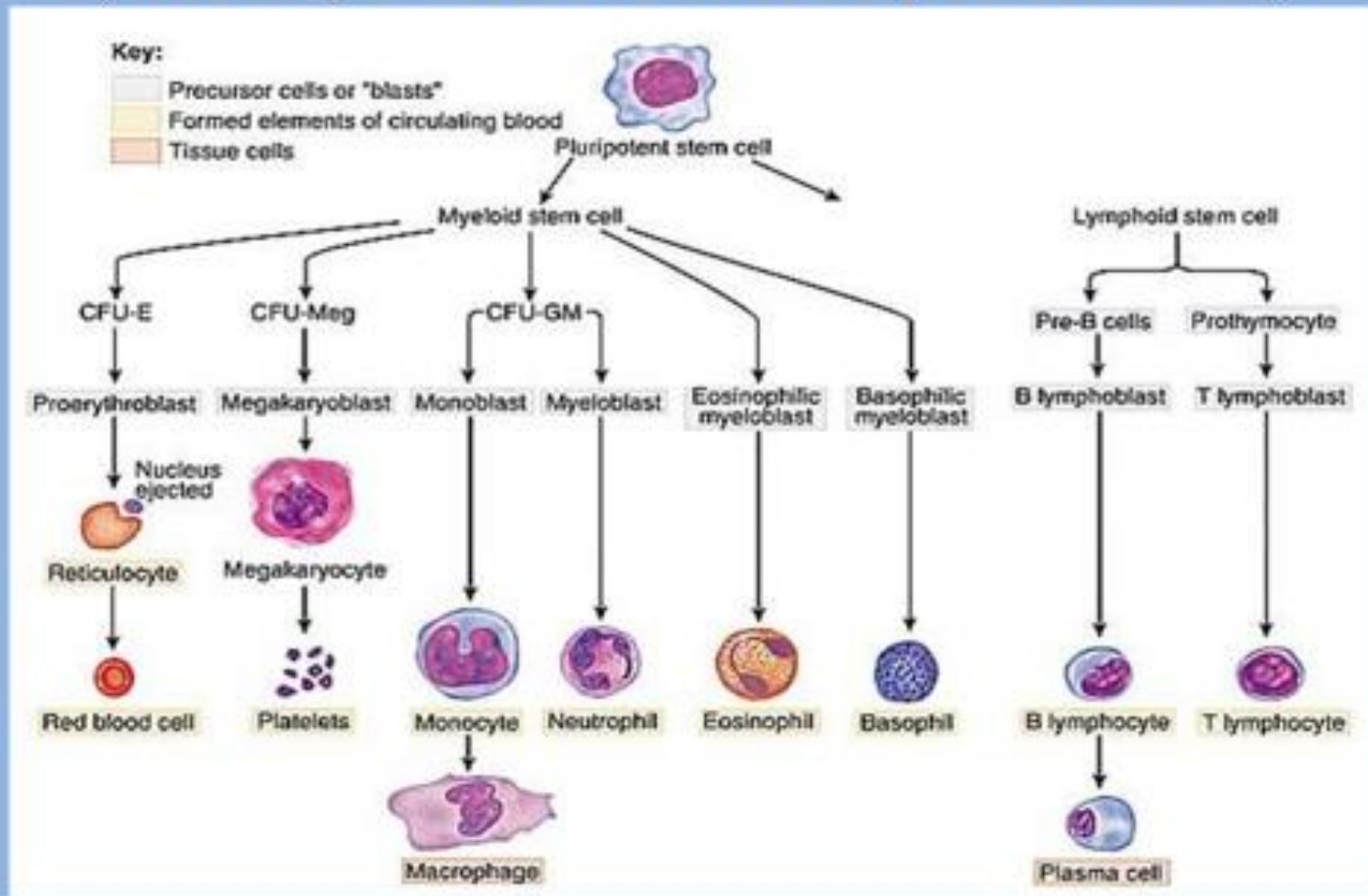


# **Childhood Leukemia**

**Professor: Nourz Elgheriani**

# Cell hierarchy (Haemopoiesis schematic representation)



Leukemia is a malignant disease in which genetic abnormalities in a hematopoietic cell in the bone marrow give rise to an uncontrolled proliferation of blood cells leads to disruption of normal marrow function and replaced by leukemic cells causing bone marrow failure then spread to blood and other organs.

If not treated, it is lethal within 1 - 6 months.

It has a different immunological subtypes.

# Childhood Leukemia

The **most frequent malignancy** in children (30%)  
followed by Lymphoma  
then CNS tumors

Acute Lymphoblastic Leukemia ALL is the most common  
type of leukemia in children (80%)

## Types of leukemia

**ALL** Acute Lymphoblastic Leukemia (80%)

**AML** Acute Myeloid Leukemia 15%

**CML** Chronic Myeloid Leukemia < 5%

**CLL** not in children(chronic lymphoblastic L)

**Each type of leukemia is divided to subtypes according to the following investigations:**

Morphological L1, L2, L3 (FAB classification ) (microscopically)

Immunological, flow cytometry; pre-B cell, B-cell, T-cell.

Cytogenetic (Karyotyping) abnormal chromosomes.

Biochemical

Molecular genetic.

**each subtype has different response to treatment.**

## Syndromes & congenital disorders with high risk of leukemia

- Identical twin with leukemia
- Trisomy 21 (Down syndrome) (14 times higher)
- Turner syndrome
- Klinefelter syndrome
- Neurofibromatosis type 1
- Fanconi anemia (high fragility of chromosomes)
- Monosomy 7
- Syndromes: (Bloom, Kostmann, Shwachman-Diamond)
- Ataxia- teleangiectasia
- Congenital agammaglobulinemia
- Wiskott- Aldrich S
- Severe Combined Immunodeficiency

**Genetic predisposition**

**&**

**Environmental causes:**

Ionizing Radiation

Chemotherapy

Viruses (EBV, HIV)

Pesticides



**ALL**

Acute Lymphoblastic Leukemia

# Acute Lymphoblastic Leukemia ALL

Most common type of childhood Leukemia (80%)

Peak age: 2-5 years

Males > females

white children > (twice) non-white children

# Signs & Symptoms of ALL

=

Signs & Symptoms of **Pancytopenia** (medullary site, bone marrow)

+

**Organomegaly**

+ -

The signs & symptoms of **under lining syndrome**

+ -

Signs & Symptoms of extramedullary sites  
**CNS leukemia & Testicular leukemia**

## The signs & symptoms of ALL

### **Anemia:**

pallor, fatigue, tachycardia, dyspnoea, may cardiovascular decompensation (heart failure)

### **Leucopenia (low WBC count) or Leucocytosis high count of non-functional WBCs:**

Fever

Sign & symptoms of infection commonly respiratory infections.

### **Thrombocytopenia:**

Bleeding: Petechial rash, ecchymosis, Bruises, mucosal bleeding; epistaxis, gum bleeding.

## The signs & symptoms of ALL

### Organomegaly:

Hepatomegaly

Splenomegaly may cause abdominal pain

Lymphadenopathy (Generalized)

Mediastinal Mass (T-cell leukemia)

Joint swelling (arthritis), bone pain, bone tenderness & limping

## Signs of extramedullary sites (CNS & Testes)

### CNS Leukemia

at time of diagnosis 5% of patients have CNS Leukemia with meningeal signs:

morning headache,

vomiting,

papilledema,

Cranial Nerve Palsies & any other neurological signs

### Testicular involvement

Painless testicular swelling

priapism is occasionally associated with elevated WBC

## **Bone and joint involvement:**

Bone pain:  
present in 25 % to 50% of patients.

Joint swelling & tenderness:  
due to leukemic infiltration of the periosteum.

Differential Diagnosis:  
rheumatic fever, rheumatoid arthritis

## Mediastinum enlargement

anterior mediastinal mass due to leukemic cells infiltration in lymph nodes and /or thymus (thymus in T-cell leukemia)

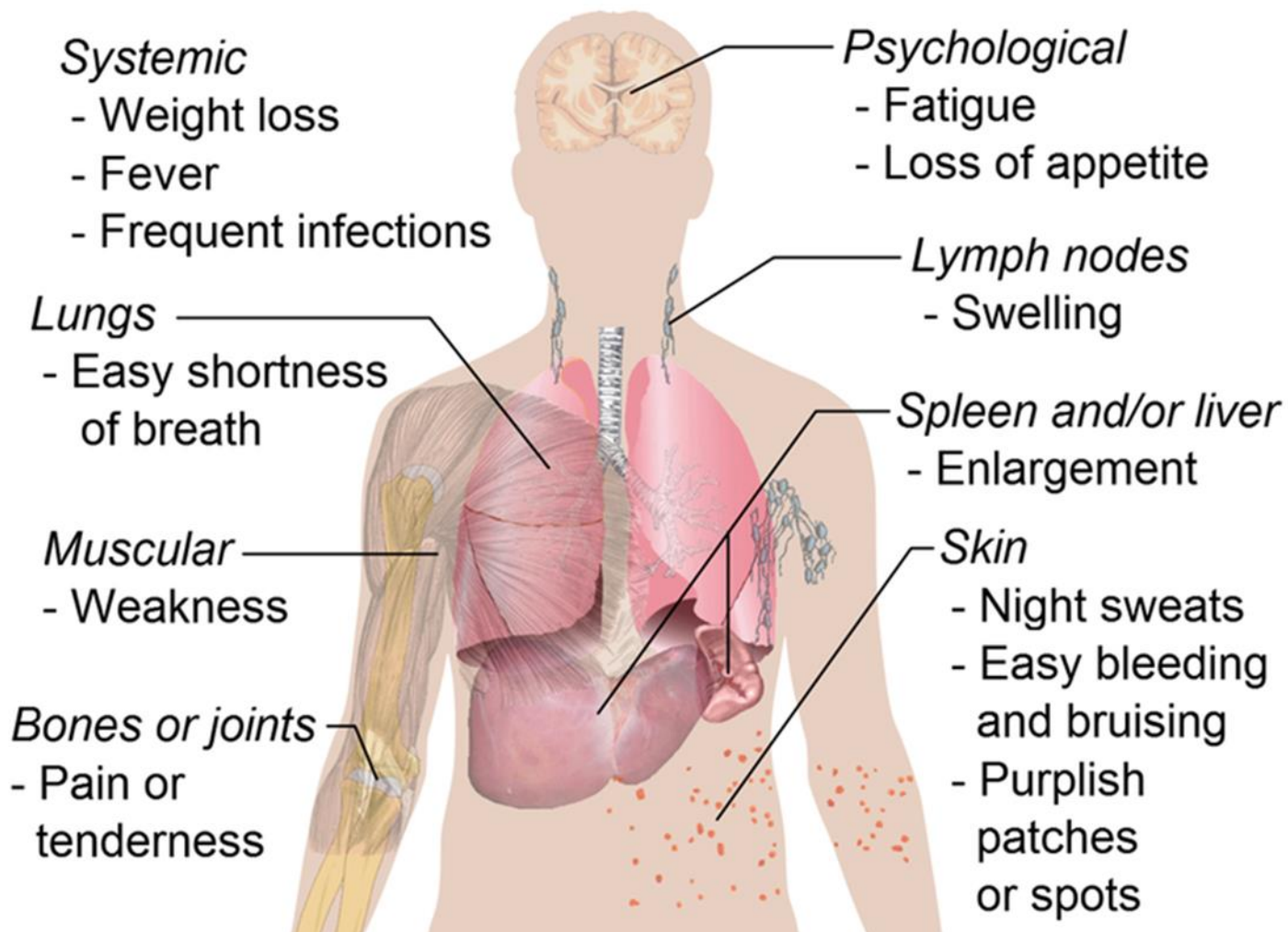
Kidney enlargement due to leukemic cells infiltration

## Very rare Cardiac involvement

due to pericardial infiltration by leukemic cells, tachycardia, low blood pressure, other signs of cardiac insufficiency



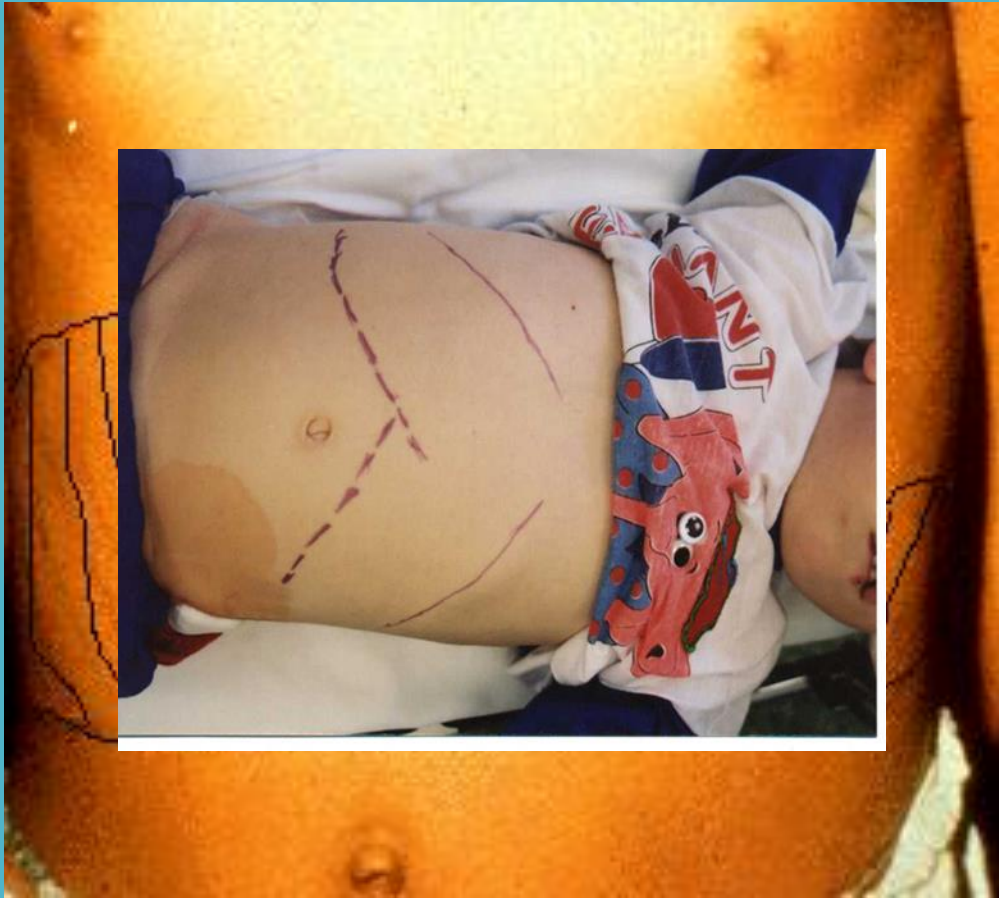
Common symptoms of  
**Leukemia**



**Petechiaie**







# Investigations for ALL

## 1. CBC

WBC count: ↑ or ↓ **Leucocytosis or Leucopenia**

Hemoglobin: **Anemia**

Platelet count: **Thrombocytopenia**

MCV, MCH, MCHC are normal

## **2. Peripheral Blood Film**

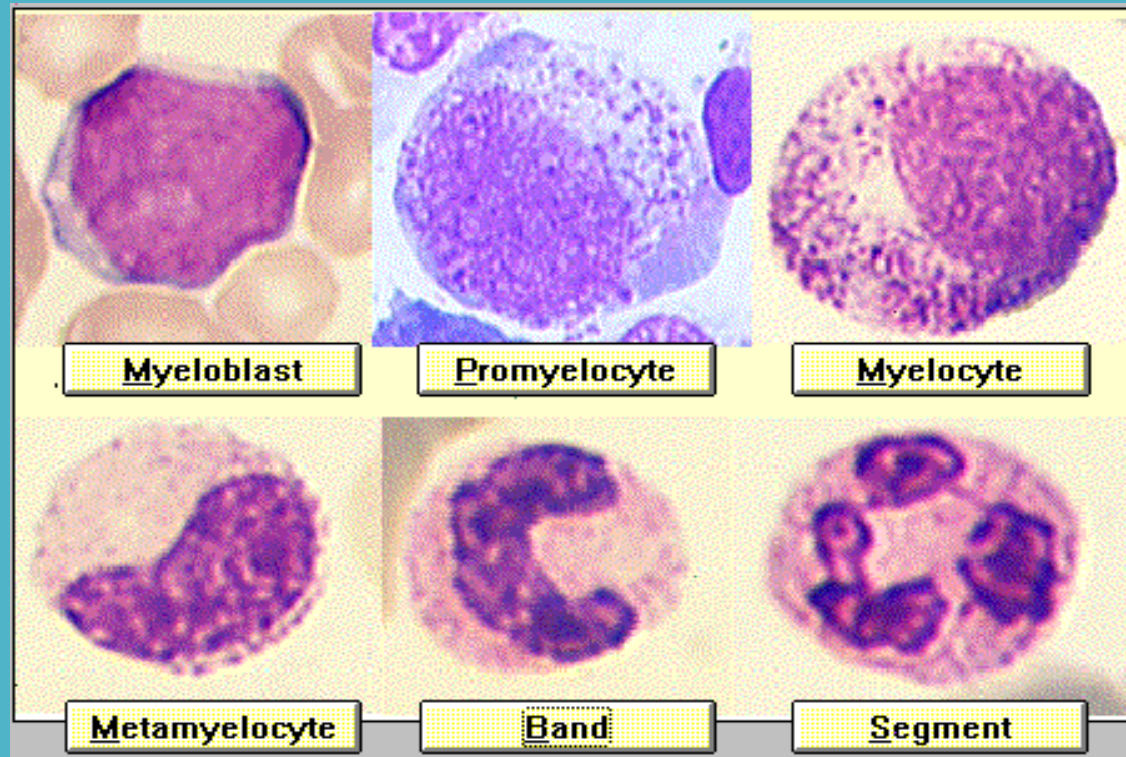
### 3. Bone Marrow Aspiration or Biopsy

> 25% blast cells

Morphology  
Cytochemistry  
Immunophenotyping  
Genetics

# Bone marrow examination

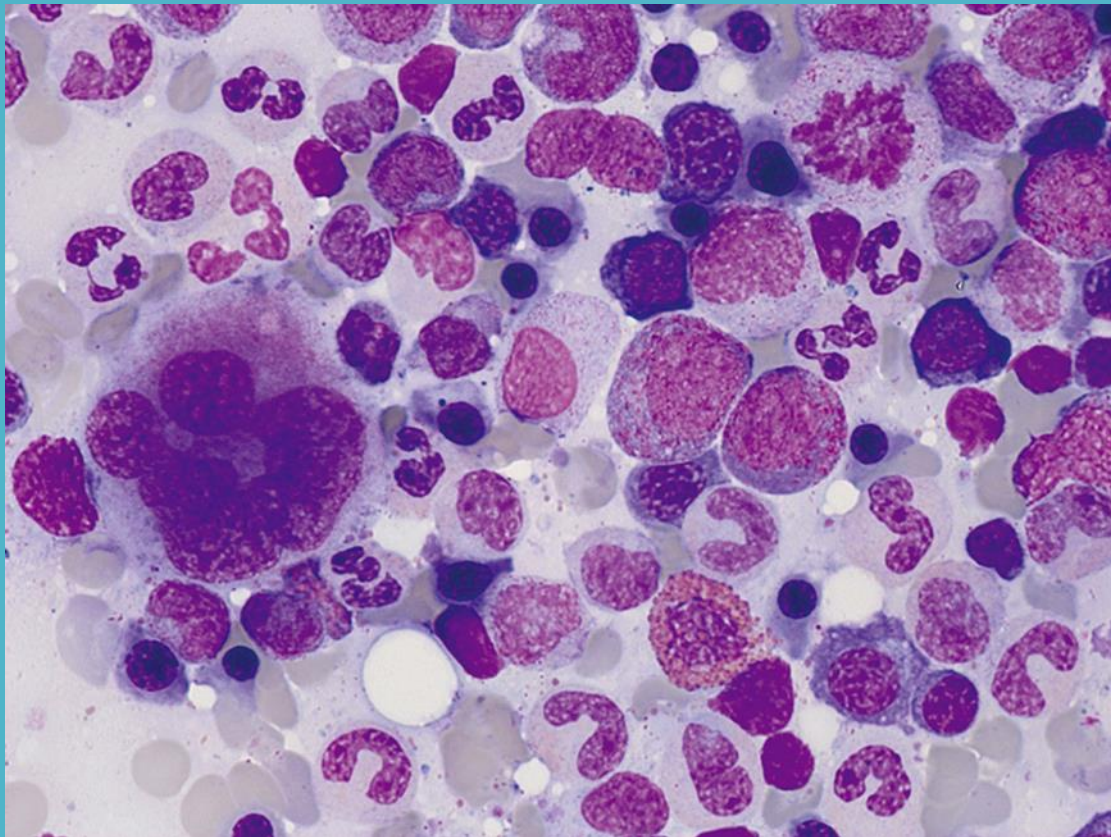
## Morphology



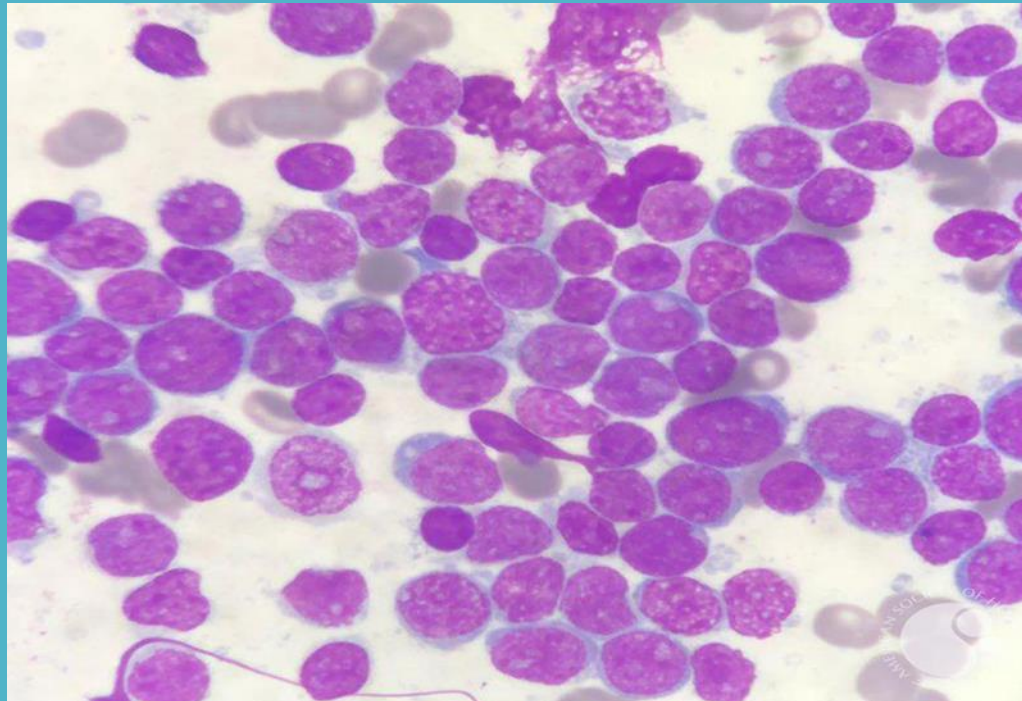


# Bone marrow examination

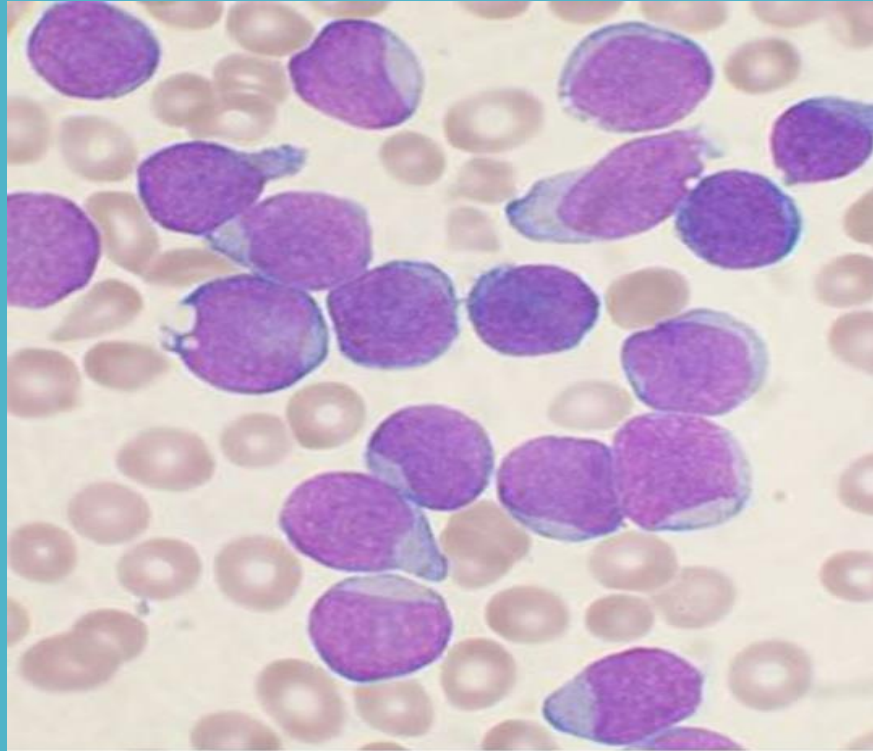
## Morphology of Normal bone marrow



Bone marrow aspiration  
morphology of ALL  
(Acute lymphoblastic leukemia)



Bone marrow aspiration  
morphology of ALL  
(Acute lymphoblastic leukemia)



Morphology: FAB classification:

ALL - L1

ALL - L2

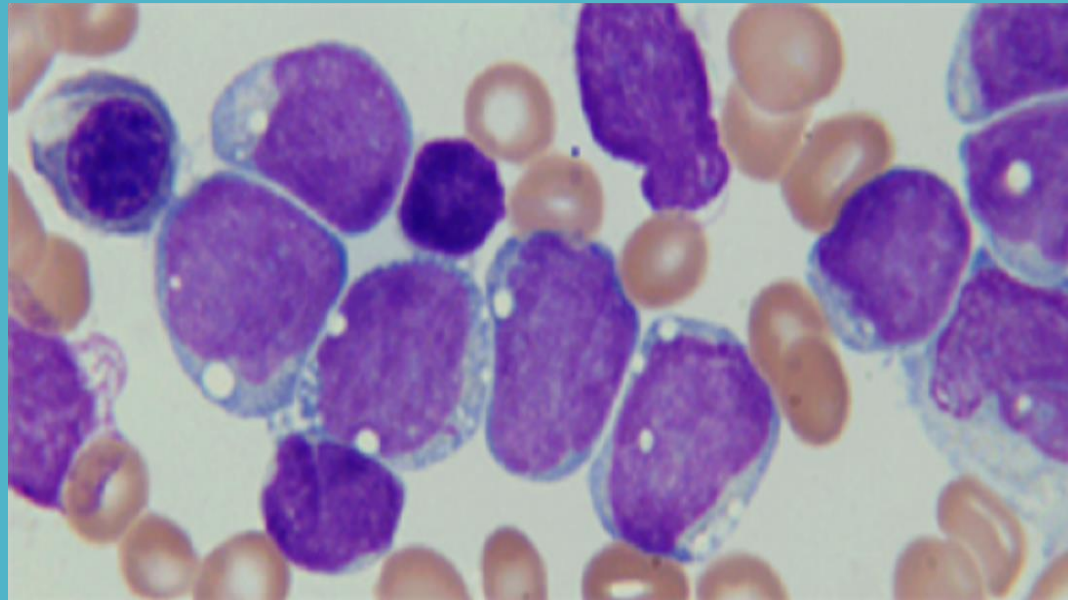
ALL - L3

chemistry:

ALL: + periodic acid Schiff(PAS)

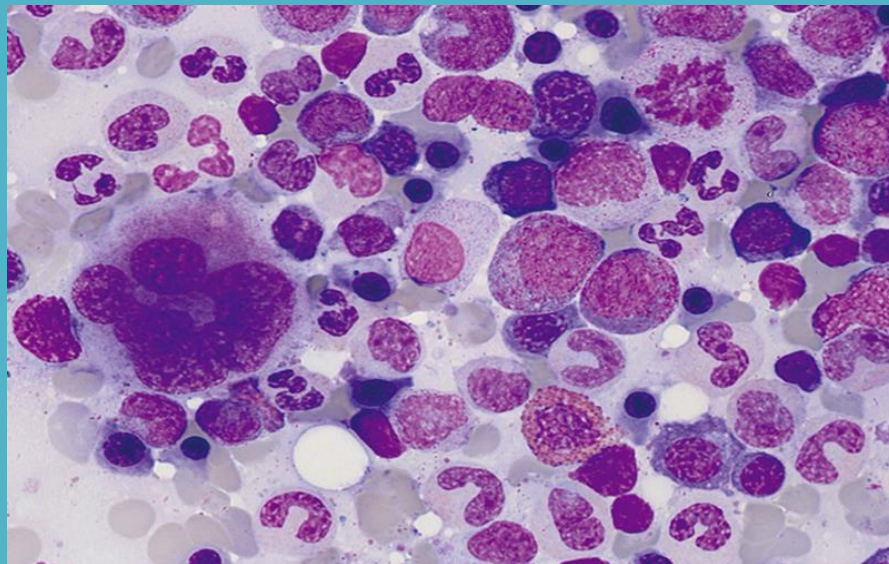
AML: + Sudan black, + peroxidase

Bone marrow aspiration  
Morphology of  
Acute lymphoblastic leukemia  
ALL-L3 (vacuoles)

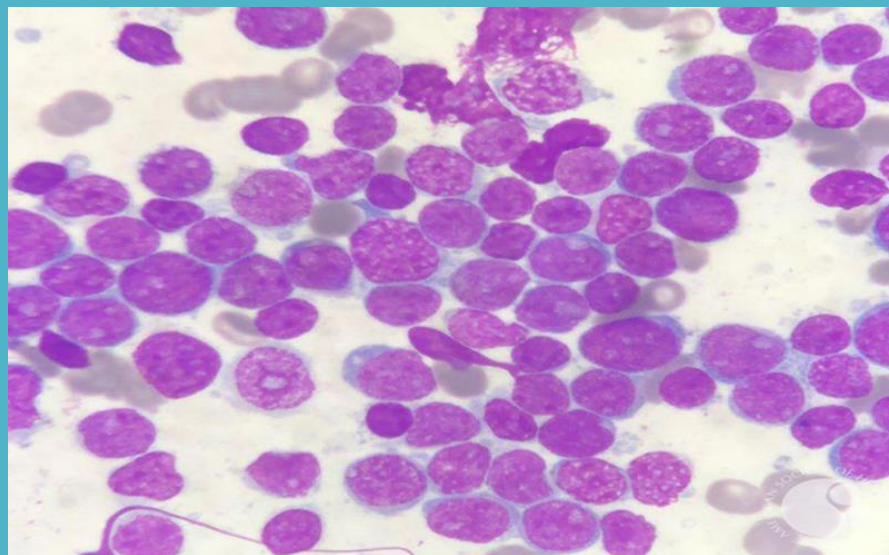


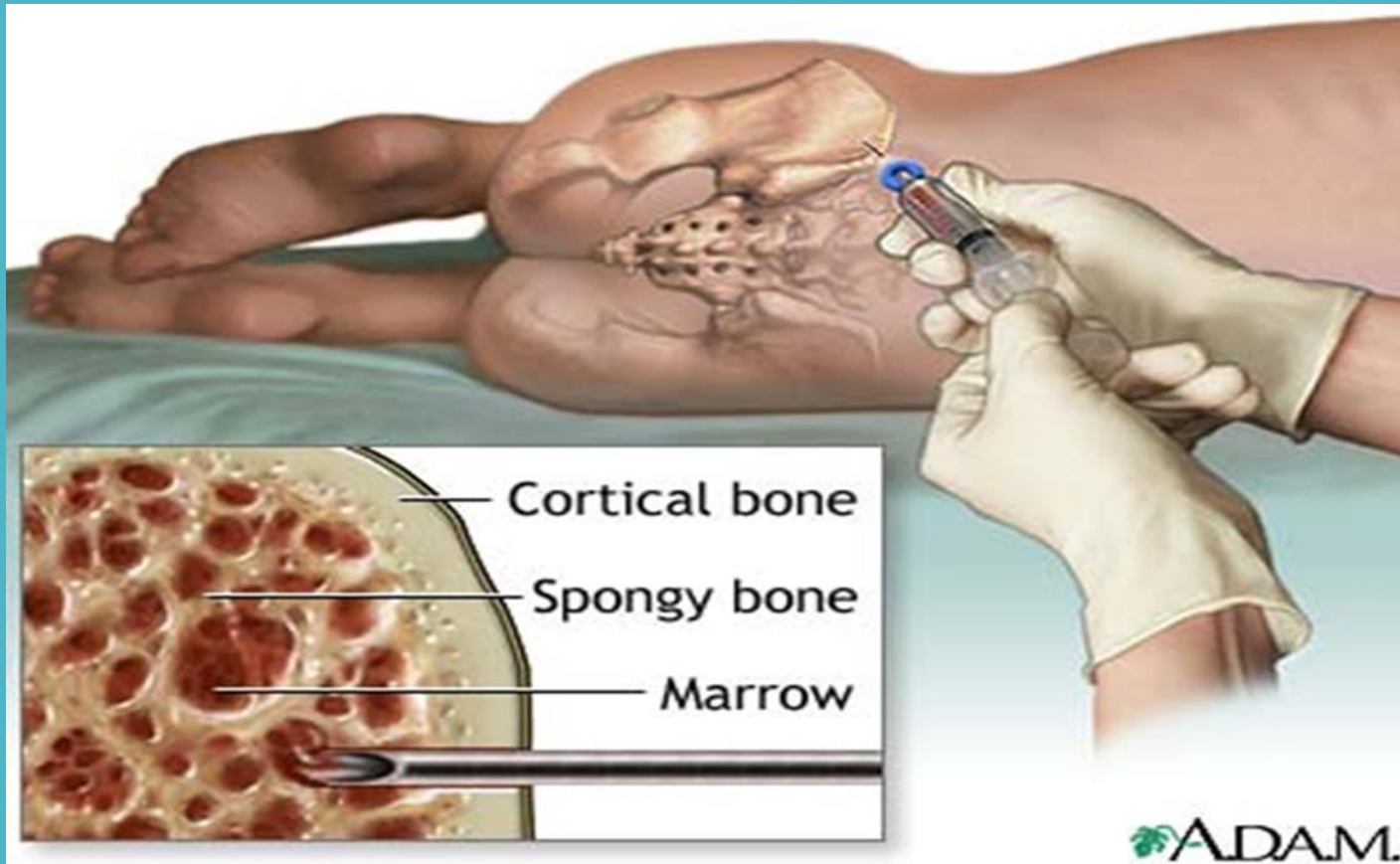


Normal Bone Marrow



ALL

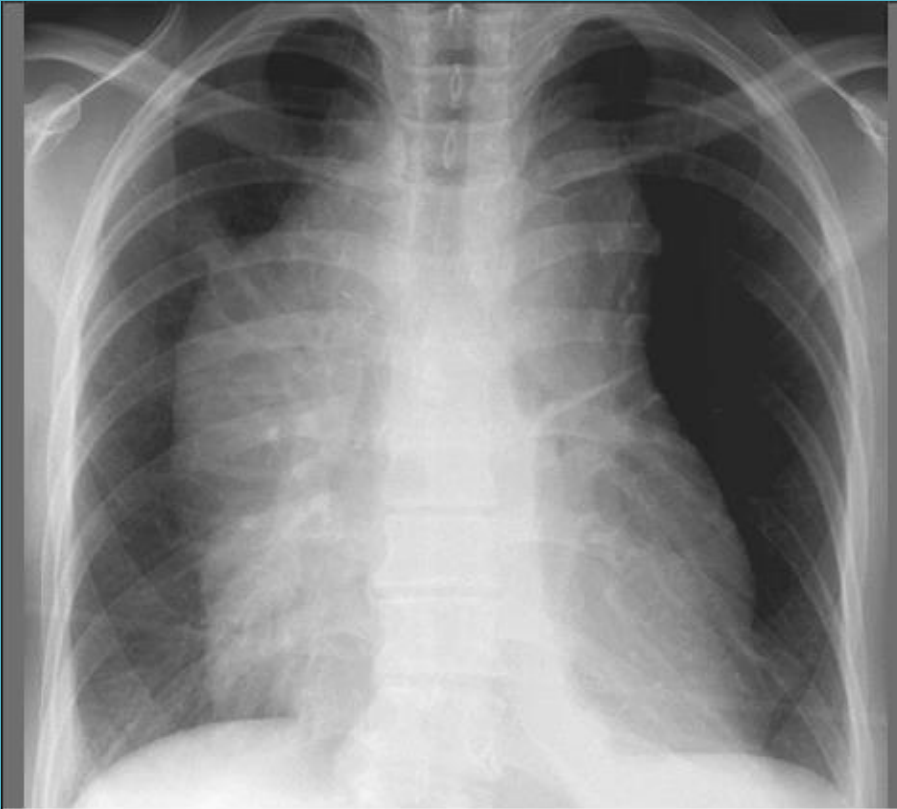




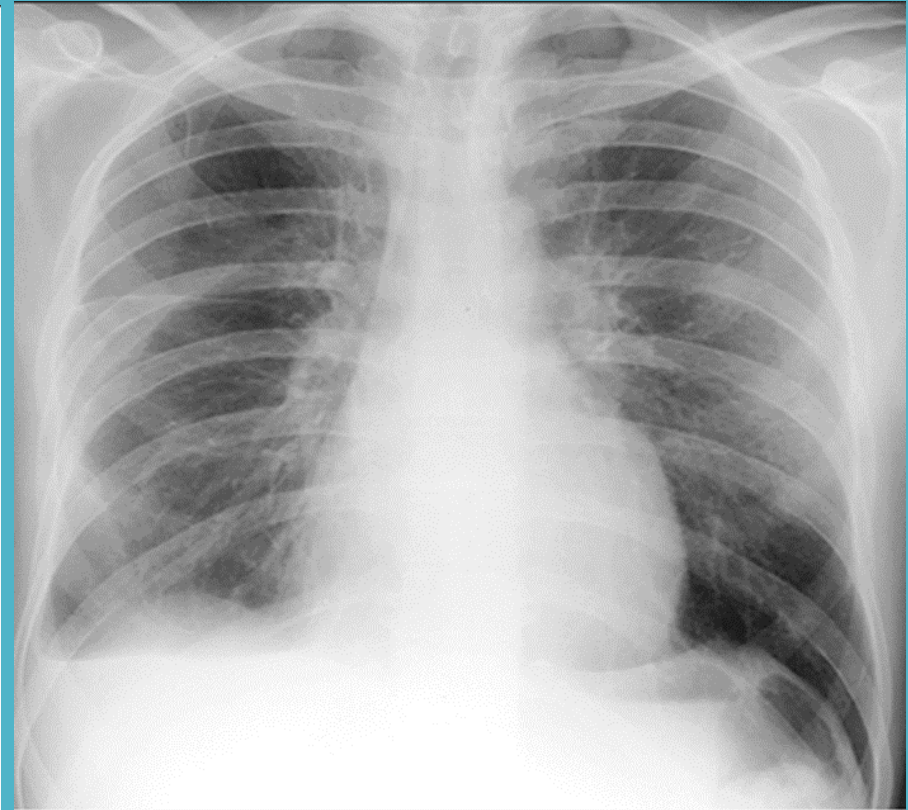
Bone Marrow Aspiration

## 4. Chest X-ray

for mediastinal mass in T cell leukemia



Chest X ray shows  
Mediastinal Mass



Normal chest X ray



## 5. Lumber Puncture

for **Cerebrospinal fluid** examination

for blast cells in **CNS leukemia**

## 6. Renal function tests

Tumor lysis syndrome:

High uric acid

High K

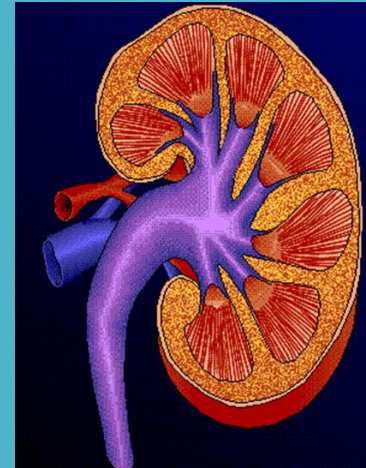
High PO<sub>2</sub>

High creatinine

High urea

Low Ca

Low Na



## 7. Flow Cytometry Immunological study

Monoclonal Antibodies to leukemia-associated antigens differentiate between types of leukemic cells:

- \*lymphoid stem cells: CD19, HLA-DR, CD 24 (+/-)
- \* early pre-B cells: CD19, HLA-DR, CD24
- \* pre-B cells: CD19, HLA-DR, CD24, CD10, CD20(+/-)
- \* B-precursors cell: CD19, HLA-DR, CD24, CD10, CD20
- \*T-cell lineage: CD7, CD2, CD1, CD4, CD8,CD3

## 8. Cytogenetic studies of bone marrow; Karyotyping

To study structure of chromosomes and their ploidy

**Hyperploidy** (extra-chromosome) has good prognosis

**Hypoploidy** (chromosomes less than 46) has poor prognosis

**Trisomies** have favourable prognosis

t(9;22) BCR/ABL translocation (**Philadelphia chromosome**)  
has unfavourable prognosis

# Bone marrow Cytogenetics study

**Translocation**

**t (1;22)**

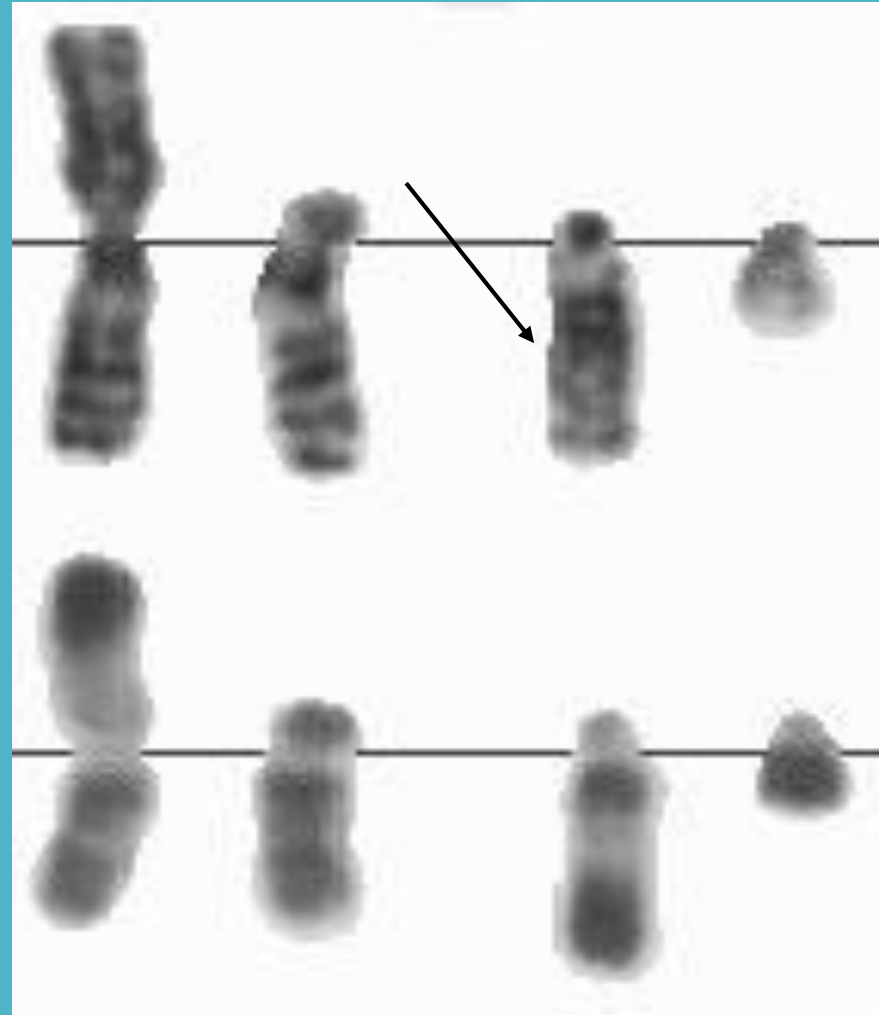
**Infant M7 AML**

**Very poor prognosis**

**Hypodiploidy**

**t(9:22)**

**iAMP 21**



# Prognostic Factors of ALL

## Standard Risk with favourable prognosis:

WBCs count in CBC  $< 50 \times 10^9/L$

Age between 1 - 10 years

Early response to chemotherapy (steroid)

Pre-B cell subtype

Hyperploidy (Trisomy)

No CNS involvement

## High Risk with unfavourable prognosis:

WBCs count in CBC  $> 50 \times 10^9/L$

Age below 1 year (infant) & above 10 years

No early response to chemotherapy (steroid)

B cell & T cell subtypes

Hypoploidy & certain chromosomal abnormality as Philadelphia

CNS leukemia

# Differential Diagnosis of ALL

- **Viral infection (infectious mononucleosis)**  
Fever, upper respiratory infection, splenomegaly & skin rash)
- **Aplastic Anemia**  
Pancytopenia with out organomegaly.
- **ITP**  
mild bleeding (petechial rash, ecchymosis, gum bleeding & epistaxis)
- **Bone marrow infiltration by other tumour** as (lymphoma, Neuroblastoma)
- **Rheumatoid arthritis, Lupus:**  
arthritis
- **Leukemoid reaction** in bacterial infection
- **Transient Erythroblastic Anemia of Childhood**

## Symptomatic treatment

1. Anemia: **packed cell transfusion**,  
(must be CMV-negative, irradiated)
2. Thrombocytopenia: **platelet transfusion**  
(must be CMV-negative, irradiated)
3. Sepsis / infection  
**Antibiotics, antifungal, etc**
4. Tumour lysis syndrome  
**IV fluid, diuretic, Allopurinol**



Transfusion of **CMV-negative, irradiated,**  
packed cells, platelet, granulocytes



# Chemotherapy

**Induction of Remission**

**Consolidation with CNS prophylaxis** (Methotrexate)

**Reintensification**

**Maintenance phase**

Steroids (prednisolone, dexamethasone)

Vincristine IV

Adriamycin IV

Asparaginase

Intrathecal chemotherapy (Cytarabine & Methotrexate)

6-Mercaptopurine orally

Methotrexate IV

Ara-C IV

# **Stem Cell Transplantation**

**(Bone Marrow Transplantation)**

for selected cases with high risk

5-years survival rate of ALL is 90%

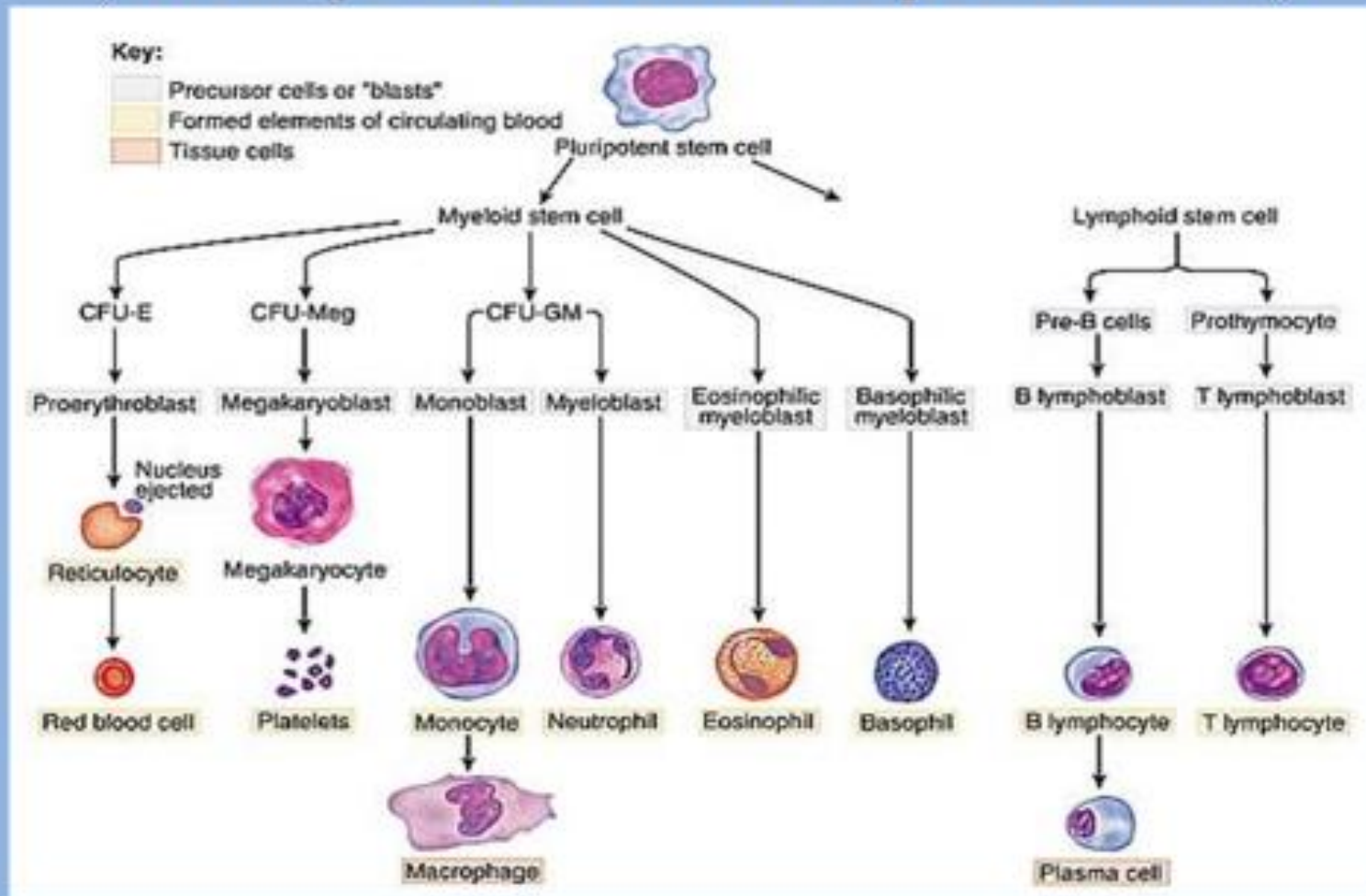
Prof. Nourz Elgheriani

# Acute myeloid leukemia

## AML

Heterogeneous group of malignant hematological precursor cells of the **myeloid, monocytic, erythroid or megakaryocytic** cell lineage

# Cell hierarchy (Haemopoiesis schematic representation)



## **FAB classification of AML**

M0: immature myeloblastic leukemia

M1: myeloblastic leukemia

M2: myeloblastic leukemia with signs of maturation

M3: promyelocytic leukemia

M4: myelomonocytic leukemia

M5: monocytic leukemia

M6: erythroleukemia (RBCs precursor Leukemia)

M7: megakaryocytic leukemia (Platelet precursor Leukemia)

ALL

80%

2 - 5 years

90% cure rate

AML

15%

all ages

65% cure rate



Gum Hypertrophy in  
AML  
(acute myeloid leukemia)



## Auer rods in AML M1/M2





# THANK YOU

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