ACUTE LEUKEMIA

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Objectives :-

= diagrammatic explanation to hematopoiesis .

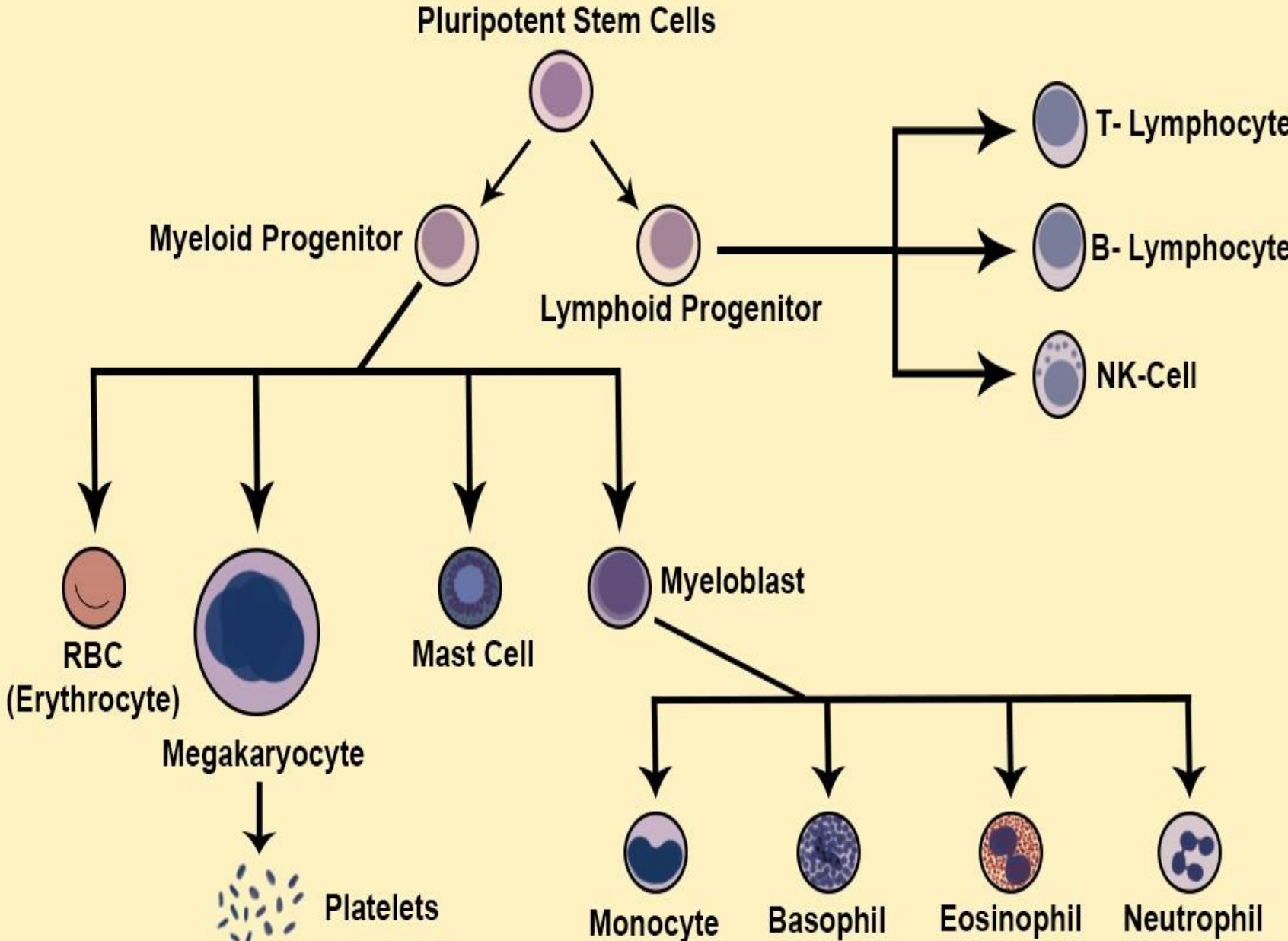
= types of leukemia .

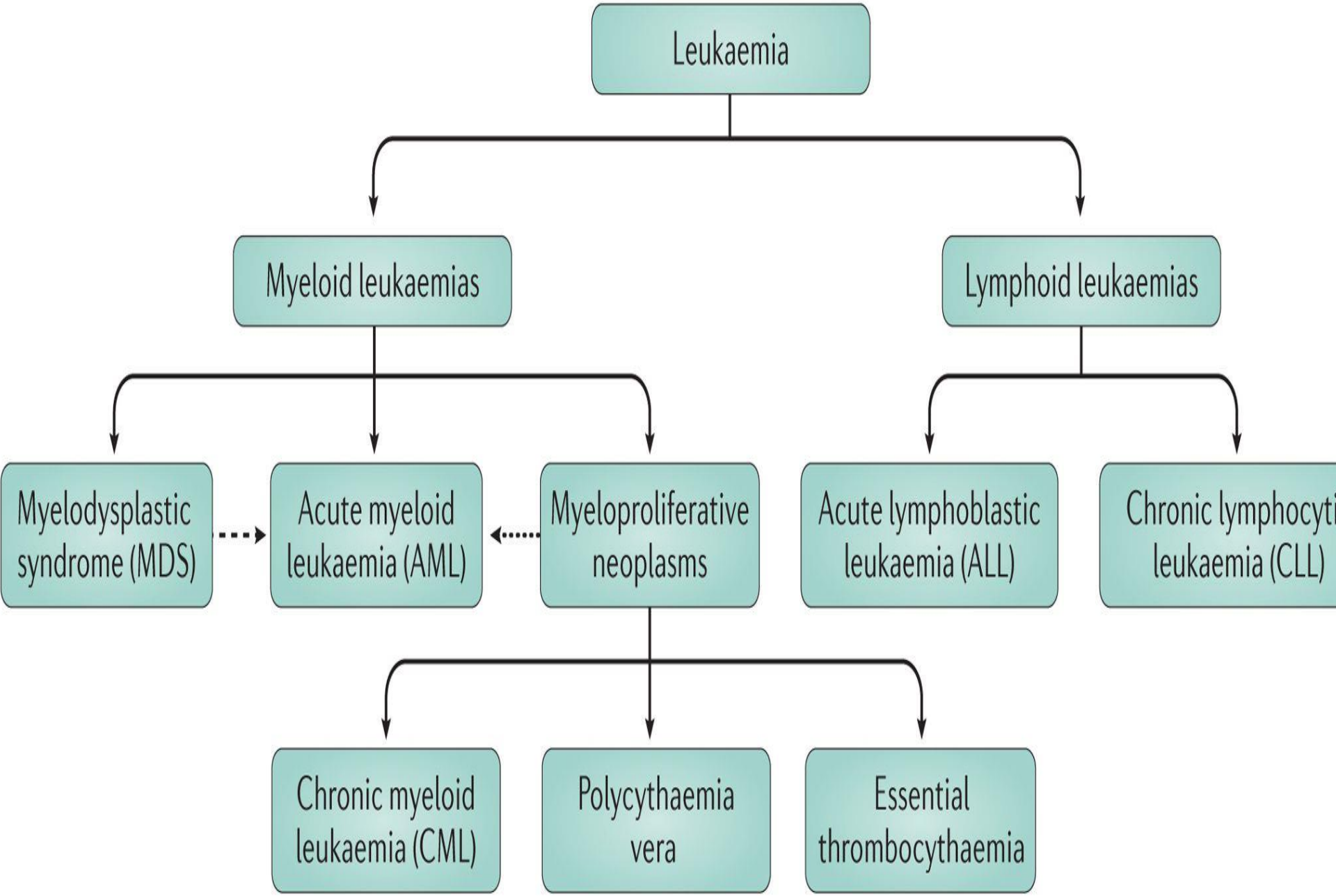
= general consideration of acute leukemia concerning presentation, etiology , diagnosis & treatment.

= acute lymphoblastic leukemia : classification , management .

= acute myeloid leukemia : etiology , classification , management.

Blood Cell Differential




Leukaemia
Myeloid leukaemias
Lymphoid leukaemias
Myelodysplastic syndrome (MDS)
Acute myeloid leukaemia (AML)
Myeloproliferative neoplasms
Acute lymphoblastic leukaemia (ALL)
Chronic lymphocyti leukaemia (CLL)
Chronic myeloid leukaemia (CML)
Polycythaemia vera
Essential thrombocythaemia

ACUTE LEUKEMIA

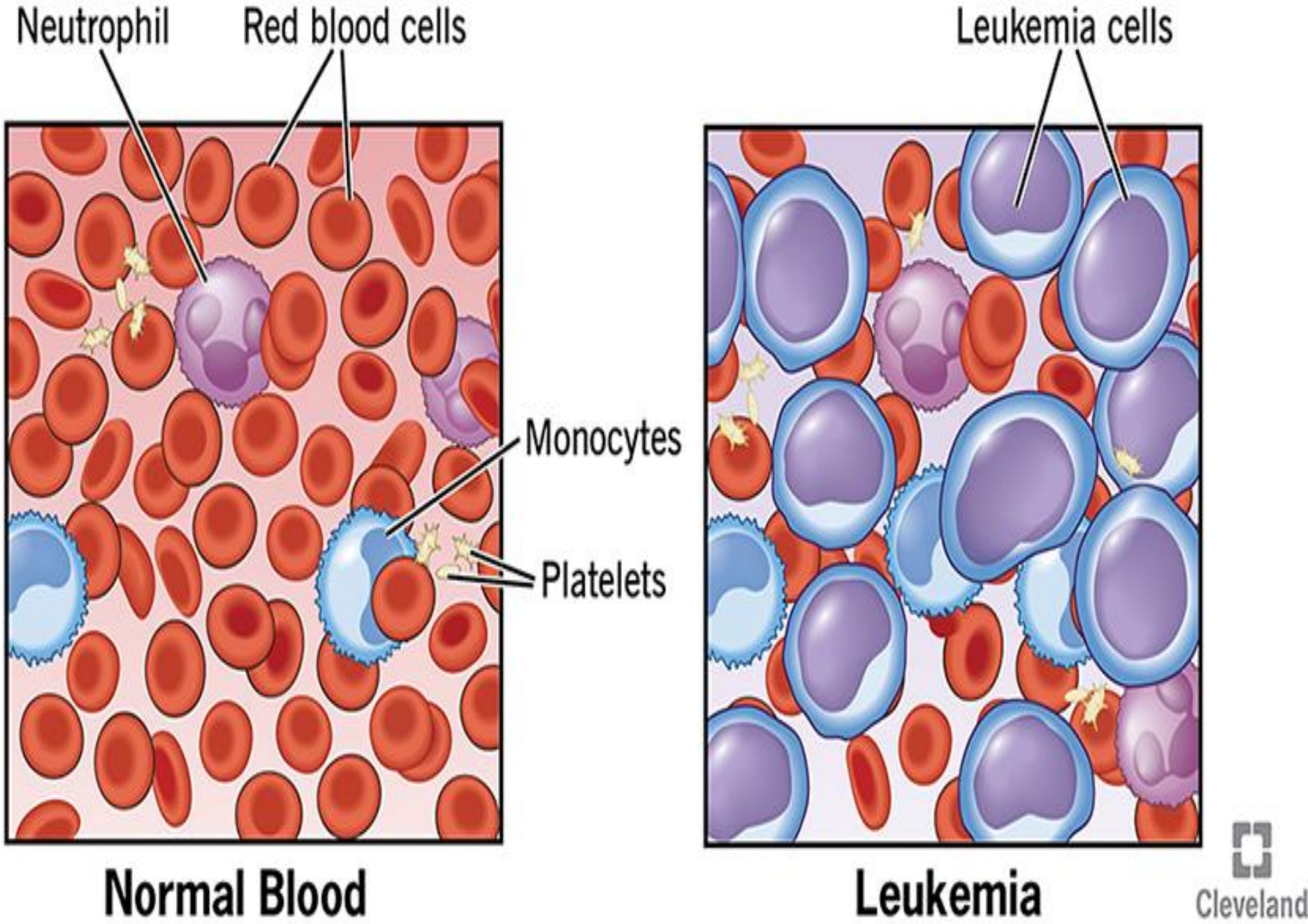
Malignant proliferation of the hematopoietic stem cell in the bone marrow leading to accumulation of immature cells on the expense of normal hematopoiesis.

EPIDEMOLOGY :-

* The incidence is 3-5/100.000 annually.
* Male/female ratio 2:1.
* Geographical variation in incidence does occur.

* Acute leukemia occurs at all ages , ALL shows a peak of incidence in children aged 1-5 years, AML incidence increased over the age of 50.

* AML/ALL ratio 4:1 in adults while the reverse is true in children.


Neutrophil
Red blood cells
Monocytes
Platelets
Normal Blood
Leukemia cells
Leukemia
Cleveland Clinic
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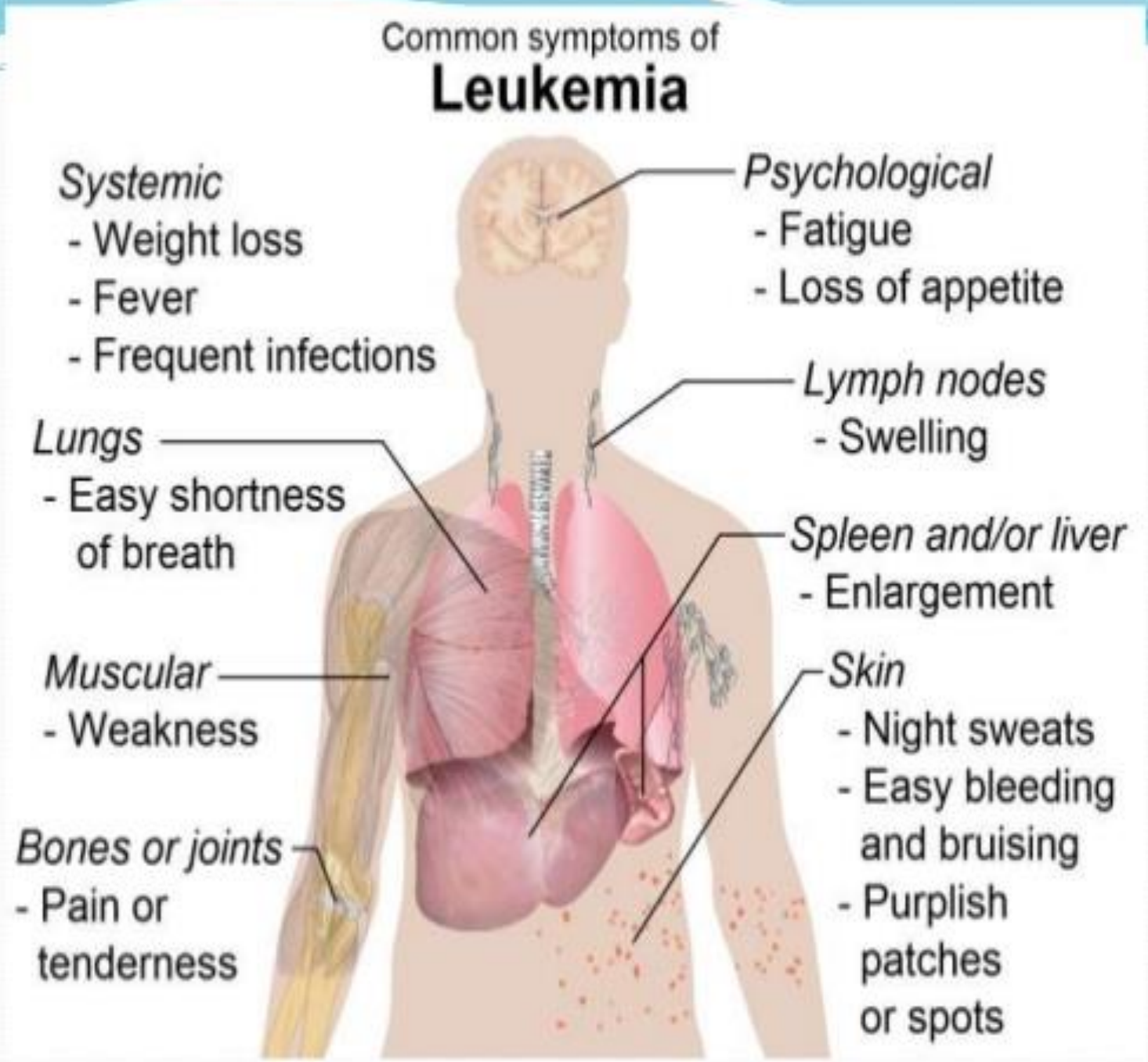
CLINICAL FEATURES :-

- common systemic symptoms: fatigue , anorexia , wt. loss , sweating , fever .

- Anemia (symptomatic , asymptomatic) .

- Bleeding (purpura , mucous membrane , systemic) .
- Infection (bacterial , viral , fungal) .


Common symptoms of
Leukemia
Systemic
- Weight loss
- Fever
- Frequent infections
Psychological
- Fatigue
- Loss of appetite
Lymph nodes
- Swelling
Lungs
- Easy shortness of breath
Spleen and/or liver
- Enlargement
Muscular
- Weakness
Skin
- Night sweats
- Easy bleeding and bruising
- Purplish patches or spots
Bones or joints
- Pain or tenderness

ETIOLOGY :-

* Unknown in majority of cases, But some risk factors were recognized :
  - Ionizing radiation (Atomic bombing, radiotherapy, diagnostic x-ray of fetus)
  - cytotoxic drugs: (alkylating agents, industrial exposure to benzene).
  - Retrovirus: (human T-cell lymphotropic virus).
  - Genetic: (down's syndrome).
  - Immunological: (Hypogammaglobulinemia).

DIAGNOSIS :-

requires morphological, cytochemical, immunophenotyping, cytogenetic and molecular analysis.

- Morphological: CBC, PBF, BMA (hypercellular, blasts > 20%).

-Cytochemical : ALL (PAS) , AML (SB, MPO).

- Immunophenotyping : Flowcytometry on PB,BM.

ALL : CD10 ,CD19 ,CD20 ,CD79a,
CD22 (B-lymphoid).
CD3, CD7, CD2 (T- lymphoid).

AML :CD13 , CD33 , CDw65 ,CDII7 and anti-MPO.

- Cytogenetic analysis: karyotyping, Philadelphia chromosome, mutations.
- Biochemistry (RFT, LFT, UA, LDH).
- Coagulation profile.
- CXR, CT SCAN.
- Lumber puncture.

DIAGNOSIS OF ACUTE LEUKEMIA

- Peripheral Blood smear
- Bone marrow aspiration smear
- Cytochemistry
- Immunophenotyping
- Cytogenetic analysis
- Molecular genetic analysis

MANEGMENT :

A- Supportive :

- Identify & treat infection, prophylaxis by antibacteriacl, antifungal and antiviral.
- Correction of anemia
- Platelet concentrate transfusion.
- Good venous access by central line insertion.
- Assessment & prevention of tumor lysis syndrome by fluid, allopurinol.
- Careful & detailed explaination to the patient about chemotherapy.
- Obtain consent.

B- Specific :

Combination chemotherapy in phases

- Induction of remission.
- Consolidation.
- Maintenance.
- Intrathecal chem., cranial radiation in All
- Allogenic H.S.C.T.

PROGNOSIS :

- Untreated patients survival rate 5 weeks.
- Patient treated supportively survive for few months.

- Patient treated with specific therapy their survival rate is extending months to years in about 60 - 80% they achieve complete remission.

- The evaluation of minimal residual disease (MRD) shows a powerful prognostic factor.

- Introduction of all- transretinoic acid (ATRA) give a high remission rate in AML/M3.

Acute Lymphoblastic Leukemia

malignant proliferation of hematopoietic precursor cells of lymphoid lineage in bone marrow.

- Etiology , incidence .

-FAB classification :

L1 & L2 & L3 " Burkitt".

- Immunological classification :

B- lineage ALL (85 %).

* proB-ALL , Common ALL, preB-ALL , B-cell ALL .

T- lineage ALL (15 %) .

* Pre-T ALL , T-cell ALL.

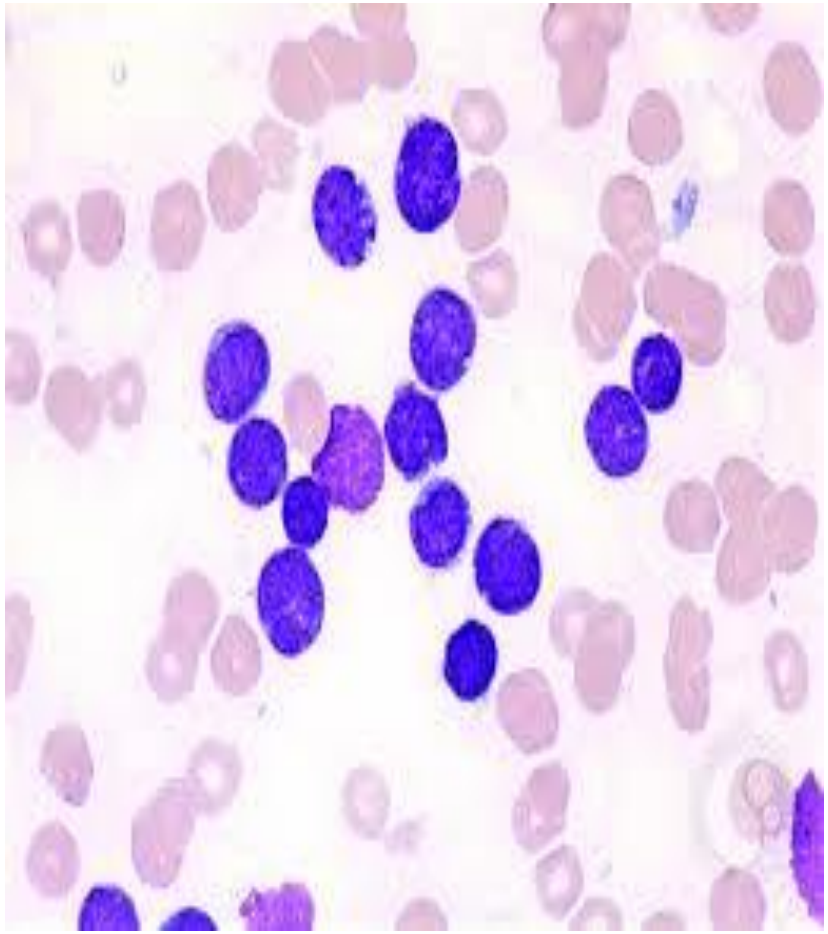
CLINICAL FETURES :

- Bleeding – infection – anemia .
- Lymphadenopathey.
- Hepatomegaly & splenomegaly.
- Mediastinal mass.
- Signs of leucostasis .
- CNS involvement.
- Other organ involvement.

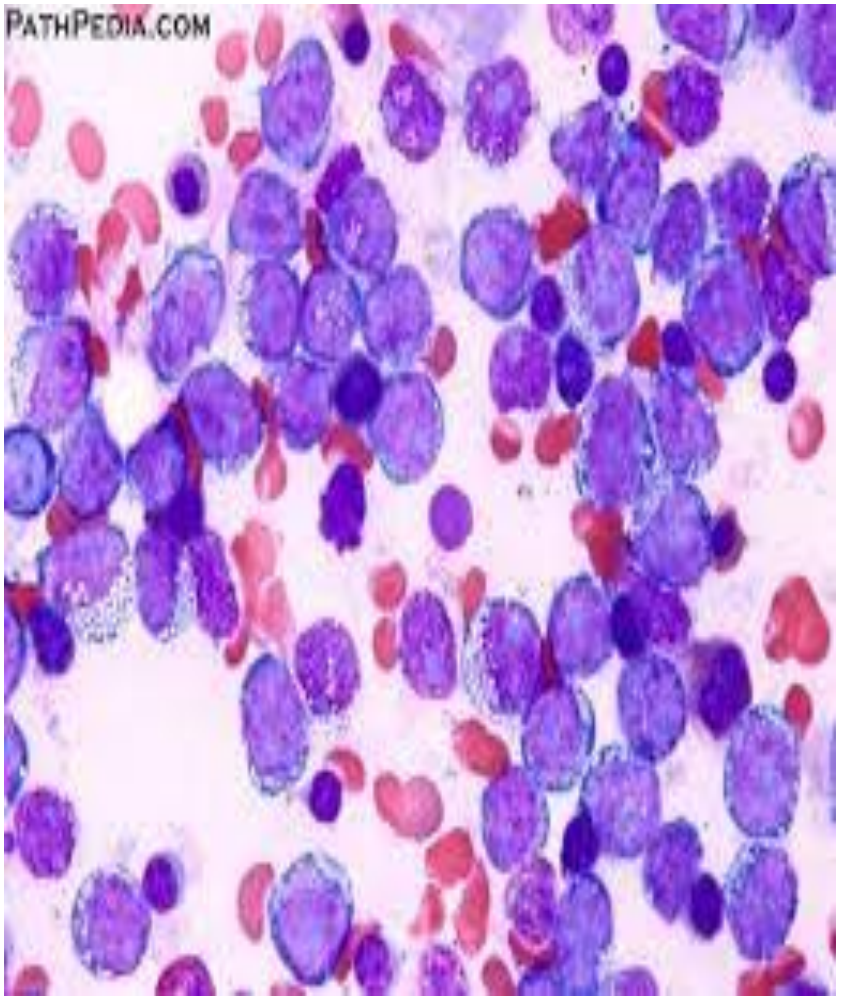
DIAGNOSIS & INVESTIGATION :

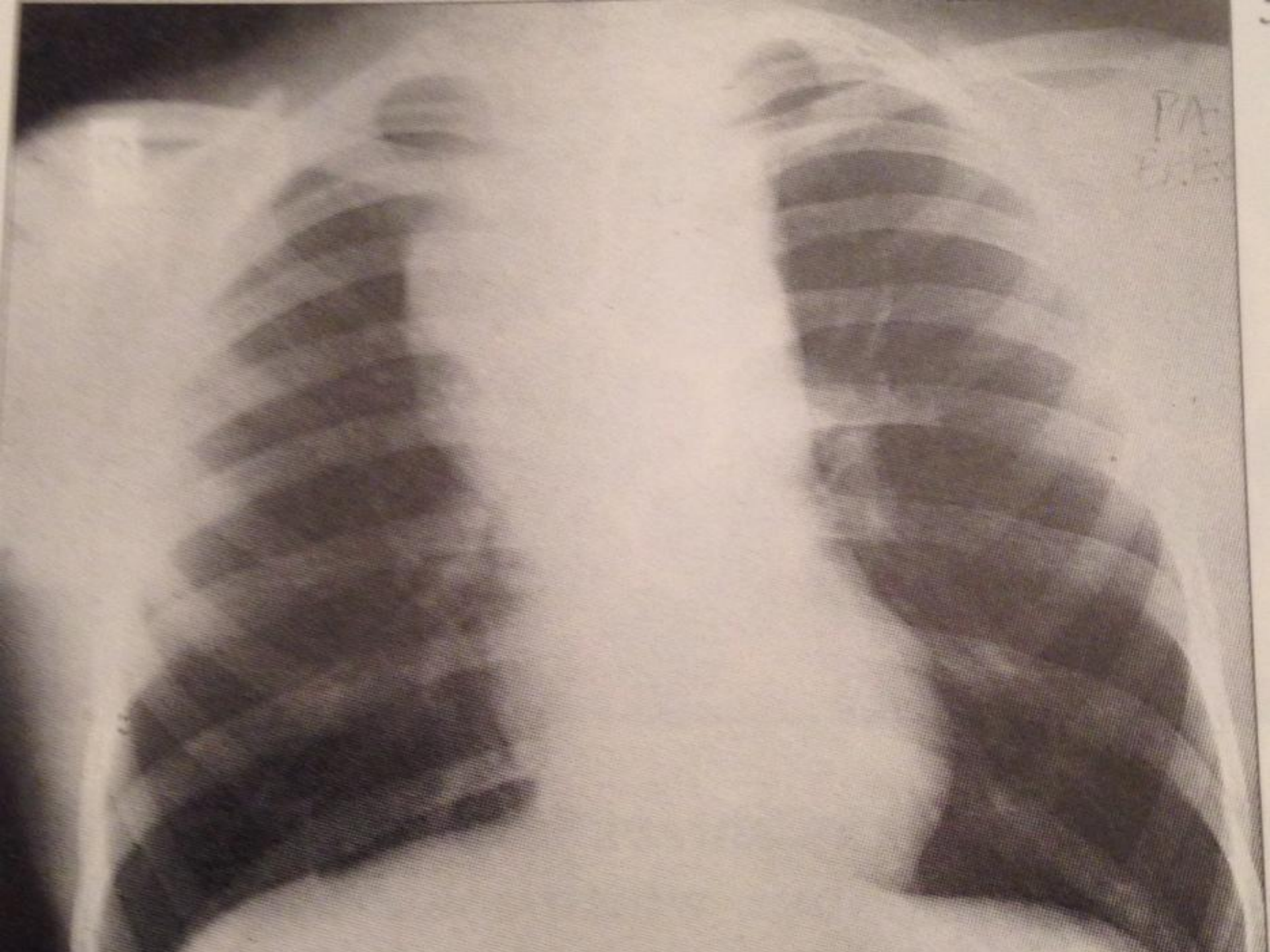
Already discussed.

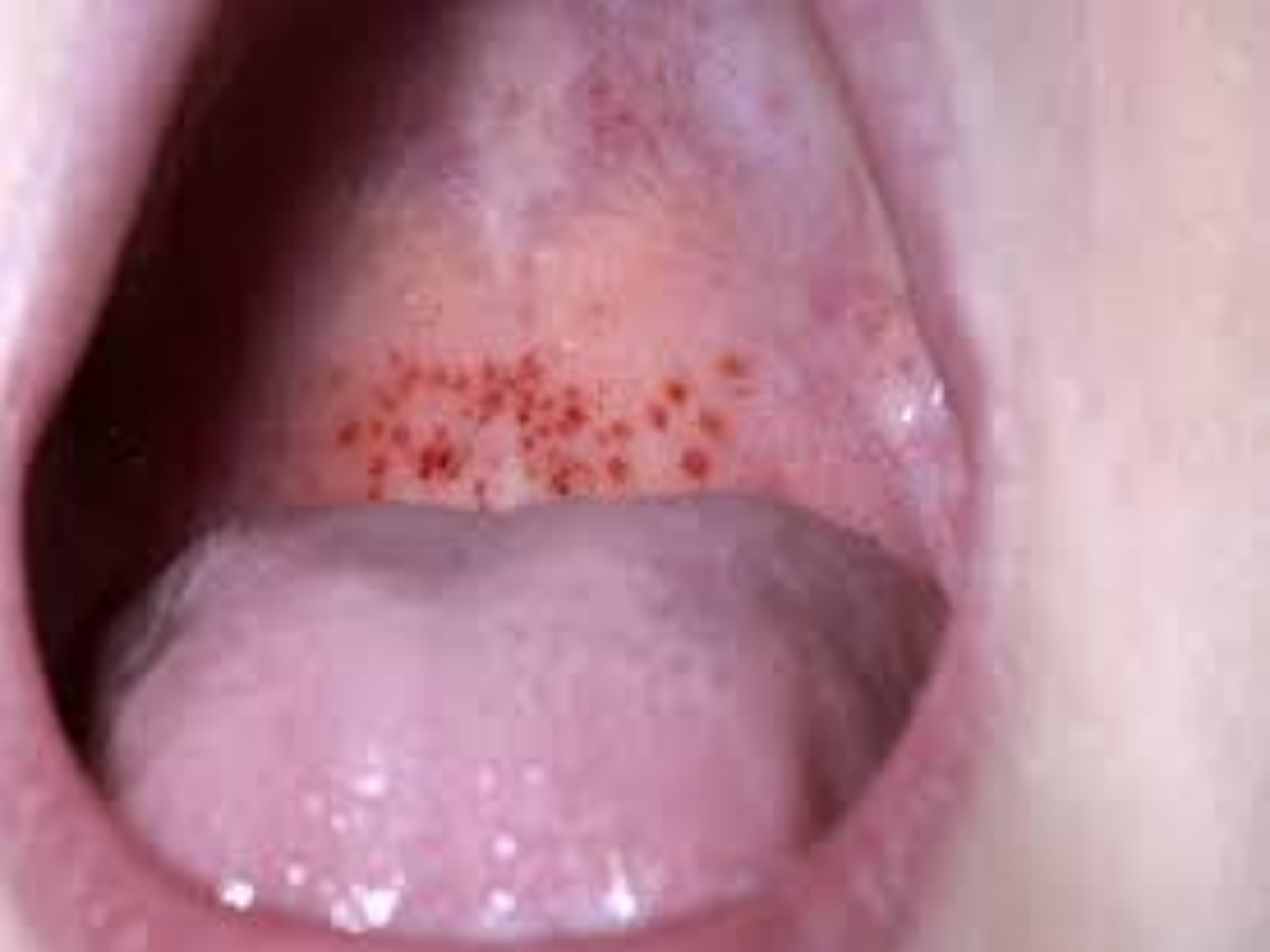
PBF



BMA







MANEGMENT :

A- Supportive.

B- Specific :

- Induction of remission :

Vincrestine , pred., anthracycline and asparginase.

- CNS prophylaxis :

* Cranial radiation.

* Intrathecal methotrexate, cytosar, pred. weekly 4 injection.

- Consolidation :

High dose methotrexate, cytosar, etoposide, anthracycline, cyclophosphamide.

- **Maintenance**:

2-3 years.

a- Oral dose daily with 6 mercaptopurine with once weekly methotrexate.

b- IT. Methotrexate every 3 months.

C- Allogenic H.S.C.T.

Acute Myeloid leukemia

malignant tumor of myeloid lineage in BM

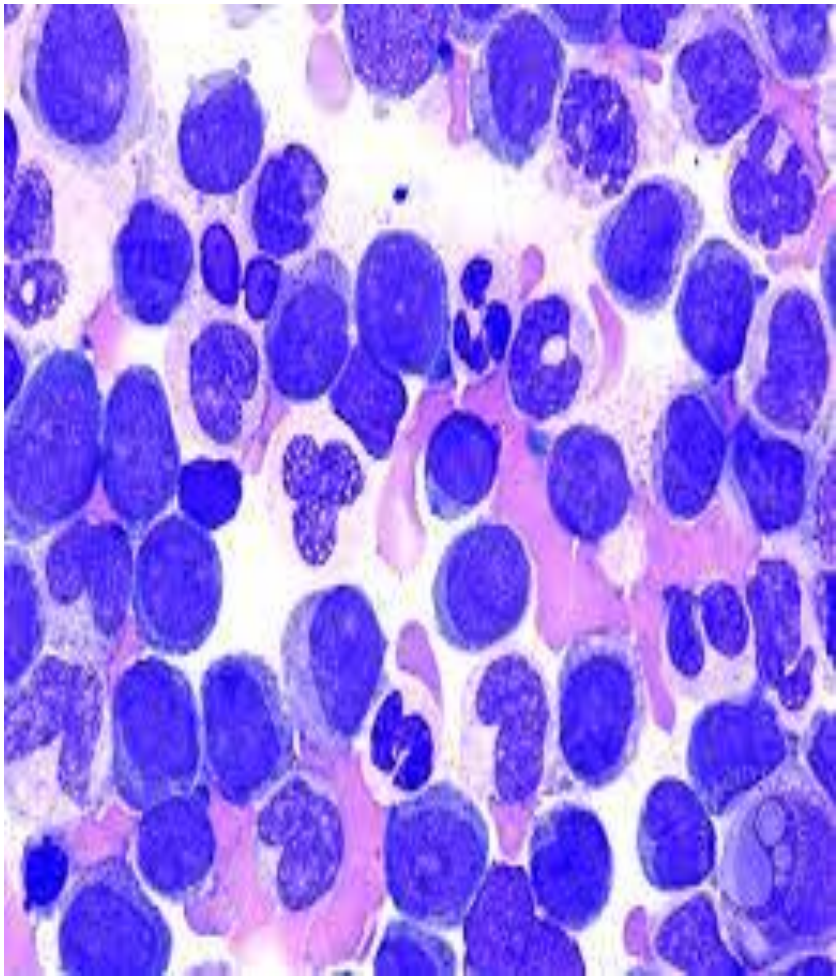
Etiology :

- Denovoux.
- Associated with pre- existing MDS, MPN, previous chemotherapy, radiation , benzene exposure .

DIAGNOSIS :

CBC, PBF, BMA.

BMA



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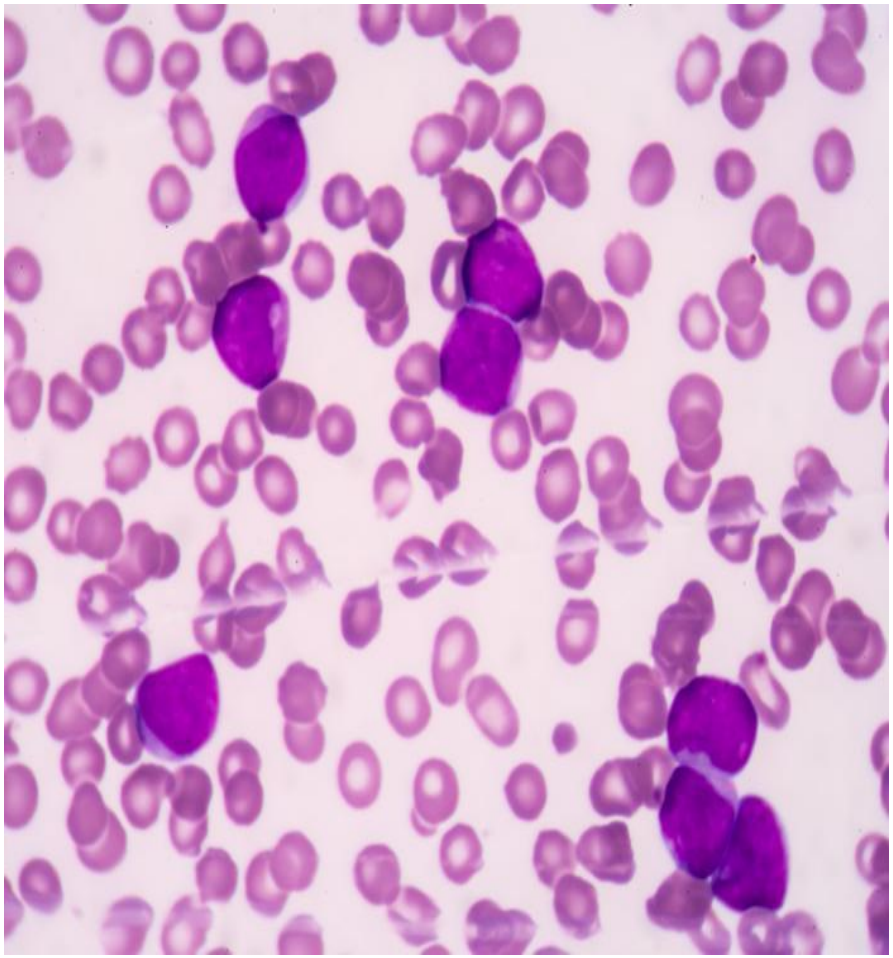

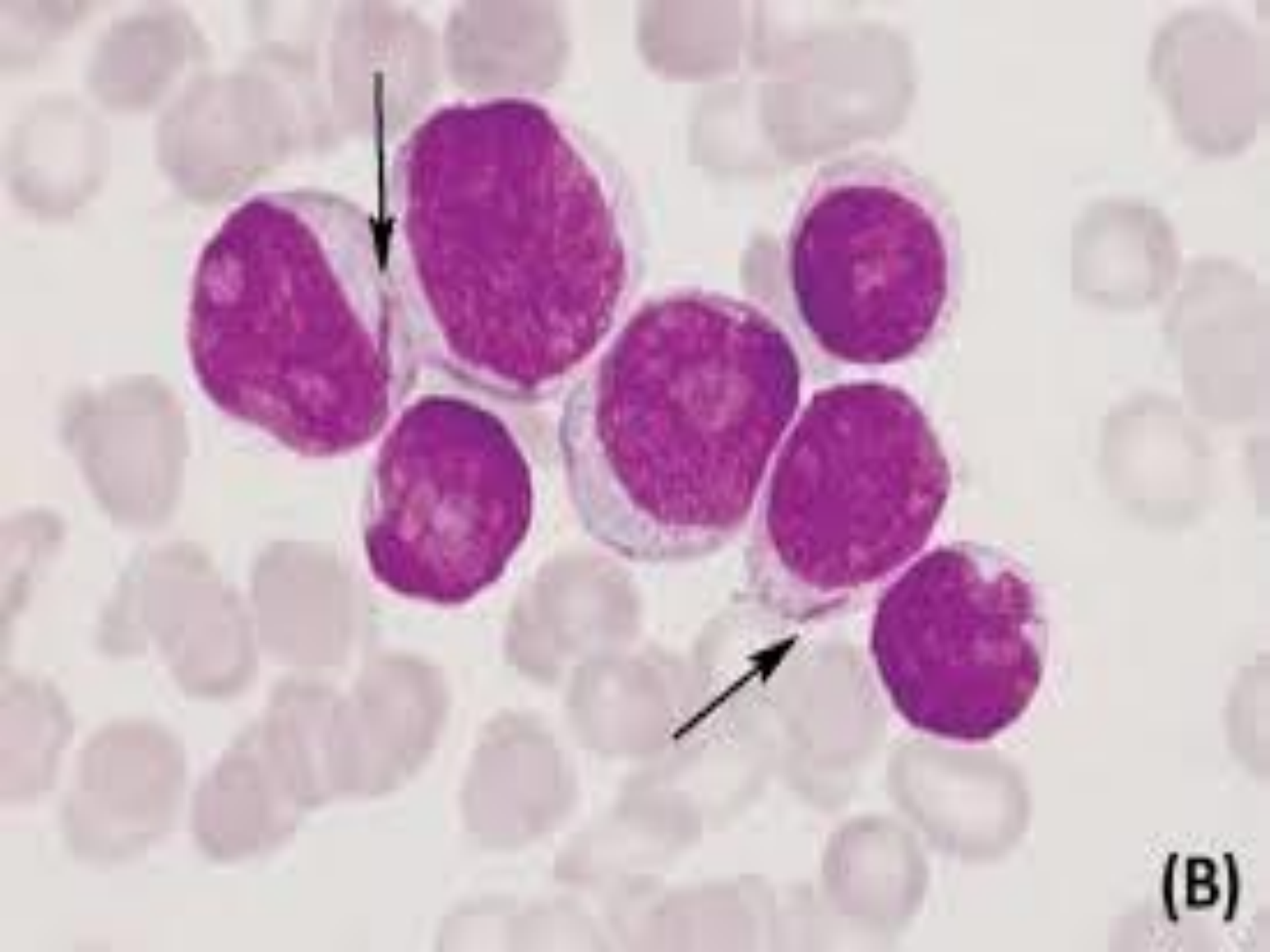
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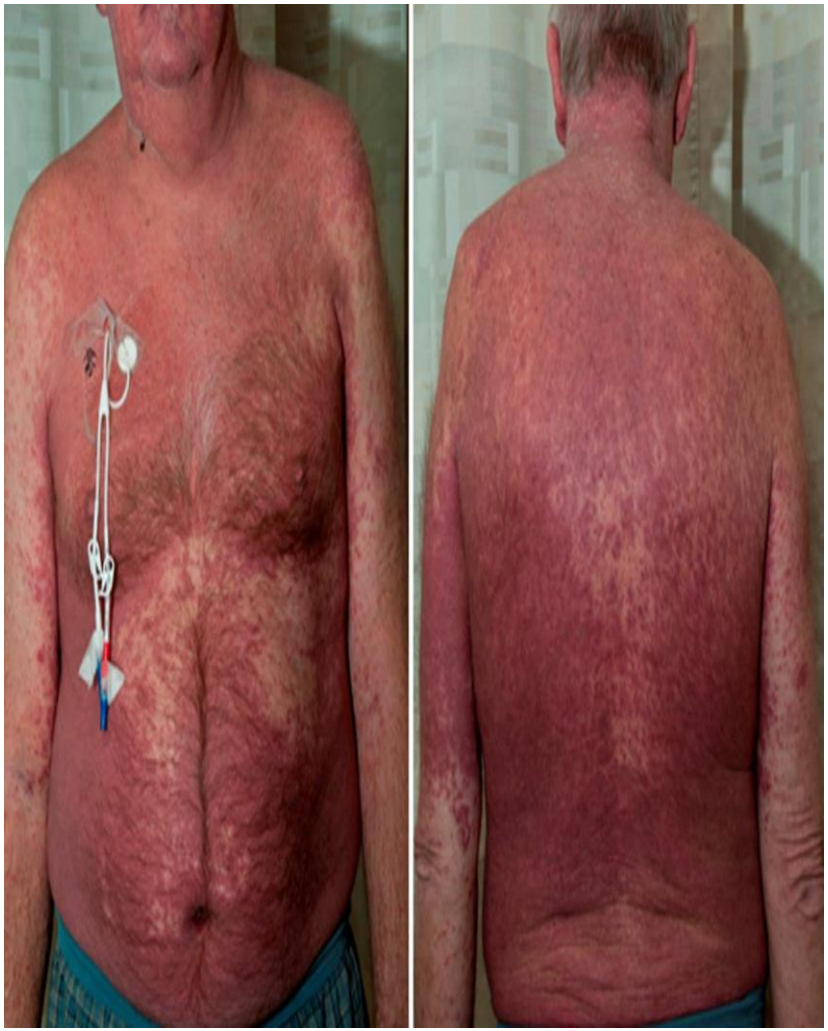
FAB CLASSIFICATION : " Mo ⟶ M7 "

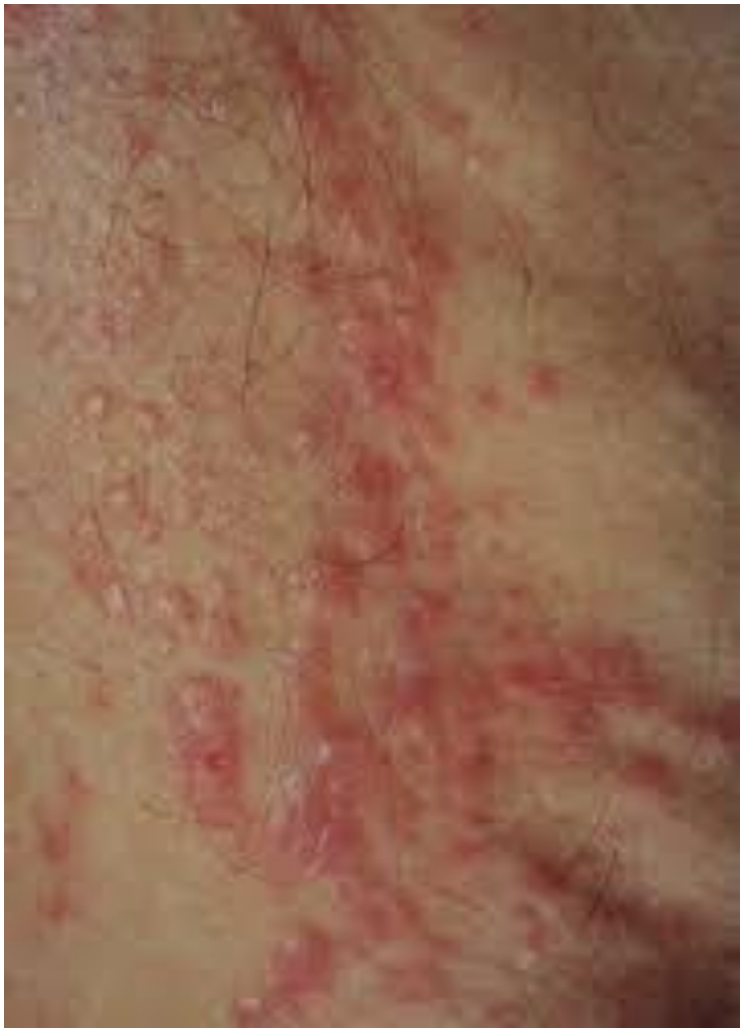
WHO CLASSIFICATION :

- AML with recurrent genetic abnormality.
- AML with myelodysplasia related changes.
- Therapy related myeloid neoplasm.
- Myeloid sarcoma.
- Myeloid proliferation related to down's syndrome.
- AML not otherwise specified.

CLINICAL FEATURES :

- Acute presentation as critical sick patient.
- Infection , Bleeding.
- Symptoms & signs of anemia.
- Gum hypertrophy.
- Skin infiltration.
- Symptoms of luecostasis.
- Hepatomegaly & splenomegaly.
- CNS involvement.





TREATMENT :

A - Supportive.

B - Specific : Age related.

- pts. > 60 years planned for less intensive chemotherapy and rarely need BMT.
- pts > 75 years ± comorbidities planned for supportive treatment ± low dose single agent chemotherapy.
- pts < 60 years are candidates for intensive chemotherapy + BMT.

Induction of remission:

1-2 courses anthracyclins + cytosar, then evaluate for CR by PBF, BMA & MRD.

NB: if the subtype is promeloblastic “M3” induction by ATRA or Arsenic trioxide is added to the induction phase.

Consolidation:

2-4 courses of high dose cytosar “ HIDAC”.

Maintenance:

For 2 years indicated for APML “M3” pts.

Allogenic HSCT:

For pts < 60 years after CR1 in high risk patient CR2 in standard risk pts.

ALL Vs AML

	ALL	AML
Age	Mainly children	Mainly adults
Lymphadenopathy	Usually present	Usually absent
Hepatosplenomegaly	+ve mild	+ve mild
Gum hypertrophy	-ve	+ve in M4/M5
Skin infiltration	-ve	+ve in M4/M5
CNS involvement	+ve in some	+ve in some
Granulocytic sarcoma	-ve	+ve in few cases
Mediastinal mass	+ve in T-ALL	-
Associated DIC	-ve	+ve in M3
Serum muramidase	Normal	In M4/M5 (monocytic type)
Prognosis	Good	Bad

THANK YOU