Hematology

"Haematology"

Benign & Malignant Leukocyte Disorders

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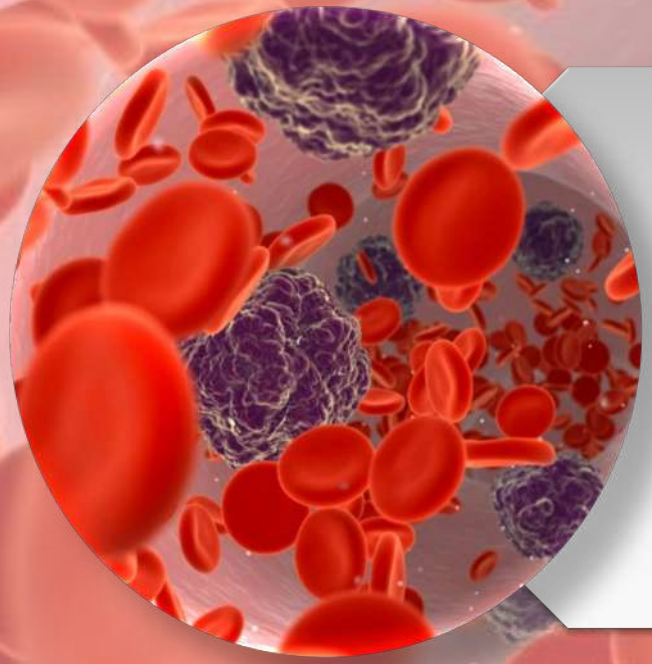
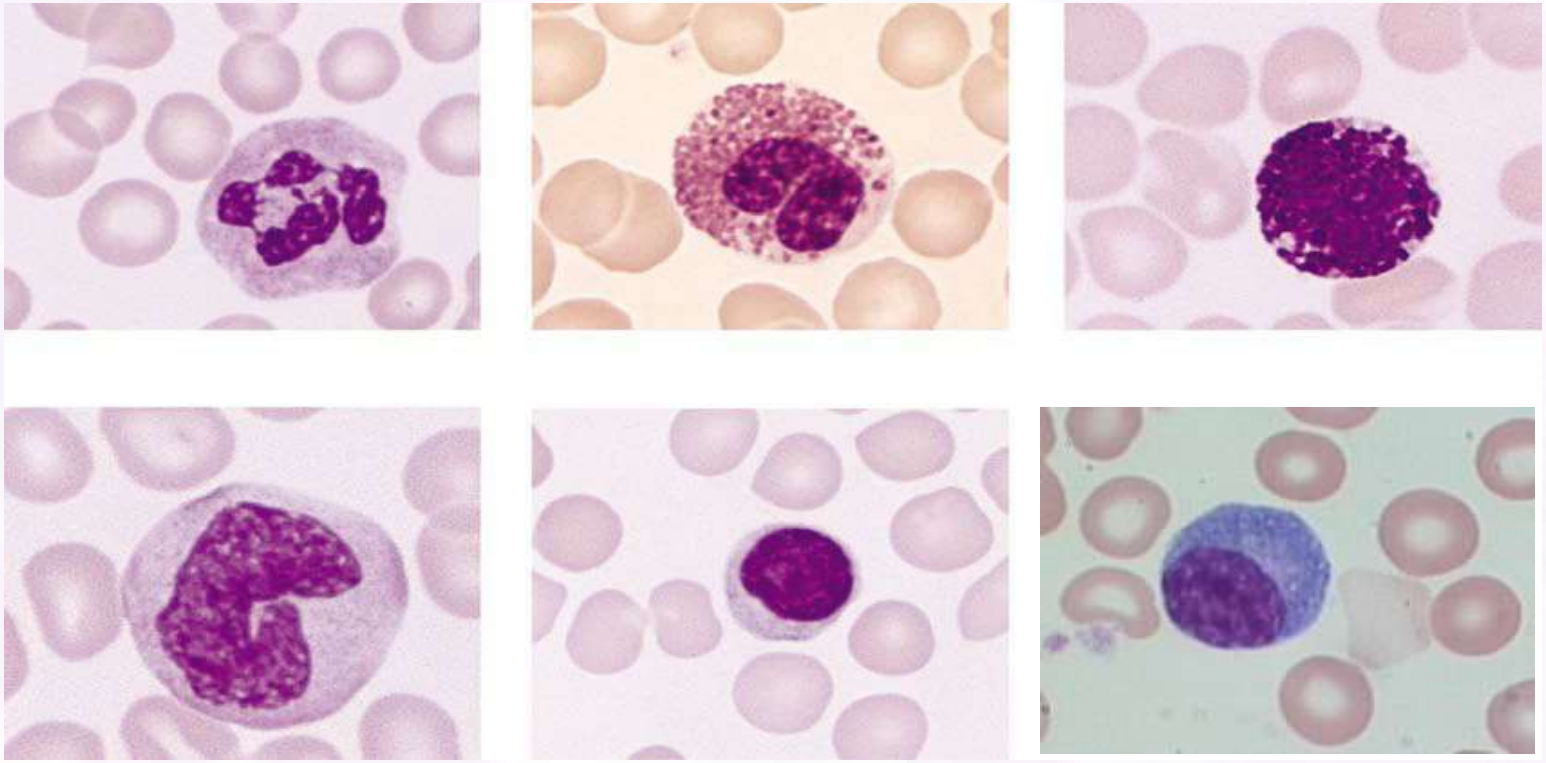


Benign Leukocytes Disorders

White Blood Cells (Leukocytes)

- ✓ Phagocytes; granulocytes; (neutrophils, eosinophils and basophils) and monocytes.
- ✓ Immunocytes; lymphocytes and plasma cells.



Normal leukocytes values

Adults	Blood count (%)	Children	
Total leucocytes	4.00–10.0 × 10^9/L*	Total leucocytes	
Neutrophils	2.0–7.0 × 10^9/L* (40-80%)	**Neonates**	10.0–25.0 × 10^9/L
Lymphocytes	1.0–3.0 × 10^9/L (20-40%)	**1 year**	6.0–18.0 × 10^9/L
Monocytes	0.2–1.0 × 10^9/L (2-10%)	**4–7 years**	6.0–15.0 × 10^9/L
Eosinophils	0.02–0.5 × 10^9/L (1-6%)	**8–12 years**	4.5–13.5 × 10^9/L
Basophils	0.02–0.1 × 10^9/L (1-2%)		

Normal black and Middle Eastern subjects may have lower counts.

Normally there is a diurnal variation in total WBC count

In normal pregnancy the upper limits: total leucocytes 14.5 × 10^9/L and neutrophils 11 × 10^9/L.

Leukocytosis; (Leucocytosis)

An increase in the number of white cells in the blood.

1- Increase production in the marrow;

- ✓ Chronic infection or inflammation (growth factor-dependent)
- ✓ Paraneoplastic (e.g., Hodgkin lymphoma; growth factor-dependent)
- ✓ Myeloproliferative disorders (e.g., chronic myeloid leukemia; growth factor-independent)

2- Increase release from the marrow;

- ✓ Endotoxemia
- ✓ Infection
- ✓ Hypoxia

3- Decreased margination;

- ✓ Exercise
- ✓ Catecholamines

4- Decreased extravasation into tissues; Glucocorticoids

Leukocytosis

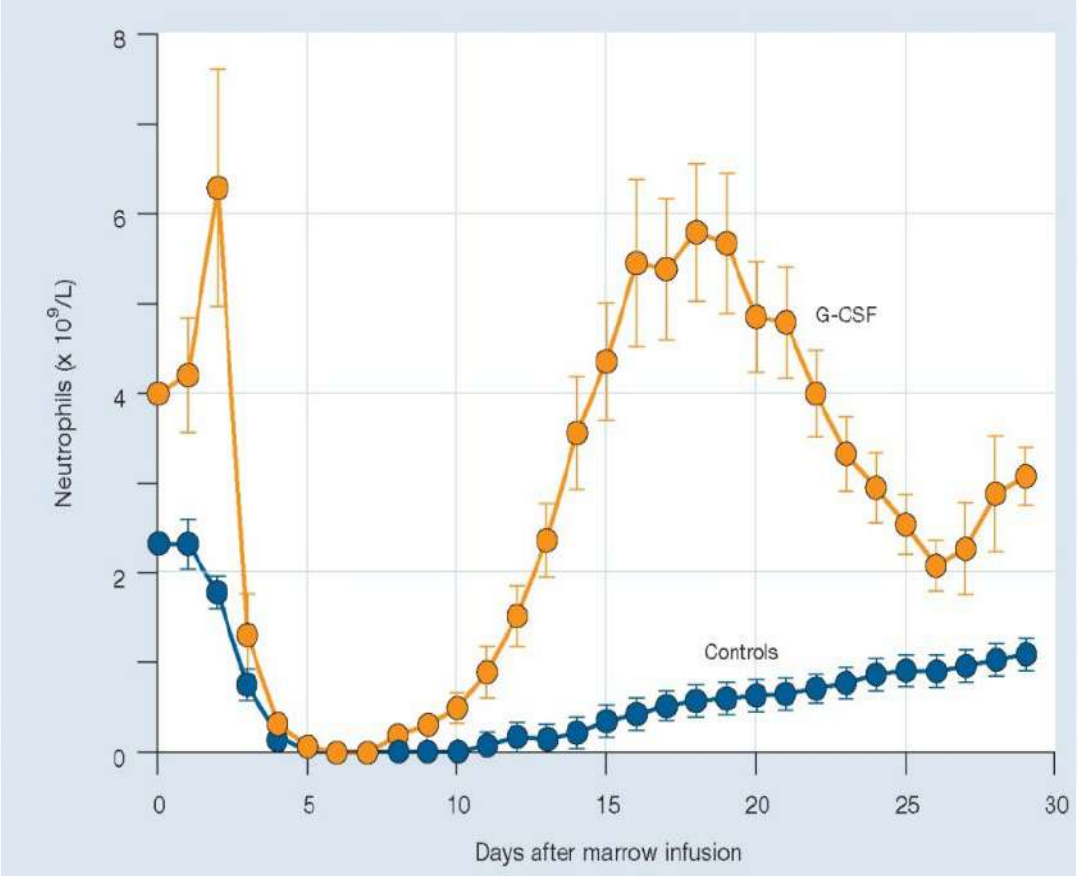
Cell type	Causes
Neutrophilia	Acute bacterial infections; especially those caused by pyogenic organisms, sterile inflammation caused by, e.g; tissue necrosis (myocardial infarction, burns)
Lymphocytosis	Viral infections (e.g.; HA,CMV, EB virus); *Bordetella pertussis*. Accompanies monocytosis in many disorders associated with chronic immunological stimulation (e.g.; tuberculosis, brucellosis)
Monocytosis	Chronic infections (e.g., tuberculosis), bacterial endocarditis, rickettsiosis, and malaria, collagen vascular diseases (e.g., systemic lupus erythematosus); inflammatory bowel diseases (e.g., ulcerative colitis)
Eosinophilia	Allergic disorders such as asthma, hay fever; certain skin diseases, parasitic infestations, drug reactions, certain malignancies (e.g.; lymphomas, mainly Hodgkin's), collagen vascular disorders and some vasculitides (autoimmune disorders) e.g; vasculitis.
Basophilia	Rare, often indicative of a myeloproliferative disease (e.g.; chronic myeloid leukemia)

Granulopoiesis:

- ✓ Formation of the granulocytic series within the marrow.
- ✓ More than the erythroid (G:E ratio; 2:1-12:1) in the BM as it represents the 'reserve pool' (storage) component.
- ✓ Neutrophils spend 6-10 hrs in the circulation and then transfer to the tissue to stay for 4-5 days before its destruction during defective activity.
- ✓ Many controlling factors controlling the maturation, including interleukins (ILs), colony stimulating factors (CSFs), the CSFs are working also for the proliferation and differentiation, mainly the G-CSF.

Clinical applications of G-CSF:

- ✓ IV or SC can used to increase the circulating neutrophils
- ✓ Post-chemotherapy, radiotherapy and stem cell transplantation
- ✓ Acute leukemias.
- ✓ Myelodysplasia ((MDS)
- ✓ Lymphomas.
- ✓ Severe infections and severe neutropenia.
- ✓ Stem cell harvesting in the peripheral blood.

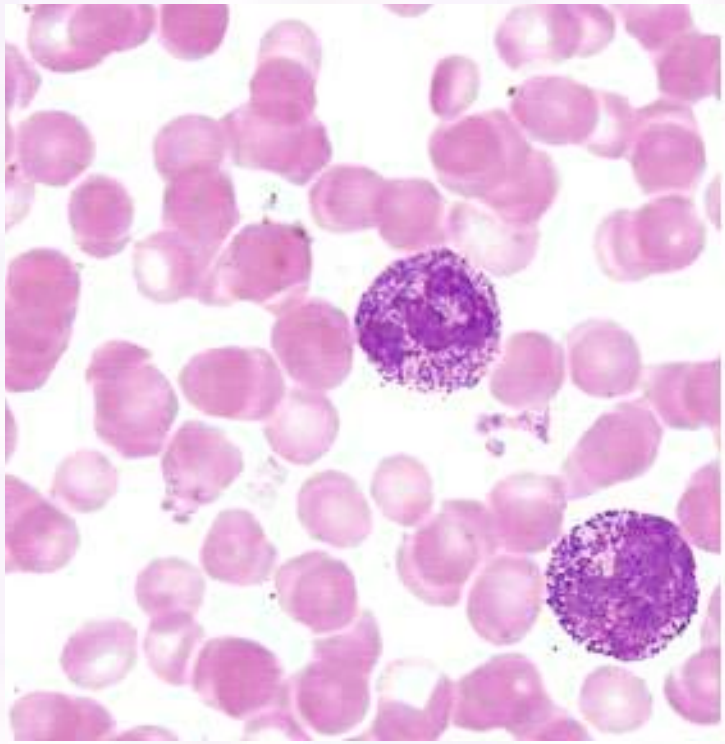


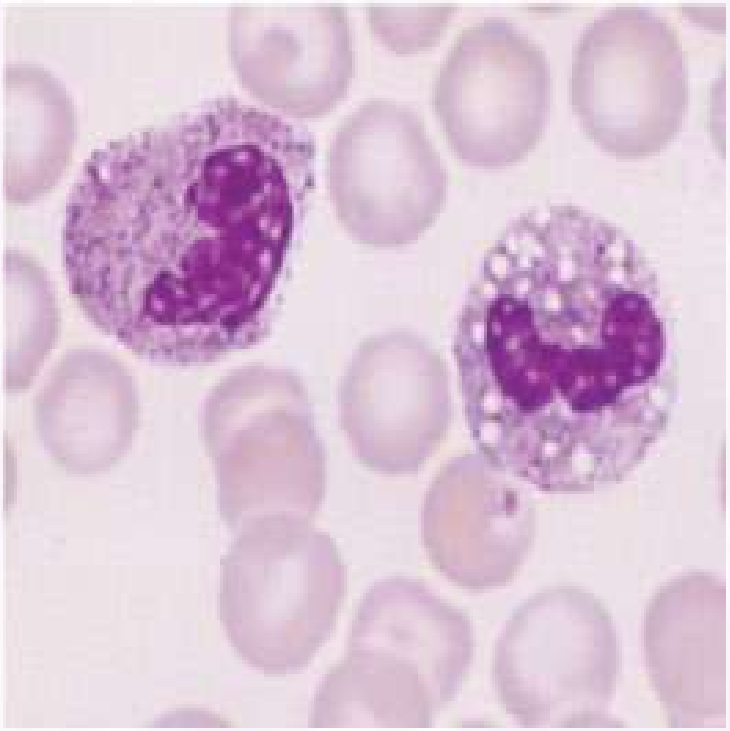
Disorders of the Granulocytes:

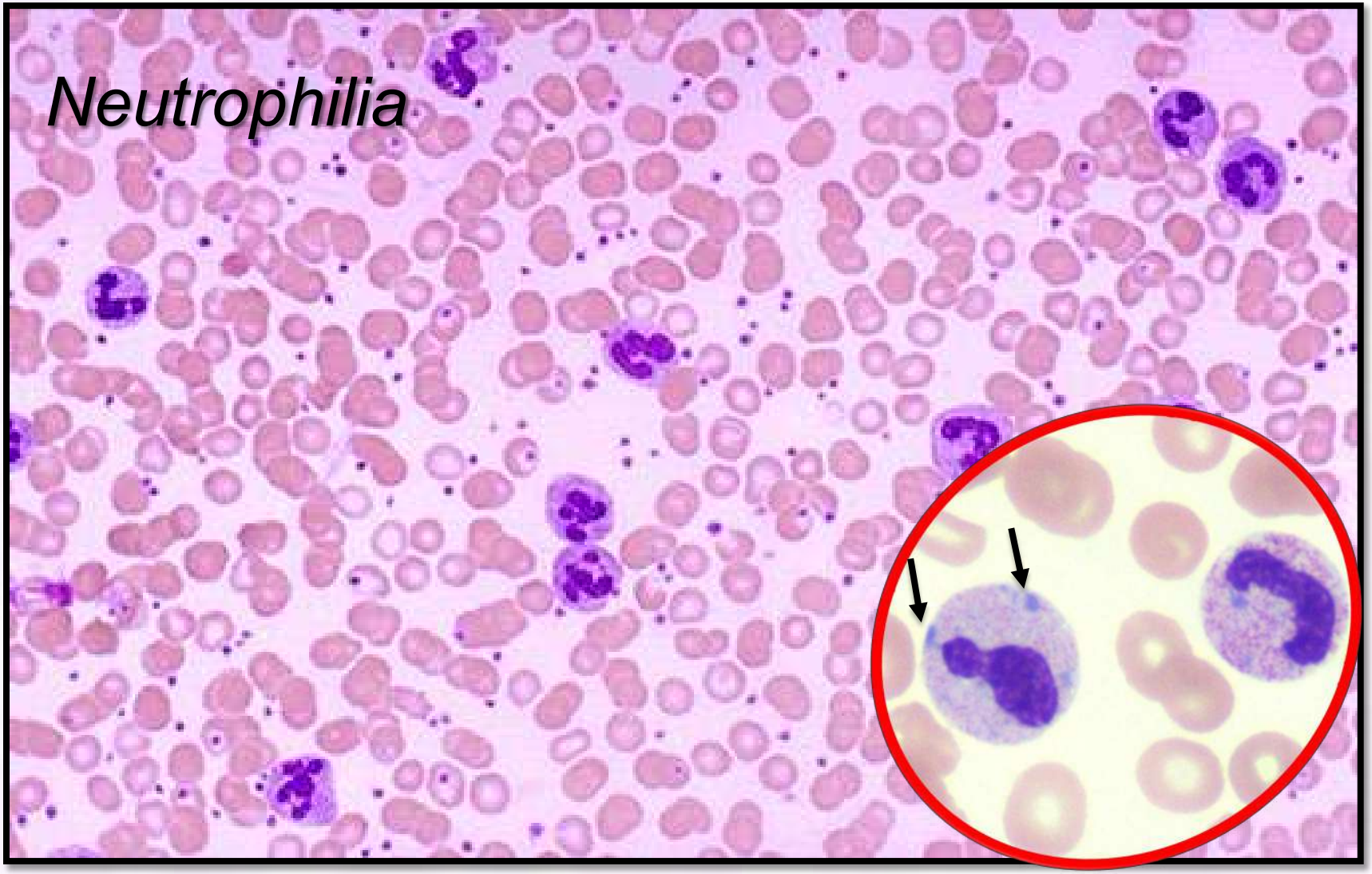
1. Quantitative (increase or decrease numbers);

Leukocytosis (increased WBCs count); benign or malignant.

- ✓ Absolute Neutrophilia; means increased its count, while the relative means only increase of its percentage.





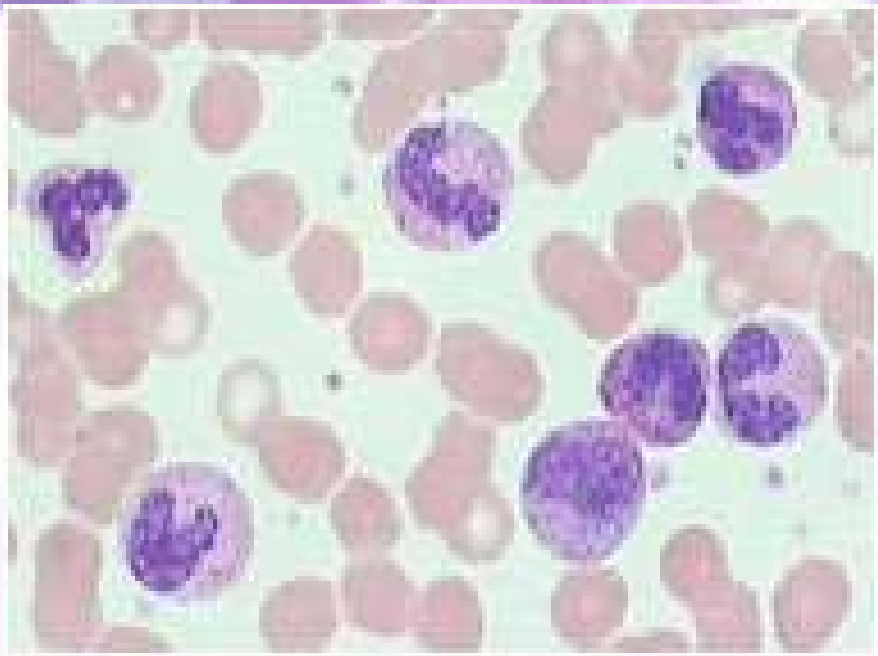


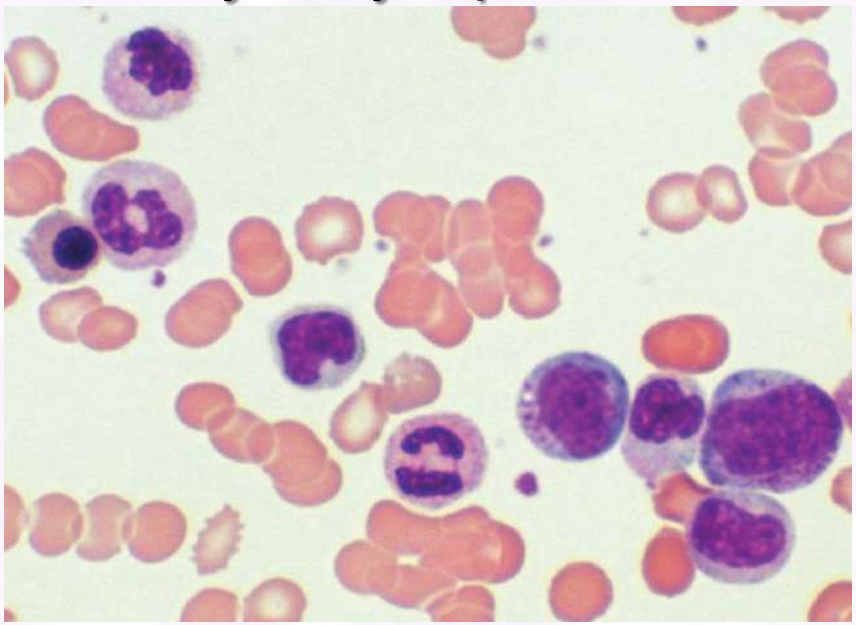
Neutrophilia: toxic changes shown by the presence of red-purple granules in the neutrophils. Döhle body (arrows), remnant of rough endoplasmic reticulum, can be seen in the cytoplasm of the neutrophil.

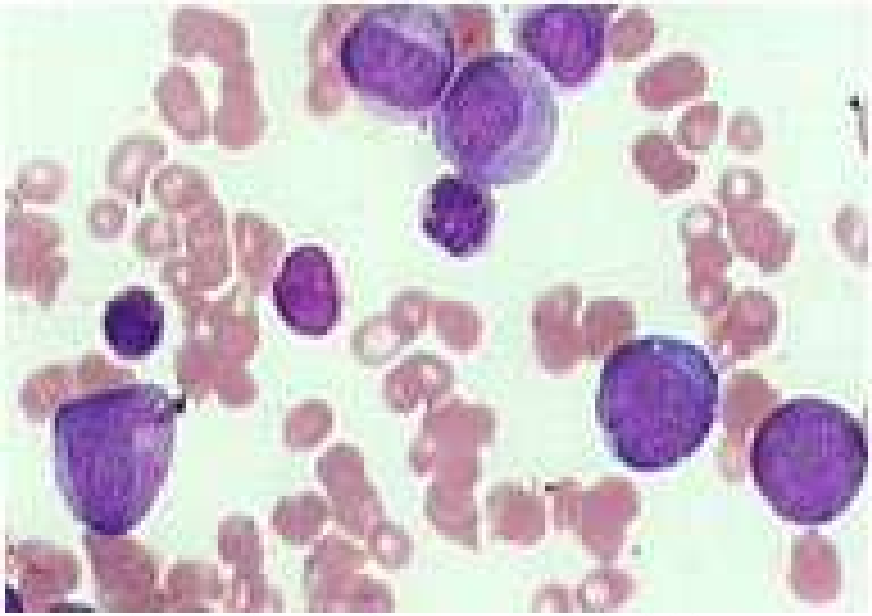
❖ Causes of Neutrophilia:

1. Bacterial infections (especially pyogenic bacterial).
2. Inflammation and tissue necrosis; (e.g. myositis, cardiac infarct, trauma).
3. Myeloproliferative diseases: CML, polycythemia vera, myelofibrosis, essential thrombocythemia.
4. Metabolic disorders (e.g. uremia, eclampsia, acidosis…)
5. Acute hemorrhage or hemolysis.
6. Drugs; e.g. corticosteroid therapy (inhibits margination).
7. Use of myeloid growth factors (e.g. G-CSF).

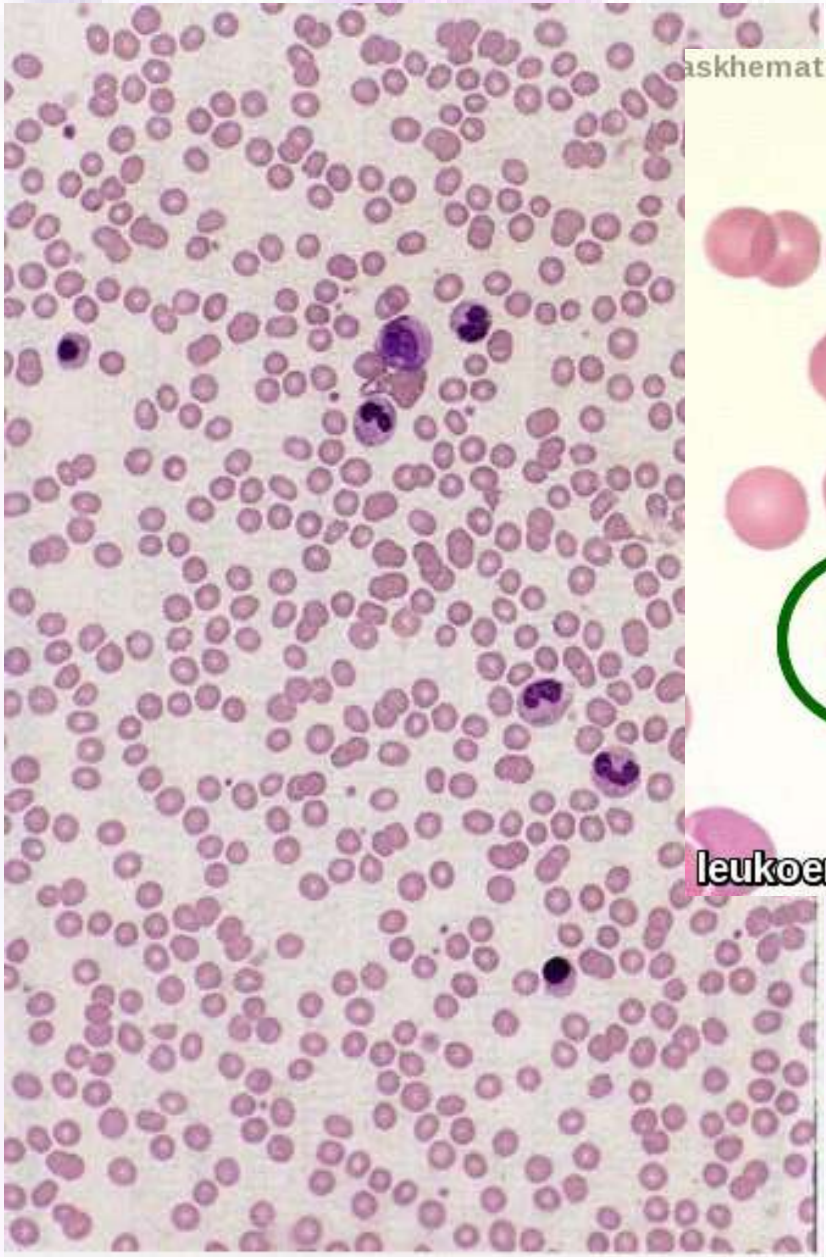
- ✓ **Leukemoid** reaction; Means presence of immature granulocytic cells (left shift) in the peripheral blood.
- ✓ **Leukoerythroblastic** picture; means presence of nRBCs with myelocyte precursors.

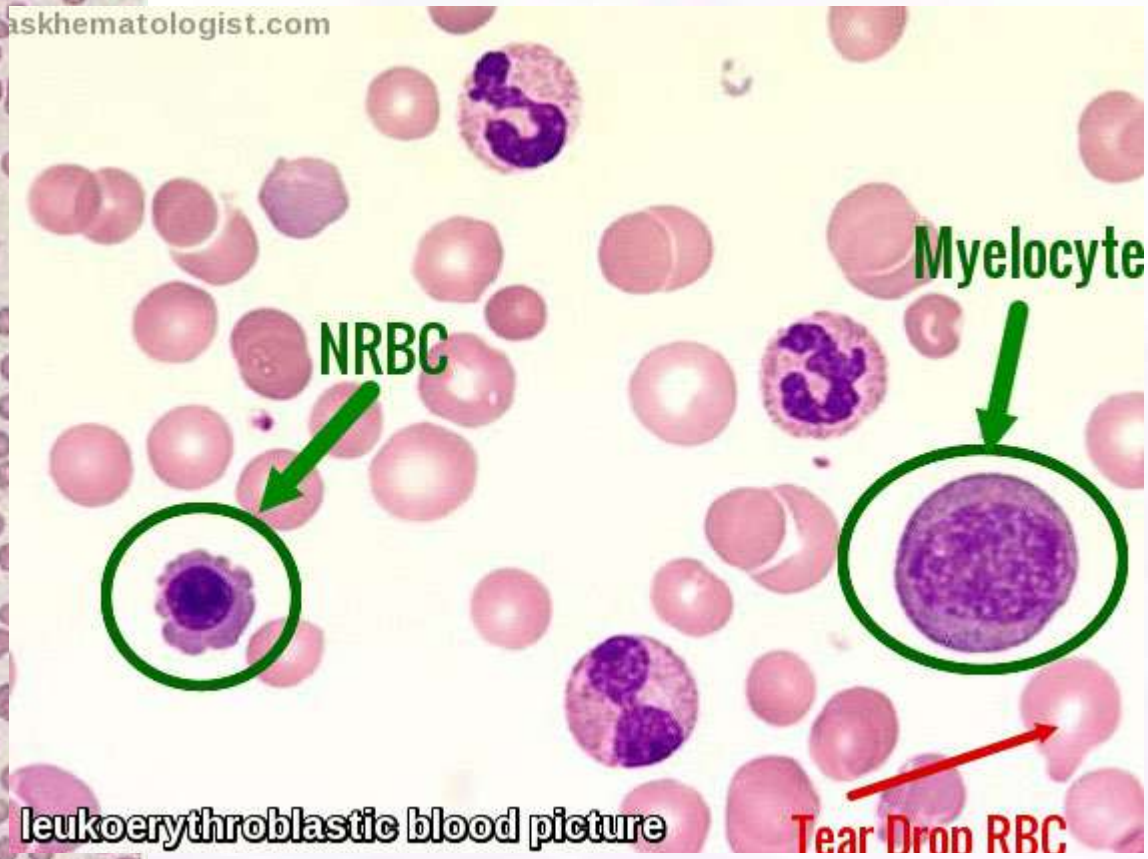






Leukoerythroblastic picture; Mild (left) and sever (right)





Leukoerythroblastic Picture

❖ Causes of Leukoerythroblastic Picture:

1. Reactive; due to increased BM activity, such as in hemorrhage or hemolysis, which leads to increased myeloid activity in addition to the erythroid lineage

2. Abnormal BM activity; Severe megaloblastic anemia

3. Myelophthisis (Abnormal BM element proliferation); may associate extramedullary hematopoiesis;

- ✓ Metastatic neoplasm in the marrow
- ✓ Primary myelofibrosis
- ✓ Myeloid leukemia, myeloma, lymphoma
- ✓ Miliary tuberculosis.

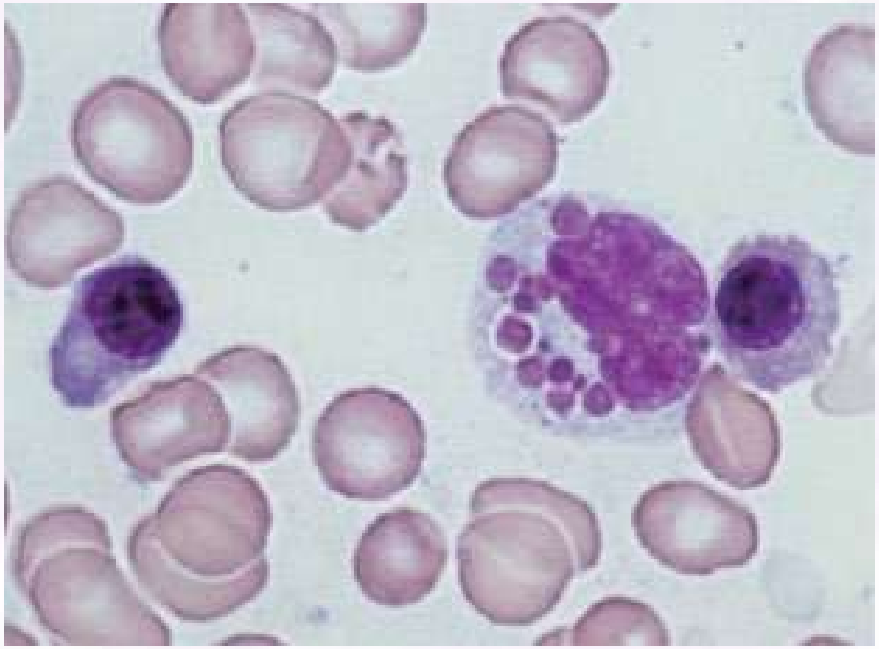
4. Corticosteroid therapy

2. Qualitative (functional);

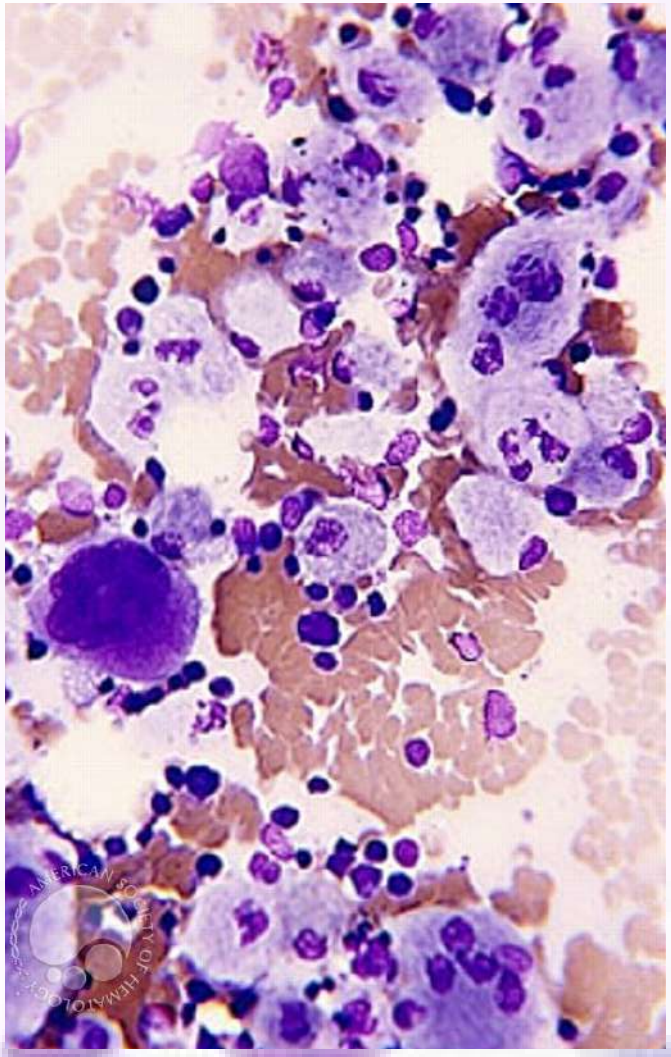
Defective phagocytic cell activities;

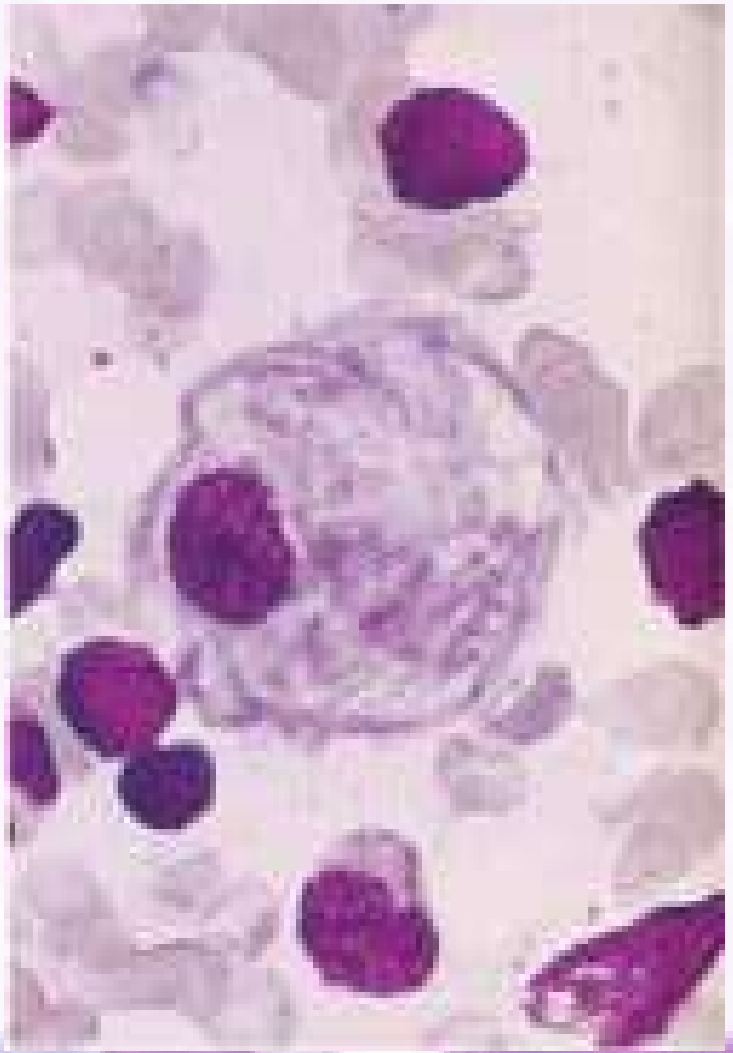
- ✓ Lazy leukocyte syndrome, which due to chemotactic defects. Can be congenital or due to corticosteroid therapy which also occur in MPNs.
- ✓ Hypergammaglobulinemia; there is defect in phagocytosis.
- ✓ Chédiak-Higashi syndrome;

an autosomal recessive killing defect effects, while the acquired can occur in MPNs. Multiple large azurophilic granules which seen in the cytoplasm of the neutrophil.

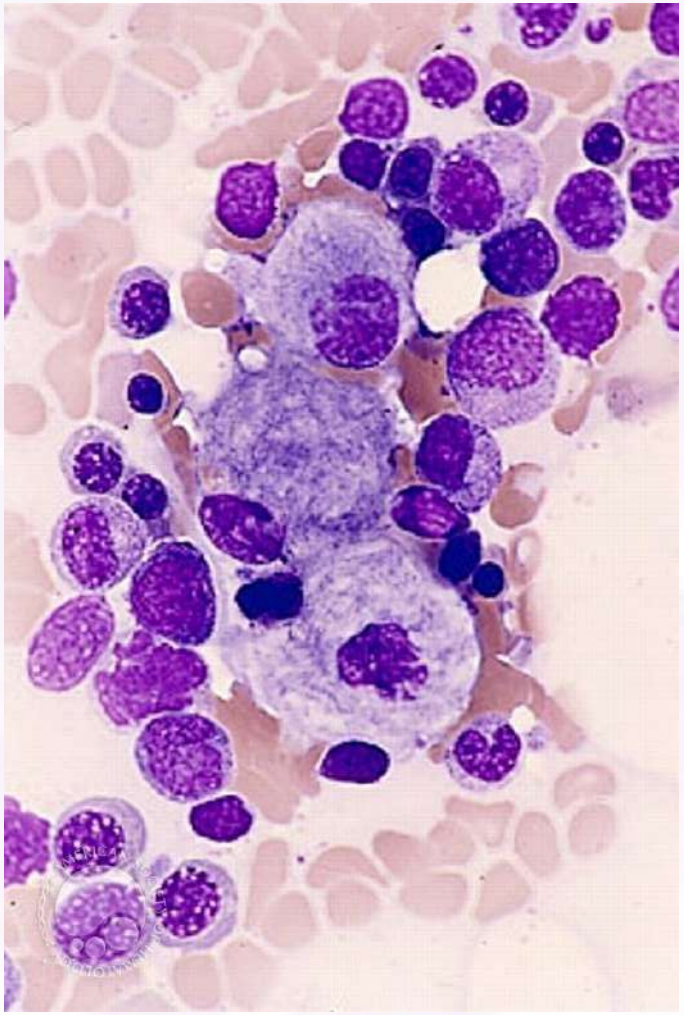


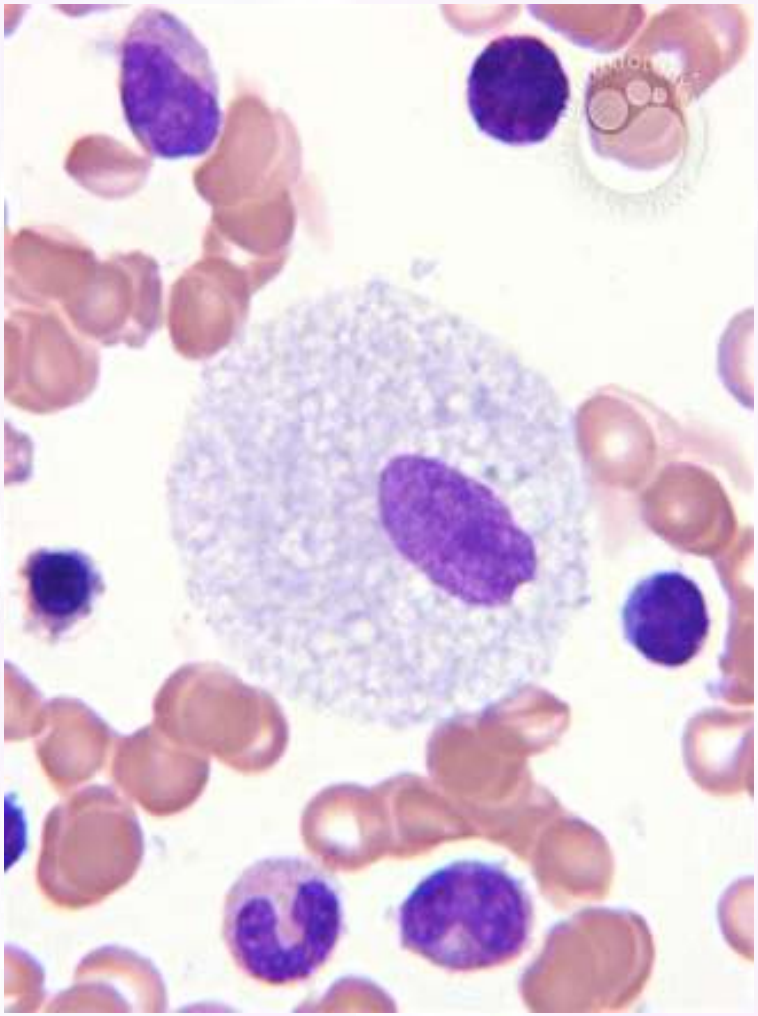
- ✓ Gaucher's disease; glucocerebrosidase enzyme deficiency leads to unprocessed glucocerebroside accumulation within the macrophages





- ✓ Niemann-Pick; sphingomyelin and cholesterol accumulation which due to abnormal lipid metabolism from hereditary sphingomyelinase deficiency.





❖ ***Causes of Neutropenia;*** *(Neutr.; less than 2.0 X 10^9/L)*

1. Drug-induced; long list, e.g; anti-inflammatory drugs or antibacterial drugs.

2. Benign; racial or familial

3. Cyclical (rare enzymatic syndrome).

4. Immune; autoimmune, systemic lupus erythematosus, hypersensitivity and anaphylaxis

5. Infections; Viral (e.g. hepatitis, influenza, HIV), Fulminant bacterial infection (e.g. typhoid, miliary tuberculosis)

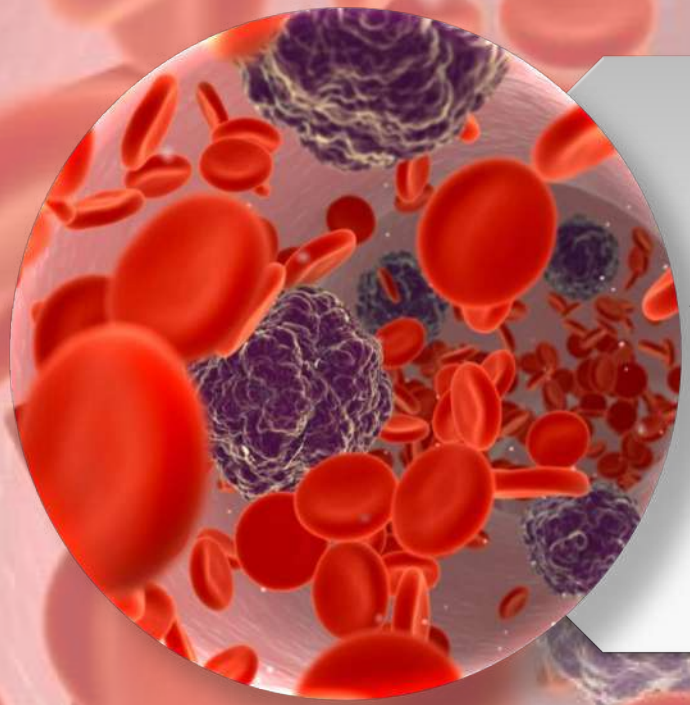
6. Part of general pancytopenia; (Bone marrow failure and splenomegaly)

❖ *Causes of Eosinophilia*

1. Allergic diseases, especially hypersensitivity of the atopic type (e.g. bronchial asthma, hay fever, urticaria and food sensitivity)
2. Parasitic diseases (e.g. amoebiasis, hookworm, ascariasis, tapeworm infestation, filariasis, schistosomiasis and trichinosis)
3. Certain skin diseases (e.g. psoriasis, pemphigus and dermatitis herpetiformis, urticaria and angioedema, atopic dermatitis)
4. Drug sensitivity
5. Lymphoma, mostly Hodgkin.
6. Hypereosinophilic syndrome & Chronic eosinophilic leukemia
7. Myeloproliferative disorders.

❖ ***Causes of Monocytosis:***

1. Chronic bacterial infections: tuberculosis, brucellosis, bacterial endocarditis, typhoid
2. Connective tissue diseases; SLE, rheumatoid arthritis
3. Protozoan infections
4. Chronic neutropenia
5. Chronic myelomonocytic leukemia (CMML)



Hematological Malignancies

Hematological Malignancies

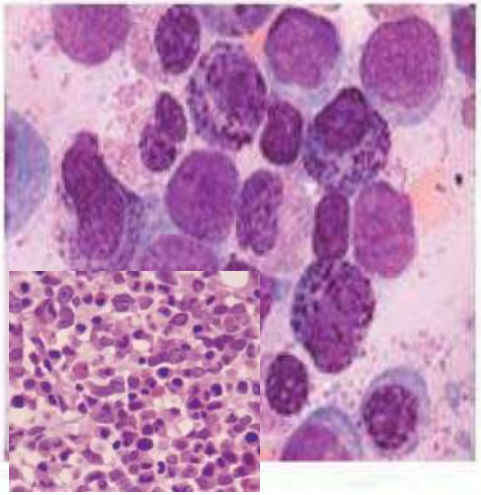
- Clonal diseases (neoplastic proliferation) that derive from a single cell in the marrow or peripheral lymphoid tissue that has undergone genetic alteration.
- Nearly 40% of the population will develop cancer in their lifetime. Hematological malignancies represent approximately 7% of all malignant diseases.

❖ Diagnostic Methods:

- Morphology; (cyto- & histo-logical) by presence of malignant cells.
- Cytochemistry; (cyto- & histo-chemical) using special stains for the cells.
- Karyotype chromosomal analysis (microscopical chromosomal morphology).
- immunochemistry (immunocyto- &histochemistry); Antibodies can also be used to stain cells or tissue sections with fluorescent markers.
- Fluorescence *in situ* hybridization analysis (FISH); Involves using of fluorescent-labelled genetic probes which hybridize to specific parts of the genome.

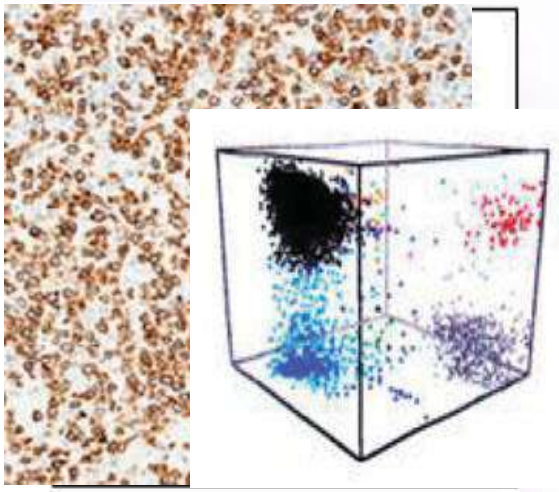
- Flow cytometry; Antibodies labelled with different fluorochromes recognize the pattern and intensity of expression of different antigens on the surface of normal and leukemic cells.
- Polymerase chain reaction (PCR); can be performed on blood or bone marrow for a number of specific translocations.
- DNA microarray platforms.

Morphology (cyto&hist)

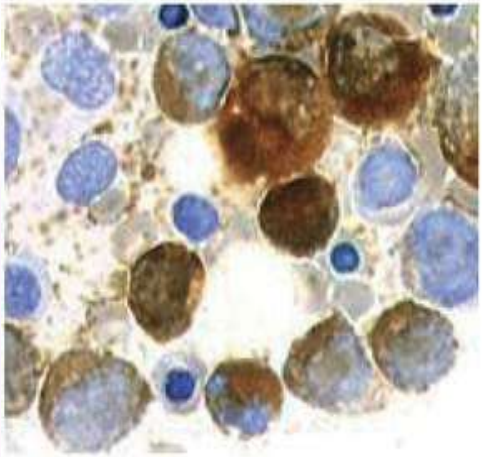


Cytogenetics

Immunophenotyping



Cytochemistry (cyto&hist)



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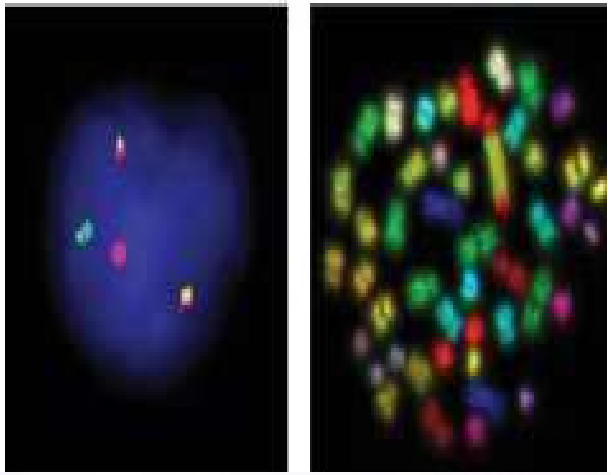
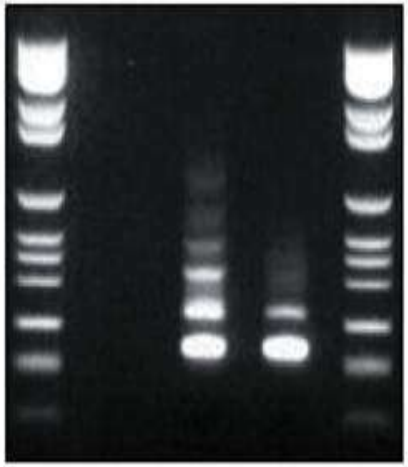


Molecular Biology



❖ Value of Genetic Markers:

1. Initial diagnosis.
2. Treatment protocol.
3. Monitoring the response to therapy minimal residual disease (MRD).

❖ General Support Therapy:

- ➢ Insertion of a central venous catheter (for the chemotherapy and nutrition).
- ➢ Blood product;
- Blood transfusion mostly to patients with Hb < 8 g/dL.
- Platelet transfusion is typically a platelet count $<10\times10^9$/L.
- ➢ Recombinant erythropoietin (EPo); to reduce the need for blood transfusion and improve patient well-being.
- ➢ Antiemetic therapy; for the nausea and vomiting due to chemotherapy side-effects.
- ➢ Psychological support, infections (bacterial, viral and fungal) and pain need to be considered.

❖ Neoplastic Proliferation of White Blood Cells

They can be divided into three broad categories based on the origin of the neoplastic cells:

A. Lymphoid neoplasms, which include; lymphocytic leukemias, non-Hodgkin lymphomas (NHLs), Hodgkin lymphomas (discussed later), and plasma cell dyscrasias and related disorders.

B. Myeloid neoplasms; arise from stem cells that normally give rise to the formed elements of the blood: granulocytes, red cells, and platelets.

The myeloid neoplasms fall into three fairly distinct subcategories:-

1- Acute myelogenous leukemias, in which immature progenitor cells accumulate in the bone marrow.

2- Chronic myeloproliferative disorders, in which inappropriately increased production of formed blood elements leads to elevated blood cell counts.

3- Myelodysplastic syndromes, which are characteristically associated with ineffective hematopoiesis and cytopenias.

C. Histiocytic neoplasms: represent proliferative lesions of histiocytes. Of special interest is a spectrum of proliferations comprising Langerhans cells (the Langerhans cell histiocytoses).

LEUKEMIAS

Leukemias are a group of disorders characterized by neoplastic proliferation of WBCs with accumulation of malignant leukocytes in the bone marrow and blood, leading to features of marrow failure and organs infiltration

- It is either; chronic or acute which can be either myeloid or lymphoid.
- The chronic leukemias usually less progress in comparison with the acute, but the acute respond more to treatment.

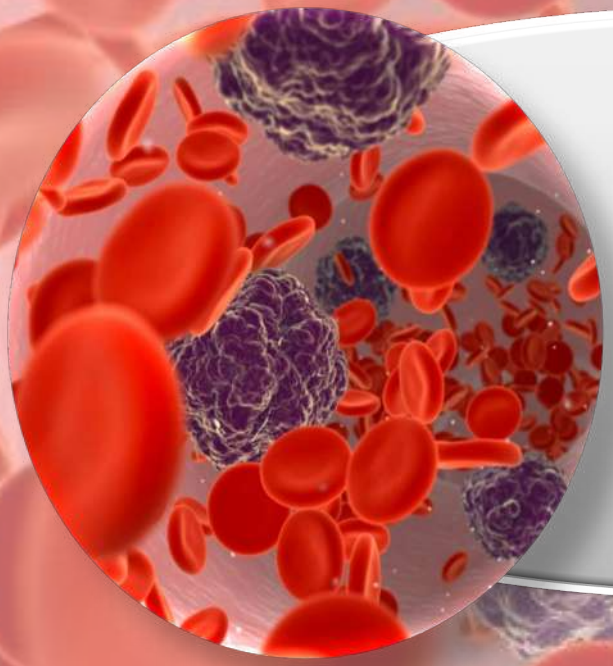
❖ Epidemiology

- The incidence of leukemia of all types in the population is approximately 10/100,000 per annum.
- Males are affected more frequently than females, with a ratio being about 3:2 in acute leukemia. 2:1 in chronic lymphocytic leukemia and 1.3:1 in chronic myeloid leukemia.
- Acute leukemia occurs at all ages; ALL; in children aged 1-5 years and AML there is a striking rise over the age of 50, while chronic leukemias occur mainly in middle and old age groups.

❖ Etiology:

Unknown, but as in most diseases it is the combination of genetic background and environmental influence that determines the risk of developing a malignancy.

- **Genetic;**
- Down's syndrome; (where acute leukemia occurs with a 20-30 fold increased frequency).
- Fanconi's anemia.
- Ataxia telangiectasia and Bloom's syndrome.
- **Environmental;**
- Chemicals, Drugs and Radiation
- Viral infections; (Human T-lymphotropic virus type1, Epstein-Barr virus (EBV)… etc.



ACUTE LEUKEMIAS

ACUTE LEUKEMIAS

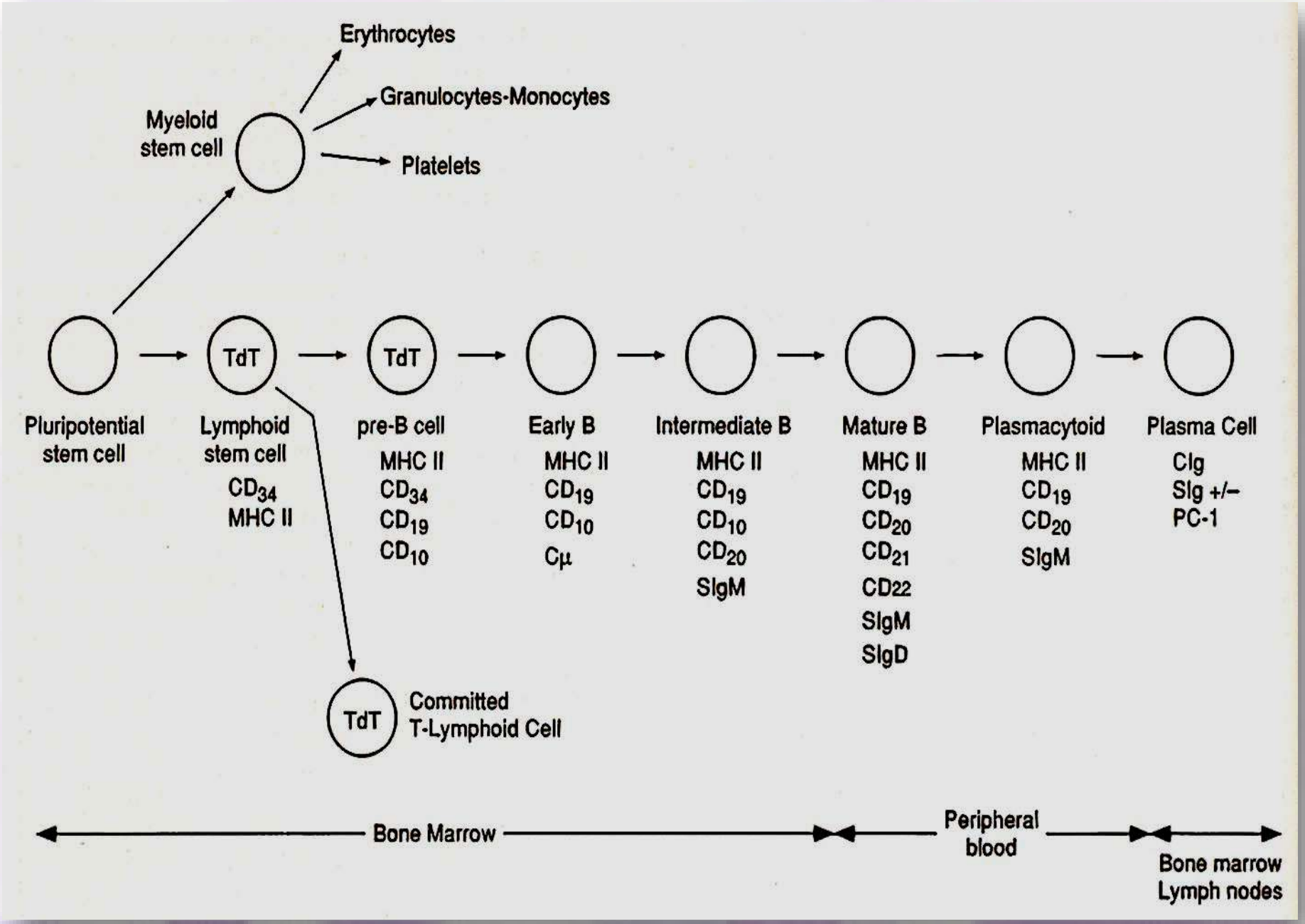
Aggressive disease characterized by malignant transformation of stem cells or early progenitor cells leading to accumulation of the early hemopoietic cells (blasts).

- Usually fatal if not treated.
- 2 major types; Myeloid (AML) or lymphoid (ALL).
- The mechanisms of these changes;
  1. Increased **proliferation** rate.
  2. Reduced **apoptosis**.
  3. Block of **differentiation**.

Defined by:

1- Presence of **blast cells of >20%** in the peripheral blood or marrow.

2- Leukemic cytogenetic or molecular genetic (clonality) abnormality even with less than 20% blasts.


Erythrocytes
Granulocytes-Monocytes
Platelets
Myeloid stem cell
TdT
TdT
Pluripotential stem cell
Lymphoid stem cell
CD34
MHC II
pre-B cell
MHC II
CD34
CD19
CD10
Early B
MHC II
CD19
CD10
Cμ
Intermediate B
MHC II
CD19
CD10
CD20
SIgM
Mature B
MHC II
CD19
CD20
CD21
CD22
SIgM
SIgD
Plasmacytoid
MHC II
CD19
CD20
SIgM
Plasma Cell
CIg
SIg +/–
PC-1
TdT
Committed T-Lymphoid Cell
Bone Marrow
Peripheral blood
Bone marrow
Lymph nodes

ACUTE MYELOID LEUKEMIA (AML)

- Most common form of leukemias in adult age group and less in children (10-15%).
- French-American-British (FAB); divided AML to M0 through M7, based on the type of cell the leukemia develops from and how mature the cells are. depending on the morphology of the leukemia cells looked under the microscope after routine staining.
- WHO scheme (2008); depending on the specific gene abnormalities with the advanced techniques specially the genetics.

FAB Classification

Subtype	Name
M0	Undifferentiated AML
M1	AML with minimal maturation
M2	AML with maturation
M3	Acute promyelocytic leukemia (APL); hypergranular M3 variant; APL hypogranular
M4	Acute myelomonocytic leukemia (AMML)
M4 eos	Acute myelomonocytic leukemia with eosinophilia
M5	Acute monocytic leukemia M5a; Monoblastic, M5b; Monocytic
M6	Acute erythroid leukemia (DiGuglielmo's disease)
M7	Acute megakaryoblastic leukemia

WHO Classification of AML

1- AML with recurrent cytogenetic abnormalities.

2- AML with multilineage dysplasia.

- Following MDS or MDS/MPD.
- Not related to MDS.

3- AML and MDS, therapy related (t-AML).

Alkylating agents, topoisomerase type II inhibitors.

4- AML not otherwise categorized.

- FAB; M0-M7, basophilic leukemia, panmyelosis, myeloid sarcoma.
- Acute leukemia of ambiguous lineage.
- Undifferentiated, bilineal, biphenotypic.

WHO Classification AML 2008 (modified)

- ***Acute myeloid leukemia with recurrent genetic abnormalities;***

AML with t(8;21)(q22;q22); RUNX1-RUNX1T1
AML with inv(16)(p13.1q22) or t(16;6)(p13.1;q22); CBFB-MYH11
AML with t(15;17)(q22;q12); PML-RARA
Provisional entity: AML with mutated NPM1
Provisional entity: AML with mutated CEBPA

- ***Acute myeloid leukemia with myelodysplasia-related changes***
- ***Therapy-related myeloid neoplasms (t-AML)***
- ***Acute myeloid leukemia, not otherwise specified;***

AML with minimal differentiation
AML without differentiation
AML with maturation
Acute myelomonocytic leukemia
Acute monoblastic/monocytic leukemia
Acute erythroid leukemia
Acute megakaryoblastic leukemia
Acute basophilic leukemia
Acute panmyelosis with myelofibrosis

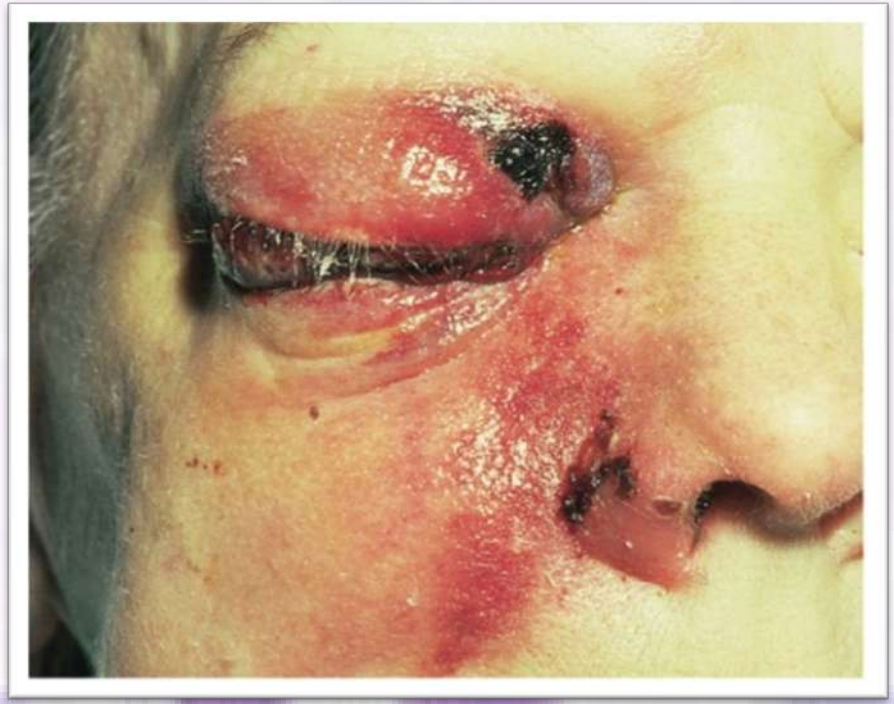
- ***Myeloid sarcoma***
- ***Myeloid proliferations related to Down syndrome***
- ***Transient abnormal myelopoiesis myeloid leukemia***

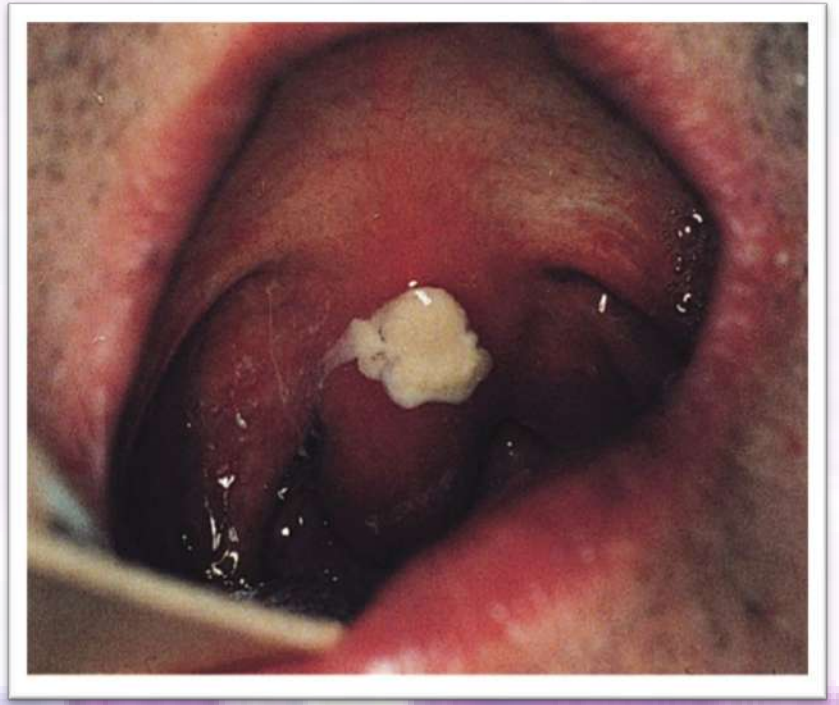
❖Clinical Features:

General features of illness; fever, malaise,… with the features of bone marrow failure, due to its involvement by malignant cells.

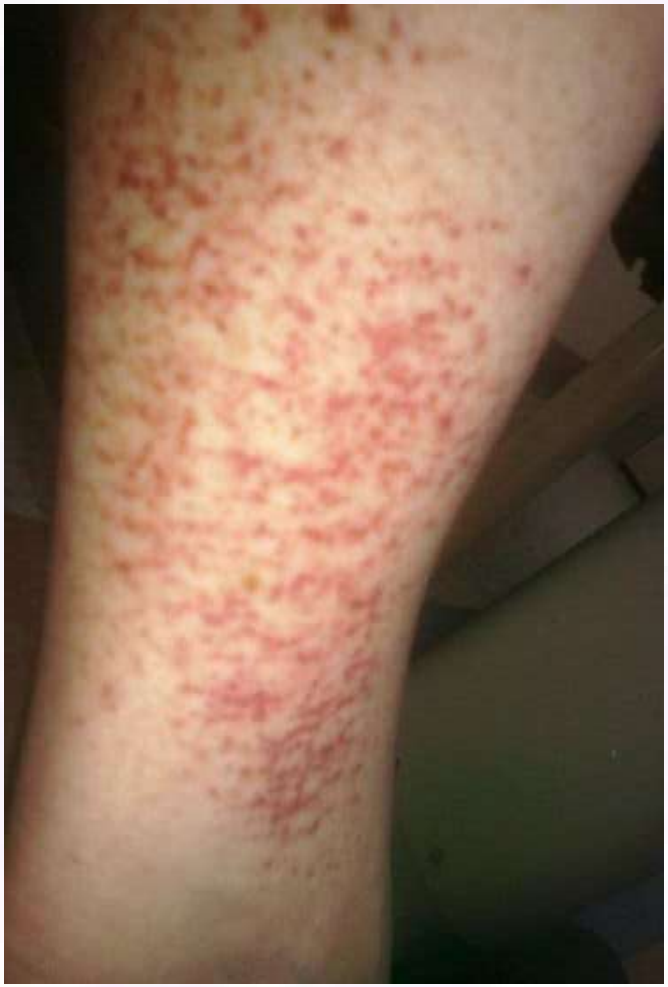
Can presented in a wide spectrum of manifestations;

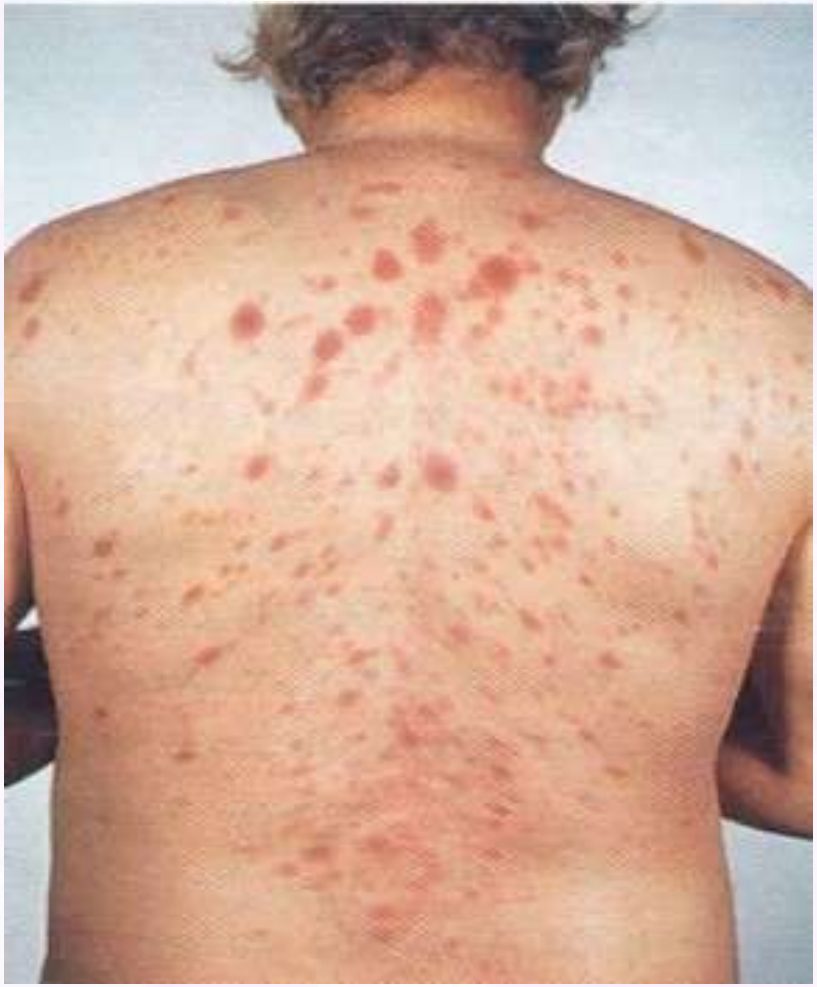
- Infections; are frequent due to loss of normal leukocytes functions. It could be bacteria, viral or fungal.



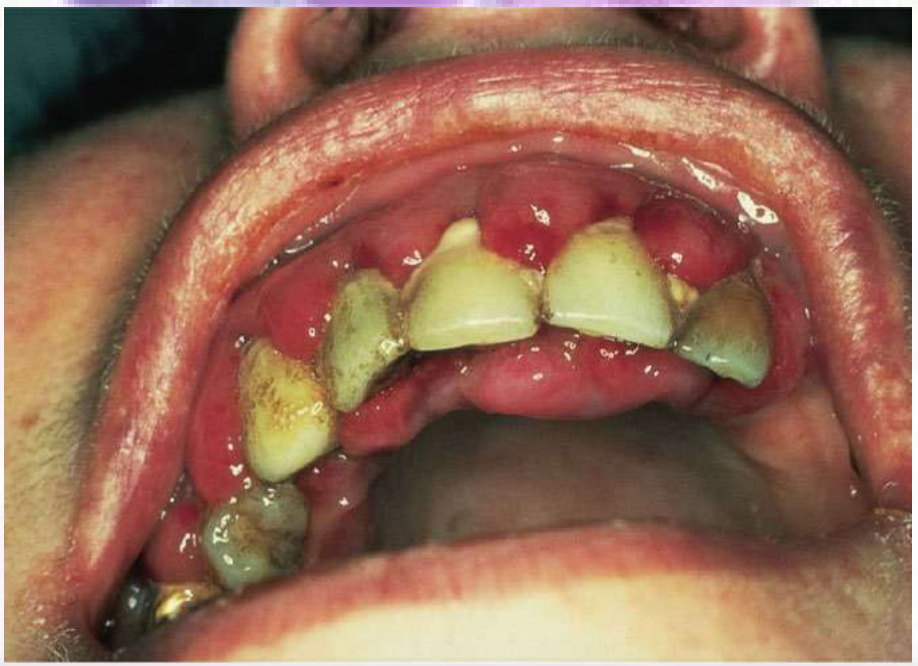


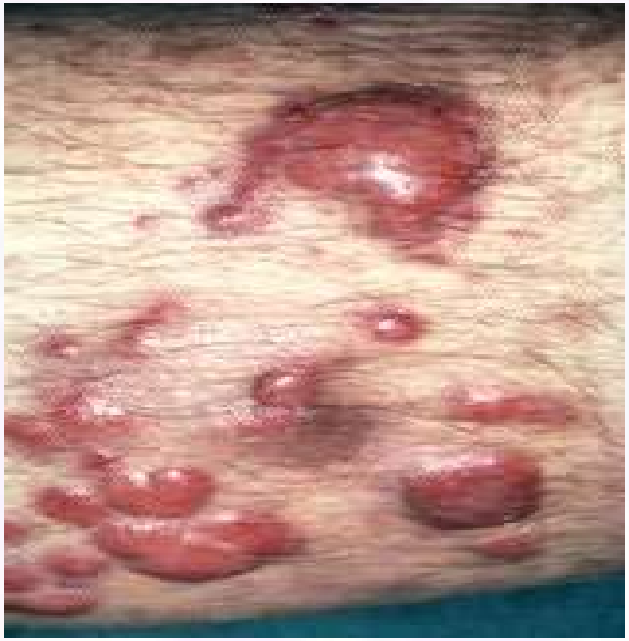
- Anemia; due to failure of erythropoiesis.
- Bleeding; due thrombocytopenia.
- DIC; characteristic of M3 variant.





- Tissue involvements (infiltrations); gum hypertrophy, skin (erythem-matous or nodular skin lesi-ons) and CNS involvement are characteristic of AML-M4 and M5 subtypes.





Laboratory Features:

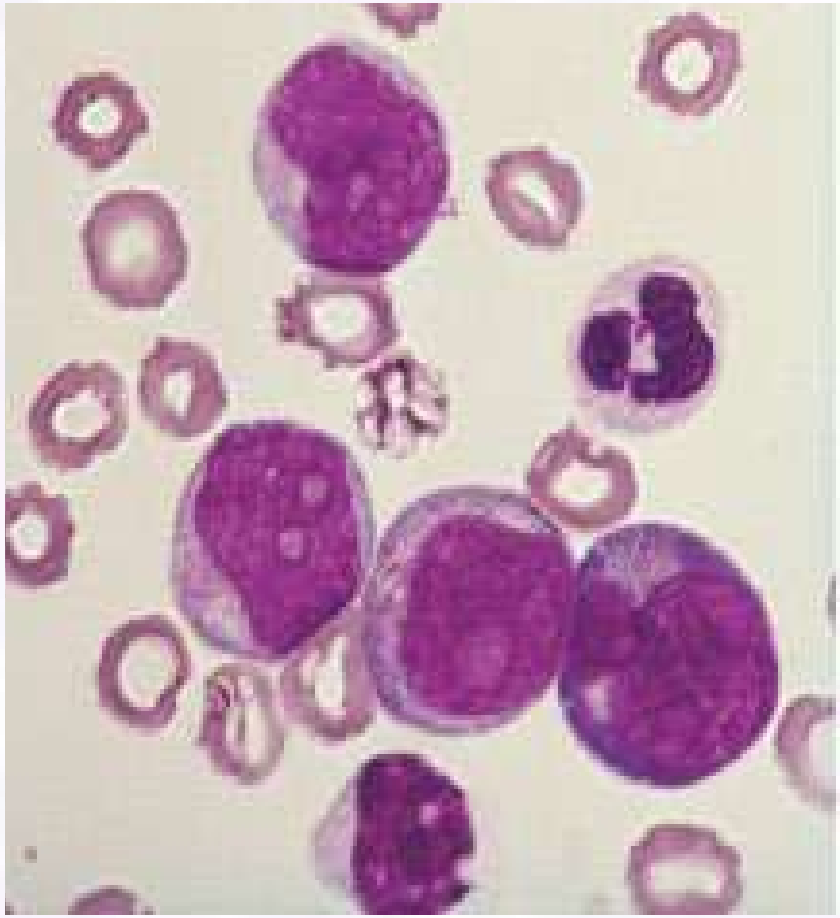
- Anemia; normochromic normocytic.
- Thrombocytopenia; in most cases.
- WBC; mostly high. Morphological with presence of blast cells of variable numbers and types.

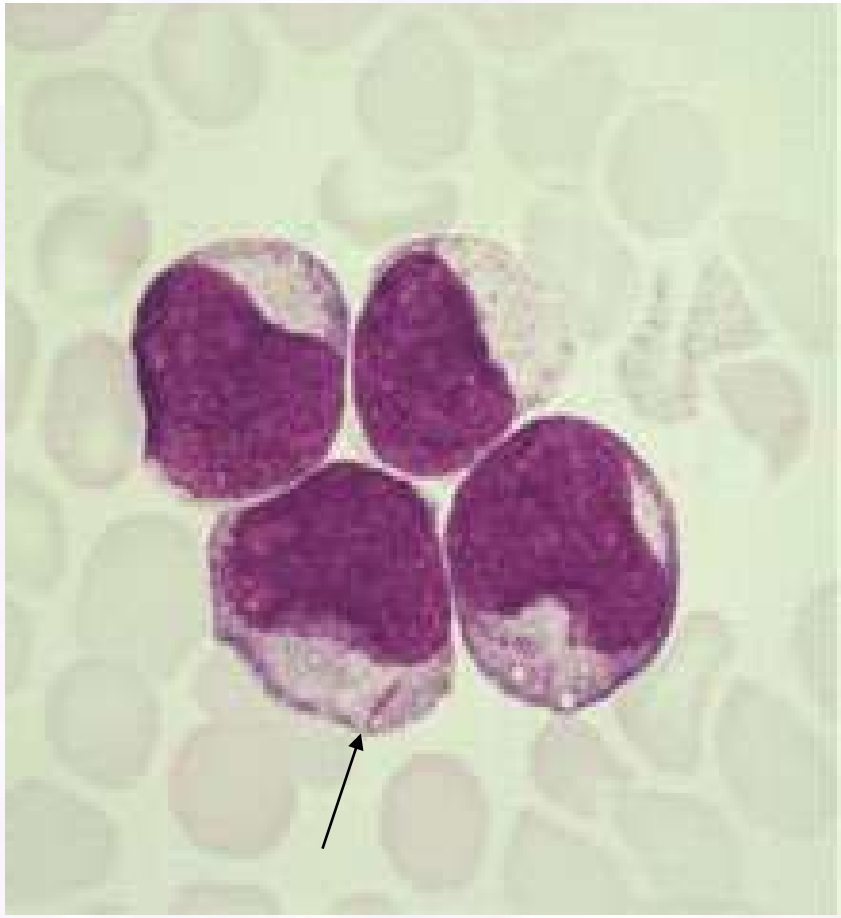
Usually with Auer rods and

Multiple Auer rods (faggot) in M3.

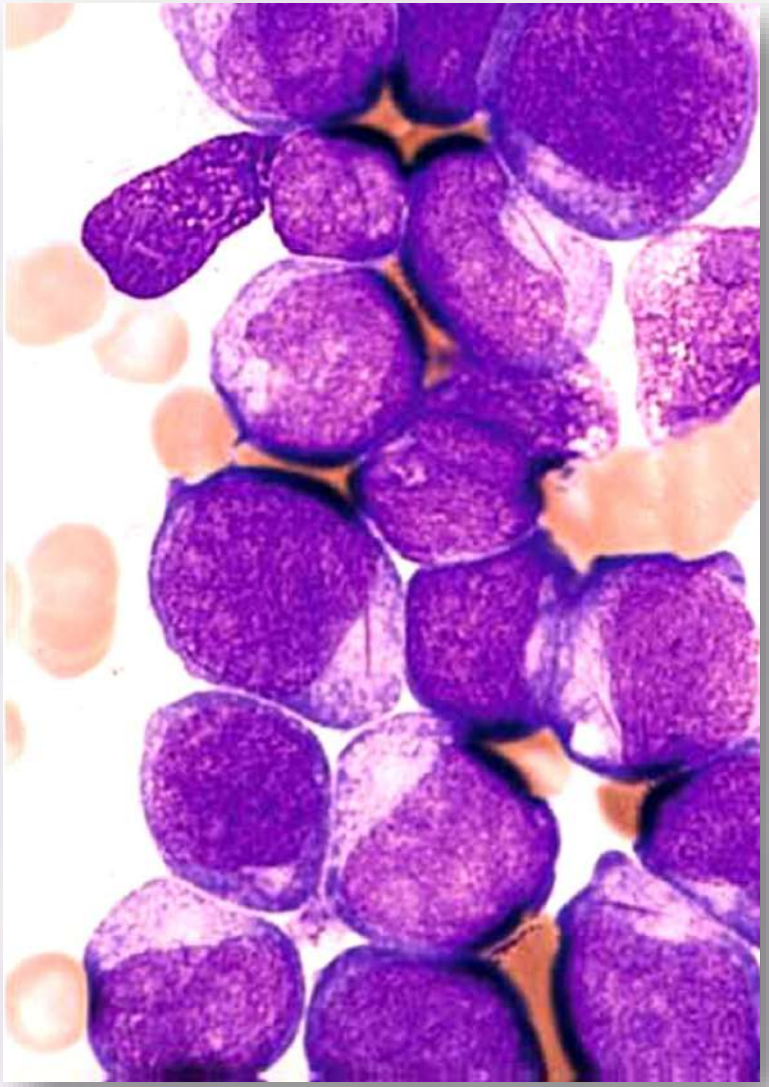
Monocytic morphology seen in M4 and M5a.

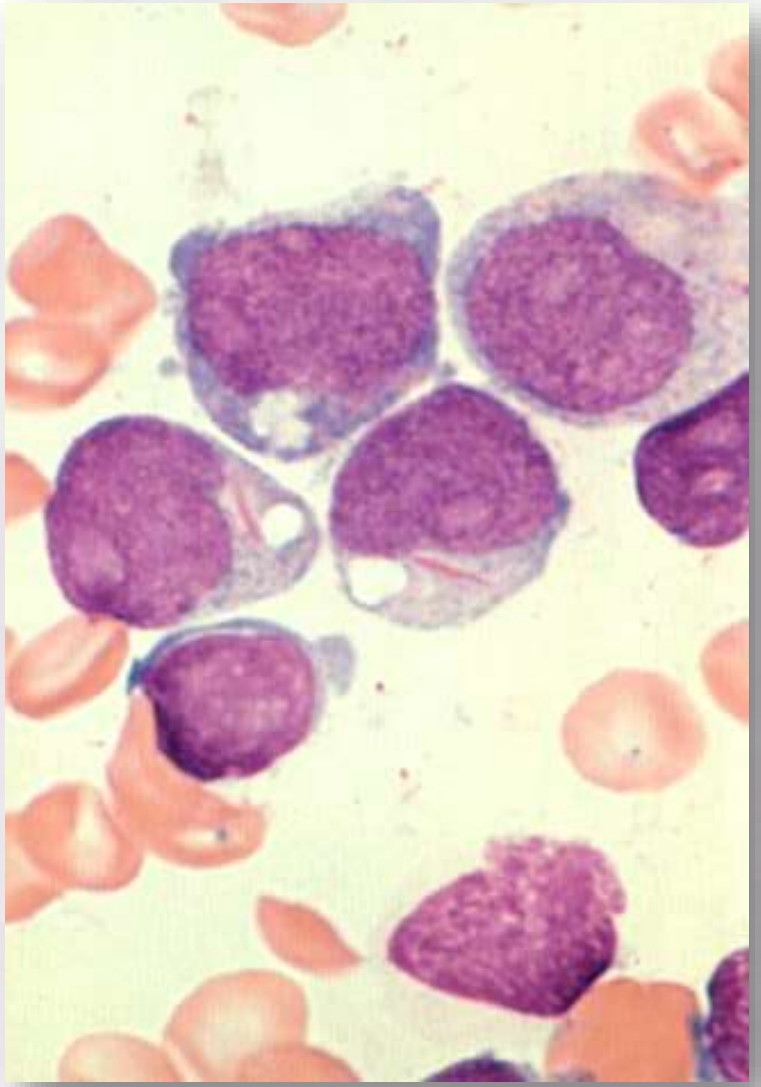
- BMA; hypercellular with suppression of other hemopoietic activity and blasts >20%.



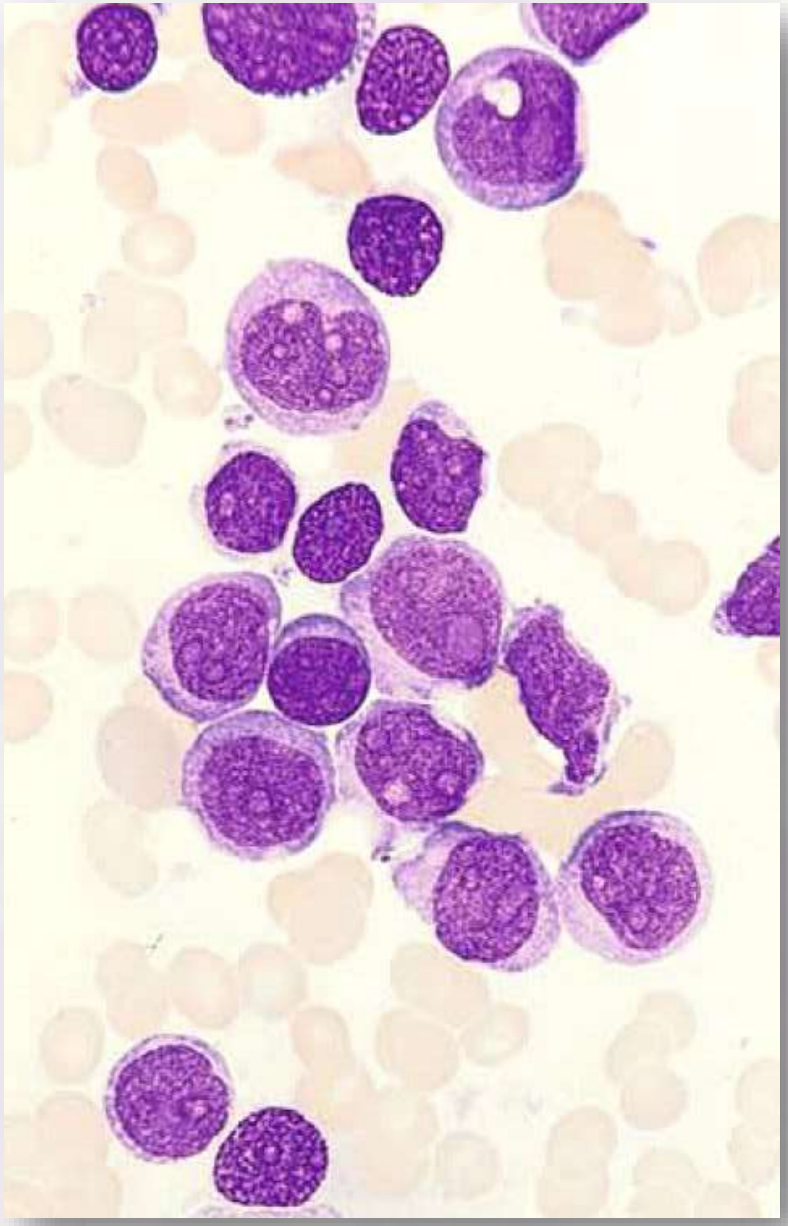


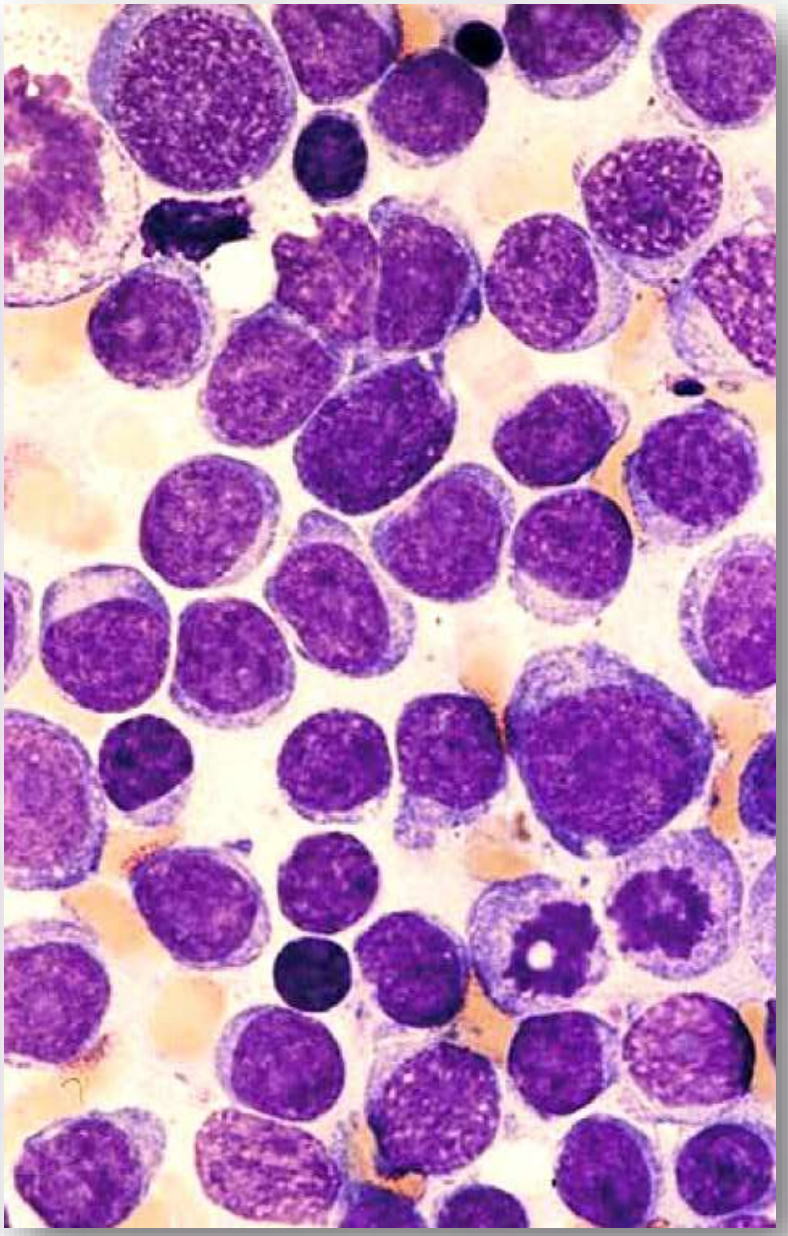
AML; showing blast cells of large size with high amount of cytoplasm (low N/C ratio) containing Auer rods (arrow) and irregular nuclear outline with prominent nucleoli.

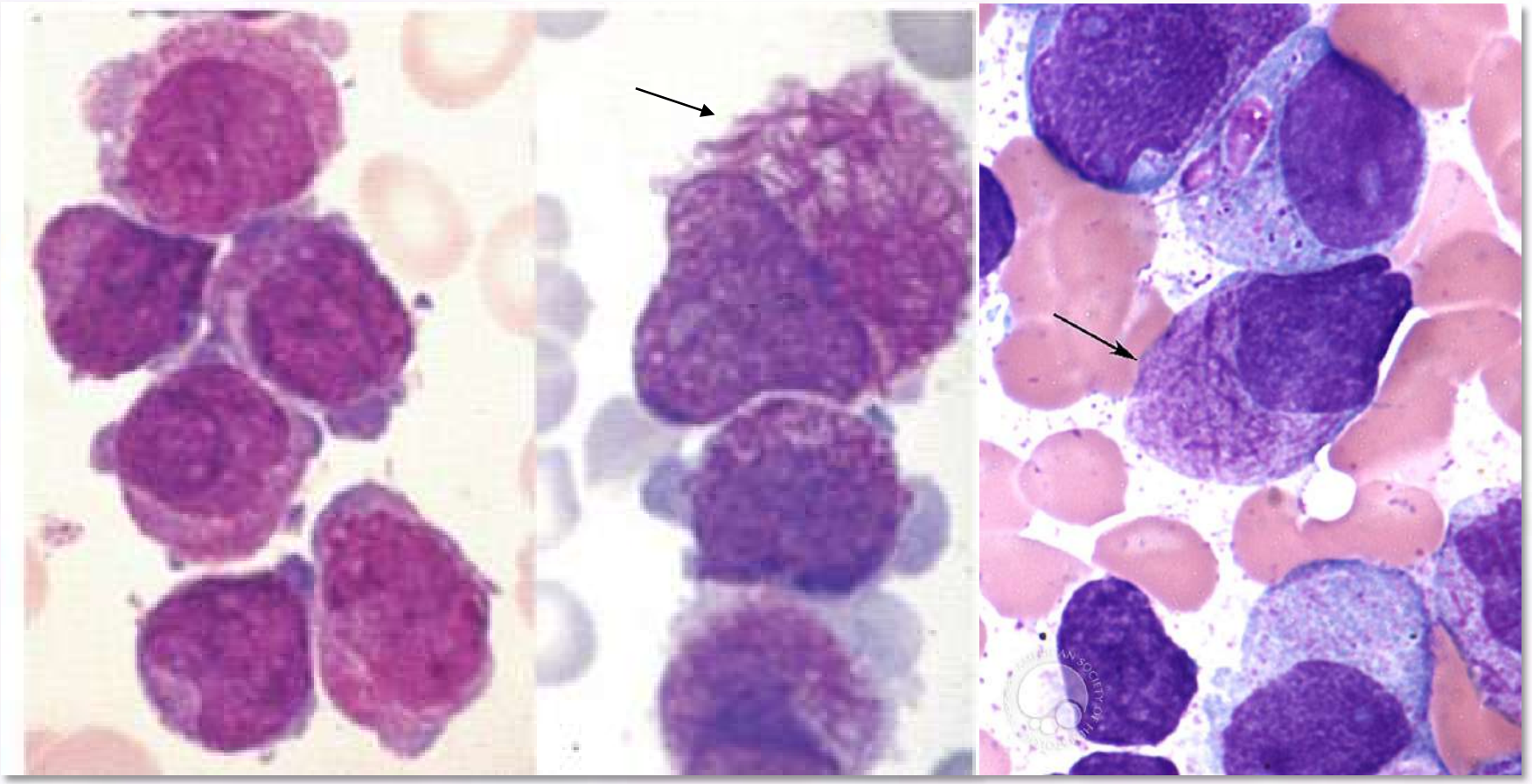




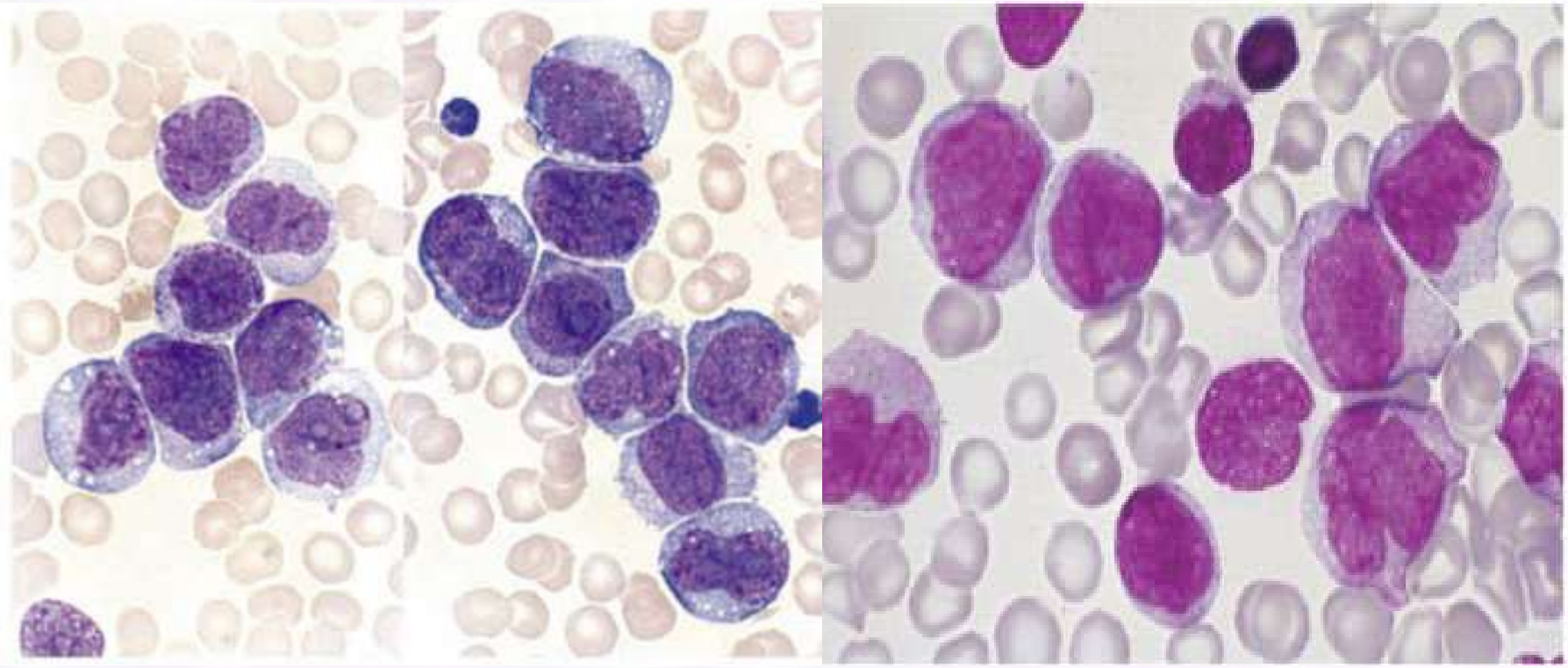
AML; showing large blast cells with prominent nucleoli .
Auer rods.







AML-M3 (APL); Neoplastic promyelocytes with abnormally coarse and numerous azurophilic granules. Other characteristic findings include the presence of several cells with multiple needle-like Auer rods *(Faggot cells)*



AML; another example, shows monocytic morphology (M4 and M5)

Characterization the type of leukemia for its treatment and prognosis by;

- Cytochemical.
- Immunological (flow cytometry).
- Cytogenetic.

Special Tests for AML

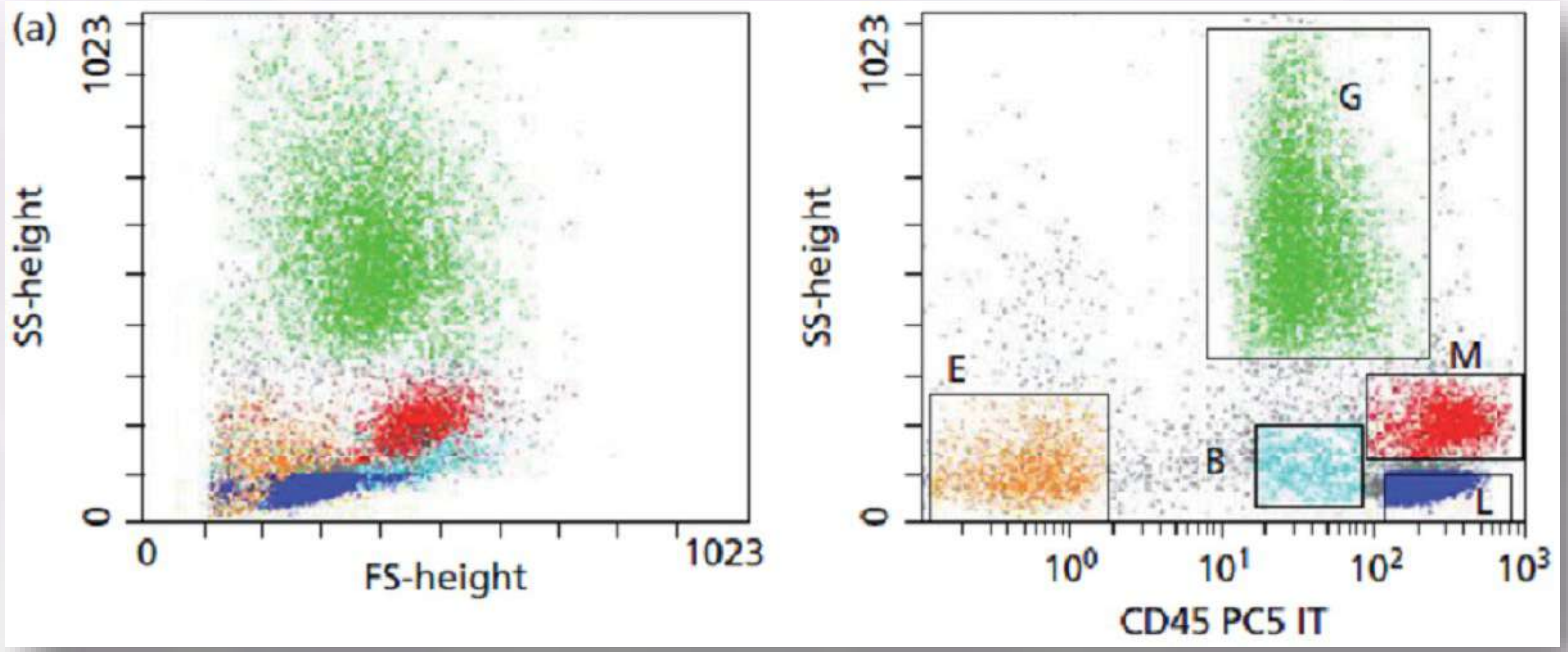
➢ ***Cytochemistry***	
- Myeloperoxidase	+ (including Auer rods)
- Sudan black	+ (including Auer rods)
- Non-specific esterase	+ in M4 & M5
➢ ***Immunological markers (flow cytometry)***	
- CD13, CD33, CD117	+
- Glycophorin	+ (erythroid)
- Platelet antigens. e.g;CD41	+ (megakaryoblastic)
- Myeloperoxidase	+ (undifferentiated)
➢ ***Chromosome and genetic analysis***	

❑ Example of Flow cytometry immunophenotyping;

Showing improvement of separation of populations by CD45 and sideways light scatter (SSC) gating. Forward light scatter (FSC) is also shown.

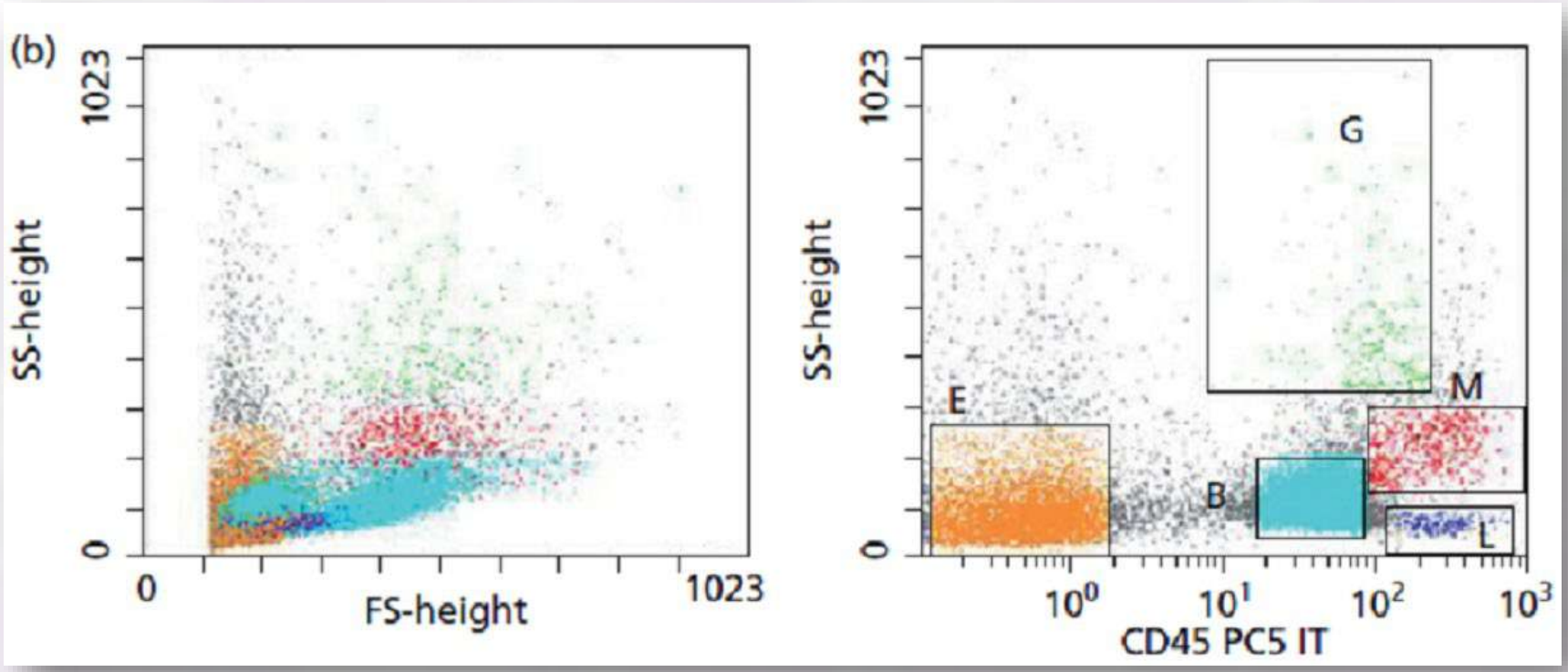
SSC-CD45 gating permits isolation of bone marrow blasts from all other populations, which is not possible by SSC-FSC gating.

(a) Normal bone marrow (left, SSC-FSC plot; right, SSC-CD45 plot)



((G, granulocytes; M, monocytes; L, lymphocytes; E, erythrocytes; B, blasts.))

(b) Acute myeloid leukemia bone marrow (left, SSC-FSC plot; right, SSC-CD45 plot).



((G, granulocytes; M, monocytes; L, lymphocytes; E, erythrocytes; B, blasts.))

Treatment:

The aim of the treatment; to achieve complete remission(CR); marrow blasts <5%, normal blood count and performance status.

- The main steps include; induction, consolidation and BMT
- General supportive therapy.
- Specific; depends on age, performance status, and genetic lesions.
- Chemotherapy.
- Targeting treatment and Immunotherapy are new drugs can be used.
- Allogenic stem cell transplant (SCT); may be curative treatment in relapsed disease, especially for the young patients.

❖Prognosis:

The treatment outcome depends on:

- Age; the age of <60yrs have better than the older.
- Leukocyte count.
- The cytogenetic and molecular abnormalities are most important to indicate prognosis, in addition to the classification.
- Minimal residual disease (MRD); an important guide for the treatment.

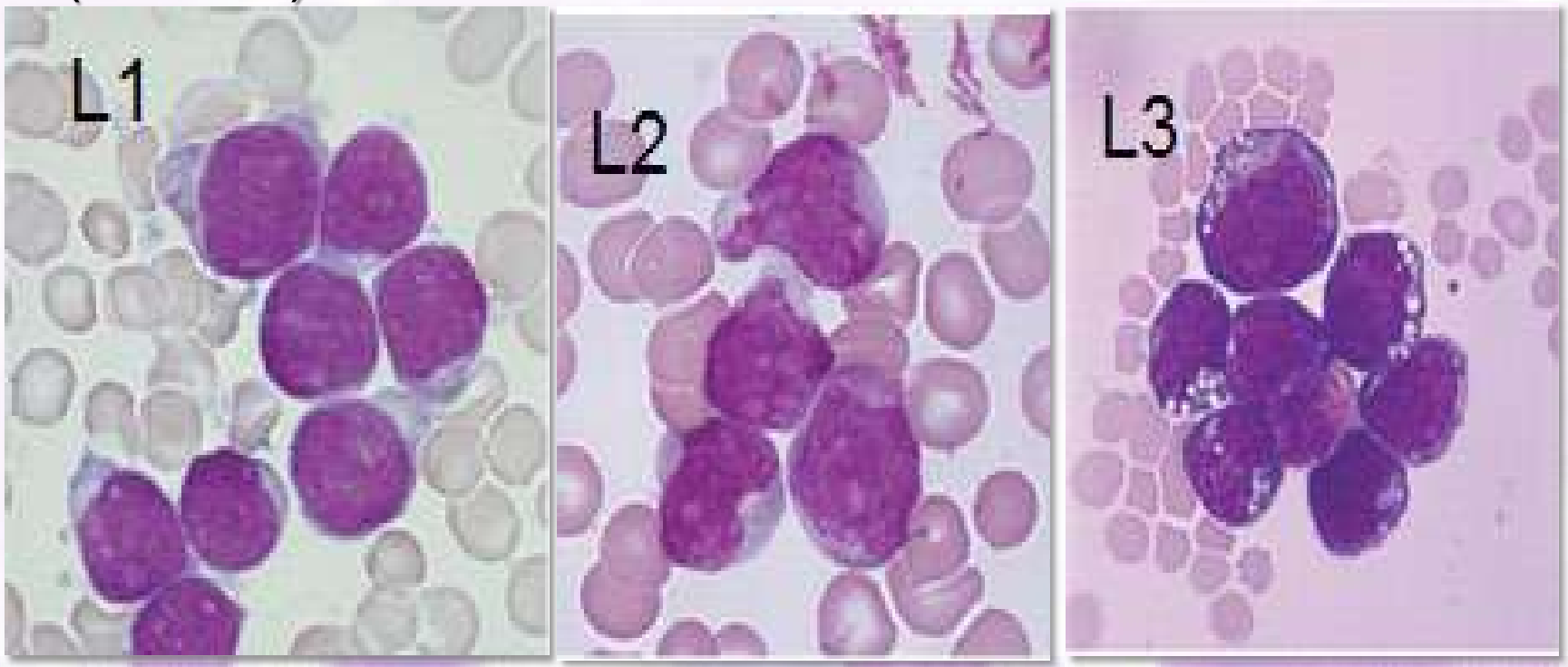
Prognostic Criteria for AML:

	Favorable	Intermediate	Unfavorable
Cytogenetics	t(15; 17) t(8; 21) inv(16) APL	Normal Other non-complex changes	Deletions (-5 or -7) Abnormal (3q) t(6; 11), t(10; 11), t(9; 22) Complex rearrangments; >3
Bone marrow response to remission induction	<5% blasts after first course		>20% blasts after first course
Age			>60 years

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

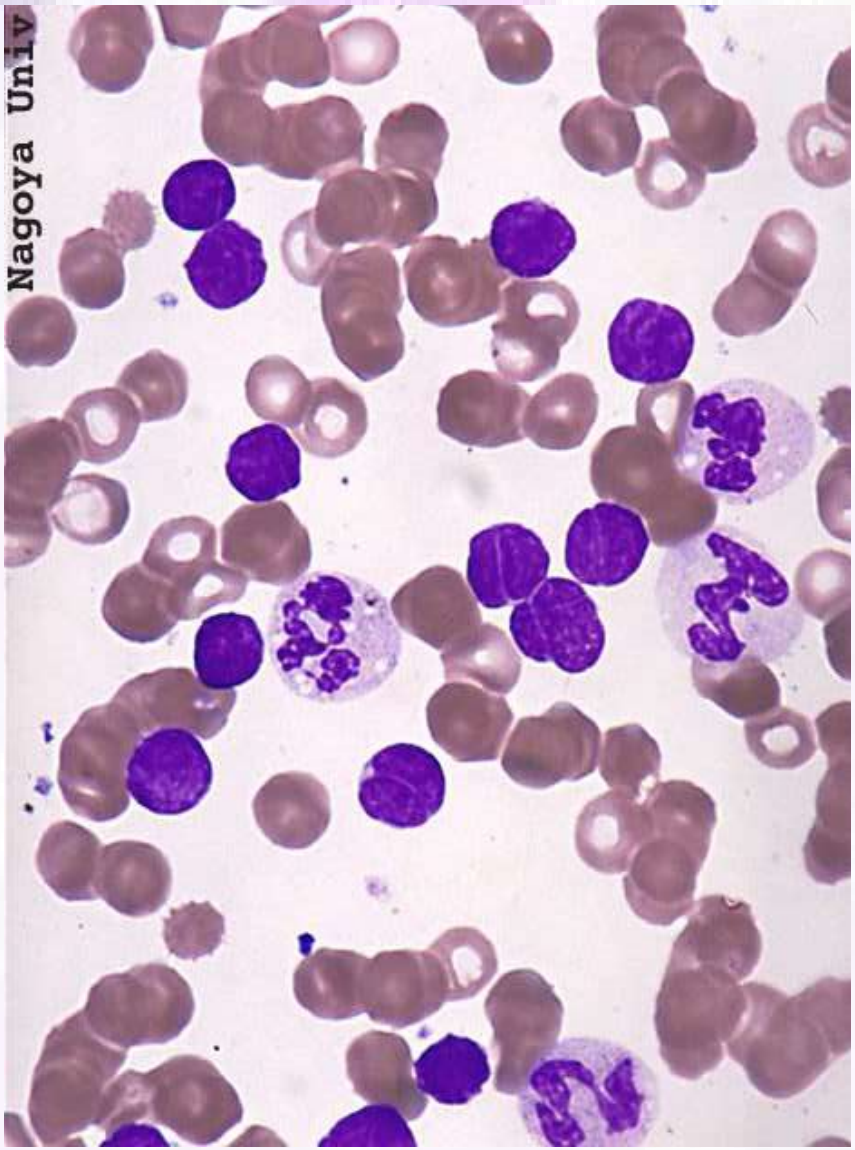
Accumulation of lymphoblasts within the bone marrow.

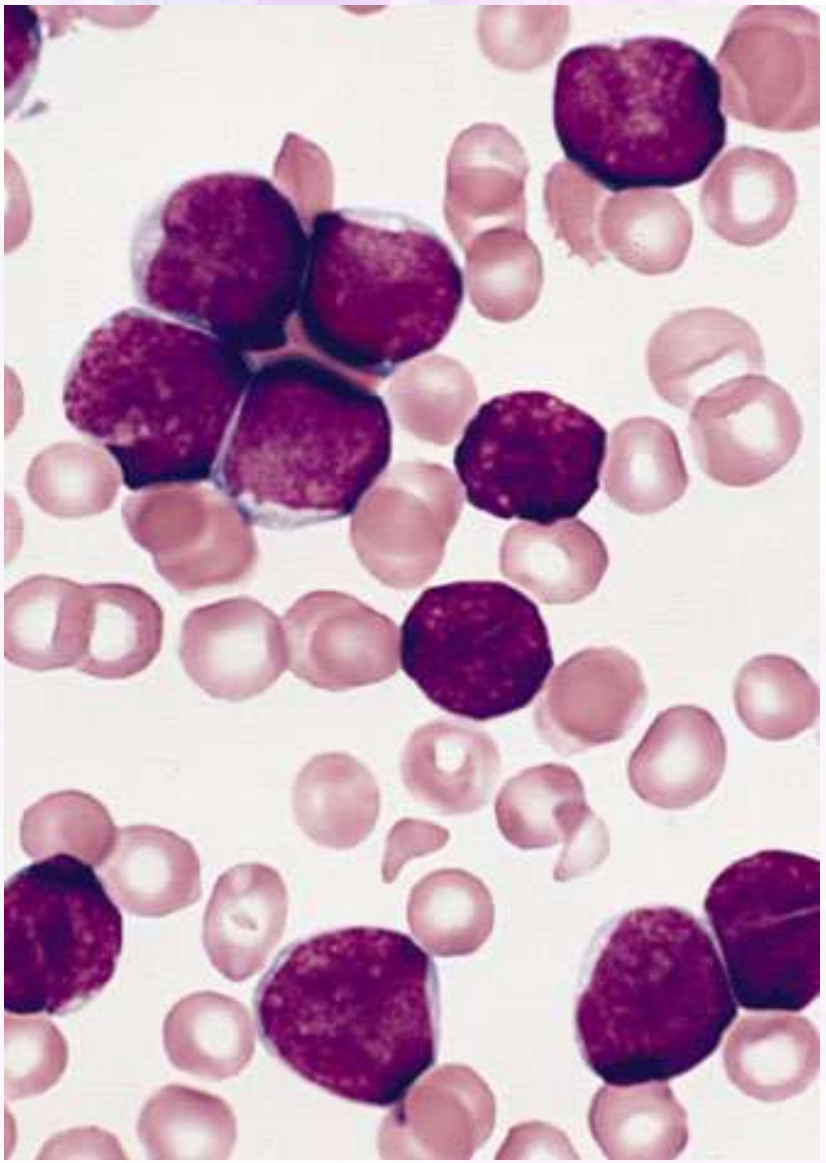
- Most common malignancy in childhood, and mostly of B-cell origin.
- Mainly classified morphologically into; L1, L2, and L3 (Burkitt's).



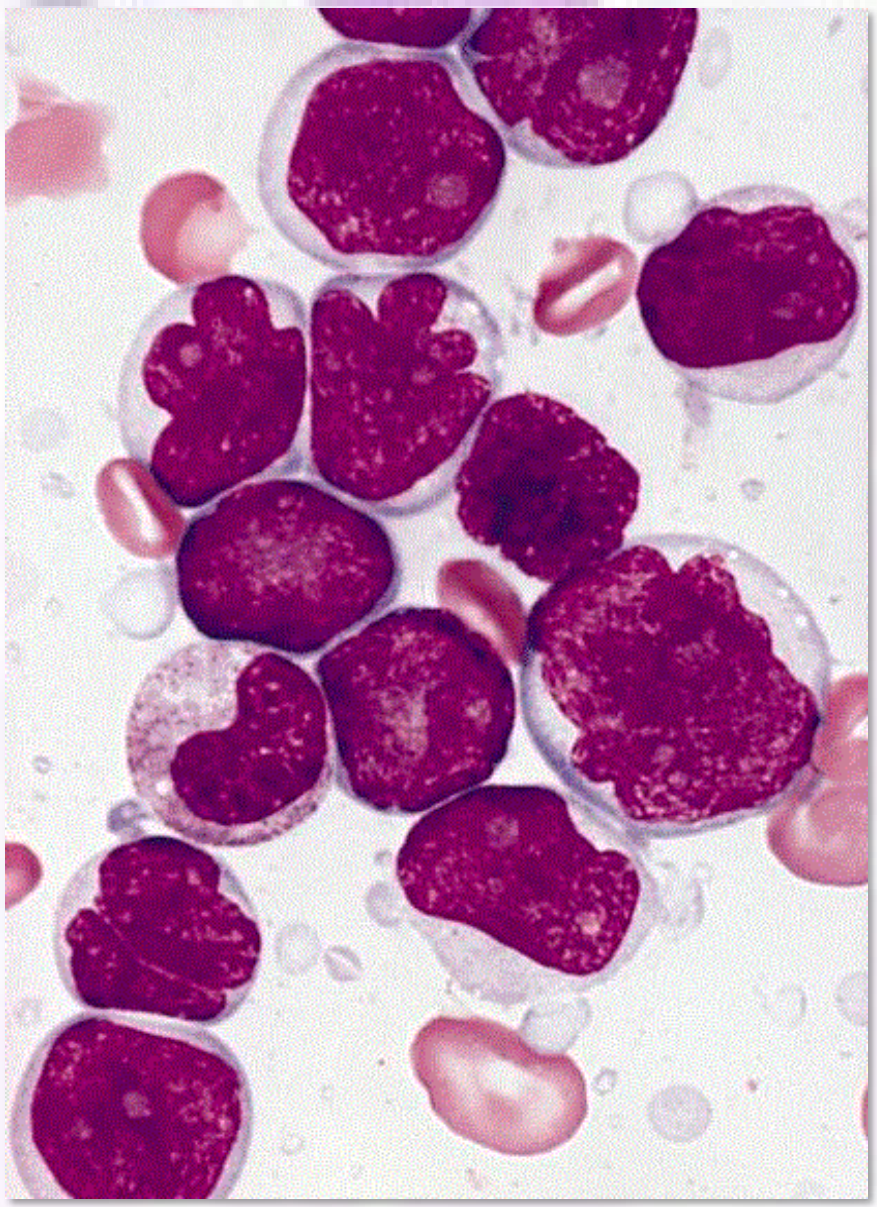
Morphological Classification
French-American-British (FAB)

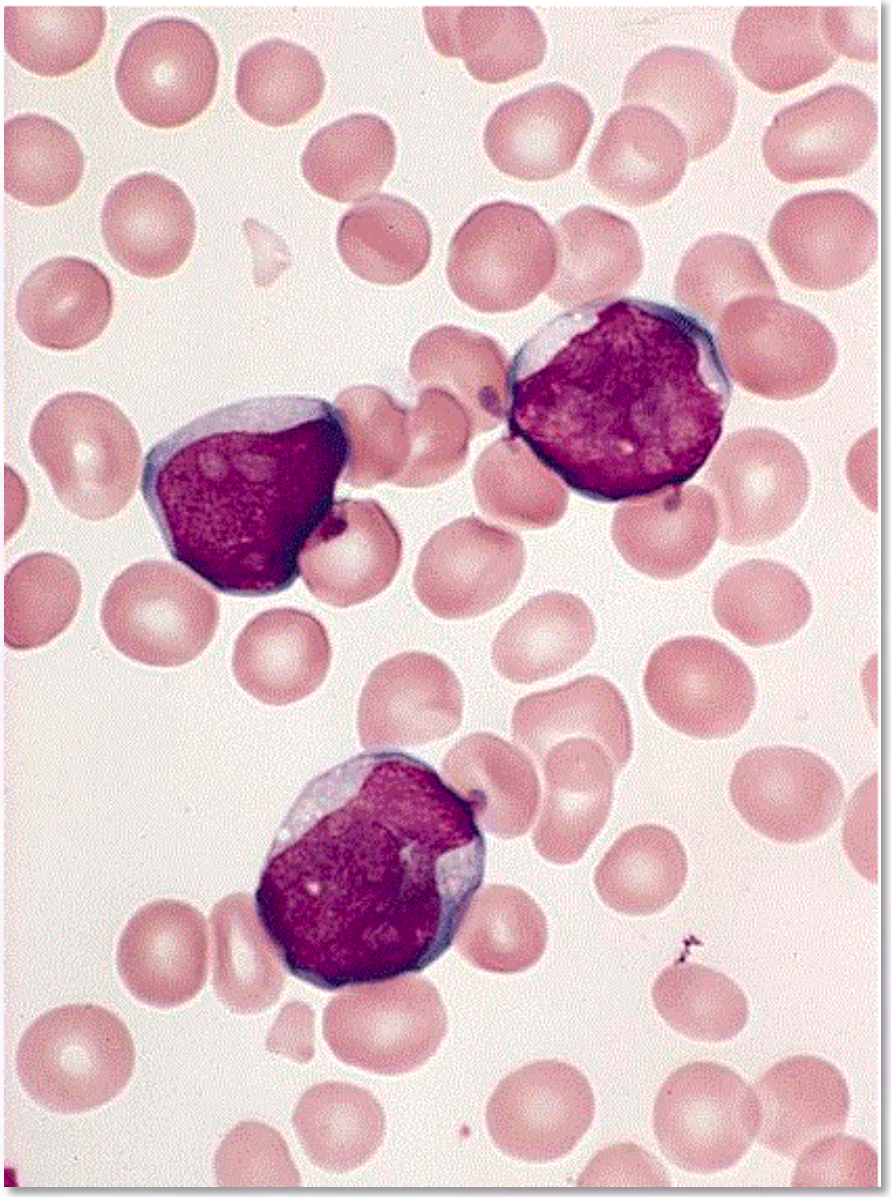
L1 ALL	Typical morphology of childhood cases of ALL; there are small to medium-sized blasts with a high nucleo-cytoplasmic ratio (N:C ratio) and a regular nuclear and cellular outline with inconspicuous nucleoli
L2 ALL	Cells are larger and more pleomorphic than those of L1 ALL; the outline and the nuclei may be irregular in shape and nucleoli may be large or prominent
L3 ALL	Cells are regular in shape but have strongly basophilic cytoplasm and prominent cytoplasmic vacuolation



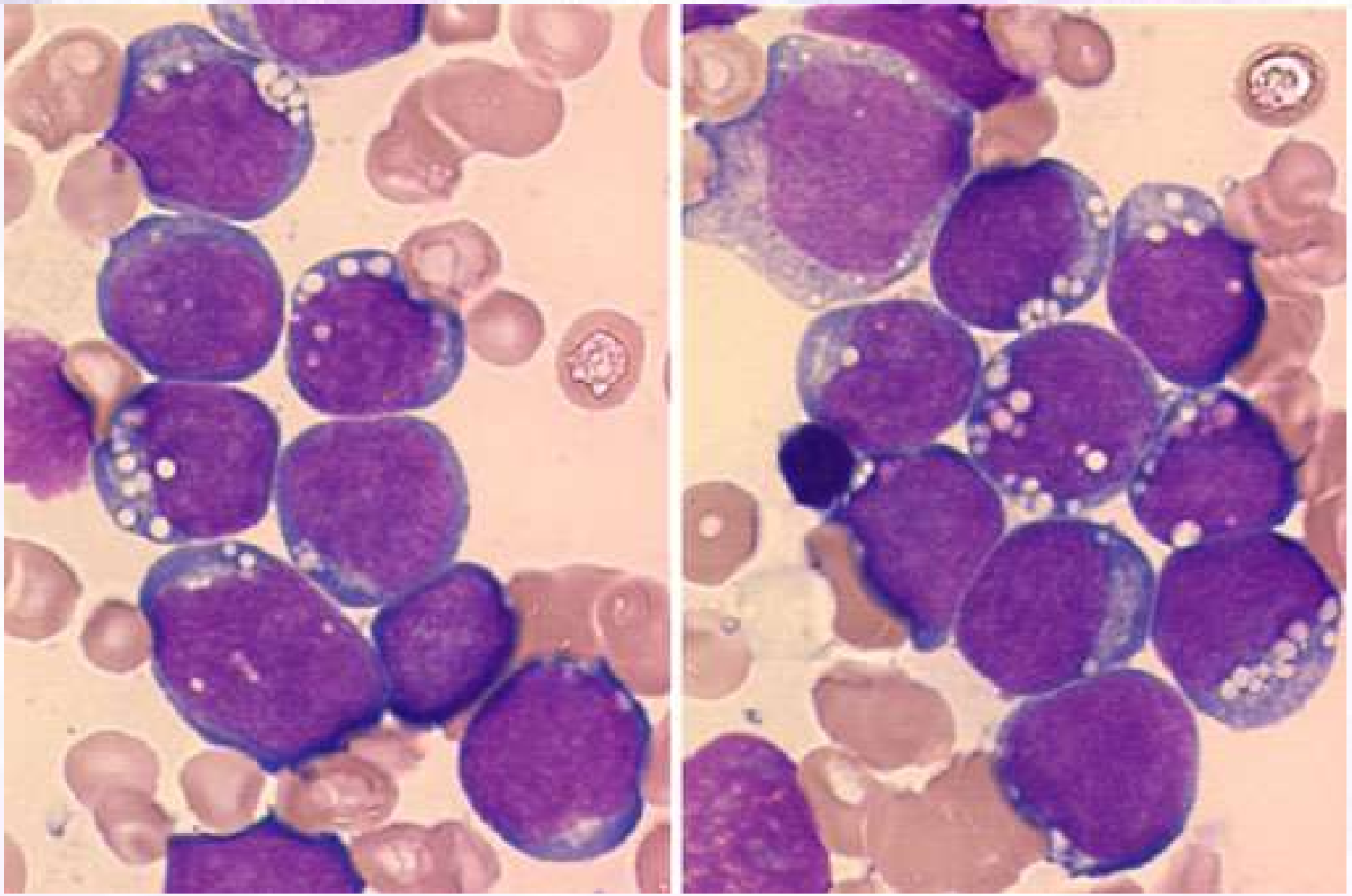


ALL- L1; Homogeneous population of small lymphoblasts with scanty cytoplasm, round regular nuclei and invisible nucleoli





ALL-2; heterogenous lymphoblasts of variable size, moderate cytoplasm, markedly large irregular nuclei with prominent nucleoli.



ALL-L3; diffuse monotonous cells with round nuclei and deeply basophilic cytoplasm which usually contains vacuoles.

FAB CLASSIFICATION OF ALL

CYTOLOGIC FEATURES	L1	L2	L3
Cell size	Small cells predominate,homogenous	Large,heterogenous in size	Large homogenous
cytoplasm	Scanty	Variable,often moderately abundant	Moderately abundant
nucleoli	Small	One or more,often large	One or more,prominent
Nuclear shape	Homogenous	Variable, heterogenous	Stippled, homogenous
Nuclear shape	Regular	Irregular clefts	regular
Cyt.basophilia	variable	variable	Intensely basophilic
Cyt.vacuolation	variable	variable	prominent

World Health Organization (WHO) Classification:

WHO classification of acute leukemias is based on :

- Clinical.
- Morphologic.
- Immunophenotypic.
- Cytogenetic.
- Molecular features.

Morphological Classification French-American-British (FAB)

Immunopheno-Subtype	FAB Subtype	Cytogenetic Abnormalities
Pre-B ALL	L1, L2	t(9;22), t(4;11), t(1;19)
T-cell ALL	L1, L2	14q11 or 7q34
B cell ALL	L3	t(8;14), t(8;22), t(2;8)

The New WHO Classification, Genetic Defects

Precursor lymphoid neoplasms
B lymphoblastic leukemia/lymphoma
B lymphoblastic leukemia/lymphoma, NOS (not otherwise specified)
B lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities
B lymphoblastic leukemia/lymphoma with t(9; 22)(q34; q11.2); BCR-ABL1
B lymphoblastic leukemia/lymphoma with t(v; 11q23); MLL rearranged
B lymphoblastic leukemia/lymphoma with t(12; 21)(p13; q22);TEL-AML1(ETV6-RUNX1)
B lymphoblastic leukemia/lymphoma with hyperdiploidy
B lymphoblastic leukemia/lymphoma with hypodiploidy (hypodiploid ALL)
T lymphoblastic leukemia/lymphoma

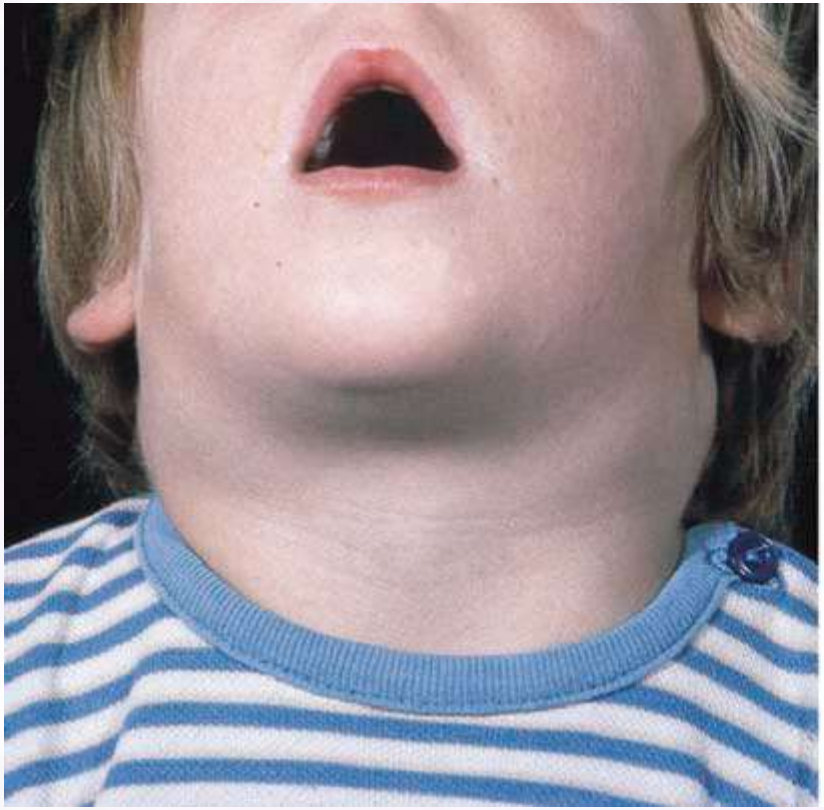
❖ Clinical features:

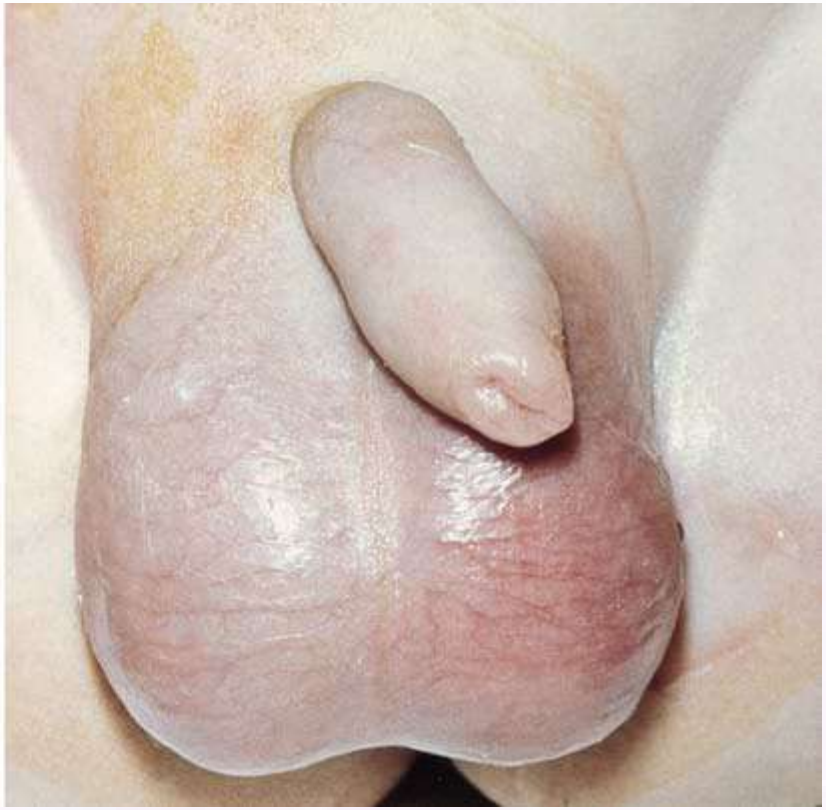
➢ Bone marrow failure:

- Anemia; (pallor, lethargy and dyspnea)
- Neutropenia; (fever and infections)
- Thrombocytopenia; (spontaneous bruises, purpura, bleeding gums and menorrhagia).

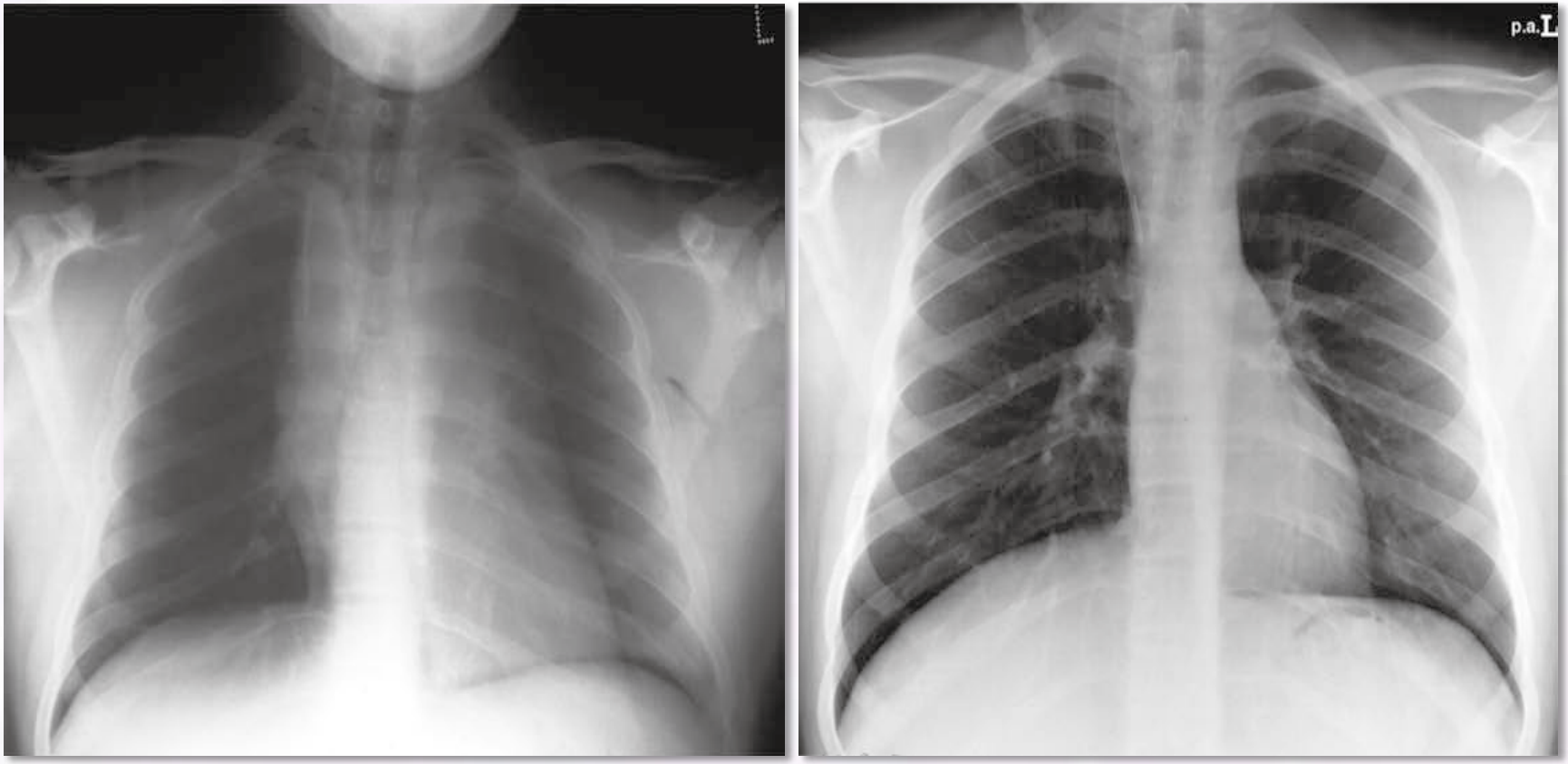
➢ Organ involvement:

- Pain, swelling and tender bones.
- Lymphadenopathy.
- Moderate hepatosplenomegaly.
- Testicular swelling.
- Meningeal involvement; headache, nausea and vomiting, blurring of vision and diplopia. Fundal examination may reveal papilledema and sometimes hemorrhage (CVA).
- Mediastinal mass; in T-ALL.





A boy with acute lymphoblastic leukemia. Marked cervical lymphadenopathy (left) and testicular swelling and erythema on the left - hand side of the scrotum caused by testicular infiltration (right).



Chest X-ray of a boy with T-ALL; There is a large mediastinal mass caused by thymic enlargement at presentation (left), which resolved after 1 week of therapy.

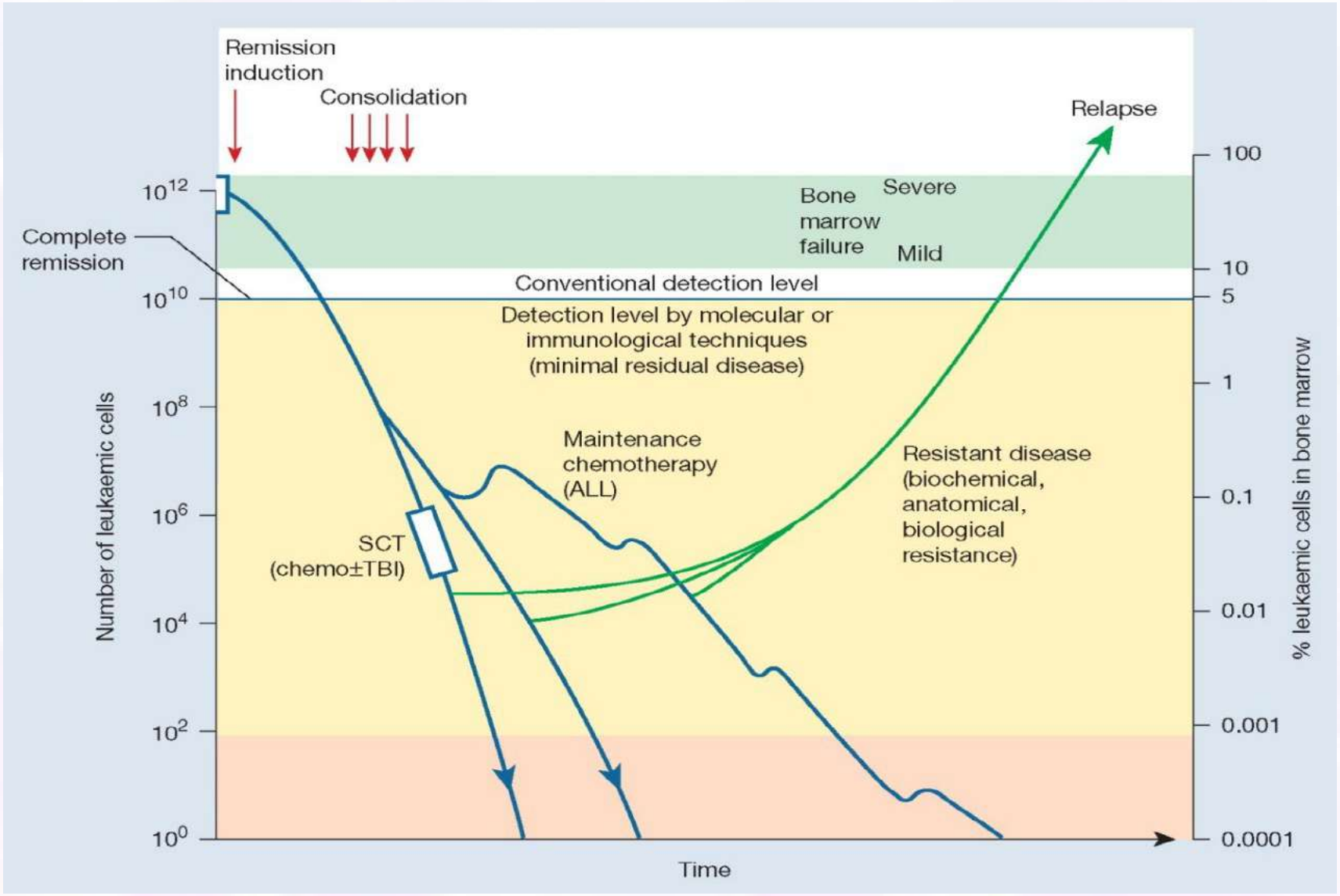
❖ Laboratory features:

- Anemia; normochromic normocytic.
- Thrombocytopenia.
- WBC count; variable, usually high and sometimes up to 200×10^9/L or more
- Blood film; variable numbers of blast cells of L1, L2 or L3
- Bone marrow; usually hypercellular with >20% blasts and sometimes hypoplastic in 5% of cases.
- CSF: Involved in 5% at presentation.
- Cytochemistry, immunological tests and cytogenetic analysis. Important to determine treatment protocol and to detect minimal residual disease (MRD) during follow-up.

❖ Treatment:

- General supportive therapy; central line, blood product, treatment of fever
- Specific, includes; induction of remission, intensification, CNS treatment and maintenance.
- Chemotherapy with or without radiotherapy.
- CNS involvement; treated seriously and use intrathecal cytotoxic.
- SCT (allogenic); may be indicated in cases with relapse

Acute leukemia: principles of therapy. ALL, acute lymphoblastic leukemia; SCT, stem cell transplantation; TBI, total body irradiation.



- The prognosis is good in children and cure may be up to 85%, while its less than 5% in old age group.

- It depends on WBC, age, sex, immunological and cytogenetic abnormalities in addition to CNS involvement and time of treatment response. MRD; an important criterion.

	Good	Poor
WBC	Low <10 × 10^9/L	High (e.g. >50 × 10^9/L)
Sex	Girls	Boys
Age	Child	Adult (or infant <1 year)
CNS at presentation	Absent	Present
Time to clear bd blasts	<1 week	>1 week
Time to remission	<4 weeks	>4 weeks
Immunophenotype	B-ALL	T-ALL (in children)
Cytogenetics	Normal or hyperdiploidy; TEL rearrangement	Ph+, 11q23 rearrangements MLL gene rearrangement Hypodiploidy (<44chromosomes)
MRD	(-ve) at 1-3 months	Still positive at 3–6 months

شكراً جزيلاً
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рахмат
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謝謝
spas
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Баярлалаа
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спасибо
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