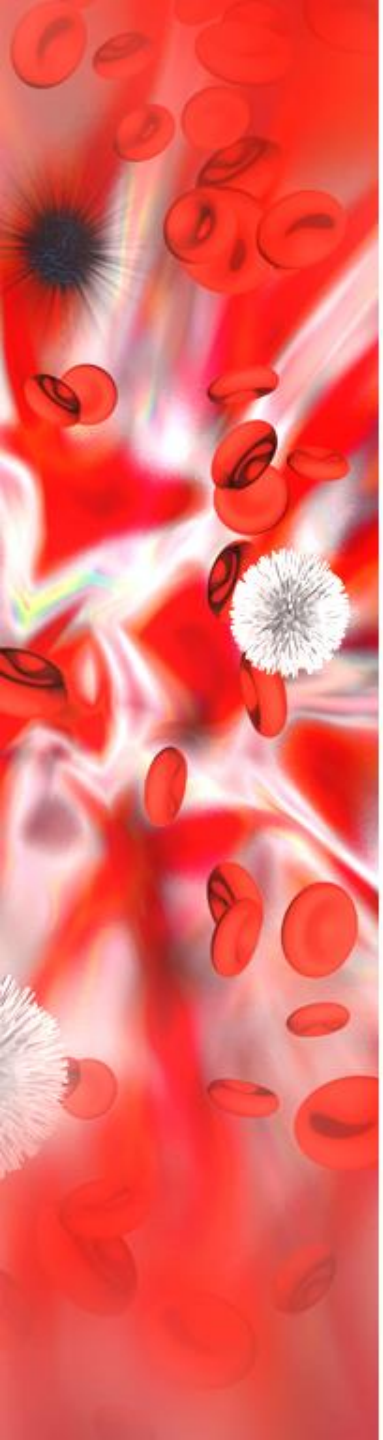
Lecture7 : Acute leukemia II



Acute lymphoblastic leukemia

- **ALL**
- Acute leukemia characterized by **proliferation of malignant lymphoid blasts** in bone marrow and blood.
- More common in Children and has better prognosis than AML.

(the principle pathogenic defect is **a block of differentiation**, form acquired mutations in transcription factors regulate differentiation of immature progenitors, or blasts accumulating in the bone marrow suppress the growth of normal hematopoietic cells)

- **Clinical Features of ALL**

1- Pancytopenia*:

Acute onset:

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

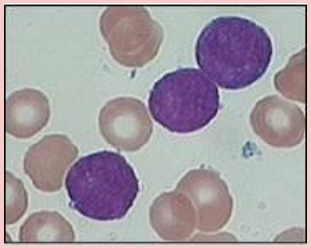
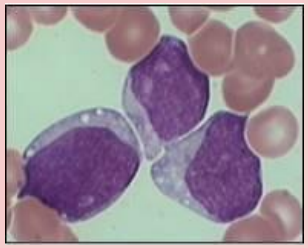
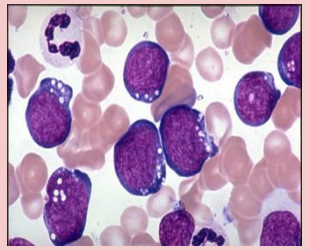
2- Organ infiltration:

- Lymphadenopathy* (very common).
- Hepatosplenomegaly.
- Testicles involvement.
- CNS disease (including headache, vomiting and nerve palsies) .
- Mediastinal mass (Characteristic for T-ALL).

* Because lymphoid blast will accumulate in marrow and this will take the place of other blast

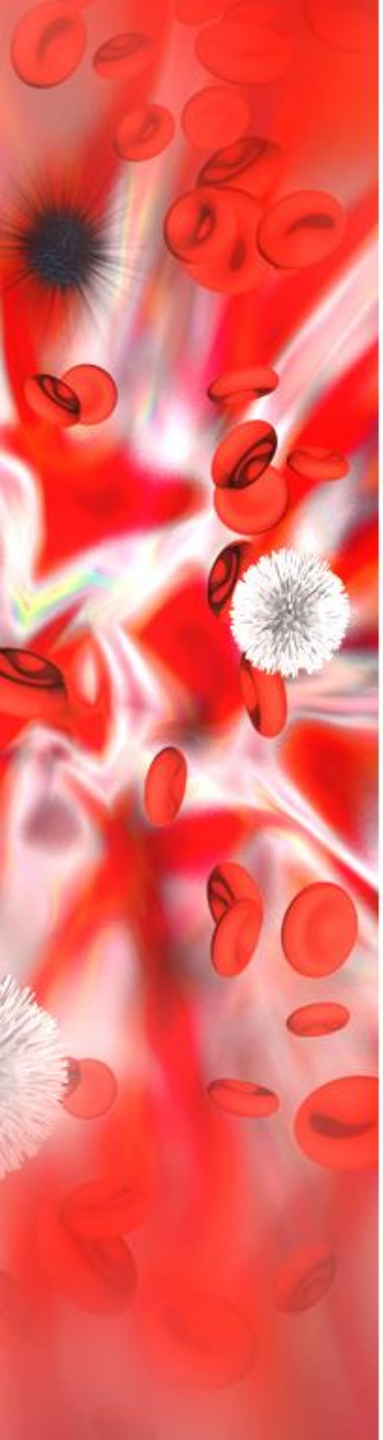
*Abnormal enlargement of lymph nods

FAB morphological subtypes

Characterstics	L1	L2	L3 (Burkitt's)
On microscopy			
Morphology	Homogenous*	Heterogeneous**	Homogenous*
Size	Small	Variable	Small
Cytoplasm	Little	More	Vaculated
Nucleoli	Not prominent	Prominent	Prominent
Genetics	Variable	Variable	T(8;14) c-myc

- **L3 (Burkitt's) represents mature lymphoid neoplasm so, it is a type of lymphoma not Acute lymphoblastic leukemia.**

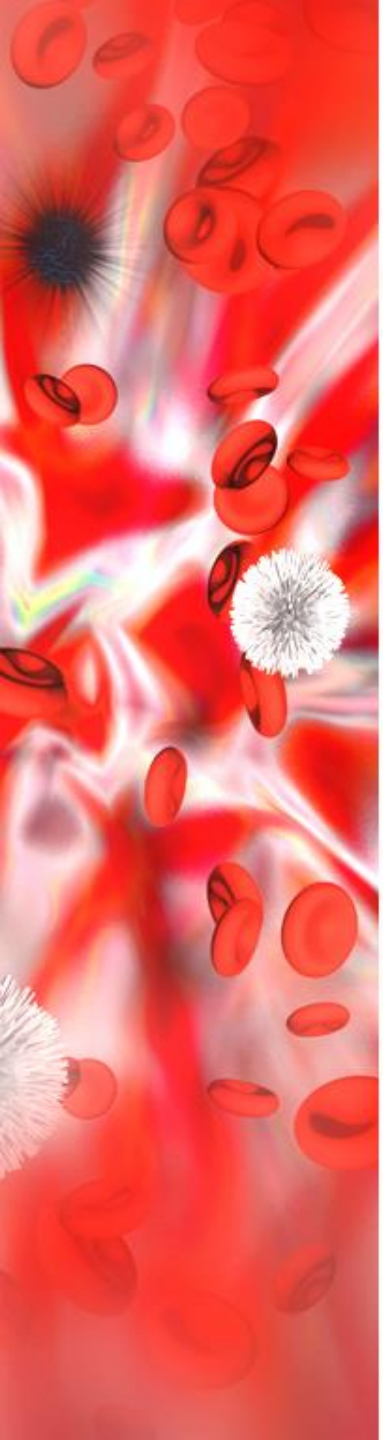
*Homogenous: single type of leukocytes.
**hetergenous: variation in WBC's counts of neutrophils, lymphocytes, monocytes…



WHO immunophenotypic subtypes

	B-cell	T-cell
Markers	CD19 (main one), cd10,cd79a	CD3 (the main)
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)***	---------

* t(9;22) nowadays has promising treatment
** t(4;11) could be congenital
*** t(12;21) More cure rate

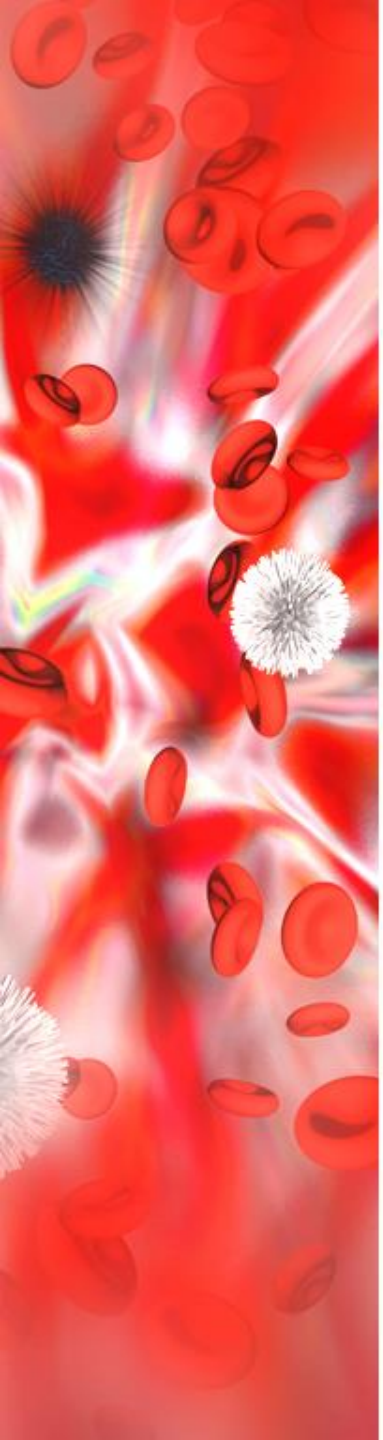


Types of ALL

Types		B-ALL		T-ALL	
Subtype		**Precursor B-cell B-ALL**	**Mature B-cell** or **Burkitt's**	**Precursor T-cell** or **T-ALL**	**Mature T-cell** or **T-cell lymphoma**
Markers	For one subtype	**CD34 & TDT** (should be +ve)	**Surface immunoglobulin**	**cCD3** (cytoplasm CD)	**sCD3** (surface CD3)
		CD10* (if **+ve** called **common B-cell**)		**CD4&CD8*** (-ve or +ve for both)	**CD4&CD8*** (+ve for only one of them)
	Common	**CD19,CD20 &CD79a**		**CD2,CD5&CD7**	

*CD10 +ve is good prognostic sign but if it's –ve is bad sign

* You test for CD4 and CD8 if both –ve or both +ve this mean its precursor T-cell subtype (malignant), but if only one +ve either CD4 or CD8 it means its Mature T-cell subtype (Benign)



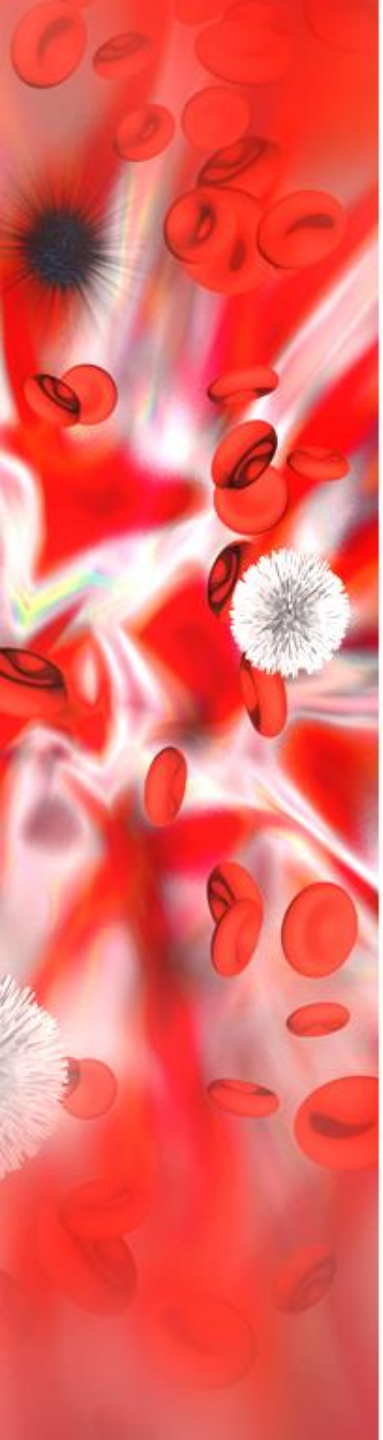
Prognosis

Better prognosis	Bad prognosis
- 2 - 10 yrs of age.	- < 2 or >10 yrs of age.
- Female.	- Male.
- Low WBC count.	- High WBC count.
- B-cell (common B-ALL)	- T-cell.
- Hyperdiploidy* t(12;21).	- Hypodiploidy* t(9;22).
- No CNS involvement	- CNS involvement.

Treatment

1) Chemotherapy: has high cure rate.
2) Stem cell transplantation.

*Hyperdiploidy → chromosomes are more than **50**
*Hypodiploidy → chromosomes are less than **44**



Summary from essential hematology for ALL

- Acute lymphoblastic leukaemia (ALL) is caused by an accumulation of lymphoblasts in the bone marrow. It is the most common malignant disease of childhood – 75% of cases occur before the age of 6 years. Eighty-five per cent of cases are of B-cell lineage with the rest being of T-cell lineage.
- The first genetic mutation occurs in many cases *in utero*, with a secondary genetic event occurring later in childhood, possibly as a reaction to an infection.
- The clinical presentation is with the features of bone marrow failure (anaemia, infection and bleeding) together with symptoms of tissue infiltration by tumour cells, leading to bone pain or swollen lymph nodes.
- Diagnosis is by examination of blood and bone marrow. Important tests include microscopic examination of the tumour cells, immunophenotyping and genetic analysis.
- ALL is subclassified according to the underlying genetic defect and a wide variety of genetic lesions are seen. The number of chromosomes in the tumour cell has prognostic importance: *Hyperdiploid* cells have >50 chromosomes and generally have a good prognosis whereas *hypodiploid* cases (<44 chromosomes) carry a poor prognosis.
- Treatment protocols for ALL are extremely complex and usually have four components – remission induction, intensification, CNS-directed therapy and maintenance.
- Treatment is *risk adjusted* to reduce the treatment given to patients with good prognosis. This is based on age, gender, white cell count and cytogenetics at presentation.
- Small numbers of tumour cells may sometimes be detected by FACS or molecular analysis even when the blood and bone marrow appear to be clear of leukaemia. This *minimal residual disease* has prognostic significance and is used in planning therapy.
- If relapse occurs during chemotherapy the outlook is poor but if it happens after years off all treatment the outlook is better. Further chemotherapy and allogeneic SCT should be considered.
- Overall, 85% of children can now expect to be cured. The cure rate in adults drops significantly to less than 5% over the age of 70 years.

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