

Acute Lymphoblastic Leukemia



Media output



Learning Objectives

- Etiology
- Classification
- Clinical Features
- Investigations
- Complications
- Treatment
- Follow up

- Greek origin;

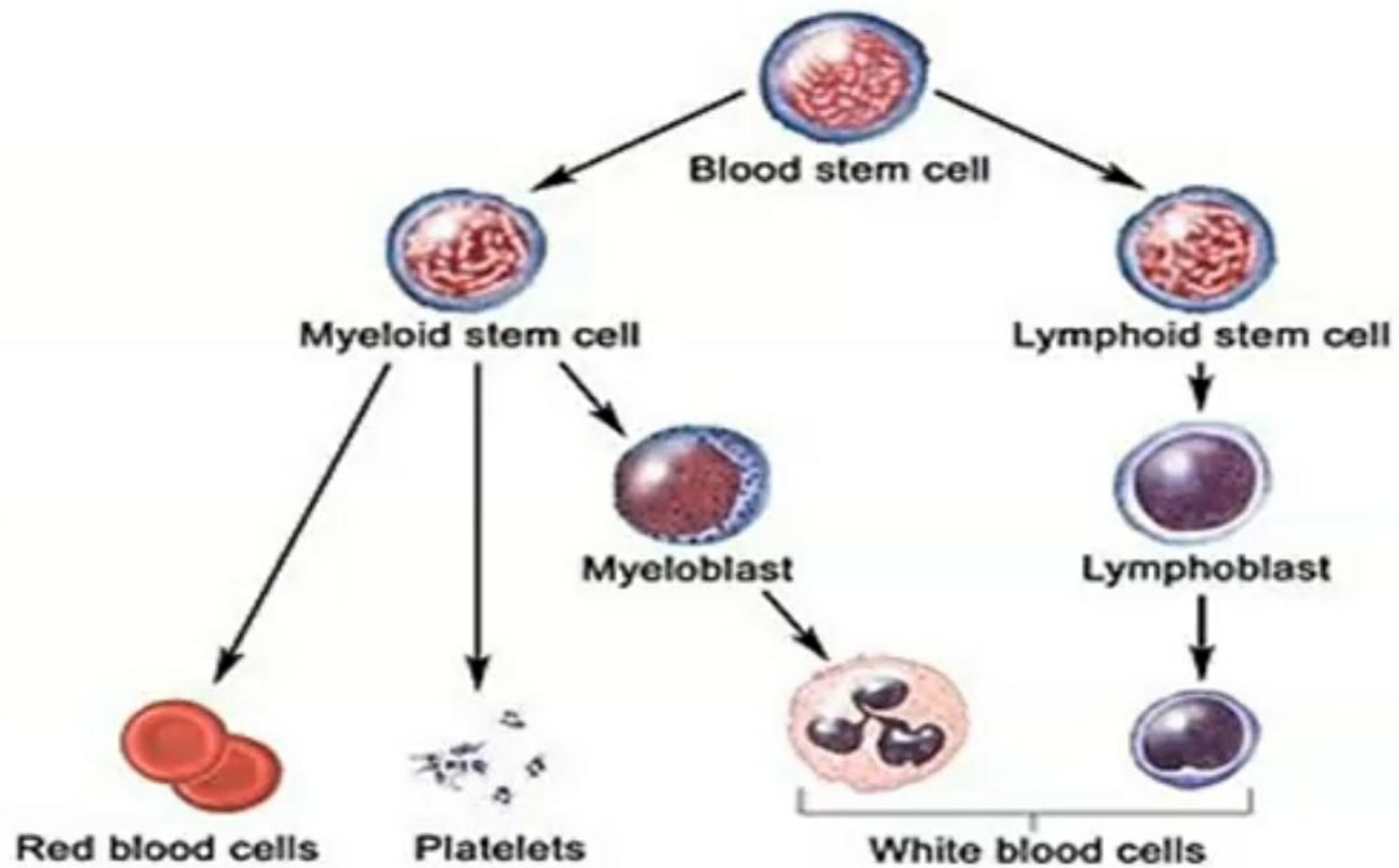
leukos which means "white"

aima which means "blood"

Monoclonal proliferation of immature "blast" cells that fail to participate in the normal maturation process

- as the cells accumulate, they spill over into the peripheral blood

PATHOPHYSIOLOGY



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Epidemiology

- Most common childhood malignancy;

31% of all in children <15 years

ALL.....77%

AML.....11%

CML.....2-3%

JMML.....1%

- white : non-white = 2 : 1
- male > female
- Peak incidence 2-6years

Etiology

GENETIC	ENVIRONMENTAL
<u>Downs, turner, klinefelter</u>	<u>Ionising radiation</u>
<u>Fanconi, diamond blackfan</u> →	Drugs
NF Type 1	<u>alkylating agents</u>
<u>Ataxia telangiectasia</u>	<u>nitrosourea</u>
SCID	<u>epipodophyllotoxin</u>
PNH	benzene exposure
<u>Li-fraumeni syndrome</u>	advanced maternal age
Blooms syndrome	paternal smoking

Classification

- *Done on basis of*
 - Morphology
 - Cell surface markers
 - Molecular genetics
- *Essential for*
 - Diagnosis
 - Prognosis
 - Choice of appropriate therapy

FAB Classification

- On the basis of Morphology
 - L1: small uniform blasts
 - L2: larger, more variable sized blasts
 - L3: uniform cells with basophilic and sometimes vacuolated cytoplasm (mature B cell ALL).

Classification of ALL(WHO)

Immunologic subtype	% of cases	FAB subtype	Cytogenetic abnormalities
B Cell ALL	85	L1,L2	t(9;22),t(4;11)t(1;19)
T cell ALL	15	L1,L2	14q11 or 7q34
Mature B cell ALL(Burkitt leukemia)	1	L3	t(8;14)

CLINICAL FEATURES

- SYMPTOMS {
 - Due to infiltration of marrow
 - Due to decreased production of normal marrow elements

CLINICAL FEATURES

- Pallor
- Fever
- Fatigue, weight loss
- Bleeding, Petechiae
- Bones Pains
- Stridor (Mediastinal mass)
- Headache, vomiting
- Testicular Mass

EXAMINATION

- Pallor
- Petechial Rash
- Mucosal Bleed
- Lymphadenopathy
- Hepatosplenomegaly
- Cranial Nerves involvement
- Papilledema, Retinal hemorrhage

INVESTIGATIONS

- Supportive
- Diagnostic
- Prognostic
- Staging
- Pre-chemotherapy

Investigations

Complete blood count-

Anemia, thrombocytopenia, leucopenia or leucocytosis.

Peripheral smear study-

circulating blast can be seen, Atypical Lymphocytes.

CHEST XRAY

CSF EXAMINATION

BONE MARROW ASP/TREPHINE

Immunohistochemistry

Flow cytometry & Immunophenotyping

Testicular Biopsy

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- NO NEED FOR BONE MARROW ASPIRATION IF
BLAST CELLS >70% ON SMEAR OR
TLC > 50,000
- SEND FLOW CYTOMETRY ON BLOOD SAMPLE

Investigations (cont)

CYTOGENETICS & MOLECULAR STUDIES

- Karyotyping
- FISH
- PCR

9;22	poor prognosis
10;14	poor prognosis
12;21	good prognosis
Trisomy 4, 10	good prognosis

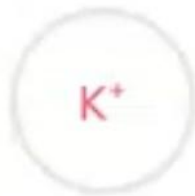
Prognostic factors in ALL

Determinants	<u>Favourable</u>	<u>Unfavourable</u>
WBC Counts	<10,000	>2,00,000
Age	2-10 years	<1yr,>10yr
Gender	female	male
Ethnicity	white	black
<u>Node.liver,splenomegaly</u>	absent	massive
Testicular enlargement	absent	present
CNS involvement	absent	<u>Csf blast and pleocytosis</u>
FAB Type	L1	L2
<u>Cytogenetics</u>	T(12;21)(TEL-AML1) <u>Trisomies 4,10,17</u>	t(9;22)(bcr-abl) t(4;11)(MLL-AF4)
<u>Ploidy</u>	<u>hyperdipoidy</u>	<u>hypodiploidy</u>
Time to remission	<14days	>28days

Risk stratification

- **High risk**
 - Age
 - Mediastinal mass
 - CNS disease
 - WBC>50,000
 - M3 at day 8
 - M2 at day 35
 - T Cell ALL
 - Philadelphia Chromosome

TUMOR LYSIS SYNDROME



Hyperkalaemia



Hyperuricaemia



Hyperphosphataemia



Hypocalcaemia



TUMOR LYSIS SYNDROME

- If TLC count is high
- Solid tumor
- Age >10
- Mediastinal mass
- LDH is high
- Uric acid >7.5
- Hyperphosphatemia

MANAGEMENT

Supportive Care

- Hydration
- Electrolytes
- Nutritional Support
- RCC ,Platelets Transfusion
- Antibiotics

Table 2

Prophylactic Management of TLS

- Central venous access and on an oncology or intensive care unit
- Baseline electrocardiogram
- Rigorous hydration – approximately 3 liters/m²/day to maintain urine output of at least 100 ml/m²/day. If necessary, diuretics such as furosemide and/or mannitol may be used to maintain urine output.
- Baseline lab values including: LDH, uric acid, sodium, potassium, creatinine, BUN, phosphorus and calcium. These labs should be checked every 6 to 8 hours for the first 48 to 72 hours after therapy, and then tapered according to risk.
- Administer allopurinol 200-300 mg/m²/day or rasburicase 0.20mg/kg/day, intravenously over 30 minutes for 3 to 7 days.
- (Optional) Alkalinization of urine with sodium bicarbonate in IV fluids.

Treatment

- Remission Induction
- Consolidation Therapy
- Intensification
- Maintenance Therapy
- CNS Prophylaxis
- Allogeneic Stem Cell Transplant

Remission Induction

- Eradicate leukemic cells from bone marrow, given for 4 weeks.
- Vincristine--- weekly
- Dexamethasone or Prednisolone daily
- L Asparaginase-- biweekly
- Intrathecal Methotrexate--twice

Remission< 5% Blasts

- For re-induction and resistant cases either Daunorubicin or cytosine given.

Consolidation

- Therapy given for 4 weeks
- Cyclophosphamide-- 2 weekly
- Cytarabine-- 4 consecutive days every week
- 6-Mercaptopurine daily

Intensification

- Therapy of 14-28 weeks
- Delayed Intensification
- Interim Maintenance
- Cyclophosphamide, L asparaginase, vincristine, 6 mercaptopurine.

Maintenance Phase

- Therapy given for 2-3 years

Mercaptopurine --daily

Methotrexate --weekly

Vincristine and corticosteroids
intermittently.

Relapse

- Bone Marrow--intensive chemo and BMT
- CNS—intrathecal medication and cranial irradiation
- Testicular—chemotherapy plus local irradiation

Click to add title

Stem Cell Transplant

–Indications:

- Usually done in second remission.
- Can be done in first remission in high risk patients
 - WBC>25,000
 - Philadelphia chromosome positive
 - poor initial response to remission induction

FOLLOW UP

- Monitor Blood counts
- Any new symptoms
- Antibiotic prophylaxis against PCP
- Fluconazole for candidiasis
- If the patient completes chemotherapy for 2 years without relapse-stop chemo and follow up
- No relapse within 5 years-can be declared as cured