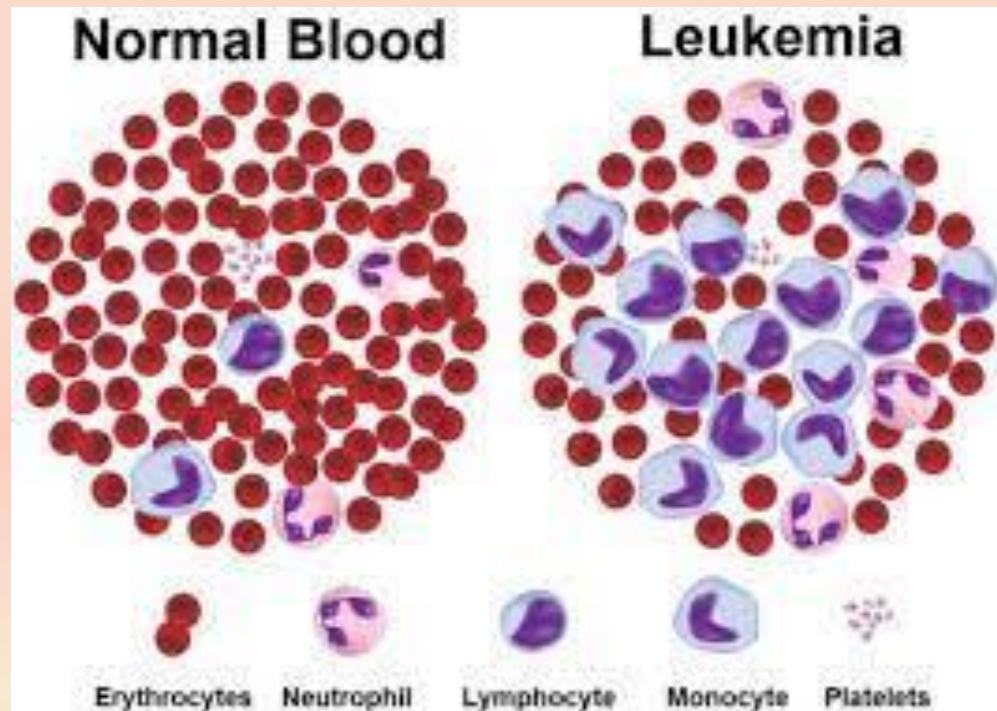


LEUKEMIA

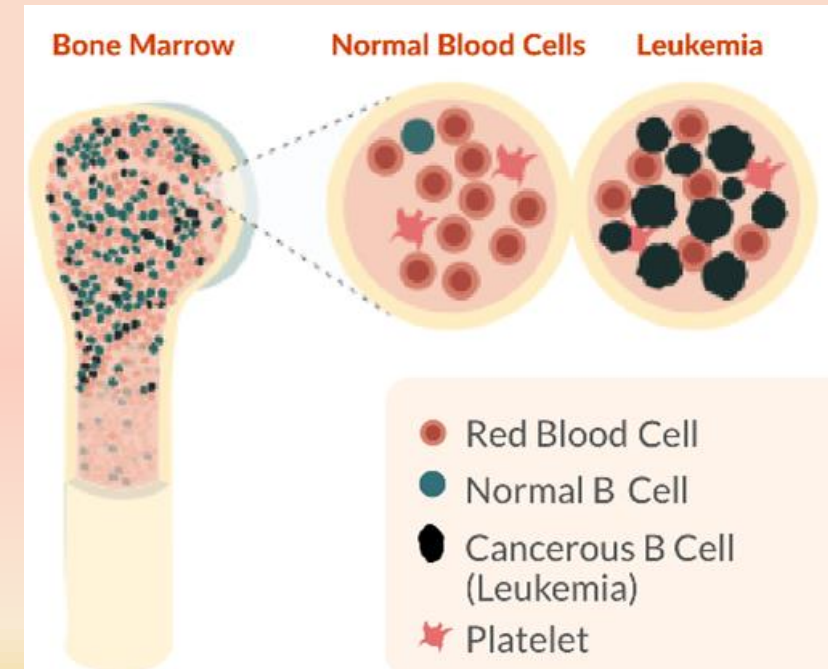
ACUTE LEUKEMIA



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Leukemia is a heterogeneous group of hematologic malignancies characterized by the uncontrolled proliferation of abnormal blood-forming cells (blasts) in the bone marrow. These immature cells:

- Accumulate in the bone marrow
 - Inhibit normal blood cell production
- } □ leading to **anemia, neutropenia, and thrombocytopenia.**
- Leukemic blasts may also infiltrate extramedullary tissues such as:
 1. Lymph nodes
 2. Liver and spleen
 3. Skin
 4. Kidneys
 5. Central nervous system (CNS)
 6. Testes



Leukemia is classified by two main criteria:

1. By Cell Lineage (Origin):

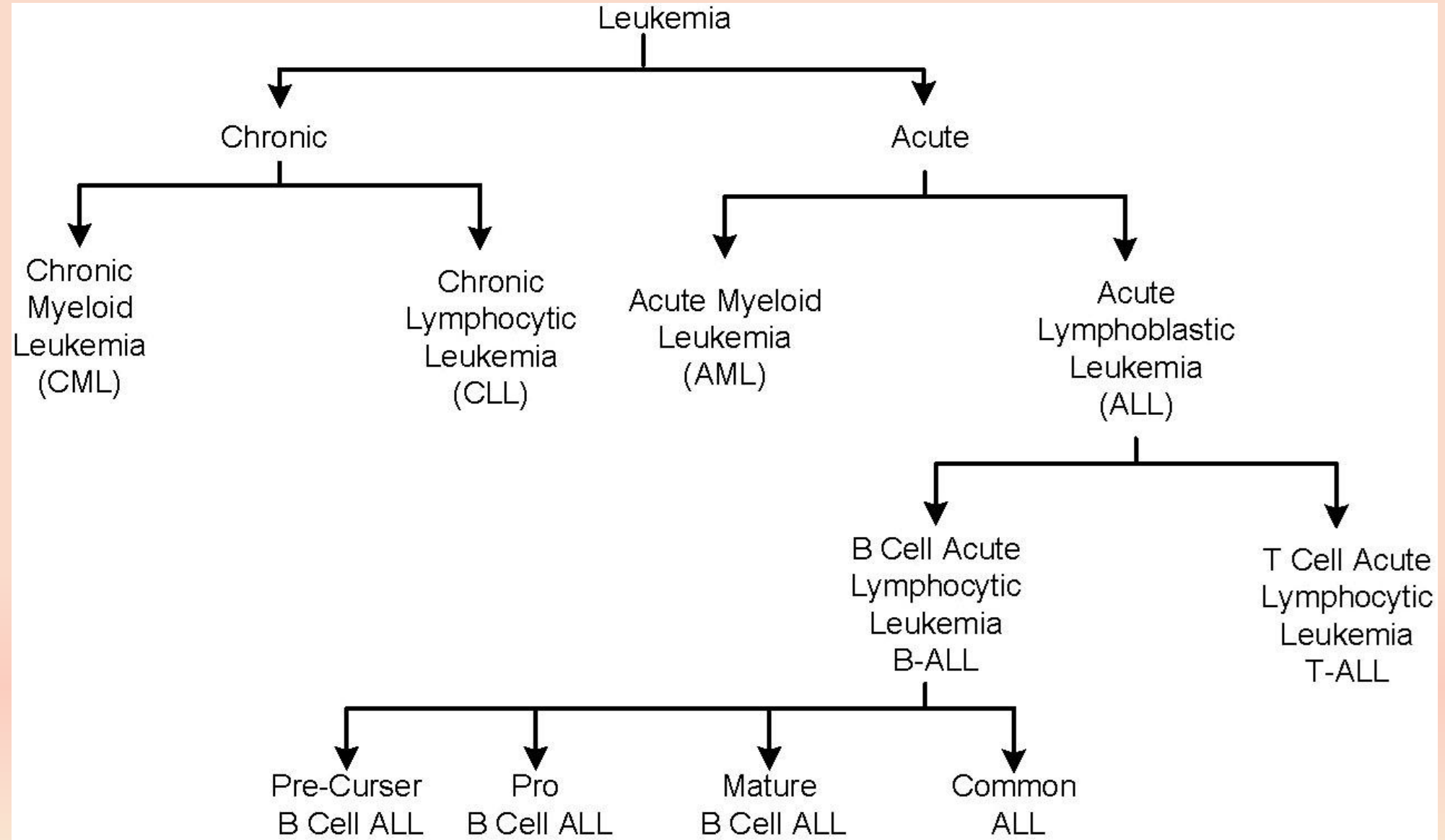
- Lymphoid (Lymphocytic) → derived from lymphoid progenitors
- Myeloid (Myelogenous) → derived from myeloid progenitors

2. By Clinical Course:

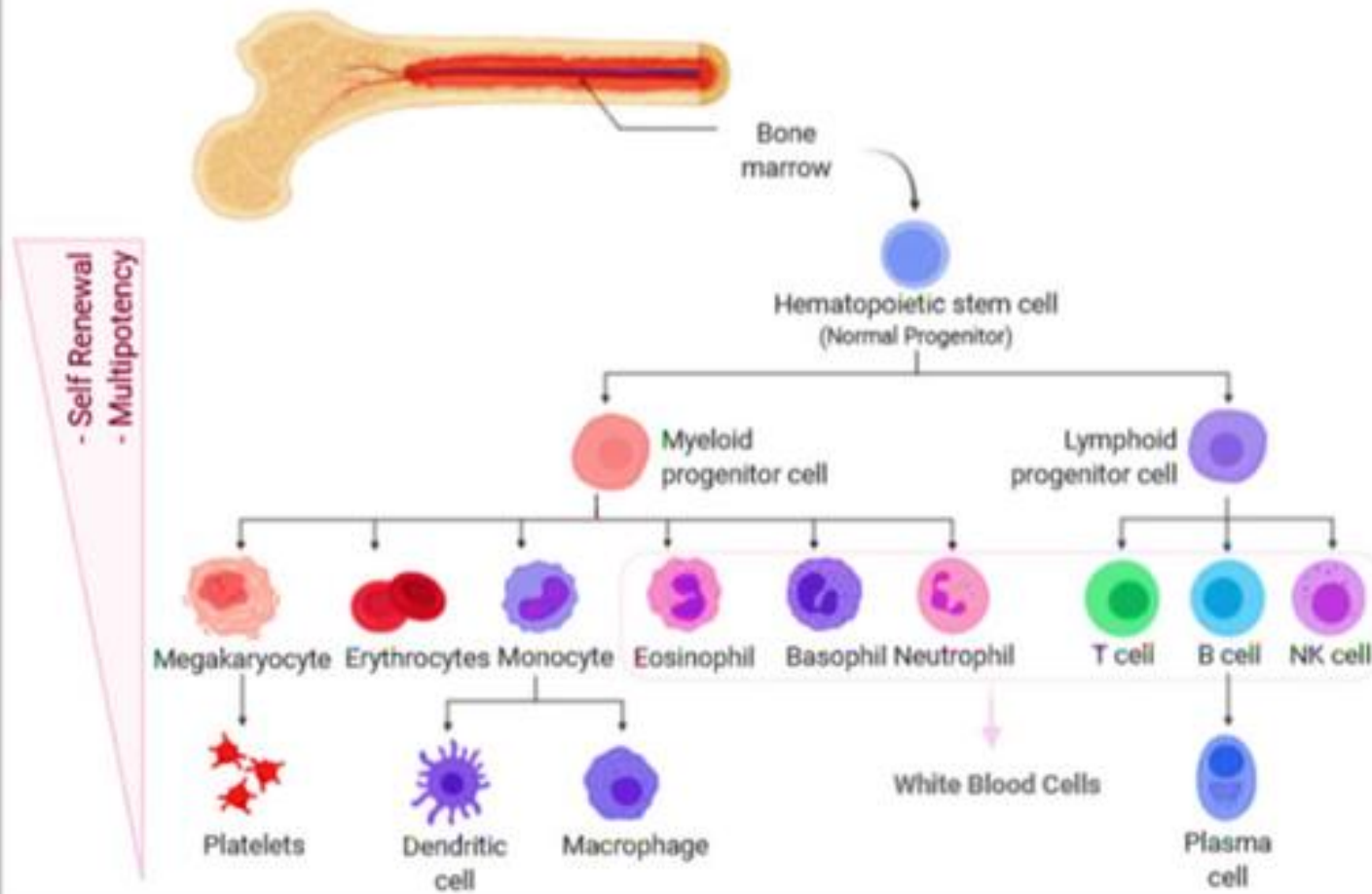
- Acute: Rapid onset and aggressive course, immature blasts dominate
- Chronic: Slow progression, cells are more mature and differentiated

The Four Major Types of Leukemia:

Type	Cell Line	Clinical Course	Predominant Age Group
Acute Lymphoblastic Leukemia (ALL)	Lymphoid	Acute	Children
Acute Myeloid Leukemia (AML)	Myeloid	Acute	Adults
Chronic Lymphocytic Leukemia (CLL)	Lymphoid	Chronic	Older Adults
Chronic Myeloid Leukemia (CML)	Myeloid	Chronic	Adults

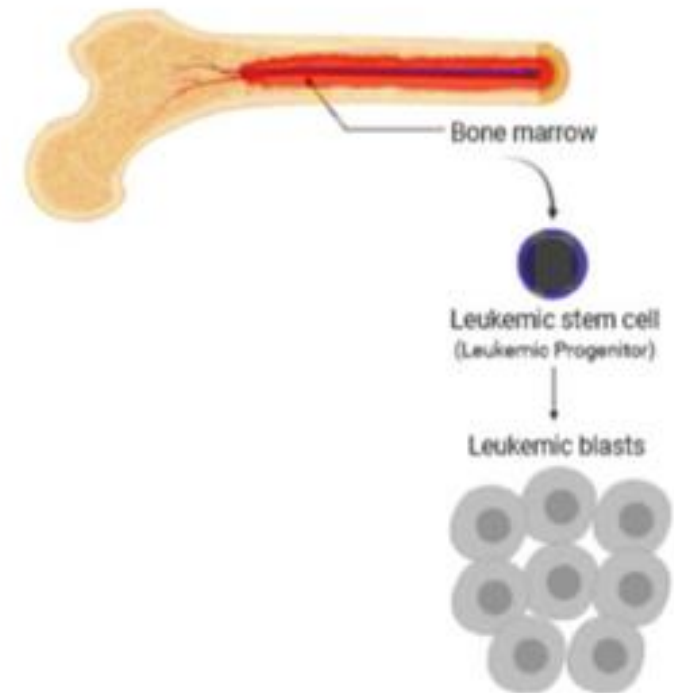


Normal Stem Cells

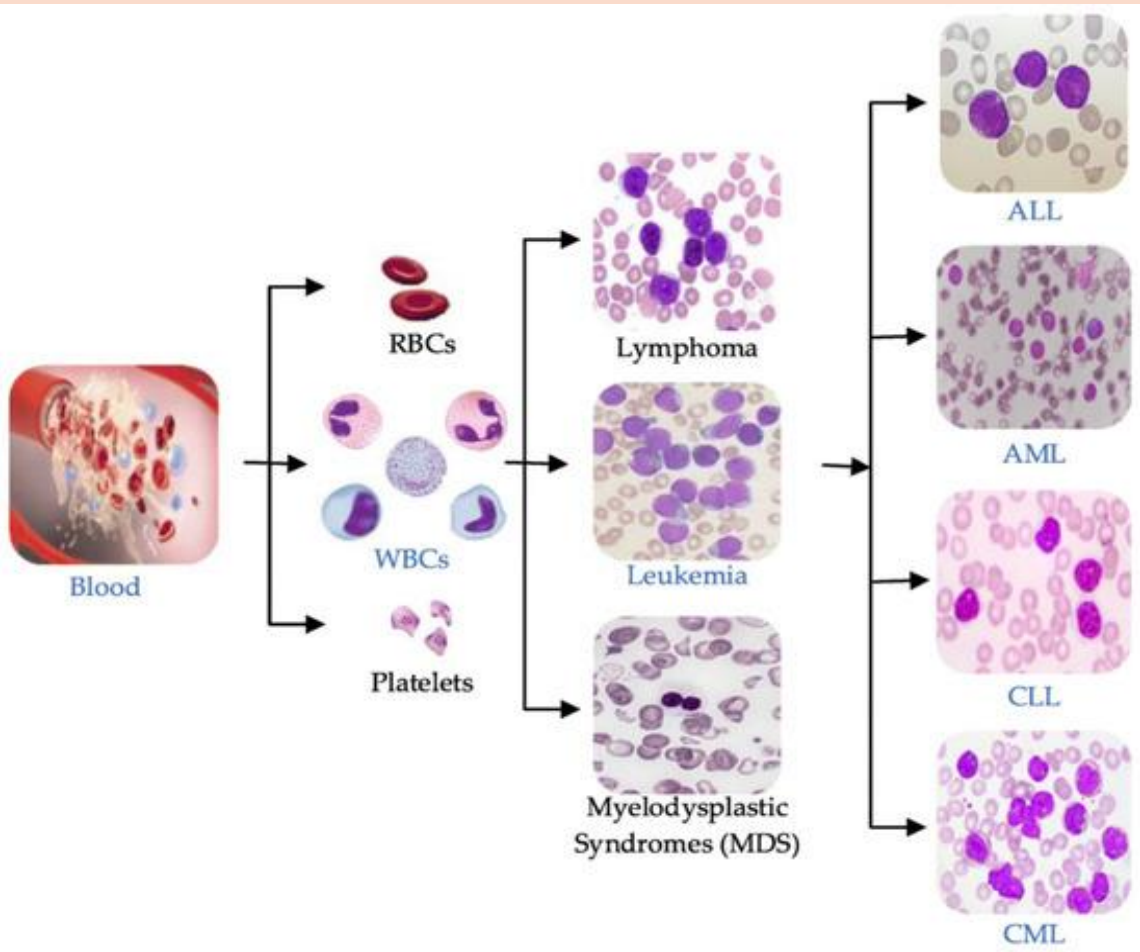
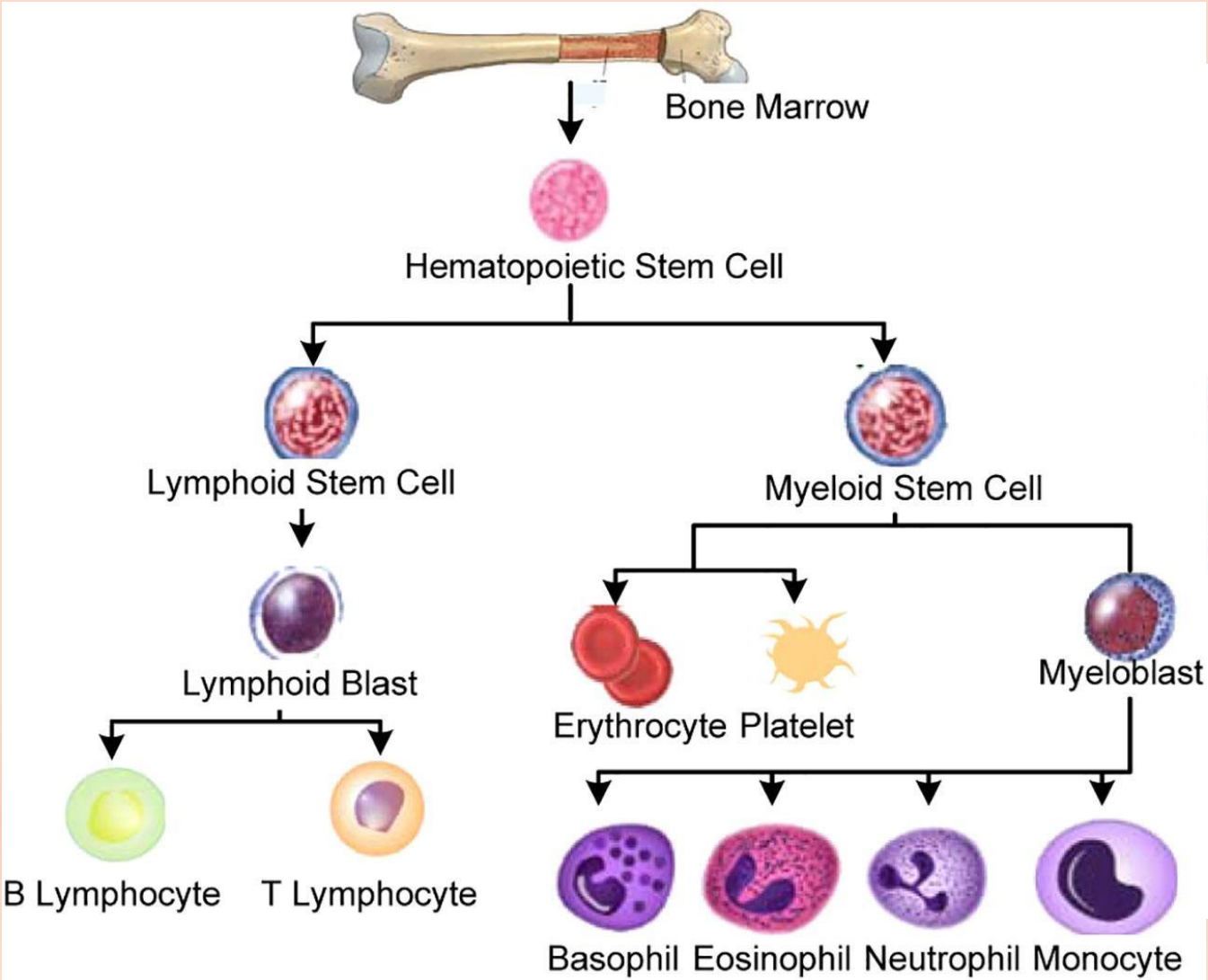


(A)

Leukemic Stem Cells



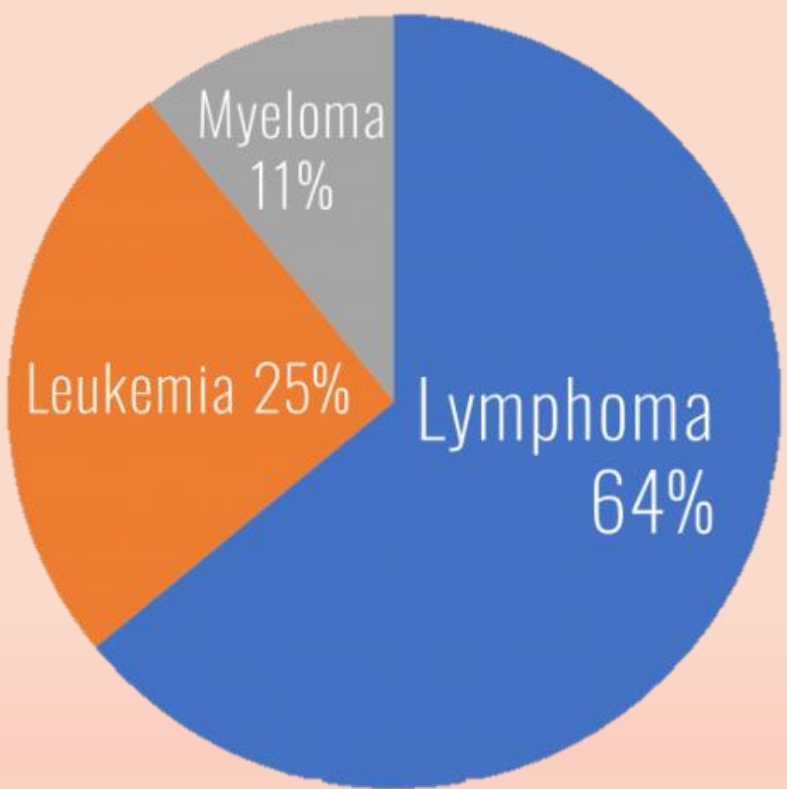
(B)



EPIDEMIOLOGY

- Acute leukemia is fatal within weeks to months if untreated
- Leukemia accounts for ~1.5% of all cancers diagnosed annually
- Causes about 2% of all cancer-related deaths
- >90% of leukemia cases occur in adults
- In adults with acute leukemia: 80% AML, 20% ALL
- In children: 75% ALL, 25% AML

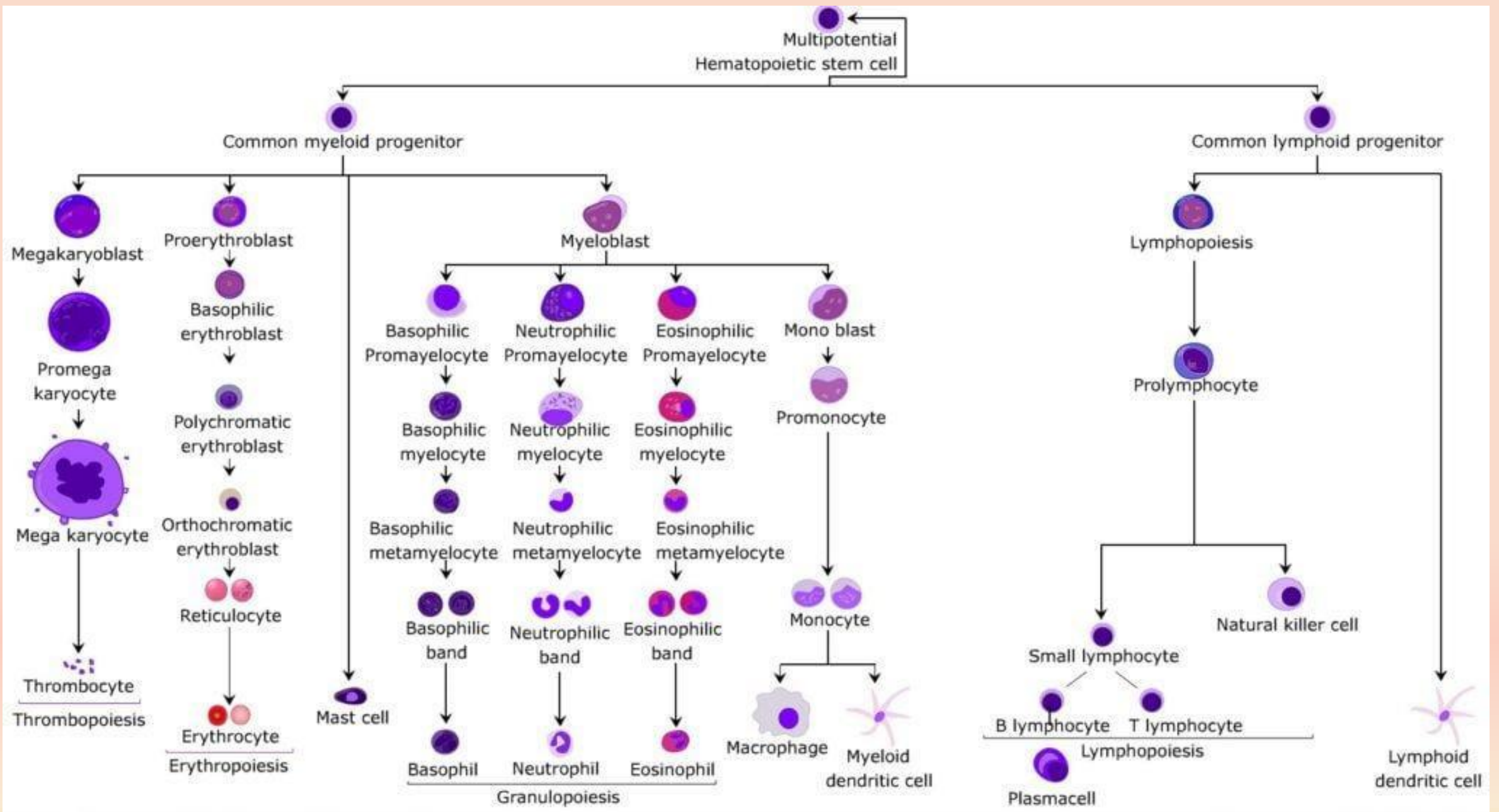
India Ranks 3rd in Blood Cancer



Age Group	Leukemia Type	Notes
< 20 years	ALL (High), AML (less)	Leukemia is the most common cancer in this age group (27% of all childhood cancers)
20–39 years	Leukemia	Leading cause of cancer-related death
> 40 years	AML, CLL, CML	Less common but more likely to occur in adults and elderly

Normal Hematopoiesis

1. **Origin:** All blood cells arise from pluripotent hematopoietic stem cells (HSCs) in the bone marrow.
2. **Differentiation Pathways:**
 - a. Myeloid stem cells → Erythrocytes, platelets, neutrophils, eosinophils, basophils, monocytes.
 - b. Lymphoid stem cells → T lymphocytes, B lymphocytes, natural killer (NK) cells.
3. **Processes Involved:** Hematopoiesis involves proliferation, differentiation, and maturation of cells under tight genetic control.



PATHOPHYSIOLOGY OF LEUKEMIA

1. Clonal Origin of Leukemia

- Leukemia begins with a single abnormal (leukemic) cell.
- This cell undergoes genetic mutations → gains the ability to proliferate uncontrollably.
- Results in a monoclonal population of abnormal blasts (myeloblasts or lymphoblasts).

2. Imbalance in Cell Development

- a. There is a failure to maintain balance between:
 - a) Proliferation (cell multiplication)
 - b) Differentiation (maturation into functional blood cells)
- b. Cells are arrested at an immature stage → accumulate as blasts.
- c. Normal hematopoiesis is suppressed, leading to:
 - i. Anemia (↓ RBCs)
 - ii. Thrombocytopenia (↓ platelets)
 - iii. Neutropenia (↓ mature WBCs)

3. Site and Stage of Origin Varies by Type

a. Acute Myeloid Leukemia (AML):

- Usually originates from pluripotent stem cell or early myeloid precursor.

b. Acute Lymphoblastic Leukemia (ALL):

- Arises from lymphopoietic stem cell or early lymphoid precursor.
- Leads to accumulation of lymphoblasts.

4. Crowding Out Effect

- Proliferating blasts overcrowd bone marrow, reducing space for normal cells.
- Leads to:
 - Decreased production of functional RBCs, WBCs, and platelets.
 - Clinical signs: fatigue, infections, bleeding tendencies.

5. Not Due to Rapid Proliferation Alone

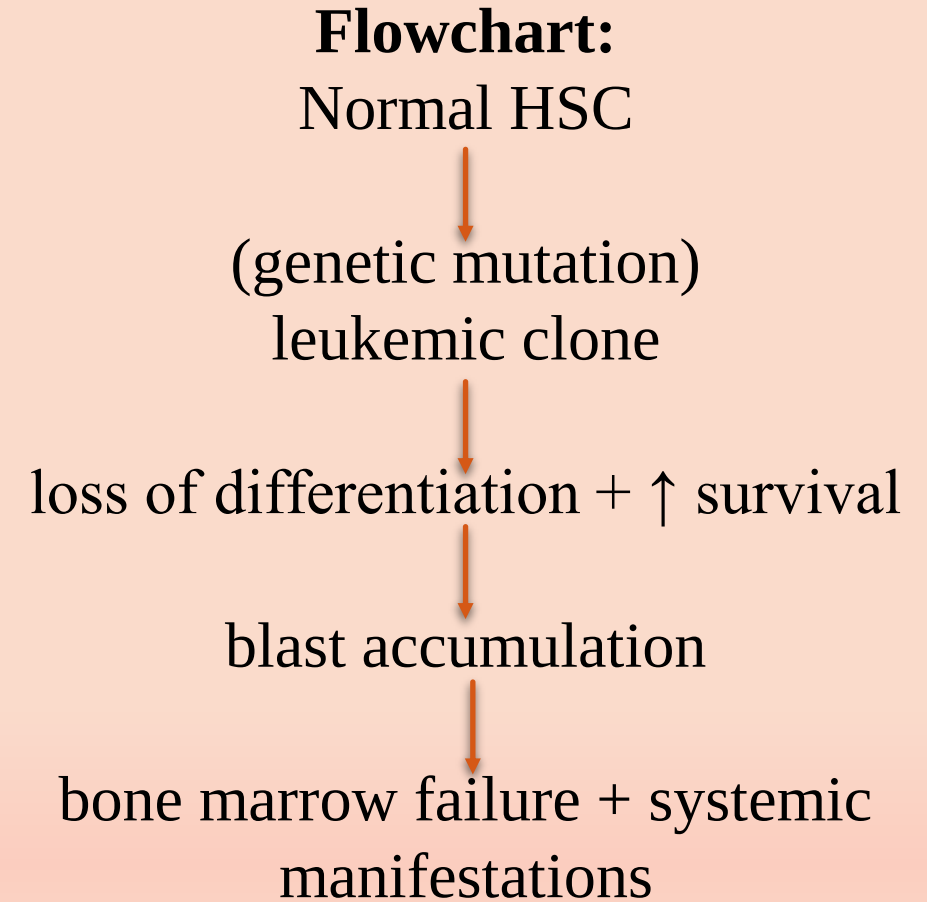
- Leukemic cells may not proliferate faster, but:
 - They survive longer (↓ apoptosis).
 - They may secrete factors that:
 - Inhibit normal cell proliferation/differentiation.
 - Protect themselves from apoptosis.

6. Genetic and Molecular Abnormalities

- Leukemogenesis involves multiple genetic alterations, including:
 - a. Proto-oncogene activation → forms oncogenes that drive proliferation.
 - b. Differentiation arrest → loss of signals needed for proper maturation.
 - c. Loss of tumor suppressor genes → unchecked cell division.
 - d. Impaired apoptosis → cells avoid programmed cell death, resist therapy.

7. Affected Cellular Processes

- Signal transduction
- RNA transcription
- Cell cycle regulation
- Differentiation and maturation
- Apoptosis (programmed cell death)



ACUTE LEUKEMIA

Etiology and Risk Factors of Acute Leukemia

Acute leukemia results from genetic mutations in hematopoietic stem cells, leading to:

1. Unregulated proliferation of immature white blood cells (blasts)
2. Blocked differentiation into mature blood cells
3. These mutations may be:
 - a. Acquired (somatic) → due to environmental exposures, drugs, infections, etc.
 - b. Inherited (germline) → due to genetic syndromes

Etiology and Risk Factors of Acute Leukemia

Genetic Conditions

Down syndrome	Fanconi anemia
Fanconi anemia	Ataxia telangiectasia
Bloom syndrome	Kostmann syndrome
Ataxia telangiectasia	Dyskeratosis congenita
Kostmann syndrome	Li-Fraumeni syndrome
Diamond-Blackfan anemia	Neurofibromatosis synoome
Dyskeratosis congenita	Wiskott-Aldrich syndrome
Li-Fraumeni syndrome	Noonan syndrome

Drugs

Therapy-related leukemia particularly afterchemothera-
Alkylating agents
Anthracyclines
Epipodophyllotoxins

Radiation

Ionizing radiation
(atomic bomb, raditherapy)

Chemical Exposures

Benzene
Pesticides
Pyrethroid-based shampoos

Radiation

Ionizing radiation
(atomic bombs, radiotherapy)

Social and Maternal Habits

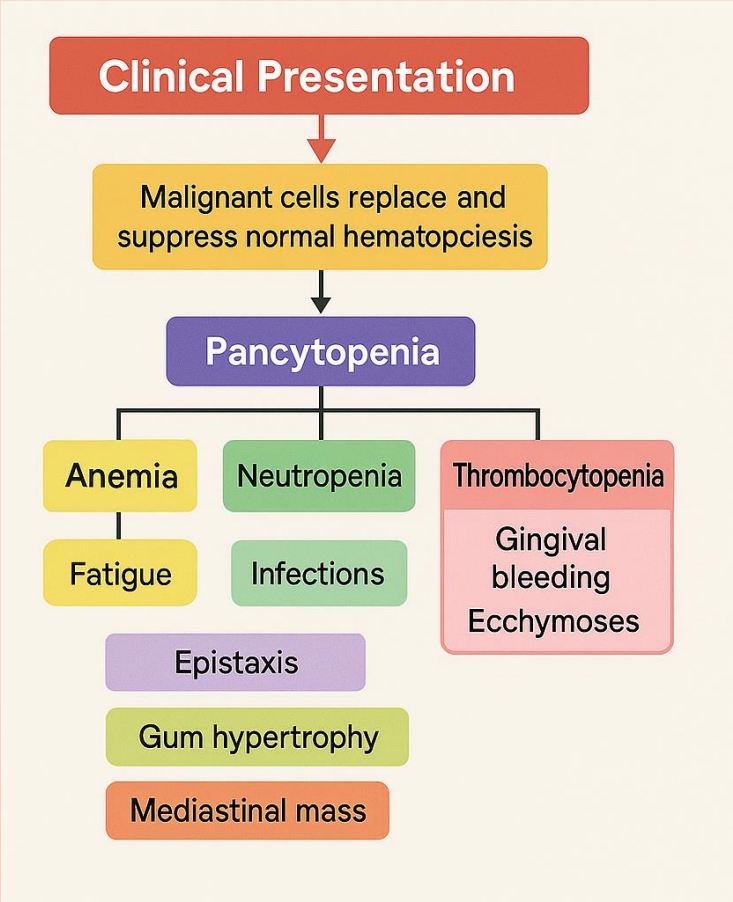
Certain perinatal exposures may increase leukemia risk

Viral Infections

Epstein-Barr virus
Human T-lymphocyte virus (HTLV-1 and HTLV-2)

Clinical Presentation

Manifestation	Cause	Clinical Features
Anemia	↓ RBCs	Fatigue, weakness, pallor, dizziness
Neutropenia	↓ Neutrophils	Frequent infections, fever, oral ulcers
Thrombocytopenia	↓ Platelets	Easy bruising, petechiae, bleeding gums, epistaxis, menorrhagia
Leukemic infiltration	Accumulation of blasts in tissues	Gum hypertrophy (especially in monocytic AML), bone pain, lymphadenopathy, hepatosplenomegaly
CNS involvement	Leukemic cells in cerebrospinal fluid	Headache, vomiting, cranial nerve palsies, visual changes
Mediastinal mass	Thymic infiltration (esp. in T-cell ALL)	Cough, dyspnea, chest pain, SVC syndrome



Diagnosis

1. Complete Blood Count (CBC) and Peripheral Blood Smear:

Anemia / Neutropenia / Thrombocytopenia / Circulating blasts

2. Bone Marrow Aspiration and Biopsy: Gold Standard for Diagnosis

- Evaluates cellular morphology and blast percentage.
- >20% blasts in marrow is diagnostic for acute leukemia (as per WHO criteria).
- Samples undergo:
 - Flow cytometry: Identifies immunophenotype of blasts (e.g., CD markers to differentiate ALL vs AML).
 - Cytogenetics (karyotyping): Detects chromosomal abnormalities (e.g., t(8;21), inv(16), t(15;17) in AML).
 - Molecular studies: Detect gene mutations (e.g., FLT3, NPM1 in AML; BCR-ABL1 in ALL).

3. Lumbar Puncture (LP)

- Done to check for CNS involvement.
- Especially important in ALL (common CNS spread), not routine in AML unless CNS symptoms are present.

4. Imaging Studies

- Chest X-ray or CT scan to detect mediastinal mass, commonly seen in T-cell ALL.
- CT/MRI may be used for evaluating extramedullary disease or CNS infiltration.

[Patient presents with fatigue, infections, bleeding]



CBC shows cytopenia or abnormal WBC



Peripheral smear shows possible blasts



Bone Marrow Biopsy + Aspirate (Confirmatory)

↳ Morphology, Flow Cytometry,
Cytogenetics



Lumbar Puncture (if CNS symptoms or ALL)

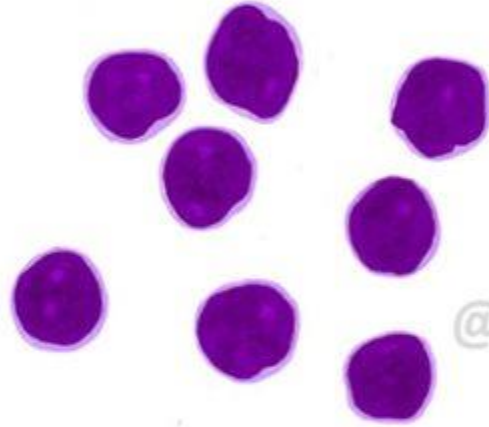


Imaging (mediastinal mass, etc.)



Diagnosis + Risk Stratification + Treatment Plan

ALL-L1



Small uniform cells. Nuclei regular with condensed chromatin, inconspicuous nucleoli. Scant cytoplasm

ALL-L2



Large, heterogenous cell population. Nuclei irregular/clefting with occasional nucleoli. Mild to moderate cytoplasm

ALL-L3



Large, homogeneous cell population. Nuclei regular with fine chromatin and 1-2 nucleoli. Moderate to abundant vacuolated cytoplasm

Risk and Risk Classification of Acute Leukemia (with Emphasis on Acute Lymphoblastic Leukemia - ALL)

- Acute leukemia, especially Acute Lymphoblastic Leukemia (ALL), is a clinically and biologically heterogeneous disease.
- The response to treatment and long-term survival varies depending on several prognostic factors.
- These are used to stratify patients into risk categories, guiding therapy intensity through risk-adapted treatment strategies.

Purpose of Risk Classification

- Predict response to therapy (complete remission, duration of remission)
- Estimate risk of relapse and long-term survival
- Customize intensity of therapy:
 - Lower intensity in standard risk to avoid long-term toxicities
 - Higher intensity in high or very-high risk to improve cure rates

Major Risk Factor Categories

Category	Examples
1. Patient Characteristics	Age, sex, race/ethnicity, initial WBC count
2. Leukemic Cell Features	Immunophenotype, cytogenetics, molecular abnormalities
3. Early Response to Therapy	Marrow response, Minimal Residual Disease (MRD), response to steroids

NCI Risk Stratification (Pediatric ALL)

Developed by the National Cancer Institute (NCI) to standardize initial therapy stratification in children:

Category	Criteria
Standard Risk	Age 1–9 years and WBC < 50,000/ μ L
High Risk	Age <1 or $\geq$ 10 years or WBC $\geq$ 50,000/ μ L

Prognostic Genetic and Cytogenetic Abnormalities

Favorable	Unfavorable / High Risk
- Trisomy 4 & 10	- Hypodiploidy (<44 chromosomes)
- High hyperdiploidy (>50 chromosomes, DNA index >1.16)	- MLL rearrangements
- ETV6-RUNX1 (t(12;21))	- Philadelphia chromosome (BCR-ABL1)
	- Ph-like ALL (JAK pathway mutations, ABL-class fusions)
	- Intrachromosomal amplification of chromosome 21 (iAMP21)
	- IKZF1 deletions (common in Ph+ and Ph-like ALL)

Response to Therapy:

1. Minimal Residual Disease (MRD)

1. Best predictor of long-term outcome
2. Measured by flow cytometry or PCR
3. Goal: MRD $<0.01\%$ at end of induction
4. MRD $\geq 0.01\%$: 3–5 $\times$ higher risk of relapse and death

2. Other Early Responses

1. Response to steroids in first 7 days
2. Marrow blast clearance after 1–2 weeks of induction

Immunophenotype and Cell Lineage

Subtype	Characteristics
B-cell ALL (~85%)	More common, better prognosis overall
T-cell ALL (~15%)	More often in older males, African Americans, higher WBC, mediastinal mass, CNS involvement; historically worse prognosis but improved with intensive therapy

Demographics and Prognosis

Demographic Factor	Impact
Sex	Males have slightly worse outcomes
Race/Ethnicity	Hispanics have highest incidence; African Americans lowest
Age	Ages 1–9 have best outcomes due to more favorable genetics

CNS and Testicular Involvement

Feature	Prognostic Implication
CNS disease at diagnosis	Higher relapse rate
Testicular disease (2% of males)	Mixed evidence; may warrant therapy intensification

RISK AND RISK CLASSIFICATION OF ACUTE LEUKEMIA

(a Acute Lymphoblastic Leukemia (ALL))

PURPOSE

- ✓ Predist response to therapy (complete remission, duration of remission)
- ✓ Estimate risk of relapse and long-term survival
- ✓ Customize intensity of therapy (risk-adapted (reatment))

MAJOR RISK FACTOR CATEGORIES

- 1 Patient Characteristics

Age, sex, race/ethnicity;
initial WBC count
- 2 Leukemic Cell Features

Immunophenotype, MRD
response to steroids
- 3 Early Response to Therapy

PROGNOSTIC FACTORS

NCI Risk Stratification
(Pediatric ALL)

Standard Risk

- Age 1-0 years
- WBC $\leq 50,000$ //pL

High Risk

- Age < 1 of ≥ 10 years
- WBC $\geq 50,000$ m/L

Response to Therapy

Minimal Residual Disease
(MRD), goal, MRD $\leq 0.01\%$
at end of induction



Genetic Abnormalities

Favorable

- Hypodiploidy
(>44
chi-omosomes)
- MLL
rearrangments
- Ph-like ALL

Untavorable /
High Risk

- MLL rearrengements
- Phlisdeiphie
chromosome
(PCR-ABL1)
- Ph-like ALL
- intrachromosomal
amplification of
chromosome 21



CNS and Testicular Involvement
Potential warrant intesification

POST-INDUCTION RISK RECLASSIFICATION

Risk Group	Criteria
Low Risk	Trisomy 4 &10 or ETV6=RUNX1, MRD $< 0,01\%$ no CNS/testicular involvement
Standard Risk	MRD $< 0.01\%$, but without favorable genetics
High Risk	MRD $\geq 0,01\%$, CNS/testicular disease, steroids prior to diagnosis

TREATMENT AND MANAGEMENT OF ALL

GOALS OF TREATMENT

1. **Short-term goal:** Achieve *complete remission (CR)*—disappearance of physical and bone marrow evidence of leukemia (normal marrow cellularity with <5% blasts) and restoration of normal hematopoiesis.
2. **Long-term goal:** Maintain continuous CR to achieve cure.
 - Children in CR for **5 years** are generally considered cured.
 - MRD (Minimal Residual Disease) is a crucial predictor of relapse.
 - **CR (Complete Remission):** No evidence of disease; normal blood counts; <5% blasts in marrow.
 - **MRD (Minimal Residual Disease):** Presence of residual leukemic cells detected by sensitive assays even after CR.

Phases of ALL Treatment

Treatment spans **2–3 years**, and ALL therapy has 5–6 major phases, with CNS prophylaxis administered throughout.

1. Induction
2. CNS Prophylaxis (throughout)
3. Consolidation
4. Interim Maintenance
5. Delayed Intensification
6. Maintenance Therapy

1. Induction Therapy

- **Goal:** Rapidly induce complete remission.
- **CR rates:**
 - ~98% in standard-risk children
 - 60–85% in adults (lower due to more poor-risk features)
- **Common Drug Regimens:**
 1. **Standard-risk:**
 1. Vincristine
 2. Dexamethasone or Prednisone
 3. Asparaginase: Pegaspargase
 2. **High-risk:**
 1. Add **Daunorubicin** (4-drug regimen)

Vincristine

- Inhibits mitosis by binding to tubulin → arrests leukemic lymphoblasts in metaphase → apoptosis.
- Primarily cytotoxic to actively dividing cells, particularly effective against lymphoid blasts.
- Backbone agent in ALL induction for both standard- and high-risk patients.
- Active against B- and T-cell precursors.
- No significant myelosuppression, so it pairs well with myelosuppressive drugs.
- Toxicities: Neurotoxicity, SIADH, alopecia
- **Glucocorticoids:**
 1. **Dexamethasone:** Better CNS penetration, ↓ CNS relapse, but ↑ risk of: Osteonecrosis , Infections, Hyperglycemia, myopathy
 2. **Prednisone:** Preferred in adolescents or patients with Down syndrome to ↓ toxicities

- **Asparaginase :**

- Enzyme that depletes asparagine → leukemic cells die due to dependence

1. Pegaspargase (pegylated E. coli form): Long half-life, less immunogenic, IV/IM

2. Erwinia asparaginase: Used if allergic to pegaspargase (requires 3x/week dosing)

Key Toxicity:

- Hypersensitivity (8–42%): Can be clinical or “silent inactivation”
- Use therapeutic drug monitoring to detect inadequate enzyme activity
- Switch to Erwinia product if inactivation is detected

- **Daunorubicin**

- Used primarily in high-risk or very-high-risk patients as part of a 4-drug induction regimen.
- Enhances depth of remission by inducing DNA damage, apoptosis in leukemic cells.
- Broad cytotoxic activity
- Potentiates efficacy of vincristine and steroids
- Frequently used with pegaspargase and corticosteroids
- Toxicities: Myelosuppression, Cardiotoxicity, Mucositis, alopecia

2. CNS Prophylaxis

Goal:

1. The CNS is a sanctuary site; most systemic chemo doesn't cross the BBB.
2. Prevent leukemic relapse in the CNS ("sanctuary site").
 - CNS involvement at diagnosis: ~3%
 - CNS relapse without prophylaxis: >50%

Agents with CNS penetration:

- High-dose methotrexate, Cytarabine, Dexamethasone (preferred over prednisone)

Modalities:

1. Intrathecal Chemotherapy:

1. Methotrexate $\pm$ Cytarabine $\pm$ Hydrocortisone (triple therapy)

2. Systemic High-Dose Therapy:

High-dose methotrexate or cytarabine

3. Cranial Irradiation:

1. Limited due to long-term neurotoxicity
2. Used only for CNS+ or very-high-risk cases

CNS relapse risk factors: Male sex, T-cell phenotype, CNS2 status, bloody lumbar puncture, hepatomegaly, age extremes

3. Consolidation Therapy

- **Goal:** Eliminate MRD and "consolidate" remission.
- Duration: ~4 weeks
- Standard regimen:
 - Vincristine + mercaptopurine + intrathecal methotrexate
- Intensified for high-risk patients: Add pegaspargase, cyclophosphamide, cytarabine
- T-cell ALL: Add nelarabine—targets T-lymphoblasts via conversion to ara-GTP

4 & 5. Interim Maintenance and Delayed Intensification

These reinduction phases extend remission, prevent drug resistance, and reduce late relapse.

Interim Maintenance:

- **Standard-risk:**
 - Escalating low-dose methotrexate + vincristine
- **High-risk:**
 - High-dose methotrexate + mercaptopurine
 - Later cycles may include asparaginase

Delayed Intensification: Reduce tumor burden, prevent resistant clones

- Combines drugs from induction + consolidation:
 - Vincristine, steroid, doxorubicin, asparaginase
 - Cyclophosphamide, cytarabine, thioguanine

Toxicity Consideration:

- ↑ antimicrobial use, transfusions, but no ↑ in mortality

6. Maintenance Therapy

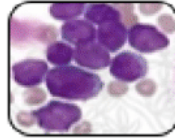
- **Goal:** Suppress residual leukemic clones and prolong remission.
- Duration: Female: 2 years Male: 3 years (↓ late relapse in trials)
- Regimen:
 1. Daily oral mercaptopurine
 2. Weekly oral methotrexate
 3. Monthly vincristine + steroid pulse
- Pharmacologic Considerations:
 1. **Adherence:**
 - <95% adherence to mercaptopurine → 2.7× risk of relapse
 - Adolescents, single-parent homes, lower SES = higher risk of non-adherence
 2. **Administration:**
 - Timing with food/milk used to matter (xanthine oxidase in milk), but newer data → no significant effect on thioguanine levels

Acute Myeloid Leukemia (AML)

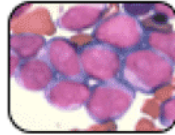
Acute Myeloid Leukemia (AML) is a clonal malignancy of the myeloid line of blood cells characterized by:

- Rapid proliferation of immature myeloid blasts.
- Disruption of normal hematopoiesis, leading to anemia, thrombocytopenia, and neutropenia.
- Without treatment, AML progresses rapidly and is fatal within weeks to months.

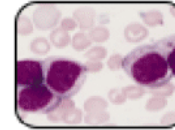
FAB CLASSIFICATION



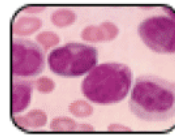
M0: Undifferentiated acute myeloblastic leukemia (5%)



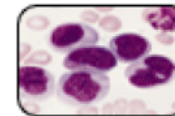
M1: Greater number of myeloblasts with <10% granulocytic differentiation.



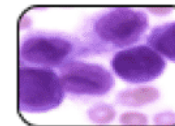
M2: Myeloblasts in great number with granulocytic differentiation >10% , NSE <20%.



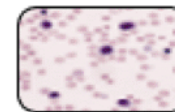
M3: Promyelocytes that are hyper granular with many Auer rods on CAE or Wright-stain and variant form cells with reniform nuclei, multilobed or bibbed, primeval cells with multiple Auer rods or relative scarcity of Hypergranular promyelocytes.



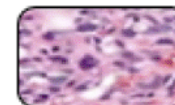
M4: >20% but <80% NSE-butyrate positivity in Monocytic cells



M5: Monocytic cells with >80% NSE positivity. (a) Monocytic differentiated (b) Monocytic, differentiated.



M6: >30% myeloblasts with more than 50% erythroblasts eliminating the erythroid cells.



M7: Acute megakaryoblastic leukemia <5%

Risk in AML

AML prognosis and treatment response vary widely and are determined by both **patient-related** and **disease-related** factors.

A. Patient-Related Prognostic Factors

1. Age:

1. Patients ≥ 60 years have worse outcomes due to:
 1. More resistant disease biology.
 2. Comorbidities and lower tolerance to intensive chemotherapy.

2. Performance status:

1. Poor status correlates with increased treatment-related mortality.

3. Sociodemographic factors:

1. Lower educational level, lack of social support, and treatment at lower-volume centers are associated with worse outcomes.

B. Disease-Related Prognostic Factors

1. White Blood Cell Count:

1. WBC $> 100,000$ cells/mm³ at diagnosis indicates high tumor burden and poor prognosis.

2. Therapy-related AML (t-AML):

1. AML developing after chemotherapy/radiation for another cancer is associated with poor response and survival.

3. Genetic and Molecular Features:

1. Includes cytogenetic abnormalities and mutations in key genes like FLT3, NPM1, CEBPA, TP53, etc.

Risk Stratification in AML

AML is classified into Favorable, Intermediate, and Poor-Risk categories based on:

- Cytogenetics (karyotype abnormalities).
- Molecular mutations (specific gene changes).

These guide treatment decisions and prognosis.

CYTOGENETICS + MOLECULAR TESTING

- Before assigning a risk group, each AML patient's karyotype (chromosomal structure) and gene mutations are evaluated.
- These genetic markers strongly preadict treatment response and long-term survival.

Clinical Application

- **Favorable risk:** Treated with intensive chemotherapy only; transplant usually not required.
- **Intermediate risk:** Treatment individualized; may consider transplant based on MRD or response.
- **Poor risk:** Usually offered allogeneic hematopoietic stem cell transplantation (allo-HSCT) in first remission.

RISK STRATIFICATION IN AML



CYTOGENETICS + 
MOLECULAR TESTING

RISK STRATIFICATION

FAVORABLE

- inv(16)
t(8;21)
- NPM1 mutation
(without FLT3-ITD)
- Biallelic CEBPA mutation

- Complex karyotype
- Monosomal karyotype

INTERMEDIATE

- Normal cytogenetics
- t(9;11)
- KIT mutation
- Mutated NPM1 and FLT3-ITD^{high}

- Monosomal karyotype
- TP53 mutation

POOR

- Complex karyotype
- Monosomal karyotype
- TP53 mutation
- RUNX1 mutation
- FLT3-ITD^{high}

- PP53 mutation
- RUNX1 mutation
- FLT3-ITD^{high}

TREATMENT AND MANAGEMENT OF

AML ROLE OF HEMATOPOIETIC GROWTH FACTORS (HGFs) IN AML

Hematopoietic growth factors (HGFs) are proteins that stimulate the proliferation, differentiation, and activation of hematopoietic cells in the bone marrow.

Examples include:

1. Filgrastim (G-CSF)
2. Sargramostim (GM-CSF)
3. Pegfilgrastim (long-acting G-CSF)

Goal:

- Shorten the duration of neutropenia
- Decrease infection risk
- Promote faster marrow recovery after chemotherapy
- Improve patient tolerance to intensive chemotherapy

ASCO Guidelines: Use of HGFs after induction is reasonable; not recommended concurrently during chemotherapy. After chemotherapy modest benefit.

Indicated to

1.Enhance chemotherapy cytotoxicity

Administered during chemotherapy (“priming”) to recruit leukemic cells into the cell cycle, making them more susceptible to cell-cycle–specific drugs (e.g., cytarabine).

2.Reduce neutropenia

Shorten the duration of neutropenia post-chemotherapy to reduce infection risk and hospital stay.

3.Accelerate marrow recovery

Help normal hematopoietic cells recover faster after intensive chemotherapy.

Agent	Type	FDA Approval	Notes
Filgrastim (G-CSF)	Granulocyte	✓	Commonly used post-induction
Sargramostim (GM-CSF)	Granulocyte + macrophage	✓	Less commonly used
Pegfilgrastim	Long-acting G-CSF	✗ (off-label in AML)	Supported by studies
Filgrastim-sndz / Filgrastim-aafi	Biosimilars	✓	Used in AML induction/consolidation

II. SUPPORTIVE CARE IN AML

- AML patients are at high risk for complications due to bone marrow suppression and cytopenias. Effective supportive care is essential to prevent mortality from infections, bleeding, and tumor lysis.
- AML treatment causes profound and prolonged **myelosuppression**, increasing risks for:
 1. Infections
 2. Tumor lysis syndrome
 3. Anemia and thrombocytopenia
 4. Myelosuppression monitoring

1. Infection Prevention & Management

a. General Measures

1. Hand hygiene, isolation (reverse/HEPA filter rooms)
2. Daily temperature monitoring
3. Avoid raw/uncooked foods (low-bacterial diet)

b. Antimicrobial Prophylaxis

Agent	Indication
Fluoroquinolones (e.g., levofloxacin)	ANC <100/mm ³ for >7 days
Antifungals (e.g., fluconazole, posaconazole)	Primary prophylaxis in AML/HSCT
Pneumocystis prophylaxis (e.g., TMP-SMX)	If >3.5% pneumonia risk
Acyclovir	HSV+ patients during induction

c. Pediatrics

1. **Levofloxacin:** Decreases febrile episodes in pediatric AML
2. **Antifungals:** Essential in AML/HSCT

2. Tumor Lysis Syndrome (TLS) Management

AML with high tumor burden (e.g., high WBC) is prone to TLS:

1. Hyperuricemia
2. Hyperkalemia
3. Hyperphosphatemia
4. Hypocalcemia
5. Renal failure

Pathophysiology

- Rapid destruction of leukemia cells → release of uric acid, K^+ , PO_4^{3-}
- Can cause: renal failure, arrhythmias, seizures

Prevention: Avoid rasburicase in G6PD deficiency → risk of methemoglobinemia.

Drug	Use	Notes
Hydration	All patients	Maintain high urine output
Allopurinol	Xanthine oxidase inhibitor	Blocks uric acid formation
Rasburicase	Urate oxidase enzyme	Rapidly lowers uric acid, single-dose often used

3. Transfusion Support

- **Red Blood Cells**
 - Transfuse if **Hb <8 g/dL** or symptomatic (fatigue, dyspnea, chest pain)
- **Platelets**
 - Transfuse if:
 - Count <10,000 cells/mm³ (prophylactic)
 - Active bleeding
 - Planned invasive procedures

4. Myelosuppression & Blood Cell Monitoring

Component	Strategy
CBC/ANC	Daily monitoring during treatment
Anemia	PRBC transfusion if Hb <8 g/dL or symptomatic
Thrombocytopenia	Platelet transfusion if <10,000/mm ³ or bleeding
Nadir	Marrow suppression peaks ~7–14 days, lasts 1–2 weeks

Limitations

- Can interfere with bone marrow biopsy interpretation if given within 7 days → immature myeloid cells may mimic leukemia
- Optimal timing, dose, and agent are still debated
- ASCO Guidelines: Reasonable after induction, especially in older patients