

## “Chronic Leukemias”

Chronic leukemias are clonal neoplastic disorders characterized by proliferation of relatively mature, differentiated hematopoietic cells with a slow, insidious onset.

### General Features ✨

- Gradual onset
  - Often detected incidentally
  - Hepatosplenomegaly and generalized lymphadenopathy common
  - Long clinical course compared to acute leukemias
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## Chronic Lymphocytic Leukemia (CLL)

### Definition

CLL is a neoplastic disorder of mature B-lymphocytes, characterized by monoclonal proliferation of immunologically incompetent, slowly dividing B cells.

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## Pathogenesis

Key mechanisms:

- Prolonged survival of B cells (not increased proliferation)
    - due to BCL-2 overexpression (anti-apoptotic)
  - Chromosomal deletions → loss of tumor suppressor genes
  - B-cell receptor (BCR) signaling promotes survival
  - Immune dysregulation:
    - Hypogammaglobulinemia → recurrent infections
    - Autoantibody formation → autoimmune hemolytic anemia / thrombocytopenia
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## Clinical Features

- 25% asymptomatic (accidental diagnosis)
  - Nonspecific symptoms: fatigue, weight loss
  - Anemia
  - Generalized, non-tender lymphadenopathy
  - Hepatosplenomegaly (50-60%)
  - Recurrent bacterial & fungal infections
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## Laboratory Findings

### Complete Blood Picture (CBP)

- TLC > 50,000 /cmm
  - Absolute lymphocytosis (>80%)
  - RBCs ↓ and Platelets ↓ (marrow infiltration / immune destruction)
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## Morphology

### Peripheral Smear

- Small mature-looking lymphocytes
  - High N:C ratio
  - Round to oval nucleus with clumped chromatin
  - Smudge cells (fragile lymphocytes damaged during smear preparation) – characteristic ★
  - ~15% cases show prolymphocytes → CLL/PLL variant
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## Bone Marrow Examination

### Aspiration:

- Replacement of marrow by lymphocytes
- Lymphocytes form 25–95% of marrow cells

### Trephine Biopsy:

- Interstitial / Nodular / Diffuse infiltration
  - Diffuse pattern = poorer prognosis
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## Immunophenotyping

- CD5 positive (aberrant T-cell marker on B cells - classic for CLL)
  - CD20 positive
  - Confirms B-cell lineage
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## Genetics

- del(13q) - most common, good prognosis
  - del(11q)
  - del(17p) (p53 loss) - poor prognosis
  - Trisomy 12
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## Prognosis

Parameter	Favorable	Unfavorable
Gender	Female	Male
BM pattern	Nodular	Diffuse
Cytogenetics	del(13q14)	Trisomy 12, del(11q)
p53	Normal	Deleted

VH genes	Hypermutated	Unmutated
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## Diagnostic Criteria

- 1] Absolute lymphocyte count  $>10 \times 10^9/L$
- 2] Bone marrow lymphocytes  $>30\%$
- 3] Immunophenotyping confirms B-cell markers

 Diagnosis requires 2 of 3 criteria:

- Either (1+2) or (1+3)
  - If lymphocyte count  $<10 \times 10^9/L \rightarrow$  both 2 and 3 required
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## Transformation

- Prolymphocytic transformation
  - Richter transformation  $\rightarrow$  Diffuse Large B-Cell Lymphoma (DLBCL)
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# Chronic Myeloid Leukemia (CML) 🔥

## Definition

CML is a chronic myeloproliferative neoplasm arising from a pluripotent hematopoietic stem cell, characterized by uncontrolled proliferation of myeloid lineage cells.

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## Epidemiology 📌

- Male : Female = 1.4 : 1
  - Peak age: 40-60 years
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## Pathogenesis 🧠

Central event:

- BCR-ABL fusion gene
- Caused by t(9;22) → Philadelphia chromosome (>90%)

Effects of BCR-ABL tyrosine kinase:

- Increased proliferation

- Decreased apoptosis
  - Genomic instability → disease progression
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## Clinical Features

- 40% asymptomatic
  - Symptoms of hypermetabolism
  - Massive splenomegaly 
  - Features of anemia
  - Platelet dysfunction → bleeding
  - Hyperuricemia → gout, renal impairment
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## Laboratory Diagnosis

### Blood CBP

- TLC  $>100 \times 10^9/L$
- Normocytic / macrocytic anemia
- Platelets usually increased

### Peripheral Smear

- Full spectrum of myeloid cells (myeloblast → neutrophil)
  - Bimodal peak: Myelocytes + neutrophils
  - Basophils ↑ (important clue)
  - Eosinophils ↑
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### Bone Marrow Findings

- Hypercellular marrow
  - Marked granulocytic hyperplasia
  - Trepine biopsy shows variable fibrosis
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### LAP / NAP Score

- Very low or absent in CML
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### CML vs Leukemoid Reaction

Feature	CML	Leukemoid Reaction
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Age	>40 years	Any age
TLC	>100,000	30-50,000
Basophilia	Present	Usually absent
Splenomegaly	Prominent	Absent/mild
Philadelphia chromosome	Present	Absent
LAP score	Low	High
Progression to acute leukemia	Yes	No

## Phases of CML

Chronic Phase (3-5 years):

- Asymptomatic or mild symptoms

Accelerated Phase:

- Blasts  $\geq 15\%$
- Basophils  $> 20\%$
- Platelets  $< 100,000/\mu\text{L}$
- Clonal evolution

Blast Crisis:

- Blasts  $\geq 30\%$
  - Extramedullary blast infiltration
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## Treatment

- Tyrosine Kinase Inhibitors (Imatinib / Gleevec) - first line 
  - Stem Cell Transplant - only curative therapy
  - Hydroxyurea - cytoreduction
  - Interferon- $\alpha$  - selected cases
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## Causes of Massive Splenomegaly (Exam Favorite!)

- 1] Chronic malaria
- 2] CML
- 3] Myelofibrosis
- 4] Leishmaniasis
- 5] Storage disorders
- 6] Thalassemia

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MCQ Pearl 

Most common clinical feature in CML:

 Enlarged spleen 

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-> The End <-