

Myeloid Neoplasms & AML

General Overview

- The most important disorders of white cells are neoplasms.
- Virtually all are considered to be malignant, but they have a wide range of behaviors, from very aggressive cancers to indolent ones.
- As a group, they are quite common.
- They occur at all ages, but some preferentially affect:
 - Infants
 - Children
 - Young adults
 - The very old

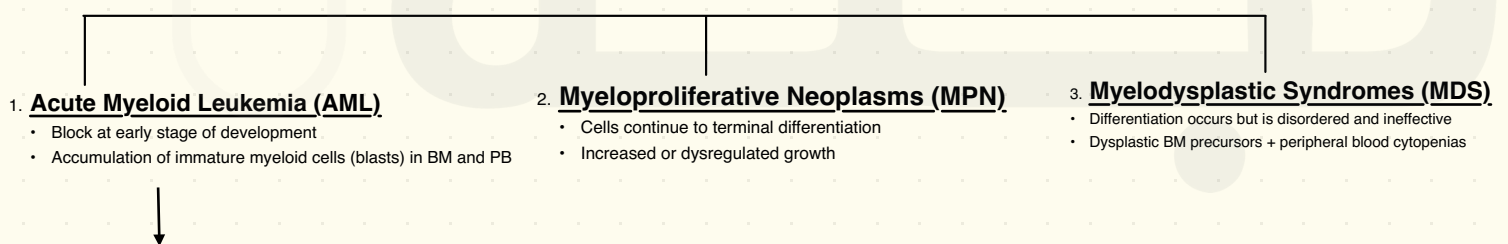
Classification (based on cell of origin & differentiation)

1. Lymphoid neoplasms
2. Myeloid neoplasms
3. Histiocytic neoplasms

Myeloid Neoplasms

- Neoplasms originating from **hematopoietic progenitors**
- Primarily involve the bone marrow, replacing normal marrow elements
- Secondary involvement of:
 - Lymph nodes (LN)
 - Spleen
 - Liver

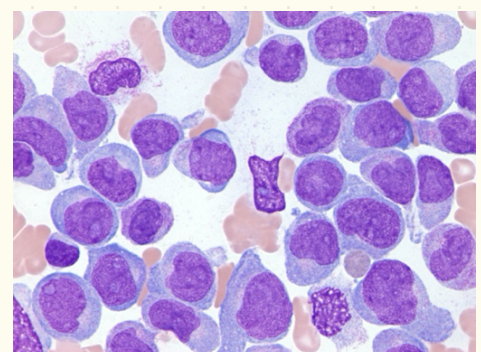
Three Broad Categories



Acute Myeloid Leukemia (AML)

General Features

- Affects all age groups (peak > 60 years)
- Symptoms result from replacement of normal marrow elements:
 - Anemia
 - Thrombocytopenia
 - Neutropenia
- Acute disease → develops within weeks
- Splenomegaly & lymphadenopathy are less prominent than ALL



Risk Factors

- Increasing age
- Male sex ♂
- Previous cancer treatment
- Radiation exposure
- Chemical exposure (e.g., benzene)
- Smoking (linked due to benzene)
- Other blood disorders (MDS, MPN)
- Genetic disorders (e.g., Down syndrome)

Pathogenesis

- Mutations in genes encoding transcription factors → block myeloid differentiation
- Leads to accumulation of blasts in bone marrow

Example: t(15;17) in APL acute promyelocytic Leukemia

- Fusion of:
- RARA gene (chr 17)
- PML gene (chr 15)
- **Forms PML/RARA fusion protein**
- Blocks differentiation at **promyelocyte stage**

Treatment Insight

- **ATRA (all-trans retinoic acid):**
- Overcomes differentiation block
- Converts promyelocytes → neutrophils
- Highly specific effect
- AML with t(15;17):
- Best prognosis
- 90% curable

Morphology

- Diagnosis requires:
- **≥20% myeloid blasts or promyelocytes in bone marrow**

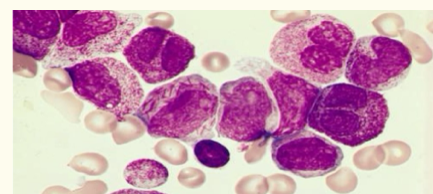
Myeloblasts

- Delicate nuclear chromatin
- 2–4 nucleoli
- Larger cytoplasm than lymphoblasts
- Fine azurophilic granules

Auer Rods

- Red-staining, needle-like granules
- Common in AML
- Numerous in APL

Auer Rods



Other Findings

- Different subtypes may show:
- Monoblasts
- Erythroblasts
- Megakaryoblasts
- Blasts may be absent in PB → **aleukemic leukemia**
- Bone marrow exam is essential in pancytopenia

TABLE 1. WHO classifications for AML subtypes		Table 12.11 WHO Classification of AML	
Type	Name	Class	Prognosis
M0	Minimally differentiated acute myeloblastic leukemia	I. AML With Recurrent Chromosomal Translocations	Favorable
M1	Acute myeloblastic leukemia (M2)(t(8;21)(q22;q22))		
M2	Acute myeloblastic leukemia (M2)(t(8;21)(q22;q22))		
M3	Acute promyelocytic leukemia (APL)		
M4	Acute myelomonocytic leukemia		
M4eo	Myelomonocytic leukemia with bone marrow eosinophilia	II. AML With Multi-lineage Dysplasia	Variable
M5	• Acute monoblastic leukemia (M5a) • Acute monocytic leukemia (M5b)		
M6	Acute erythroid leukemias, including —Erythroleukemia (M6a) —Acute pure erythroid leukemia (M6b)	III. AML, Therapy-Related	Very poor
M7	Acute megakaryoblastic leukemia		
M8	Acute thrombocytic leukemia	IV. AML, Not Otherwise Classified	Intermediate
M9	AML, acute myeloid leukemia, blastocytosis (M9), with pathologic signification		

Monoblasts

- Folded or lobulated nuclei
- No Auer rods

Immunophenotype

- Common markers:
- CD13, CD33, CD14, CD15, CD117 (KIT)
- CD34 → stem cell marker
- **Myeloperoxidase (MPO)** → **most specific**
- Helps:
- Distinguish AML from ALL
- Identify poorly differentiated AML

Clinical Features

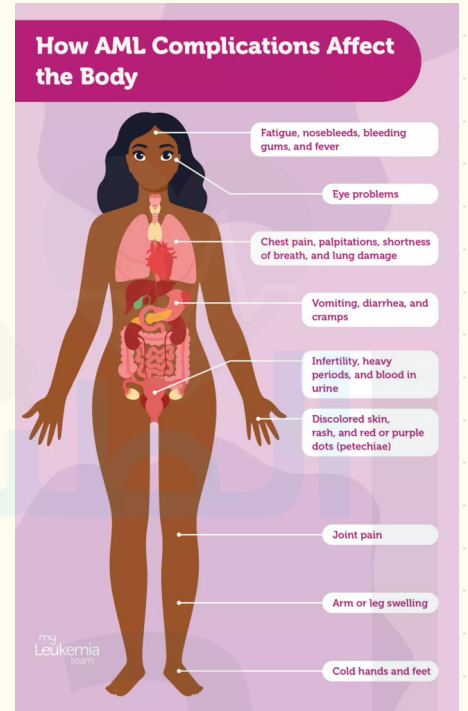
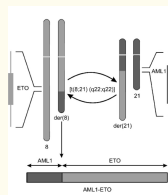
- Rapid onset (weeks to months)
- Symptoms:
- Fatigue (anemia)
- Fever (neutropenia)
- Bleeding (thrombocytopenia)
- CNS involvement: less common than ALL

Special Features

- t(15;17) AML:
- High risk of **DIC** (due to procoagulants)
- Monocytic AML:
- Skin infiltration (leukemia cutis)
- Gingival involvement
- Can present as:
- **Myeloblastoma / granulocytic sarcoma**

Prognosis

- Generally poor disease
- Good-risk cytogenetics:
- t(8;21)
- inv(16)
- ~50% long-term survival
- Overall survival:
- **15–30%** with conventional chemotherapy



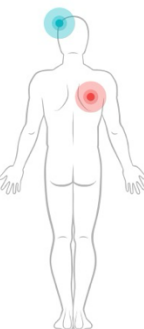
Acute vs Chronic leukemia

Acute leukemia

- ▶ Blasts
- ▶ Rapid proliferation of cells.
- ▶ Rapidly Fatal (<6 months without Tx)
- ▶ Lymphoid...ALL
- ▶ Myeloid...AML

Chronic leukemia

- ▶ Mature cells
- ▶ Gradual proliferation.
- ▶ More indolent disease. (2-6 years without Tx)
- ▶ Lymphoid...CLL
- ▶ MPN...CML



لَا حَوْلَ وَلَا قُوَّةَ إِلَّا بِاللَّهِ

"من كنوز الجنة"