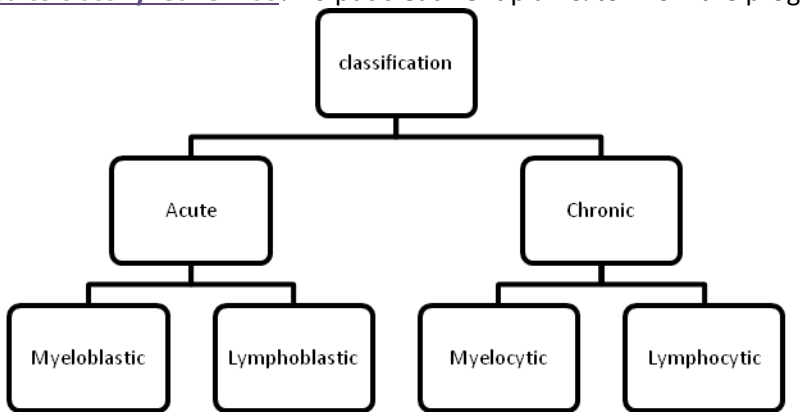
Problem 3 – Unit 6 – Clinical: leukemia classification

- **Definition of leukemias**: they are malignant disorders affecting the bone marrow, lymphatic system and the spleen (mainly).
- **Why do we need to classify leukemias**? To put treatment plan & to know the prognosis.



- **To differentiate between different types of leukemia:**
  - **Morphology & cytochemistry:**
    - ✓ Myeloperoxidase (+), Sudan black (+) ---> AML
    - ✓ PAS (+) ---> ALL
  - **Flow cytometry:**
    - ✓ CD13, CD33, CD117 ---> AML
    - ✓ TdT, CD10, CD19, CD22 ---> ALL (B-cell)
    - ✓ TdT, CD2, CD3, CD7 ---> ALL (T-cell).
  - **Cytogenetics:**
    - ✓ Karyotyping---> Ph chromosome in CML.
    - ✓ PCR & FISH ---> BCR-ABL1 fusion gene in CML.

Acute Lymphoblastic Leukemia (B-cell or T-cell)

- **Morphology**: ↑nuclear to cytoplasm ratio, mirror-type appearance, open chromatin & presence of nucleoli.
- **Genetic abnormalities:**

Favorable	Unfavorable
* t(12,21) in childhood * Hyperdiploidy (> 50 chromosomes)	* t (9,22) in adults. * t (11q23). * Hypodiploidy (<44 chromosomes).

- **Molecular findings:**
  - **B-cell**: clonal rearrangement of immunoglobulin gene.
  - **T-cell**: clonal rearrangement of TCR gene.

Acute Myeloblastic Leukemia

- **Morphology**: ↓nuclear to cytoplasm ratio, presence of auer rods & larger cells than lymphoblasts.
- **Types**:
  - **AML with recurrent genetic abnormalities**: t(8,21), inv (16), t(15,17).
  - **AML with myelodysplasia-related changes**: microscopic features of dysplasia in at least 50% of cells in at least two lineages.
  - **Therapy related AML (t-AML):** examples include etoposide & alkylating agents ---> causing mutations in MLL gene.
  - **AML, not otherwise specified**: absence of cytogenetic abnormalities. Mutations are more frequent especially in NPM & FLT3 genes.
  - **Myeloid sarcoma**: resemble a solid tumor but is composed of myeloid blast cells.

- **Acute promyelocytic leukemia:**
  - T (15,17) ---> PML-RAR
  - **Morphology**: multiple Auer rods (faggot cells) and hypergranular
  - **Clinical features & complications**: thrombocytopenia + DIC & hemorrhagic syndrome.
  - **Treatment**: ATRA-therapy.
- **Prognosis of AML:**

Table 13.3 Prognostic factors in acute myeloid leukaemia (AML).

	Favourable	Intermediate	Unfavourable
Cytogenetics	t(15; 17) t(8; 21) inv(16) *NPM* mutation *CEBPA* mutation	Normal Other non-complex changes	Deletions of chromosome 5 or 7 Abnormal (3q) t(6; 11) t(10; 11) t(9; 22) Complex rearrangements (>3 unrelated abnormalities) *FLT3* internal tandem repeat
Bone marrow response to remission induction	<5% blasts after first course		>20% blasts after first course
Age			>60 years

Chronic Myelocytic Leukemia

- ↑WBCs (leukocytosis) & blast cells < 5%
- **Genetic abnormality**: t(9,22) resulting in Ph chromosome (BCR-ABL1 fusion gene) which has increased tyrosine kinase activity leading to enhancement of cell proliferation and prevention of apoptosis.

Chronic Lymphocytic Leukemia

- ↑ in adults & western countries.
- There is familial genetic predisposition.
- CD5, CD19 & CD23
- **Staging (Binet):**
  - **Stage (A)**: enlargement of less than 3 lymphoid areas.
  - **Stage (B)**: enlargement of more than 3 lymphoid areas.
  - **Stage (C)**: anemia (Hb<10) & thrombocytopenia.