Leukemia:

Malignant disorder of Haematopoeitic stem cells. characterised by ↑ WBCs.

Epidemiology:
- Age → Older age, Male : Femal = 3 : 2.
- 10/100,000 per annum patient.
- Asea - Chinese people.

Risk factors
1) Ionising radiation → Radiotherapy. X rays in fetus. Atom bombing in Japanese (Myeloid).
2) Cytotoxic drugs.
3) Retrovirus - 4) Genetic : Twins. Down syndrome.
5) Immunodeficiency states.

Acute
- Immature Blast cells
- More symptoms

Chronic.
- Partially Mature Blast cells.
- Asymptomatic.

Acute leukemia — Acute Myeloid leukemia (Old age)
— Acute lymphoblastic leukemia (Children).

Acute leukemia

Acute myeloid leukemia.

- Myeloid blast progenitors are proliferated like (Monocytes & Granulocytes) Older age
- Subclassification — 1) chromosomal translocation
  2) Morphology of myeloblast.

Morphology

1) AML without maturation
2) AML with minimal maturation
3) AML with maturation.
4) Acute Promyelocytic leukemia t(15:17) → Absence of Retinoic acid receptor gene.
5) Acute myelomonocytic leukemia
6) Acute monocytic leukemia
7) Acute Erythroid leukemia
8) Acute Megakaryoblastic "

Causes:

1) Myelodysplastic syndrome (Defective maturation of myeloid cells).
2) Down syndrome (Both AML & CML) Trisomy 21
3) Risky → Radiotherapy, Alkylating chemotherapy.

Pathogenesis

Mutation — lose ability to differentiate → Stuck in Blast stage → Dont function effectively.
Divide uncontrollably → Crowds → Cytopenia.
Settle in organs & Tissues → Organomegaly.

Acute lymphoblastic leukemia.

- lymphoid progenitors (T & B cells). proliferation.

Classification — Younger age

i) T cell ALL ii) B cell ALL.

Causes:

1) Translocation of t(12:21).
2) Translocation of t(9:22) Philadelphia chromosome.
3) Down syndrome.
4) Risk factors.
5) Abnormal chromosome numbers.

Pathogenesis:

- Same and with organs they also settle in Thymus and lymph nodes due to T-cells.

Clinical Features of Both ALL & AML

1) Fatigue → Anemia 2) ↑Infection → leukopenia
3) Easy Bleeding → Thrombocytopenia
4) Pain and Tenderness in Bones.
5) Pain in lymphnodes. } More in ALL.
6) Hepatosplenomegaly
7) Thymus enlargement → ALL
8) Swelling of gums → Monocytic variety of AML.

Investigation - ↑WBC → $1 \times 10^9/L$ to $500 \times 10^9/L$ or more, ↓RBC, ↓Platlets.

Blood smear → Myeloblasts → AML & Lymphoblast → ALL.

Bone Marrow Biopsy → ↑↑ Blast cells - >20% Blast cells.

→ Myeloblast → Large cells, Auer rods (Fine chromatins)
Lymphoblast → Smaller cells. Coarse chromatins → Contain Glycogen granules

→ Auer rods are seen in Promyelocytic leukemia, which are crystallized aggregates of myeloperoxidase enzyme.

Treatment → Immunophenotyping (ALL).

→ Tdt (DNA Polymerase only in lymphoblast).

→ CD10 (Surface marker of Pre-B cells).

Treatment → ↓↓ Number of Blast cells.

→ Depends upon type and stage of cancer.

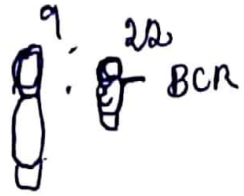
1) Chemotherapy
2) Biological therapy
3) Stem cell replacement
4) Bone Marrow transplant.

→ Acute promyelocytic leukemia

→ ALL Trans Retinoic acid (ATRA).

Chronic Myeloid leukemia:

- Myeloproliferative disorder affecting predominantly Granulocytes series, Partially matured.



Causes:

→ Chromosome Abnormality
(Philadelphia chromosome)
↳ Shortened 22 chromosome due to the reciprocal translocation of the long arm of 9 with long arm of 22. (t (9 : 22)).

- BCR gene from 22 joints with ABL oncogene from 9.
(Breakpoint cluster region)

Fusion gene = BCR-ABL fusion gene
↓
Codes for Tyrosine Kinase enzymes
↓
Oncogene causing increased cell division and prodifferation of the Granulocytes.
↓
Excess Buildup
↓
Mover in Blood and cause.
Hepatosplenomegaly.

Natural History

1) Chronic Phase
- Usually asymptomatic and responds to treatment.
- Lasts for 3-5 years.
- Symptoms → Fatigue from anemia.
  - Abdominal Fullness and satiety → Splenomegaly
  - Frequent infection and Bleeding → WBC + platlet dysfunction.

2) Accelerated Phase
- Cellular proliferation increases.
- Disease control becomes very difficult.

3) Blast Phase (Blast Crisis):
↓
Becomes acute leukemia (Blastic).

AML (70%) ALL (30%)
↳ Due to gene mutation

Leukemoid Reaction Differentiate from that by,
↳ They are normal overreactions of Bone marrow to infections or stressors. by WBC > 40,000. and left shift.
→ Normal leucocyte take up Leucocyte Alkaline Phosphatase (LAP) where CML don't take it.

Investigation:

① Bone Marrow Biopsy.
↑ Ratio of Myeloid : Erythroid (3 : 1 Normal)
↳ Non-Specific, increased in Infection.

② Blast Cells.
Chronic phase : 10%.
Accelerated phase : 10-20%.
Blast crisis : > 20%.

③ Karyotyping analysis
↳ FISH (Fluorescent in situ Hybridization)
method → Philadelphia chromosome t(9:22).

④ Normocytic normochromic anemia.

⑤ Leucocytes → 10 to 600 × 10^9/L, ↑ Granulocytes.

Chronic ~~Acute~~ lymphocytic leukemia
- Male to Femal : 2 : 1, 65-70 years.
- B cells usually activated only responding to the the antigens.
↓
But due the unknown cause.
↓
Increased B cells proliferate,
↓
Travel to the Blood and Cause,
Build up
↓
lymphonodes (Lymphoma)
small lymphocytic
↙ ↘
Autoimmune hemolytic anemia
Hypogammaglobunemia

Investigations

① Bone Marrow Biopsy.
↳ >30% lymphocytes.

② Flow Cytometry → CD_5, CD_{19}, CD_{23}.

③ Blood Smears → Count >5000.

④ ↓ Serum ~~Hem~~ Immunoglobulin

⑤ Coombs Test → Autoimmune Hemolytic anemia.

Hairy cell leukemia

- Rare chronic B-cell lymphoproliferative disorder
- 6:1 male to femal ration.
- Common Symptoms → Pancytopenia ↓↓↓
- Splenomegaly → Rupture

CBC, Blood Smear → leukemic cell with Hair like projection

Cytometry → CD 25, CD 103.

→ Medical Emergency