WBC DISORDERS

Pleuripotent stem cells (CD34+)

↓

multipotent stem cells

↓

Common myeloid progenitor

- CFU Gl/M
  - Neutrophils
  - Basophils
  - Eosinophils
  - Monocytes
- CFU M/E
  - Megakaryocytes
  - Erythrocytes.

Common lymphoid progenitor

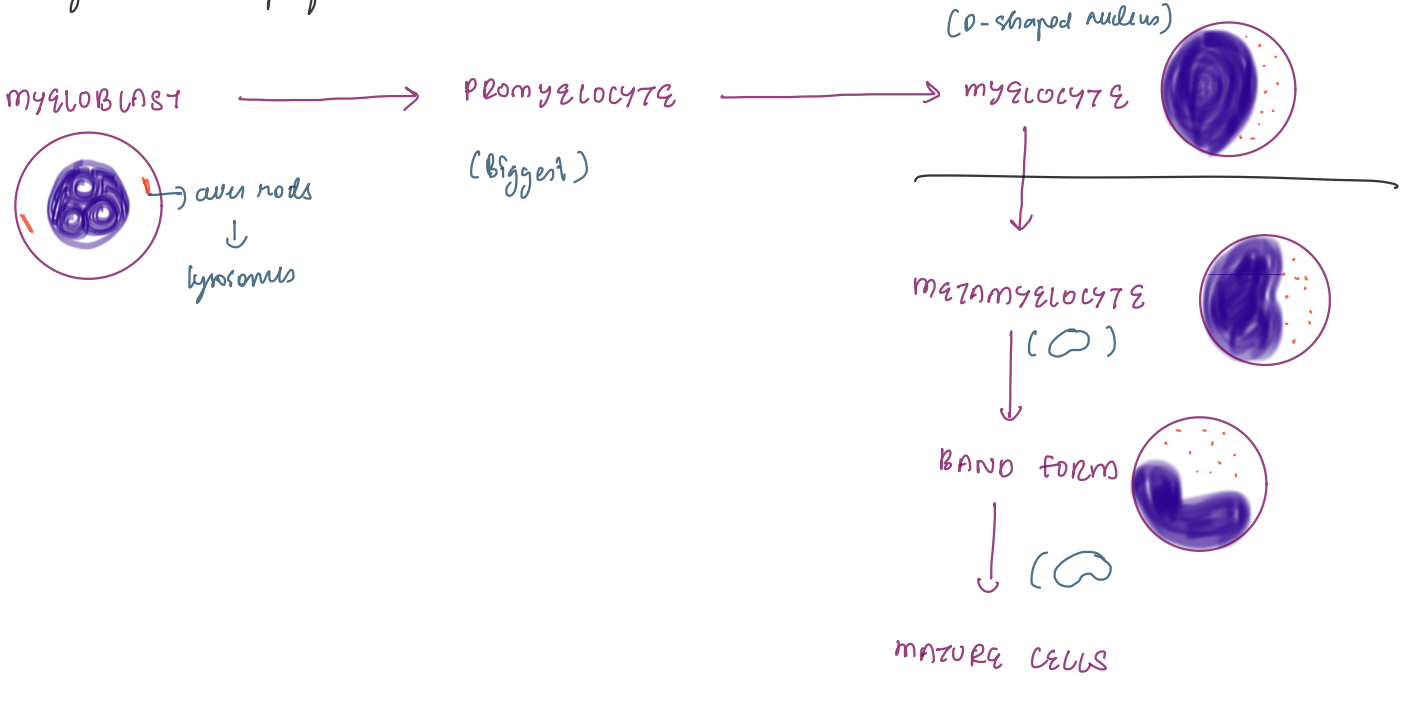
- T
- B
- NK

STAINS :

i) Myeloblast : MPO, sudan black B, CAE

ii) Lymphoblast : PAS, Acid phosphatase

iii) Monocytes : Non-specific esterase



Normal values [Never let monkey eat bananas]

Neutrophil : 2000 – 7000 cells/mm^3 → ↑ in acute inflammation, Bacterial inf

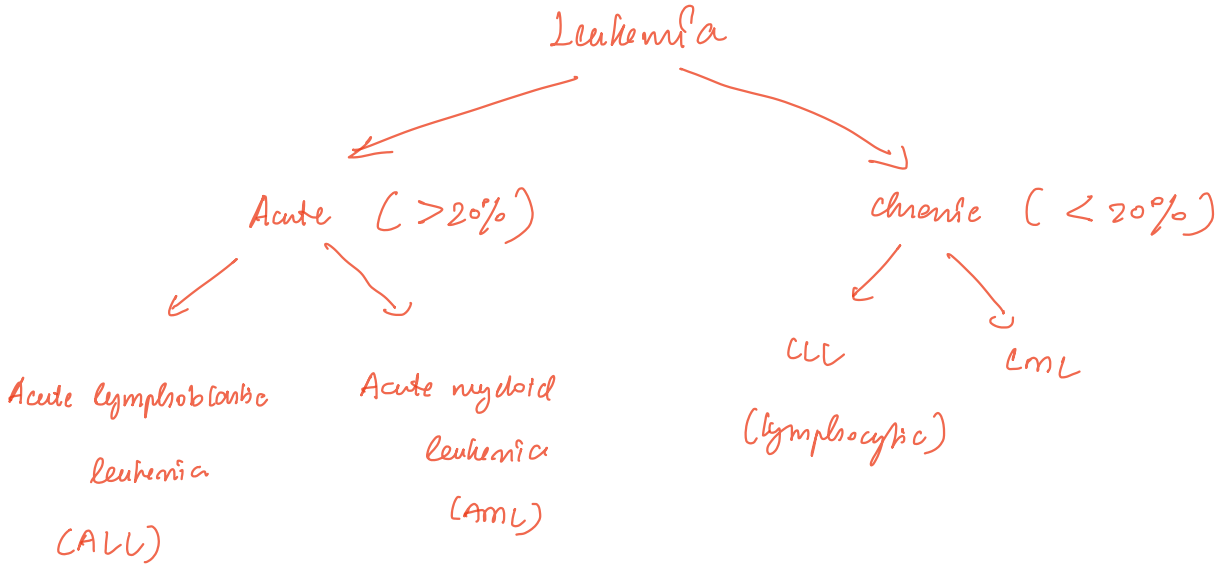
Lymphocyte : 1000 – 3000 /mm^3 → ↑ viral infection, Chronic inflammation, typhoid, TB

Monocyte : 200 – 1000 /mm^3 → ↑ in malaria, chronic myelomonocytic L

Eosinophil : 50 – 500/ mm^3 → ↑ allergy, parasitic infections

Basophil : 0 – 100/ mm^3 → CML, PV

- Hypersegmented neutrophil (>5 lobes) → megaloblastic anaemia
- Hyposegmented neutrophil - Pelger Huet anomaly
- Dohle bodies → in sepsis
  → made of dilated ER



Acute lymphoblastic anaemia (ALL)

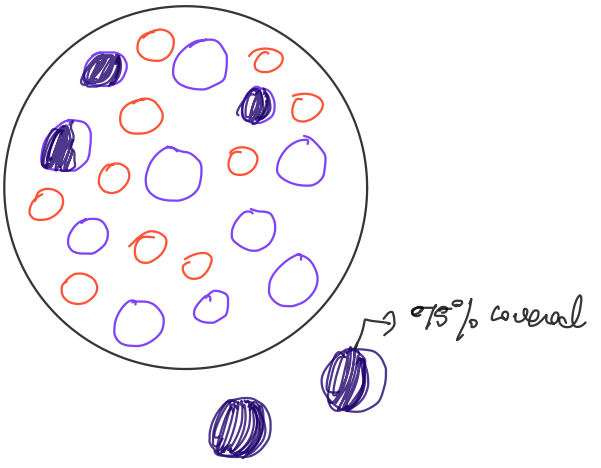
- m/c in children (< 6yrs)
- C/F : hepatosplenomegaly, CNS infiltration, testicular enlargement, mediastinal mass, pleural effusion, anaemia, neutropenia, thrombocytopenia, lymphadenopathy

Lab finding

* Blood examination : Anemia, thrombocytopenia, (leukopenia → normal → leukocytosis) variation
  - lymphoblasts > 20% - high NC ratio

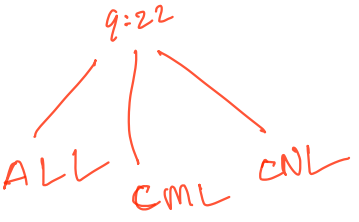
* BM exam^{n} - 20-90% of malignant undifferentiated cells of precursor B or T cells.
  PAS & acid phosphatase (+) on lymphoblast.

* Cytochemistry
  PAS, acid phosphatase = +
  MPO - -ve
  Sudan black : -ve
  NSE : -ve



* Immunophenotyping :
  BALL : CD19, CD10
  TALL : CD1, CD2, CD3, CD5, CD7

* Cytogenetic & molecular testing :
  B-ALL → t(9:22) Philadelphia chromosome.



Treatment :
Chemotherapy - vincristine, prednisolone, anthracyclines
BM transplantation

Acute myeloid leukemia **

- mainly a disease of adults
- develops due to inhibition of maturation of myeloid stem cells due to mutations.

classification

AML M0 → M7 (FAB classification)

AML M0 → AML undifferentiated

AML M1 → AML w/o maturation

AML M2 → AML with maturation (m/c) = RUNX1 : RUNX1T1

AML M3 → acute promyelocytic leukemia (APML) = PML : RARA

↑ promyelocyte → with non auer rodes (faggot cell) → contains procoagulant material

i.e. causes DIC

↓ No chemotherapy

AML M4 → Acute myelomonocytic leukemia [myelocyte + monocyte ↑]

AML M5 → Acute monocytic leukemia

AML M6 → Acute erythroid leukemia (Di guglielmo syndrome)

AML M7 → Acute megakaryocytic leukemia

↳ m/c in downs

→ Dry tap.

CF :

* Due to BM failure → Anemia, bleeding manifestations (gum bleeding **), infections, fever

* Due to organ infiltration → pain & tenderness of bones, splenomegaly, gum hypertrophy, meningeal involvement, testicular swelling.

↳ gum bleeding

lab diagnosis :

* Blood picture

- Anaemia : Normochromic
- Thrombocytopenia

- WBC : ↓ / ↑

Acute : Blood picture
↳ Anaemia, thrombocytopenia, leukopenia

* Bm exam^n
  - Cellularity - hypercellular
  - My : dry tap.

- Leukoplerite : - Bm highly packed with leukaemic blast cells.
- Erythropoiesis - ↓
- Megakaryocyte - ↓

* Cytogenetics - RUNX1 : RUNX1 T1
  PML : RARA

Predominant cell → myeloblast

* Cytochemistry.
  MPO - +ve in immature myeloid cells
  Sudan black - +ve in immature cells.
  PAS - M6 +ve
  NSE - M4 & M5

PAS - lymphoblast & erythroid
MPO & Sudan black - myeloid series

Treatment (T)

* T of anaemia & haemorrhage
* Cytotoxic dry tap
* Bm replacement

Chronic lymphocytic leukemia (CLL)

C/F : Anaemia → weakness, fatigue, dyspnoea

lymphadenopathy

hepatosplenomegaly

Haemorrhagic manifestations

less common finding : mediastinal m, bone & joint pains

Lab findings :

* Blood picture
  - Anaemia
  - WBC : marked leukocytosis

    90% of leukocytes are mature small lymphocytes

    Smudge cells present due to decayed nuclei of fragile malignant lymphocytes.
  - Platelets : Normal / ↓

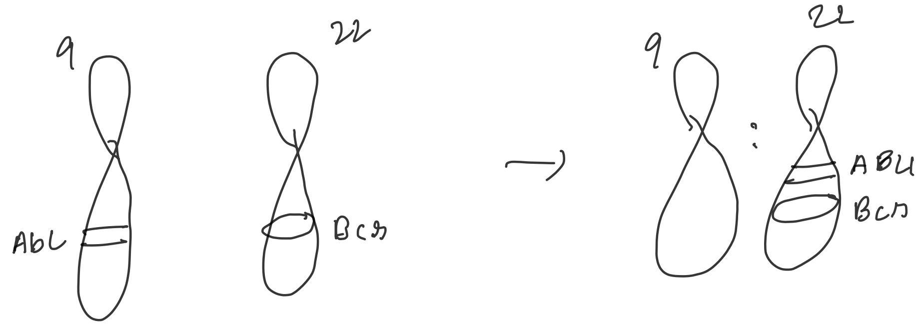
ALL CML CNL

* BM examination
  - ↑ lymphocyte count
  - ↓ myeloid precursors
  - ↓ erythroid precursors

Chronic myeloid leukemia (CML)

- due to the balanced reciprocal translocation b/w chr. 9 & 22 → Philadelphia chromosome

BCR-ABL1



} fusion → ↑ tyrosine kinase

BCR ABL

ABL1
BCR

C/F → Anaemia, hypermetabolism, splenomegaly, bleeding, juvenile CML

* lab finding - Blood picture
  - Anaemia : normocytic normochromic
  - WBC : leukocytosis

3 phases - CAB

- Chronic phase : < 10% blasts in peripheral blood & BM
  - ↑ in the proportion of basophils up to 10%

<10
10

- Accelerated phase :
  10-19% → myeloblast
  > 20% → Basophil

10-19
>20

- Blastic phase
  ≥ 20% blasts

- Platelets : ↑ / Normal

* Bone marrow exam^n
  - Cellularity - hypercellularity
  - Myeloid cells : predominates
  - erythropoiesis - normoblastic, but there is reduction in erythropoietic cells
  - Megakaryocytes : smaller in size than normal

* Cytogenetics : Philadelphia chromosome

* cytochemistry : ↓ NAP score

* other investigation
  - ↑ B_{12} & vit B_{12} binding capacity
  - ↑ serum uric acid

Hodgkin's lymphoma

Classification :

I Classical HL
- Nodular sclerosis
- mixed cellularity
- lymphocyte rich
- lymphocyte depleted

II Nodular lymphocyte predominant HL

Histologic type	Pathology	m/s	Prognosis
1. CLASSICAL HL			
Nodular sclerosis	lymphoid nodules, collagen bands Lacunar RS type	• Bands of collagen - present in the involved lymph nodes • Lacunar type RS cells	Very good
Mixed cellularity	mixed infiltrate classical RS cells	The entire affected lymph node is replaced by heterogenous mixture of various types of apparently normal cells - (proliferating lymphocytes, histiocytes, eosinophils, neutrophils)	Good
Lymphocyte rich	Proliferating lymphocytes, a few histiocytes classical RS cell	diffuse pattern of proliferation of small lymphocytes admixed with a varying number of histiocytes - classical RS cells	Excellent

Lymphocyte - depleted	Scanty lymphocytes, few histiocytes Diffuse fibrosis pleomorphic RS cell	• Entire LN is replaced by diffused fibrosis, appearing as homogenous, fibrillar hyalin material. • Reticular variant - typical & pleomorphic RS cells.	Poor
II Nodular - lymphocyte predominant HL	Proliferation of small lymphocytes, nodular pattern of growth	Sparse (scattered) number of RS cells Polyploid RS cell (popcorn cells)	Chronic relapsing, may transform into large B cell NHL

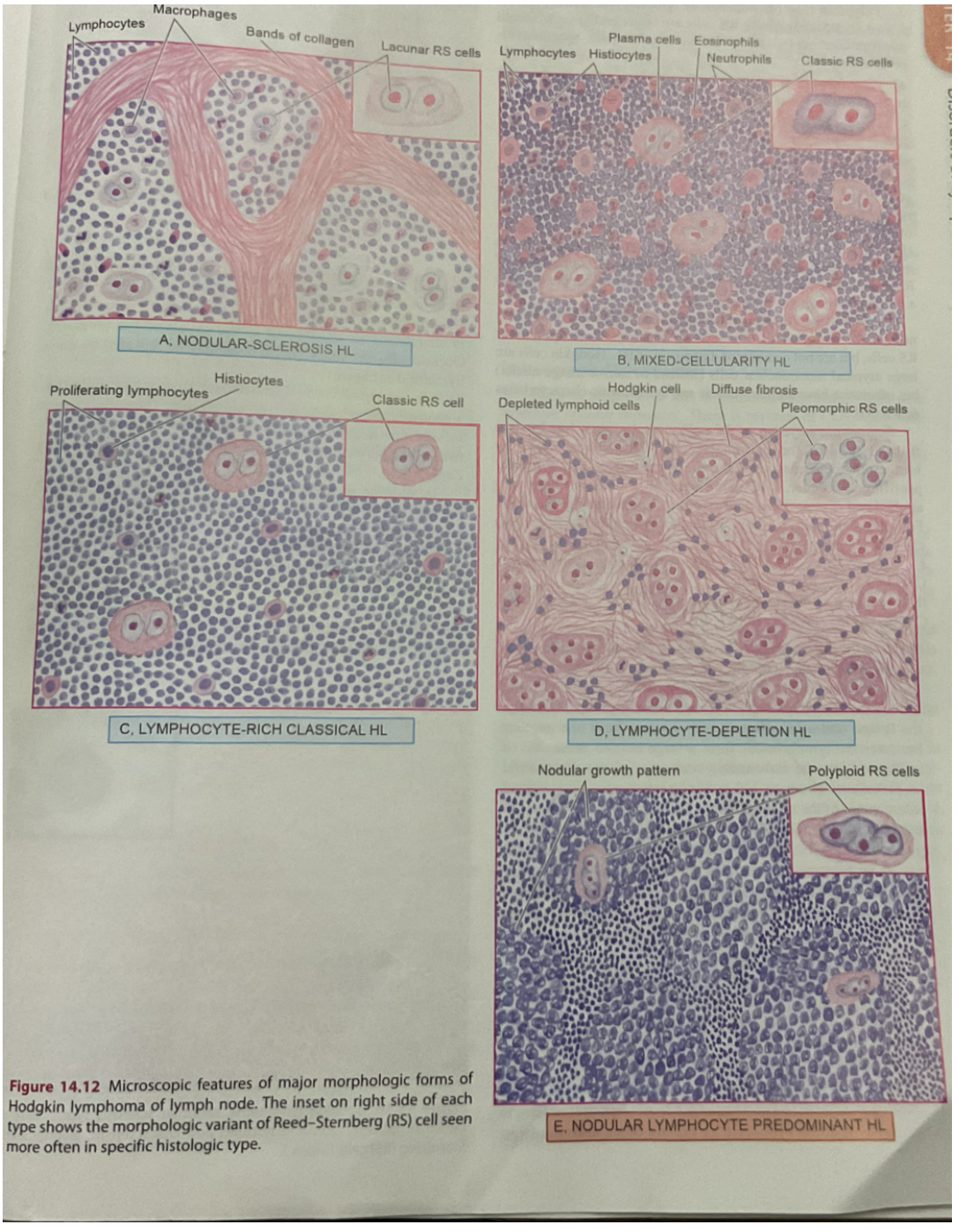


Figure 14.12 Microscopic features of major morphologic forms of Hodgkin lymphoma of lymph node. The inset on right side of each type shows the morphologic variant of Reed–Sternberg (RS) cell seen more often in specific histologic type.

Burkitt lymphoma

* Uncommon tumor in adults
* Corresponds to L_3 ALL of FAB group
* 3 subgroups : African endemic (Jaw tumor)
  Sporadic BL
  Immunodeficiency-associated BL

Pathology

. Histologically, all 3 types of BL are similar

cross - Tumor cells are medium sized & homogenous in size & shape

m/s - Nuclei are round-oval
Contains 2-5 nucleoli
Cytoplasm is basophilic
Contains lipid vacuolation

- have high mitotic rate
- Presence of numerous macrophages in the background of this tumor containing phagocytosed tumor debris giving it 'starry sky' appearance.

. Tumor cells are positive for CD10, BCL6, BCL2 & high Ki-67 index.

. t(8:14) & t(8;22) involving MYC gene on chromosome 8, with overexpression of MYC protein.