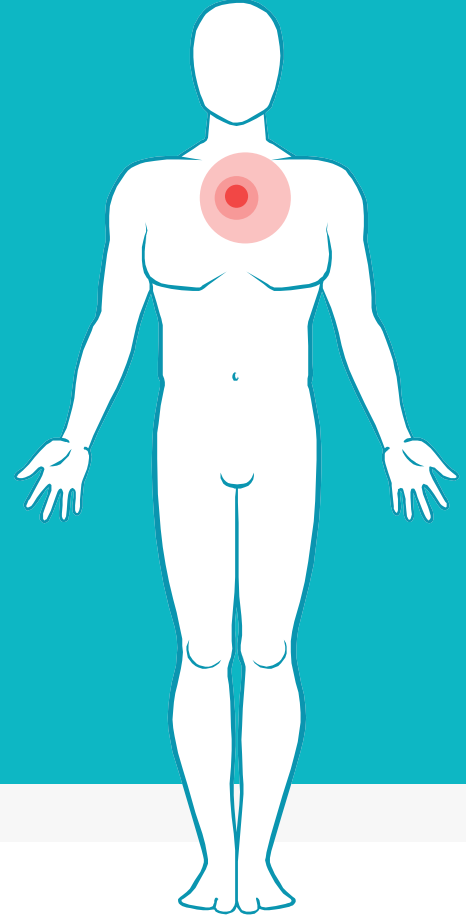


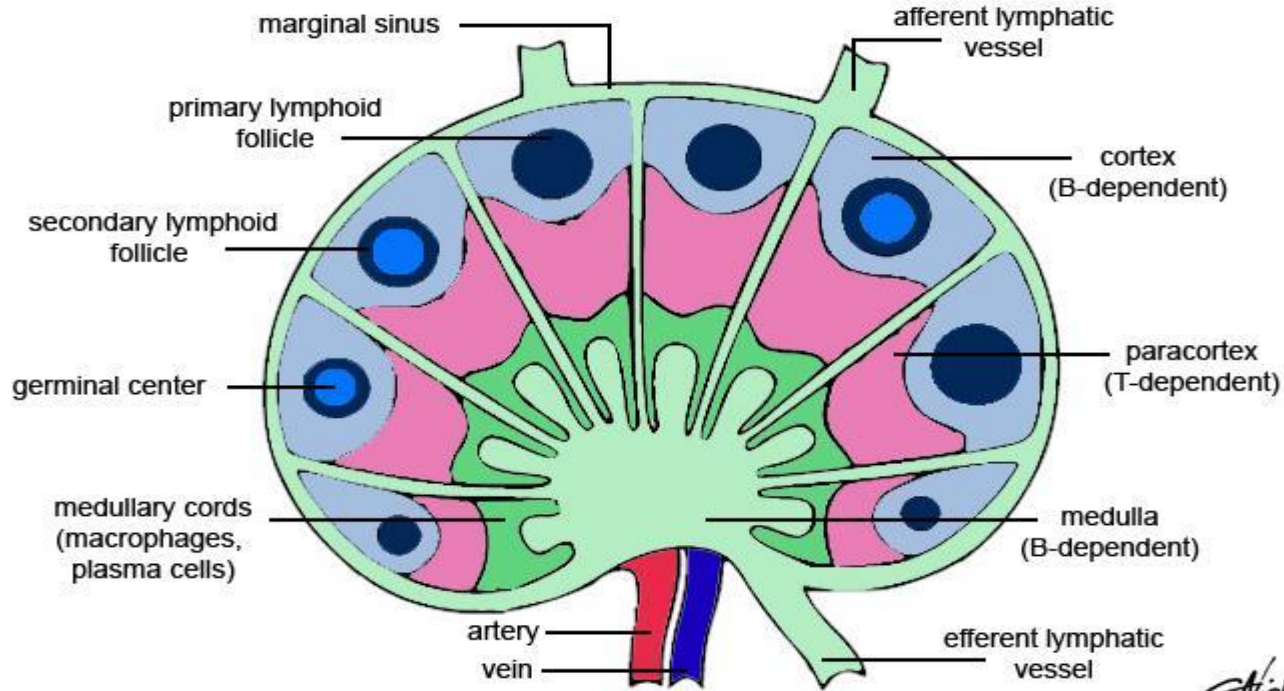
# Hematopoietic & Lymphoid System

## White Cell disorders



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6/4/2026

# Reactive Lymphadenitis



*E. Vigliani*

2.

# Neoplastic Proliferations of White Cells

**~ Lymphoid Neoplasms**

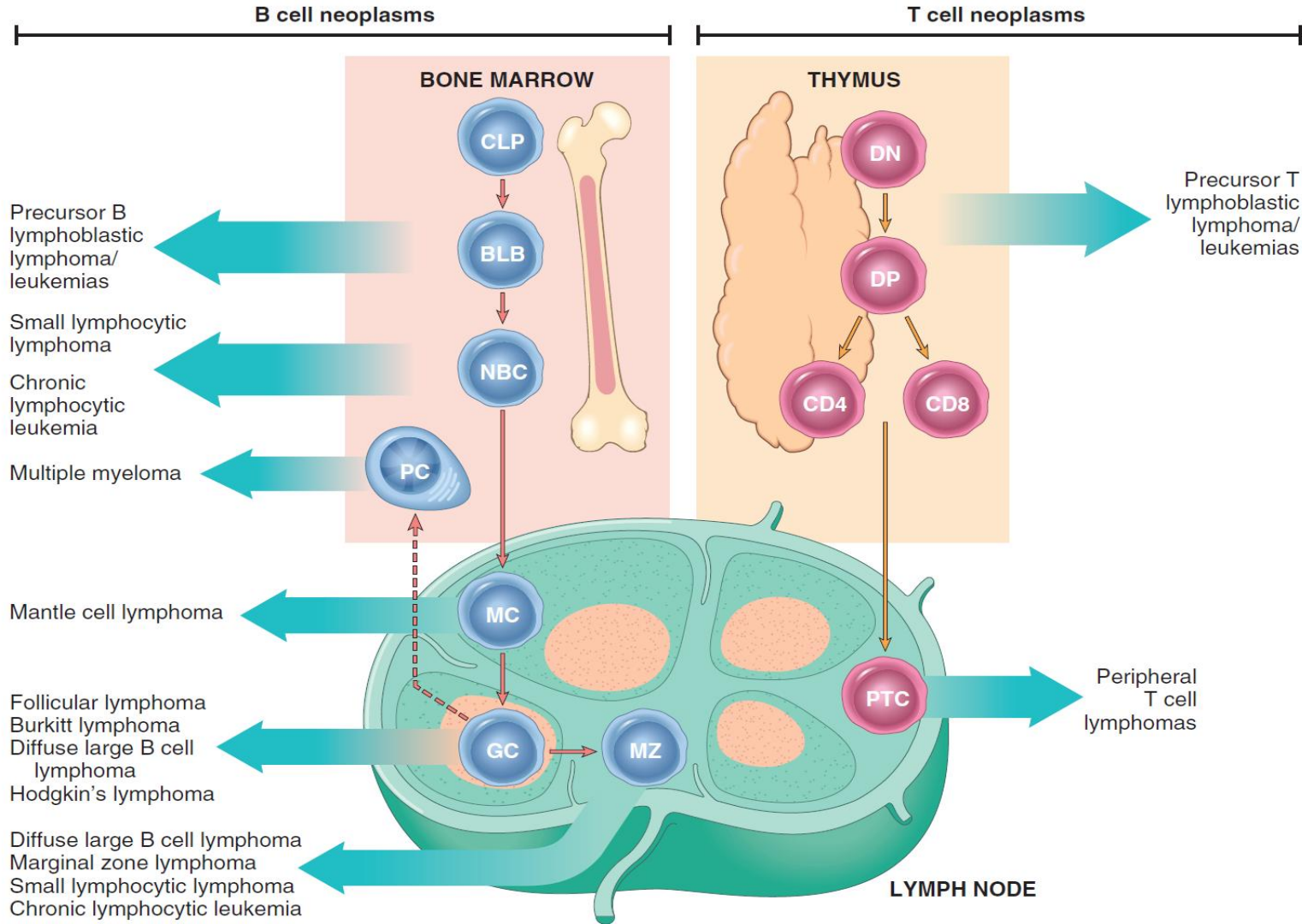
# Lymphoid Neoplasms

## They can manifest as:

- ✓ Leukemias: involvement of the bone marrow (BM) & the peripheral blood (PB) (usually, not always)
- ✓ Lymphomas: tumors that produce masses in lymph nodes or other tissues.
- ✓ Other (plasma cell neoplasm)
- ✓ All can spread to lymph nodes & other tissues (liver, spleen, bone marrow, and peripheral blood)

# Lymphoid Neoplasms

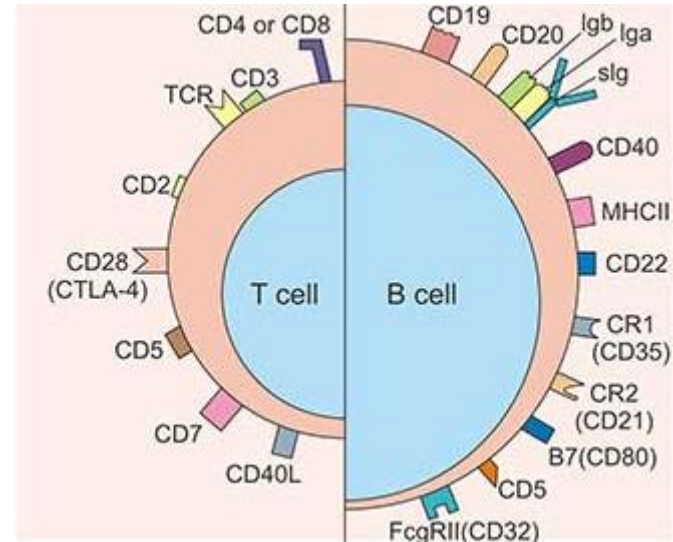
- ▶ B and T cell tumors are composed of cells that are **arrested at or derived from a specific stage** of normal lymphocyte differentiation
- ▶ Diagnosis & classification → rely on tests (immunohistochemistry or flow cytometry) that **detect lineage-specific antigens** (e.g., B cell, T cell, & NK cell markers) and markers of **maturity**.
- ▶ Many such markers are identified by their **cluster of differentiation (CD)** number. (e.g., CD8, CD4, or CD20).



# Lymphoid Neoplasms

- ▶ **Cluster of differentiation antigen (CD):** commonly used as cell markers in immunophenotyping, allowing cells to be defined based on what molecules are present on their surface.

- 1) B-cell markers: **CD19**, CD79, and CD20
  - 2) T-cell markers: CD3 (either CD4 or CD8)
- ▶ **TdT:** a marker of early lymphoid origin (B & T lymphoblasts)



# Lymphoid Neoplasms

- ✓ Upon antigen stimulation → B cells enter germinal centers → undergoes Class switching and Somatic hypermutation (Goal is: antibody Diversification)
- ✓ This is a mistake-prone forms of regulated genomic instability that place germinal center B cells at relatively high risk for potentially transforming mutations. (genetic errors that occur during antigen receptor gene rearrangement and diversification) → most of B-cell lymphomas.

# Lymphoid Neoplasms

- ▶ Lymphoid neoplasms and immune system function.
  - 1) Can cause **Immunodeficiency** ( ↑ susceptibility to infection).
  - 2) Can cause **Autoimmunity**
  - 3) **Inherited or acquired immune deficiencies** ↑ the risk for the development of certain lymphomas (usually EBV associated)

# Lymphoid Neoplasms

- ▶ So they are either B or T cell neoplasms.
- ▶ Two groups of lymphomas are recognized : Hodgkin lymphomas (HD) & non-Hodgkin lymphomas (NHL)
- ▶ The World Health Organization (WHO) has formulated a widely accepted classification scheme, relies on a combination of **morphologic, phenotypic, genotypic, and clinical features.**

# Lymphoid Neoplasms

## Precursor B Cell Neoplasms

*Precursor B cell leukemia/lymphoma (B-ALL)*

## Peripheral B Cell Neoplasms

*B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)*

B cell prolymphocytic leukemia

Lymphoplasmacytic lymphoma

*Mantle cell lymphoma*

Follicular lymphoma

Extranodal marginal zone lymphoma

Splenic and nodal marginal zone lymphoma

Hairy cell leukemia

Plasmacytoma/plasma cell myeloma

Diffuse large B cell lymphoma (multiple subtypes)

Burkitt lymphoma

## Precursor T Cell Neoplasms

*Precursor T cell leukemia/lymphoma (T-ALL)*

## Peripheral T/NK Cell Neoplasms

T cell prolymphocytic leukemia

T cell granular lymphocytic leukemia

*Mycosis fungoides/Sézary syndrome*

*Peripheral T cell lymphoma, unspecified*

Angioimmunoblastic T cell lymphoma

Anaplastic large cell lymphoma

Enteropathy-type T cell lymphoma

Panniculitis-like T cell lymphoma

Hepatosplenic  $\gamma\delta$  T cell lymphoma

Adult T cell lymphoma/leukemia

Extranodal NK/T cell lymphoma

Aggressive NK cell leukemia

## Hodgkin Lymphoma

*Nodular sclerosis*

*Mixed cellularity*

Lymphocyte-rich

Lymphocyte-depleted

Lymphocyte predominant

# Acute Lymphoblastic Leukemia/Lymphoma (ALL)

- ▶ Neoplasms composed of immature B (pre-B) or T (pre-T) cells → called **Lymphoblasts**.

- ▶ 85% B-cells , commonly manifest as acute LEUKEMIA

The most common cancer of children (Peak : 3 years)

- ▶ 15% T-cells, commonly manifest as thymic LYMPHOMA

Peak: adolescence

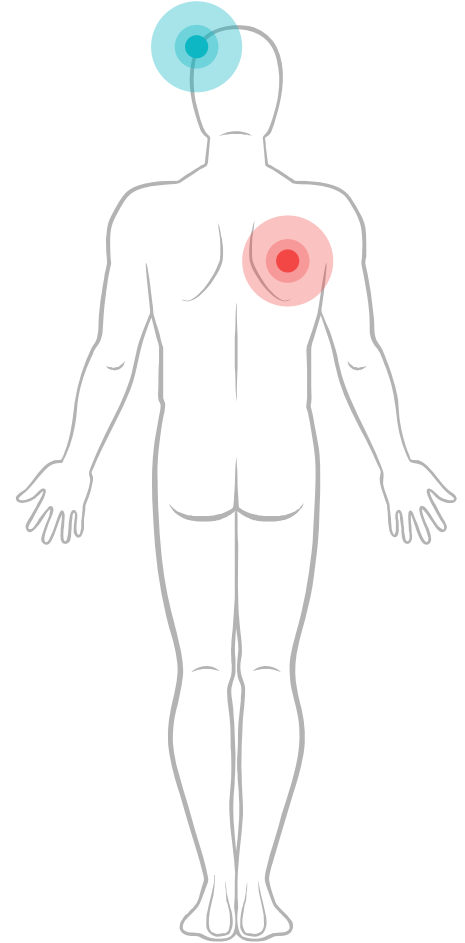
# Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Genetics

## Pre-B cell

- ▶ Hyperdiploidy (> 50 chromosomes/cell)
- ▶ t(12;21).
- ▶ t(9;22) involving *ABL* & *BCR* genes.

## Pre-T cell

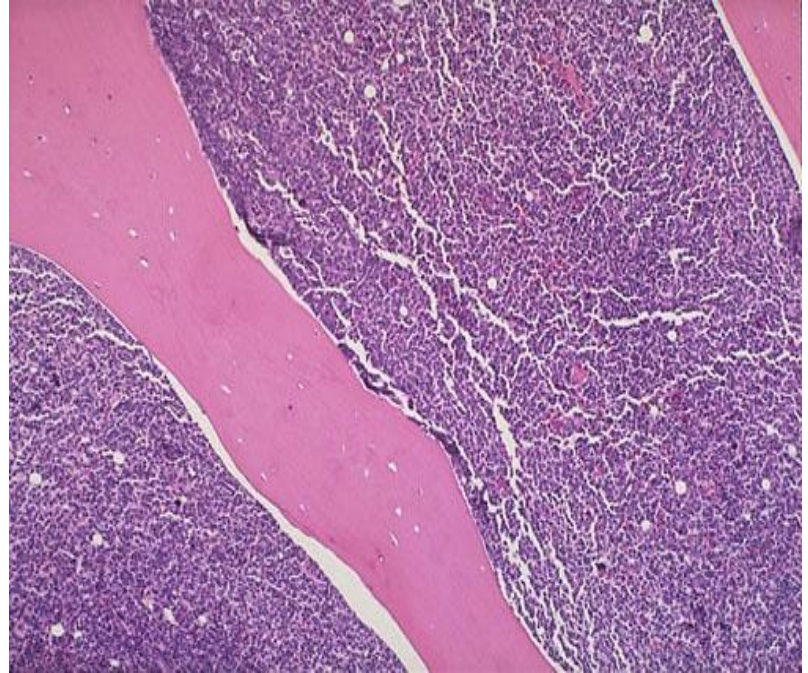
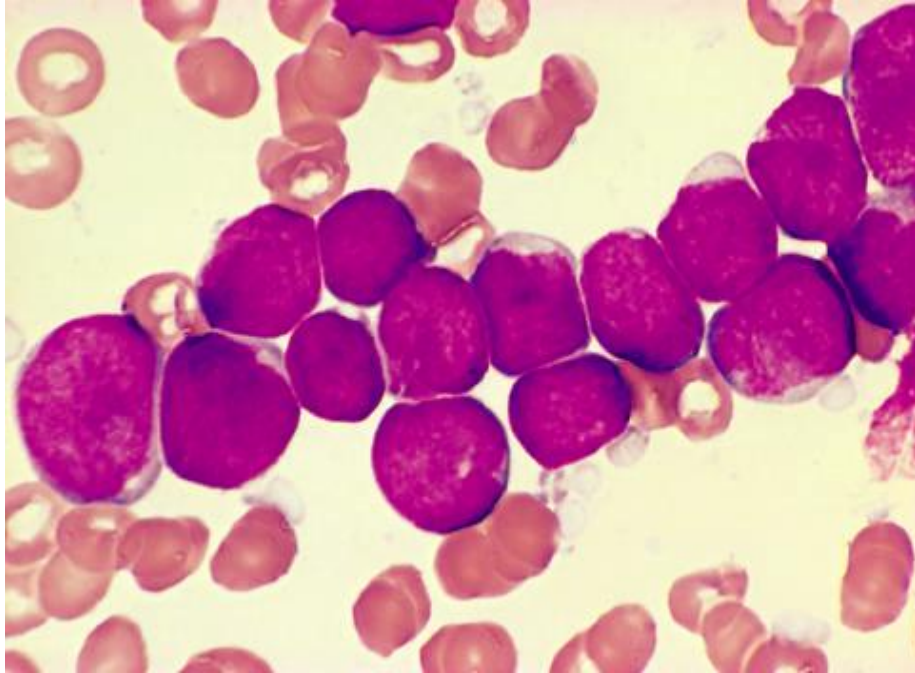
- ▶ NOTCH1 mutations
- ▶ CDKN2A mutations



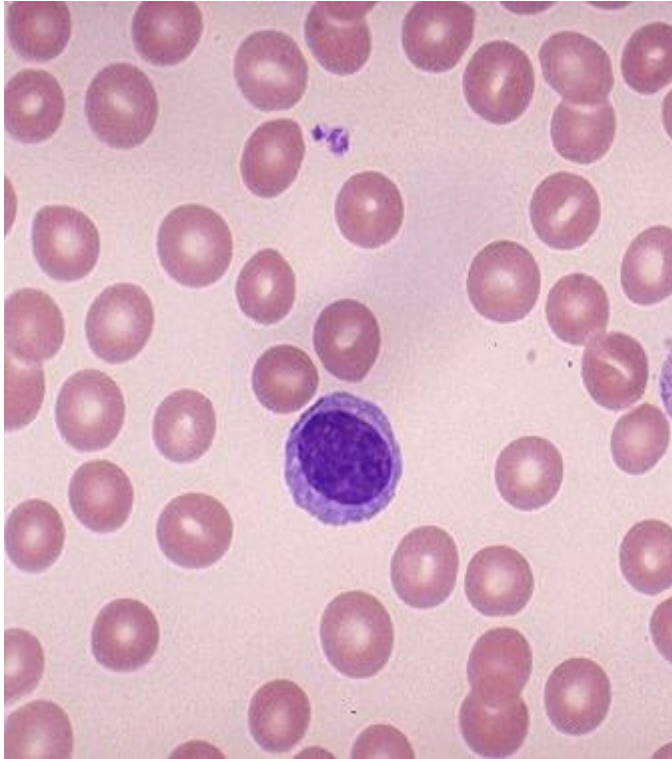
## Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Morphology

- ▶ **Leukemia** : the marrow is hypercellular & packed with lymphoblasts → replace normal marrow elements.
- ▶ **Lymphoma** : Mediastinal (thymic) mass & is more likely to involve lymph nodes & spleen.
- ▶ **Blasts**: scant basophilic cytoplasm and nuclei with delicate, finely stippled chromatin & small nucleoli.
- ▶ In pre-B & pre-T ALLs the blasts are identical in routine stains (immunophenotype is needed)

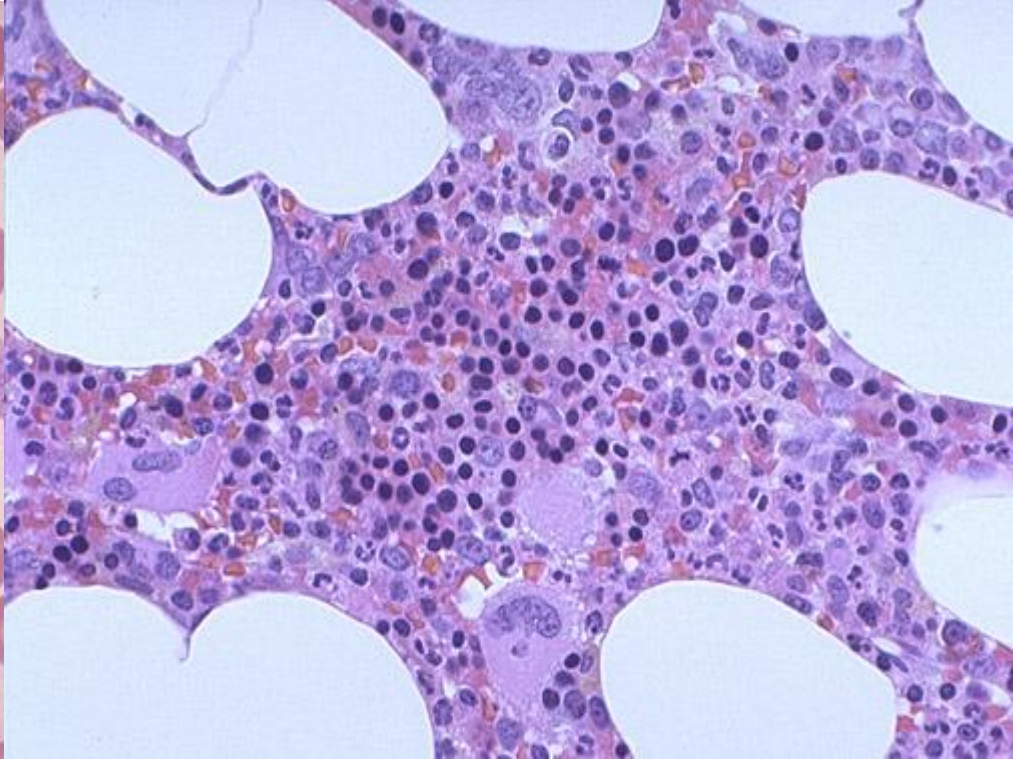
# Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Morphology



Normal mature lymphocyte



Normal bone marrow



## Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Clinical features

### ▶ Presentation:

- 1) Symptoms related to depression of marrow function; anemia, neutropenia & bleeding.
  - 2) Mass effects → neoplastic infiltration; bone pain
  - 3) CNS manifestations headache, vomiting, and nerve palsies.
- ▶ Aggressive but curable (85% cure rate in children), but remains the leading cause of cancer deaths in children

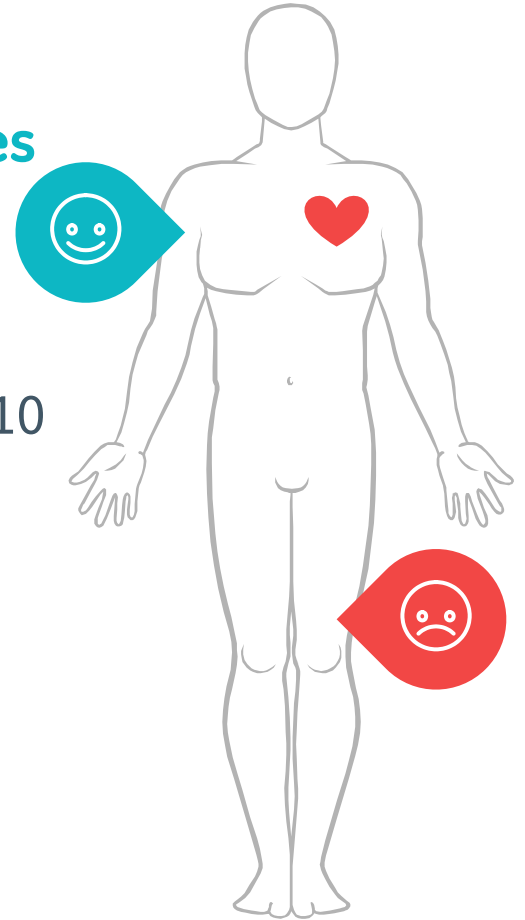
# Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Clinical features

## Worse prognosis

- ▶ Younger than 2
- ▶ Older than 10
- ▶ PB WBC count > 100,000
- ▶ t(9;22)

## Favorable prognosis

- ▶ Age between 2-10
- ▶ PB Low WBC count
- ▶ Hyperdiploidy
- ▶ t(12;21)



# Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

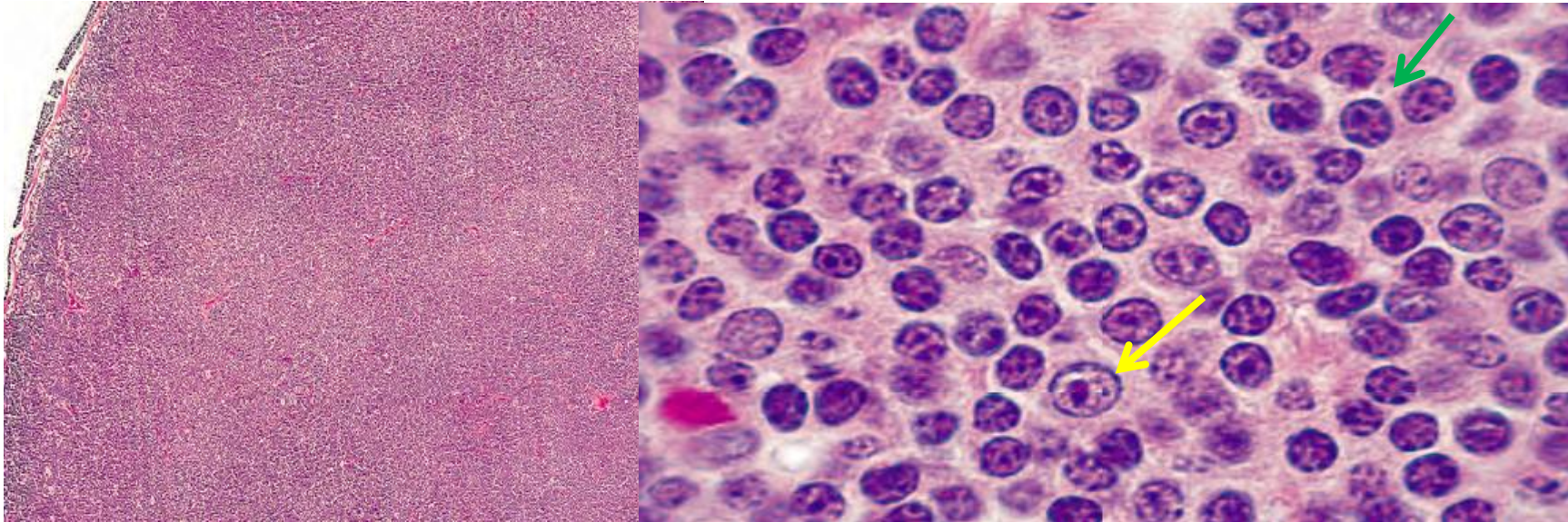
- ▶ An **indolent**, slowly growing tumor (increased tumor cell survival is more important than tumor proliferation)
- ▶ CLL & SLL are essentially identical.
- ▶ CLL → If PB involvement count exceeds 5000 cells/ $\mu\text{L}$
- ▶ The most common leukemia of adults in the West.

## Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) : Morphology

- ▶ Involved lymph nodes are effaced by:
  - 1) Sheets of small lymphocytes with dark, round nuclei, **clumped** chromatin & scanty cytoplasm.
  - 2) Small percentage of large lymphocytes with prominent centrally located nucleoli → **prolymphocytes**.

## Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) : Morphology

**Green** arrow: cells w Clumped chromatin & white areas in between conferring a “soccer ball” appearance. **Yellow** arrow : prolymphocytes



## Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) : Immunophenotype

- ▶ A neoplasm of mature B cells → expressing the CD20.
- ▶ The tumor cells also express CD5 (diagnostic clue, only SLL & MCL express it)

# Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) : Clinical features

- ▶ Old age. Often asymptomatic. But symptoms are nonspecific; easy fatigability, weight loss, anorexia, generalized lymphadenopathy & hepatosplenomegaly.
- ▶ Peripheral lymphocytosis ( $>5000$ )
- ▶ Indolent disease but cure may only be achieved with hematopoietic stem cell transplantation (HSCT)
- ▶ 10-15% develop autoimmune hemolytic anemia & thrombocytopenia.

# Follicular Lymphoma

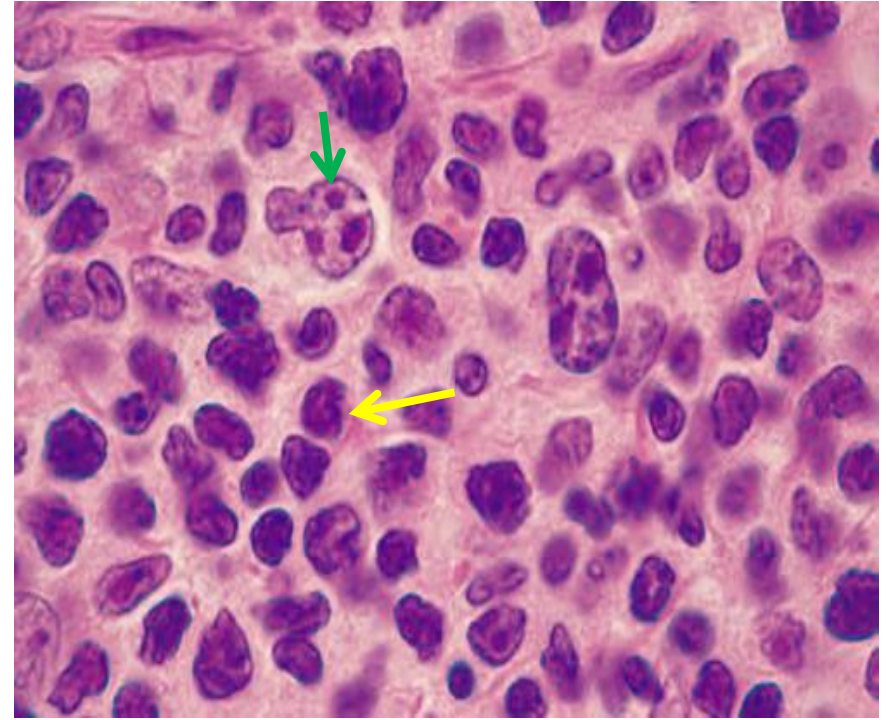
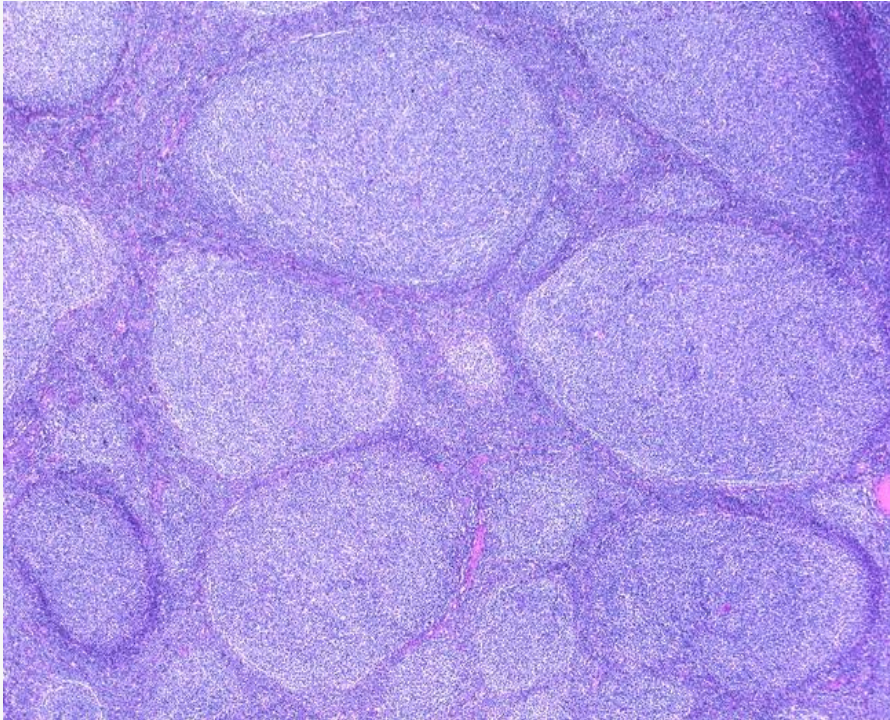
- ▶ Relatively common tumor → 40% of the adult NHLs
- ▶ **Pathogenesis:** a characteristic (14;18) translocation that fuses the BCL2 gene on chromosome 18 to the IgH locus on chromosome 14 → inappropriate “overexpression” of BCL2 protein (an inhibitor of apoptosis) → contributes to cell survival)

## Follicular Lymphoma - Morphology

- ▶ Lymph nodes usually are effaced by a distinctly nodular (follicular) proliferation
- ▶ Two types of neoplastic cells,
  - 1) the predominant called **centrocytes** have angular “cleaved” & indistinct nucleoli,
  - 2) the other **centroblasts**, larger cells with vesicular chromatin, several nucleoli.

# Follicular Lymphoma - Morphology

Centrocyte  
centroblast



## Follicular Lymphoma - Immunophenotype

- ▶ B-cells markers (mature B cell neoplasm).
- ▶ CD10 → GC marker (expressed in Burkitt lymphoma, B-ALL & some DLBCL)

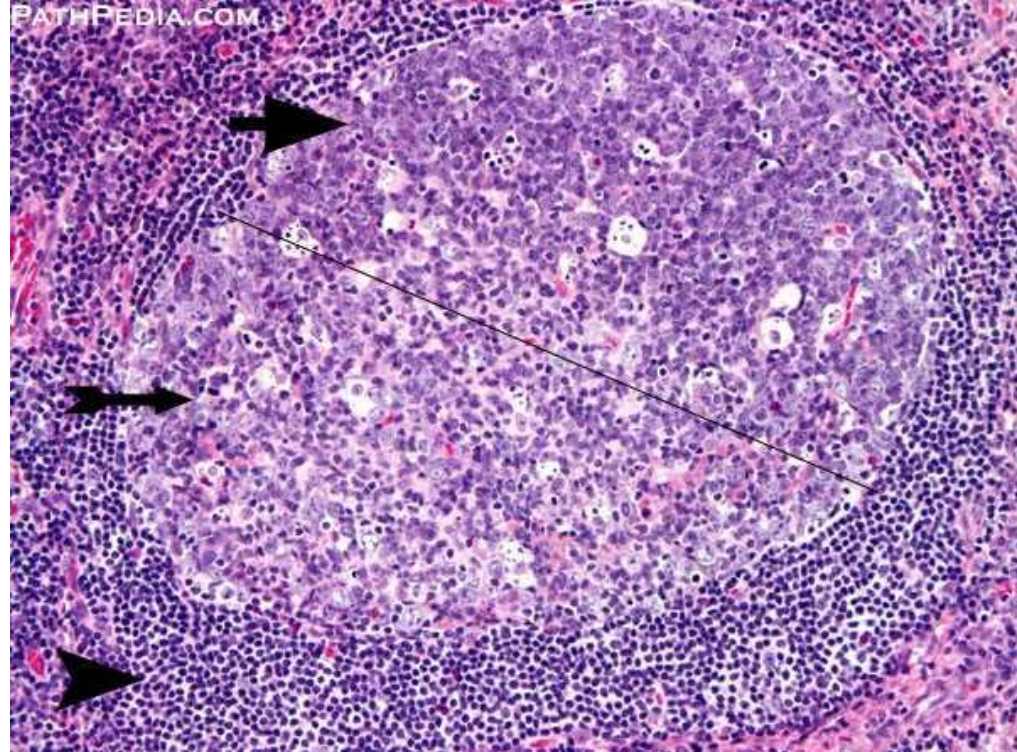
## Follicular Lymphoma - Clinical features

- ▶ Older than 50
- ▶ Generalized painless lymphadenopathy
- ▶ Bone marrow is involved in 80% of cases
- ▶ Prolonged survival, not curable disease (indolent)
- ▶ 40% transform into DLBCL, **dismal** prognosis

# Mantle Cell Lymphoma

- ▶ composed of cells resembling the naive B cells found in the mantle zones of normal lymphoid follicles.
- ▶ mainly in men older than 50 years of age

Normal GC, Arrowhead: mantle zone



## Mantle Cell Lymphoma – Pathogenesis & immuno.

- ▶ All tumors have an (11;14) translocation → fuses the cyclin D1 gene to the IgH locus → overexpression of cyclin D1 → stimulates growth by promoting the progression of cell cycle from G1 to S phases)
- ▶ **Immunophenotype:**
  - 1) B cell markers.
  - 2) CD5 (as CLL/SLL)
  - 3) Cyclin D1 ( not expressed in CLL/SLL)

## Mantle Cell Lymphoma – Morphology

- ▶ A diffuse involvement of the lymph node.
- ▶ The tumor cells are slightly larger than normal lymphocytes with irregular nucleus, inconspicuous (not clear) nucleoli.
- ▶ Bone marrow is involved in most cases.
- ▶ sometimes arises in the GIT as multifocal polyps (**lymphomatoid polyposis**).

## Mantle Cell Lymphoma – Clinical features

- ▶ Patients Present with fatigue & lymphadenopathy → found to have generalized disease involving the bone marrow, spleen, liver, and (often) GIT.
- ▶ Moderately aggressive & incurable.
- ▶ The median survival is 4-6

THANK YOU!