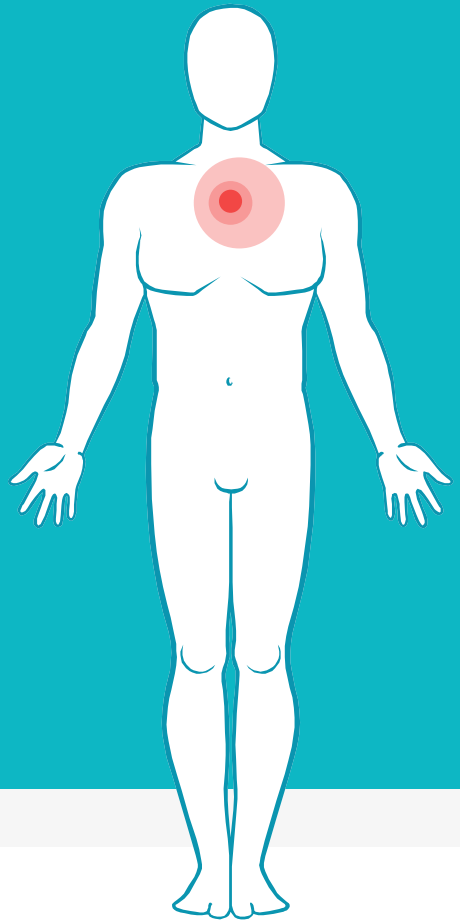
26/3/25

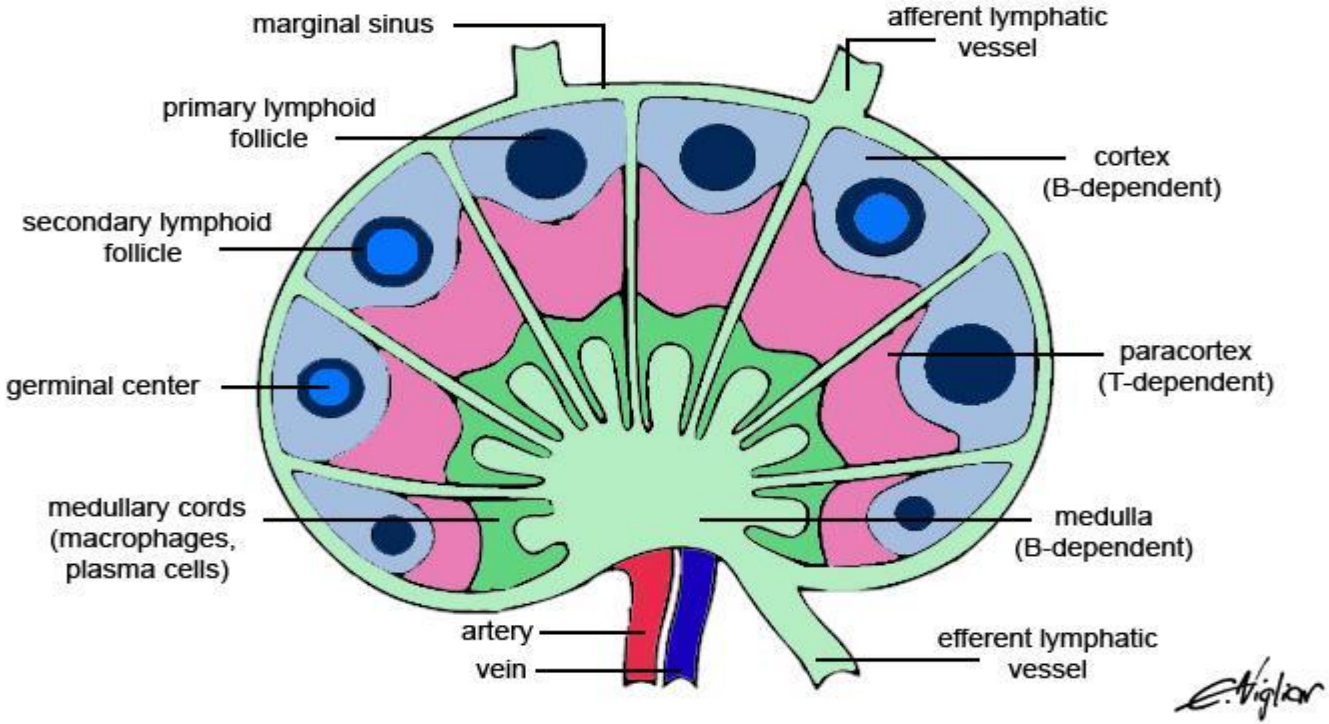
Hematopoietic & Lymphoid System

White Cell disorders



Ghadeer Hayel, M.D.
Assistant professor of Pathology
Mutah University
Consultant hematopathologist
3/26/2025

Reactive Lymphadenitis



- The most important disorders of white cells are neoplasms.
- Virtually all are considered to be malignant, but have a wide range of behaviors, ranging from the most aggressive cancers of man to indolent.
- As a group they are quite common.
- Occur at all ages , some preferentially affect infants, children, young adults, & the very old.
- In our discussion we'll divide them into three broad categories based on the **cell of origin** & differentiation of tumor cells:

1) Lymphoid neoplasms.

2) Myeloid neoplasms.

3) Histiocytic neoplasms

2.
Neoplastic Proliferations of White Cells

~ Lymphoid Neoplasms

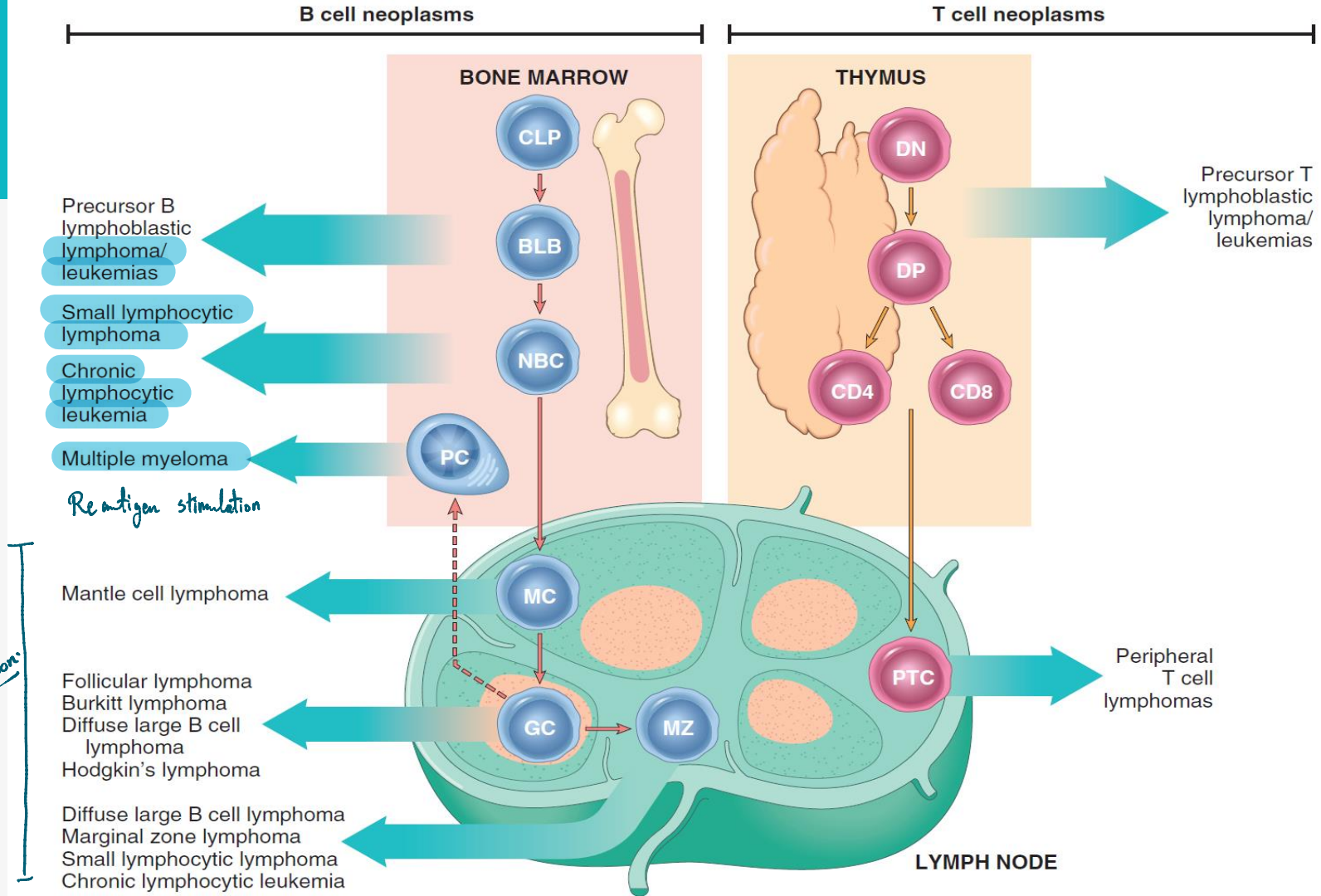
Lymphoid Neoplasms

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).

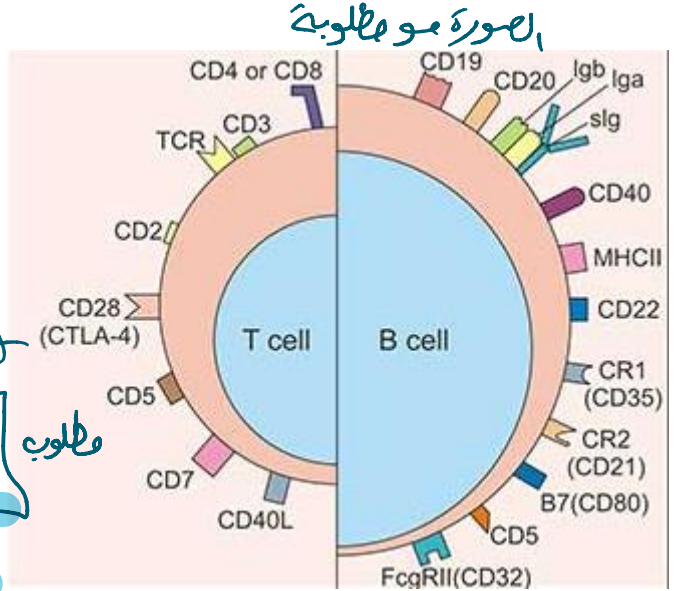

B cell neoplasms
T cell neoplasms
BONE MARROW
THYMUS
CLP
BLB
NBC
PC
DN
DP
CD4
CD8
Precursor B lymphoblastic lymphoma/ leukemias
Small lymphocytic lymphoma
Chronic lymphocytic leukemia
Multiple myeloma
Re antigen stimulation
Precursor T lymphoblastic lymphoma/ leukemias
Mantle cell lymphoma
MC
Follicular lymphoma
Burkitt lymphoma
Diffuse large B cell lymphoma
Hodgkin's lymphoma
GC
MZ
PTC
Peripheral T cell lymphomas
Diffuse large B cell lymphoma
Marginal zone lymphoma
Small lymphocytic lymphoma
Chronic lymphocytic leukemia
LYMPH NODE
Differentiation

Lymphoid Neoplasms

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

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)
  precursor / immature.



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

As a result of lymphoma.

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.

Molecular changing

Lymphoid Neoplasms

مشى لعنا
بس عشان
نعرف العدد انه
كبير

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)

Common الأطفال والمراهقين (Adolescent)

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

arrest of maturation.

pre-B من BM

pre-T من Thymus

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

only بشكل

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

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

Peak: adolescence

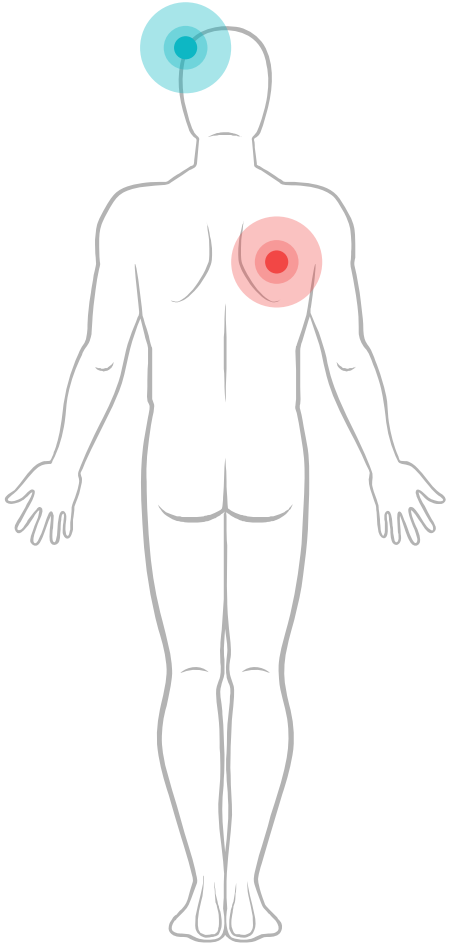
Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Genetics

Pre–B cell

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

Pre–T cell

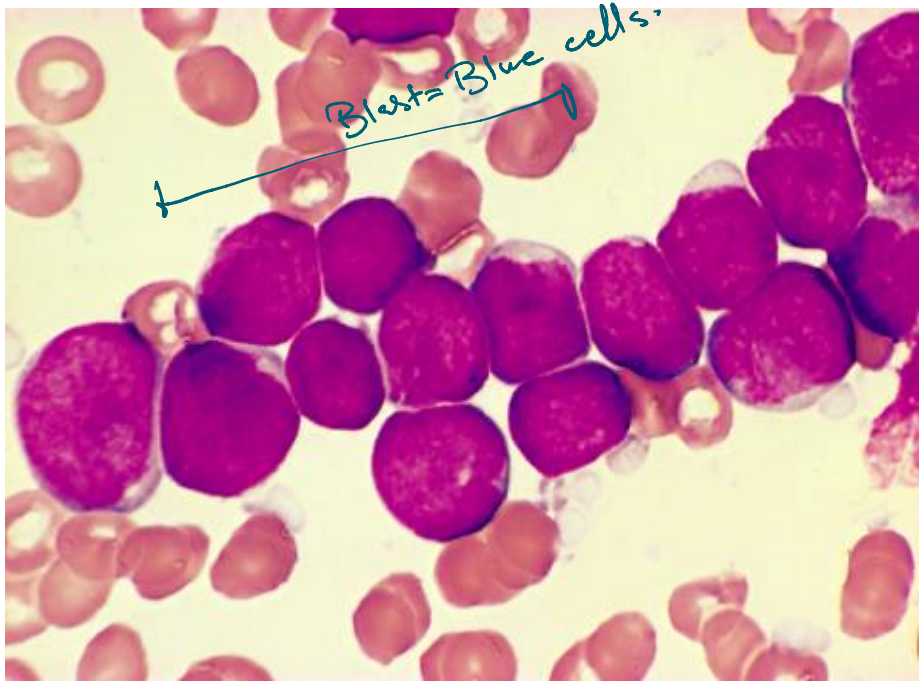
- NOTCH1 mutations
- CDKN2A mutations

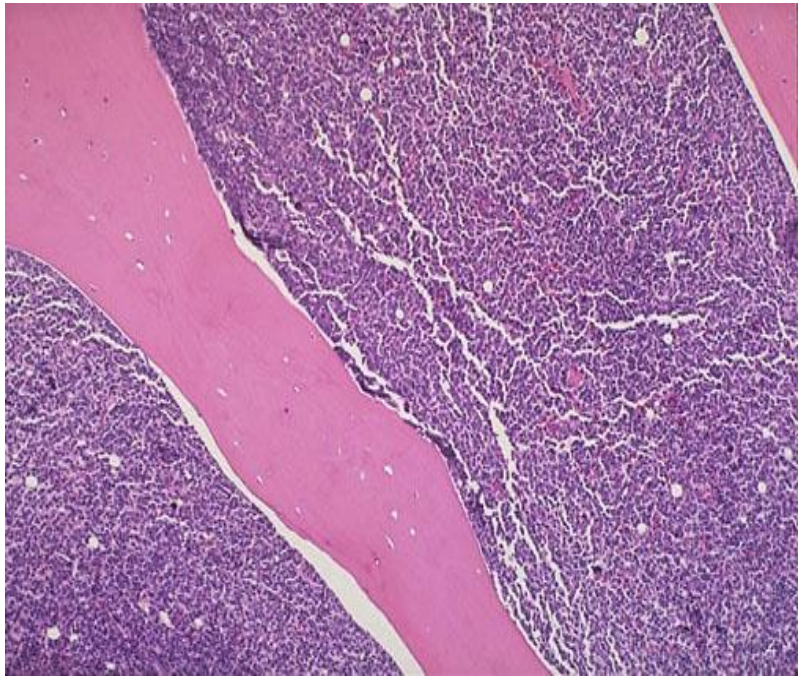


Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Morphology

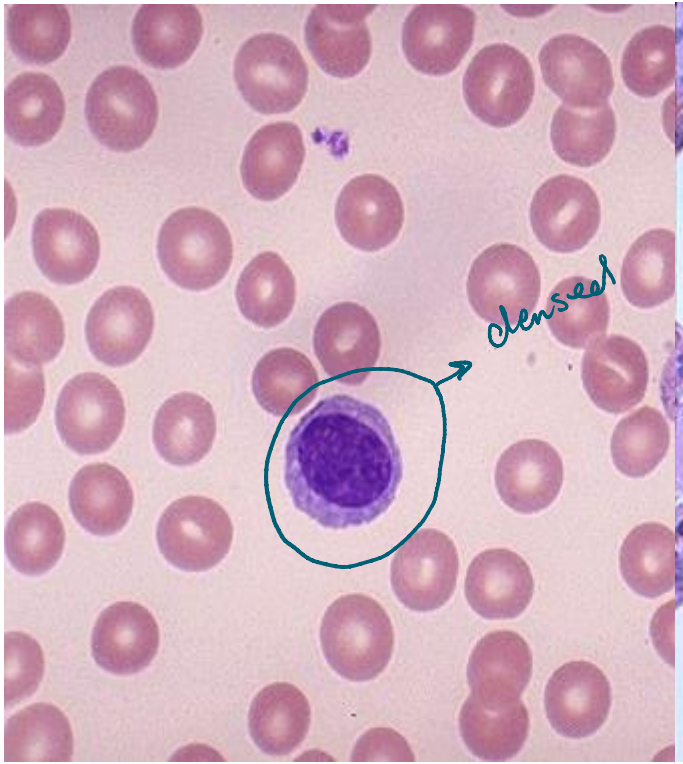
- Leukemia : the marrow is hypercellular & packed with lymphoblasts → replace normal marrow elements.
- Lymphoma : Mediastinal (thymic) mass & is more likely to involve lymph nodes & spleen.
- Blasts: scant basophilic cytoplasm and nuclei with delicate, finely stippled chromatin & small nucleoli.
- In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

Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Morphology

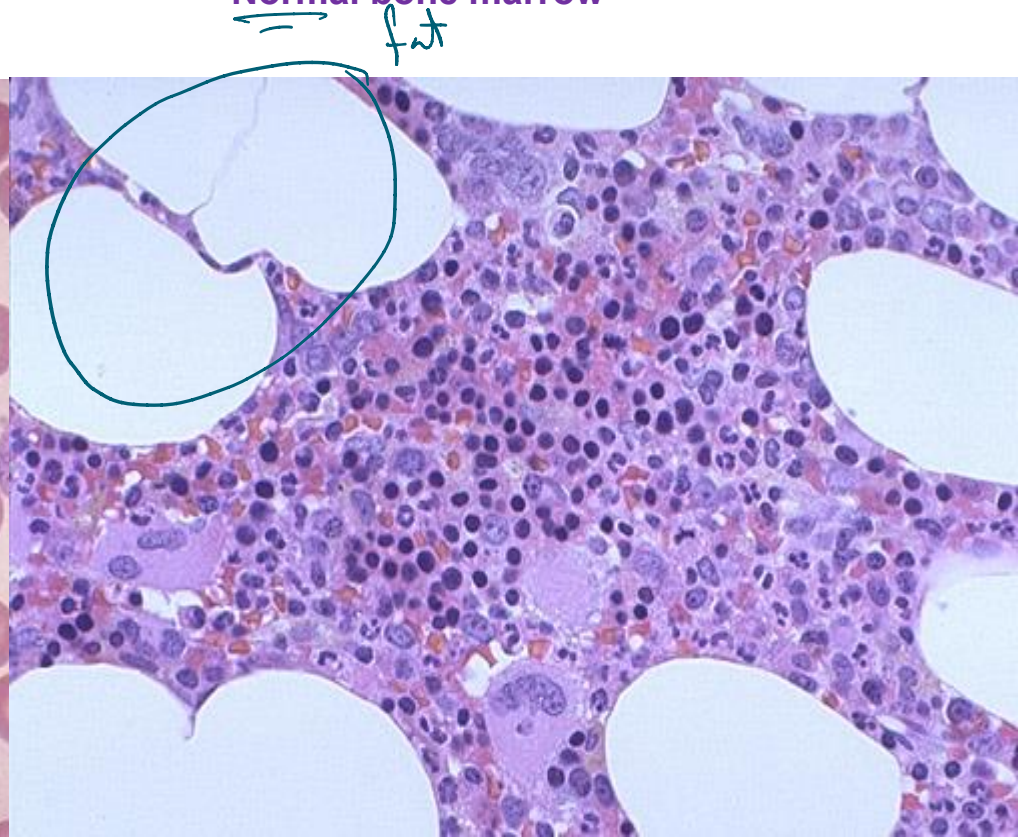




Normal mature lymphocyte



Normal bone marrow



Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Clinical features

- **Presentation:** In cases of replacement.

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

good prognosis in high chemotherapy.

Acute Lymphoblastic Leukemia/Lymphoma (ALL) : Clinical features

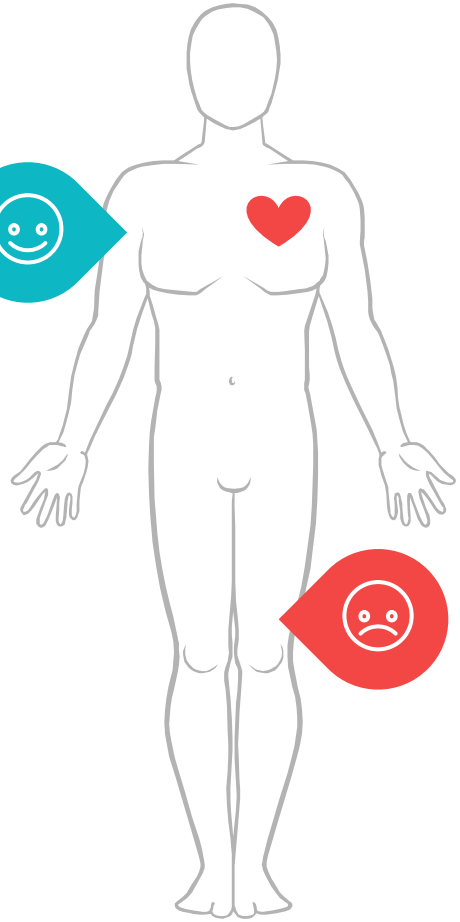
حسب الحجم دكتور كيف عم نميز المريض وبشو أعالجه

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/μL
- The most common leukemia of adults in the West.

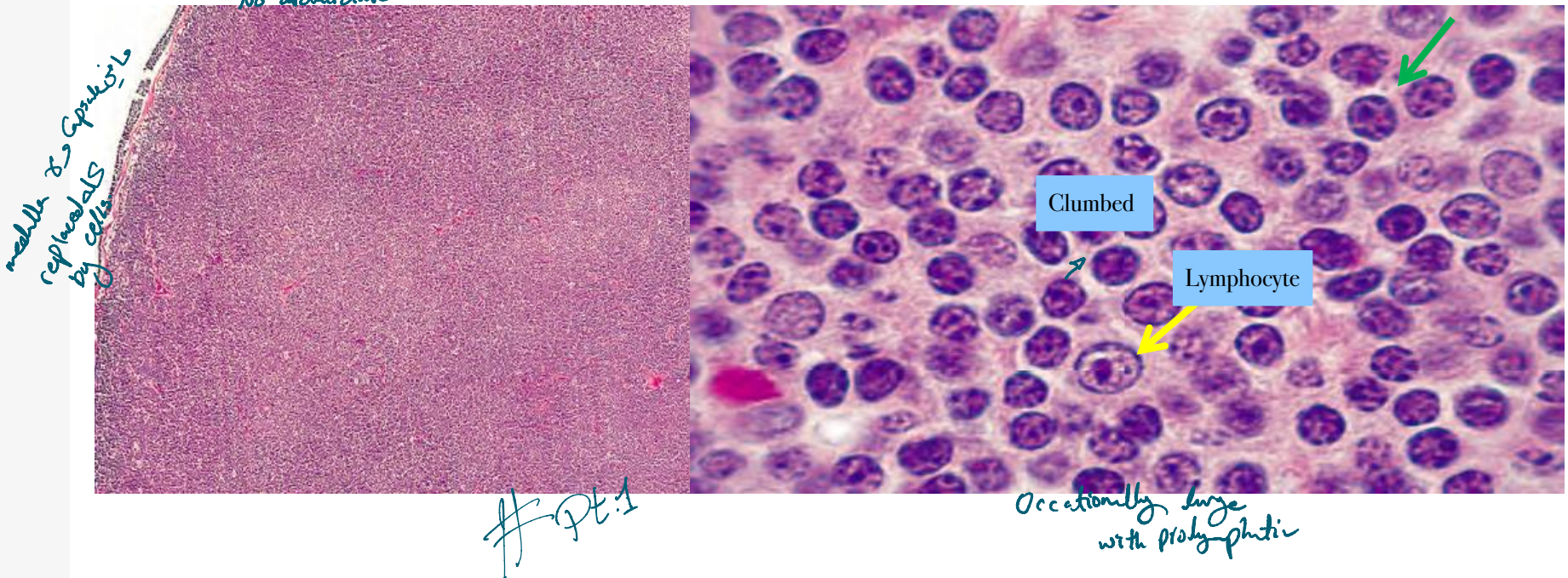
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) : Morphology

- 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



27/3/25

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)

↓ Marker of B cells.

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

- Old age. Often asyptomatic. 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

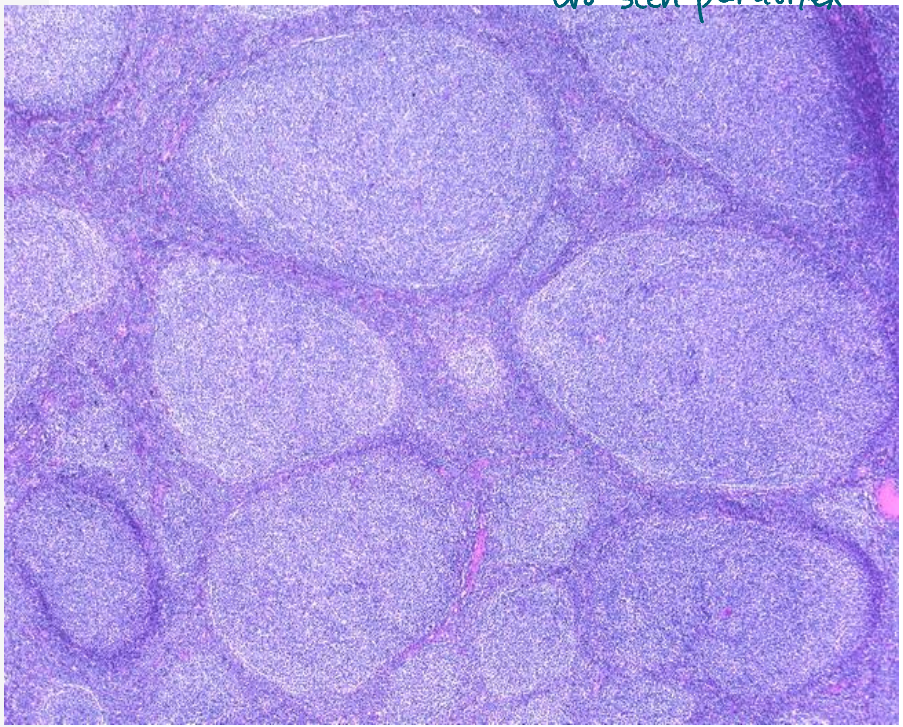
- Lymph nodes usually are effaced by a distinctly nodular (follicular) proliferation
- Two types of neoplastic cells,

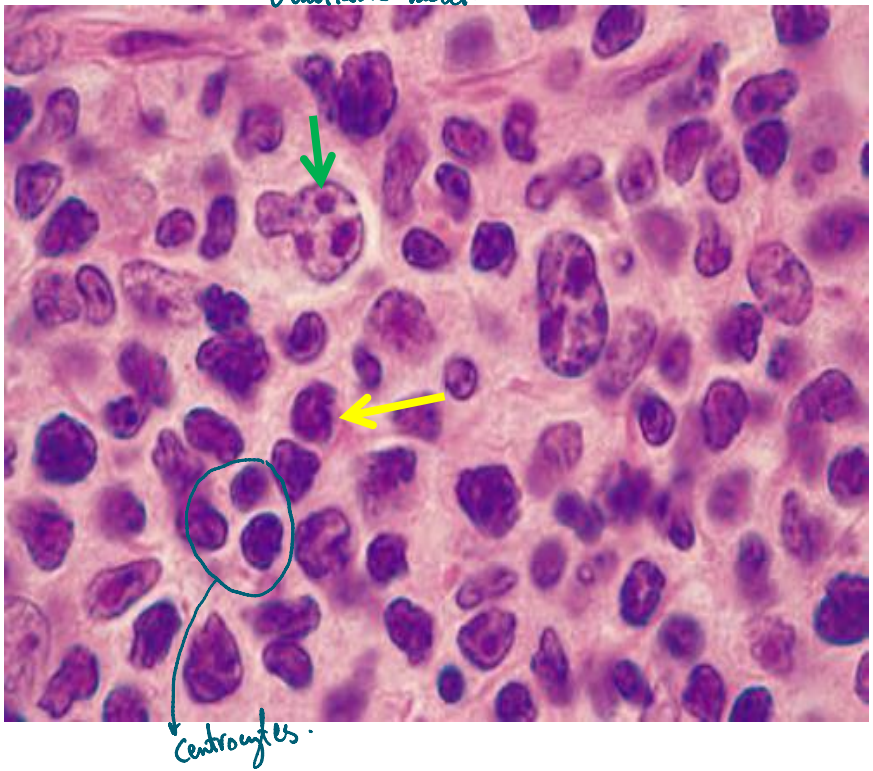
1) the predominant called centrocytes have angular "cleaved" & indistinct nucleoli,
2) the other centroblasts, larger cells with vesicular chromatin, several nucleoli.

Very dark و طعوجلة

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)

germinal center marker

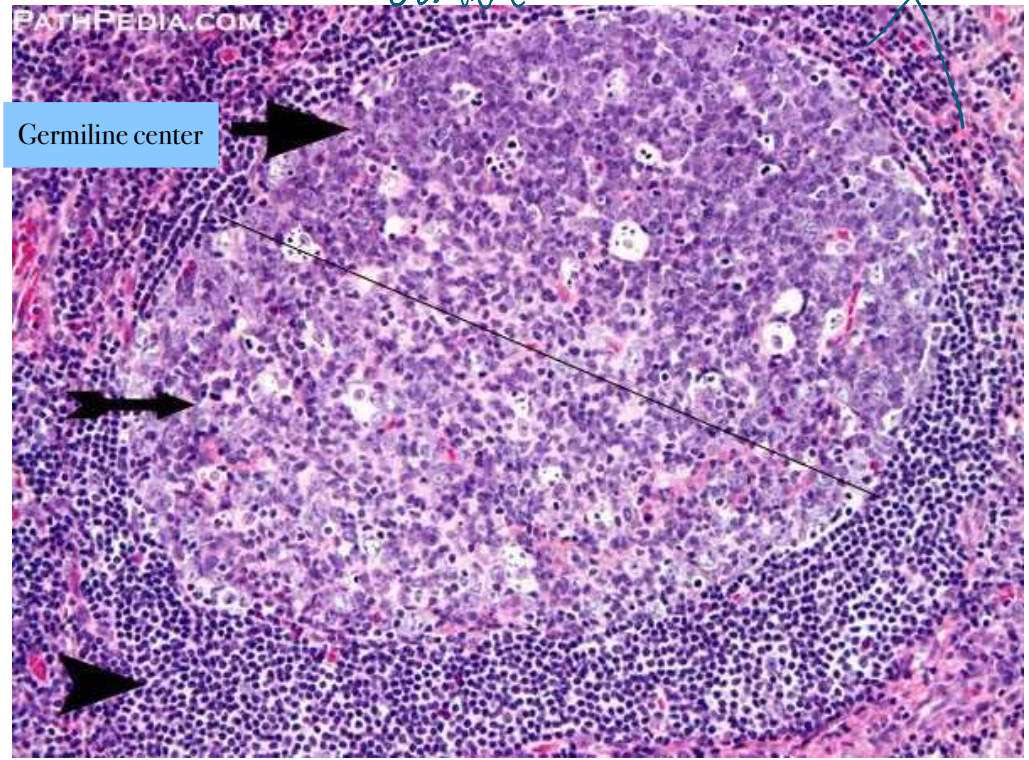
Blast → TBT

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



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

Mildly aggressive

- 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