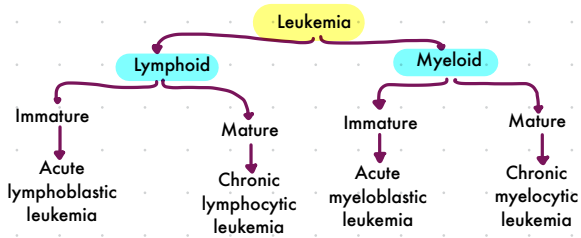
Neoplastic Proliferationsof White Cells

General definitions:

leukemia: lymphoid or myeloid neoplasm originated from bone marrow and can spread to peripheral blood (not always)

lymphoma: Discrete tumor mass originated from lymph nodes. And they are two types Hodgkin (HL) and Non Hodgkin (NHL)

Both of them can spread to other regions as:
(LN,BM, spleen, liver, etc...)



Note:

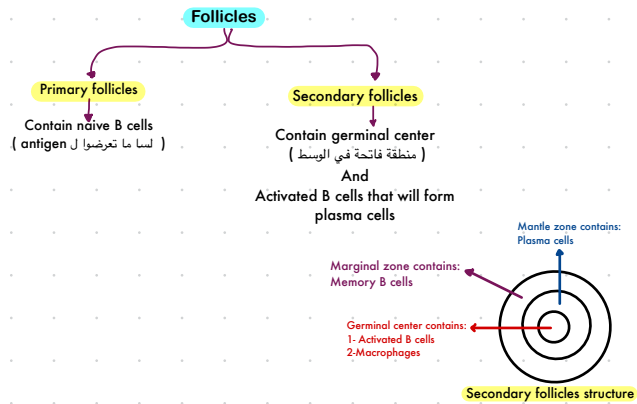
leukemia can be from immature cells (lymphoblastic or myeloblastic)
or mature cell (Lymphocytic or myelocytic)
* if it's immature we call it Acute
* if it's mature we call it chronic

Remember:

* B cells formed and become mature in bone marrow
-After that B cells stay in follicles of LN.
* T cells formed in bone marrow, mature in thymus
-After that T cells stay in parafollicular area of LN.

*WBCs neoplasms:

1-Common neoplasms. 2-Range from aggressive to indolent
3-Can occur at all ages



Why B cells neoplasms are more than T cells neoplasms ?

Because B cells in germinal centers undergo class switching and somatic hypermutation (the process of forming specific antibody to the antigen "Antibody diversification"
And this process involves a lot of mutations on antigen receptor to reach the most specific AB-> that's why B cell neoplasms are more common.

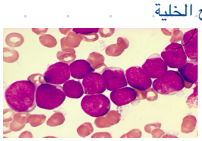
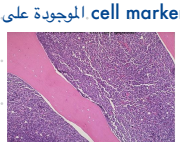
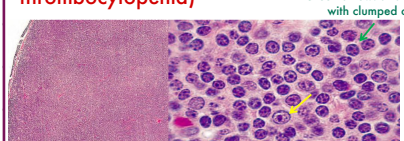
Patients who have lymphoid neoplasms are:

1-Immunodeficient 2-Can have autoimmunity
3-Can have inherited or acquired immune deficiencies; so increased risk of lymphomas (usually EBV associated)

ال tumor يعتمد على المرحلة إلي طلع منها لأنه كل tumor يتكون من
(Cells that arrested at or derived from specific stage of lymphocyte differentiation)

التشخيص يعتمد على ال immunohistochemistry and flow cytometry عشان أحدد مَن الخلية المتأثرة بالزبط

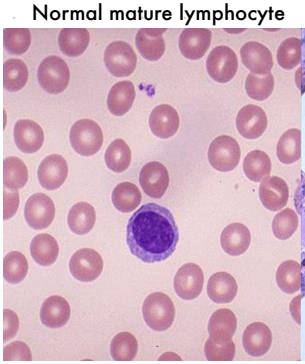
Lymphocytes contain cell markers:
1- CD19,CD20,CD21,CD79—>B cells
2- CD3,CD4—>T helper cells
3- CD3,CD8—>T cytotoxic cells
4- TdT: marker of early lymphoid origin "immature" (T and B lymphoblast)

	Acute lymphoblastic leukemia / lymphoma (ALL)	Chronic lymphocytic leukemia / Small lymphocytic lymphoma (CLL / SLL)
Cells involved	Immature B or T cells (preB, preT)= lymphoblasts 85% B cells commonly manifest as acute leukemia 15% T cells commonly manifest as thymic lymphoma	Mature B or T cells= lymphocytes But B cells more commonly affected *CLL and SLL are essentially identical
Affected Persons	B cells are commonly affected in children (peak: 3years) T cells are commonly affected in adolescence	It's the most common leukemia of Adults in the west It also affects old age
Cause of neoplasms	**Pre-B cell:** ▷ Hyperdiploidy (> 50 chromosomes/cell) ▷ t(12;21). Good prognosis ▷ t(9;22) involving ABL & BCR genes. **Pre-T cell:** ▷ NOTCH1 mutations ▷ CDKN2A mutations	It's an indolent tumor (increase tumor cells survival more important than tumor proliferation) " الفكرة في هذا tumor مش إنه زادت عملية تصنيع الخلايا بقدر ما الخلايا صاروا مقاومين لعملية ال apoptosis و هذا أدى إلى زيادة عددهم "
Histologic features	Leukemia → BM is hypercellular and packed with lymphoblast → Lymphoblast replace BM Lymphoma → There will be mediastinal thymic mass → More likely to infiltrate LNs and spleen **Lymphoblast:** 1- Scant basophilic cytoplasm 2- Nucleus with delicate, finely stippled chromatin 3- Small nucleoli من ناحية ال histology مش رح نقدر نميز هل هي T or B لنعرف immunophenotype عشان هيك نتّجه lymphoblast الموجودة على سطح الخلية cell markers  Abnormal lymphoblast  Abnormal BM CBC: 1- Low RBC 2- Low platelets 3- Low or increased WBCs but even if they are increased they are unfunctional	Lymphocytic count >5000 cells/ML *Incidentally found tumor Neoplasm of mature B cells express CD20 This tumor express CD5 (diagnostic feature) If lymph nodes are involved they will have: 1- Small lymphocytes with: *Scanty cytoplasm *Dark,round nuclei *Clumped chromatin 2-Large Lymphocytes (prolymphocytes) with: *prominent centrally located nucleoli Small lymphocytes > prolymphocytes **10-15% develop (Autoimmune hemolytic anemia and thrombocytopenia)  Green arrow: small lymphocytes with clumped chromatin Yellow arrow: Prolymphocytes
Clinical symptoms	1) Depression of marrow function leading to: 1- Anemia 2- Neutropenia 3- Bleeding 2) Mass effects → neoplastic infiltration; bone pain 3) CNS manifestations 1-Headache 2-Vomiting 3- Nerve palsies ▷ Aggressive but curable (85% cure rate in children) **Leading cause of cancer deaths in children	Often asyptomatic. But symptoms are nonspecific 1- Easy fatigability 2-Weight loss 3-Anorexia, 4-Generalized lymphadenopathy 5- Hepatosplenomegaly.

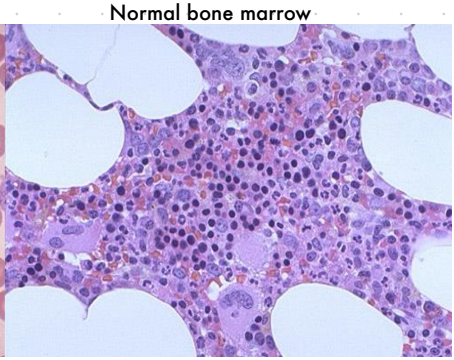
Prognosis	**Worse prognosis** ▷ Younger than 2 ▷ Older than 10 ▷ PB WBC count >100,000 ▷ t(9;22)	**Favorable prognosis** ▷ Age between 2-10 ▷ PB Low WBC count ▷ Hyperdiploidy ▷ t(12;21)	**Cure may only be achieved with hematopoietic stem cell transplantation (HSCT) **Note:** Mantle cell lymphoma can also express CD5 as CLL/SLL

when diagnosing:
**Leukemia —> We use bone marrow biopsy
↳ But in CLL we use flow cytometry
**lymphoma —> We use lymph node biopsy

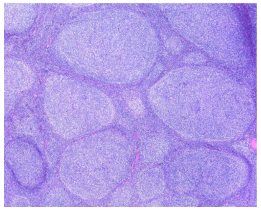
Normal mature lymphocyte

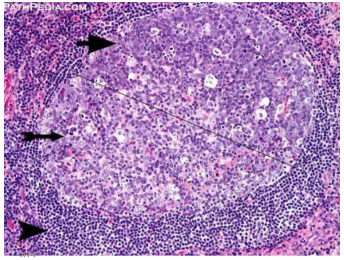


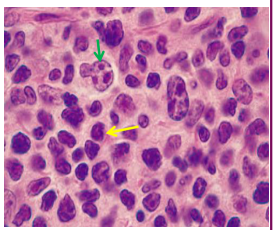
Normal bone marrow



	Follicular Lymphoma	Mantle Cell Lymphoma
Cells involved		composed of cells resembling the naive B cells found in the mantle zones of normal lymphoid follicles.
Affected Persons	Relatively common tumor ↳ 40% of the adult NHLs	mainly in men older than 50 years of age
Cause of neoplasms	characteristic (14;18) translocation fuses the BCL2 gene on chromosome 18 to the IgH locus onchromosome 14 - inappropriate "overexpression" of BCL2 protein (an inhibitor of apoptosis) -> contributes tocell survival) indolent B cell lymphoma	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)
Histologic features	Lymph nodes usually are effaced by a distinctly nodular (follicular) proliferation B-cells markers (mature B cell neoplasm). CD10 → GC marker (expressed in Burkitt lymphoma, B-ALL & some DLBCL) ▸ 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.	▸ **Immunophenotype**: 1) B cell markers. 2) CD5 (as CLL/SLL) 3) Cyclin D1 (not expressed in CLL/SLL) ▸ 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**).
Clinical symptoms	▸ 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	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







صح وجوده اكثر

Centrocyte
centroblast