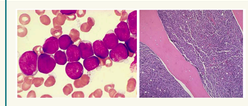
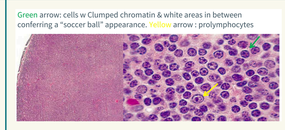
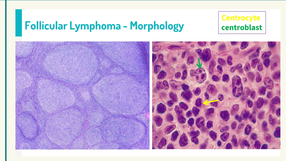
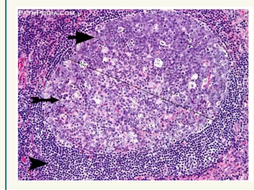
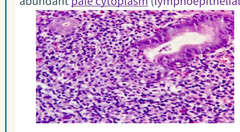
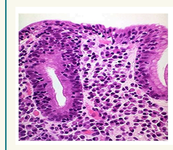
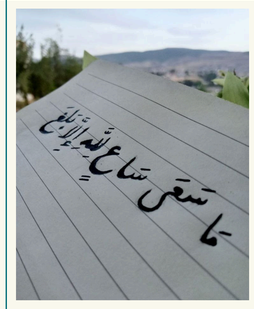
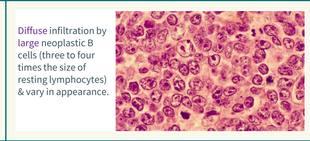
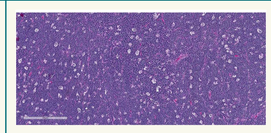
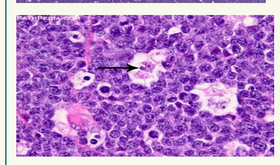
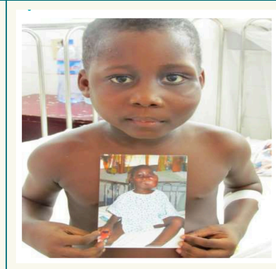
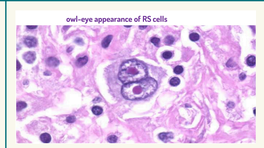
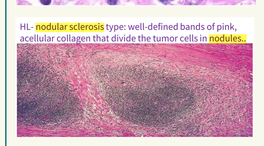
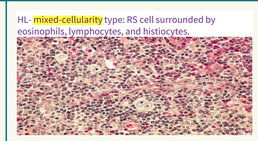
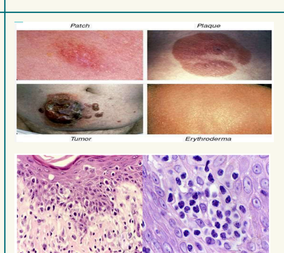
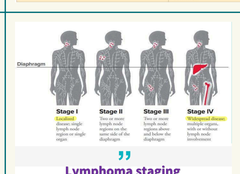
Lymphoid Neoplasms

	description	pathogenesis	morphology	Immunophenotype	clinical fatures	histology	notes
ALL	Neoplasms composed of immature B (pre-B) or T (pre-T) cells called **Lymphoblasts**.	**Pre-B cell** ▹ Hyperdiploidy (> 50 chromosomes/cell) ▹ t(12;21). ▹ t(9;22) involving *ABL* & *BCR* genes. **Pre-T cell** ▹ NOTCH1 mutations ▹ CDKN2A mutations	▹ **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)		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		**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)
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.		▹ 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.**	▹ A neoplasm of **mature B cells** (expressing the CD20). ▹ The tumor cells also express **CD5** (diagnostic clue, **only SLL & MCL express it**) MCL = mantle cell lymphoma	▹ **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 NHL = Non-Hodgken lymphoma	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	▹ 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.	▹ **B-cells markers** (mature B cell neoplasm). ▹ **CD10** = GC marker (expressed in Burkitt lymphoma, B-ALL & some DLBCL) GC = germinal center	▹ **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** N.B : lymphadenopathy caused from non-inflammatory process usually painless (from record lec 7 by dr.Ghadeer)		
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** N.B : mantle zone = zone around follicles, filled by naive B-cells	▹ 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)	▹ 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).**	1) **B cell markers.** 2) **CD5** (as CLL/SLL) 3) **Cyclin D1** (not expressed in CLL/SLL)	▹ 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**		**Cyclin D1 distinguish between MZL & CLL/SLL**
Extranodal Marginal Zone Lymphoma	▹ An **indolent** B cell tumor arises most commonly **in epithelial tissues** (e.g. GIT, salivary glands, lungs, orbit, & breast) ▹ an example of a cancer arises within & is sustained by chronic inflammation: 1) **autoimmune disorders** (salivary gland in Sjögren syndrome & thyroid gland in Hashimoto thyroiditis) 2) **Chronic infection** (such as H.pylori gastritis). N.B : MALToma are type of this cancer when infiltration in gastric epitheilium		▹ B-cells characteristically infiltrate the epithelium of involved tissues (in small aggregates) 👉 called **lymphoepithelial lesions.** ▹ Characteristic features: tumor cells accumulate **abundant pale cytoplasm** or exhibit plasma cell differentiation. ✅ Gastric MZL (MALT lymphoma) showing intraepithelial atypical lymphocytes (lymphoepithelial lesion) and plasma cell differentiation in the lamina propria. ✅ Another MALT lymphoma where tumor cells accumulate abundant pale cytoplasm (lymphoepithelial lesion)	**B-cell markers.**	▹ Present as **swelling** of the salivary gland, thyroid or orbit or are discovered incidentally in the setting of H. pylori–induced gastritis. ▹ When localized, they are often **cured** by simple excision followed by radiotherapy.	Another MALT lymphoma where tumor cells accumulate abundant pale cytoplasm (lymphoepithelial lesion)   Gastric MZL (MALT lymphoma) showing intraepithelial atypical lymphocytes (lymphoepithelial lesion) and plasma cell differentiation in the lamina propria.	
Diffuse Large B Cell Lymphoma	▹ **Most common adult lymphoma** ▹ **Either de novo or transformation from other low grade tumors (follicular lymphoma).**	Most of them = Mutations & rearrangements of the **BCL6 gene** 👉 increased levels of BCL6 protein (an important transcriptional regulator of gene expression) in GC B-cells.	**Diffuse infiltration** by large neoplastic B cells (three to four times the size of resting lymphocytes) & vary in appearance. N.B : it has **polymorphism charecteristic** (from record)	**B-cell markers**, CD10 in some tumors	▹ **Median > 60 years of age** (but Can occur at any age) ▹ Generalized lymphadenopathy ▹ Can occur in extranodal sites (GIT) ▹ An **aggressive and rapidly fatal lymphoma if not treated** ▹ **50% cure with treatment.**		
Burkitt Lymphoma	▹ **Highly aggressive** tumor which can be: 1) **Endemic** in parts of Africa (ass with EBV) 2) Sporadically in other geographic areas ✅ **The fastest growing human tumor!!** N.B : **endemicity are charecteristic of burkitt lymphoma (record)**	translocations involving **MYC gene** on **chr. 8** 👉 MYC overexpression (a master regulator of Warburg metabolism (aerobic glycolysis), a cancer **hallmark that is associated with rapid cell growth).** **The fastest growing human tumor!!** N.B : tumor cells here activate metabolic activity for macromolecules not for ATP (record)	▹ **Intermediate size lymphocytes** (Variable cytoplasm, several nucleoli). ▹ Very **high rates of proliferation and apoptosis** (high turnover) 👉 numerous mitoses & **tissue macrophages containing ingested nuclear debris.** ▹ These benign macrophages often are surrounded by a clear space, creating a **"starry sky" pattern.**	**B-cell markers** **CD10** N.B : CD10 are marker for GC , appears with Burkuitt's & follicular lymphomas	▹ Both types affect children & young adults (**Not elderly = record**) ▹ Usually **arises at extranodal sites**: 1) Endemic 👉 **maxillary or mandibular masses** 2) Sporadic 👉 abdominal tumors (bowel & ovaries) ▹ **Highly aggressive**; **can be cured** with very intensive chemotherapy regimens. N.B : because chemotherapy affect highly proliferative cells mainly , so Burkuitt's lymphoma cured by chemotherapy because its highly growing charecteristic (record)	 	
Hodgkin Lymphoma	▹ A distinctive group of B-cell neoplasms , characterized by the presence of **RS cell. (Reed-Sternberg)** ▹ Unlike most NHLs, they **arise in a single lymph node or group** & **spread in a stepwise fashion to anatomically contiguous nodes.** **Hodgkin Lymphoma – major subtypes** ▹ Classic HL ▸ Nodular sclerosis ▸ Mixed cellularity ▸ Lymphocyte-rich ▸ Lymphocyte-depleted } The two most common forms ▹ Nodular lymphocyte predominant HL (NLP HL)		▹ **Reed-Sternberg (RS) cell**: a **very large** cell with an enormous **multilobate nucleus**, exceptionally prominent nucleoli (inclusion-like) & abundant cytoplasm. ▹ RS cells are **surrounded by a heterogeneous inflammatory infiltrate** containing small lymphocytes, eosinophils, plasma cells, and macrophages. ▹ These characteristic **nonneoplastic** inflammatory cells are generated by cytokines secreted by RS cells (IL-5,TGF-β, & IL-13).	▹ **In Classic**: Typical RS cells ✅ **express CD15 and CD30** and ❌ fail to express B-cell & T-cell markers. ▹ In NLP HL: RS variant cells ✅ **express B cell markers (e.g., CD20)** and ❌ fail to express CD15 and CD30.	▹ **Usually Young age** ▸ But can affect any age ▹ **Single lymph node or region of lymph nodes** ▸ **Cervical and mediastinal** ▪ Rarely tonsils, Waldeyer ring or extranodal sites. ▹ Manifests as **painless lymphadenopathy**, patients in advanced disease (stages III & IV 👉 see notes in next disease) are more likely to **exhibit B symptoms** (fever, weight loss, night sweats) as well as pruritus & **anemia**. N.B : B symptoms are symptoms not related to specific type of lymphoma (record) ▹ **Spreads in a contiguous manner. (from node to node = record)** ▹ **Treated** with chemotherapy, sometimes together with involved field radiotherapy. ▹ The outlook, even in advanced disease, is very good, the 5year survival rate for patients with stage 1-2 disease is more than 90%.	 	 HL is a **cardinal (essential) example of a tumor that escapes from the host immune response by expressing proteins that inhibit T cell function** 👉 **RS cells express high levels of PD (programmed death) ligands** 👉 factors that **antagonize T cell responses.** **Hodgkin Lymphoma** / **Non-Hodgkin Lymphoma** More often localized to a single axial group of nodes (cervical, mediastinal, paraaortic) / More frequent involvement of multiple peripheral nodes Orderly spread by contiguity / Noncontiguous spread Mesenteric nodes and Waldeyer ring rarely involved / Mesenteric nodes and Waldeyer ring commonly involved Extranodal involvement uncommon / Extranodal involvement common
Mycosis Fungoides and Sézary Syndrome	▹ In MF, a **neoplastic CD4+ T cells home to the skin.** ▹ So it is a form of **cutaneous T cell lymphoma.** ▹ Usually manifests in three stages: 1) A nonspecific erythrodermic rash (patches) 2) Progresses in time to a plaque phase. 3) A tumor phase. 4) sezary syndrome (record) N.Bs : - it is the only disease in our lectures related to T-Cells (record) - it is not related to fungus , but in the past they belived that this leasion caused by fungus (record) - CD4 mainly related to skin (record) - plaque = raised larger leasion (record)		Histologically, infiltration of **epidermis & upper dermis** by neoplastic T cells with marked **infolding of the nuclear membranes** 👉 a **cerebriform appearance.** N.B : these cells known as (cerebroid) because it mimic the cerebrum in appearance ~oid = mimic some thing (remember leukemoid reaction)	Tumor cells are ✅ CD4 + ❌ CD8 -	▹ Sézary syndrome: a clinical variant of MF characterized by: (1) a generalized **exfoliative erythroderma** (2) tumor cells **(Sézary cells) in the peripheral blood.** ▹ Patients diagnosed with early- stage MF survive for many years. ▹ Patients with tumor- disease, visceral disease, or Sézary syndrome survive on average for 1-3 years.		 **Lymphoma staging**

يَا بنيّ ..

أنفِق درهمك كأنّه كلّك .. وقُل :

لِلَّهِ أنا وما مَلَكْتَ .. لك أنا وإليك ..

حينها تبلُغ مقام: {يُضاعِف لِمن يَشاء} .. فإنّ الصدقة تعطيك

ما مَنحَت؛ كما مَنحَت!

د. كفاح أبو هنود

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