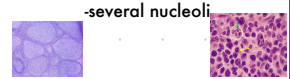
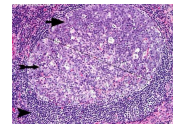
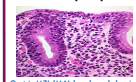
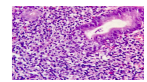
Lymphoid neoplasms II

Done by: Kareem Obeidallah

Disease	Affected persons	Cause of neoplasm	Histologic features	Diagnosing	Clinical symptoms
Follicular lymphoma	-40% of the adults non Hodgkin lymphoma -Older than 50 years old	Translocation (14;18) *fusion of BCL2 gene on chromosome 18 to the IgH locus on chromosome 14 ↓ Over expression of BCL2 protein (An inhibitor of apoptosis) ↓ Increase cell survival	*Distinctly(nodular)follicular proliferation *Two types of neoplastic cells: 1-Centrocyte "predominant cells": -angular,cleaved and indistinct (not clear) nucleoli 2-Centroblast: -Larger cells -Vesicular chromatin -several nucleoli 	▷ B-cells markers (mature B cell neoplasm) ▷ CD10 → GC marker (expressed in Burkitt lymphoma, B-ALL & some DLBCL)	1- Generalized painless lymphadenopathy 2- Bone marrow is involved in 80% of cases 3- Prolonged survival, not curable disease (indolent) 4- 40% transform into DLBCL, dismal prognosis → Poor prognosis
Mantle cell lymphoma (Composed of cells resembling naive B cells found in the mantle zone of normal lymphoid follicles)	-Mainly in men older than 50 years old	Translocation (11;14) *Fusion of Cyclin D1 gene to the IgH locus ↓ Over expression of cyclin D1 ↓ Stimulate 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. 	1) B cell markers. 2) CD5 (as CLL/SLL) 3) Cyclin D1 (not expressed in CLL/SLL) الي بخليني أميز بين ال CLl/SLL و ال mantle cell lymphoma هو ال Cyclin D1	▷ fatigue & lymphadenopathy → found to have generalized disease involving the bone marrow, spleen, liver, and (often) GIT. ▷ Bone marrow is involved in most cases. ▷ Moderately aggressive & incurable. ▷ The median survival is 4-6 ▷ sometimes arises in the GIT as multifocal polyps (lymphomatoid polyposis).
Extranodal marginal zone lymphoma (indolent B cell tumor arises most commonly in epithelial tissues (e.g. GIT, salivary glands, lungs, orbit, & breast)	-Older ages	Translocation (11;18) Cancer arises within & is sustained by chronic inflammation: 1) Autoimmune disorders - Salivary gland as in Sjögren syndrome - Thyroid gland in Hashimoto thyroiditis) 2) Chronic infection (such as H.pylori gastritis)	▷ B-cells infiltrate the epithelium of involved tissues (in small aggregates) → called lymphoepithelial lesions ▷ Tumor cells accumulate ▷ Abundant pale cytoplasm or exhibit plasma cell differentiation in lamina propria.  Gastric MZL (MAL 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.

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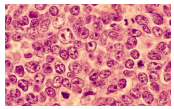
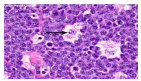
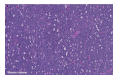
Diffuse Large B Cell Lymphoma	- Most common adult lymphoma - Median > 60 years of age (but Can occur at any age)	▷ Either de novo or transformation from other low grade tumors (follicular lymphoma) ↳ Here BCL2 will be positive ▷ Mutations & rearrangements of the BCL6 gene ↓ increased levels of BCL6 protein ↓ 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 	▷ B-cell markers ▷ CD10 in some tumors	▷ 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 (associated with EBV) 2) Sporadically in other geographic areas	-affect children & young adults	translocations MYC gene on chromosome 8 ↓ MYC overexpression (master regulator of Warburg metabolism "aerobic glycolysis") ↓ cancer hallmark that is associated with rapid cell growth	▷ Intermediate size lymphocytes (Variable cytoplasm,several nucleoli) ▷ Very high rates of proliferation and apoptosis (high turnover) numerous mitoses & tissue macrophages containing ingested nuclear debris ▷ benign macrophages surrounded by "starry sky": clear space around macrophages  	▷ B-cell markers ▷ CD10	▷ The fastest growing human tumor ▷ Arises at extranodal sites: 1) Endemic → maxillary or mandibular masses, 2) Sporadic → abdominal tumors (bowel & ovaries) ▷ Highly aggressive ▷ Cured with very intensive chemotherapy regimens

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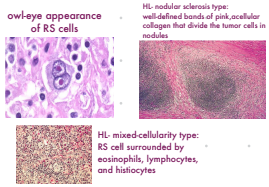
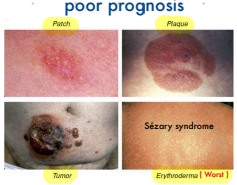
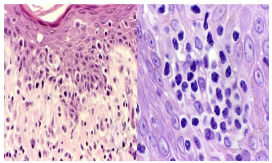
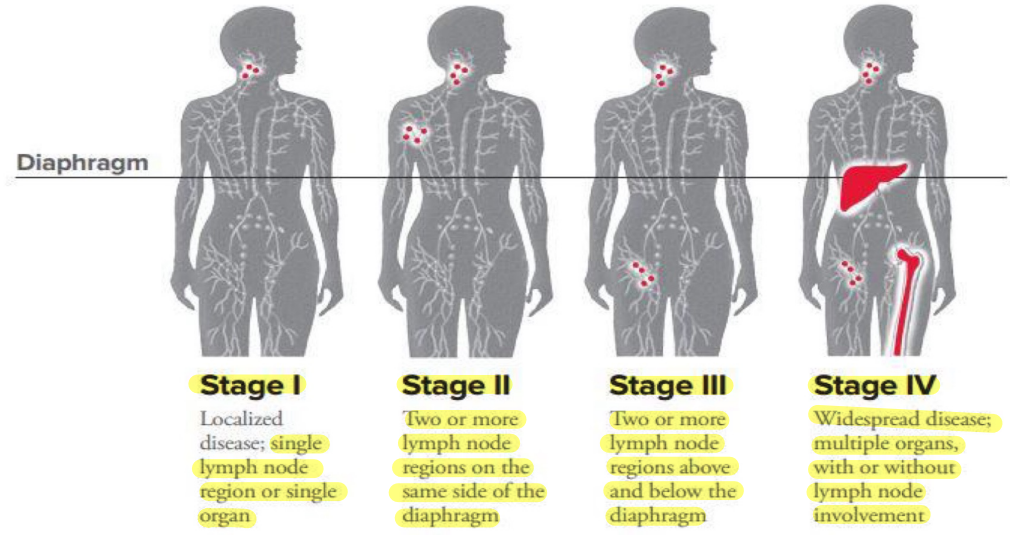
Hodgkin Lymphoma (distinctive group of B-cell neoplasms)	- Usually Young age (But can affect any age) *There are two subtypes: ▷ Classic HL: ▸ Nodular sclerosis ▸ Mixed cellularity (The two most common types) ▸ Lymphocyte-rich ▸ Lymphocyte-depleted ▷ Nodular lymphocyte predominant HL (NLP HL)	It's tumor that escapes from the host immune response by: expressing proteins that inhibit T cell function RS cells express high levels of PD ligands factors antagonize T cell responses.	Contain: ▷ **Reed-Sternberg cell**: -Large cell -Multilobate nucleus -Prominent nucleoli (inclusion-like) -Abundant cytoplasm -Surrounded by a heterogeneous inflammatory infiltration: small lymphocytes, eosinophils, plasma cells and macrophages ▷ These characteristic nonneoplastic, inflammatory cells are generated by cytokines secreted by RS cells 1) IL-5 2) TGF-β 3)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 and fail to express CD15 and CD30	▷ Affect single lymph node or region of lymph nodes and spread to contagious nodes as: 1- Cervical and mediastinal 2- Rarely tonsils,waldeyer ring or extranodal sites ▷painless lymphadenopathy ▷Stages III & IV exhibit: 1- B symptoms -fever -weight loss -night sweats 2- Pruritus & anemia *Treatment: chemotherapy + sometimes combined with radiotherapy ▷ Prognosis is very good * 5-year survival rate for patients with stage 1-2 disease is more than 90%.
Mycosis Fungoides and Sézary Syndrome (form of cutaneous T cell lymphoma)	-Old age Manifests in three stages: 1) A nonspecific erythrodermic rash (patches) 2) Progresses in time to a plaque phase 3) A tumor phase كل ما تقدمنا مرحلة لقدام رح يصير poor prognosis  	a neoplastic CD4+ T cells home to the skin *No Reed-Sternberg cell	a neoplastic CD4+ T cells home to the skin ↓ infiltration of epidermis & upper dermis by neoplastic T cells with marked infolding of the nuclear membranes ↓ cerebriform appearance 	Tumor cells are: CD4 positive CD8 negative (not exist)	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

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

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