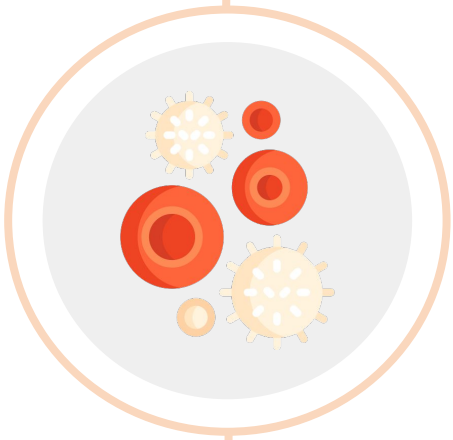
Lymphomas



Objectives: 438/BlackBoard

- ★ Describe the pathology classification of Lymphoma.
- ★ Describe the Clinical Presentation of Lymphoma.
- ★ Work up lymphoma.
- ★ Know the treatment of lymphoma.

Objectives: 439

- ★ Introduction of some important terminologies.
- ★ Know the major subtypes of lymphoma.
- ★ Know the typical presentation of the major subtypes

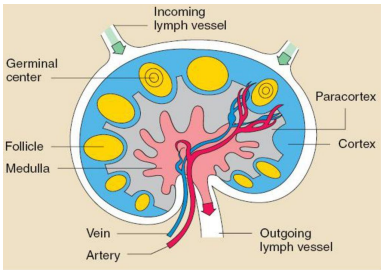
Editing file

Color index

Original text
Females slides
Males slides
Doctor's notes 438
Doctor's notes 439
Text book
Important
Golden notes
Extra

Introduction

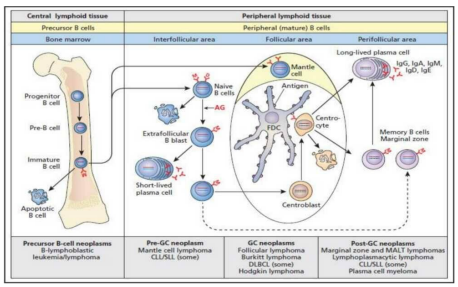
◀ Lymph Node Structure



- Consists of cortex and medulla
- Follicles are embedded within the cortex
- Germinal centers (GCs) are embedded within the follicles
- Interaction between antigens and lymphocytes occur in germinal centers (GCs)
- Location of lymphoma determines its naming

◀ B-cell development

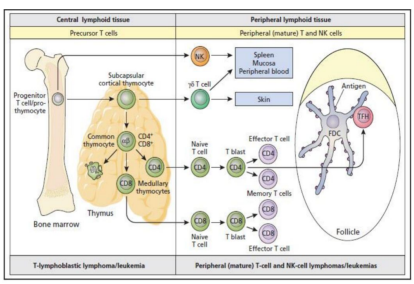
- Lymphocytes are derived from hematopoietic stem cells in the bone marrow.
- B-cell maturation occurs in the bone marrow.
- Begins with recombination of the V(ariable), D, J(unction) gene segments of the immunoglobulin heavy chain (IgH) followed by the light chain
- To generate a functional immunoglobulin that is expressed on the cell surface as B-cell receptor (BCR).
- The primary function of B-cells is to produce a vast diversity of immunoglobulins.
- Diversity come from random V, D, and J rearrangements.
- Rearrangement results in expression of IgM and IgD on the surface mature B-cells that exit the marrow.
- These are mature but (naïve B-cells) not exposed to antigens yet
- Then they get exposed to antigen in the germinal centers of secondary lymphoid organs:
  - such as lymph nodes (functions as a sewage system for the body)
  - mucosa associated lymphoid tissue (MALT)
  - or the spleen
- Here, **somatic hypermutation**[1] occurs in the V genes of the heavy and light chains:
  - Multiple antibodies with different affinity to the antigen.
  - Those with good affinity differentiate to memory B-cells or plasma cells which recognize disease for long term
  - The others undergo apoptosis. recognize disease short term
- Finally, class switching occurs in the germinal (an imp place for switching)
- center and involves changing the heavy chain to produce IgG, IgA, or IgE.



- Lymphoma can happen at any stage, lymphoblastic lymphoma[2] is the most immature type while post-GC lymphomas are most mature, as we go right, it's more aggressive but still curable (e.g. plasma cells lymphoma aka multiple myeloma)

◀ T-cell development

- In contrast to B-cell, T-cell exit the marrow and develop in the thymus
- Similar to B cells, each T cell recognizes a specific antigen, but through a T-cell receptor (TCR) rather than BCR.
- Similar to BCRs, diversity of TCRs is generated through recombination
- of V, D, and J gene segments of the four TCR genes, alpha (α), beta
- (β), gamma (γ) and delta (δ).
- Mature T-cells express either αβ TCR or γδ TCR. imp to know bc they affect prognosis & management



1-Normal mutation that leads to proliferation of B lymphocytes
2- Involvement of bone marrow → leukemia, no involvement → lymphoma

Histopathology and specialized studies

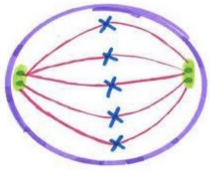
When we see an unusual lymphoid mass, our job includes:-

1) Identifying what that mass is
2) Origin of the mass
3) Unique identifiable markers

Cytogenetic techniques study the **cells**, and include: Conventional Cytogenetics & FISH
Whereas Molecular techniques studies **genetic mutations**/combinations and includes PCR

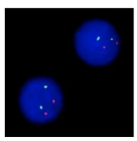
Conventional Cytogenetics

- Metaphase cytogenetics = chromosomal analysis = Conventional cytogenetic techniques = karyotyping (counting chromosomes)
  - Numeric chromosomal abnormalities (too many or too few chromosomes)
  - Deletion
  - Translocation. e.g. (8:14) in burkitt's
- Bone marrow or tissue → maintained in culture → exposed to a mitotic inhibitor → blocks formation of the spindle → arrests cell division at the metaphase stage.
- Thus, cytogenetic studies require dividing cells. So we instruct the surgeon to NOT put the sample in formalin bc that would kill it, but instead maintain it in culture with freezing and mitotic inhibitors, then measure while dividing.
- **Limitations:**
  - Require active cell division.
  - Insensitive to submicroscopic abnormalities e.g. gene mutations
  - Small number of cells are analyzed (regardless of how big the sample is, so abnormalities that come in small concentrations are harder to detect



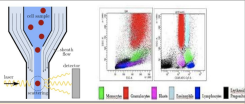
Fluorescence in situ hybridization (FISH)

- A specific single-stranded DNA probe corresponding to a gene or chromosomal region of interest is labeled for fluorescent detection.
- identify chromosomal abnormalities
- Probes are then incubated with the sample and examined by microscopy.
- Abnormal attachment indicate +ve FISH
- Abnormalities can be seen in non-dividing cells (interphase nuclei)
- Peripheral blood slides can be directly processed.
- Specific molecular abnormalities
- More sensitive than conventional cytogenetic
- You have to start with pathology and move into it as it's not done as an initial investigation, unless you have an idea of what the abnormality is (solid vs liquid).



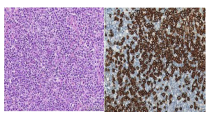
Flow cytometry

A technique for the identification, quantification, and sorting of single cells in a cell suspension
often with the use of fluorescent tagged antibodies to detect the presence of specific target antigens



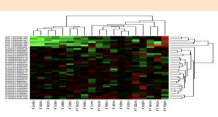
Histopathology

- Morphology
  - H&E stain, autonomous pattern of diffuse cells that are large in size and densely arranged poorly differentiated cells (with inflammation)
- Immunohistochemistry (IHC)



RNA expression arrays

- Not commonly used except in research centers to map out the genetic defects of a certain disease
- Characterization of the gene expression patterns within the cells of interest
- Referred to as a gene expression profile (GEP)

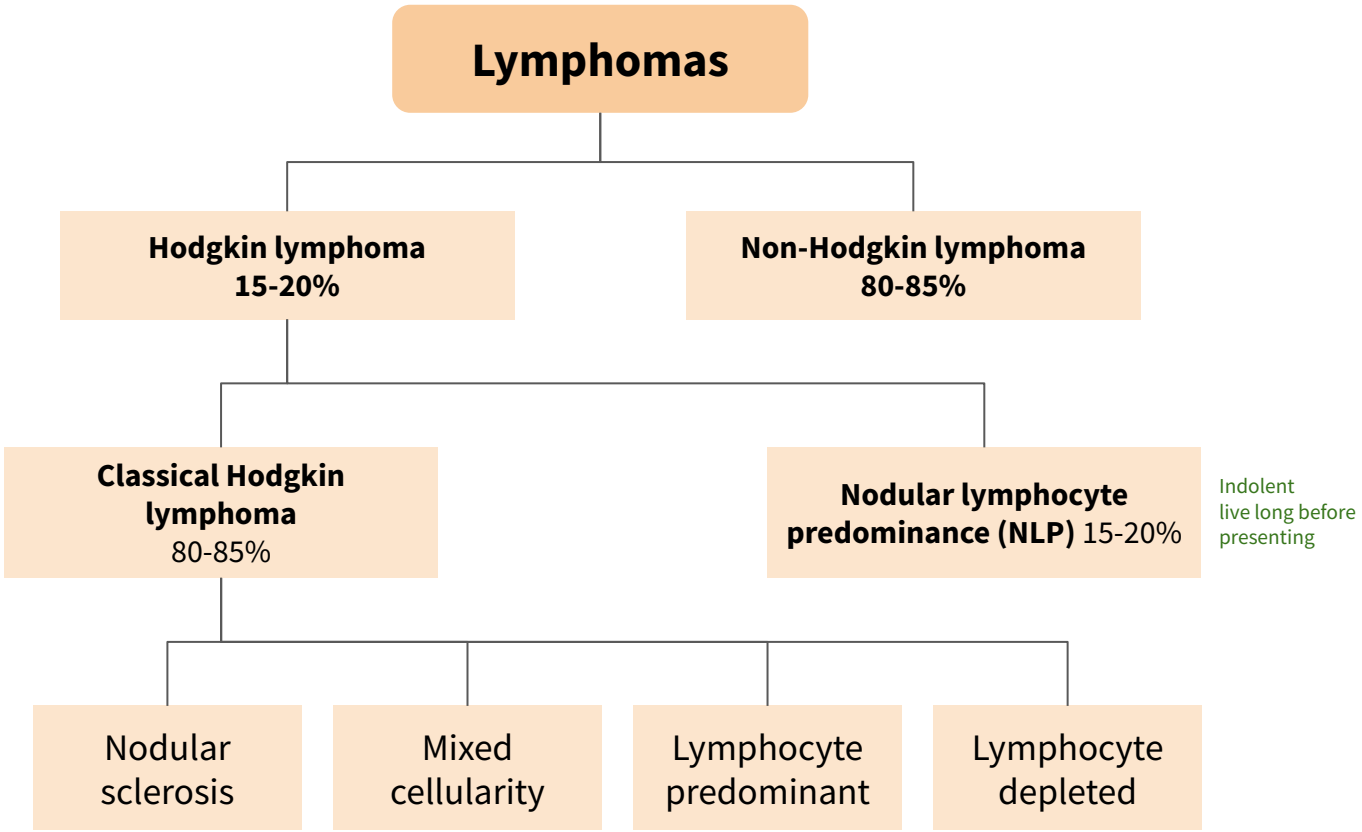


Introduction to lymphomas

Definition

- Lymphoma is a **cancer of the lymphatic system**, which is part of the body's germ-fighting network.
- It's a neoplastic proliferation of lymphoid cells that forms a mass, and may arise in LN or in extranodal sites. **The lymphatic system includes:**
  - Lymph nodes (lymph glands)
  - Spleen
  - Thymus gland
  - Bone marrow
- Lymphoma can affect all the above mentioned areas as well as other organs throughout the body. This is because every organ in the body has its own lymphatic structure. For example, the stomach can have a gastric carcinoma or lymphoma

◀ Main subtypes of lymphomas



Note: Hodgkins is more common in the Lymph nodes while NHL is more common in the lymphatic vessels

◀ WHO Classification of Hematological Neoplasms

- **Classification:**
  - **A. Myeloid**
  - **B. Lymphoid**
    - B cell neoplasms
      - Includes plasma cell myeloma
    - T cell neoplasms
    - Hodgkin's lymphoma
  - **C. Histiocytic**
  - **D. Mast Cell**

Risk factors

◀ Risk factors for lymphomas

	Hodgkin lymphoma	Non-Hodgkin lymphoma
Age	People **aged 20-30 years** and **those 55 years of age and above** have a higher risk of lymphoma.	Most lymphomas occur in people **aged 60 years** and older. However, some types are more likely to develop in children and young adults.
Sex	Slightly **more common in males** than females.	Some types are **more likely in women**. Men have a higher risk of other types.
Family history	If a sibling has Hodgkin lymphoma, the risk is slightly higher. If the sibling is an identical twin, this risk increases significantly.	-
Ethnicity and location	-	In the U.S., African American and Asian American people have a lower risk for non-Hodgkin lymphoma than white people. Non-Hodgkin Lymphoma is more common in developed nations.
Chemicals & Radiation	-	**Nuclear radiation and certain agricultural chemicals have links to non-Hodgkin lymphoma. (Job-induced malignancy)**
Immunodeficiency	**HIV infection** can weaken the immune system and increase the risk of lymphoma.	A person with a less active immune system has a higher risk. This may be due to **anti-rejection medications following a solid organ transplant or HIV.**
Autoimmune diseases		This type of disease occurs when the immune system attacks the body's own cells. Examples include **rheumatoid arthritis and celiac disease**.
Infectious factor	**Infectious mononucleosis:** The **Epstein-Barr virus (EBV)** can cause mononucleosis. This disease increases the risk of lymphoma.	Certain viral and bacterial infections that transform lymphocytes, such as the **Epstein-Barr virus (EBV),** increase the risk. This virus causes **glandular fever**.

Grouping/ subtypes	• Nodular lymphocyte-predominant HL
	• Classical HL:
	  ○ Nodular sclerosis HL
	  ○ Lymphocyte-rich classical HL
	  ○ Mixed cellularity HL
	  ○ Lymphocyte depletion HL
		• Indolent
		• Aggressive
		• Highly aggressive
		
		Formerly was:
		- Low grade
		- Intermediate grade
		- High grade

Clinical presentation

◀ Signs and symptoms of lymphoma

Painless swelling of lymph nodes (Most common presentation) in the neck , armpits or groin , get painful after drinking alcohol. (In reactive lymphadenitis (in response to infection) there will be painful lymphadenopathy and it won't be persistent)	**B symptoms:** • Persistent Fever without infection. • Night sweats • Unexplained Weight loss and reduced appetite
Persistent fatigue (This could be due to anemia or as a result of the disease process itself)	**Itchy skin** "Pruritus"
Shortness of breath (Due to enlarged mediastinal LN which may compress the respiratory tract)	

- **Some additional symptoms of non-Hodgkin lymphoma include (Depends on the location):**
  - Persistent coughing (If in the mediastinum)
  - Shortness of breath
  - Pain or swelling in the abdomen (If it involves the abdomen)
  - **Pain, weakness, paralysis, or altered sensation** may occur if an enlarged lymph node presses **against spinal nerves or the spinal cord**.
- Lymphoma can spread rapidly from the lymph nodes to other parts of the body through the lymphatic system.(Which is why it's important to act quickly) As cancerous lymphocytes spread into other tissues, the immune system cannot defend against infections as effectively. (The rapidity of spread, depends on the subtype)

◀ Diagnosis of lymphomas

Swollen lymph nodes

History

- **Painless lymphadenopathy (If painful, think of reactive lymphadenopathy)**
- **B symptoms and Performance status** (It is a subjective assessment of the patient's activity; for example 100% or 70%...)

Physical examination

- **lymph nodes, liver, spleen, oropharynx**
- **You must examine all the body's lymph nodes.** For para-aortic lymph nodes it has to be >10cm to be felt, so for mediastinal and para-aortic, you need to do imaging to discover them. Other sites can be palpated in the physical examination.

Lab tests

- **CBC** (To check WBC, plt etc.)**, Creatinine, liver function tests, LDH, calcium**
- Creatinine is used to check if the pt has any renal impairment (for future investigations/treatment)

Diagnosis *(cont.)*

Biopsy

- **A biopsy is usually required for diagnosis. What are the types of biopsy?**
  1. **Fine needle aspiration (FNA):** looks at cells not tissues (good for solid tumors)
     - Takes only few cells out. It can be done in the clinic and doesn't take time.
     - It's useful when the Dr needs to take an urgent decision and can't wait for a tru-cut biopsy.
     - Tells you there is a malignancy but doesn't tell you what type.
     - You can aspirate inflammatory cells instead of cancer cells (if both are within the same tissue)
  2. **Incisional biopsy:** tissue of lymph node) **(Tru-cut/core Biopsy)**
     - Takes small part of the lymph node, requires local anesthesia and it's done by interventional radiologists
  3. **Excisional biopsy ★ GOLD STANDARD**
     - Take the whole lymph node out, requires general anesthesia and done in OR.

How to stage lymphoma?

1. **CT scan:** Neck, Chest, Abdomen, and pelvis
2. **PET scan ★ in curable lymphomas: to follow revolution**
   a. Hodgkin lymphoma (usually more aggressive as a disease but easier to treat, unlike indolent lymphomas)
   b. Aggressive NHL: DLBCL, Burkitt's lymphoma, Peripheral T-cell lymphoma. show ↑ uptake
   c. Less role in indolent lymphomas e.g. follicular
   d. **How is it performed?** First we inject an isotope called fluorodeoxy**glucose** (FD**G**), FDG has high affinity for cancer cells, especially lymphomas. The cancer cells will take up this isotope and appear bright on imaging, this is called standardized uptake value (SUV). This technique is not used in patients with uncontrolled diabetes or an active infection bc the isotope will precipitate in these areas instead of the cancer. Also, if the LN was very small, it may not be appear in the PET-scan.
   e. PET scan can differentiate between fibrosis/necrosis from treatment, and active cancer
3. **Bone marrow biopsy: to check for EXTENSION (i.e. stage 4) not metastasis**
   a. No need in PET staged Hodgkin.
   b. We still do it in all NHL although the role in DLBCL is fading out of favor.
4. **Investigations:**
   a. CBC, LDH (marker of cell turnover), LFTs, Hepatitis serology (Hb C, Hb B core and surface antigen, HIV) to prevent reactivation with chemo, Quantitative immunoglobulins (esp in B cell).

★ International prognostic index for NHL

Clinical Risk Factor	Point per Risk Factor
Age >60	1
serum LDH>normal	1
performance status 2 - 4	1
stage 3 or 4	1
extra nodal involvement >1	1

Risk for CNS involvement based on total points: 0 - 1 points is low risk, 2 points is low to intermediate risk, 3 points is intermediate to high risk, and 4 or 5 points is high risk.

Staging system

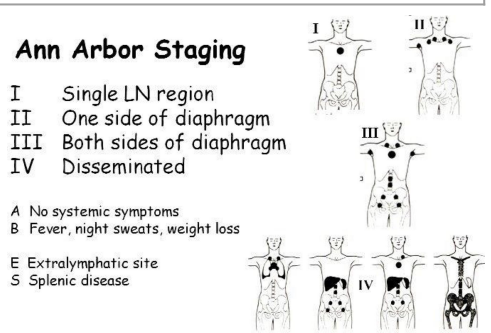
◀ Staging system

Cotswolds Meeting modification of **Ann Arbour Classification:**

- Consist of a number and a letter e.g. IA, IIIB
- Staging is based on the number of affected nodes, the presence or absence of B symptoms, and whether or not the disease is present on both sides of the diaphragm

Stage	Description
I (Early)	• Involvement of a **single lymph-node region or lymphoid structure**
II (Early)	• Involvement of **two or more lymph node regions on the same side of the diaphragm**; Example: Supraclavicular + Infraclavicular LNs involvement
III (Advanced)	• Involvement of **lymph node regions on both sides of the diaphragm (above and below)** Example: Supraclavicular + Inguinal LNs involvement
IV (Advanced)	• **Extensive extranodal disease** (more extensive than "E")
Designations applicable to any disease state	
A	• Asymptomatic
B	**One** of the following is enough: (It indicates aggressive disease → needs aggressive therapy) • **Fever:** > 38°, recurrent (Spiking up and down, not stable.) • **Night sweats:** Drenching (Excessive sweating, they change clothes frequently), recurrent. • **Weight loss:** unexplained loss of >10% of **the ideal** body weight within the previous 6 months
X	**Bulky disease:** (If you see the letter X in the description of lymphoma → Bulky)
E	• **Limited** extranodal extension from **adjacent** nodal site
S	• **Splenic disease**

II: Multiple nodes group
III: above & below diaphragm
IV: Bone marrow / non-lymphoid

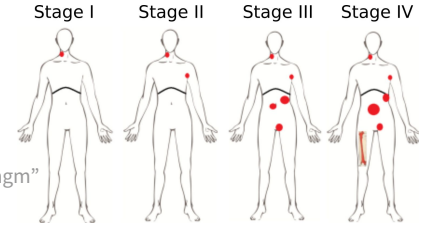


Examples: (From 437 team)

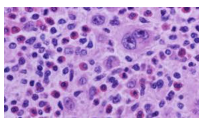
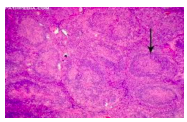
Stage IIA:
- Asymptomatic patient with ≥ 2 lymph nodes that are both 3cm in size on the same side of the diaphragm.

Stage IBx:
- Patient with B symptoms and one lymph node that is 11 cm in size "Bulky disease".

Stage IIIA:
- Asymptomatic patient with one lymph node in his neck and one lymph node in his abdomen "below the diaphragm" that are both 4 cm in size.



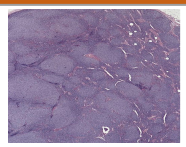
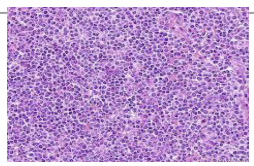
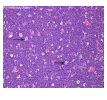
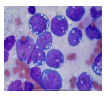
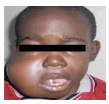
HL Vs. NHL

	Hodgkin's lymphoma	Non-Hodgkin's lymphoma
General info	• **Typical presentation is a young patient with cervical and or mediastinal LN**	
Origin	- **B-cell**	- 70% B-cell; 30% T-cell
Lymph node involvement	- Single lymph node group	- Multiple lymph node groups
Extranodal involvement	- Rare	- Common
Spread	- **Contiguous (typically neck → mediastinum → abdo/spleen)**	- Non contiguous
Clinical features	- Painless swelling of lymph nodes - B symptoms - Fatigue, itchiness - SOB (Due to enlarged mediastinal LN which may compress the respiratory tract)	
		Other symptoms depends on the location - Mediastinum: SOB, cough - GI: early satiety, GI bleeding, abdominal pain - Neuro: paralysis, focal neurologic symptoms - Skin infiltration: rash, plaques, tumors, ulcers
Histology	**Owl's Eye**  **Reed-Sternberg cells** 	Neoplastic cells of B-cell, T-cell, and natural killer (NK)
Prognosis	- **Good (highly curable >90%)**	- Bad
Subtypes	A. Nodular lymphocyte-predominant HL B. Classical hodgkin's lymphoma 1. Nodular sclerosis HL (Most common) 2. Lymphocyte-rich classical HL 3. Mixed cellularity HL (Associated with abundant eosinophils) 4. Lymphocyte depletion HL	A. According to cell type: - B cells - T cells B. According to aggressiveness: - Indolent (kills in years) - Aggressive (kills in months/weeks) - Highly aggressive (kills in days/weeks)
Treatment	• Limited stage: ○ ABVD x 2 then **PET** scan if in CR then 1-2 cycles then stop • Advanced: ○ ABVD x 2 then **PET** if in CR then 4 more cycles of AVD ○ If not in CR: consider escalation (escalated BEACOP) or continue ABVD x 4 • CR = Complete response • ABVD: abbreviation for chemotherapy used, you wont be asked what it stands for	- Check slide 12

B-cells Non-Hodgkin's lymphoma (NHL)

◀ Clinical grouping of NHL

focus on bolded types (follicular, DLBCL, BL)
pics are only for those types

Clinical grouping	Type
Indolent "low grade" (kills in years) Very chronic, think of it like DM, HTN	**Follicular lymphoma (FL) (Most common indolent subtype).** • Germinal center lymphoma (+ CD10, BCL6) • t(14:18) results in overexpression of the anti-apopototic protein bcl-2. • The translocation moves the bcl-2 gene on 18 to near the enhancer element of the immunoglobulin heavy chain on chromosome 14. • The problem is **cells don't die** (not a problem of hyperproliferation) • The proliferative rate is low (proliferative index Ki67 20-40%) low compared to BL (95%) • **Incurable but responsive to treatment** shrinks but never goes away  This is why excisional biopsy is better
	Marginal zone lymphoma • Nodal • **Extranodal (MALT): may regress with treatment of H.pylori** **Note:** Marginal zone lymphoma is associated with chronic inflammatory states e.g. Hashimoto's thyroiditis, Sjogren's syndrome, H.pylori gastritis
	Small lymphocytic lymphoma (when CLL involves LN)
	Lymphoplasmacytic (association with Waldenstrom's macroglobulinemia)
	Hairy cell leukemia (HCL)
	Mantle cell lymphoma
Aggressive "intermediate" (kills in months-weeks) Acute duration	**Diffuse large B-cell lymphoma (Most common)** (In KSA, it's 80%) • Morphological diagnosis is a key (large cells & diffuse infiltration). • The problem is with high proliferative rate (not with apoptosis) • The proliferative index is very high (Ki67 = 80-90%) • Curable (>60% cure rate). pts die due to chemo complications rather than the disease • Many clinical forms: DLBCL-NOS (most common)/ Mediastinal Large B-cell lymphoma/ Primary CNS DLBCL • 2 molecular forms: • Activated B-cell type (ABC) poor risk. so mutated that it activated in an abnormal location thus making it worse • Germinal center B-cell (GCB) better risk.  Sheets of cells that look similar
	High grade B-cell lymphoma (previously called Burkitt's-like)
	Mantle cell lymphoma • Has the 2 worse features of both DLBCL and FL. Hematologist worst nightmare • Cells don't die and they also proliferate !!! • Bad bad type! • Incurable and poor prognosis. aggressive AND doesn't respond to chemo, unlike former types • t(11:14) Cyclin D1. 14 geenrally is a key in translocation • Treated differently: takes into consideration Quality of life vs quantity • Young <60: R-chemo then ASCT • Elderly: R-chemo (BR, RCHOP, RCVP) • Ibrutinib (BTK inhibitor) in relapsed refractory cases.
Highly Aggressive (kills in days to weeks)	**Burkitt's lymphoma** • t(8:14) c-myc on chromosome 8 is translocated near the enhancer of IGH gene of chromosome 14. • Cells have a very high proliferate rate (100% ki67) double every 24hr • High rate of apoptosis (cells die easily) • **Highly curable (>90%) but fatal if you don't treat** • Very sensitive to chemotherapy. if you can get them through the 1st cycle of chemo they'll be fine • High risk for tumor lysis syndrome (like ALL, in fact ALL-3=BL)  Starry sky appearance  Cells w/ vacuoles  pt appears well one day and the next day they'd had a huge mass
	Double Hit lymphoma more aggressive than DLBCL but less than BL • Imagine a lymphoma with: 2 translocations: • Anti-apoptotic BCL-2 • C-myc • Double hit (poor prognosis) • Triple HIT: BCL-2 and BCL-6 and c-myc (poor prognosis) • Treated with dose adjusted EPOCHR more agressive • Infusional chemotherapy to target continuous cell kill • Adjusted to ANC nadir • Adding Etoposide (compared to RCHOP) more cytotoxic
	B-Lymphoblastic lymphoma (LBL)

B-cells Non-Hodgkin's lymphoma (NHL)

◀ Treatment

There is conflict in the treatment of **indolent advanced stage**, but keep in mind that all of them are right (No Qs will come on advanced stage, bc all of them are correct). For the rest just know if it's radio or chemotherapy, you don't need to know the doses or any other details

Indolent lymphoma
e.g. Follicular Grad ½, small lymphocytic, marginal zone

Limited disease (Stage I,II)	Advanced stage (Stage III, IV), relapsed, progressive

• Radiation therapy	• Asymptomatic:
	  ○ Watch and wait or chemotherapy:
	  ■ Rituximab weekly x 4 in FL
	• Symptomatic or transformed NHL:
	  ○ Single of combination therapy
	  ■ Bendamustine rituximab (BR)
	  ■ R-CHOP
	  ■ R-CVP
	R-chemo

Aggressive lymphoma

- DLBCL:
  - Limited: **RCHOP** x 3 cycles then PET if –ve 1 last cycle then stop. If + RT.
  - Advanced: **RCHOP** x 6 cycles
- PTCL:
  - Limited: **CHOP** x 3 cycles then PET if –ve 1 last cycle then stop. If + RT.
  - Advanced: **CHOP** x 6
- High grade B-cell:
  - Double HIT: DA-EPOCHR x 6
- Highly aggressive Burkitts:
  - Aggressive short course chemotherapy: (CODOX-MR/IVACR) basically the longest treatment

Relapsed/refractory lymphoma

- Salvage chemotherapy. use different combination than before
- Multiple regimens exist with equal efficacy but different side effectprofile:
  - ESHAP, EHAP, DHAP, GDP, RICE etc
  - If in CR: proceed to **auto stem cell transplant** unlike in leukemia where the issue is the stem cells
  - In not in CR: palliatiation old patient with comorbidities
- Targeted therapies exist and may be helpful in relapsed diseases
  - Brentuximab (anti CD30) in HL and some T-cell lymphomas

Relapsed/refractory lymphoma

- Plethora of new therapies in the past few years
- Very effective even in high risk pts
  - E.g. BCL-2 inhibitors (venetoclax in CLL)
- Other small molecule inhibitors (targeting BCR signalling)

B-cells Non-Hodgkin's lymphoma (NHL)

◀ Treatment (438)

MALT lymphoma

- It's an indolent subtype, but discussed separately because it has special treatment
- Marginal zone B-cell lymphoma of extranodal (MALT) type
- **Stomach:** associated with **Helicobacter pylori infection**
- **Salivary Gland:** associated with **Sjogren's syndrome**
- **Thyroid:** associated with **Hashimoto's thyroiditis**
- **Orbital** (lacrimal, conjunctiva)
- **Other:** Waldeyer's ring, breast, bladder, lung, skin

} **Chronic antigen stimulation**

Treatment of gastric MALT (Important bc it's common in KSA)

Stage IE (H. pylori +ve)	Stage IE (H. pylori -ve or antibiotic failure)	Stage 2 or higher
• **PPI, 2 antibiotics (e.g. clarithromycin, amoxicillin) (H.pylori eradication)** • Follow up gastroscopy with Biopsy every 6 month for 2 yrs, then every 1 year	• IFRT 30 Gy (95% local control) **(Local radiotherapy only)**	• Treat as indolent lymphoma + H. pylori eradication

T-cells Non-Hodgkin's lymphoma (NHL)

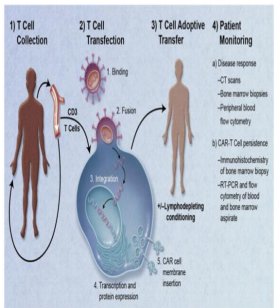
◀ Clinical grouping of NHL

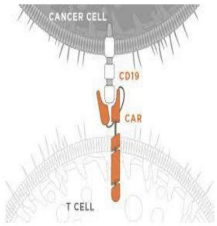
Dr: Only know the most common types
Fem: no need to know

Clinical grouping	Type
Indolent grade	**T-cell large granular lymphocytic leukemia (T-LGL)**
	Mycosis Fungoides (most common, precedes sezary syndrome)
	Primary cutaneous types
Aggressive "intermediate grade" (Rapid progression, do investigations then start treatment)	PTCL
	Angioimmunoblastic T-cell lymphoma (AITCL)
	Anaplastic T cell lymphoma • ALK negative (bad prognosis) • ALK positive (good prognosis)
	Aggressive NK-cell leukemia
	Extranodal NK / T cell lymphoma, nasal type
	Enteropathy associated T-cell lymphoma (celiac)
	Adult T-cell leukemia/lymphoma (ATLL)
	Hepatosplenic T-cell lymphoma
	Sezary syndrome can result from progression of mycosis fungoides or as de novo disease
Highly aggressive	T-Lymphoblastic lymphoma (LBL)

◀ T-cells NHL treatment

- Chop based therapy
- Some new therapies are emerging as part of the management of certain types of NHLs, including CAR-T Cells which is done by Extracting patient's T cells → genetically modifying them by adding a virus that attacks the same cluster (cancer antigen) → reinfuse to patient. The modified T cells would then kill the cancer cells





Lecture Quiz

Q1: A 19-year-old woman presents for evaluation of a nontender left axillary lymph node. She is asymptomatic and denies weight loss or night sweats. Examination reveals three rubbery firm nontender nodes in the axilla, the largest 3 cm in diameter. No other lymphadenopathy is noted; the spleen is not enlarged. Lymph node biopsy, however, reveals mixed-cellularity Hodgkin lymphoma. Liver function tests are normal. How would you manage this patient?

A- Chemotherapy 4-6 cycles followed by radiation
B- Chemotherapy 3-4 cycles followed by radiation
C- Local radiation only
D- Surgical excision

Q2: A 53-year-old man comes to the physician for recurring fever and night sweats for the past 6 months. The fevers persist for 7 to 10 days and then subside completely for about a week before returning again. During this period, he has also noticed two painless lumps on his neck that have gradually increased in size. Over the past year, he has had an 8.2-kg (18.1 lbs) weight loss. Two years ago, he had a severe sore throat and fever, which was diagnosed as infectious mononucleosis. He has smoked a pack of cigarettes daily for the past 10 years. He does not drink alcohol. His job involves monthly international travel to Asia and Africa. He takes no medications. His temperature is 39°C (102.2°F), pulse is 90/min, respirations are 22/min, and blood pressure is 105/60 mm Hg. Physical examination shows 2 enlarged, nontender, fixed cervical lymph nodes on each side of the neck. Which one of teh following would be seen in tha Microscopic examination of a specimen obtained on biopsy of a cervical lymph node?

A- Acid Fast Bacilli
B- CD15/30 positive cells (Reed-Sternberg Cells)
C- Proliferation of monomorphic lymphocytic cells on biopsy

Q3: The nurse understands that Hodgkin's disease is suspected when a client presents with a painless, swollen lymph node. Hodgkin's disease typically affects people in which age group?

A- Older adults (ages 41-50 years)
B- Teenagers (ages 13-20 years)
C- Young adults (ages 21-40 years)
D- Children (ages 6-12 years)

Q4: A 29-year-old man comes to the physician because of a 3-month history of fatigue, weight loss, and multiple painless swellings on his neck and axilla. He reports that his swellings become painful after he drinks alcohol. Physical examination shows nontender cervical and axillary lymphadenopathy. A lymph node biopsy specimen shows giant binucleate cells. Which of the following is the most likely diagnosis?

A- Adult T-cell lymphoma
B- Hodgkin lymphoma
C- Diffuse large B-cell lymphoma (DLBCL)
D- Mycobacterial infection

Q5: A 68-year-old man is evaluated because of worsening chronic epigastric pain. He now has fatigue and early satiety. He has iron deficiency anemia. Results of upper gastrointestinal endoscopy reveal diffuse gastritis, along with mucosal thickening in the gastric antrum associated with a mass lesion. Abundant Helicobacter pylori organisms are noted on biopsy, and histologic evaluation of the mass lesion shows it to be a gastric lymphoma of mucosa-associated lymphoid tissue (MALT) type. What is the most appropriate next step in the management of this patients illness?

A- Combination chemotherapy with 5-fluorouracil, doxorubicin, and mitomycin C (FAM)
B- Combination chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)
C- Eradication of Helicobacter pylori
D- Total gastrectomy followed by radiation therapy

Q6: A 70-year-old man comes to the physician because of fatigue and intermittent epigastric pain. The symptoms began about one year ago. He describes the pain as diffuse and 3 out of 10 in intensity. Recently, he has had unusually large black stools. He appears pale. His pulse is 72/min and his blood pressure is 110/70 mm Hg. Physical examination shows epigastric tenderness. A urea breath test is positive. Upper gastrointestinal endoscopy reveals an ulcerating mass in the gastric antrum. Biopsies of the mass show diffuse infiltrates of small lymphoid cells that are positive for CD20 antigen. A CT scan of the chest and abdomen shows normal regional lymph nodes. Which of the following is the most appropriate therapy with curative intent at this time?

A- Reassurance
B- Distal gastrectomy with gastrojejunostomy
C- External beam radiation therapy
D- Amoxicillin, clarithromycin, and omeprazole

Answers: Q1:A | Q2:B | Q3:C | Q4:B | Q5:C | Q6:D

Answers Explanation File!

GOOD LUCK !

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