# Diseases of LYMPH NODES

Dr. AHMED ROSHDI

## **OUTLINES**

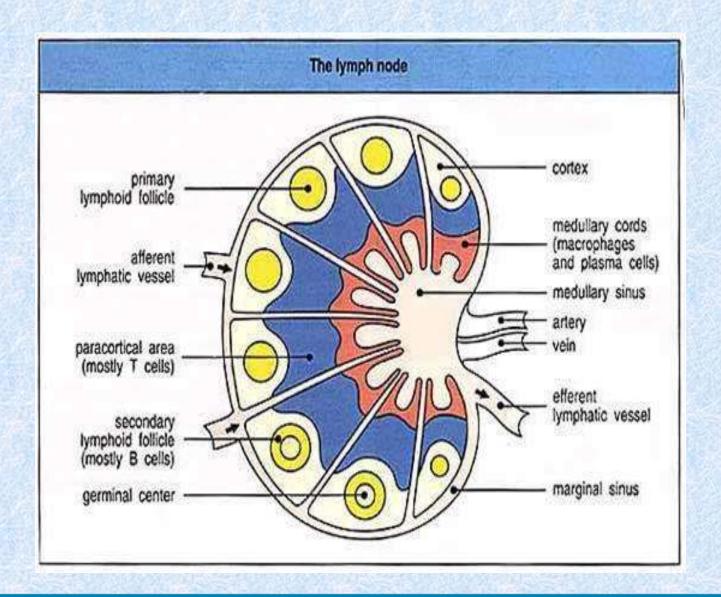
- Introduction
- Lymphadenopathy
- Lymphadenitis
- Reactive hyperplasia
- Metastatic carcinoma of the LN
- Non Hodgkin's lymphoma
- Hodgkin's lymphoma
- Splenomegally

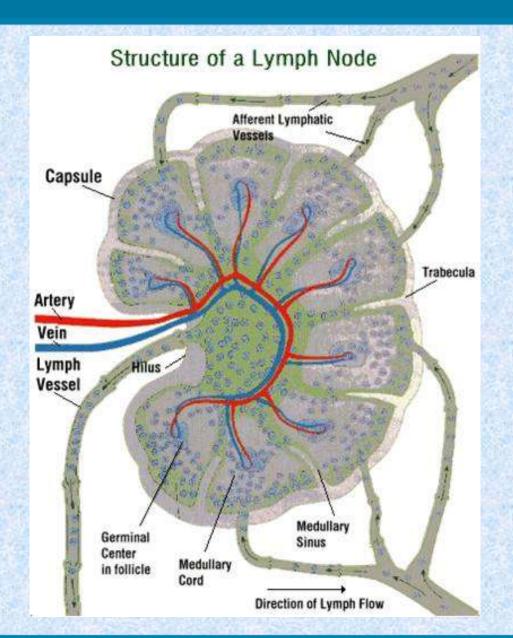
## Lymphocytes and Monocytes:

- Circulate in the blood
- Accumulate in
  - <u>Discrete organised collections</u> (RE system): LNs, spleen, thymus, tonsils, adenoids and payers' patches
  - <u>Less formed collections</u>: BM, lungs, GIT and other tissues

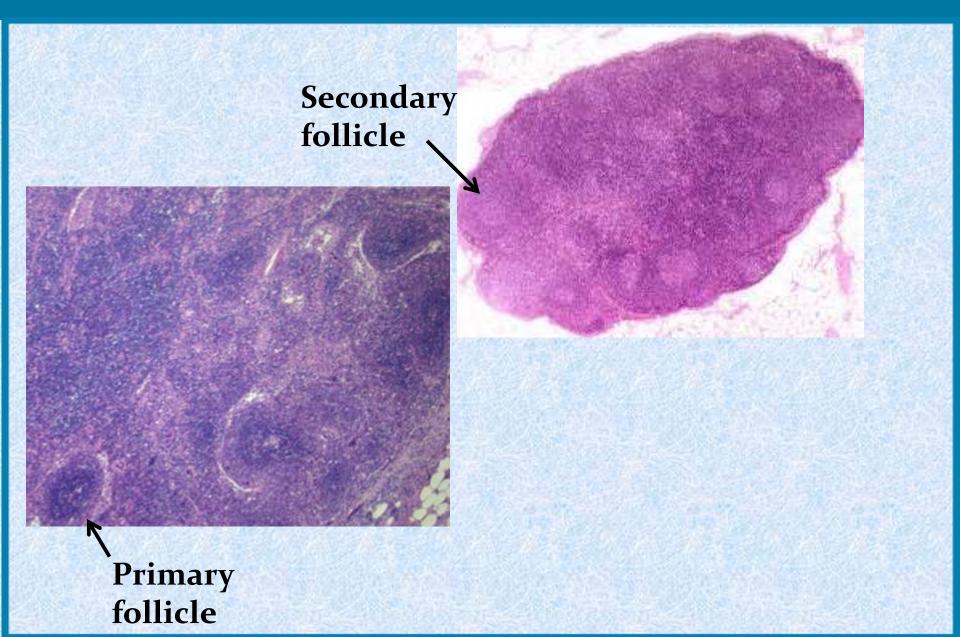
#### Normal LNs:

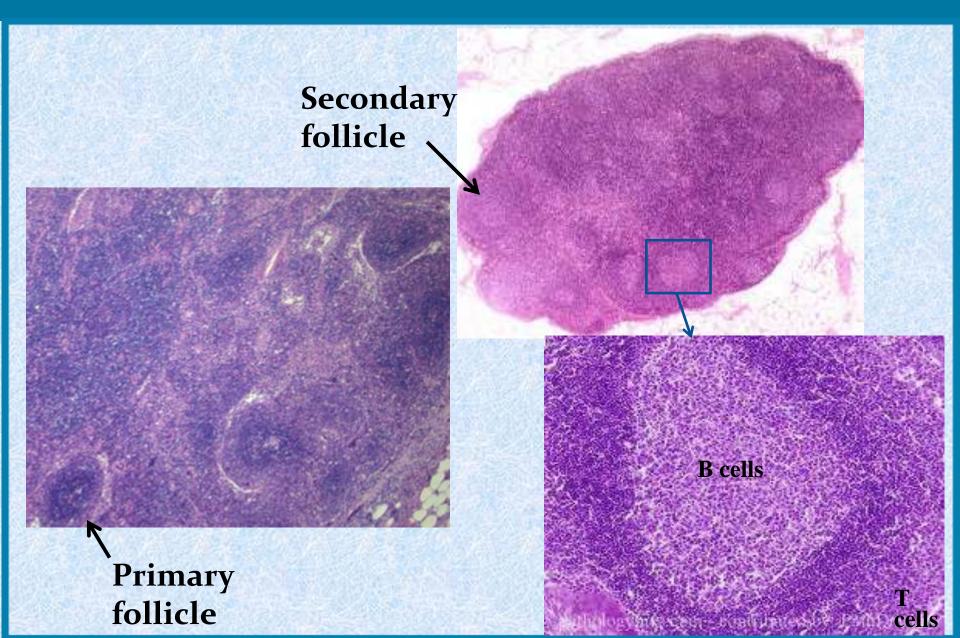
- Grossly (clinically): small, bean shaped arranged in groups (e.g. cervical, axillary and inguinal)
- Seldom palpable









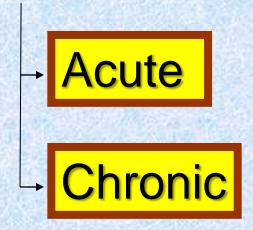


## LYMPHADENOPATHY

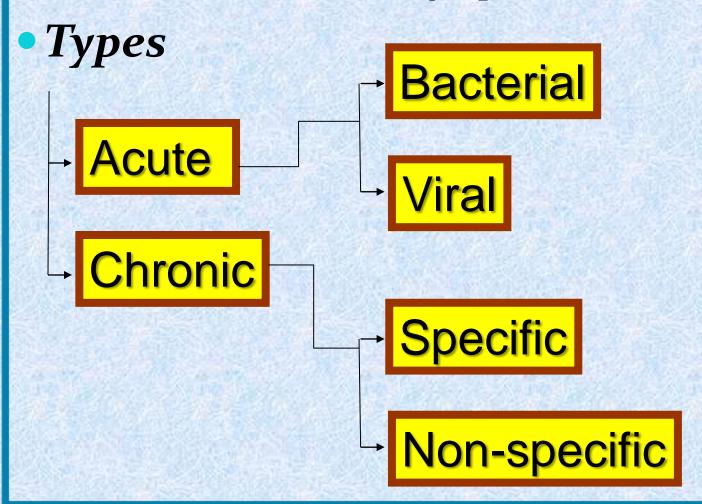
- Definition:
  - Enlargement of one or more groups of lymph nodes
- Types
  - Localized: involve one group of LNs
  - Generalized: involve more than one group of LNs
- Causes
  - □Inflammatory (lymphadenitis):
    - Acute or chronic lymphadenitis
    - Specific or non-specific lymphadenitis (examples)
  - □**Hematologic:** Leukemias
  - Metabolic: Some metabolic diseases
  - **□**Neoplastic:
    - Primary: Lymphoma
    - Secondary (metastatic): commonly carcinoma
  - □**Others:** Reactive hyperplasia of LN

- Definition:
  - Inflammation of the lymph node

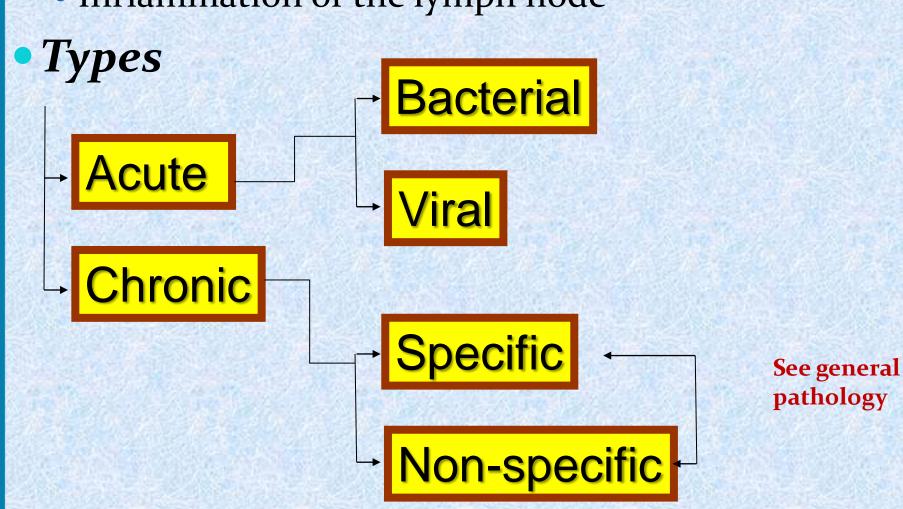
- Definition:
  - Inflammation of the lymph node
- Types



- Definition:
  - Inflammation of the lymph node



- Definition:
  - Inflammation of the lymph node



Types

Bacterial

- Affects L.Ns. draining acute infective lesions (acute tonsillitis → acute cervical lymphadenitis)
- Grossly: enlarged red and tender L.Ns.
- <u>Microscopically:</u> infiltration of the L.N. by acute inflammatory cells (mention)

Types



#### Infectious mononucleosis

- ♦ Cause: EB virus
- ◆ <u>C/P</u>: fever, sore throat, generalized lymphadenopathy
- **♦ Lymph node:**

Expansion of the inter-follicular areas by:

- numerous immunoblasts
- small lymphocytes
- plasma cells
- macrophages

- **□** Definition:
  - Non-specific, non neoplastic enlargement of the LNs due to proliferation of lymphoid tissue
- ☐ Clinically:
  - Non painful LN enlargement involving one or more groups
  - LNs are diffusely enlarged, soft, discrete and not fused.
- **☐** Significance:
  - DD of lymphoma, clinically and histologically (see later)
- ☐ Types:
  - o Follicular
  - Paracortical
  - Sinusal

#### 1. Follicular hyperplasia:

- Due to preferential stimulation of follicular B cells
- Occurs in Rheumatoid arthritis, Sjogren's syndrome and Toxoplasmosis or any irritation at draining area.

#### o M/P:

- Numerous variable sized secondary follicles.
- Large germinal centers.
- Follicles are surrounded by well-distinct mantle zones.
- Lymphocytes does not break lymph node capsule

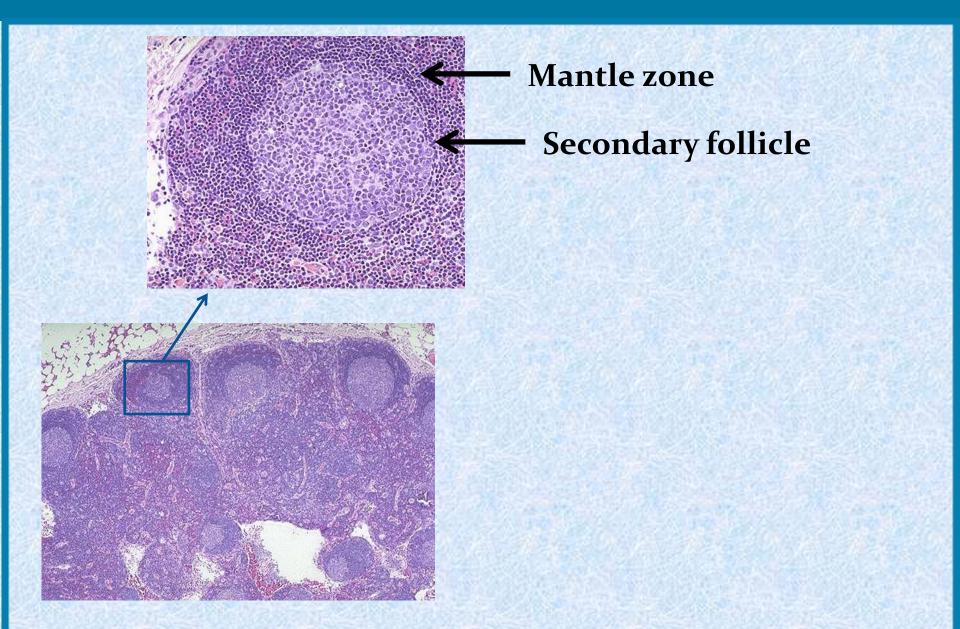
#### 2. Para-cortical hyperplasia:

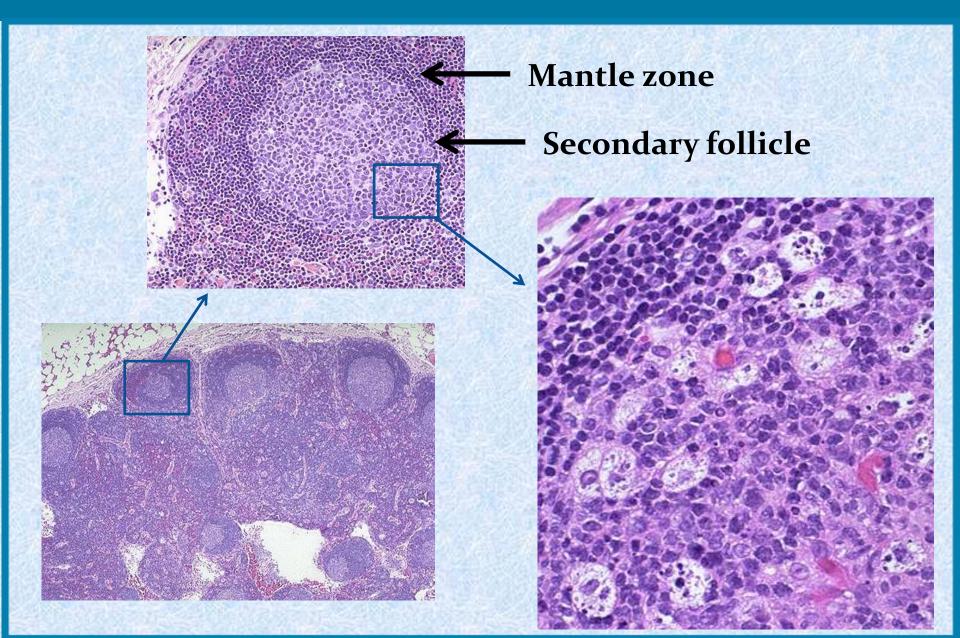
- Due to preferential stimulation of the para-follicular T cells
- o Can be seen in
  - SLE
  - viral lymphadenopathy, as infectious mononucleosis
  - drug-induced lymphadenopathy

#### 3. Sinusal hyperplasia:

- Due to preferential distention of lymph sinuses by benign histocytes accompanied by lymphocytes
  - 1. Sinus histiocytosis with massive lymphadenopathy
  - 2. Langerhans cell histiocytosis







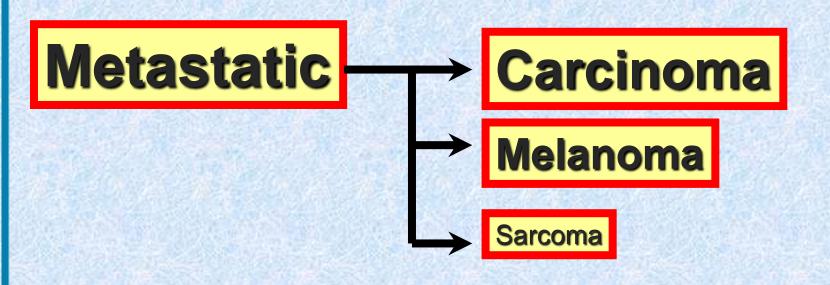
# Tumours of the lymph nodes

#### TUMOURS OF LNs

Metastatic

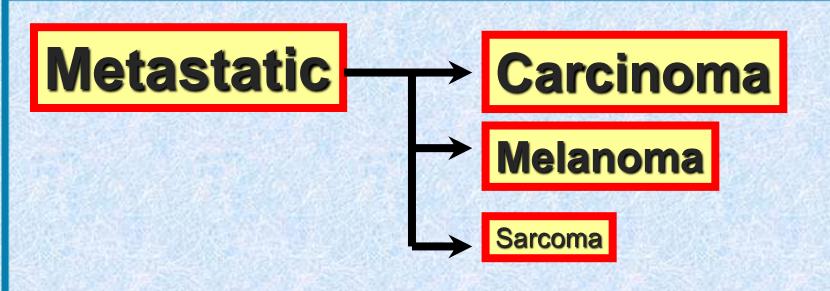
Primary (Lymphoma)

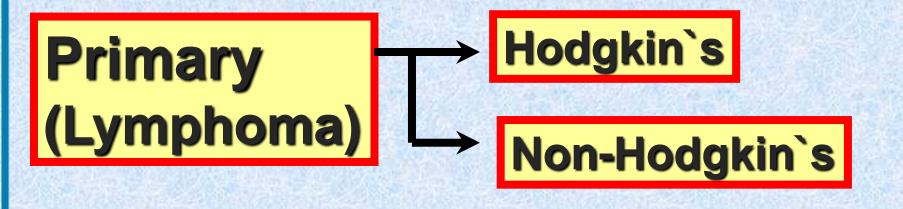
## TUMOURS OF LNs



Primary (Lymphoma)

## TUMOURS OF LNs





#### Metastatic carcinoma of the LN

- Definition:
  - Involvement of the LN tissue by malignant epithelial cells
- Common sites:
  - Axillary LN: in breast cancer
  - Cervical LN: in thyroid and naso-phareyngeal cancers
  - Porta-hepatis LN: in hepatic, GB and pancreatic cancers
  - Mesenteric LNs: in cancer colon and rectum
  - Iliac and para-aortic LN: as in cancer bladder and cancer cervix
- Grossly
  - Multiple, enlarged discrete or fused LNs with greyish white cut section

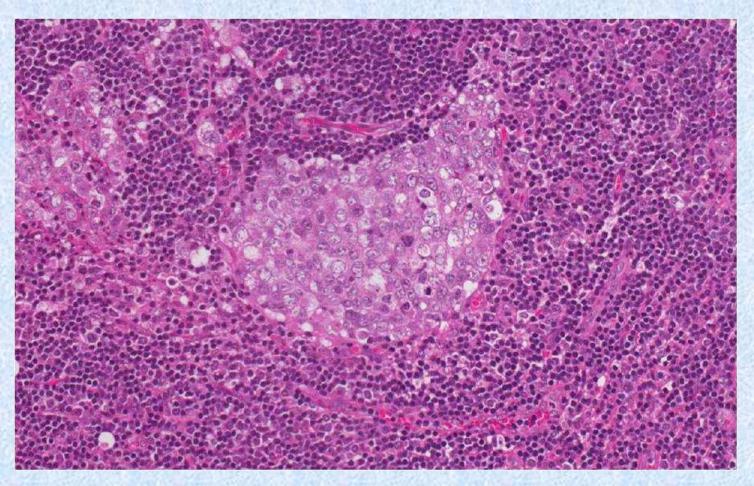
#### Metastatic carcinoma of the LN

- M/P:
  - <u>Early</u>: deposition of malignant epithelial cells in the subcapsular lymph sinuses (<u>mention features of malignancy</u>)
  - In advanced cases: LN tissue is partially, sub-totally or totally replaced by the neoplastic cells
  - The metastatic cells are similar to the primary tumour cells (arrange in sheets, nests, glands, papillae......)
  - The nearby lymphoid tissue (if present) show features of lymphoid hyperplasia

#### Clinical importance:

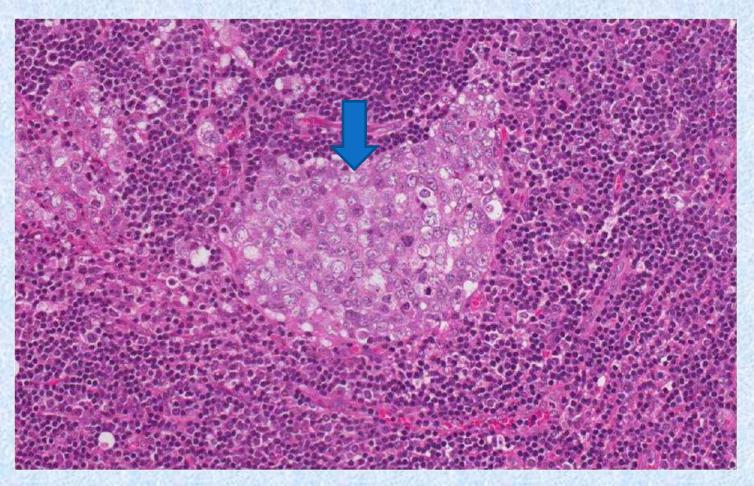
 LN metastasis is considered during TNM staging; treatment and prognosis of cancer patients

#### Metastatic carcinoma of the LN



**Comment???** 

#### Metastatic carcinoma of the LN

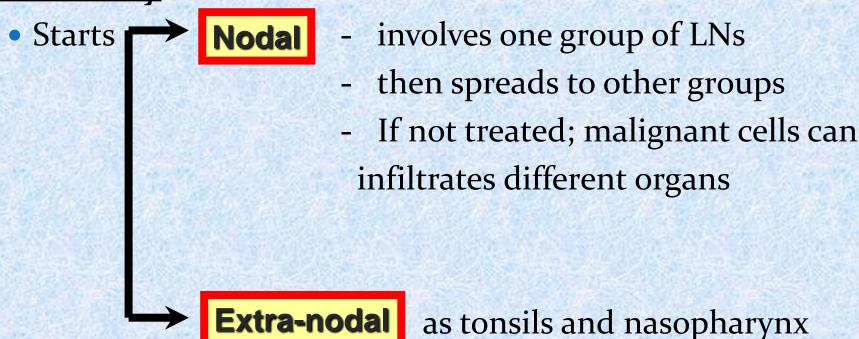


**Comment???** 

#### • Definition:

Malignant tumours of lymphoid tissue.

#### Clinically

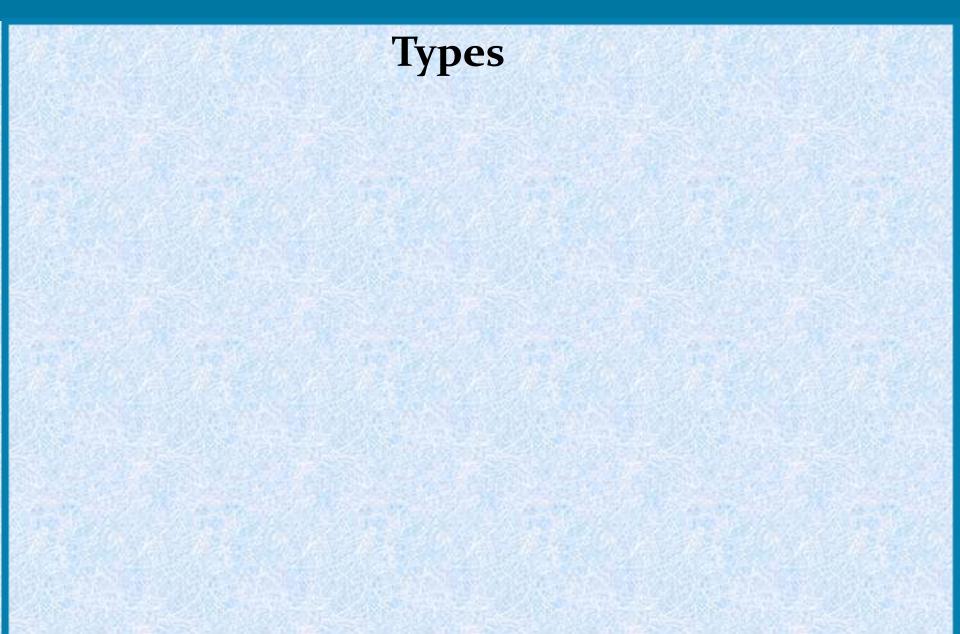


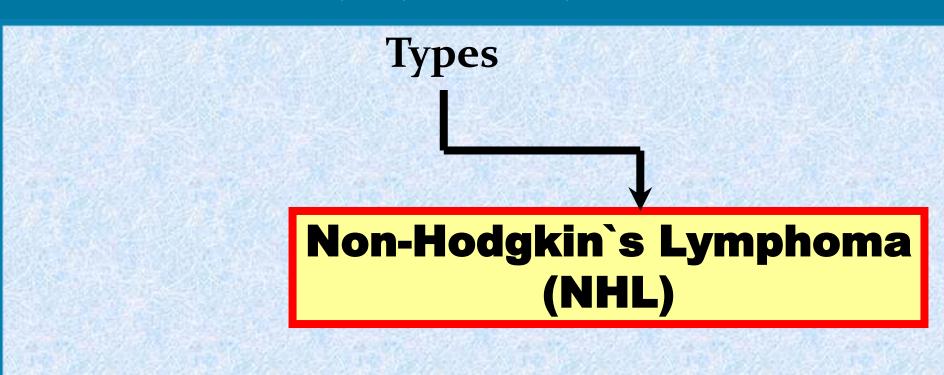
#### • Grossly:

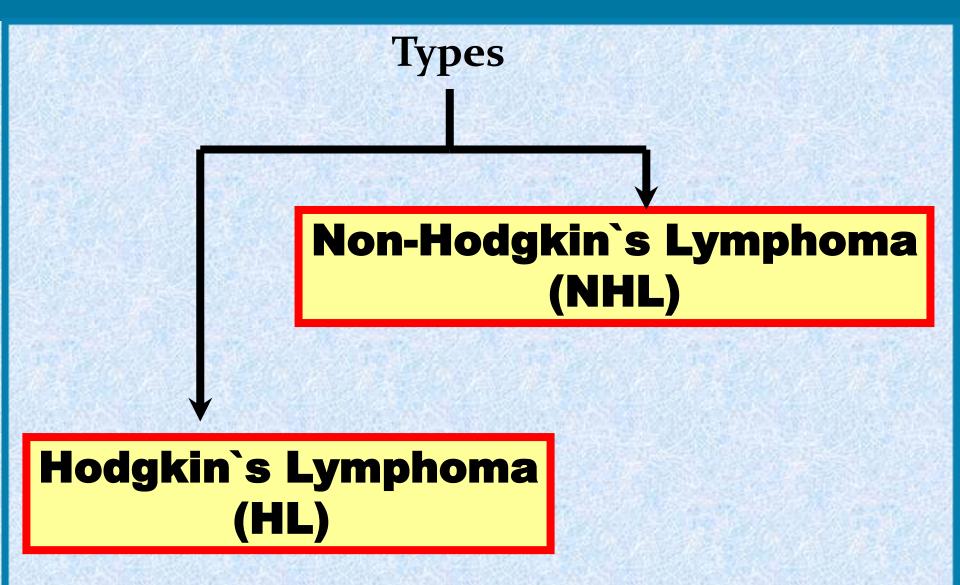
- Multiple painless lymph node enlargement
- Firstly discrete but become fused as tumor cells infiltrate peri-nodal tissues.
- Cut surface is homogenous and gray or pink in color

#### • M/P:

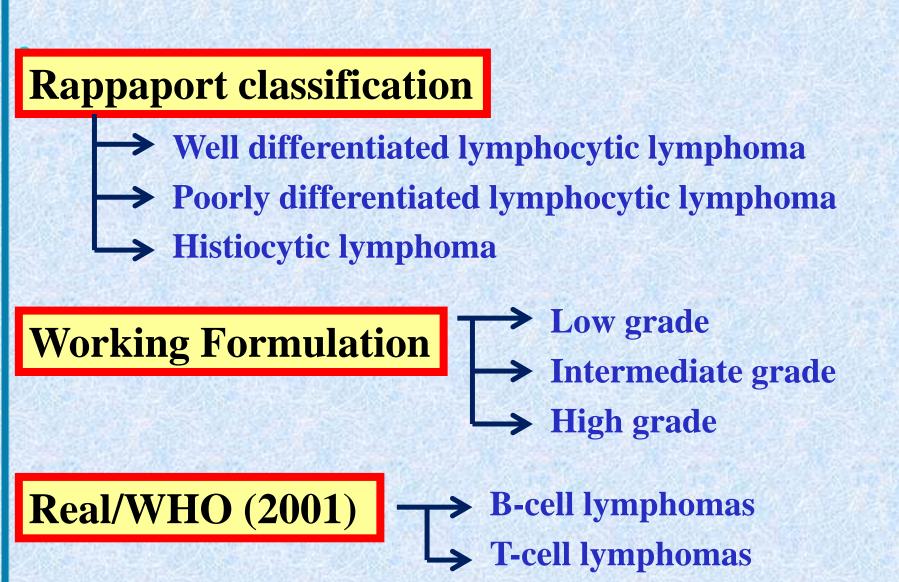
- Effacement of normal nodal architecture is a common general feature
- Other histological features vary according to the type of lymphoma







# Non-Hodgkin's Lymphoma



# Non-Hodgkin's Lymphoma

## **Real/WHO (2001)**

#### B cell lymphoma

#### Precursor B cell lymphoma

•Precursor B cell leukemia/ lymphoma

#### Peripheral B cell neoplasms

- B cell chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL)
- 2. Lymphoplasmocytic lymphoma
- 3. Mantle cell lymphoma
- 4. Follicular lymphoma
- 5. Marginal zone lymphoma
- 6. Extranodal lymphoma of mucosa associated lymphoid tissue (MALT).
- 7. Plasmacytoma/ multiple myeloma
- 8. Diffuse large B cell lymphoma
- 9. Mediastinal large B cell lymphoma
- 10. Burkitt's lymphoma

#### T cell lymphoma

#### Precursor T cell lymphoma

•Precursor T cell leukemia/ lymphoma

#### Peripheral T cell neoplasms

- 1. T cell (CLL/SLL)
- 2. Large granular lymphocytic leukemia
- 3. Mycosis fungoides & Sezary syndrome
- 4. Peripheral T cell lymphoma unspecified
- 5. Angio-immunoblasic T cell lymphoma
- 6. Natural killer/T cell lymphoma
- 7. Intestinal T cell lymphoma
- 8. Adult T cell leukemia/ lymphoma
- 9. Anaplasic large T cell lymphoma

#### **Working Formulation**

- ☐ Solely based on the morphology of H&E sections.
- ☐ Has therapeutic and prognostic validity.
- ☐ Depends on:
  - Architectural features (low magnification):
    - •follicular proliferation
    - diffuse proliferation
  - Cytological features (high magnification):

#### Cell size

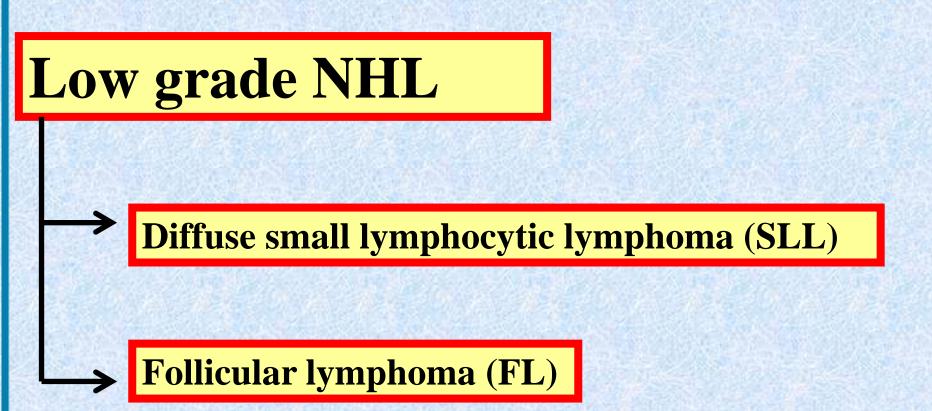
- small
- large
- mixed small and large

#### **Nuclear outline**

- cleaved (indented)
- non-cleaved

#### **Working Formulation**

Low Grade	Intermediate Grade	High Grade	
Small lymphocytic	Follicular large cell	Immunoblastic	
Follicular small cell	Diffuse small cells	Lymphblastic	
Follicular mixed small and large cell	Diffuse mixed cell Diffuse large cell	Burkitt's lymphoma	



## Low grade NHL

#### Diffuse small lymphocytic lymphoma (SLL)

#### Clinical features:

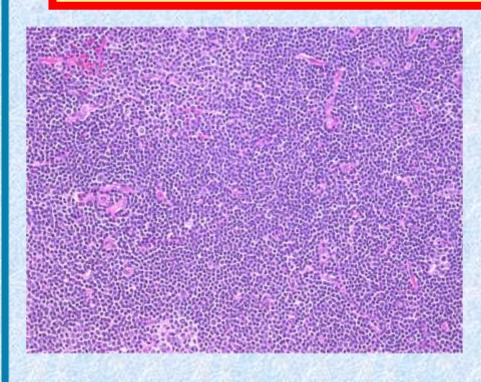
- Affects old age (~ 60 years)
- Generalized lymphadenopathy
- Hepato-splenomegaly is common.
- May be accompanied with chronic lymphocytic leukemia

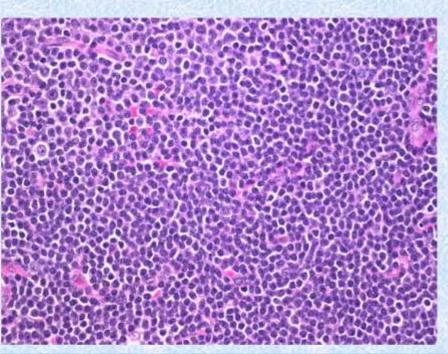
#### • Pathological features:

- ♦ Effacement of nodal architecture by a diffuse infiltrate of small lymphocytes
- ♦ The lymphocytes have:
  - scant cytoplasm
     dark stained nuclei
  - inconspicuous nucleoli. rare mitotic activity.

#### Low grade NHL

Diffuse small lymphocytic lymphoma (SLL)





#### Low grade NHL

Follicular lymphoma (FL)

#### • Clinical features:

- Affects old age (~ 60 years)
- Generalized lymphadenopathy and splenomegaly.
- Extra-nodal sites (e.g. GIT) may be involved

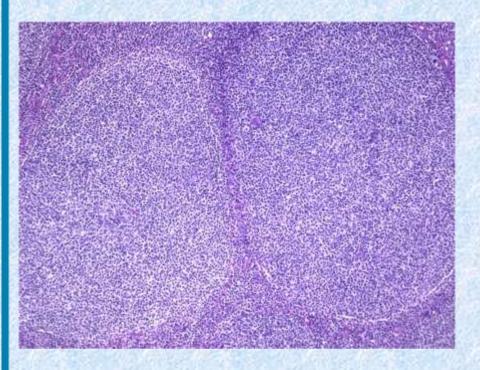
#### Pathological features:

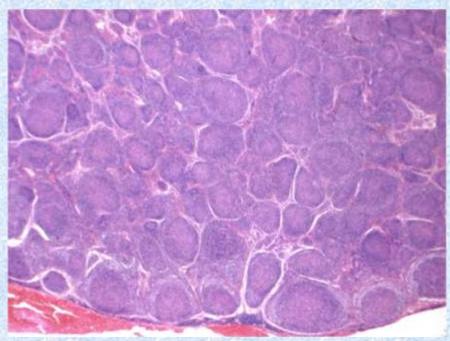
- ☐ Effacement of nodal architecture by neoplastic follicles
- ☐ The follicles resample secondary follicles, but with:
- crowding of follicles and compression of inter-follicular tissue.
- lacking mantle zones
- lacking tingible-body macrophages
- the neoplastic lymphocytes are monoclonal (by IHC)

#### Follicular lymphoma (FL)

- <u>Types:</u> Three types of FL (based on cell morphology):
  - A. FL with predominantly small cleaved cell (low grade):
    - Cells are slightly larger than normal lymphocytes
    - Scanty cytoplasm.
    - Irregular nuclear contour with prominent indentations.
    - Few mitosis
  - B. FL with mixed small and large cell type (low grade):
    - Component of the small cells described above
    - The follicles contain large number of large cleaved or non-cleaved cells accounting to 20-25% of the cell count.
  - C. FL with predominantly large cells (intermediate grade).

Follicular lymphoma (FL)

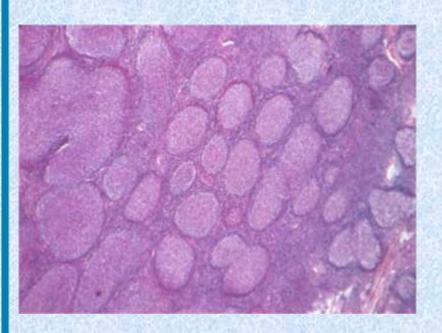




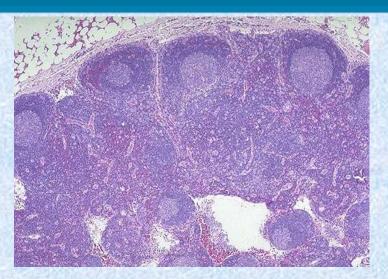
#### Follicular lymphoma (FL)

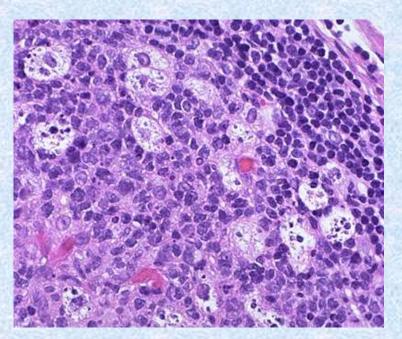
	F. Hyperplasia	F. Lymphoma
L. power	<ul> <li>Loosely packed follicles</li> <li>Polymorphic follicles</li> <li>Prominent mantle zone</li> <li>Polarized follicles</li> <li>Prominent germinal center</li> <li>Preserved open sinuses</li> <li>No capsular invasion</li> </ul>	<ul> <li>Tightly packed follicles</li> <li>Monomorphic follicles</li> <li>Absent mantle zone</li> <li>Non polarized follicles</li> <li>No detected germinal center</li> <li>Compressed or destructed sinuses</li> <li>Extension to peri-nodal tissue</li> </ul>
H. power	<ul> <li>High mitotic rate in germ center</li> <li>Tingible body macrophages</li> <li>Paracortical lymphoid cells</li> <li>between follicles</li> </ul>	<ul><li>Lower mitotic rate</li><li>No tingible body macrophages</li><li>Atypical cleaved cells between follicles</li></ul>
IHC	<ul><li>Polyclonal light chain expression</li><li>No reactivity to bcl-2 protein</li></ul>	<ul><li>Monoclonal light chain expression</li><li>85% reactivity to bcl-2 protein</li></ul>

#### Follicular lymphoma (FL)



**Comment??** 





# Intermediate grade NHL

- Follicular predominantly large cell lymphoma
- Diffuse small cleaved cell lymphoma
- Diffuse mixed small and large cell lymphoma
  - Diffuse large cell lymphoma

## Intermediate grade NHL

- Follicular predominantly large cell lymphoma
- A rare type of FL.
- Most of neoplastic cells of the follicles are large with:
  - cleaved or
  - non-cleaved nuclei.
- •Mitotic figures are more numerous
- Diffuse small cleaved cell lymphoma
- Small cleaved cells arranged diffusely

#### Intermediate grade NHL

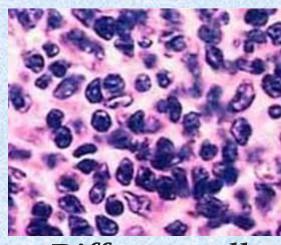
#### Diffuse mixed small and large cell lymphoma

- •A mixture of small cleaved cells and large cells.
  - •Small cleaved cells:
    - Nucleus with irregular contour and indentation
    - Scanty cytoplasm.
  - •Large cell
    - •Up to four times the size of normal lymphocyte.
    - •Round or oval nucleus with one or two nucleoli.
    - Moderate pale cytoplasm
    - •Frequent mitosis.

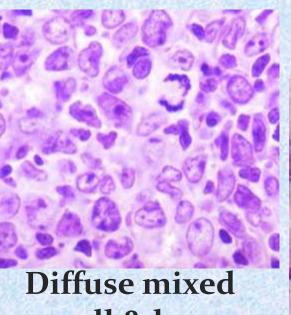
#### Diffuse large cell lymphoma

•Predominantly large cells (as described above).

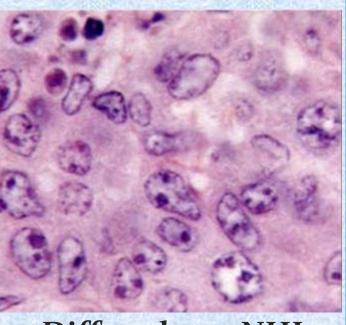
## Intermediate grade NHL



Diffuse small cleaved NHL



small & large



Diffuse large NHL



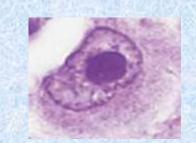
## High-grade NHL



- Diffuse B or T cell in origin
- Composed of large atypical cells with large nuclei
- The nucleoli are large and typically single and central
- Mitoses are numerous

#### Lymphoblastic lymphoma

- Diffuse B or T cell lymphoma
- Composed of large lymphoblasts
- With irregular convoluted nuclei
- Nucleoli are small
- Cytoplasm is moderate and cell borders are indistinct





## High-grade NHL

 $\rightarrow$ 

Burkitt's Lymphoma (BL)

- Only B cell lymphoma
- •Types:
  - ♦ Endemic BL:
    - Endemic in Africa
    - Affects mainly children
    - EBV infection plays important role in pathogenesis
  - ♦ <u>Sporadic BL</u>: occurs throughout the world
  - ♦ <u>Immunodeficiency-associated BL</u> (HIV-associated)

## High-grade NHL

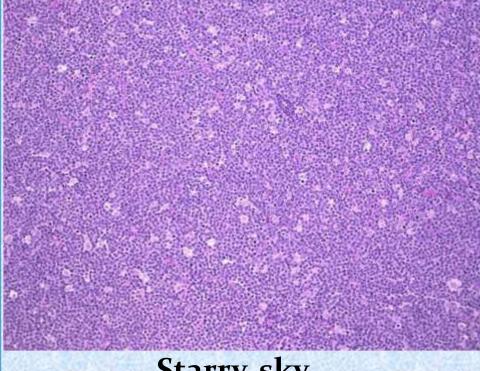
Burkitt's Lymphoma (BL)

<u>C/P</u>: masses in the jaws or abdominal masses <u>Microscopic picture</u>:

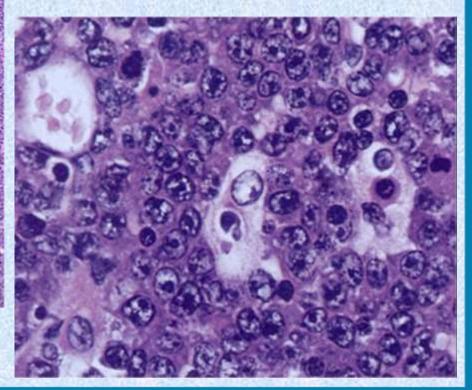
- ♦ neoplastic small lymphocytes having:
- round nuclei with two or more nucleoli
- scanty basophilic cytoplasm
- very high mitotic activity
- ♦ There are <u>scattered macrophages</u> with
- abundant pale cytoplasm,
- containing nuclear debris → Starry-Sky appearance



Burkitt's Lymphoma (BL)







#### **Definition:**

Malignant tumour of lymphoid tissue characterised by presence of:

- Large neoplastic cells (Reed-Sternberg cells)
- Polymorphic cellular background: reactive inflammatory cells (lymphocytes, plasma cells and oesinophiles)

#### **Incidence**

Common disease representing ~30% of all lymphomas.

#### **Clinically**:

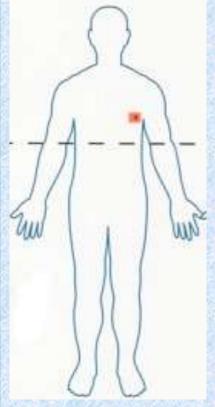
- Biphasic age incidence:
  - in early adult life (15-40 yrs)
  - in old age

#### **Clinically**:

- Usually presents by:
  - Enlarged LNs: commonly cervical & supra-clavicular LNs ± splenomegaly.
  - 2. Systemic manifestation:
    - Occurs in about 25% of cases
    - Include non-specific symptoms as:
      - intermittent fever (Pel-Ebstein fever)
      - night sweats
      - weight loss
  - 3. Clinical staging (Ann-Arbor staging)

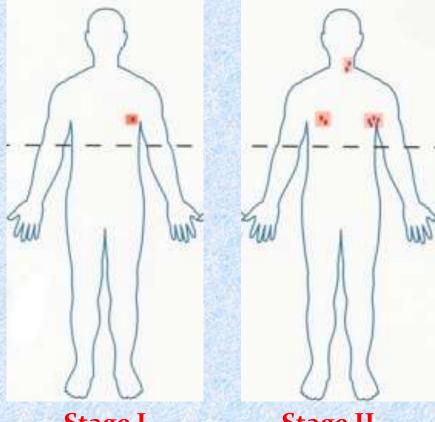
#### **Clinically**:

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Stage I Single LN group

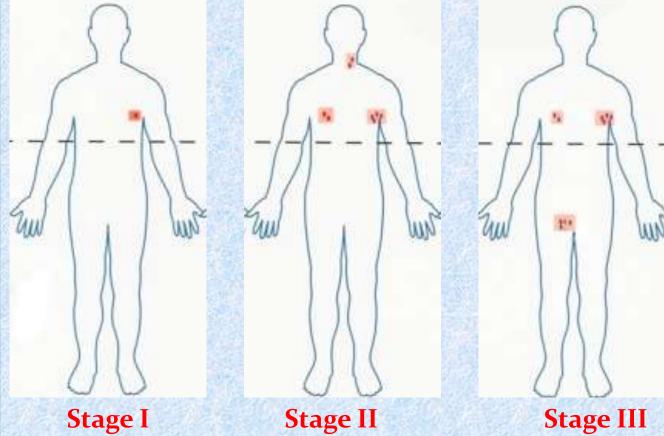
#### **Clinically**:



Stage I Single LN group

Stage II
Two groups on one side of diaphragm

#### **Clinically**:

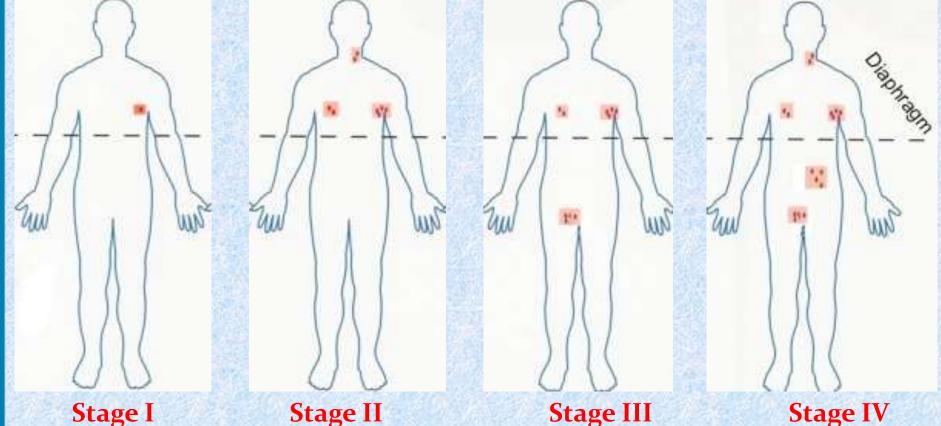


Stage I Single LN group

Two groups on one side of diaphragm

LN groups on both sides of diaphragm

#### **Clinically:**



Stage 1 Single LN group

Two groups on one side of diaphragm

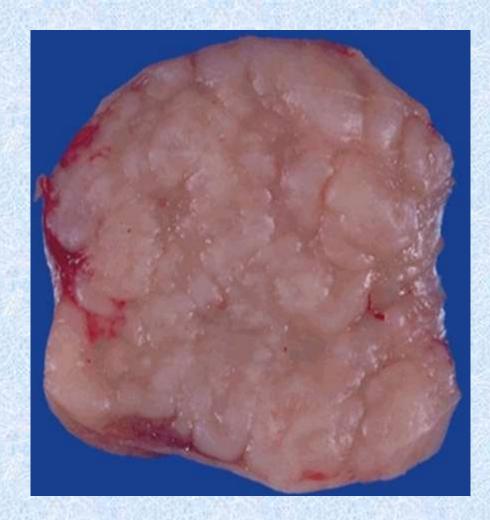
LN groups on both sides of diaphragm

Extranodal extention

#### **Gross picture:**

- **♦ Lymph Nodes:**
- Early: the affected LNs are enlarged, firm, & discrete
- Later: infiltration of the capsule & perinodal CT → fusion of the LNs → an irregular fixed mass
- <u>Cut surface</u> is homogenous grayish pink
- ♦ Spleen:
- Enlarged & firm, with grayish nodules on cut section
- ♦ Extra-nodal sites:
- As spleen, liver bon marrow may be seen (Stage IV)

#### Gross picture:





#### Microscopic picture:

♦ Partial or complete loss of normal nodal architecture

- ♦ Partial or complete loss of normal nodal architecture
- ♦ Infiltration of the LN by:

- ♦ Partial or complete loss of normal nodal architecture
- ♦ Infiltration of the LN by:
  - Reed-Sternberg cells (RS cells) or one of its variants

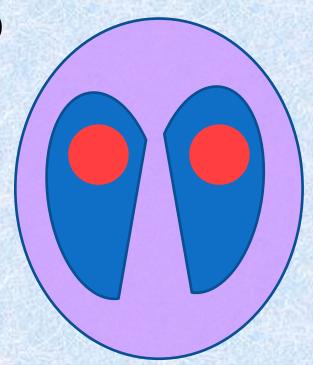
- ♦ Partial or complete loss of normal nodal architecture
- ♦ Infiltration of the LN by:
  - Reed-Sternberg cells (RS cells) or one of its variants
     Surrounded by

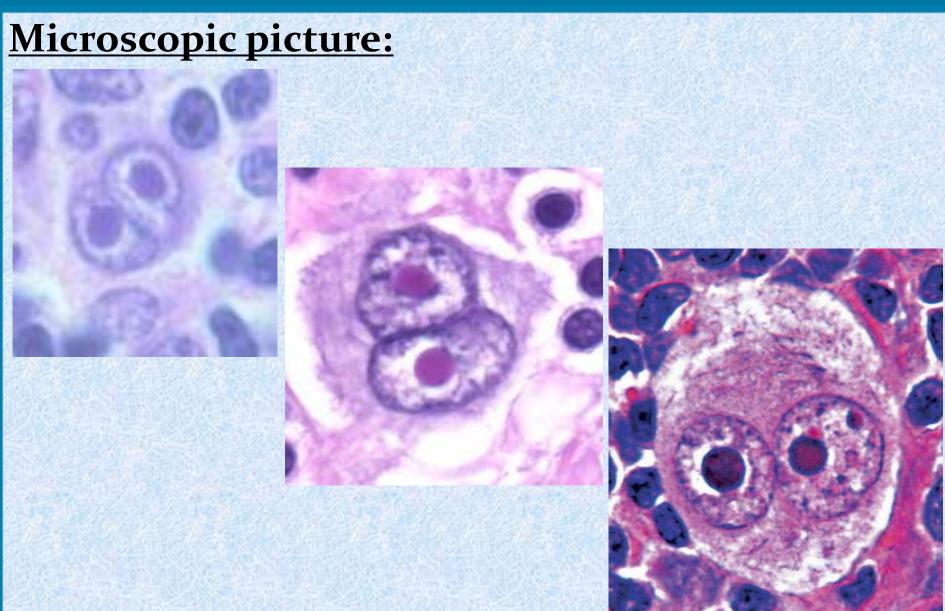
- ♦ Partial or complete loss of normal nodal architecture
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     Surrounded by
  - Reactive inflammatory cells:

- ♦ Partial or complete loss of normal nodal architecture
- ♦ Infiltration of the LN by:
  - Reed-Sternberg cells (RS cells) or one of its variants
     Surrounded by
  - Reactive inflammatory cells:
    - lymphocytes,
    - plasma cells,
    - eosinophils,
    - macrophages

- Reed-Sternberg cells:
  - Also called RS cells, Hodgkin's cell, or Dorothy Reed cells
  - It is the malignant cells in cases of Hodgkin's Lymphoma
  - Features:
    - Size: giant cell (30-60 µm in diameter)
    - Cytoplasm: abundant amphophilic
    - Nucleus:
      - o has two nuclei
      - with prominent eosinophilic nucleolus reaching size of RBC
      - Arranged in mirror image or Owl eye appearance

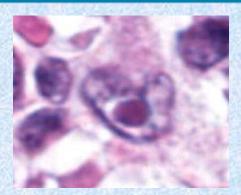
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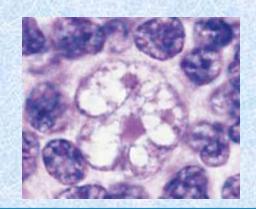


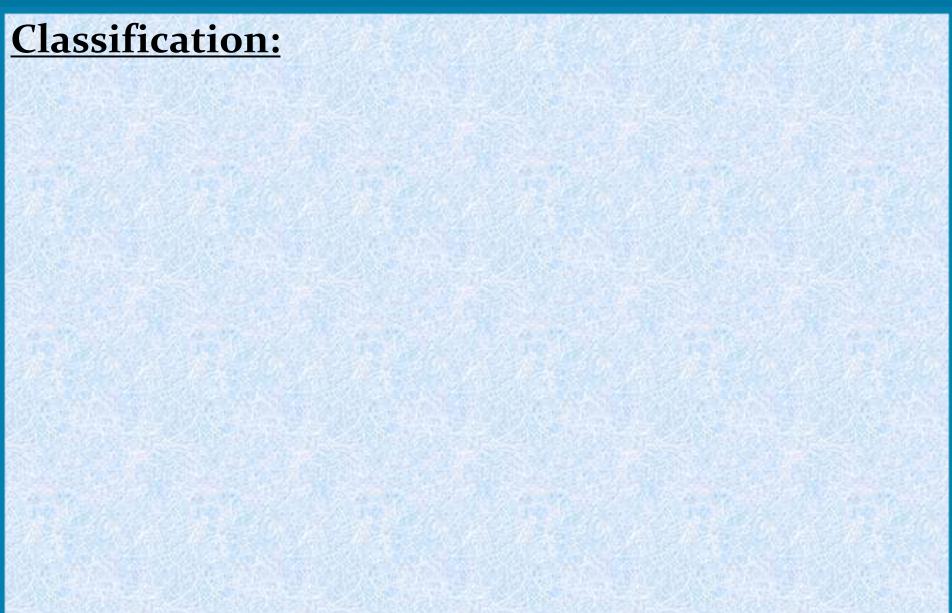
#### Microscopic picture:

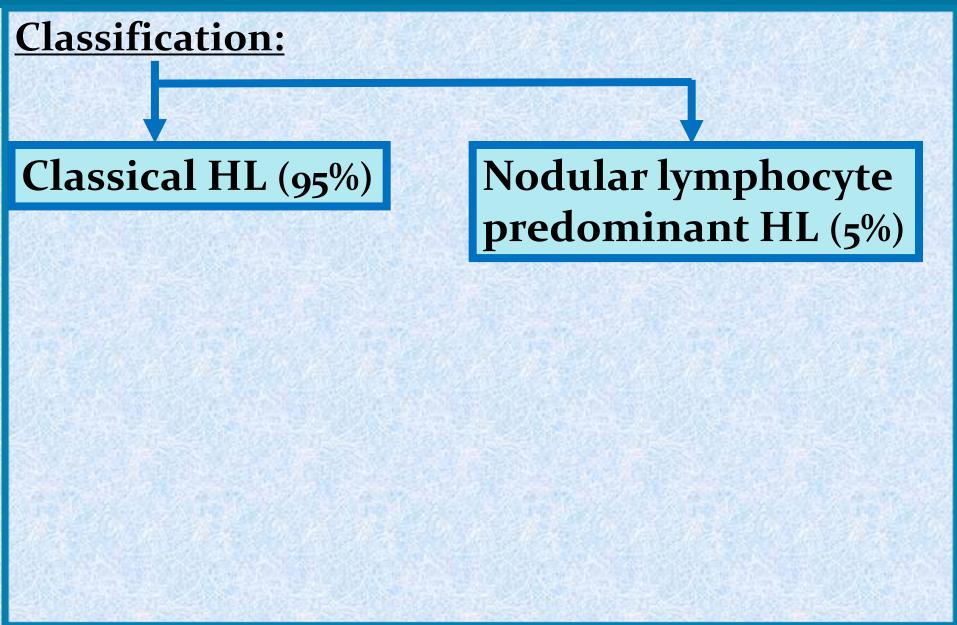
- Variants of Reed-Sternberg cells:
  - 1. <u>Mononuclear variant</u>: similar to typical RS-cell, but with a single nucleus
  - 2. <u>Lacunar cell</u>: similar to typical RS-cell, but with shrunken cytoplasm (clear space between shrunken cytoplasm & cell wall)
  - 3. Lymphocytic & Histiocytic (L&H) variant: mononuclear cells with lobed nuclei and small nucleoli (popcorn nuclei).

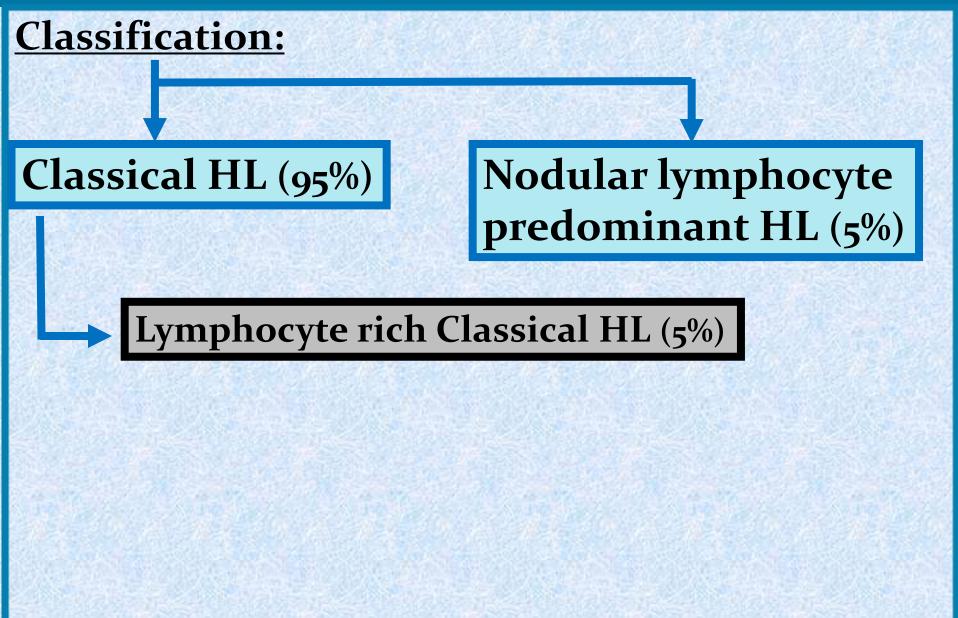


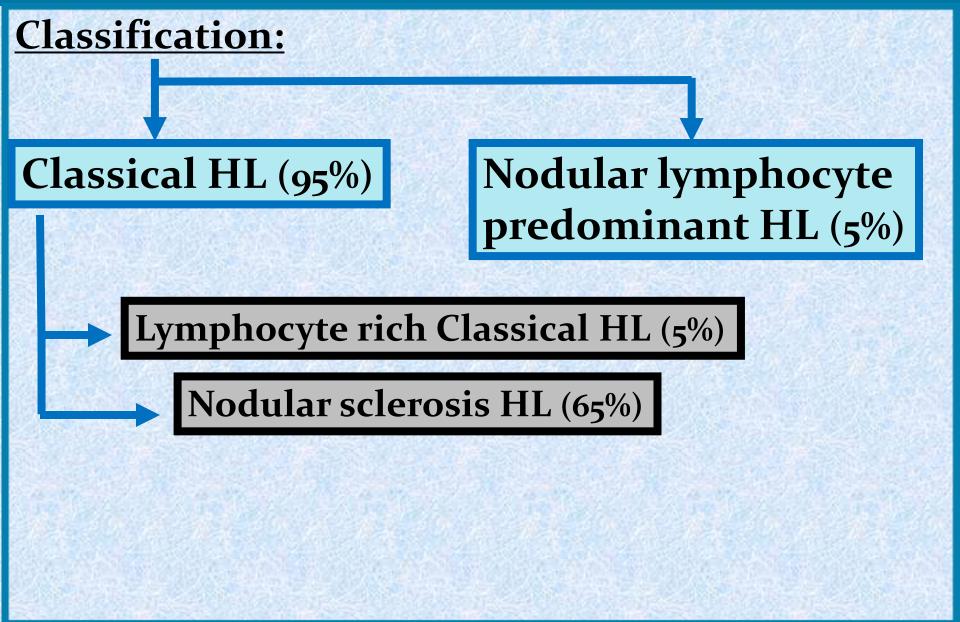


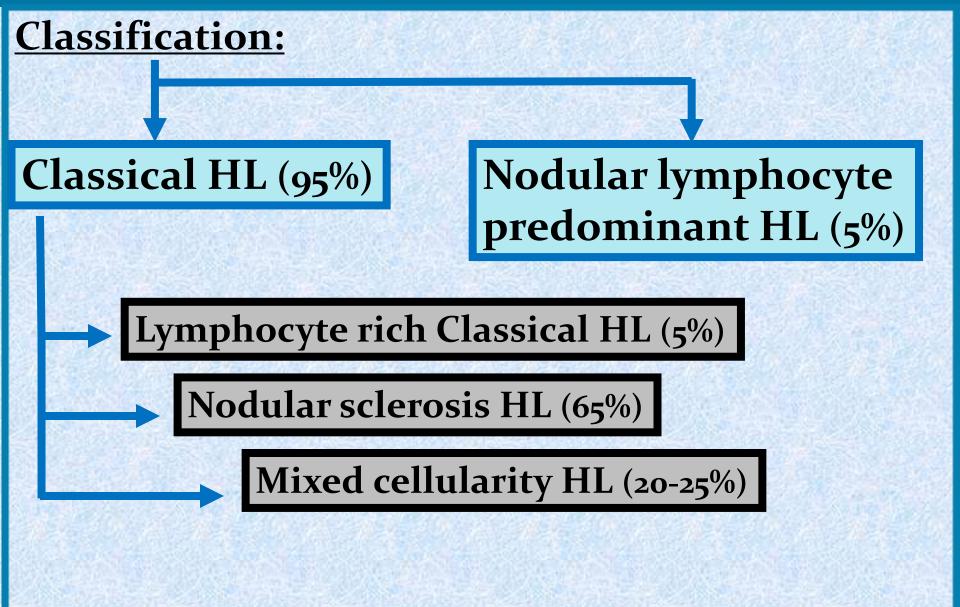


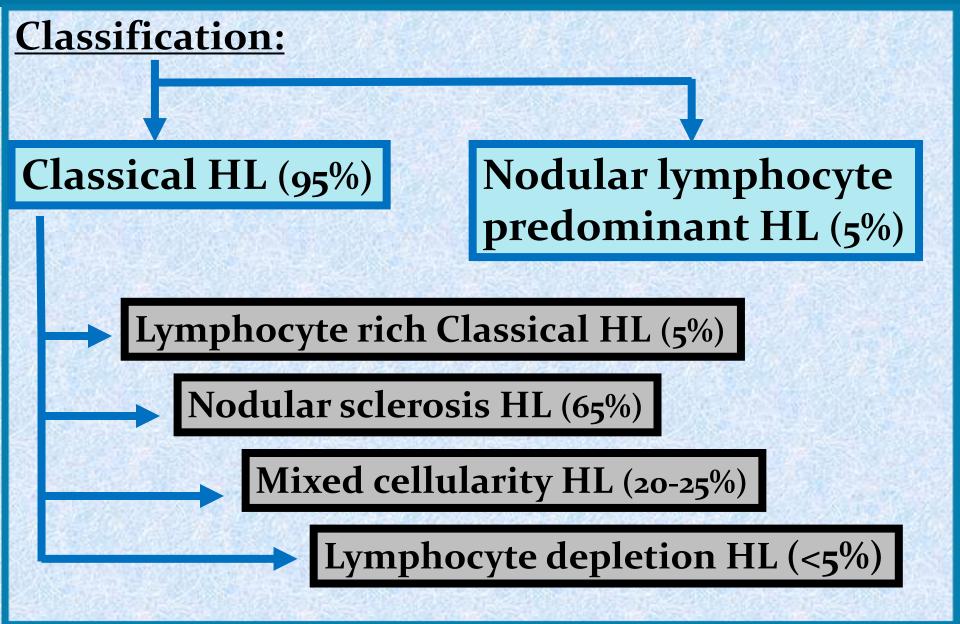








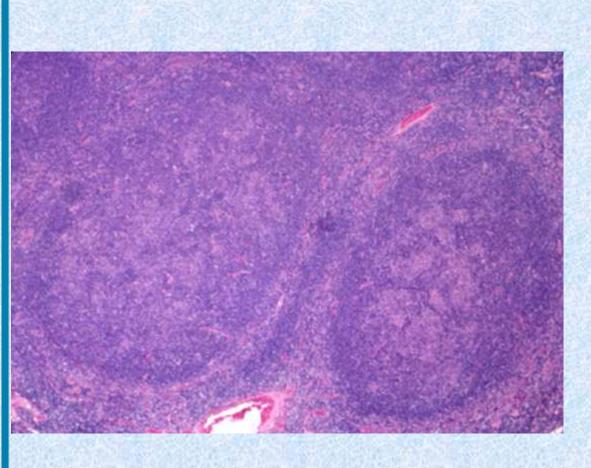


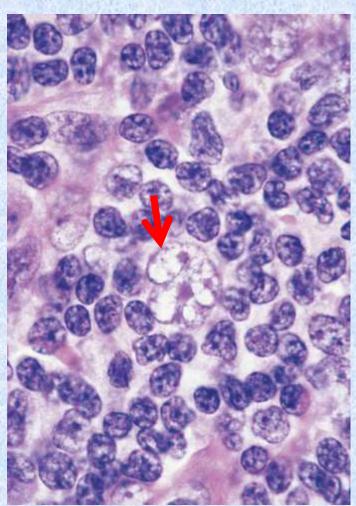


#### Nodular lymphocyte predominant HL

- Represents about 5% of all HL cases
- Has the best prognosis
- Characterised by
  - Loss of normal nodal architecture
  - Nodular infiltrate of the lymph node consists of reactive cells (predominantly lymphocytes)
  - Pop-Corn type Hodgkin's cells
  - No typical RS cells.

Nodular lymphocyte predominant HL





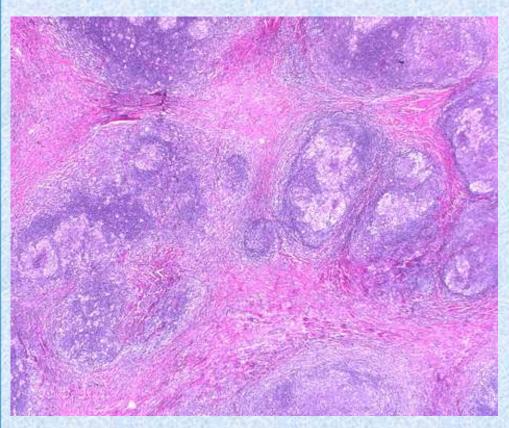
#### Lymphocyte-rich classical HL

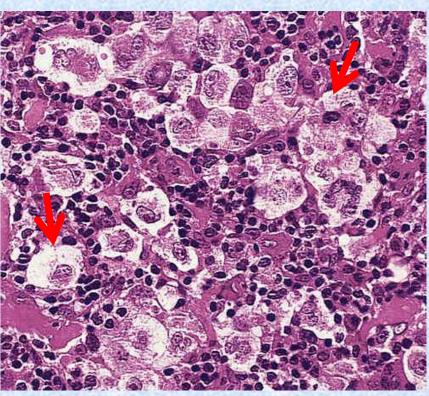
- Represents about 5% of cases
- Has good prognosis
- Characterised by
  - Loss of normal nodal architecture
  - The infiltrate consists of reactive cells (predominantly lymphocytes with oesinophiles, plasma cells and histocytes)
  - Mononuclear type Hodgkin's cells
  - Typical RS cells may be seen.

#### Nodular sclerosing HL

- Represents about 65% of HL cases
- Has good prognosis
- Characterised by
  - Loss of normal nodal architecture
  - Lymph nodal tissue is divided into nodules by thick collagen bands.
  - The reactive infiltrate consists of a cellular mixture of lymphocytes, esinophiles, plasma cells and histocytes
  - Lacunar type Hodgkin's cells
  - No or scanty typical RS cells.

Nodular sclerosing HL

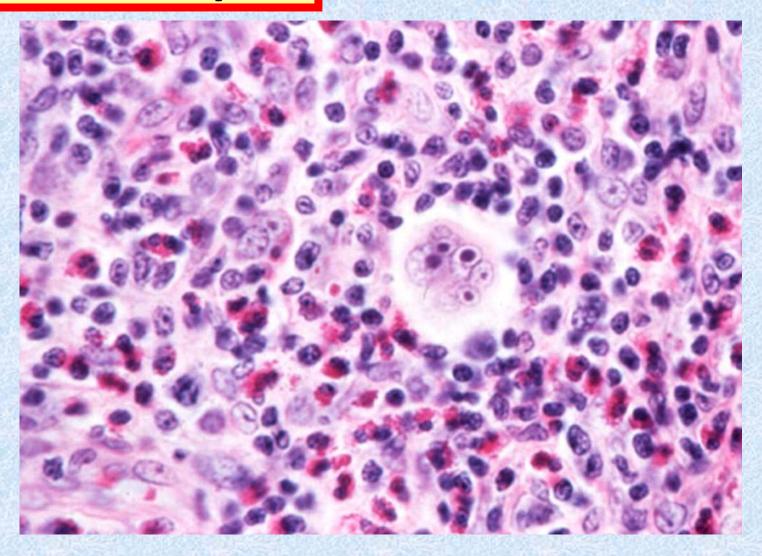




#### Mixed cellularity HL

- Represents about 20-25% of cases
- Has poor prognosis
- Characterised by
  - Loss of normal nodal architecture
  - The reactive infiltrate consists of a cellular mixture of lymphocytes, numerous oesinophiles, plasma cells and histeocytes
  - Numerous Typical RS cells
  - Mononuclear cells are commonly seen.

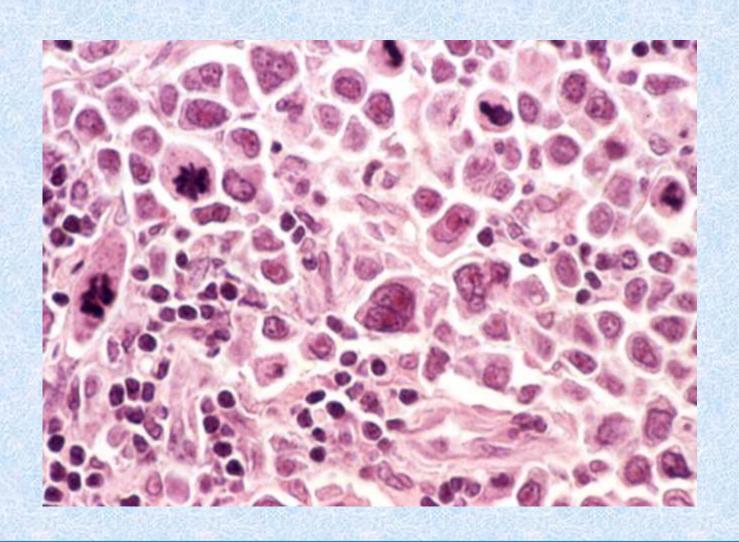
Mixed cellularity HL



#### Lymphocyte depletion HL

- Represents 1-5% of cases
- Has the worst prognosis
- Characterised by
  - Loss of normal nodal architecture
  - Infiltration of the LN by numerous Typical RS cells and Mononuclear Hodgkin's cells with frequent mitosis
  - Few reactive cells and few lymphocytes.

Lymphocyte depletion HL



#### **Prognosis:**

- Based on histological types:
  - Nodular lymphocyte predominant and Lymphocyte rich Classical HL have good prognosis
  - Nodular sclerosis HL has relatively good prognosis
  - Mixed cellularity HL has poor prognosis
  - Lymphocyte depletion HL has worse prognosis
- Clinical stage and presence of systemic infiltration are more important than histological features in determining prognosis of HL.

### NHL and HL

NHL	HL
Tend to involve more than one group of LNs	often localized to a single group of LNs
More frequent involve peripheral LN groups	More frequently involve axial LN groups
Cervical, mediastinal, para-aortic can be involved	Cervical, mediastinal, para-aortic are commonly involved
Mesenteric nodes and Waldeyer ring are commonly involved.	Mesenteric nodes and Waldeyer ring are rarely involved.
Frequent peri-nodal extension	Less frequent perinodal extension
Usually non-contiguous spread.	Spread is usually by contiguity.
Involvement of extra-nodal sites is common.	Involvement of extra-nodal sites is uncommon.

#### LYMPHOMA

#### Tissue tumour markers for diagnosis of lymphoma

- Identification of lymphoma subtype is very essential from the therapeutic and prognostic points of view
- Histological features of lymphoma subtypes <u>can be similar</u>, so <u>not conclusive</u> to separate different types
- Immunohistochemistry is mandatory to differentiate
- Examples:
  - All B cell lymphomas are CD19, CD20 and CD79 positive
  - T cell lymphomas are CD3 and CD5 positive
  - Burkitt's lymphoma and follicular lymphomas are CD10.
  - Follicular lymphoma is bcl-2 positive
  - Hogdkin's cells are CD15 and CD30 positive

#### DISEASES OF SPLEEN

#### Causes of splenomegaly

- □ Inflammatory:
  - Acute splenic swelling in septicemia and typhoid fever.
  - Viral infections as infectious mononucleosis.
  - Bacterial infections as tuberculosis.
  - Parasitic infections as bilharziasis, malaria and hydatid cyst.
- □ Circulatory disturbances
  - Chronic general venous congestion in RSHF.
  - Portal hypertension in liver cirrhosis and bilharzial hepatic fibrosis.
  - Splenic infarctions.
- □ Hematologic<u>:</u>
  - (a) Haemolytic anaemias. (c) Leukemias.
  - (b) Polycythaemia vera (d) Thrombocytopenia purpura.

#### DISEASES OF SPLEEN

#### **Causes of splenomegaly**

- □ Metabolic:
  - Amyloidosis, hemochromatosis and lipid storage diseases
- □ Neoplastic:
  - Benign tumors as fibroma, hemangioma and lymphangioma.
  - Malignant tumors as malignant lymphomas, angiosarcoma and fibrosarcoma.
- □ Hypersplenism

# Thank you

Good luck

Dr Ahmed Roshdi