

“Hematopoietic And Lymphoid System (HLS)”

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Hodgkin Lymphoma

- A primary malignant neoplasm of the lymphoid system arising from germinal center B cells.
- Unlike NHL, they arise in a single lymph node or chain of lymph nodes and spread characteristically in a stepwise fashion to the anatomically contiguous nodes then spleen, liver and BM.
- Bimodal age distribution:
 - 20 - 30 years of age.
 - > 50 years of age.
- **Cervical and supraclavicular** nodes are the most commonly affected.

❖ Clinical Presentations

- ❑ Painless lymphadenopathy.
- ❑ B-symptoms (cytokines release):
 - ❑ Fever
 - ❑ Night sweats
 - ❑ Weight loss (10% of body weight)
- ❑ Splenomegaly in 16% of the cases.
- ❑ Anemia due to bone marrow involvement in 5% of the cases.

Hodgkin Lymphoma

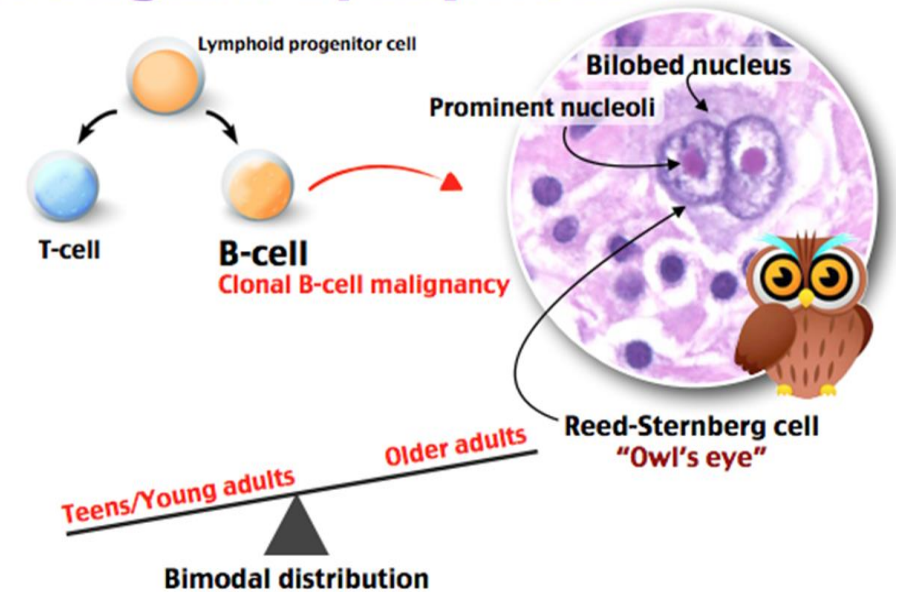
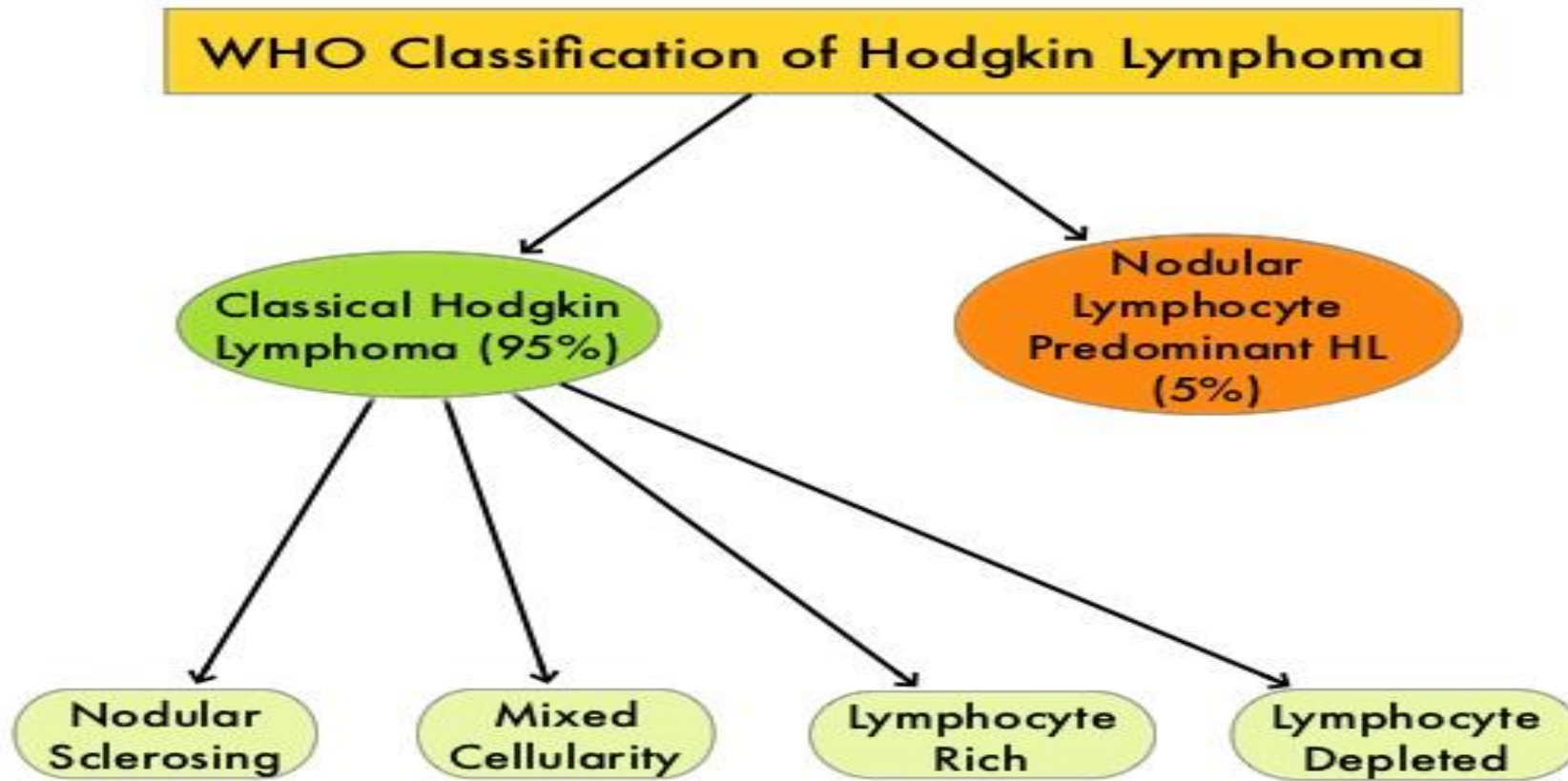




Table 12.9 Clinical Differences Between Hodgkin and Non-Hodgkin Lymphomas

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

❖ Classification Of Hodgkin lymphoma



❖ Morphology

1. **Neoplastic cells ((Reed-Sternberg cells (RS))** (derived from B cells, minor fraction).
2. Immunologic reaction to tumor:
 - Lymphocytes composed mostly of small lymphocytes with the CD4 immunophenotype.
 - Histiocytes.
 - Eosinophils
 - Plasma cells.
 - Neutrophils.
 - Fibroblasts and fibrous tissue.

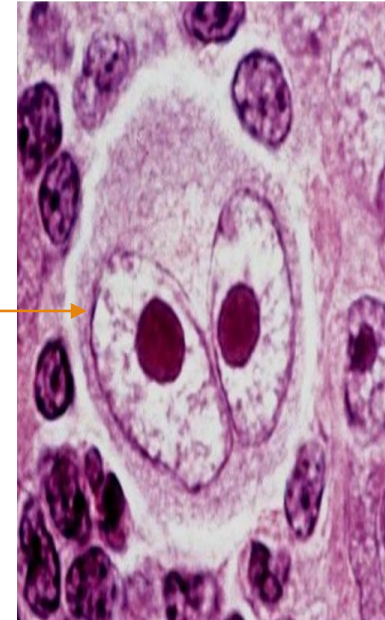


The quality and the quantity of each component determine the subtype of Hodgkin disease.

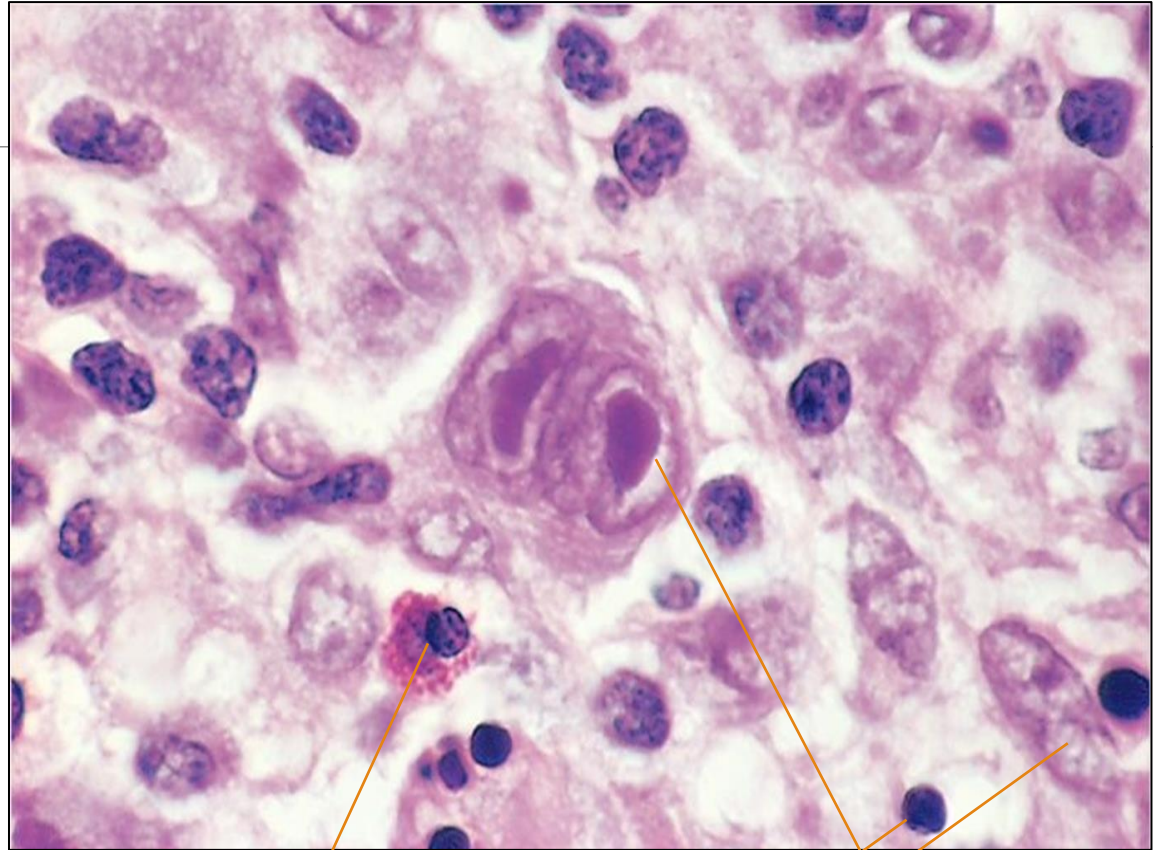
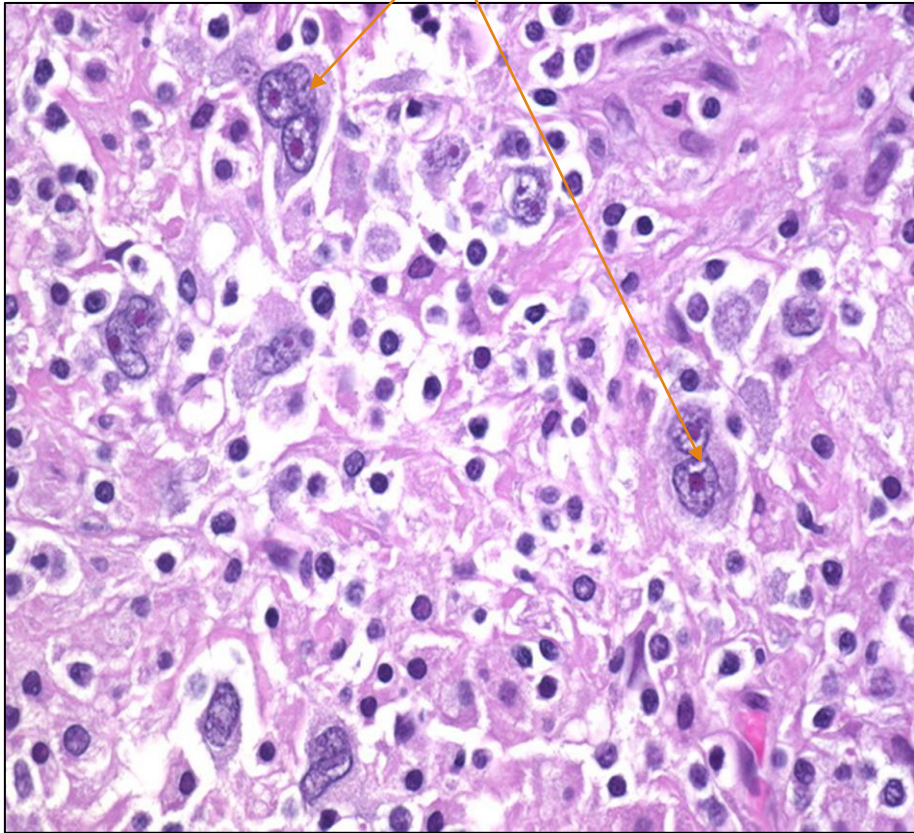


❑ Morphologic Features of CLASSIC Reed-Sternberg Cells

1. Large (15-45 μm in diameter).
 2. Enlarged polylobated nucleus.
 3. Huge round inclusion-like nucleoli.
 4. Abundant, slightly eosinophilic cytoplasm.
- **The CLASSIC RS** cells with two mirror-image nuclei or nuclear lobes, each containing a large (inclusion-like) acidophilic nucleolus surrounded by a distinctive clear zone; together, they impart an **owl-eye appearance**.



RS cells

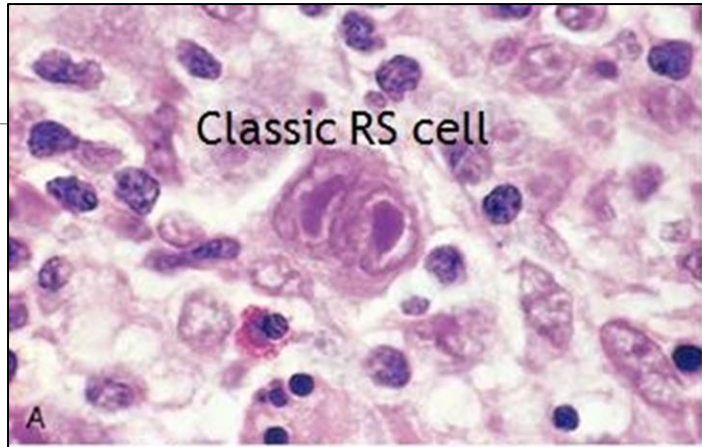


Hodgkin's Lymphoma: showing classic Reed-Sternberg cell, lymphocytes, eosinophil & histiocytes



❑ Variants of Reed-Sternberg cells

1. **Hodgkin cells (Mononuclear variant):** Insufficient for diagnosis.
2. **Mummified cells:** dark smudge degenerating cells with pyknotic nuclei and eosinophilic cytoplasm.
3. **Lacunar cells:** Large polylobated nuclei surrounded by **pale cytoplasm** and contain inconspicuous nucleoli.
4. **(LP) L&H cells:** cells with hyperlobated nuclei, finely granular chromatin, and inconspicuous small nucleoli.



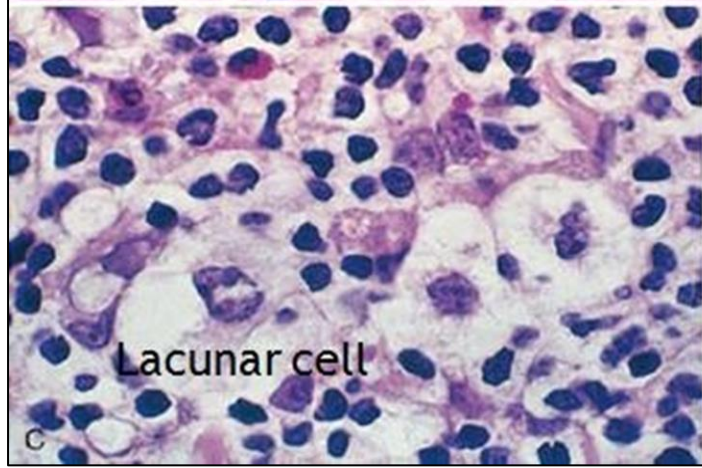
Classic RS cell

A



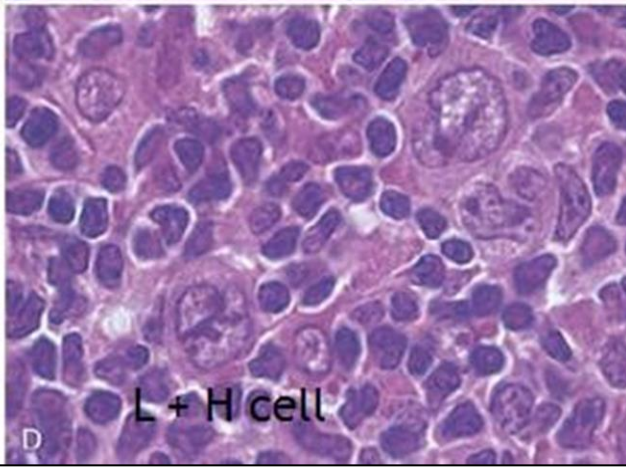
Mononuclear variant

B



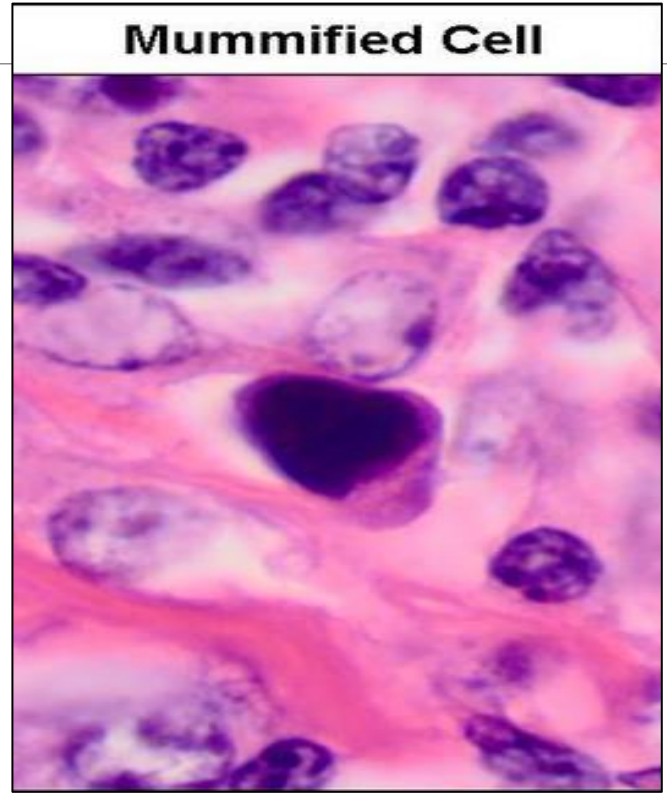
Lacunar cell

C



L + H cell

D



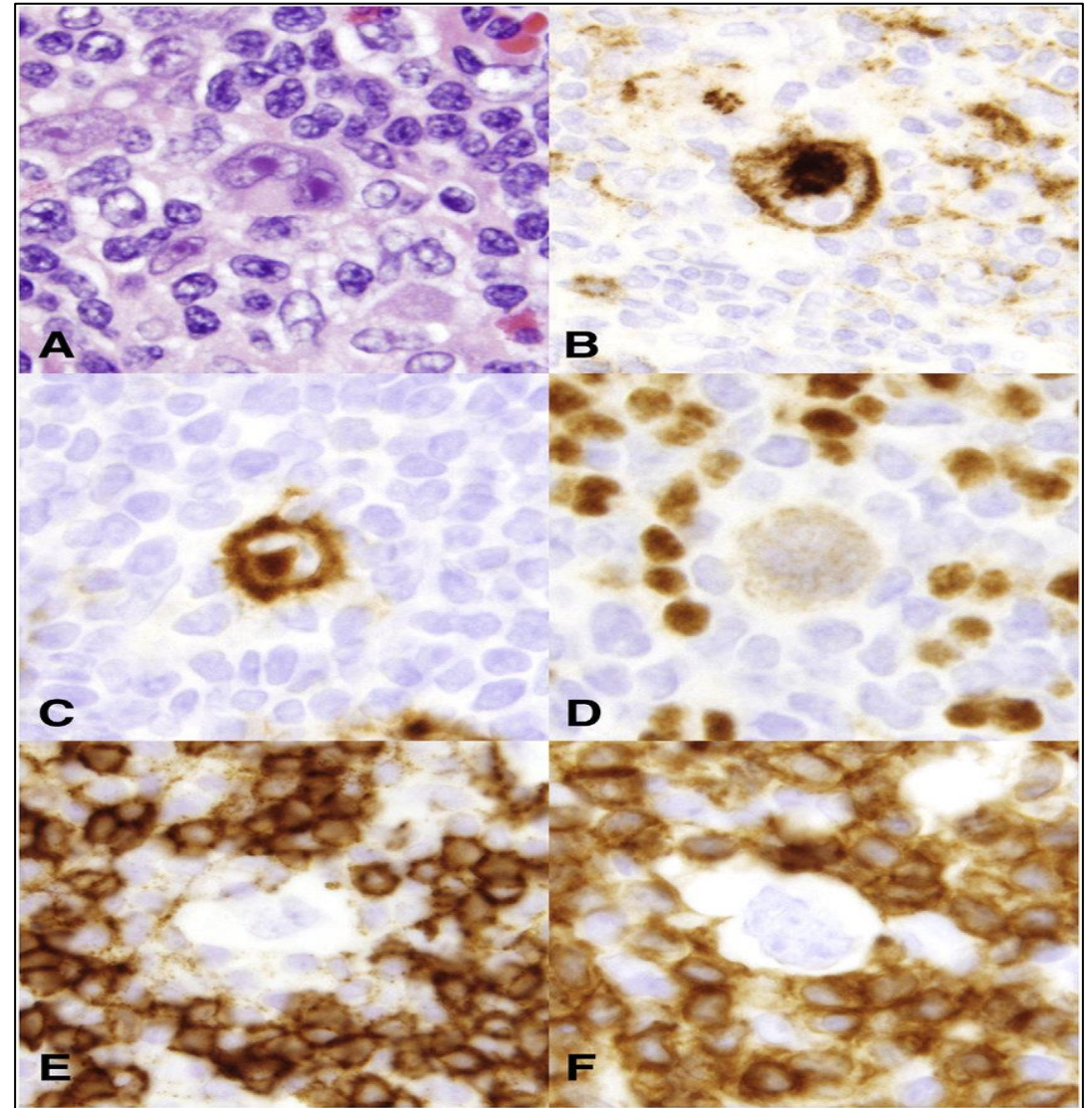
Mummified Cell

❖ Immunophenotyping Of HL

- Classical HL:
 - RS: CD45-, CD20-, CD15+, CD30+, weak variable PAX5+, MUM1+
- NLPHL:
 - RS: CD45+, CD20+, strong PAX5, CD15-, CD30-

Classic Hodgkin lymphoma:

- A. H&E
- B. CD15
- C. CD30
- D. PAX5 (note decreased intensity compared to background B cells)
- E. CD20
- F. CD3.



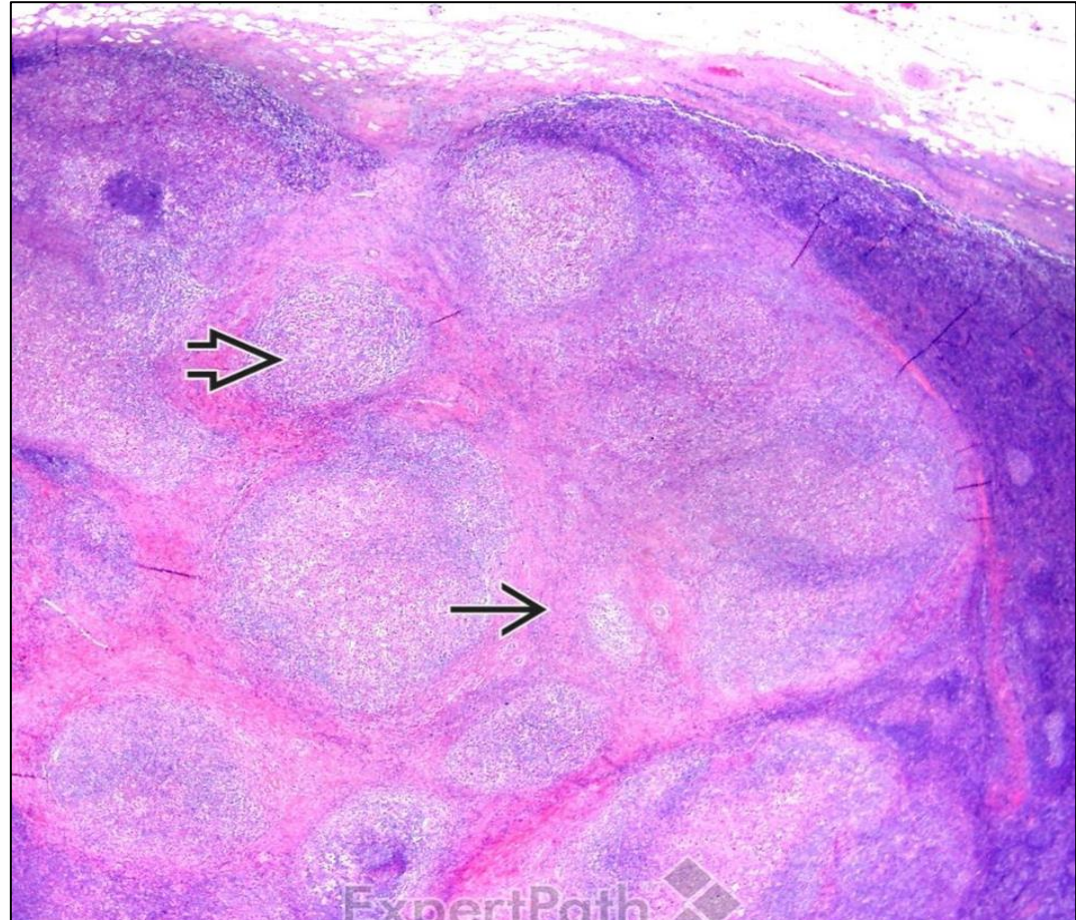
Classical Hodgkin Lymphoma

(1) Nodular Sclerosis

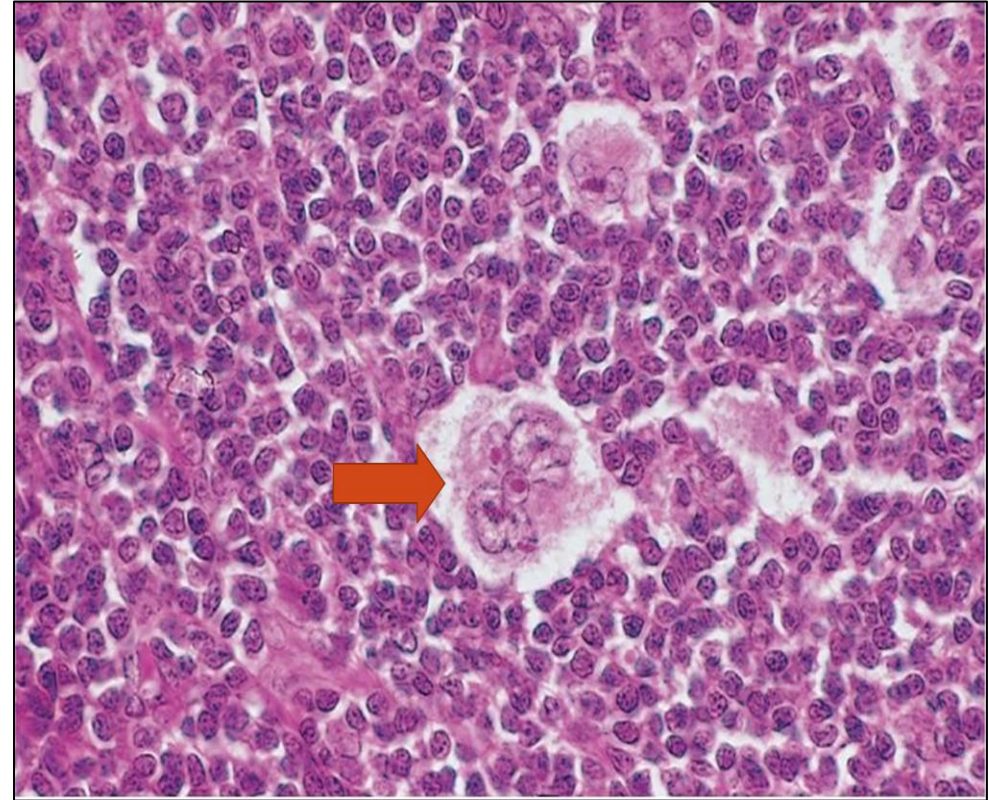
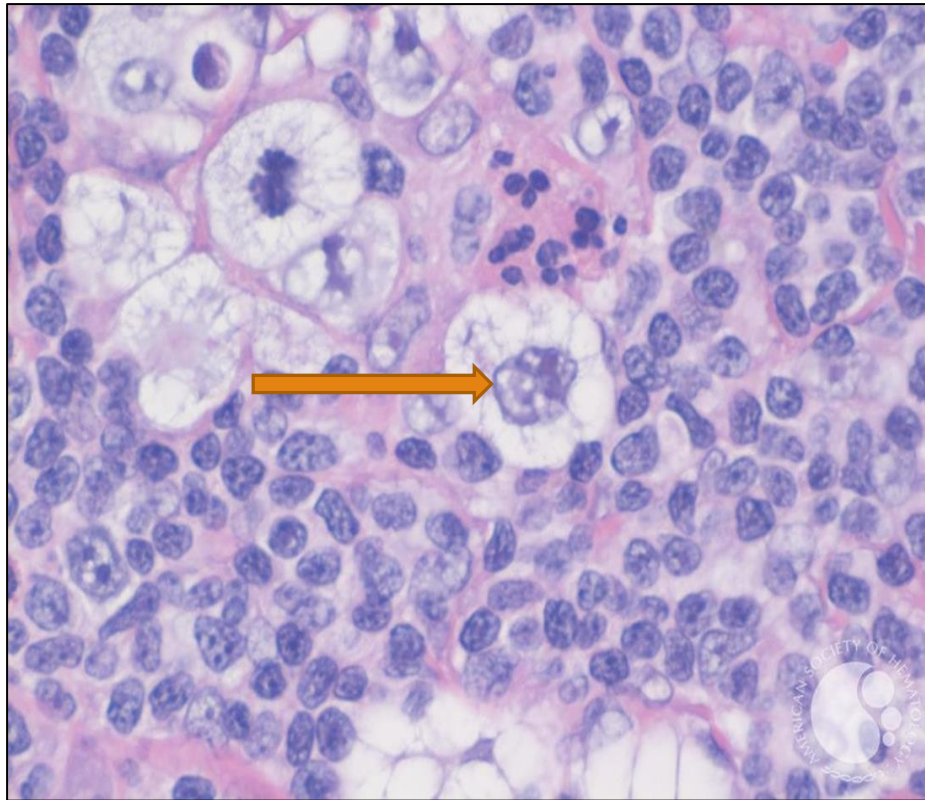
- This is the most common form.
- M=F.
- Has a striking propensity to involve the lower cervical, supraclavicular, and mediastinal lymph nodes.
- More in adolescents or young adults.
- Patients present at an early stage (I&II).
- Overall prognosis is excellent.
- EBV -

Morphology:

- The presence of **collagen bands** that divide the lymphoid tissue into **circumscribed nodules**.
- The cellular infiltrate may show varying proportions of lymphocytes, eosinophils, histiocytes, and **lacunar cells**.
- The immunophenotype of the lacunar variants is identical to that of classic RS cells.



- **The lacunar cell** (a variant of the RS cell, large and has a single multilobate nucleus with multiple small nucleoli and an abundant, pale-staining cytoplasm)
 - In formalin-fixed tissue, the cytoplasm often retracts, giving rise to the appearance of cells lying in **empty spaces or lacunae**.

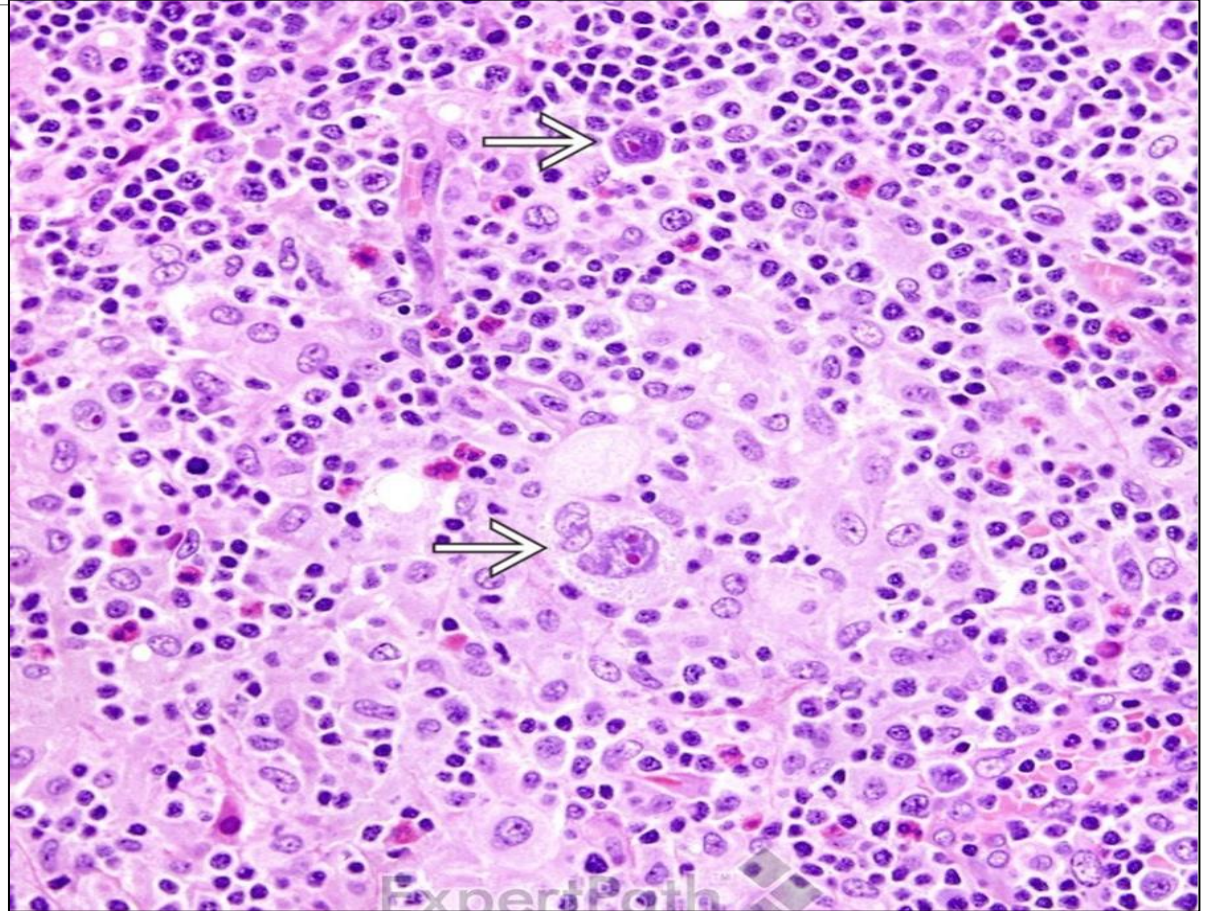


Classical Hodgkin Lymphoma

(2) Mixed Cellularity

- This is the most common form in patients > 50 yr.
- There is a Male predominance.
- Classic RS cells are **plentiful** within a distinctive heterogeneous cellular infiltrate, which includes small lymphocytes, eosinophils, plasma cells, and benign histiocytes.
- More patients have **disseminated disease and systemic manifestations.**
- It is associated with **EBV** in about **70%** of cases.
- Very **good** prognosis.

The normal architecture is effaced by Reed-Sternberg and **mononuclear Hodgkin** (RS+H) (white solid arrow) cells in a background of small lymphocytes, epithelioid histiocytes, and eosinophils.

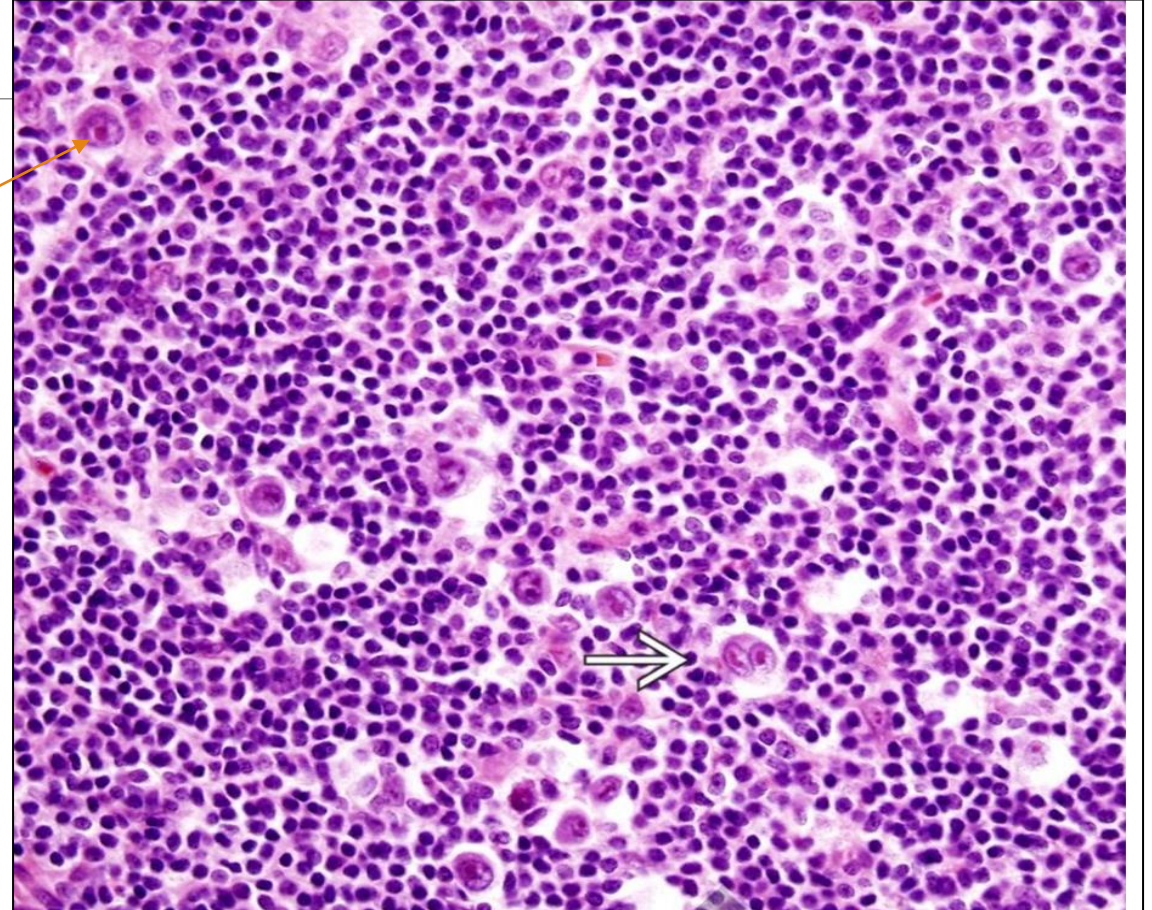


Classical Hodgkin Lymphoma

(3) Lymphocyte Rich

- The reactive lymphocytes make up most of the cellular infiltrate.
- M>F, older adults.
- This entity is distinguished from the lymphocyte predominance type by the presence of frequent mononuclear variants and diagnostic Reed-Sternberg cells with a “classical” immunophenotypic profile.
- It is associated with **EBV** in about **40%** of cases.
- Very **good to excellent** prognosis.

- Mononuclear Hodgkin cells and one Reed-Sternberg cell (white solid arrow) in a background of small lymphocytes.



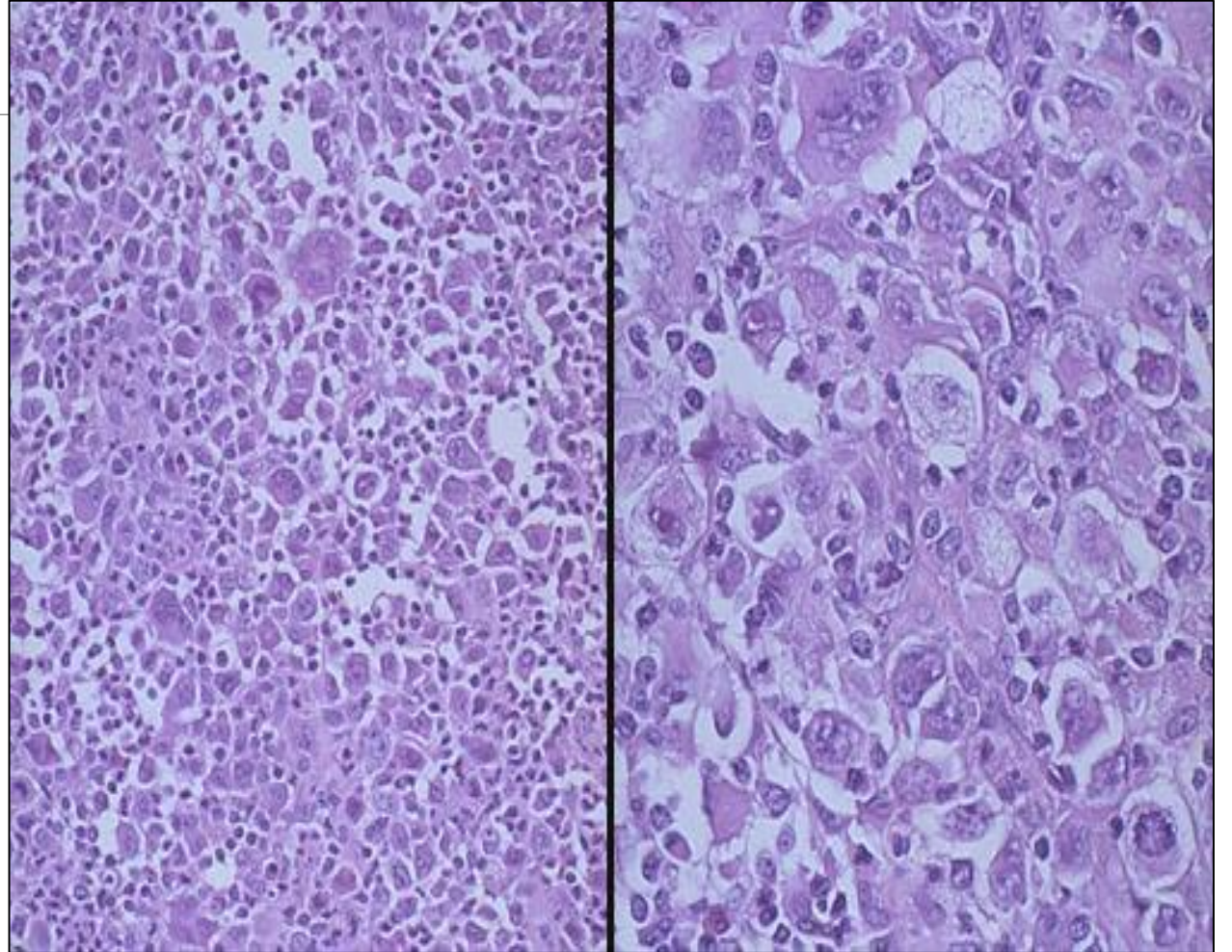
Classical Hodgkin Lymphoma

(4) Lymphocyte depleted

- An aggressive form that affects older patients.
- M>F.
- It is more common in patients with **HIV** infection
- Associated with **EBV** infection in **~90%** of cases.
- Characterized by the paucity of lymphocytic cells with the presence of numerous pleomorphic, mummified RS cells with maximum areas of necrosis.
- It has a **poor** prognosis.
- Stages **III & IV** are usual.

Lymphocyte depleted HL:

Many Reed-Sternberg cells and variants are present, and small lymphocytes are depleted.



Non-Classical Hodgkin Lymphoma

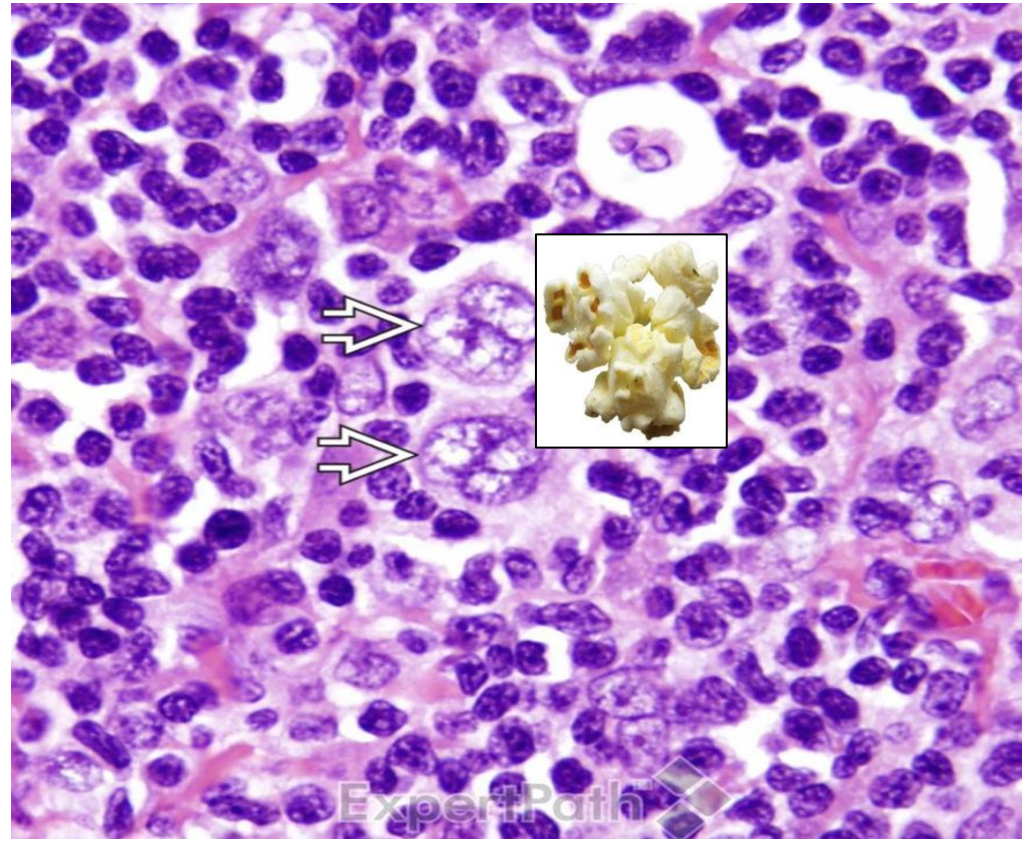
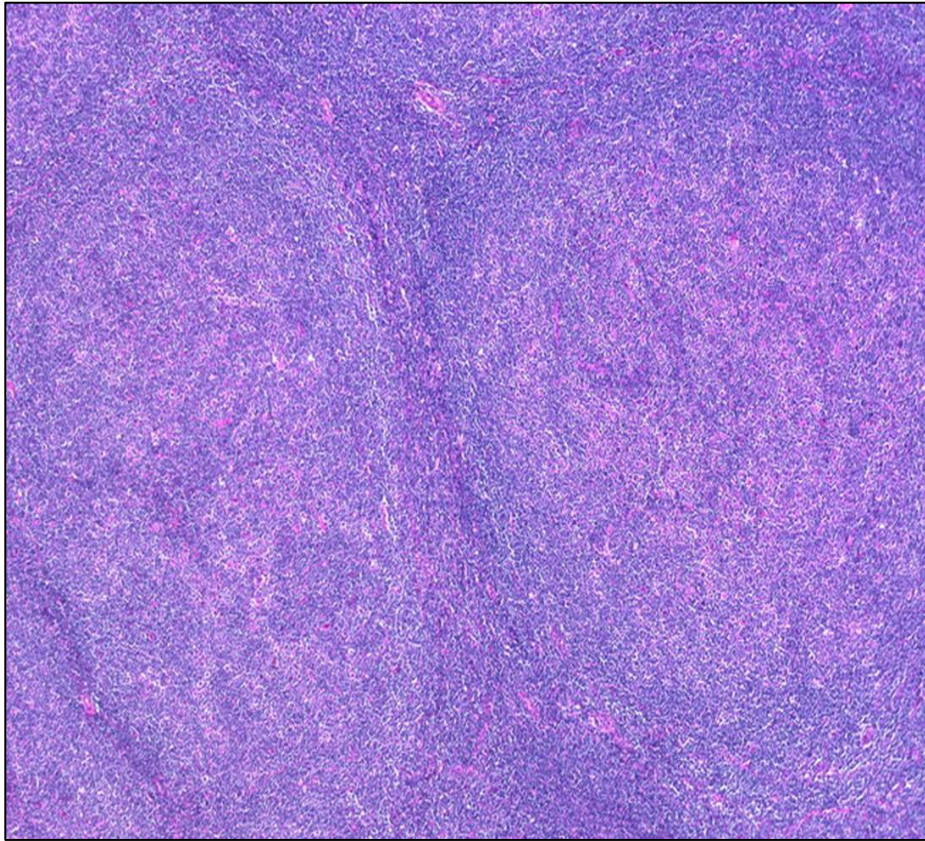
Nodular Lymphocyte predominant (NLPHL)

- 5% of Hodgkin lymphoma.
- **Diffuse or nodules** with many small resting **lymphocytes** admixed with a variable number of **histiocytes**.
- Other types of reactive cells, such as eosinophils, neutrophils, and plasma cells, are scanty or absent, and classic RS cells are extremely difficult to find.
- Scattered among the reactive cells are **lymphohistiocytic (L&H)** variant RS cells that have a delicate multilobed, puffy nucleus that has been likened to a popcorn pattern called (**popcorn cells**).
- Affects predominantly **young males (<35 years)**.
- Cervical and/or axillary nodes are the most frequently involved.
- **EBV-**
- Excellent prognosis



NLPHL involving lymph node is shown.

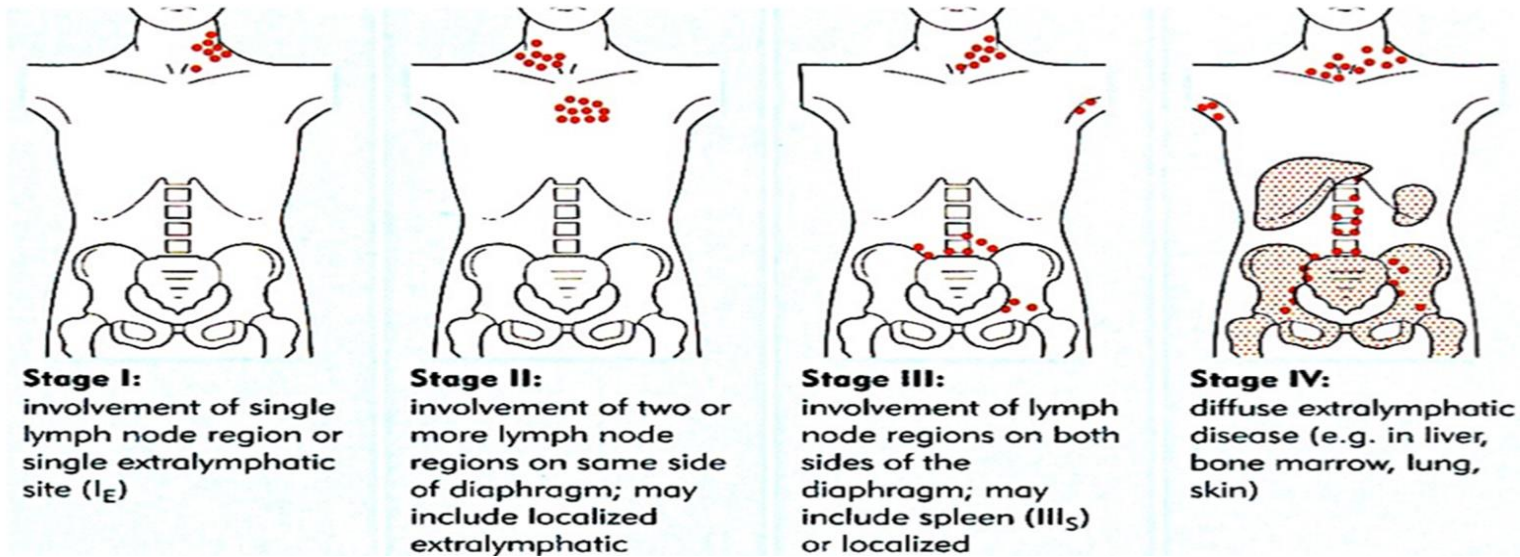
The large neoplastic cells, known as lymphocyte-predominant (LP) cells (white open arrow), often have multilobated nuclear contours and resemble popcorn.



❖ Hodgkin Lymphoma Poor Prognostic Factors

- ❑ Stage IV, and B symptoms
- ❑ Age \geq 45yr
- ❑ Male gender
- ❑ Histology (particularly the lymphocyte-depleted)
- ❑ ESR (>50)
- ❑ Albumin level ($<4\text{g/dl}$),
- ❑ Low Hb. ($<10.5\text{g/dl}$)
- ❑ Extra-nodal disease

Clinical Staging Of Hodgkin And Non-Hodgkin Lymphomas (Ann Arbor Classification):



All stages are further divided based on the absence (A) or presence (B) of the following systemic symptoms and signs: significant fever, night sweats, unexplained loss of more than 10% of normal body weight

