HODGKINS LYMPHOMA

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LEARNING OBJECTIVES

- Definition
- Classification
- Epidemiology
- Clinical presentation
- Diagnosis
- Staging

Hematopoietic Malignancies

- ***Lymphoma*** *is used for* proliferations that arise as discrete tissue masses.

- ***Leukemia*** *is used for neoplasms that present with widespread* involvement of the bone marrow and (usually, but not always) the peripheral blood.

Lymphoma

- Clonal malignant disorders that are derived from lymphoid cells: either precursor or mature T-cell or B-cell

- Majority are of B- cell origin

- Divided into 2 main types :

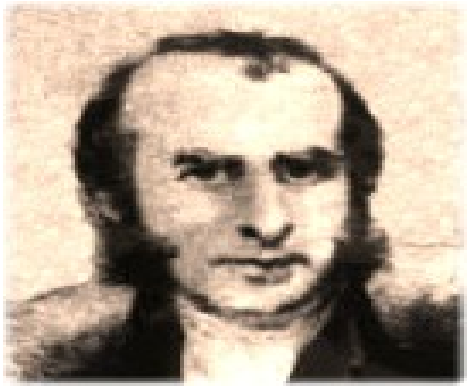
1. *Hodgkin's lymphoma*
2. *Non - Hodgkin's lymphoma*

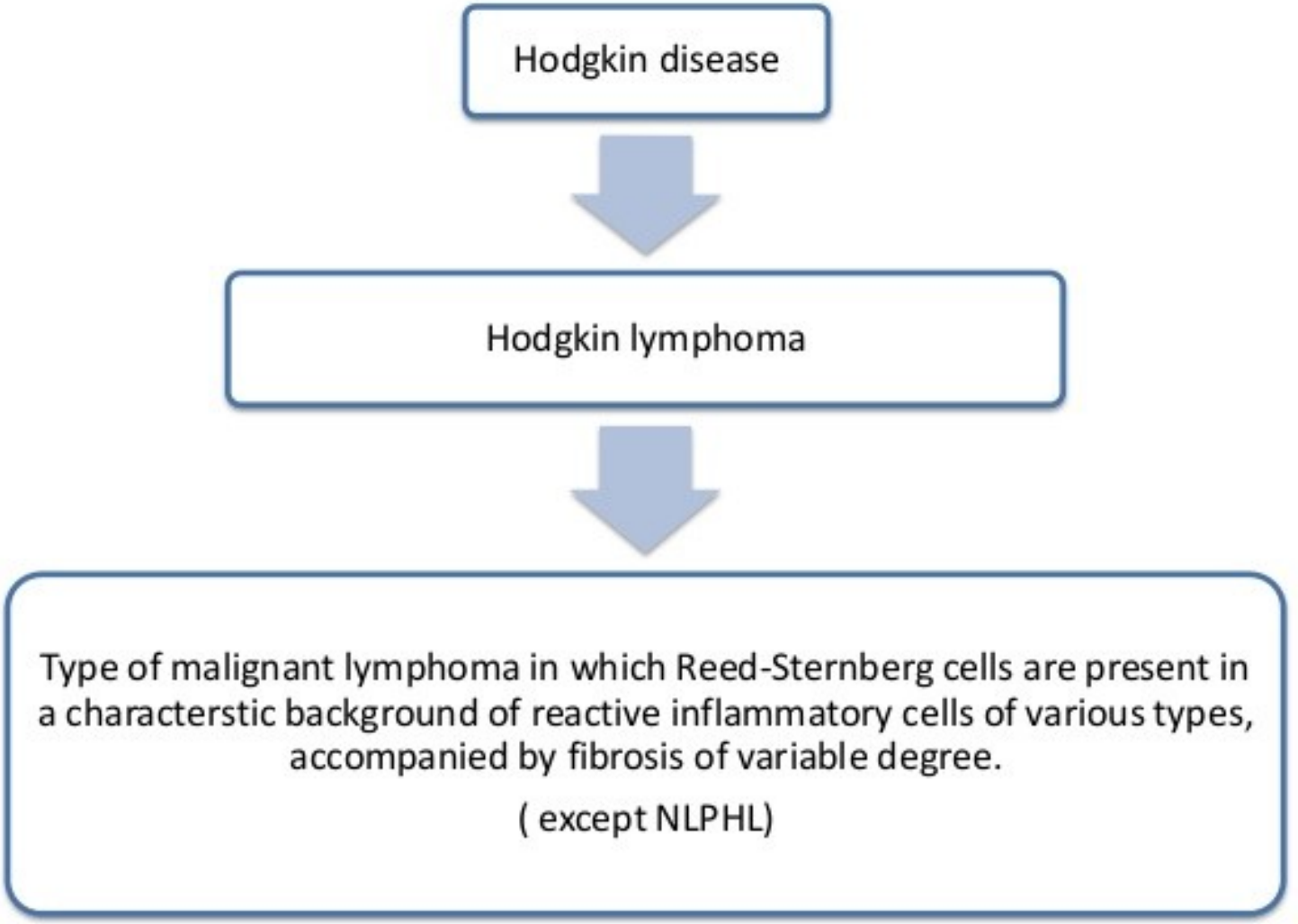
INTRODUCTION

- Are group of cancers which originate from lymphatic systems.
- It was named after Thomas Hodgkin who first described it in 1832.
- Dorothy Reed and Carl Sternberg first described the malignant cells of Hodgkin lymphoma call Reed Sternberg cells.
- Hodgkin lymphoma was the first cancer which could be successfully treated by radiation therapy and also by combination chemotherapy

Hodgkin's Disease

- Histologically & clinically a distinct malignant disease
- Predominantly, B-cell disease
- Course of the disease is variable, but the prognosis has improved with modern treatment




Hodgkin disease
Hodgkin lymphoma
Type of malignant lymphoma in which Reed-Sternberg cells are present in a characterstic background of reactive inflammatory cells of various types, accompanied by fibrosis of variable degree.
(except NLPHL)

EPIDIMIOLOGY

- **Hodgkin lymphoma accounts for 0.7% of all new cancers in the United States**
- **There are about 8000 new cases each year.**
- **The average age at diagnosis is 32 years.**
- **It is one of the most common cancers of young adults and adolescents but also occurs in the aged.**
- **It was the first human cancer to be successfully treated with radiation therapy and chemotherapy and is curable in most cases.**

WHO CLASSIFICATION

- Classical Hodgkin's Lymphoma:

  1. Nodular Sclerosis
  2. Mixed Cellularity
  3. Lymphocyte-rich
  4. Lymphocyte depletion

- Nodular lymphocyte predominant Hodgkin's lymphoma

Etiology

- **? Infection – *EBV, HIV***

- **? Environmental factors**

No clear risk factors, several implicated

- **woodworking, farming**
- **rare familial aggregations • First degree relatives have five fold increase in risk for Hodgkin lymphoma.**
- **High socio economic status.**

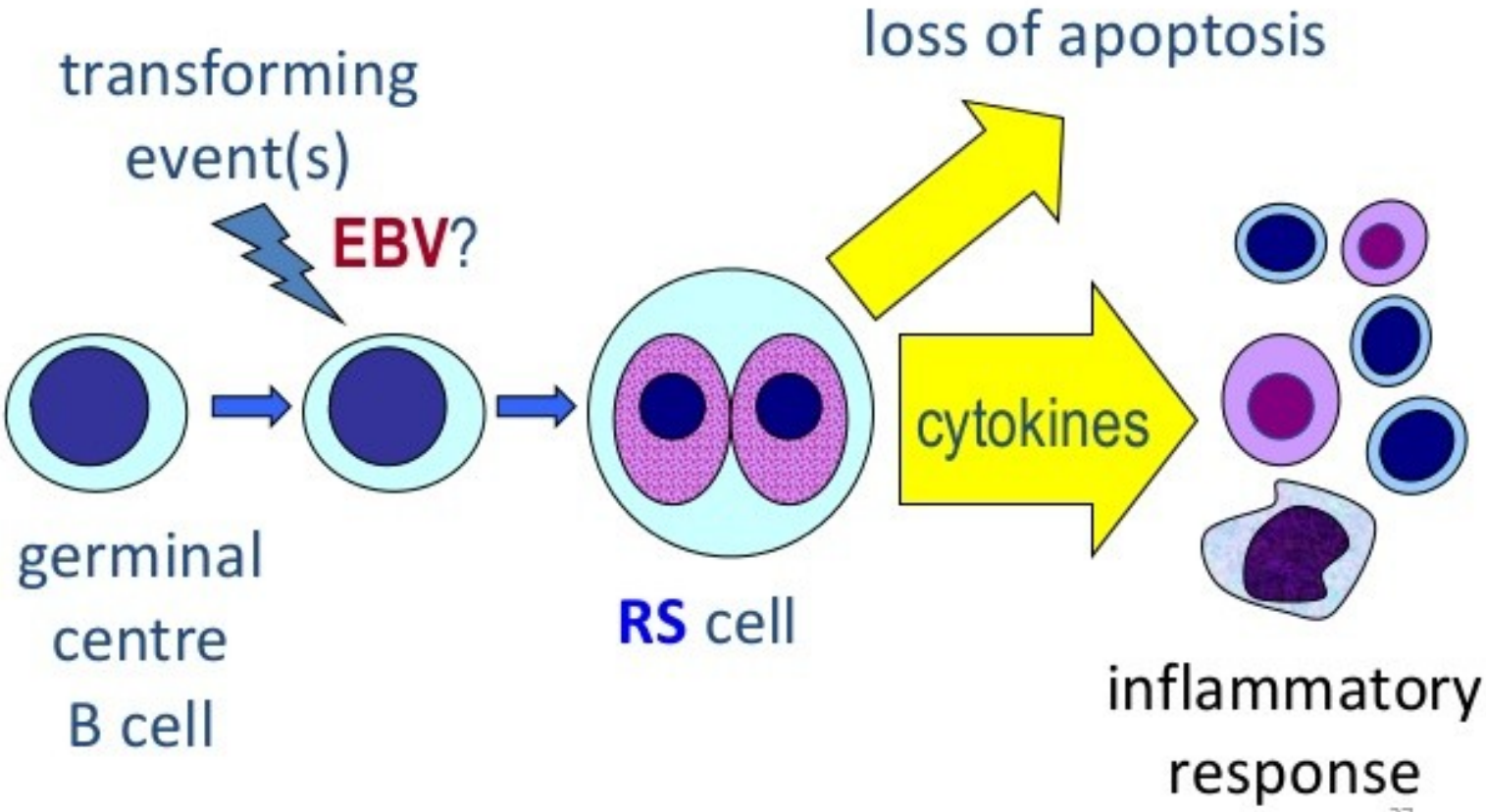
PATHOGENESIS

- **the Ig genes of Reed-Sternberg cells have undergone both V(D)J recombination and somatic hypermutation**
- **This establish an origin from a germinal center or postgerminal center B cell**
- **Despite having the genetic signature of a B cell, the Reed-Sternberg cells of classical HL fail to express most B-cell–specific genes, including the Ig genes**

PATHOGENESIS

NF-κB (**nuclear factor kappa-light-chain-enhancer of activated B cells**) is a protein complex that controls transcription of DNA, cytokine production and cell survival.

A possible model of pathogenesis



Cytokines (such as IL-5, IL-10, IL-13, and TGF-β) and ***chemokines*** (such as TARC, MDC, IP-10, and CCL28) are secreted by Reed-Sternberg cells.

They lead to florid accumulation of reactive cells in tissues involved by classical HL.

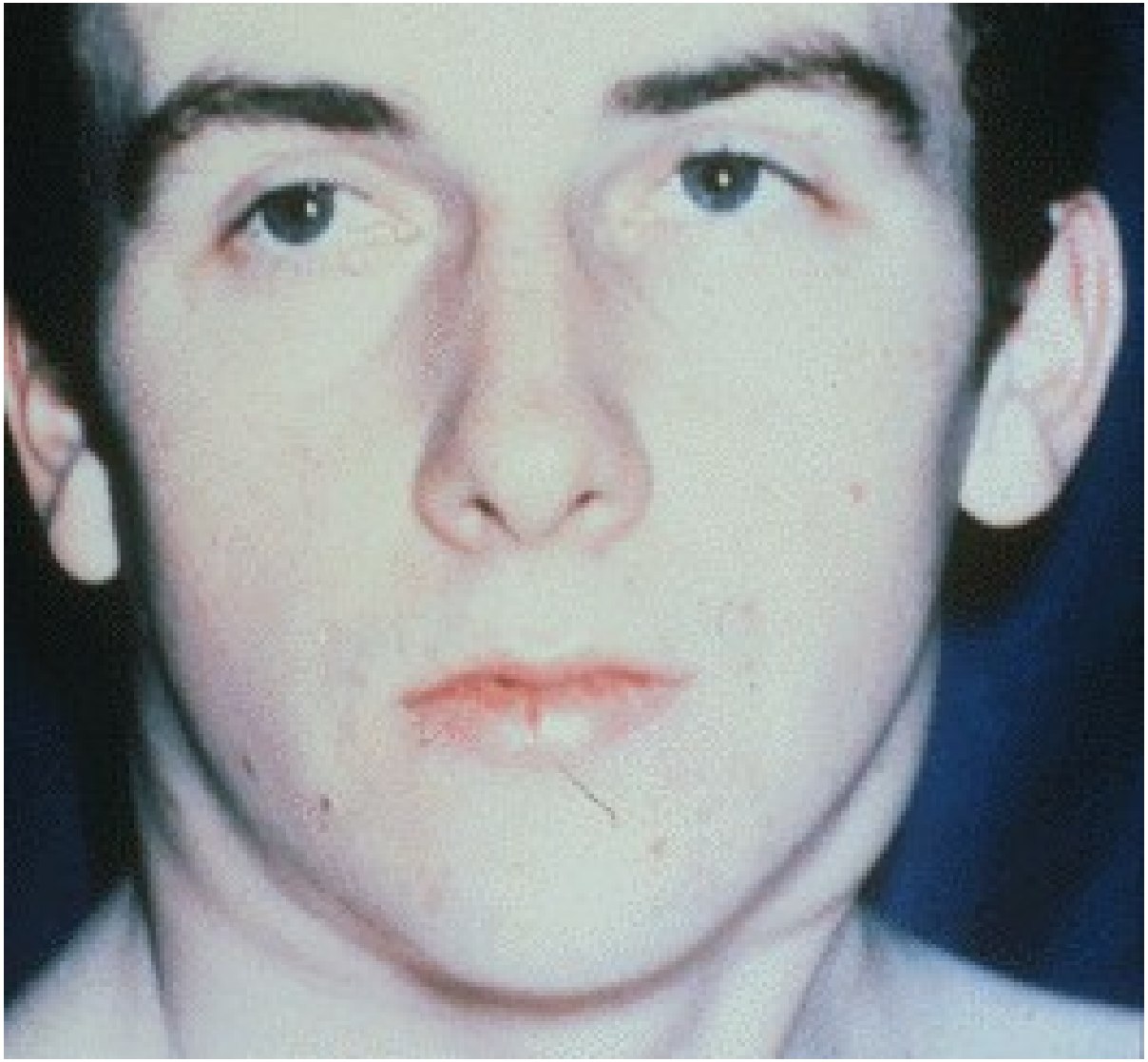
These reactive cells produce factors that support the growth and survival of the tumor cells and further modify the reactive cell response.

Clinical features

- **Bimodal age distribution :**
  - **young adults *(20-30 yrs)* & elderly *(> 50yrs)***
    ***M*ay occur at any age**
- **M > F**
- ***Lymphadenopathy*:**
  - **most often cervical region**
  - **asymmetrical, discrete**
  - **painless, non-tender**
  - **elastic character on palpation (rubbery)**
  - **not adherent to skin**
  - **fluctuate in size**

Clinical features -cont..

- *Contiguous spread via the lymphatic chain eg.* involvement of abdominal & thoracic LNs
- Extra nodal disease - rare
- Hepatosplenomegaly



- **Constitutional symptoms (*B symptoms*)**
  - *Night sweats*
  - *sustained fever > 38 degree Celsius,*
  - *loss of weight >10% of body weight in 6 months*

- Fever sometimes cyclical *('Pel-Ebstein fever')*
- Pain at the site of disease after drinking alcohol
- Pallor
- Pruritis
- Symptoms of Bulky (>10 cm) disease

Investigations

- ***COMPLETE BLOOD COUNTS***
- ***ESR***
- ***LDH***
- ***LFT***
- ***RFT***

- *CXR - mediastinal mass*

- *CT thorax / abdomen / pelvis-for staging*

- *Other: PET,* Lymphangiography , Laporotomy

LN FNAC / biopsy :

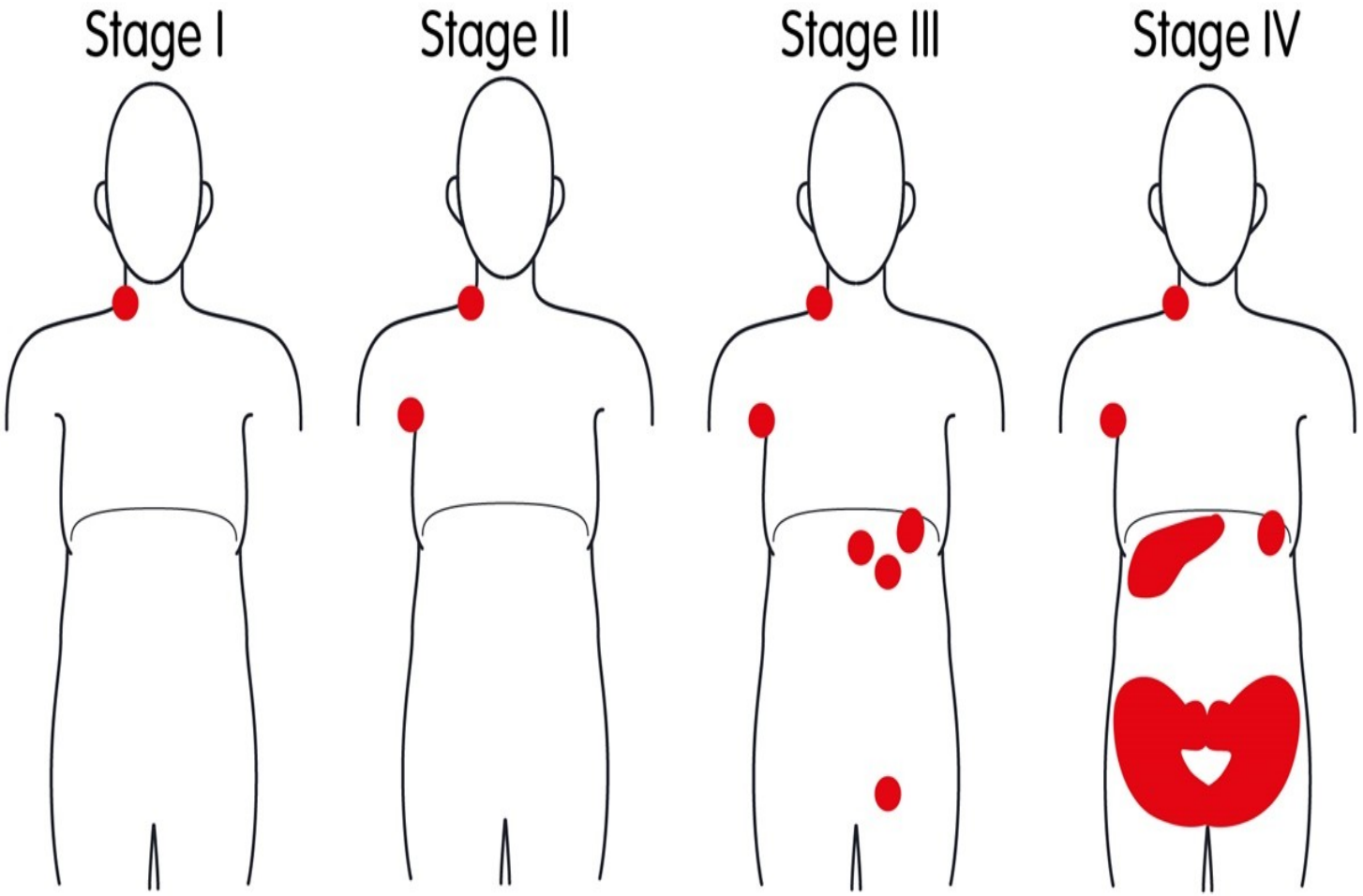
- **Malignant REED-STERNBERG (RS) Cell: Bi-nucleate cell with a prominent nucleolus derived from B cell at an early stage of differentiation**
- **Reactive background of eosinophils, lymphocytes, plasma cells**
- **Fibrous tissue**

STAGING OF DISEASE

Stage	Distribution of Disease
I	Involvement of a single lymph node region (I) or a single extralymphatic organ or site (IE)
II	Involvement of two or more lymph node regions on the same side of the diaphragm alone (II) or localized involvement of an extralymphatic organ or site (IIE)
III	Involvement of lymph node regions on both sides of the diaphragm without (III) or with (IIIE) localized involvement of an extralymphatic organ or site
IV	Diffuse involvement of one or more extralymphatic organs or sites with or without lymphatic involvement
All stages are further divided on the basis of the absence (A) or presence (B) of the following symptoms: unexplained fever, drenching night sweats, and/or unexplained weight loss of greater than 10% of normal body weight.	

Data from Carbone PT, et al: Symposium (Ann Arbor): Staging in Hodgkin's disease. *Cancer Res* 31:1707, 1971.

Staging of lymphoma



A: absence of B symptoms B: fever, night sweats, weight loss

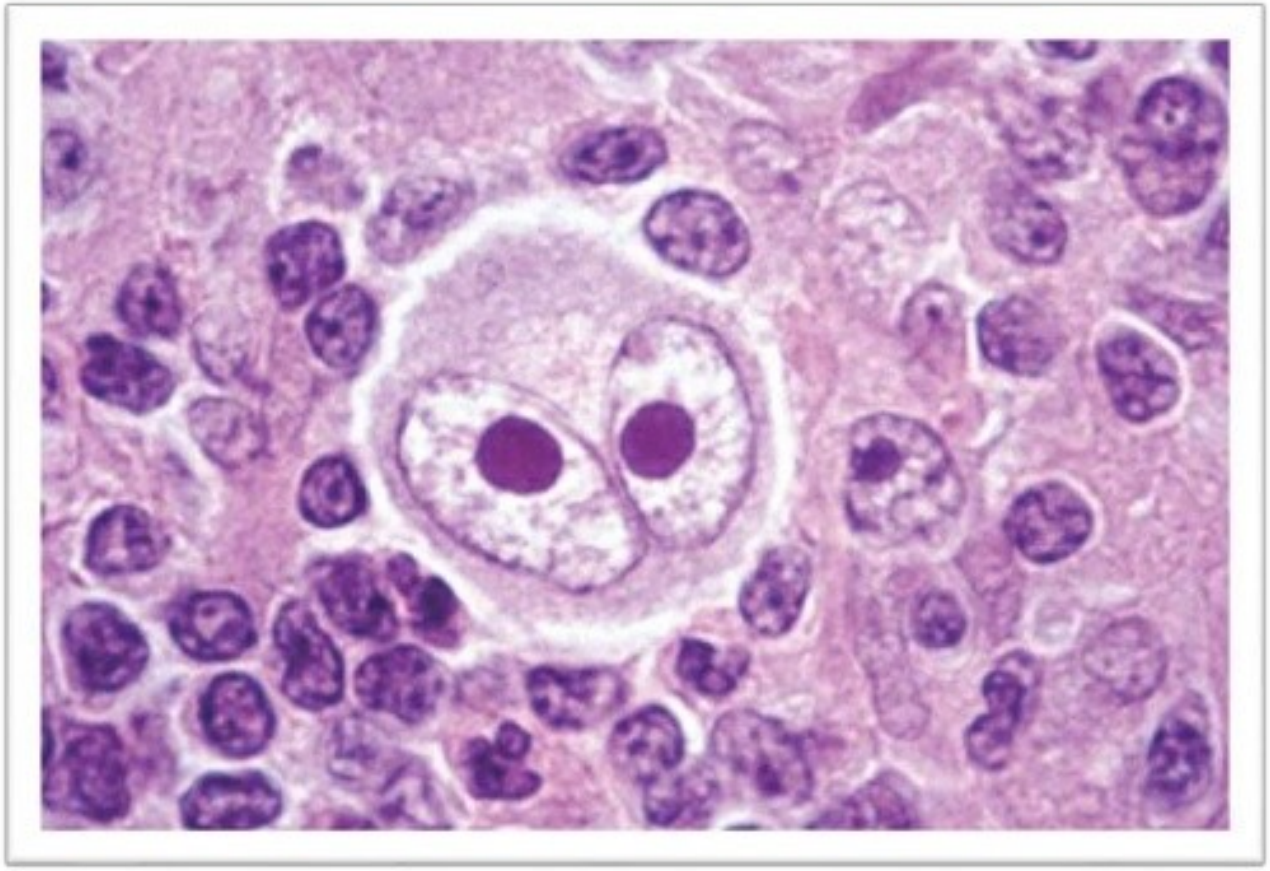
International Prognostic Index (IPI)

- Age
- Advanced stage disease
- Performance status
- Elevated LDH
- Presence of Extra nodal disease

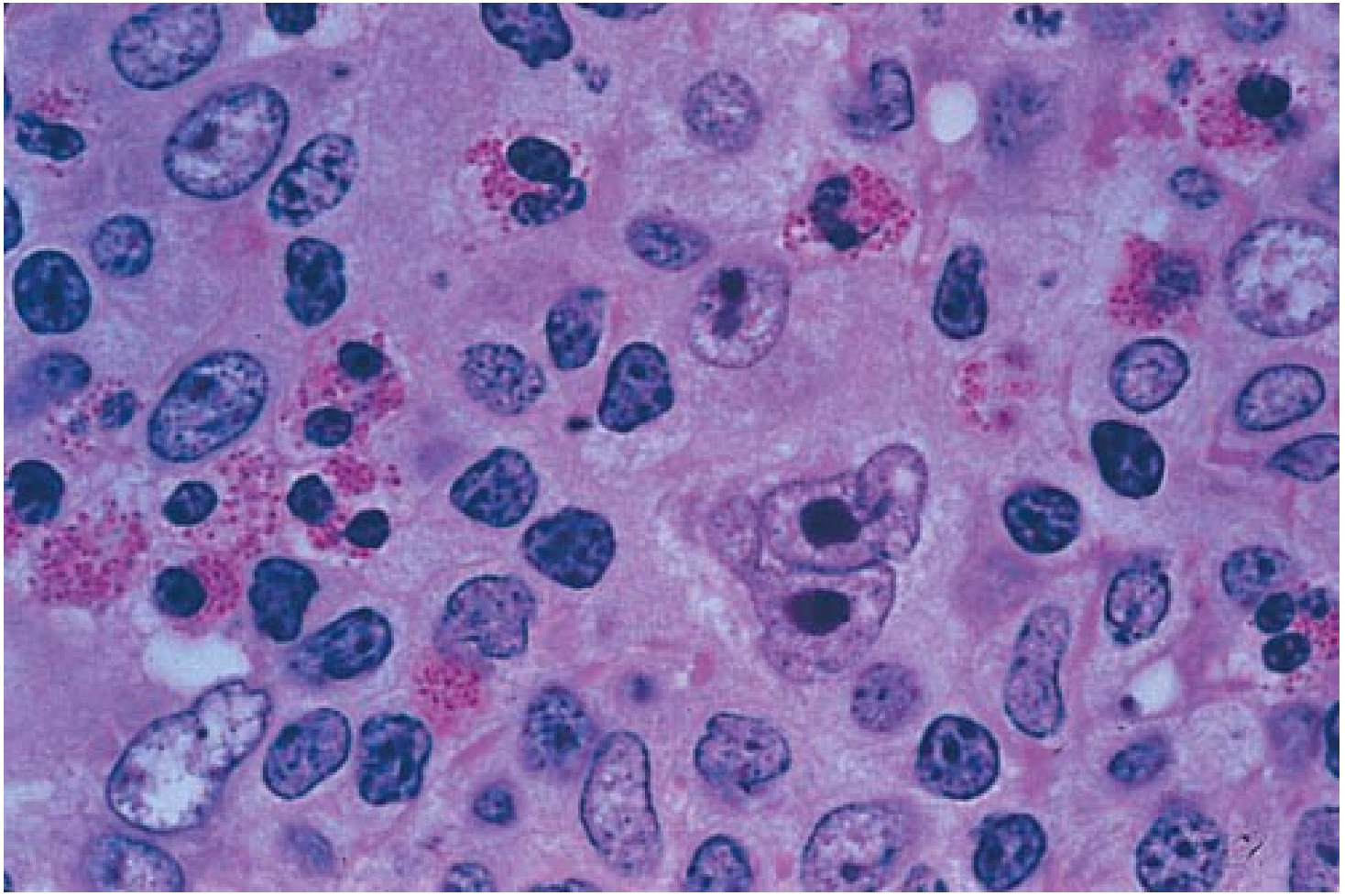
REED STERNBERG CELL

- Reed Sternberg cell common feature of ALL Hodgkin Lymphomas
- Large cells (>45um in diameter) with classically binucleate or bilobed central nucleus each with a large acidophilic central nucleoli surrounded by a clear halo. “owl’s eye appearance”
- Variants: mononuclear (Hodgkin’s cell), mummified cell, lacunar cell, L/H cell.
- Classic Reed-Sternberg cell: + CD15, CD30, CD25 – CD45
- Most current studies indicate the RS cells of HL are lymphocytic in nature and, in the great majority of cases, are of B-cell origin.

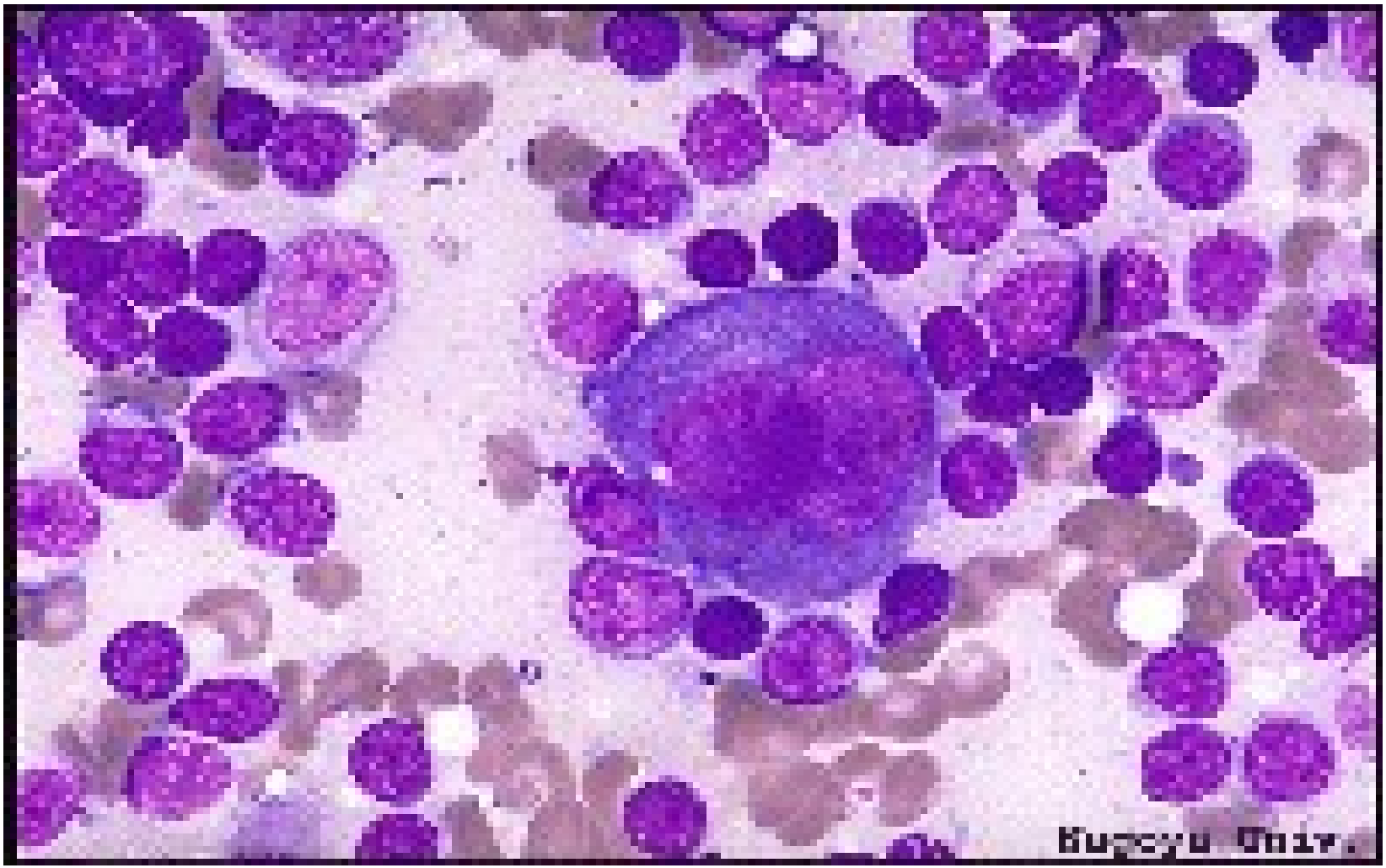
Reed-Sternberg cell



REED-STERNBERG (RS) Cell



REED-STERNBERG (RS) Cell



MORPHOLOGY

Subtype	Morphology and Immunophenotype	Typical Clinical Features
Nodular sclerosis	Frequent lacunar cells and occasional diagnostic RS cells; background infiltrate composed of T lymphocytes, eosinophils, macrophages, and plasma cells; fibrous bands dividing cellular areas into nodules. RS cells CD15+, CD30+; usually EBV–	Most common subtype; usually stage I or II disease; frequent mediastinal involvement; equal occurrence in males and females (F = M), most patients young adults
Mixed cellularity	Frequent mononuclear and diagnostic RS cells; background infiltrate rich in T lymphocytes, eosinophils, macrophages, plasma cells; RS cells CD15+, CD30+; 70% EBV+	More than 50% present as stage III or IV disease; M greater than F; biphasic incidence, peaking in young adults and again in adults older than 55
Lymphocyte rich	Frequent mononuclear and diagnostic RS cells; background infiltrate rich in T lymphocytes; RS cells CD15+, CD30+; 40% EBV–	Uncommon; M greater than F; tends to be seen in older adults
Lymphocyte depletion	Reticular variant: Frequent diagnostic RS cells and variants and a paucity of background reactive cells; RS cells CD15+, CD30+; most EBV+	Uncommon; more common in older males, HIV-infected individuals, and in developing countries; often presents with advanced disease
Lymphocyte predominance	Frequent L&H (popcorn cell) variants in a background of follicular dendritic cells and reactive B cells; RS cells CD20+, CD15–, C30–; EB–	Uncommon; young males with cervical or axillary lymphadenopathy; mediastinal

L&H, lymphohistiocytic; RS cell, Reed-Sternberg cell.

Differences between Hodgkin and Non-Hodgkin Lymphomas

Hodgkin Lymphoma	Non-Hodgkin Lymphoma
More often localized to a single axial group of nodes (cervical, mediastinal, para-aortic)	More frequent involvement of multiple peripheral nodes
Orderly spread by contiguity	Noncontiguous spread
Mesenteric nodes and Waldeyer ring rarely involved	Waldeyer ring and mesenteric nodes commonly involved
Extranodal presentation rare	Extranodal presentation common