

Hodgkin Lymphoma

Hodgkin Lymphoma

- 30% of all lymphomas
- Absolute incidence unchanged
- Arise in lymph node, cervical region
- Neoplastic tissues usually contain a small number of tumor cells

Incidence

- Bimodal age incidence 15-40, >55 years
- Childhood form (0-14) more common in developing countries
- M:F=1.5:1; in all subtypes except NS

W.H.O Classification

- Nodular lymphocyte predominant Hodgkin Lymphoma (NLPHL)
- Classical Hodgkin lymphoma
 - Nodular sclerosis (NSHL)
 - Mixed cellularity (MCHL)
 - Lymphocyte rich (LRHL)
 - Lymphocyte-depleted (LDHL)

Neoplastic cells and Hodgkin Lymphoma

- Classical Hodgkin (HRS cells):
 - Reed-Sternberg cell
 - Hodgkin cell (mononuclear)
 - Lacunar cell
- Nodular LP Hodgkin:
 - LP (lymphocyte predominant) cells, also known as L&H (lymphocytic and histiocytic) cells, “Popcorn” cells

NLPHL

- 5% of Hodgkin lymphoma
- Male; mid 30's
- Bimodal age distribution not seen
- Most present with localized peripheral lymphadenopathy, develops slowly and is responsive to therapy

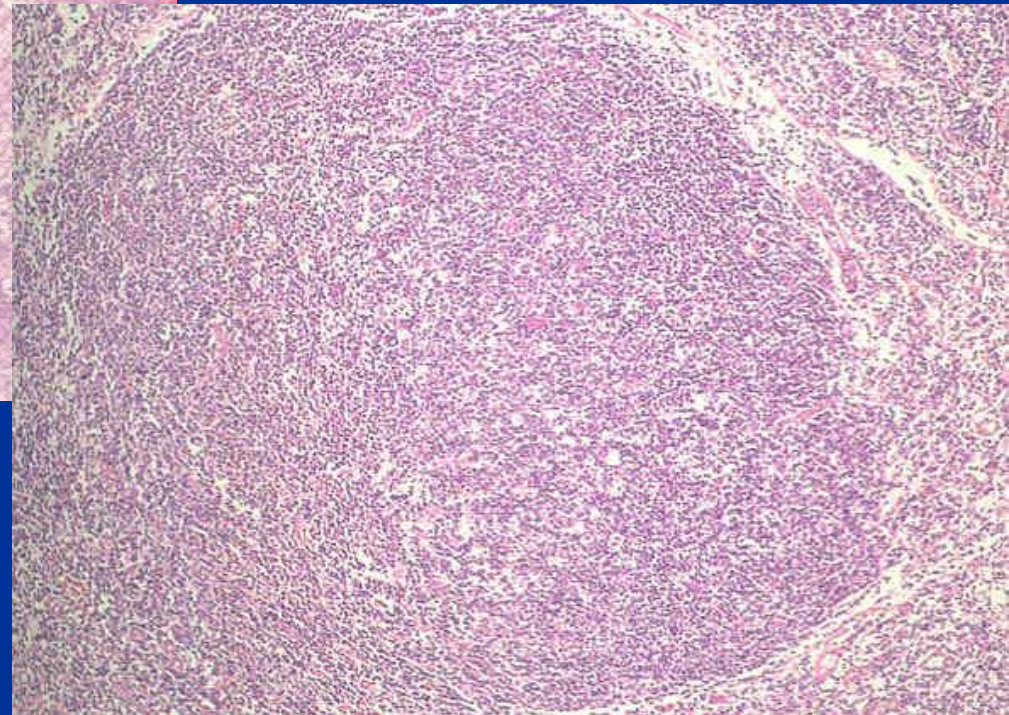
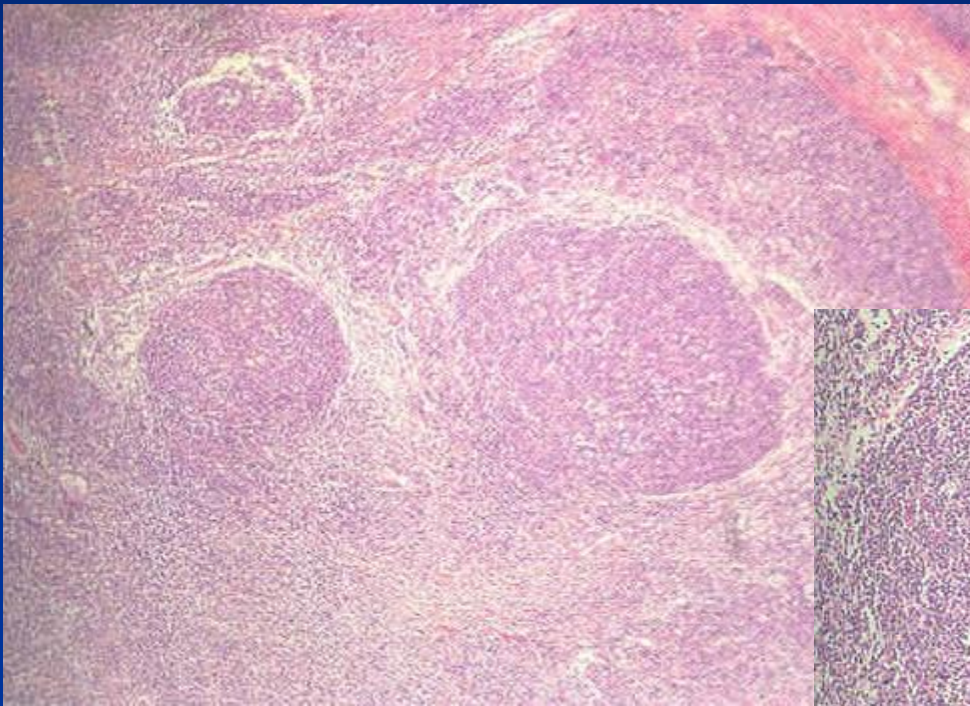
NLPHL

- Tends to spare mediastinum, spleen or BM
- Association with or progression to DLBCL (2-3%)
- Analogous to “low grade” B-cell lymphomas; but: (1) disseminated disease not usually seen, and (2) younger age.
- EBV negative

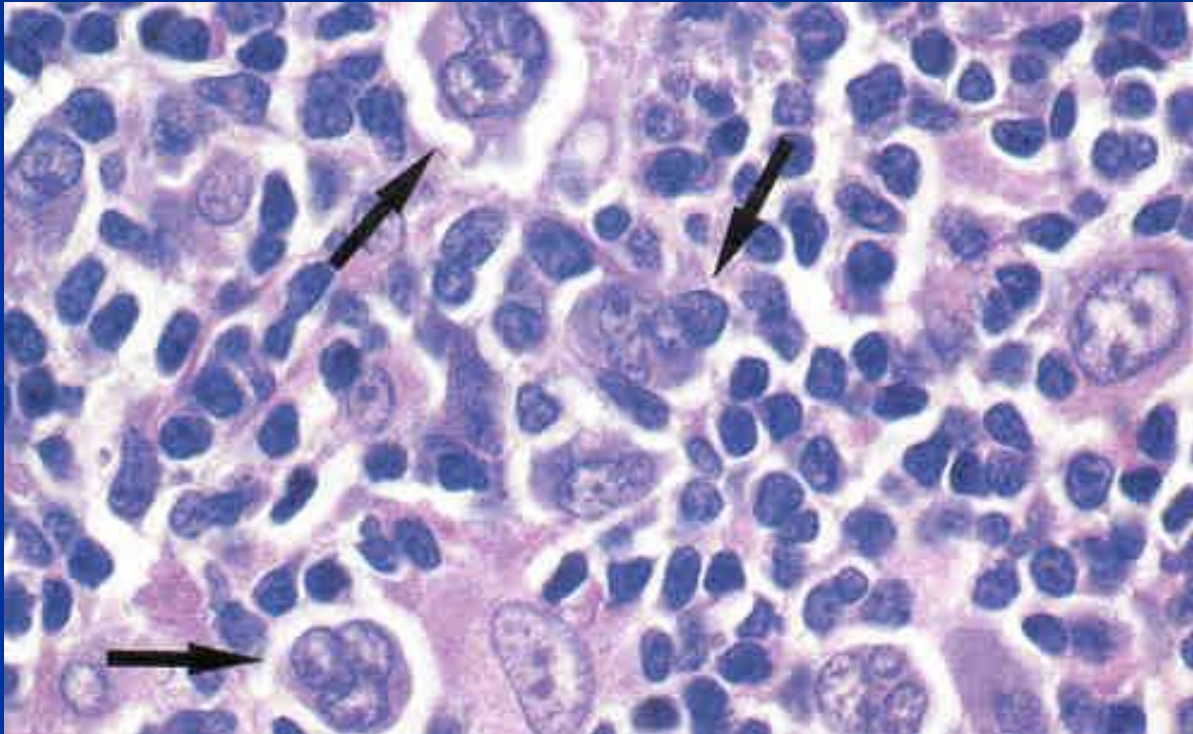
NLPHL

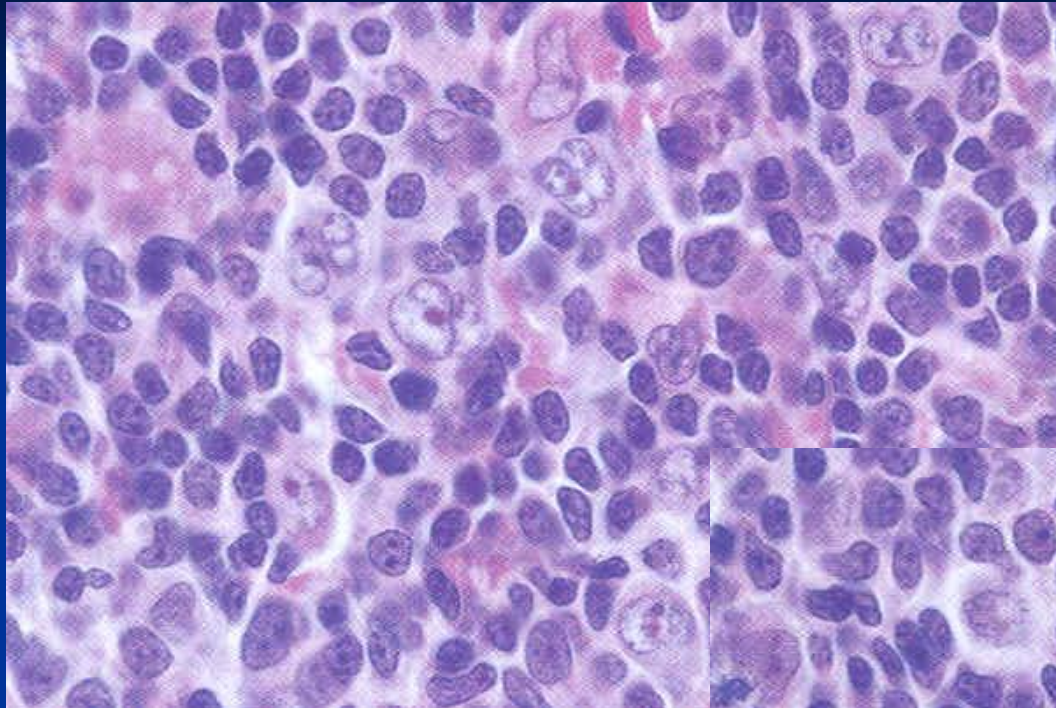
- Architecture:
 - Nodular
 - Nodular and diffuse

NLPHL

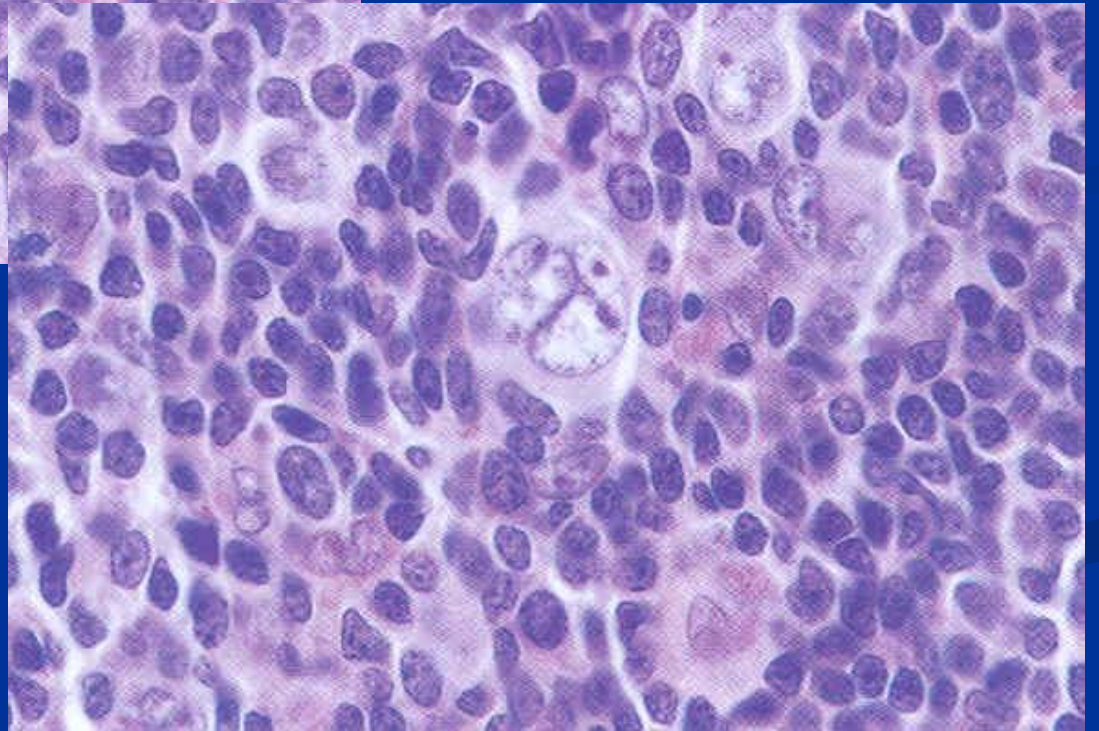


LP (L&H) cells





LP (L&H)
cells



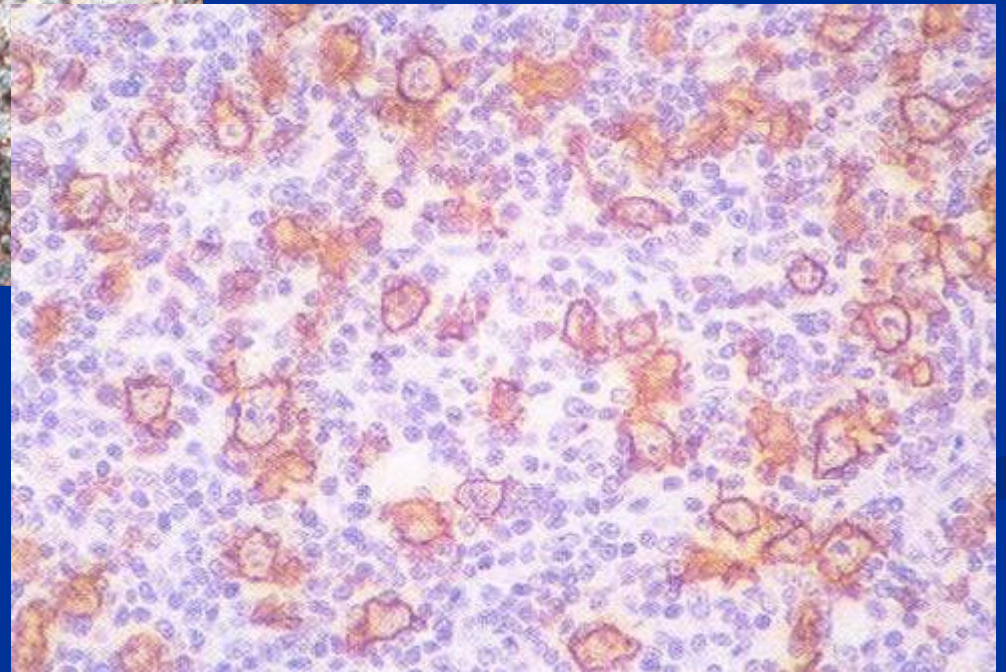
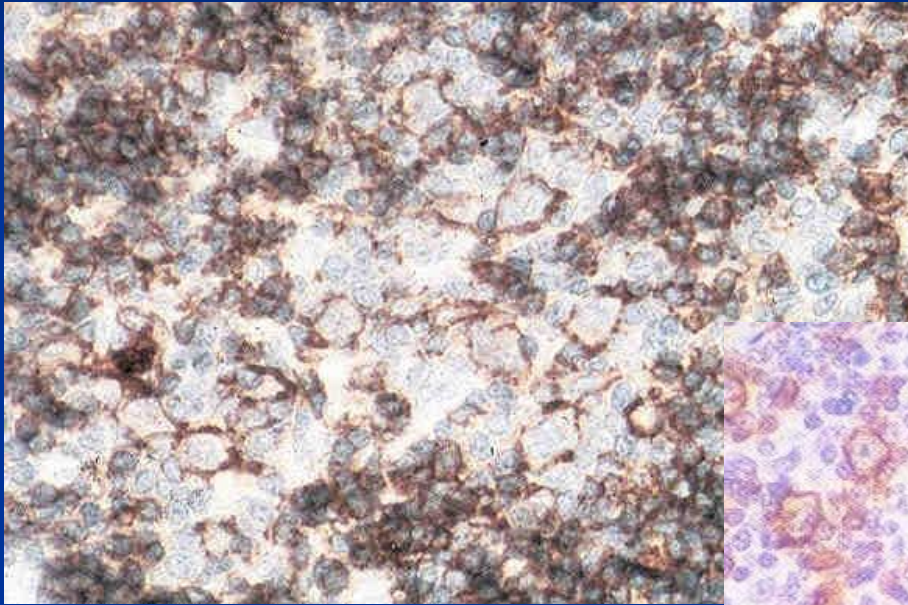
Immunophenotype (LP cells)

- CD45+
- CD20+
- EMA+ in 50% of cases
- CD 15 and CD30 are negative

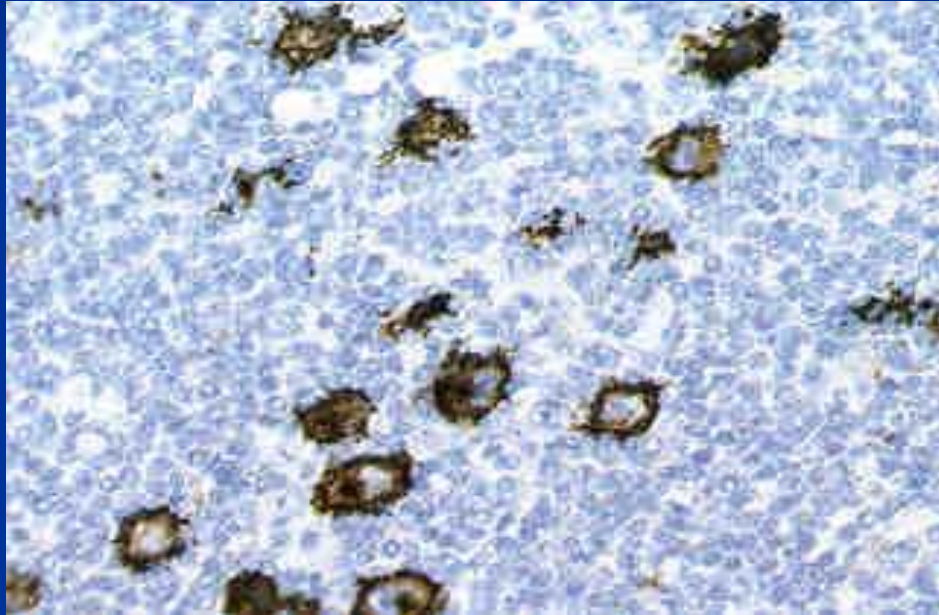
CD 20

- LP cells and the back ground cells are CD20 positive; CD20 can be used to highlight the nodularity

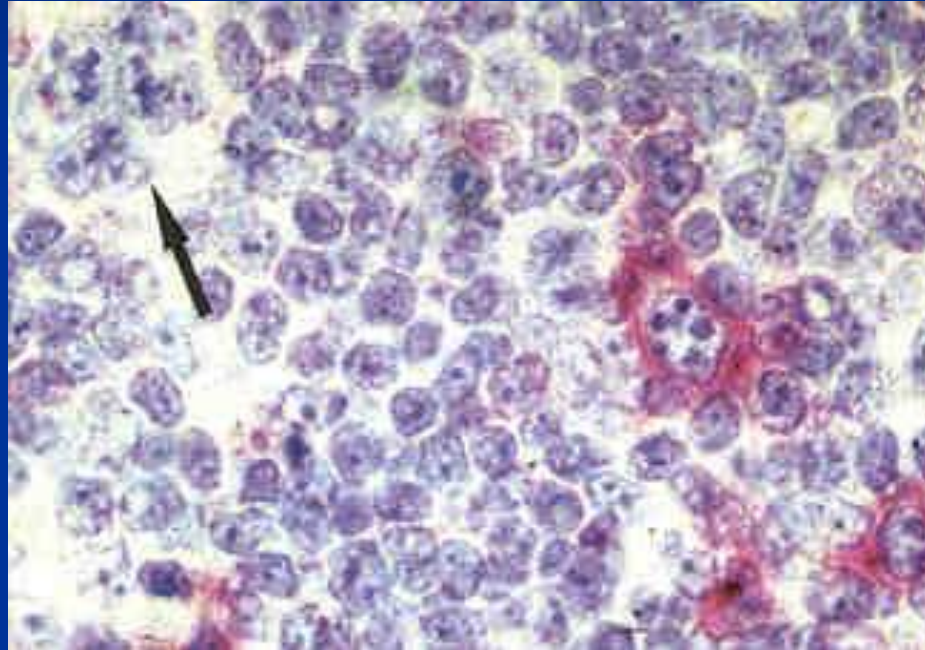
CD20 and NLPHL



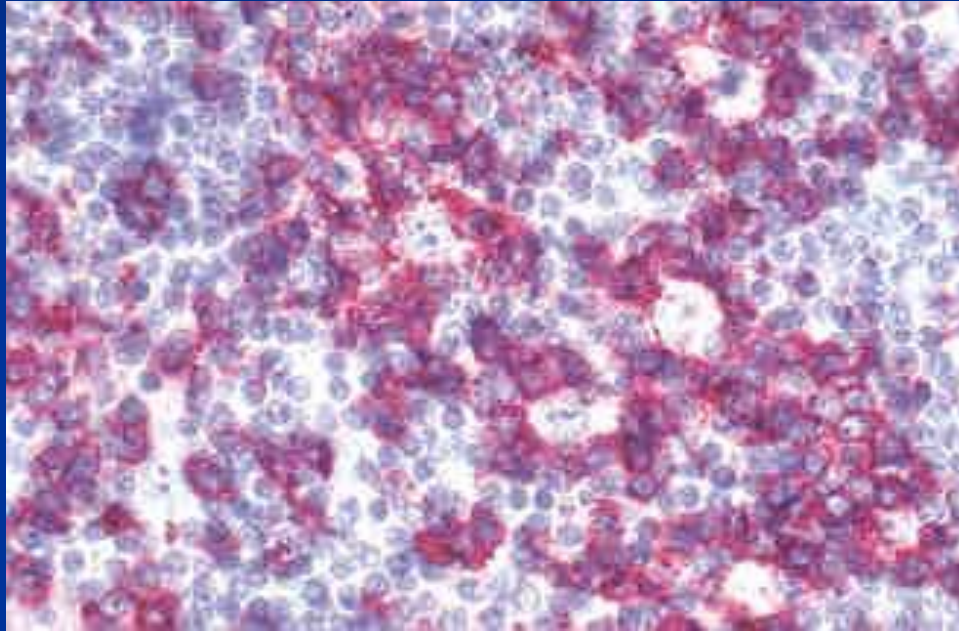
EMA



CD30



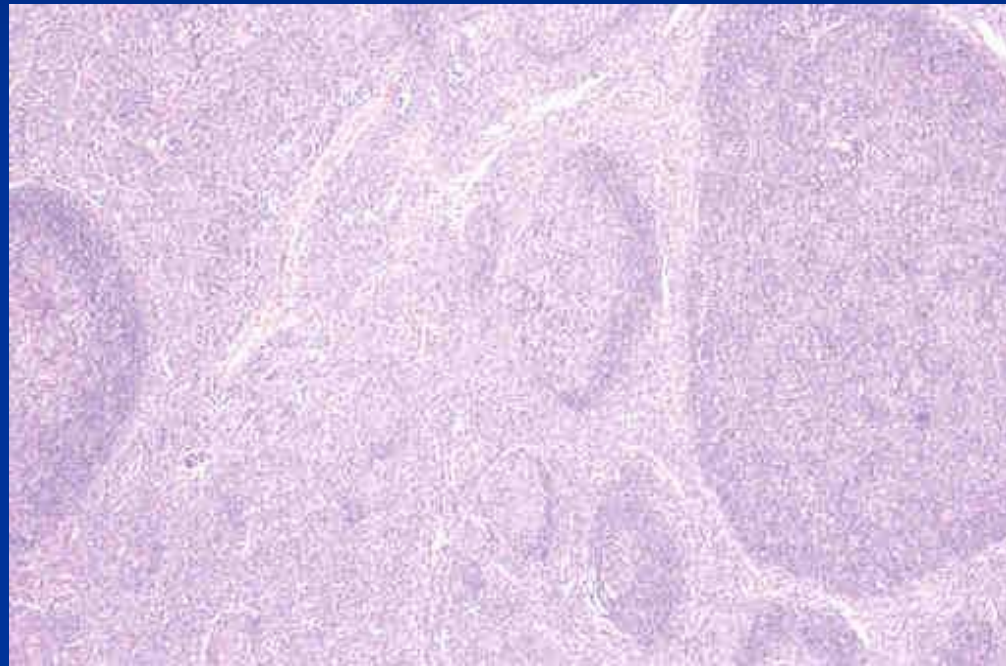
CD57

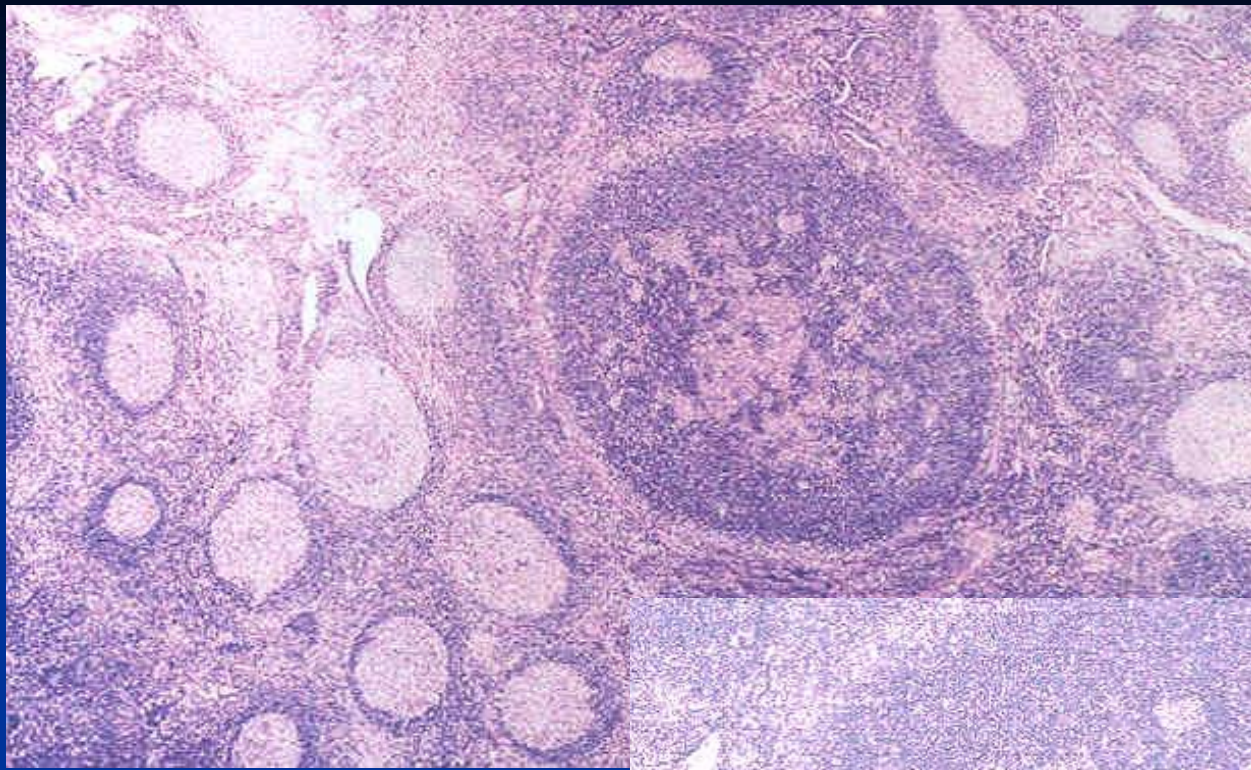


CD57 (+) T cells surround LP cells

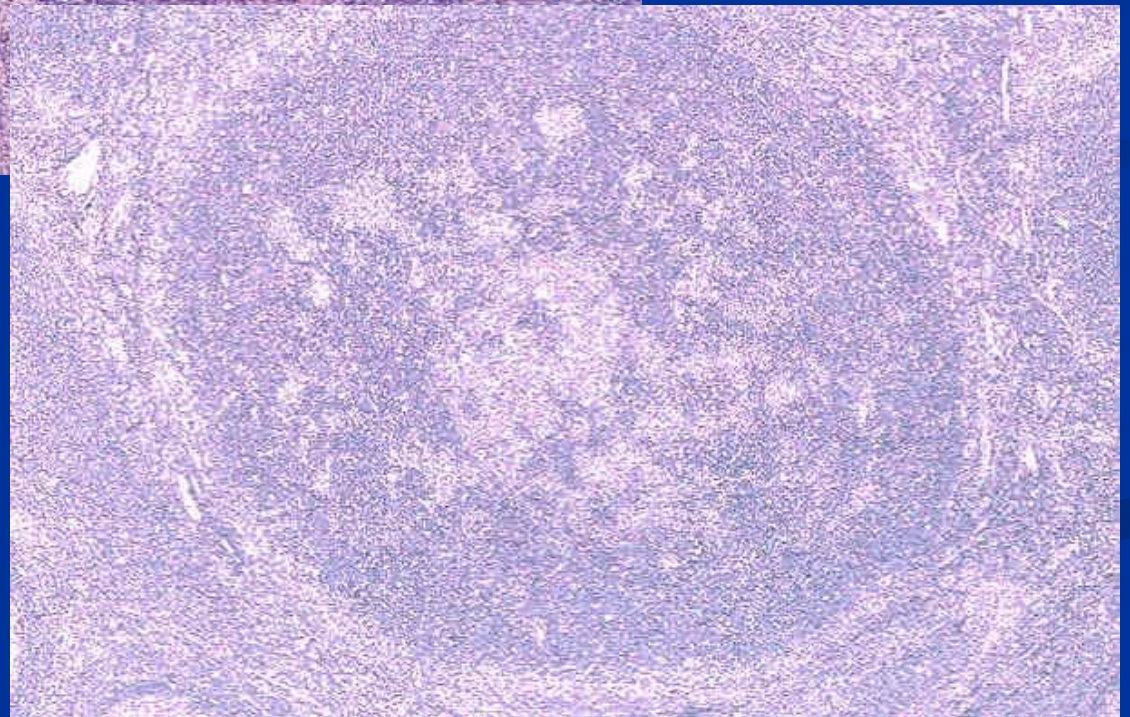
PTGC

(Progressively transformed germinal centers)





PTGC



PTGC

- Progressively transformed germinal centers (PTGC) are seen in association with NLPHL.
- It is uncertain whether these lesions are preneoplastic
- Most patient with reactive hyperplasia and PTGC do not develop HL

NLPHL

- Prognosis is good especially for earlier stage
- 2-3% of cases progress to large B-cell lymphoma

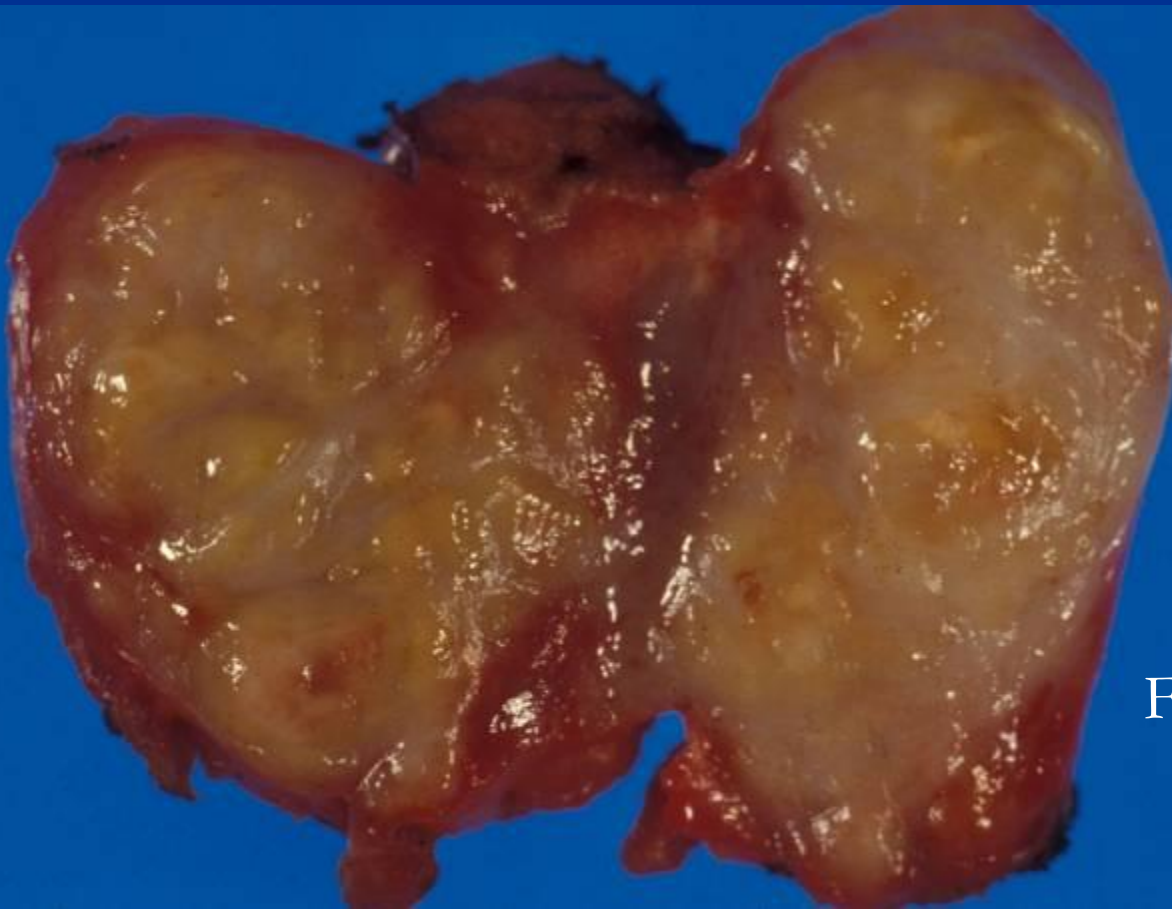
Classical Hodgkin lymphoma

- 95% of Hodgkin lymphomas
- Bimodal age distribution
- EBV has been postulated to play a role (lack of immune surveillance)

Sites of involvement

- Cervical lymph nodes
- 60% have mediastinal involvement
- Bone marrow involvement rare (5%) – stage IV disease

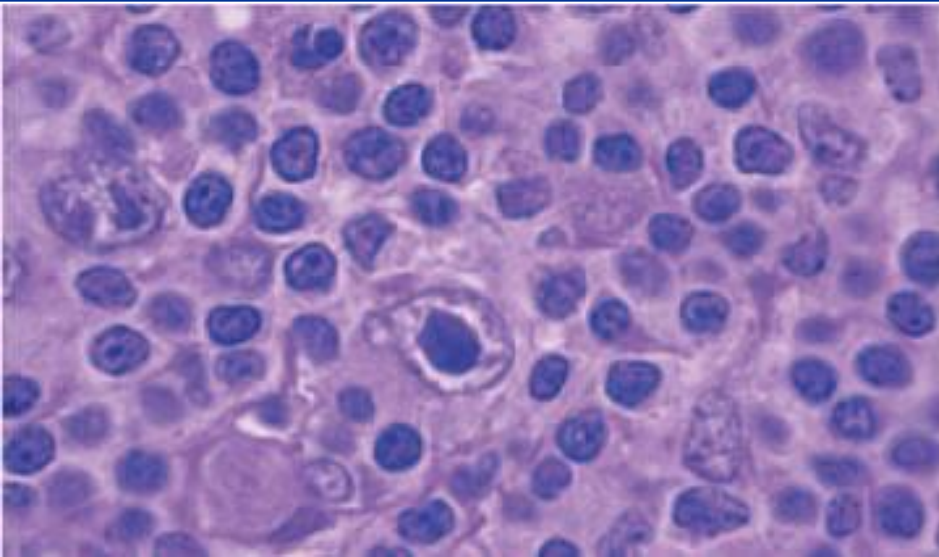
Hodgkin Lymphoma



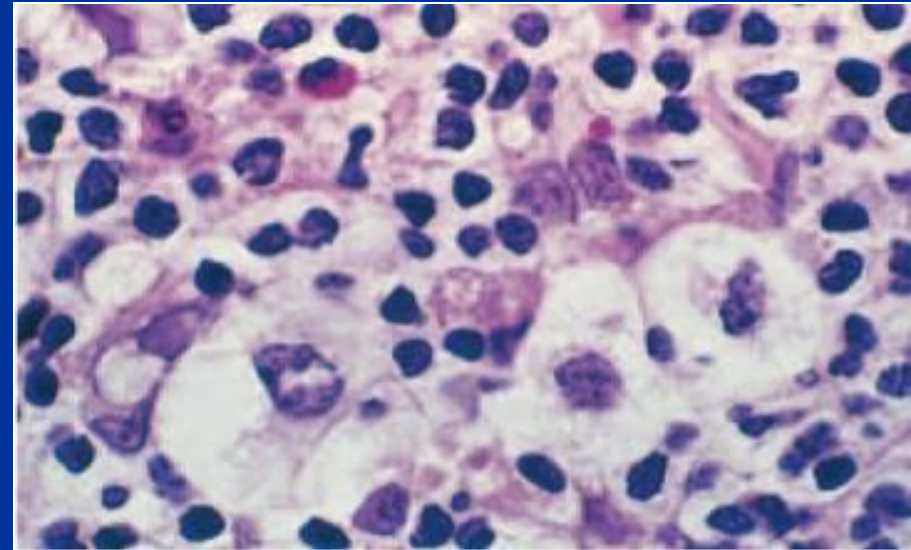
Fish-flesh tumor

Hodgkin Lymphoma

Malignant Cell Variants

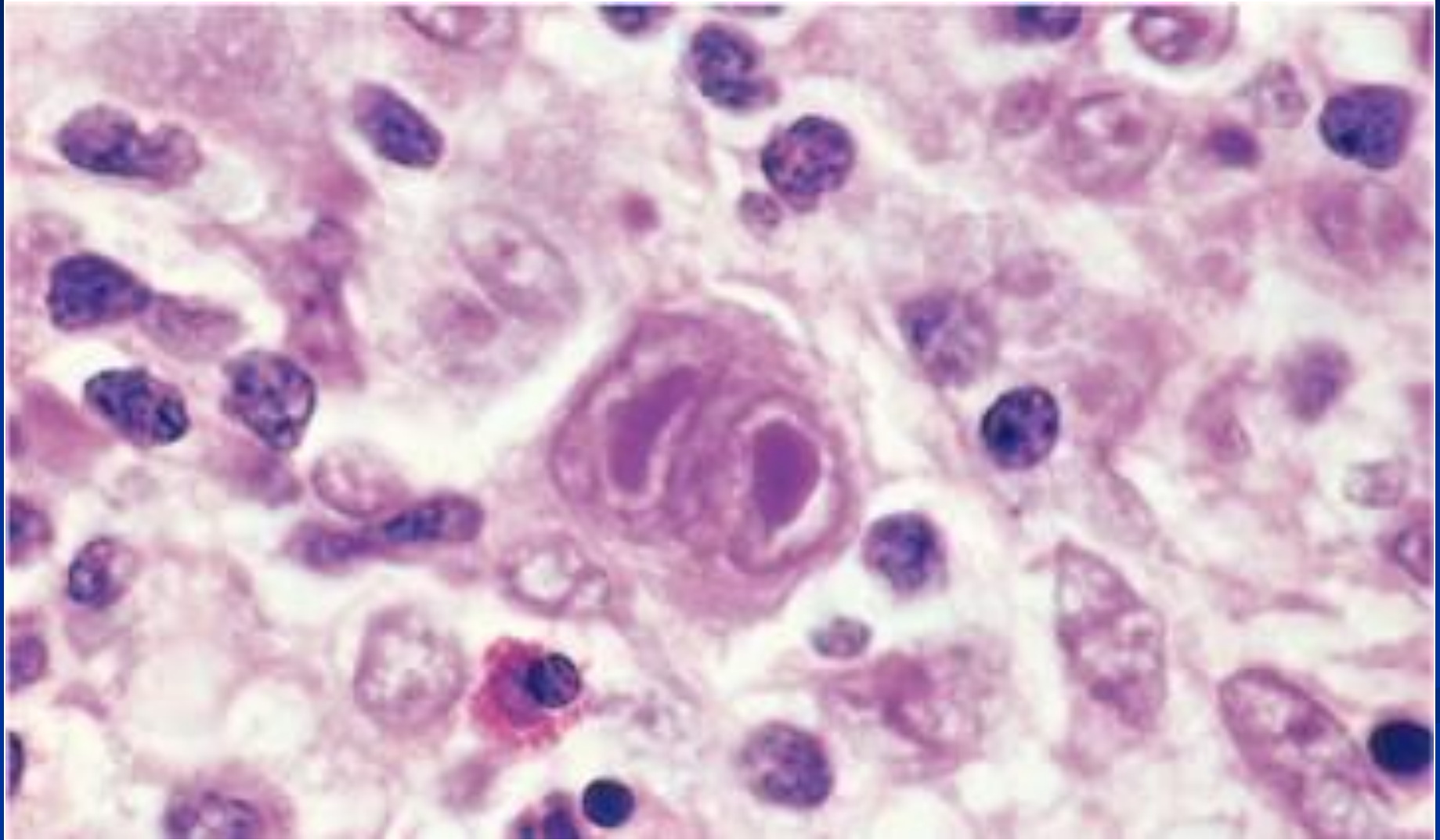


Mononuclear Hodgkin Cell



**Lacunar cells seen in nodular
sclerosis Hodgkin lymphoma**

Hodgkin Lymphoma

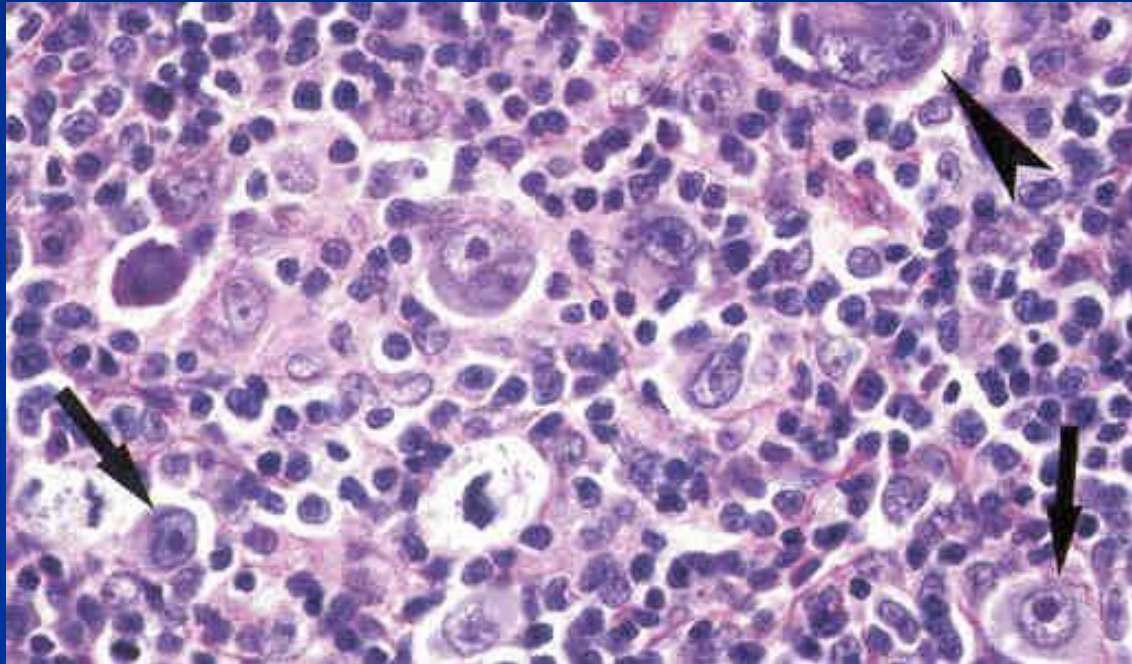


Diagnostic Reed-Sternberg cell

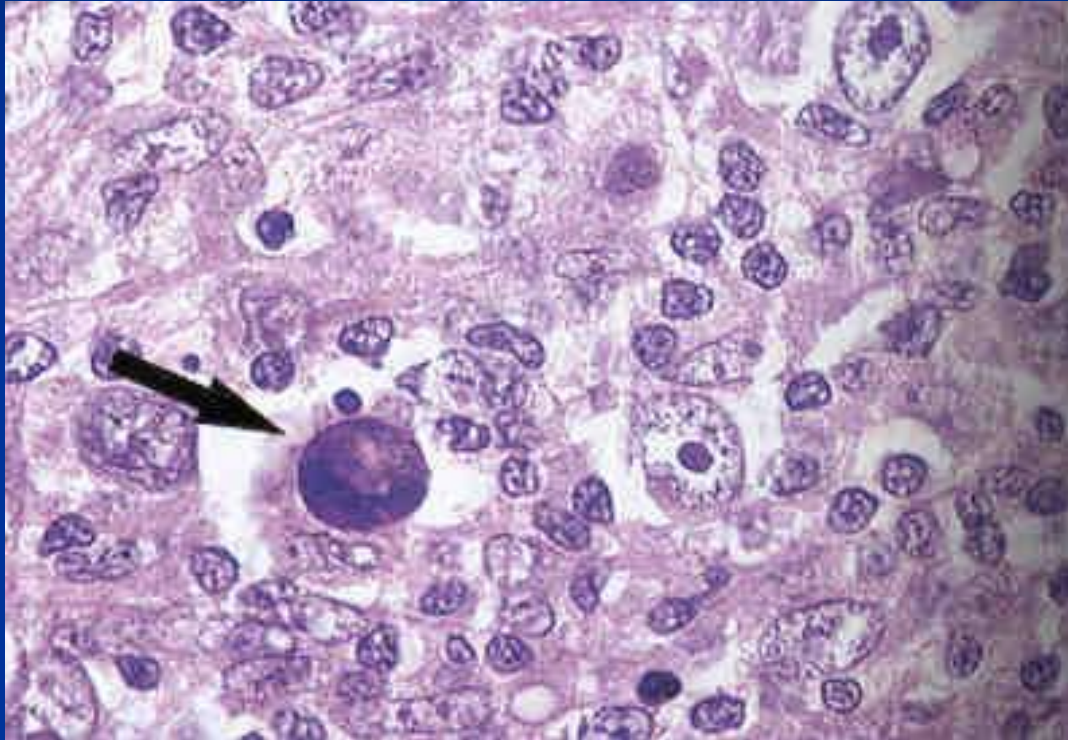
Reed-Sternberg cell



RS cells



Mummified RS cell



Defining characteristics

- RS cells in the appropriate cellular background

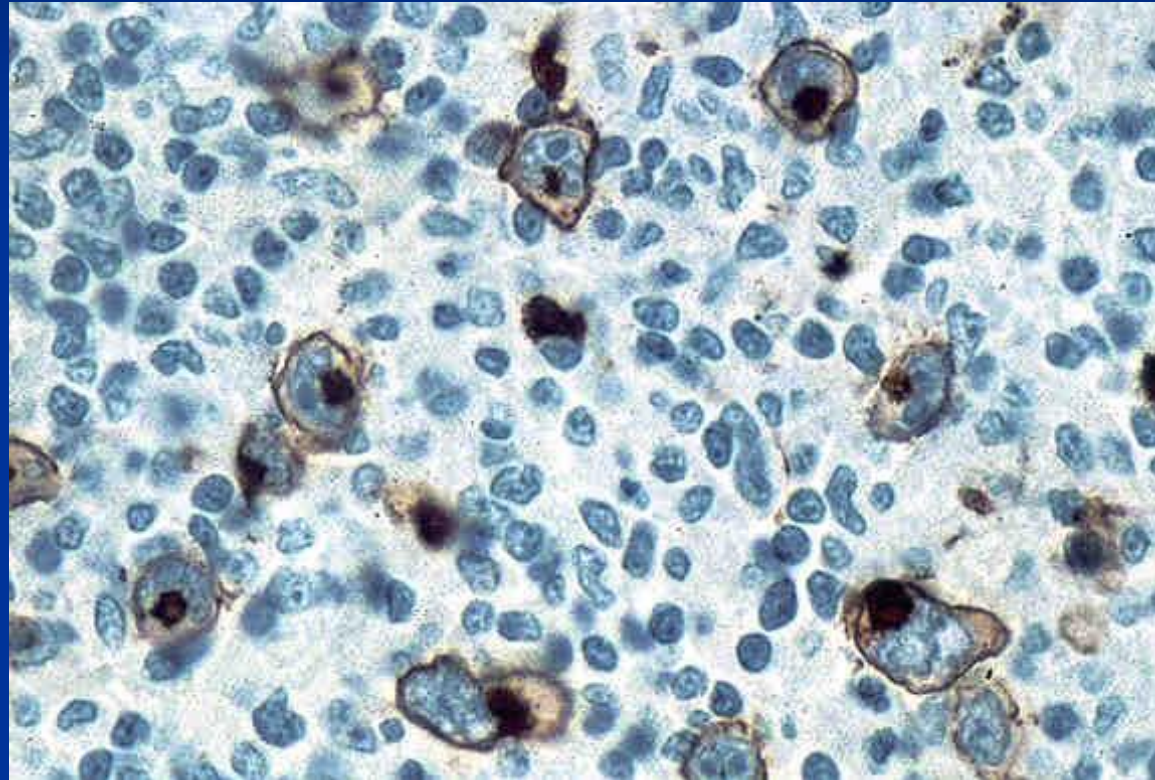
Immunophenotype (HRS cells)

CD45- , CD15+ , CD30+, PAX5+

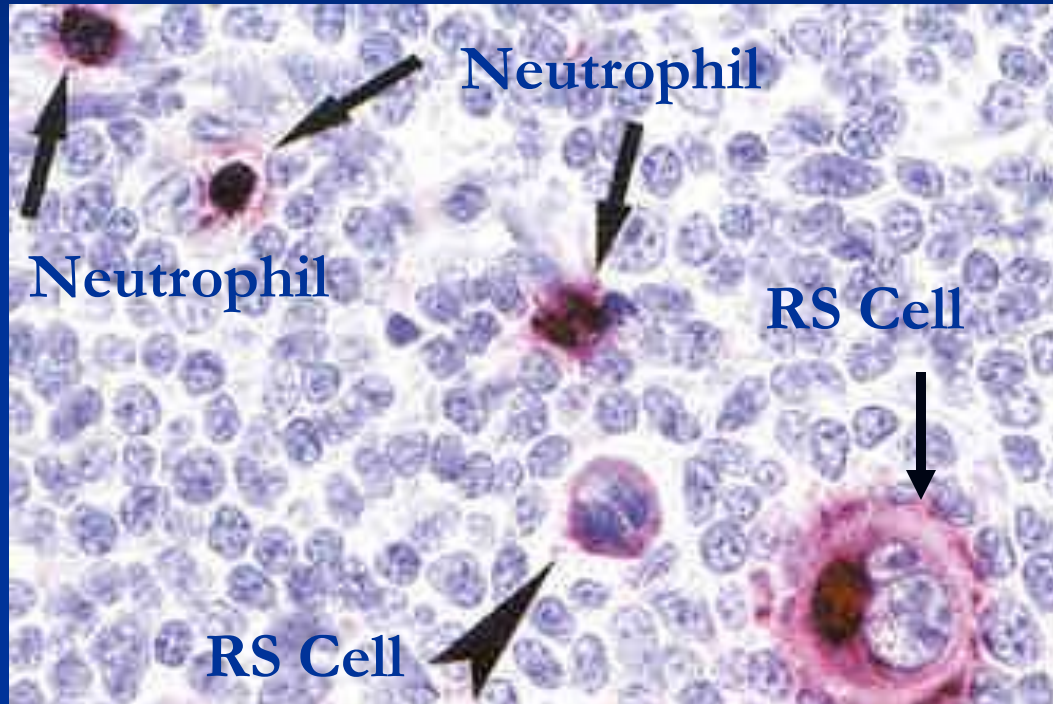
The neoplastic cells are usually not CD20 positive

The background lymphocytes are T cells (CD3 positive, CD20 negative)

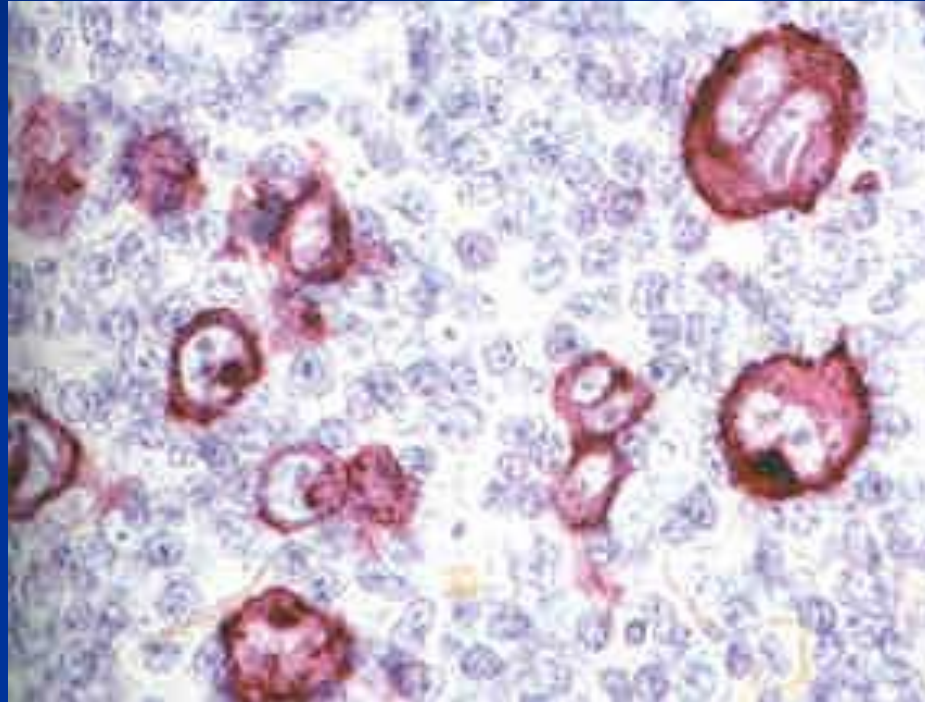
RS cells and CD15



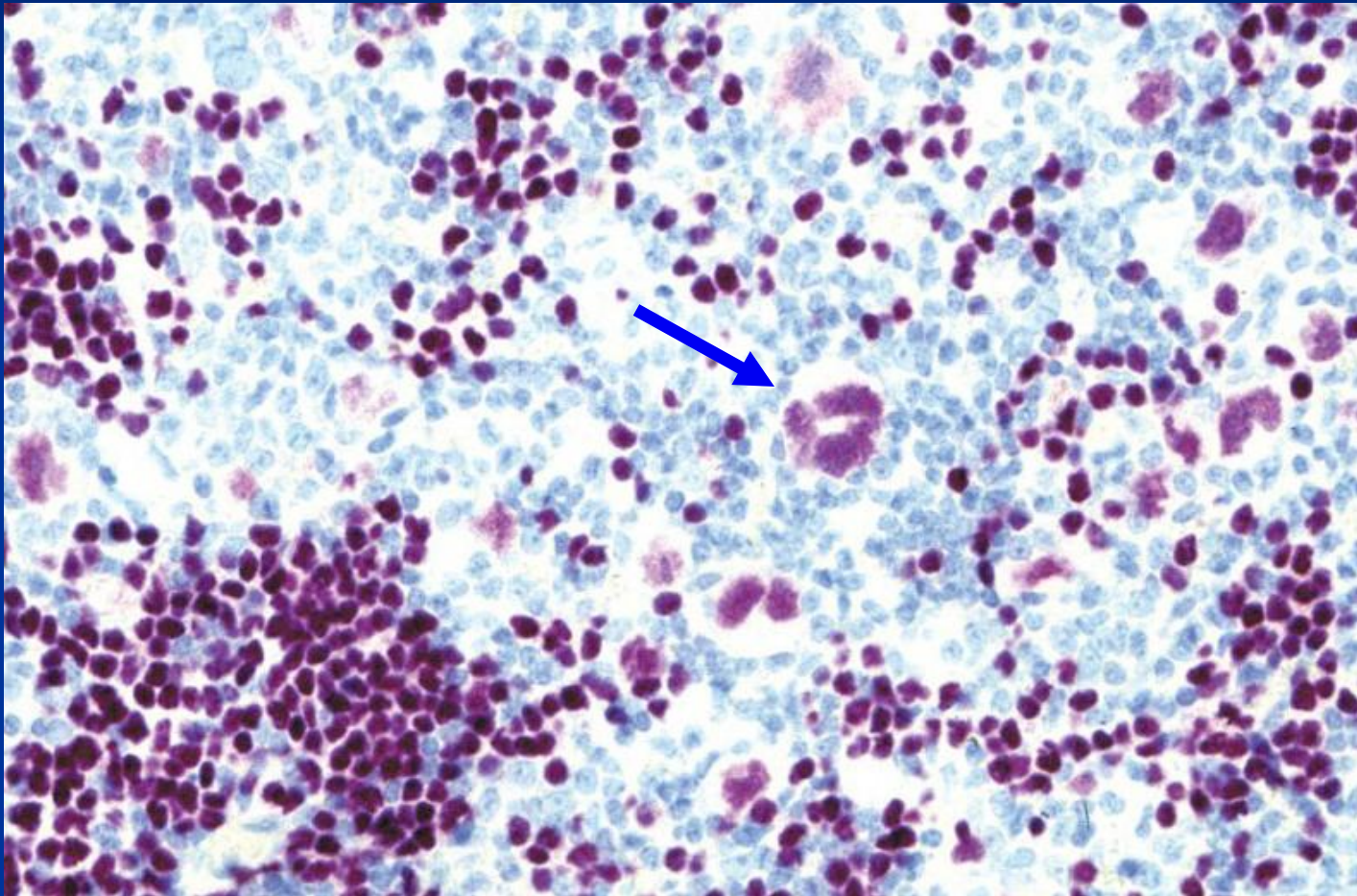
CD15



CD30



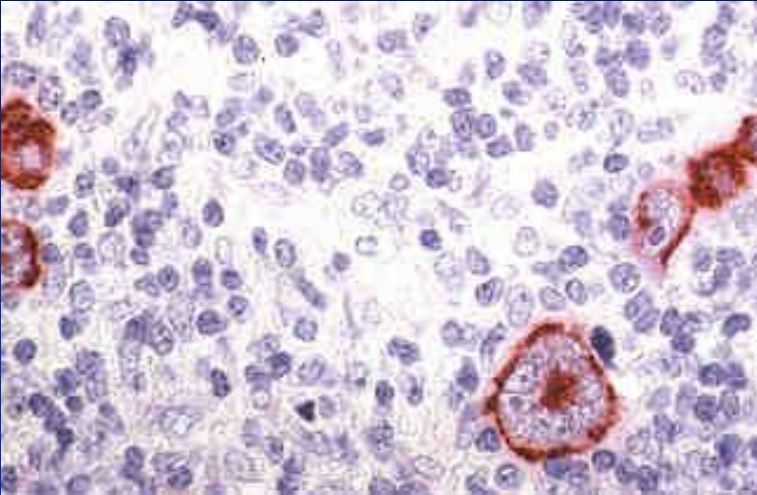
PAX5



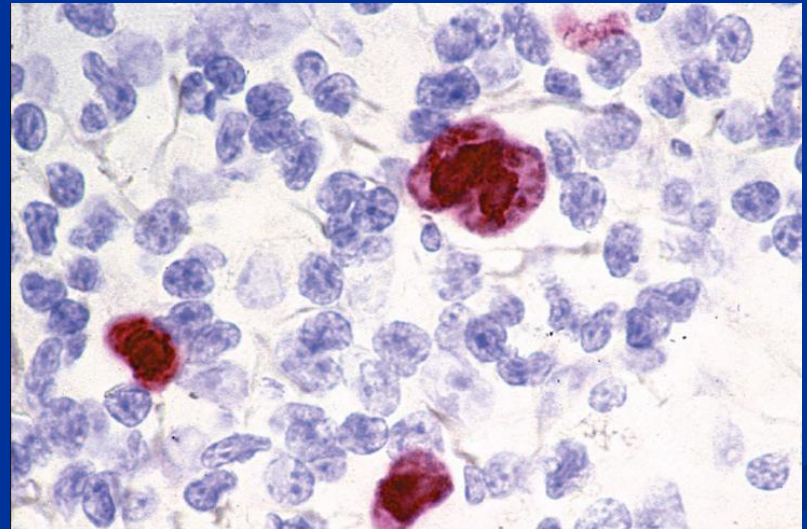
EBV

- The prevalence of EBV in RS cells varies according to the histological subtype:
 - Highest in mixed cellularity (75%)
 - Lowest in nodular sclerosis (10-40%)

EBV



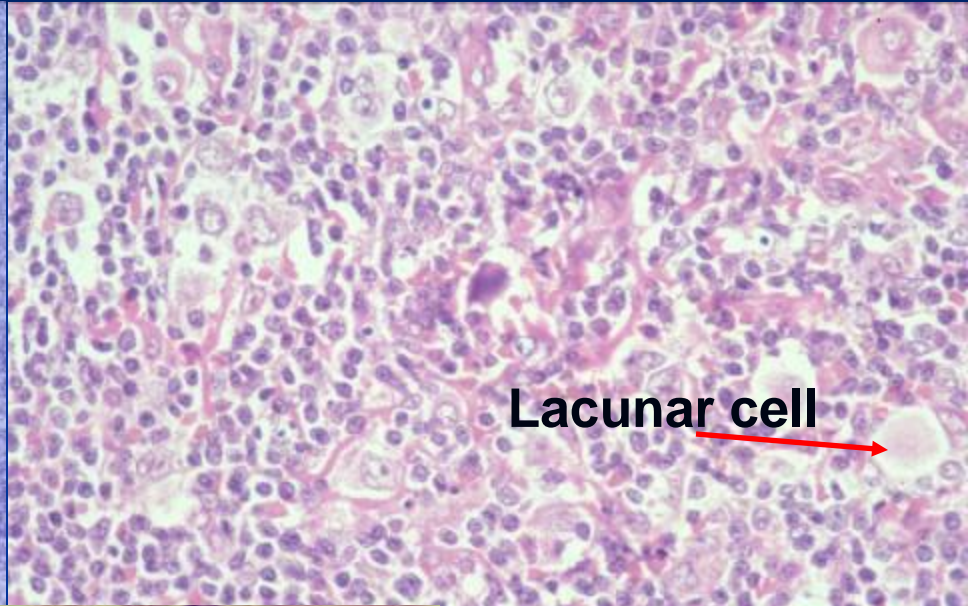
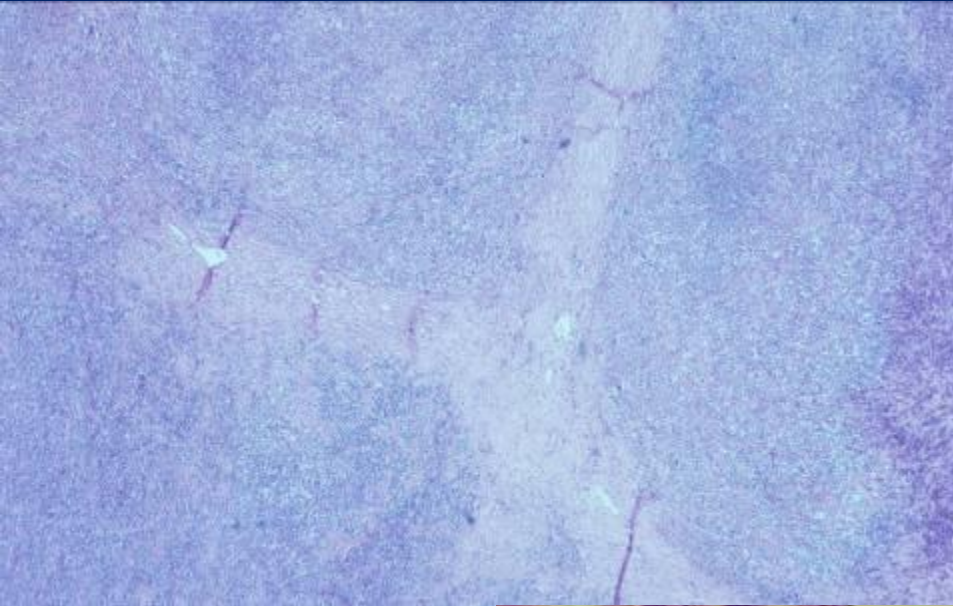
**EBV-encoded Latent
Membrane Protein 1 (LMP 1)**



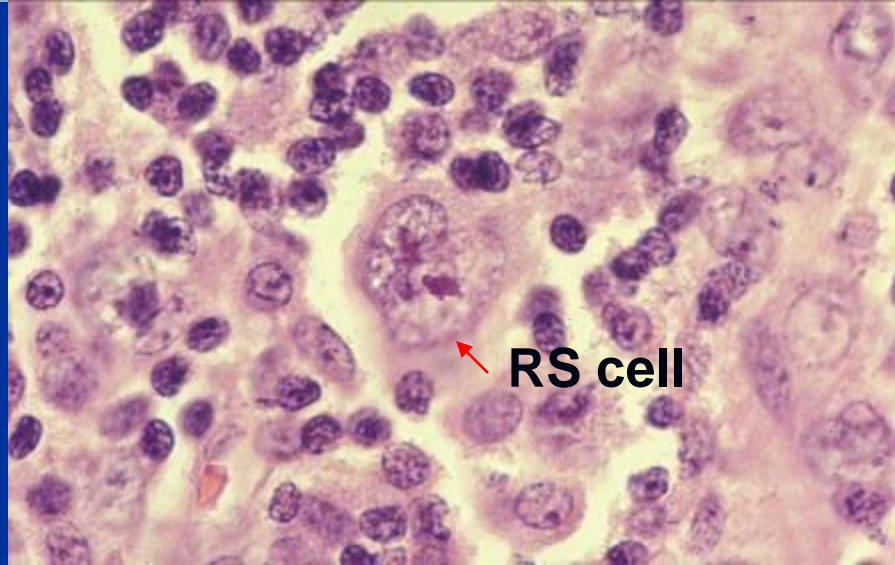
EBER-Insitu Hybridization

Hodgkin Lymphoma

Nodular Sclerosis Type



Lacunar cell

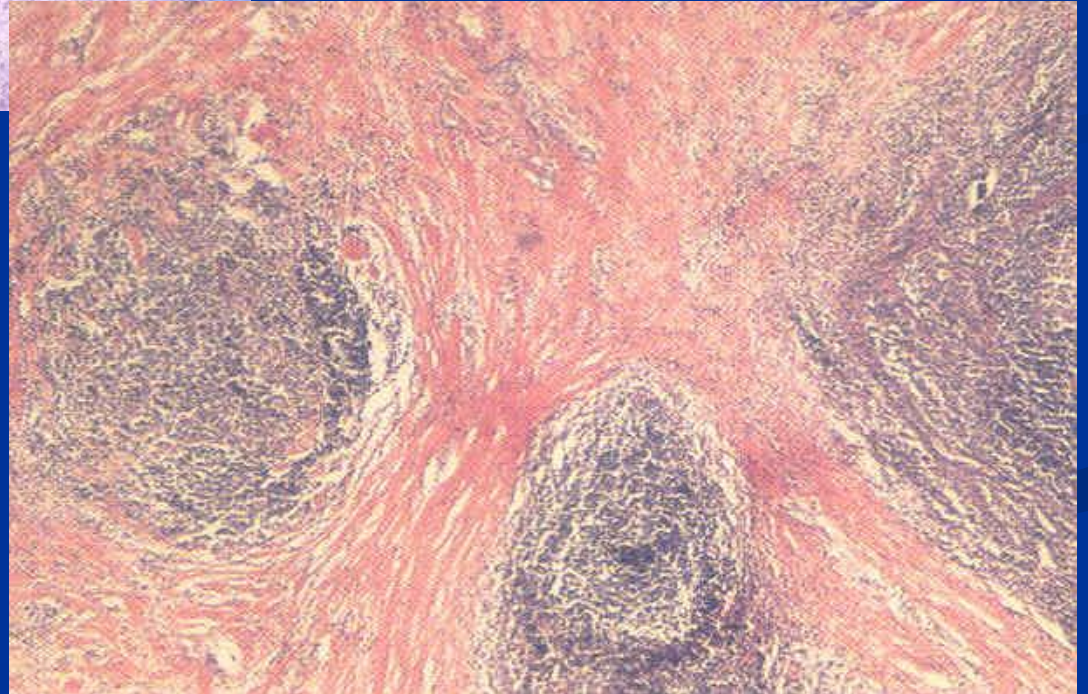
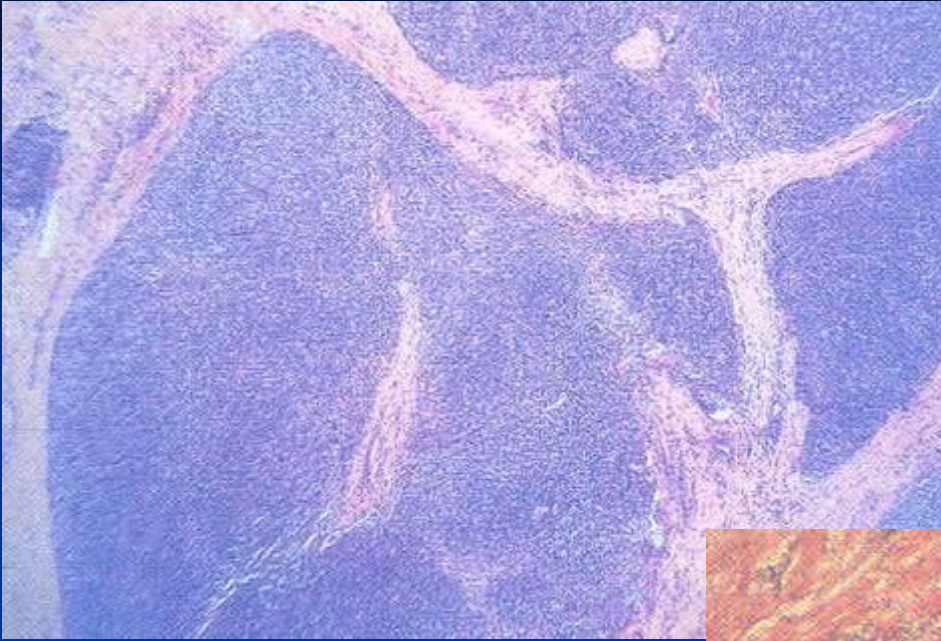


RS cell

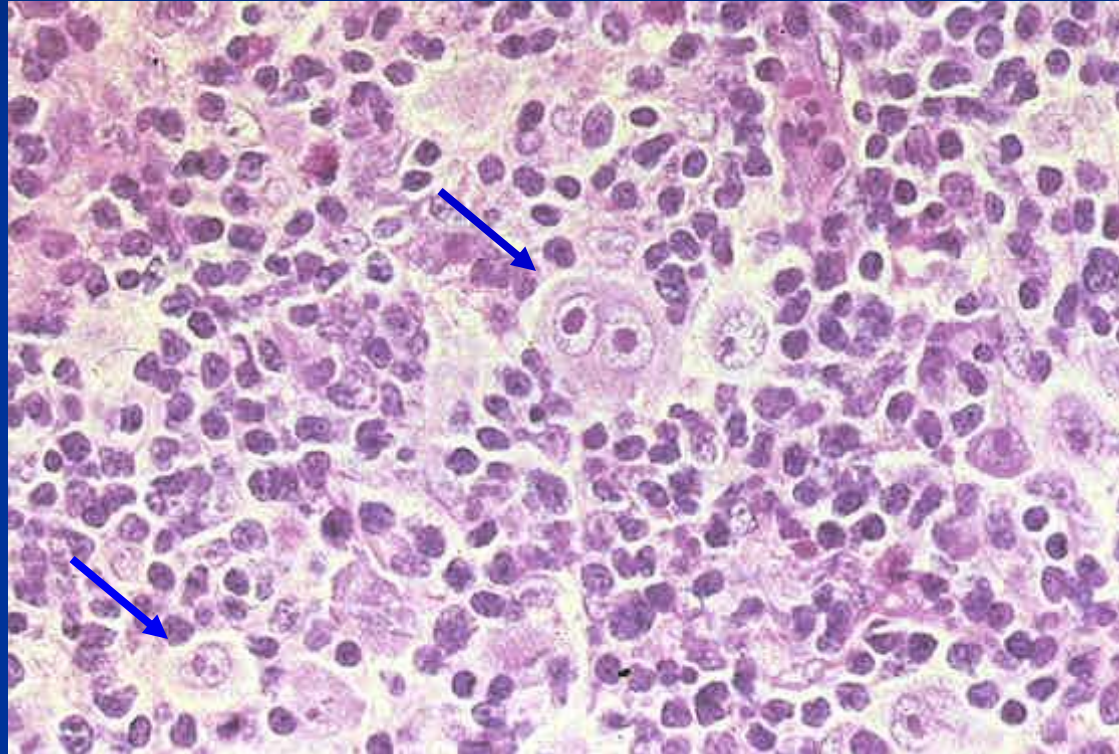
Nodular Sclerosis

- Most common type
- The only type of HL without a male predominance

Nodular Sclerosis



RS and lacunar cells



Nodular Sclerosis

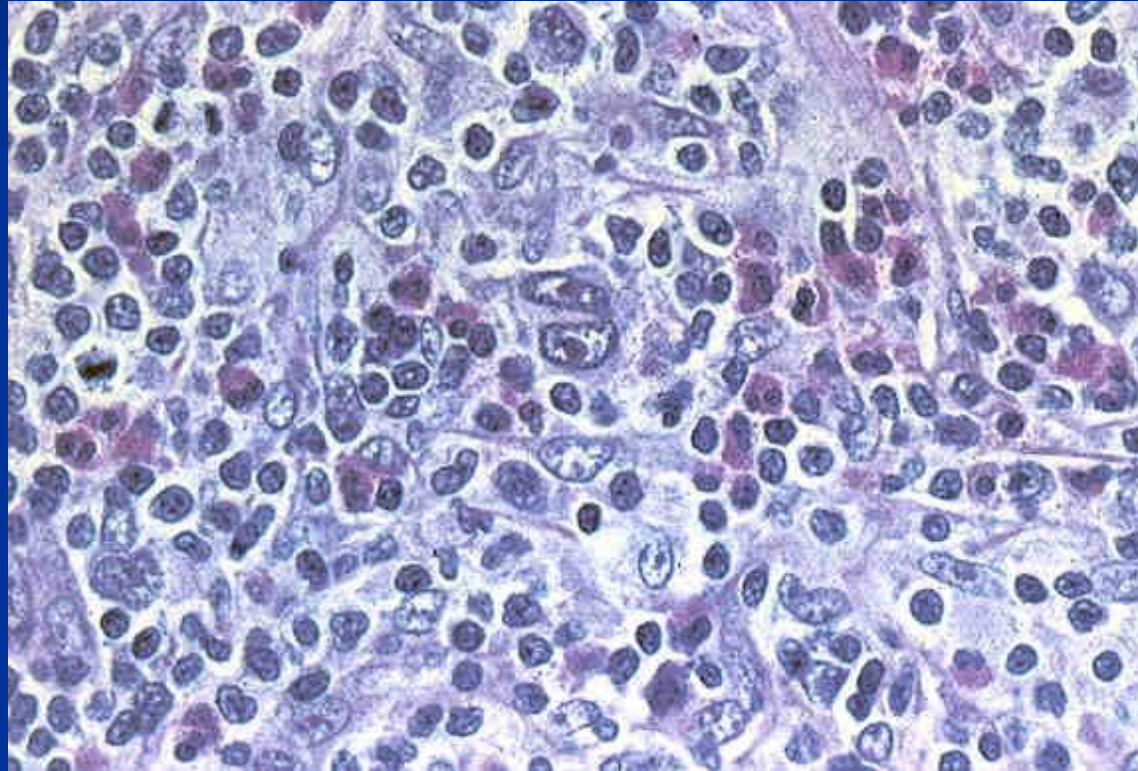
- Cellular phase
- Fibrotic phase

- Syncytial variant: an extreme form of the cellular phase (prominent aggregates of HRS cells)

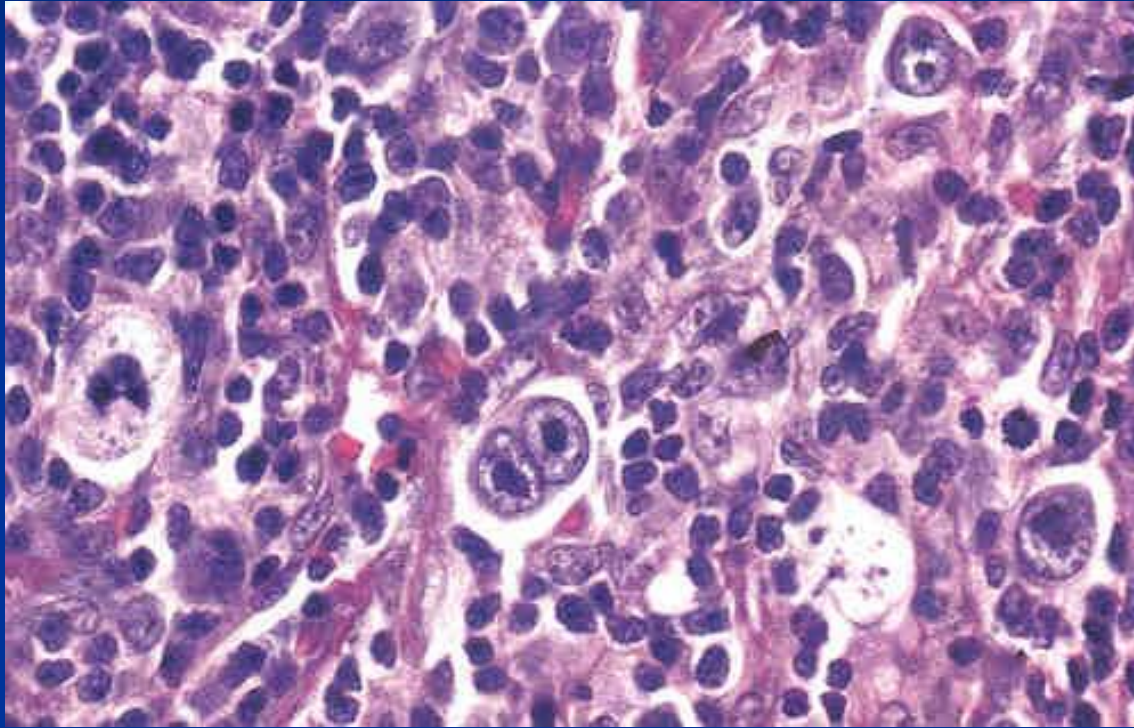
Mixed cellularity HL (MCHL)

- More frequent in patients with HIV infection and in developing countries
- A bimodal age distribution is not seen
- Often showing granulomas

Mixed cellularity



Mixed cellularity



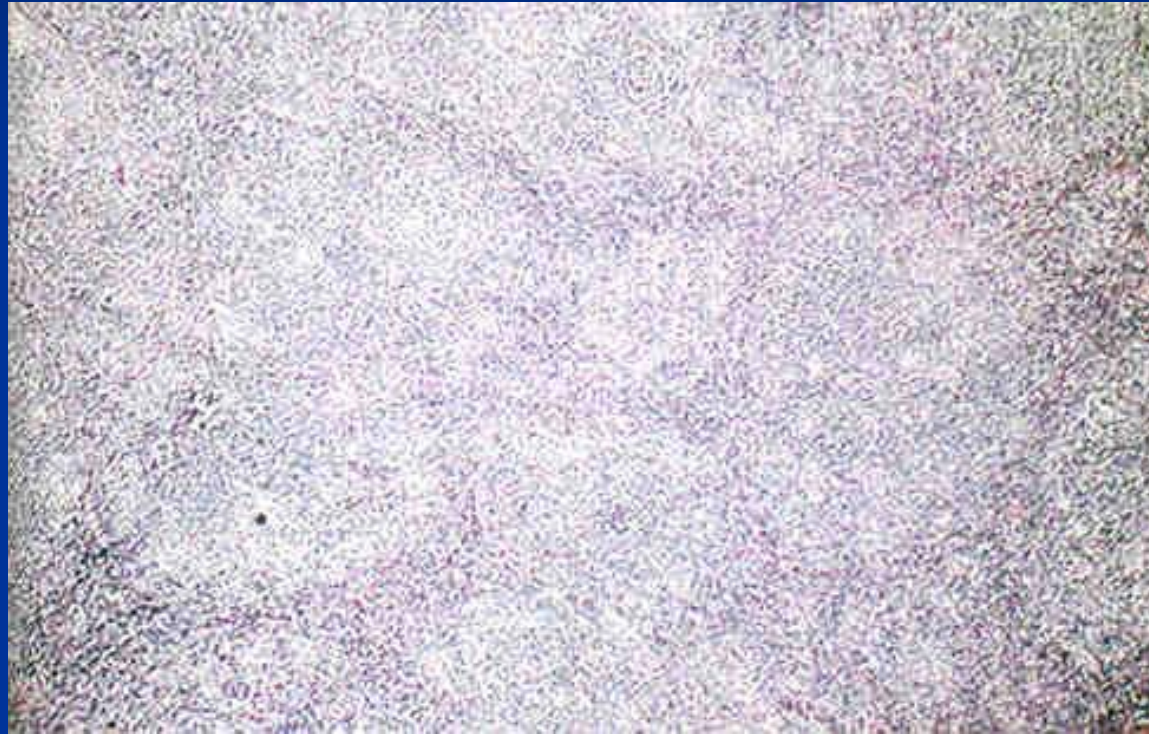
Lymphocyte rich classical Hodgkin lymphoma

- Nodular (common): background cells are B cells
- Diffuse: background cells are T cell

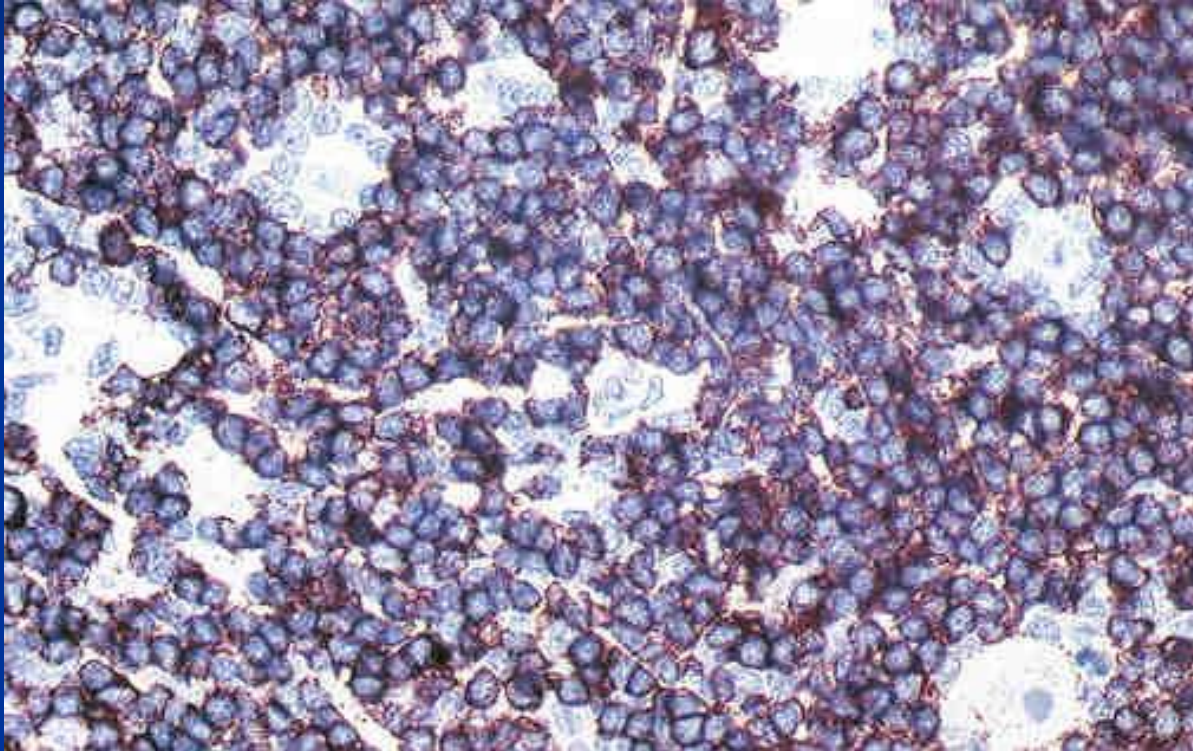
Notes:

- Histology of Nodular type resembles NLPHL
- Histology of Diffuse type resembles TCR-HR LBCL
- -No difficulty in diagnosis with HRS cell immunostains

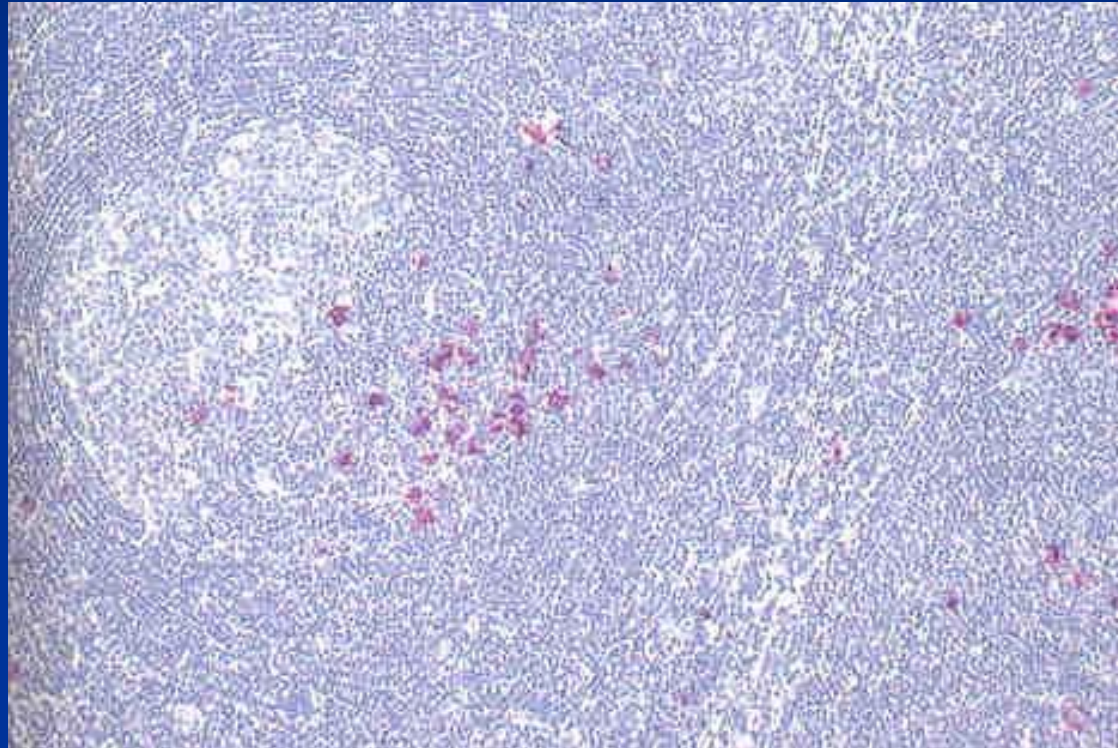
(Nodular) lymphocyte rich HL



LRHD and CD20

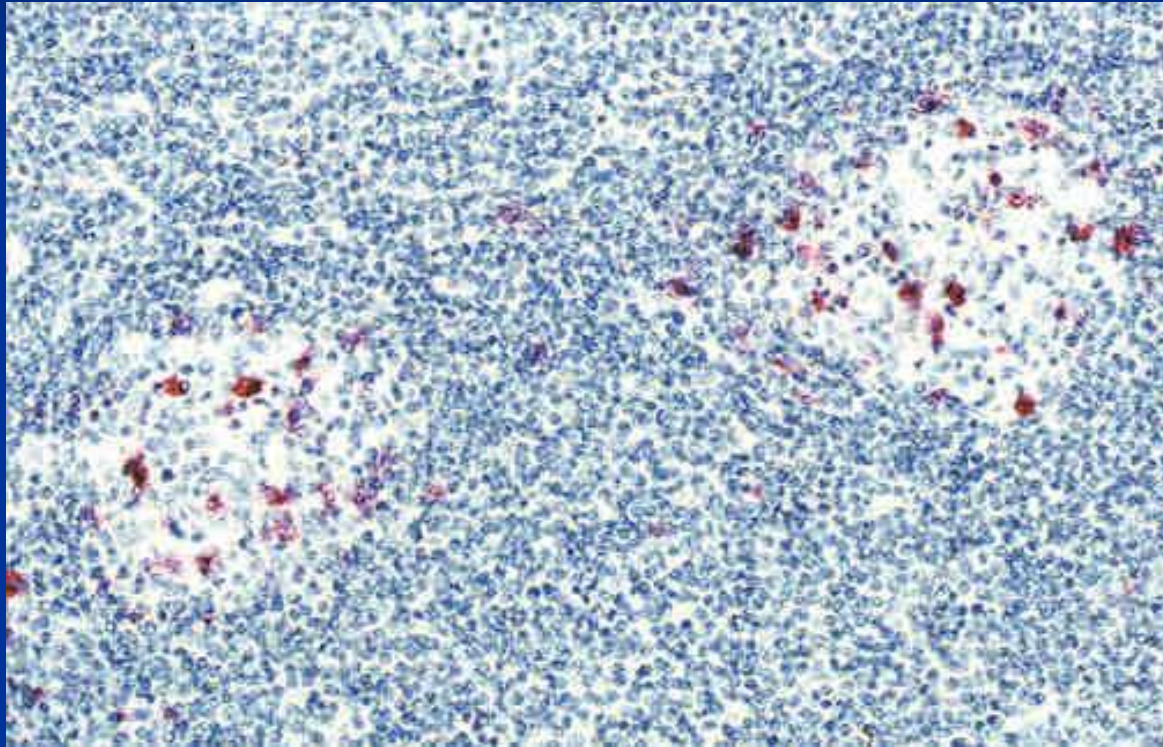


CD30 and LRHL



CD57 and LRHL

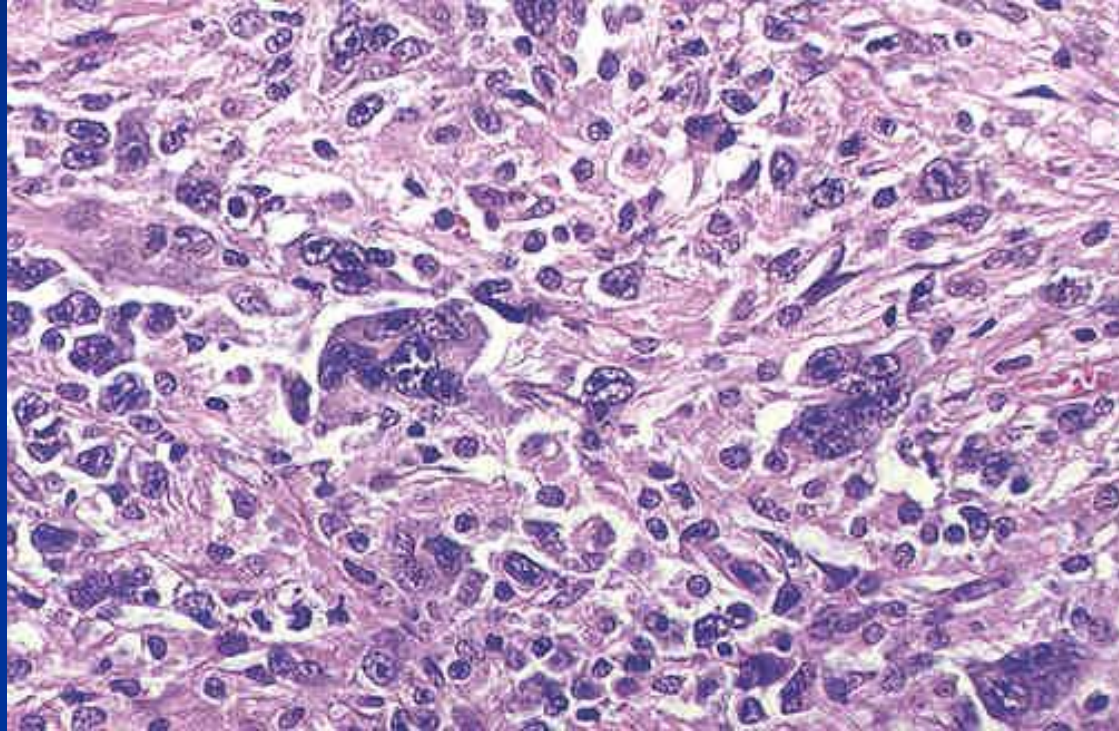
(No resetting around HRS cells)



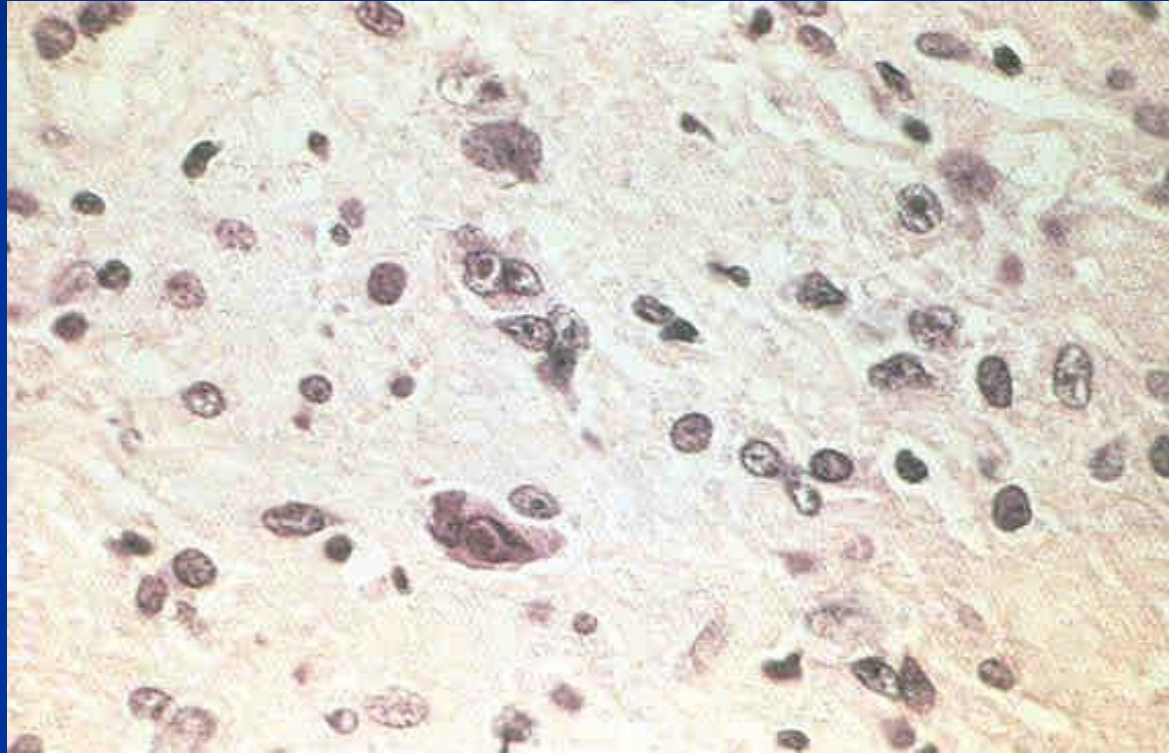
Lymphocyte depleted HL

- Relatively depleted non-neoplastic lymphocytes
- Rare subtype (<1% of cHL)
- Median age 30-37
- Often a/w HIV
- More advanced stages and with B symptoms compared to other subtypes
- May have a sarcomatous pattern
- May mimick ALTCL

Lymphocyte depleted HL



Lymphocyte depleted, diffuse fibrosis



Classical Hodgkin : Prognosis

- Prognosis is now based on the clinical stage rather than the histological subtype.
- Massive mediastinal disease is a poor prognostic factor in NS type

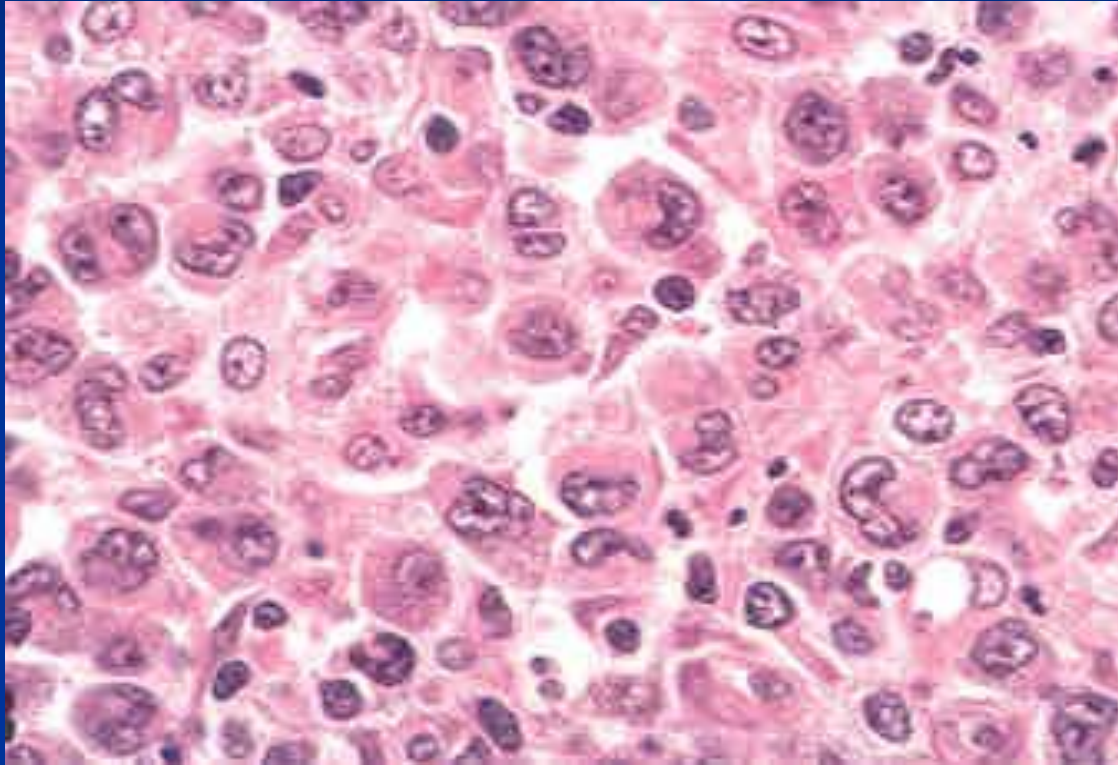
Addendum: Differential diagnosis

- Non-Hodgkin lymphoma
- LDHL, ALCL, and T-cell rich/histiocyte rich DLBCL may look histologically similar

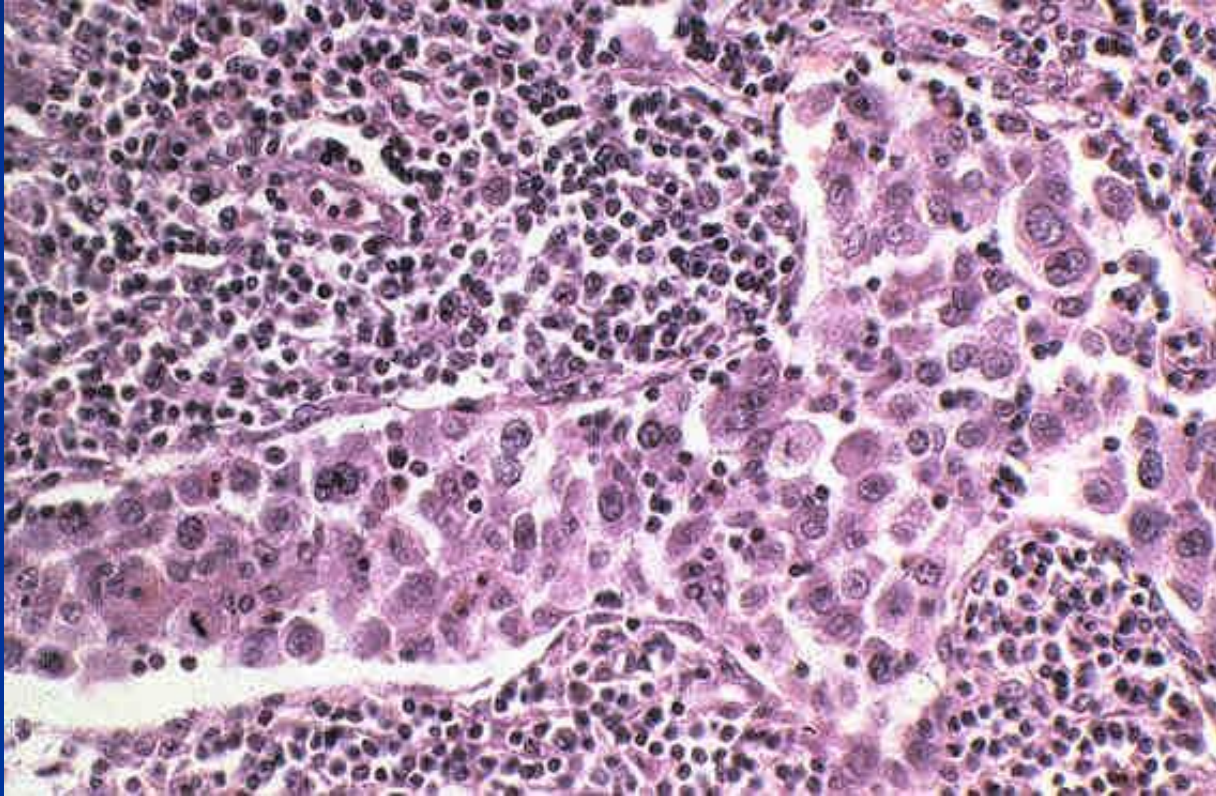
ALTCL

- Large/multinucleated cells with abundant cytoplasm
- CD20 (−)
- T- markers positive, can be “null” phenotype
- CD30 positive
- ALK1 positive (except for the provisional ALTCL-Alk1 neg)

ALCL

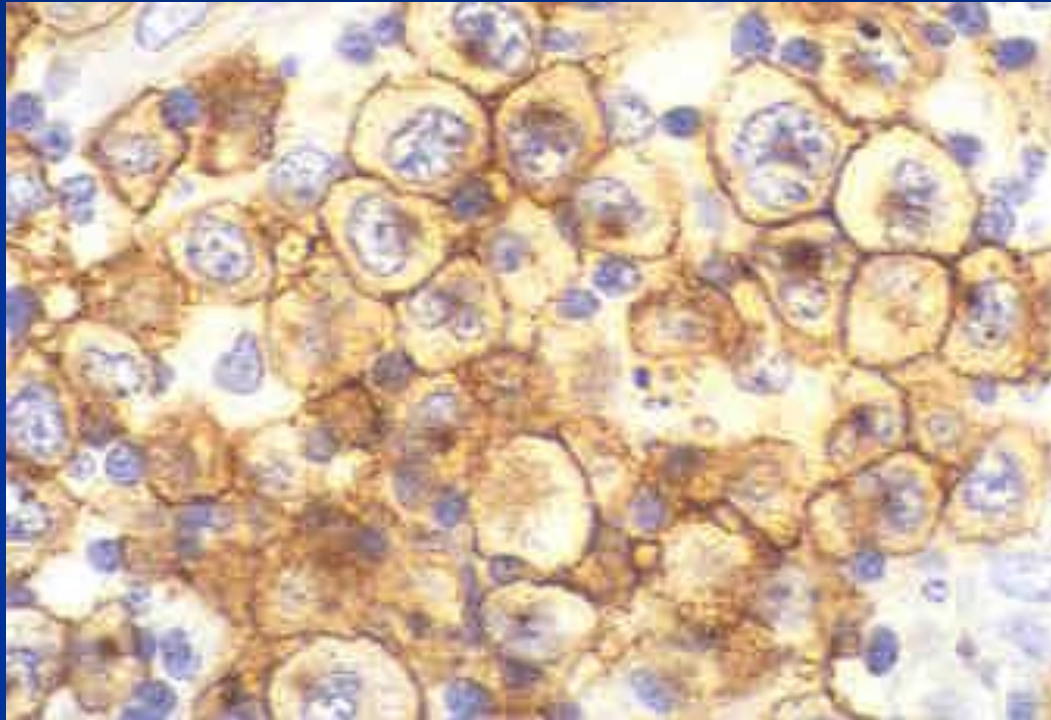


ALCL



Intra-sinusoidal infiltration

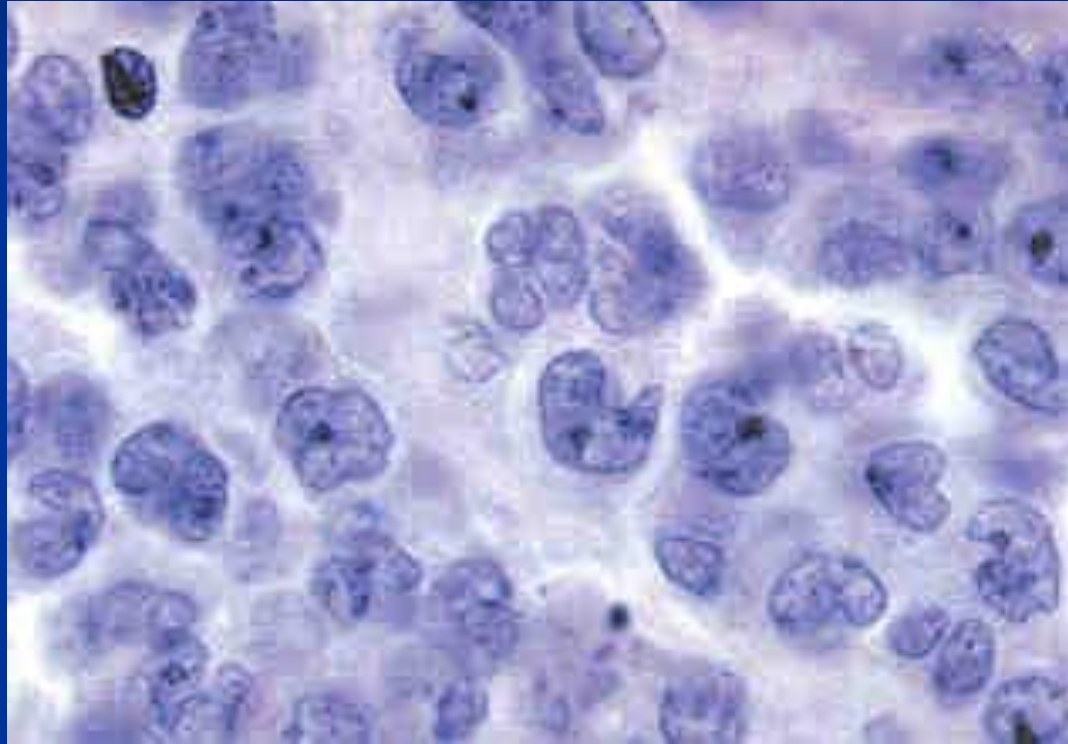
CD30



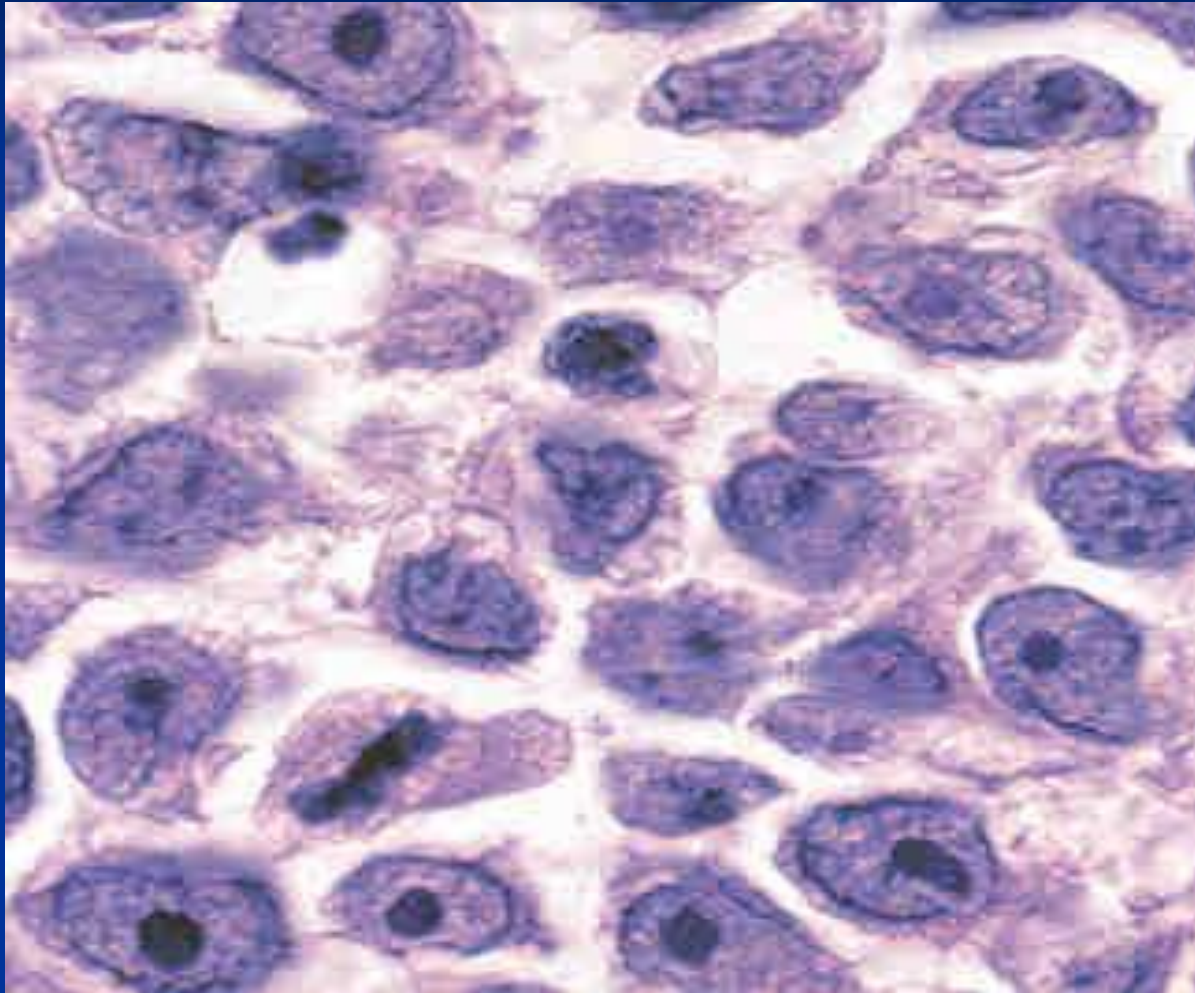
ALTCL

- Two subtypes:
 - Systemic : ALK1 +, EMA +, Clusterin +
 - Primary cutaneous : ALK1 -, EMA -, Clusterin -

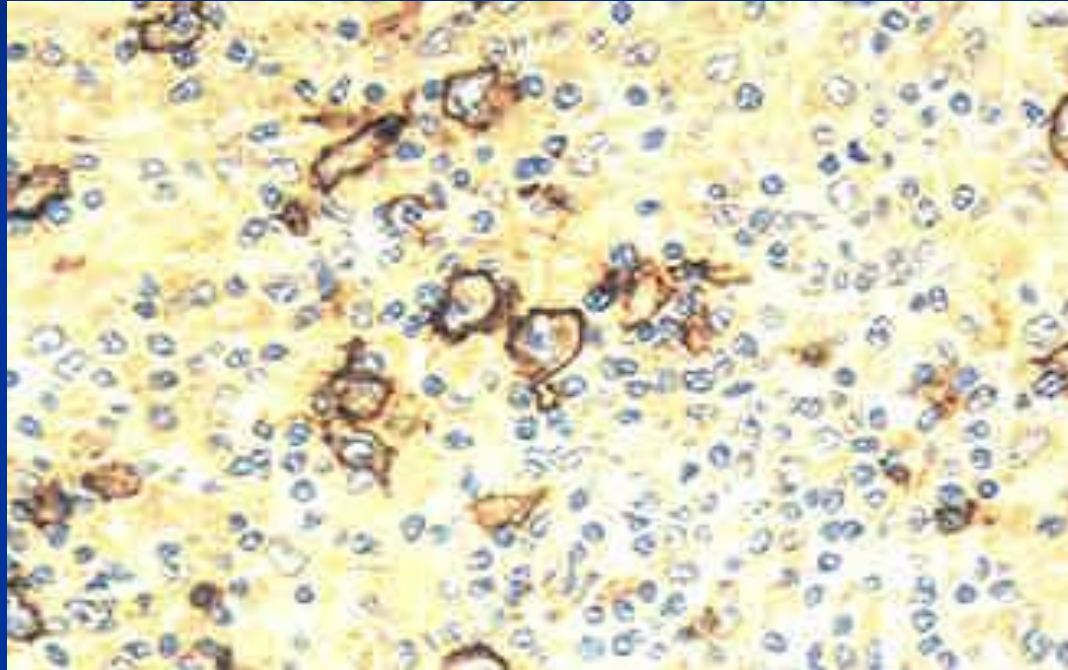
DLBCL, anaplastic variant



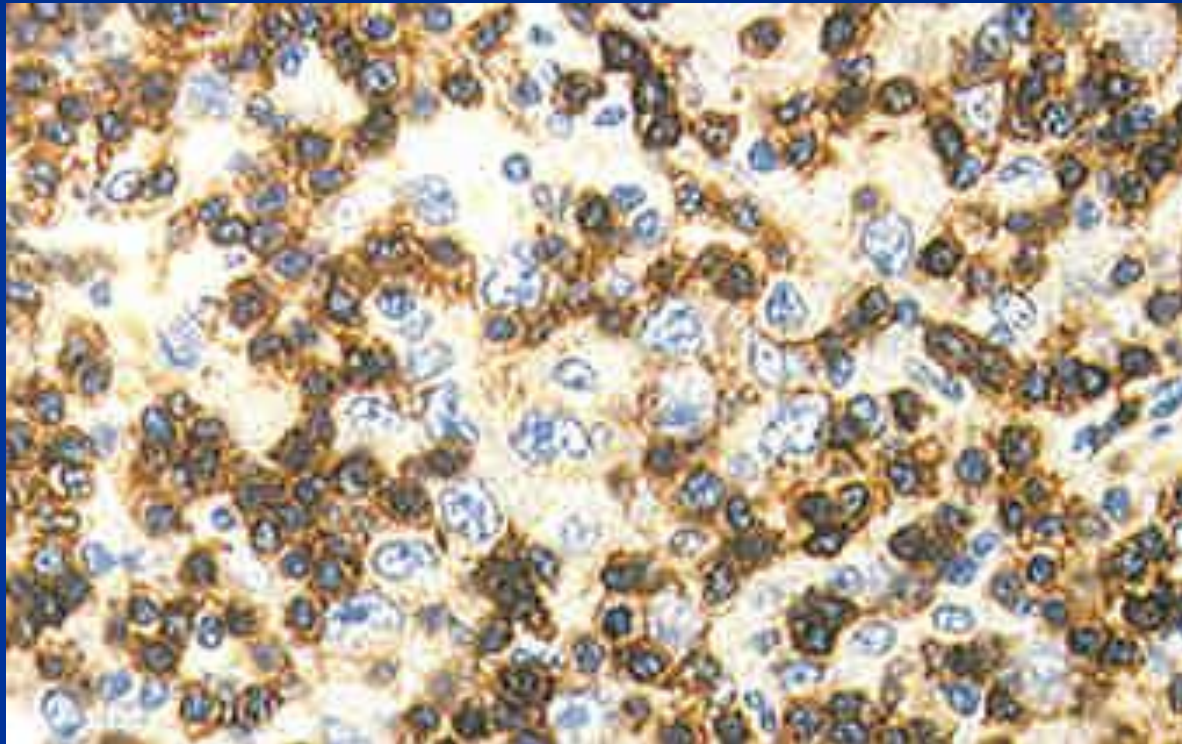
DLBCL, immunoblastic



DLBCL: CD20+



DLBCL: CD30(-)



Immunoprofile

NLPHL

CD45+ CD20+ CD15-
CD30- EMA+ PAX5+

CHL

CD45- CD3- CD20-
CD15+ CD30+ PAX5+

ALTCL

CD45+ CD20- CD3- CD4+
CD30+ ALK1+ EMA+
PAX5-

DLBCL

CD45+ CD20+ CD3-
CD30+/- PAX5+