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Lymphomas

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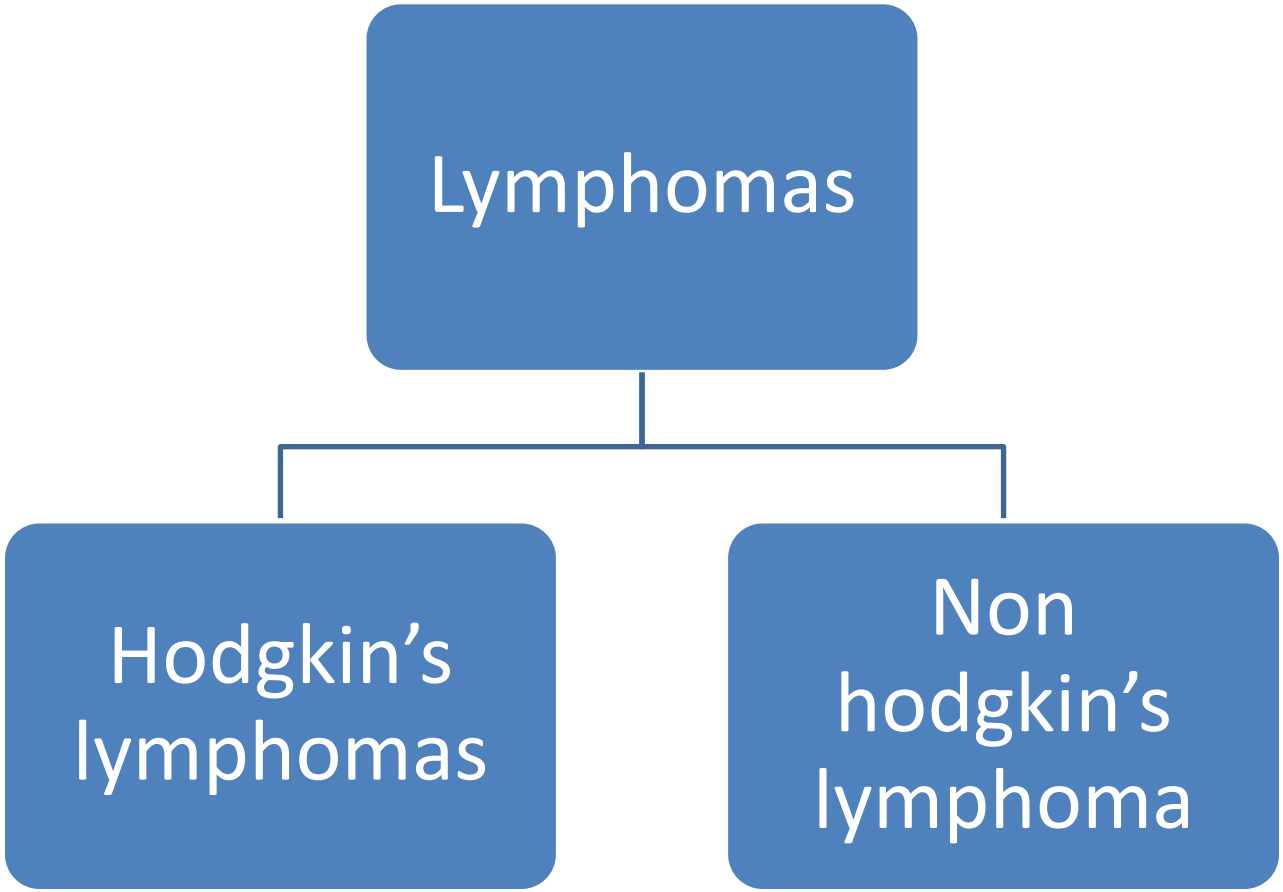
2014

Classification of lymphomas

Lymphomas are malignancies of the lymphoid cells



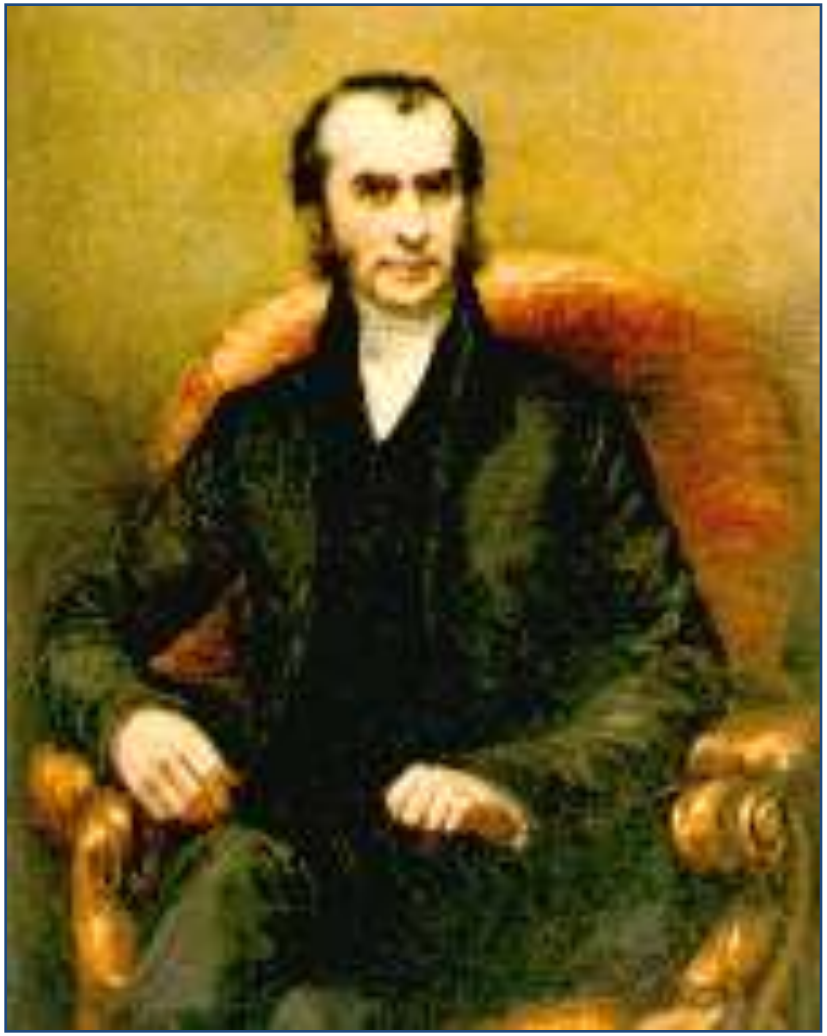
WHO classification of tumors of hematopoietic and lymphoid tissues 2008

1. Non-Hodgkin's lymphomas

2. Hodgkin's lymphoma

- B-cell lymphoma
  - account for about 85% of the diagnosed cases, and within Africa, Burkitt lymphoma is the most common B-cell tumour
- T-cell lymphoma
- NK-cell lymphomas

Hodgkin lymphoma



Dr. Thomas Hodgkin
(1798-1866)

British physician, considered one of the most prominent pathologists of his time and a pioneer in preventive medicine.
In 1832, Dr. Thomas Hodgkin, working at Guy's Hospital in London, reported a series of seven cases of enlargement of the lymph nodes and spleen, which he speculated might represent a primary disorder of those tissues rather than reactive enlargement

Dr. Dorothy Reed Mendenhall

- The first descriptions of the microscopic appearance of the affected tissues appeared in the late 1800s. However, it was not until the seminal observations by Sternberg in 1898 and Reed in 19025 that widespread attention was drawn to the curious giant cell present in many such cases, which would later come to bear their names and which would soon become regarded as a morphologic hallmark of Hodgkin's disease. Interestingly, neither Sternberg nor Reed felt that this disorder represented a neoplasm. Sternberg believed that it was a variant of tuberculosis, whereas Reed felt it to be an independent entity of inflammatory origin.

Definition

Hodgkin lymphoma (formerly, Hodgkin disease) is a potentially curable lymphoma with distinct histology, biologic behavior, and clinical characteristics.

Classification WHO (2000)

- Hodgkin lymphoma can be divided into two main types:

Classical Hodgkin lymphomas

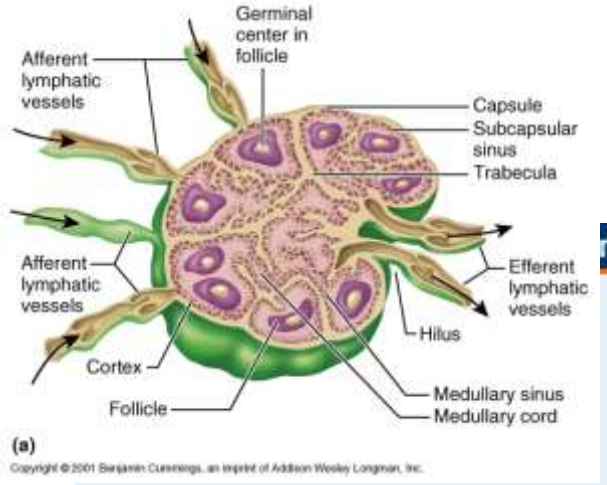
1. Nodular sclerosis
2. Mixed cellularity
3. lymphocyte-depleted
4. Lymphocyte-rich

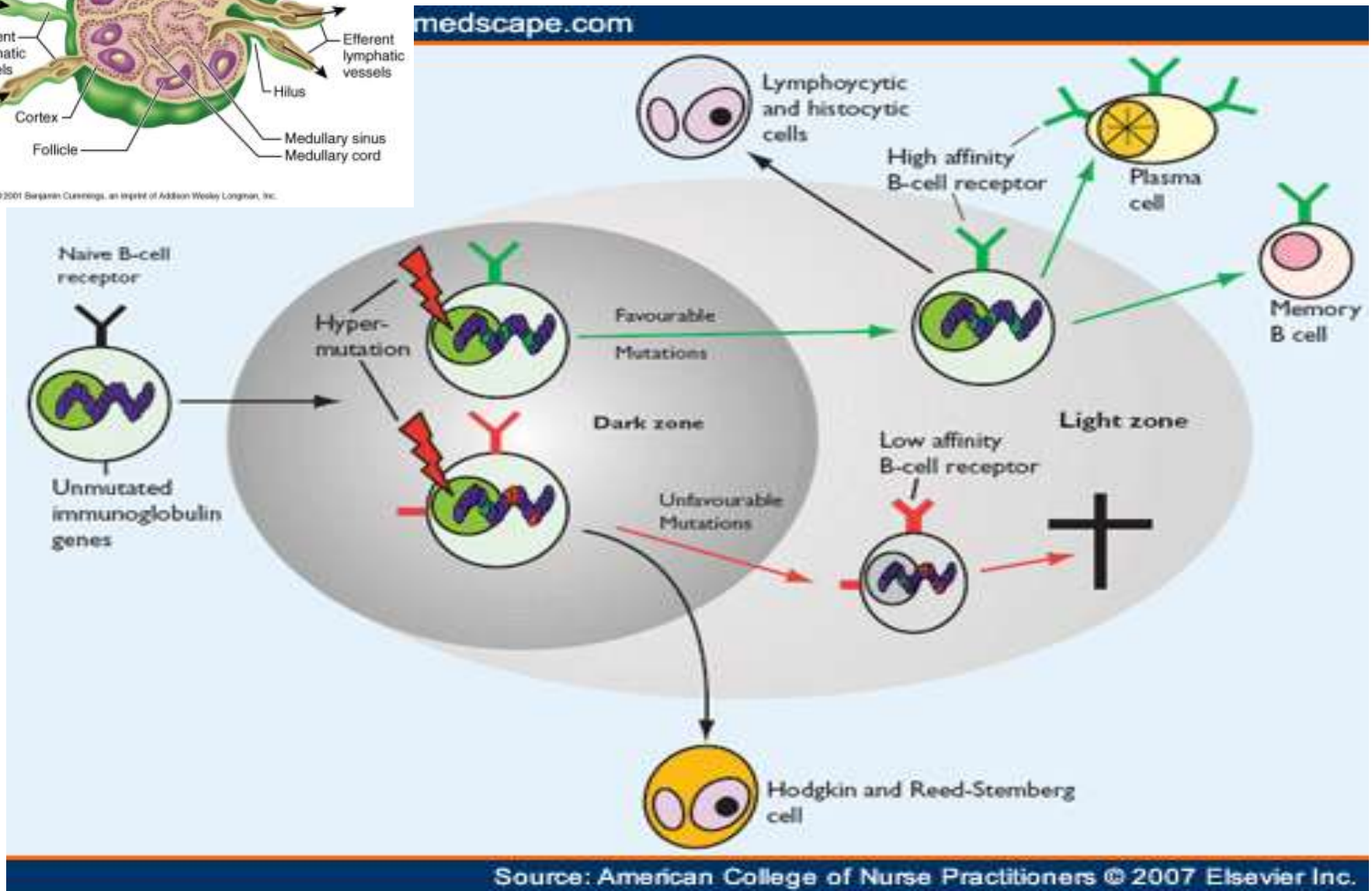
Nodular lymphocyte-predominant Hodgkin lymphoma

PATHOGENESIS

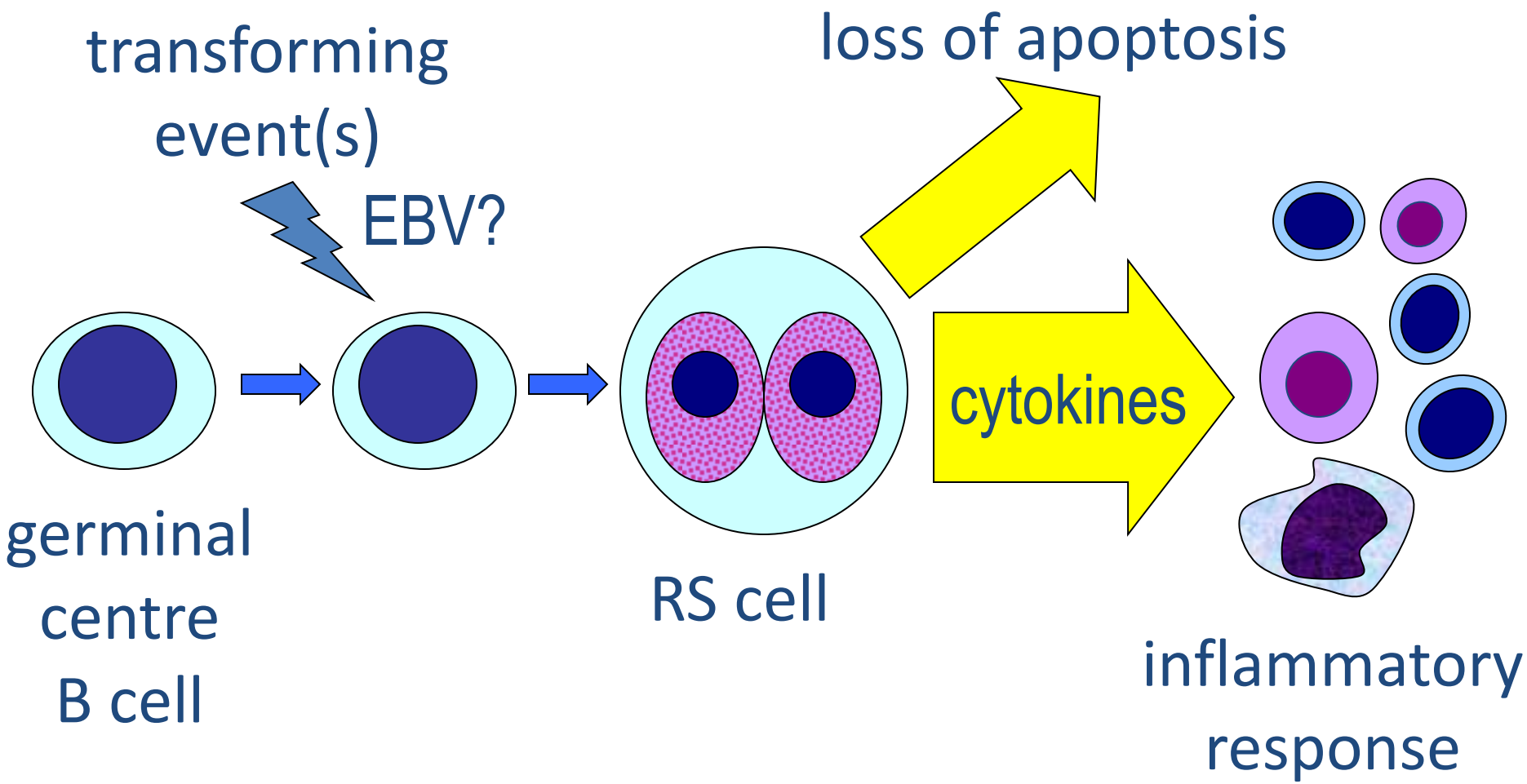
- In classic HD has been proven to be a malignant tumor of B-cell Origin
- PCR studies have provided evidence to suggest that the RS cells of classic HD are derived from germinal center B cells that have undergone unusual “crippling” mutations of their immunoglobulin genes, rendering them nonfunctional—providing a fascinating clue as to why this B-cell neoplasm appears so different from all others.
- During normal B-cell development, naïve B lymphocytes (which have few or no mutations in their immunoglobulin genes) enter germinal centers where, upon exposure to antigen, they undergo high rates of mutation of their immunoglobulin gene variable regions. This process, termed somatic hypermutation, is a key process in generating a diverse antibody repertoire and serves to increase the likelihood that high-affinity antibody is produced against a foreign antigen. Only B cells that are successful in creating immunoglobulin with high affinity for the antigen presented are permitted to leave the germinal center to become either plasma cells or memory B cells.
- B cells that cannot make antibody undergo apoptosis and die.
- Cells are “rescued” from apoptosis only if they produce high-affinity antibody; this rescue appears to involve activation of the bcl-2 anti-apoptosis gene.
- Epstein-Barr virus subsequently has been found to latently infect the RS cells in the majority of cases of classic HD. Infection by EBV can cause up-regulation of the bcl-2 gene, thereby allowing the cell to avoid apoptosis

PATHOGENESIS





PATHOGENESIS



Clinical Presentation

- **Nontender lymph nodes enlargement (localised)**
  - **neck and supraclavicular area** **60-80%**
  - **mediastinal adenopathy** **50%**
  - **other (abdominal, extranodal disease)**
- **systemic symptoms (B symptoms)** **30%**
  - **fever**
  - **night sweats**
  - **unexplained weight loss (10% per 6 months)**
- **other symptoms**
  - **fatigue, weakness, pruritus**
  - **cough , chest pain, shortness of breath, vena cava syndrome**
  - **abdominal pain, bowel disturbances, ascites**
  - **bone pain**
  - **cachexia, anemia, splenomegaly, hepatomegaly, jundice Rarely**
  - **Pel-Ebstein fever** is a rarely seen condition noted in patients with Hodgkin's lymphoma in which the patient experiences fevers which cyclicly increase then decrease over an average period of one or two weeks. A cyclic fever may also be associated with other conditions, but it is not called "Pel-Ebstein fever" unless the fever is associated with Hodgkin's.

Symptoms related lymph nodes enlargement

I. Enlarged, painless, non-tender, superficial lymph nodes

II. Alcohol-induced pain Rarely, patients with Hodgkin's lymphoma complain of severe pain following alcohol ingestion. The pain typically occurs within a few minutes after the ingestion of even a small amount of alcohol. The mechanism is unknown.

Symptoms related to mass

1. Mediastinal mass:

   retrosternal chest pain, cough, or shortness of breath.

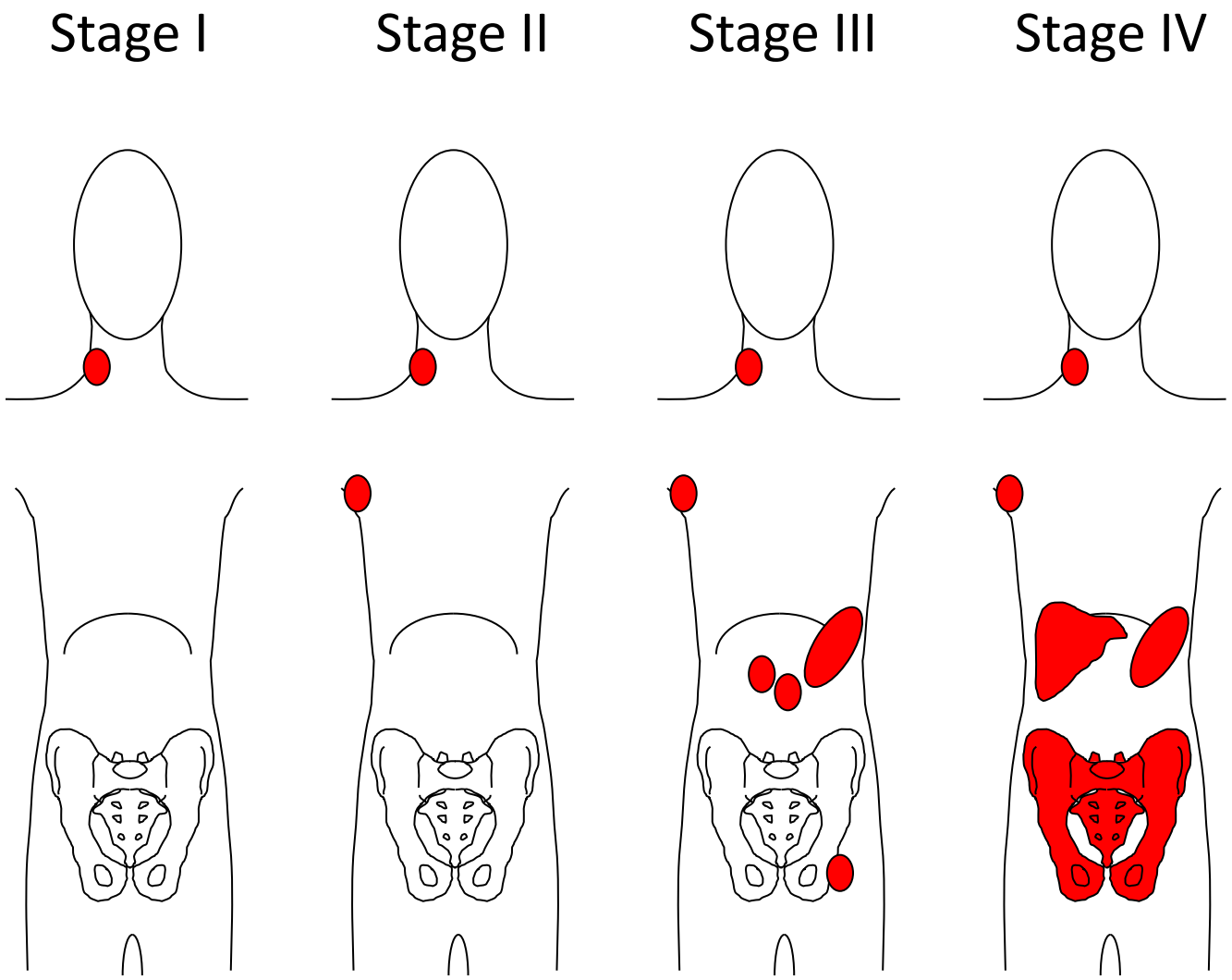
2. Retroperitoneal lymphadenopathy

   discomfort and pain in the paravertebral or loin regions, particularly in the supine position.

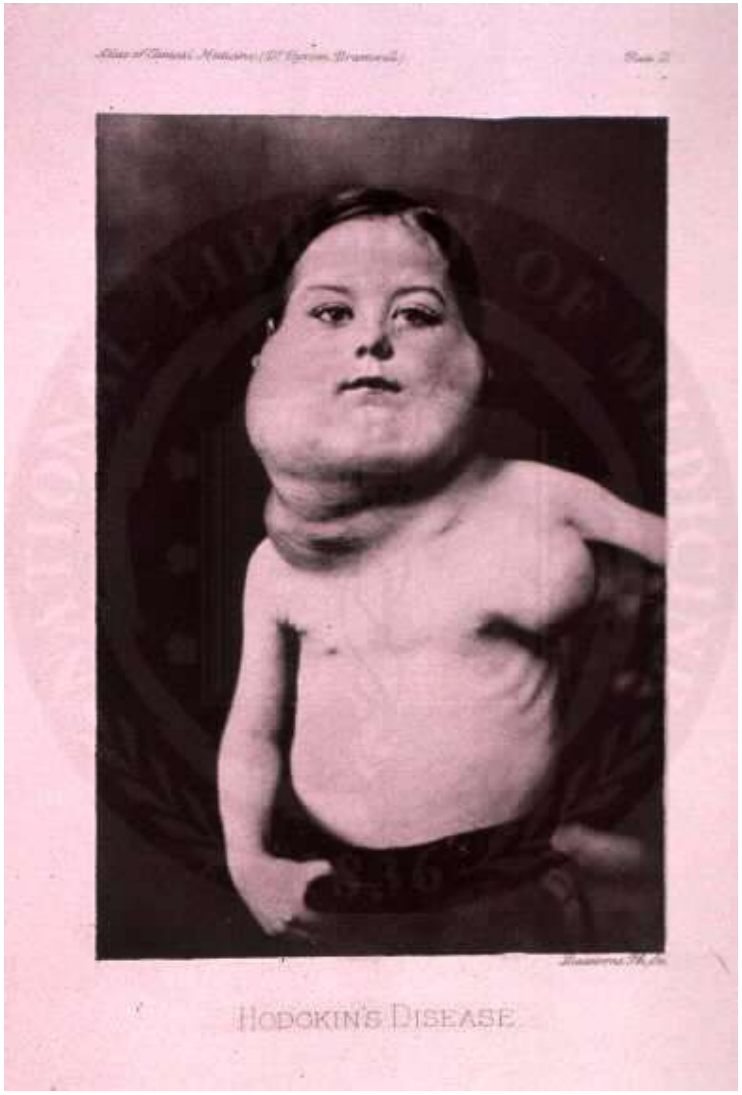
Cotswolds staging classification

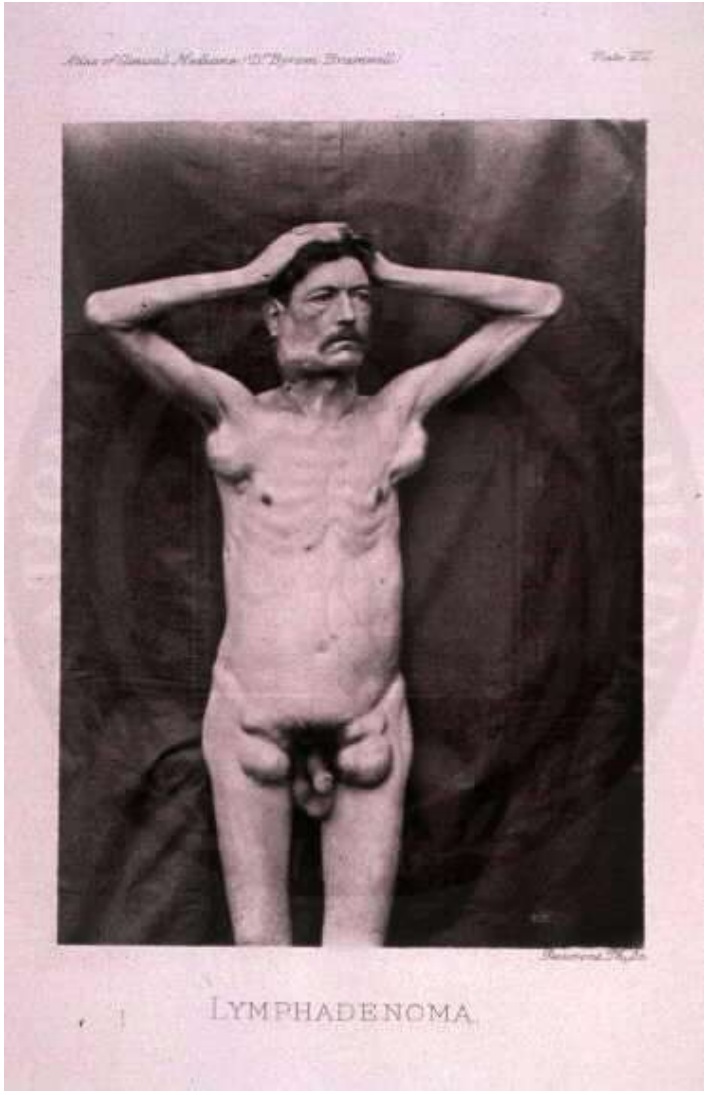
Stage	Description
Stage I	Involvement of a single lymph-node region or lymphoid structure (eg, spleen, thymus, Waldeyer's ring) or involvement of a single extralymphatic site
Stage II	Involvement of two or more lymph-node regions on the same side of the diaphragm (hilar nodes, when involved on both sides, constitute stage II disease); localised contiguous involvement of only one extranodal organ or site and lymph-node region(s) on the same side of the diaphragm (IIE). The number of anatomic regions involved should be indicated by a subscript (eg, II_3)
Stage III	Involvement of lymph-node regions on both sides of the diaphragm (III), which may also be accompanied by involvement of the spleen (III_S) or by localised contiguous involvement of only one extranodal organ site (IIIE) or both (IIISE)
III1	With or without involvement of splenic, hilar, celiac, or portal nodes
III2	With involvement of para-aortic, iliac, and mesenteric nodes
Stage IV	Diffuse or disseminated involvement of one or more extranodal organs or tissues, with or without associated lymph-node involvement
Designations applicable to any disease stage	
A	No symptoms
B	Fever (temperature >38°C), drenching night sweats, unexplained loss of more than 10% of body weight within the previous 6 months
X	Bulky disease (a widening of the mediastinum by more than one third of the presence of a nodal mass with a maximal dimension greater than 10 cm)
E	Involvement of a single extranodal site that is contiguous or proximal to the known nodal site

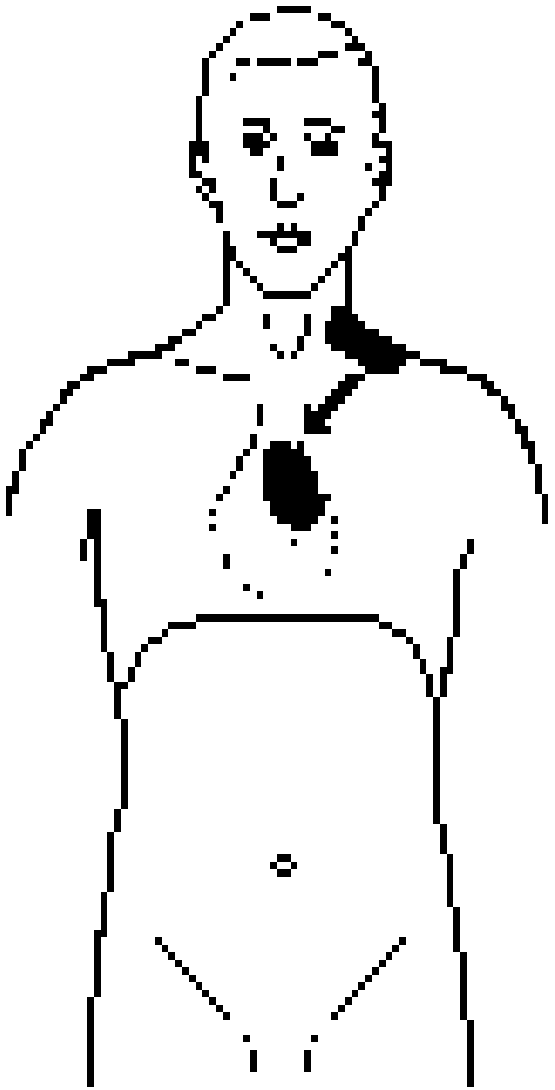
Ann Arbor classification (1971r)



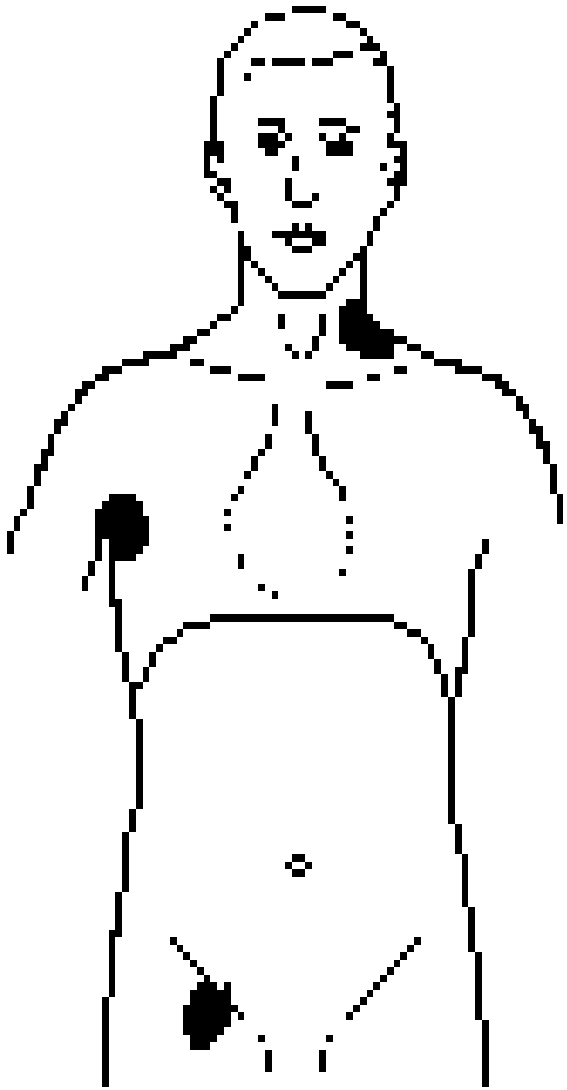
Classical Hodgkin Lymphoma





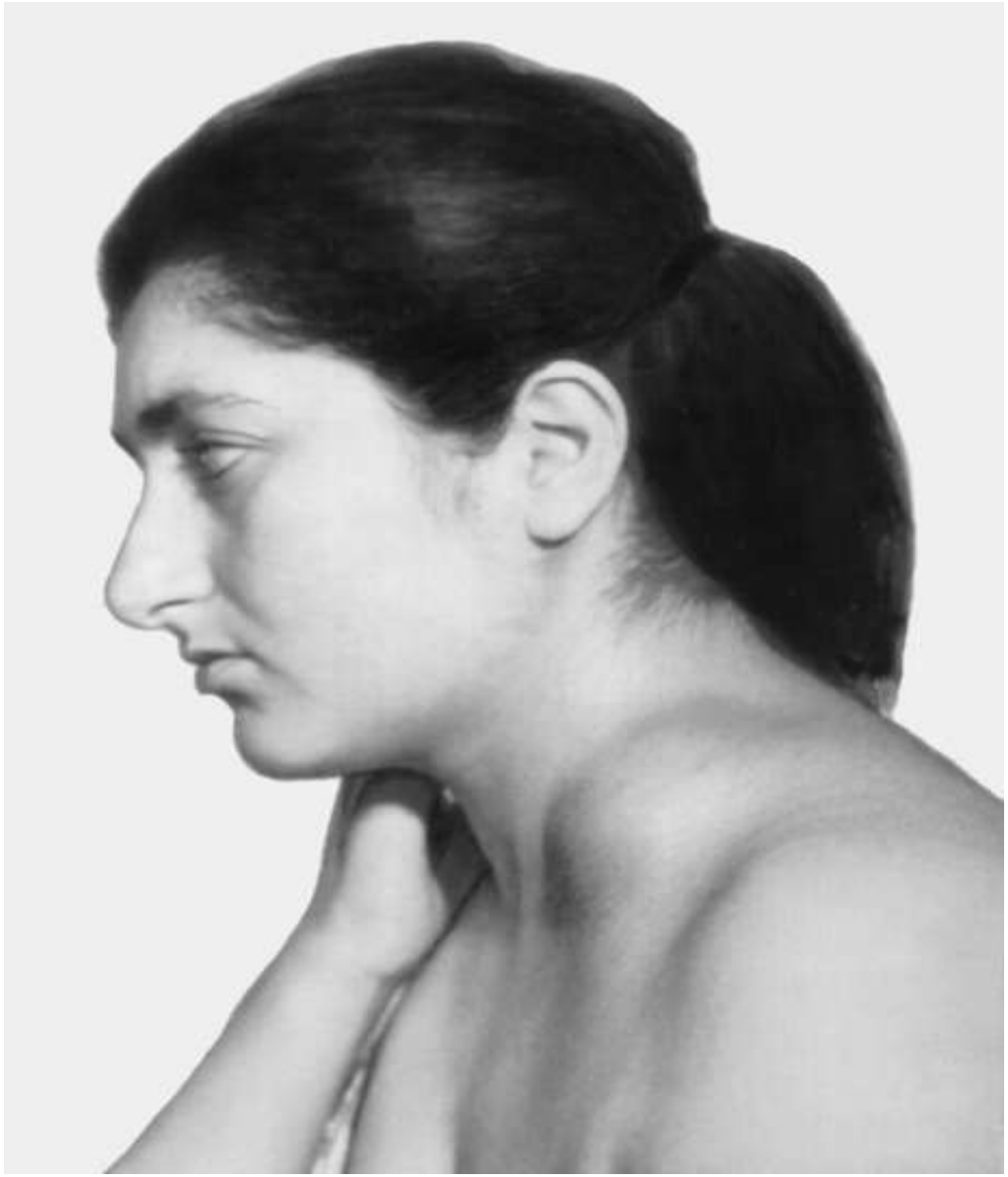


Hodgkin's Lymphoma

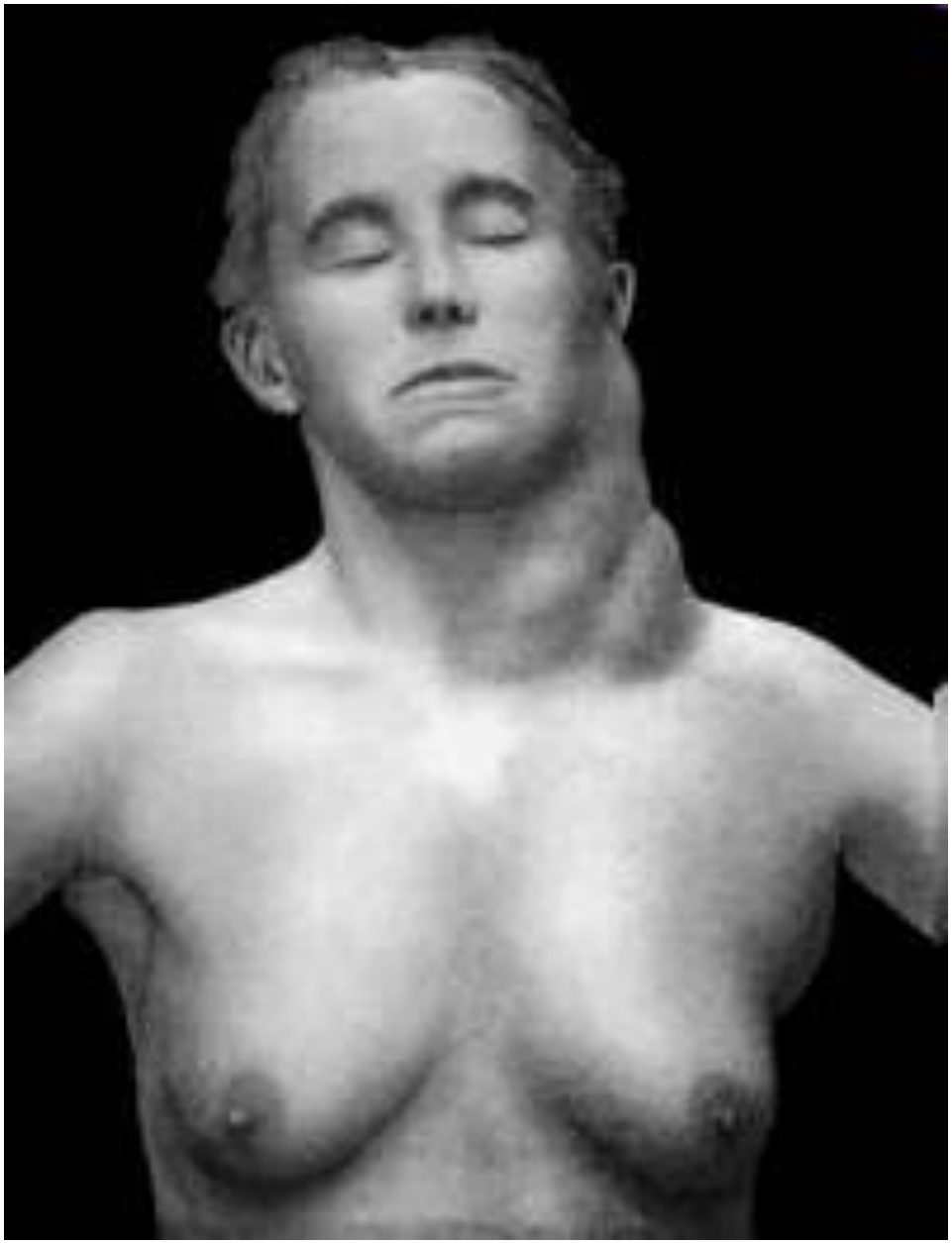


Non-Hodgkin's Lymphoma

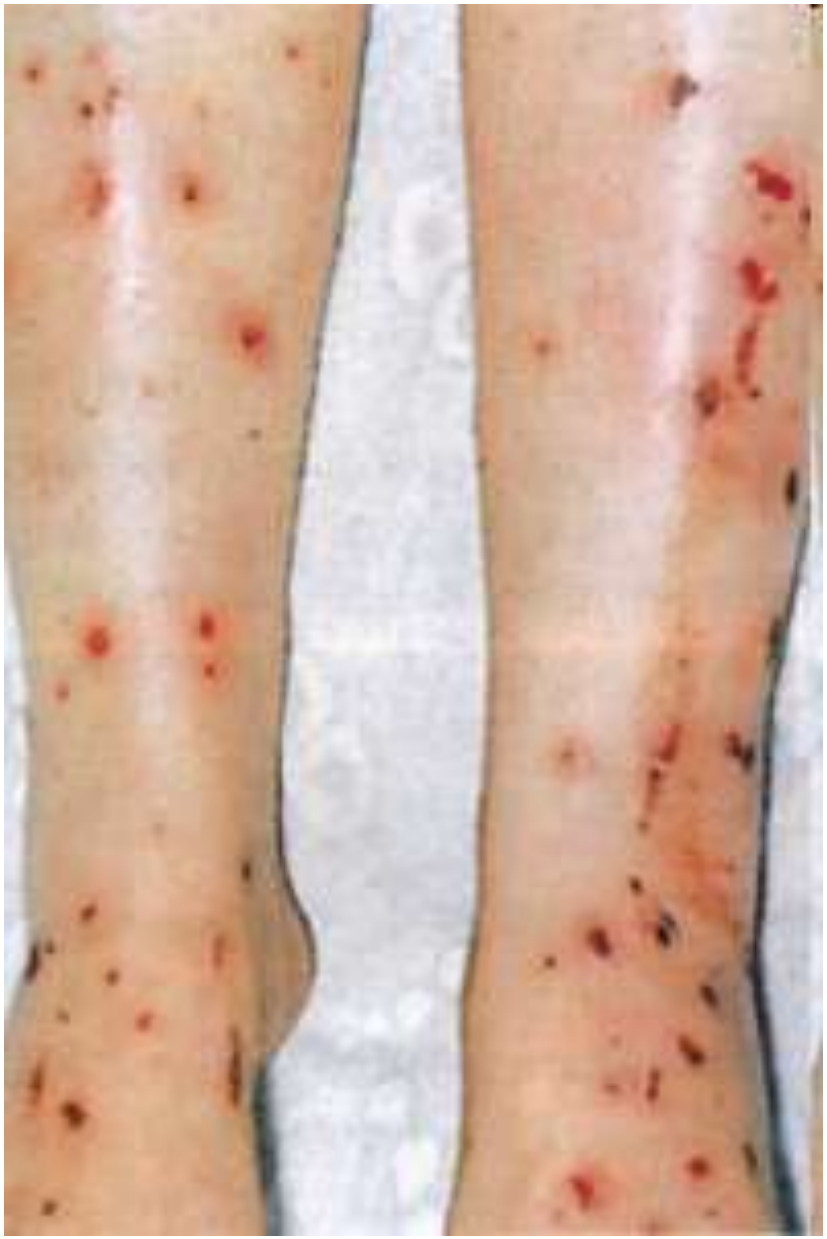
Hodgkin lymphoma generally involves contiguous nodes.
Non-Hodgkin lymphoma is noncontiguous.



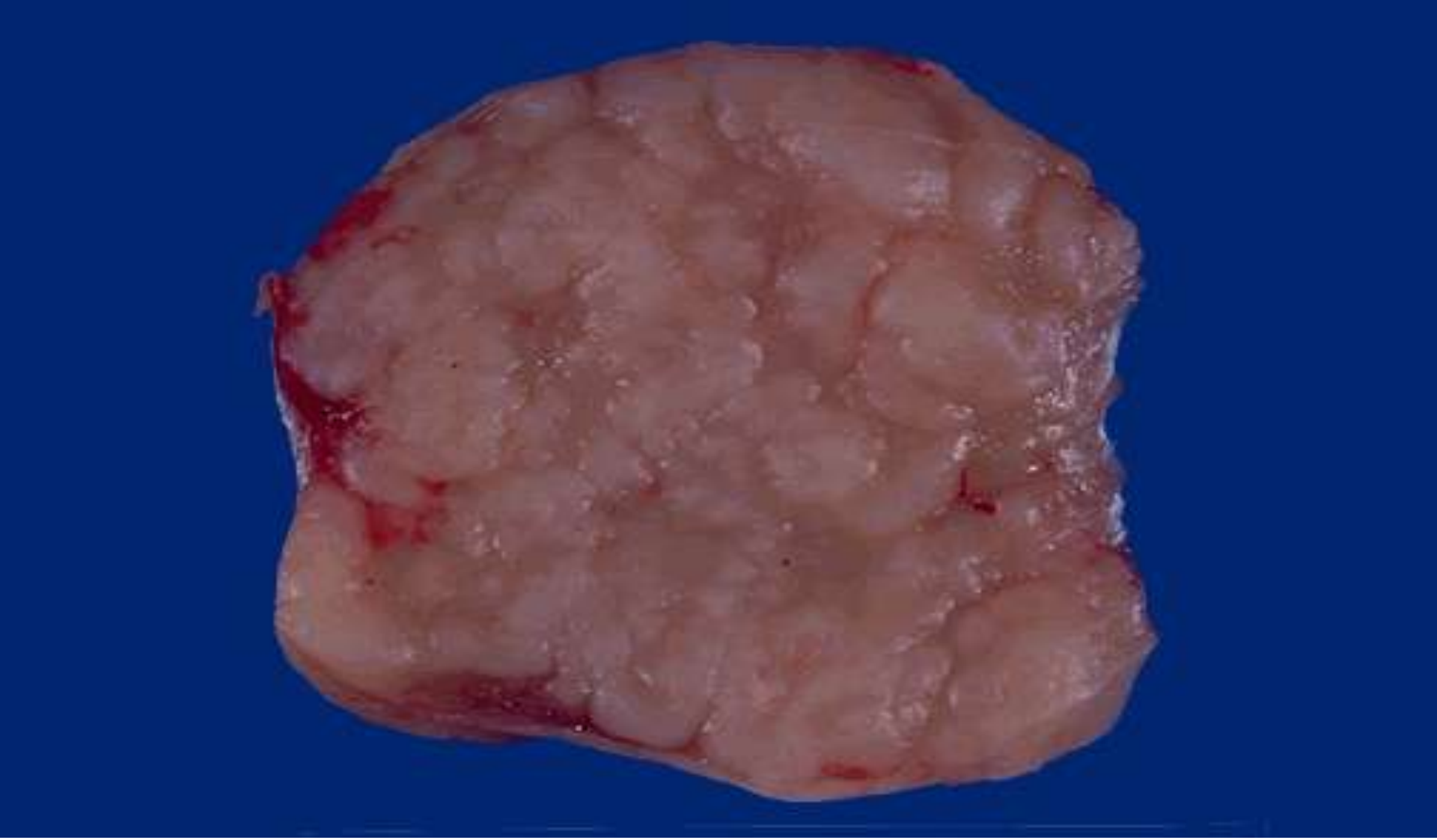
Enlarged lymph nodes in the supraclavicular region in HL patients.



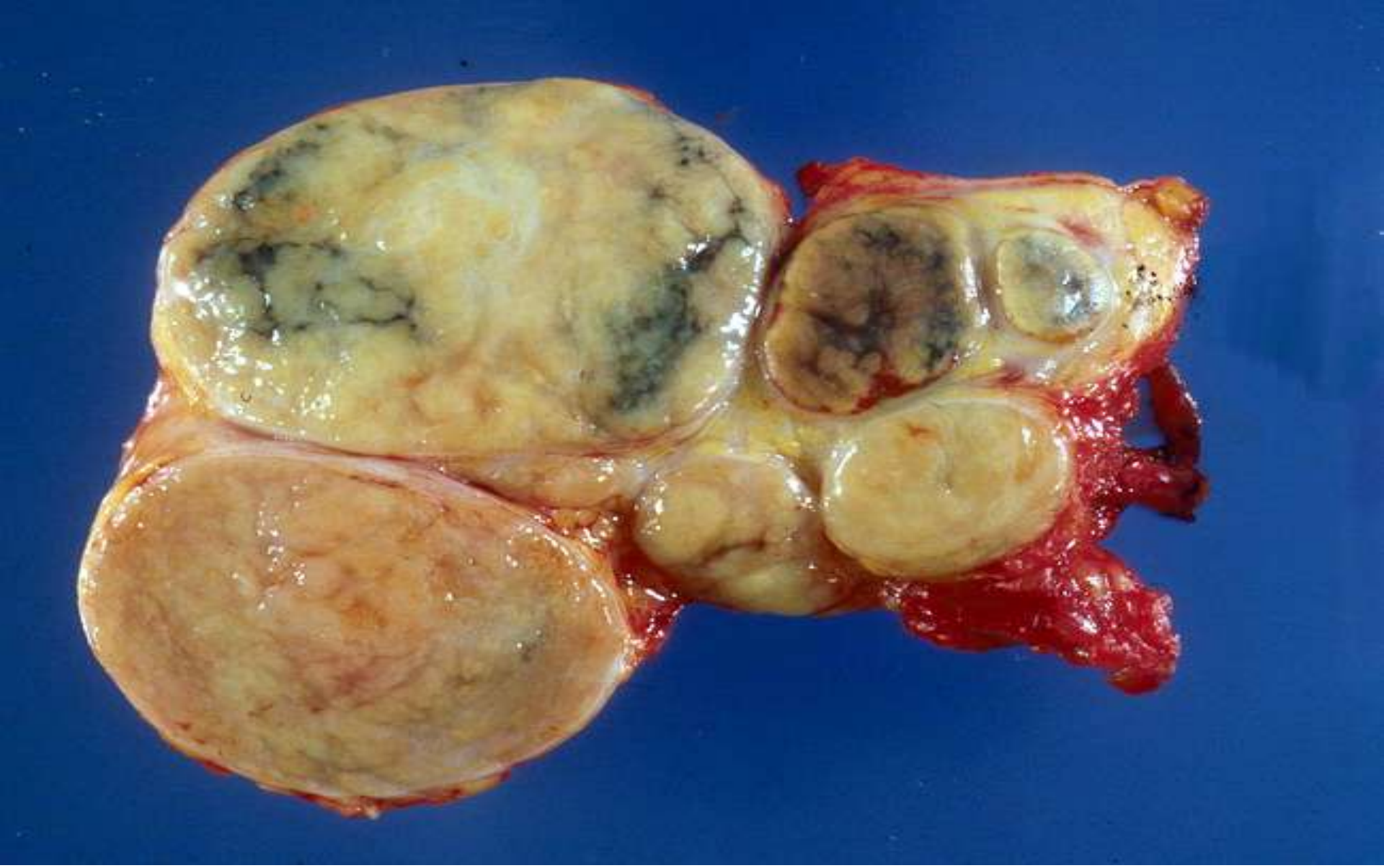
Cervical lymphadenopathy in HL



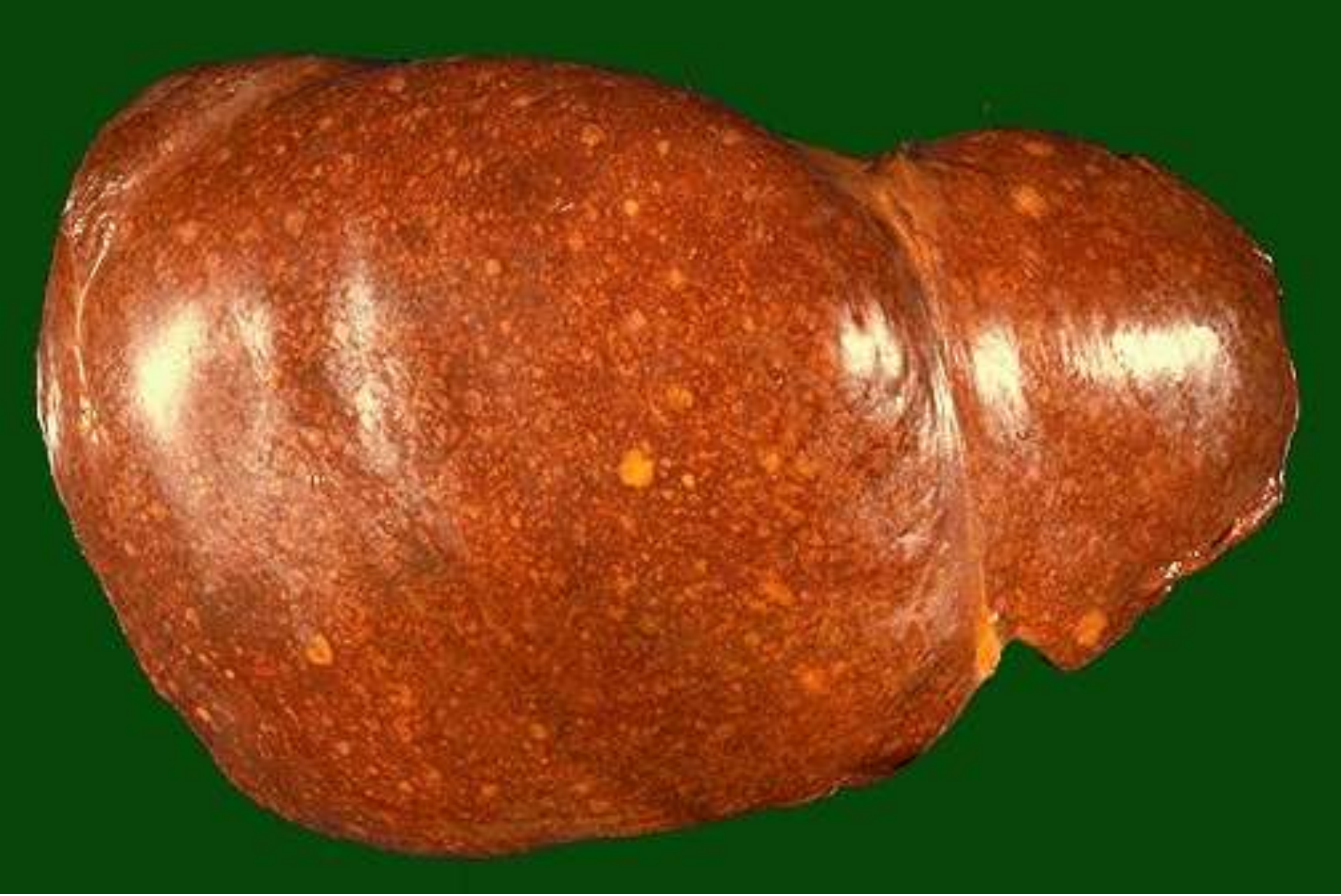
pruritus in HL



Here is a 5 cm lymph node (obviously from a patient with lymphadenopathy). The node should normally be soft and pink and less than 1 cm in size. This lymph node is involved with Hodgkin's disease. This gross appearance could pass for a non-Hodgkin's lymphoma as well.



Group of mediastinal lymph nodes. Note the anthracotic pigment in some lymph nodes. The specimen measured 12 cm. in greatest dimension.



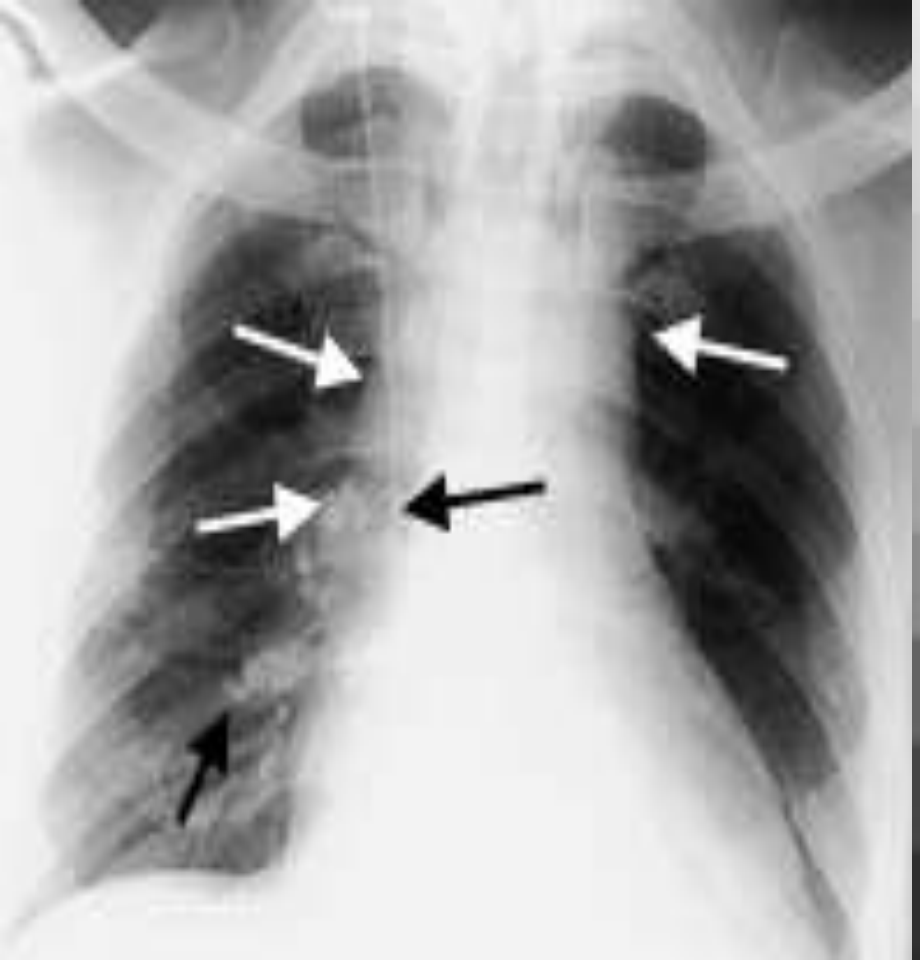
This is a liver that is involved with Hodgkin's disease.

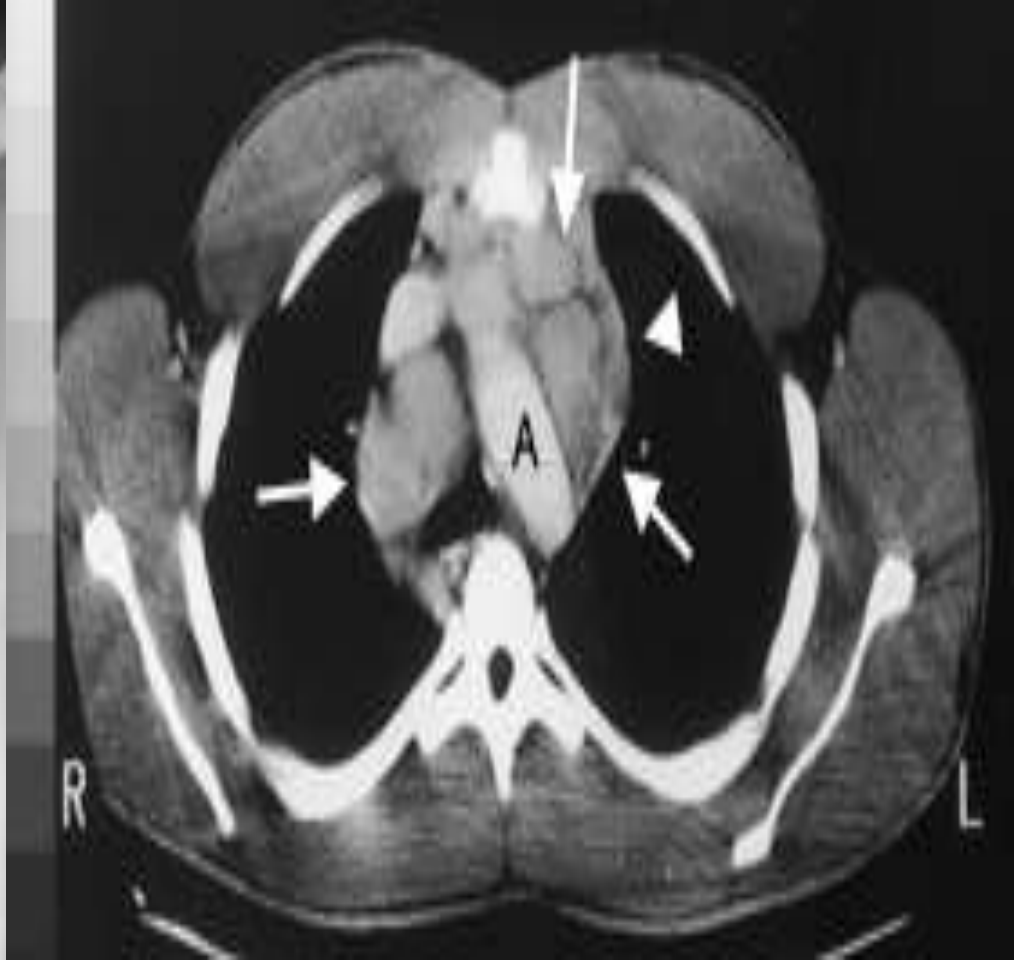
Staging evaluation for Hodgkin's Disease (1)

- **Essential**
  - **pathologic documentation by hemopathologist**
  - **physical examination**
  - **documentation of B symptoms**
  - **laboratory evaluation**
    - **complete blood count, ESR**
    - **liver function tests**
    - **renal function tests**
    - **lactate dehydrogenase**
  - **chest radiograph**
  - **ultrasonography**
  - **CT scan of chest, abdomen and pelvis**
  - **bone marrow aspiration / biopsy (bilateral)**

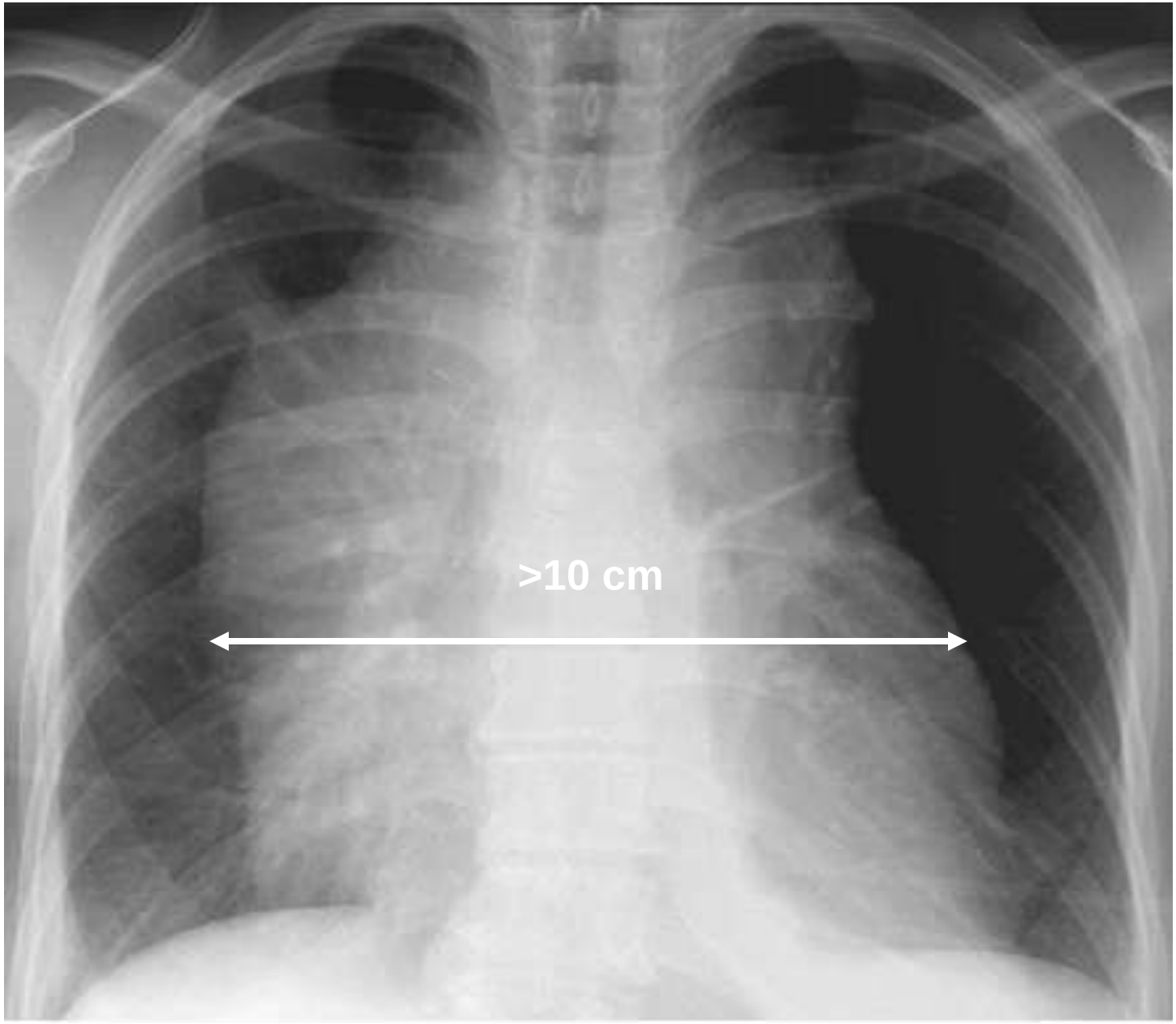
Staging evaluation for Hodgkin's Disease (2)

- **Essential under certain circumstances**
  - **liver biopsy**
  - **gallium scan**
  - **technetium bone scan**
  - **bone radiographs**
  - **MRI**
  - **bipedal lymphangiogram**
  - **staging laparotomy**
- **Useful but not essential tests**
  - **cell-surface marker phenotypic analysis**
  - **gene rearrangement analysis**

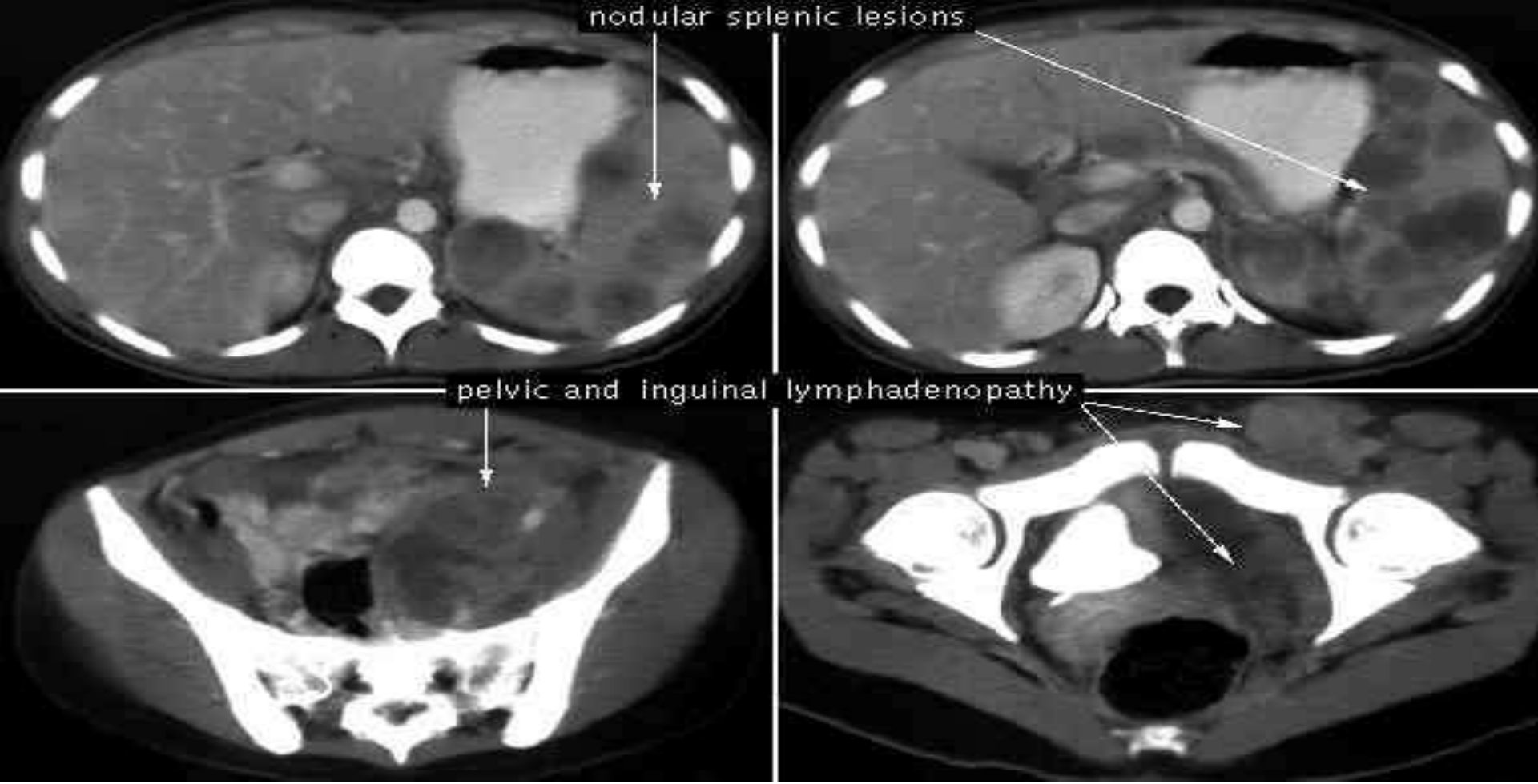




Hodgkin's disease. This contrast-enhanced computed tomographic scan of the patient in Figure 2 better delineates the extensive anterior mediastinal adenopathy *(large arrows)* from the thymus *(arrowhead)* and aorta *(A)*.

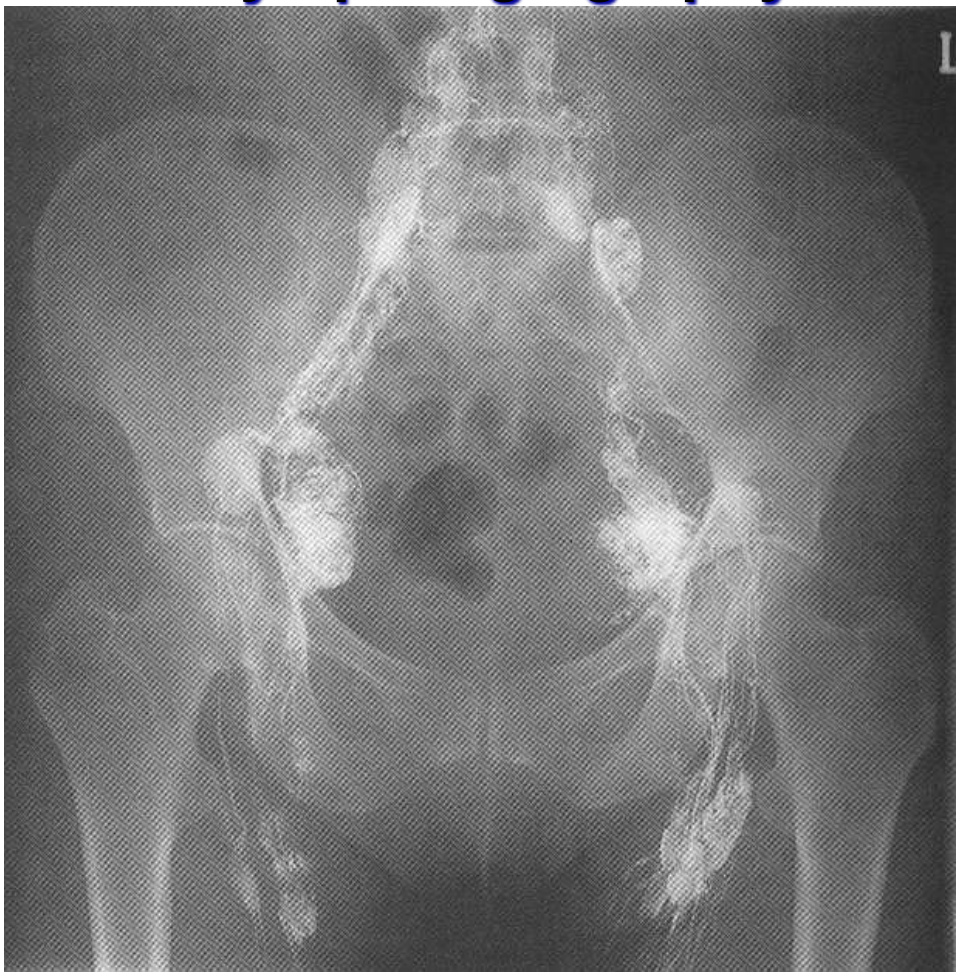


Bulky disease



This 23 y/o female with left inguinal adenopathy was referred for gallium scan. Abdominal and pelvic CT scans were subsequently performed. Selected images from the gallium scan demonstrate abnormal uptake in the left inguinal region and the left side of the pelvis. The CT scan demonstrates heterogenous masses in these regions consistent with lymphadenopathy. In addition, there are multiple low attenuation lesions in the spleen.

Lymphangiography



Abdominal lymphangiogram X-ray of a patient with Hodgkin's disease, showing the organization of lymph nodes in the pelvis and the back of the abdomen. A lymphangiogram is conducted by injecting a radio-opaque liquid dye into the lymph system through the feet. The fluid travels through the lymph system and remains visible by X-ray

Diagnosis

To diagnose Hodgkin lymphoma a histologic evaluation is always required, and an excisional lymph node biopsy is recommended for this purpose.

Comparison between two types

Classical Hodgkin lymphomas

About 19 out of 20 people with Hodgkin lymphoma.
Reed–Sternberg cell unique to this kind of Hodgkin lymphoma.

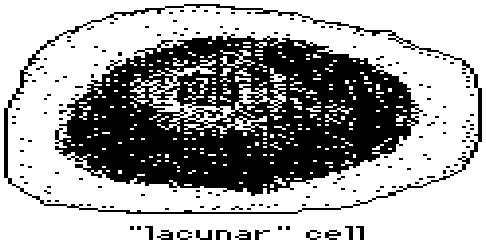
Nodular lymphocyte-predominant Hodgkin lymphoma

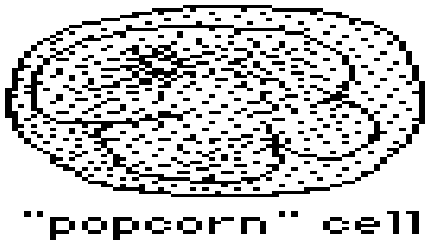
- Only 1 in 20 people with Hodgkin lymphoma. Typically affects people aged 30–50 and it is more common in men.
- So called a 'popcorn cell' is unique to this kind of Hodgkin lymphoma.
- It has a very good prognosis and over 90% of people go into remission after an excision biopsy and radiotherapy.
- NLPHL can relapse later on and require another course of treatment and this can occur after as long as 10 years after treatment has finished. In some cases, the relapse takes the form of a non-Hodgkin lymphoma (this process of a lymphoma coming back in a different form is known as 'transformation').

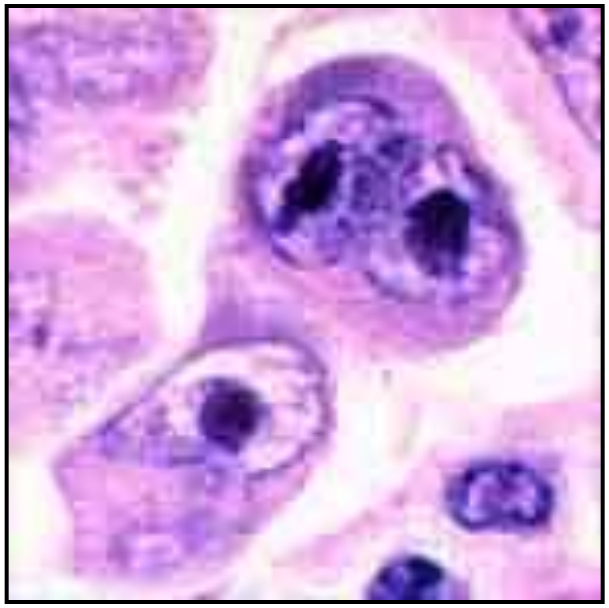
Nodular LPHL and Classical HL Morphologic and Immunophenotypic Features.

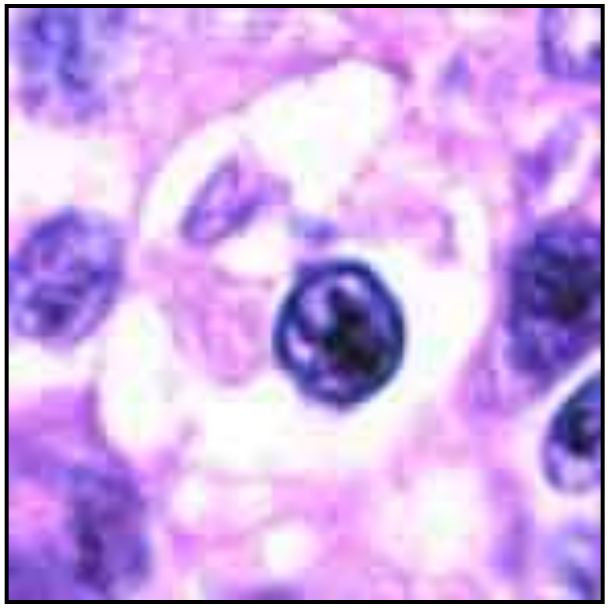
Characteristic	CHL	NLPHL
Pattern	Diffuse, Interfollicular, Nodular	Nodular, at least in part
Tumour Cells	R-S Mononuclear or Lacunar	Lymphomcytic/Histiocytic or Popcorn
Background	Lymphocytes ,histiocytes, eosinophils, plasma.	Lymphocytic, Histiocytic.
Fibrosis	Common	Rare
CD15	+ (85%)	(-)
CD30	+ (> 95%)	(-)
CD20	(- / +)	(+)
CD45	(-)	(+)
Epithelial Membrane Antigen	(-)	(+)
Nuclear BCL 6 (PTN in R-S cells)	(-)	(+)
EBV (in R-S) cells	+ (50%)	(-)
Background Lymphocytes	T -cells > B-cells	B-cells > T-cells
CD57 T-cells	(-)	(+)
Ig genes	Rearranged, Clonal, Mutated, “Crippled”	Rearranged, Clonal, Mutated, Ongoing

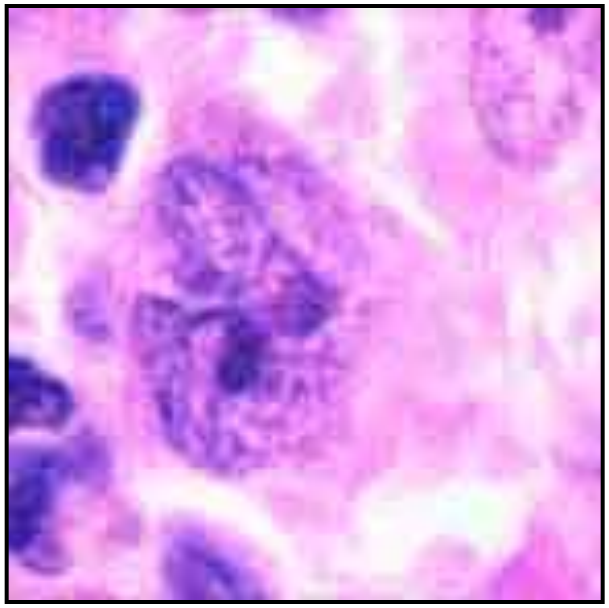
Types of cells in HL











classic RS cell

(mixed cellularity)

lacunar cell

(nodular sclerosis)

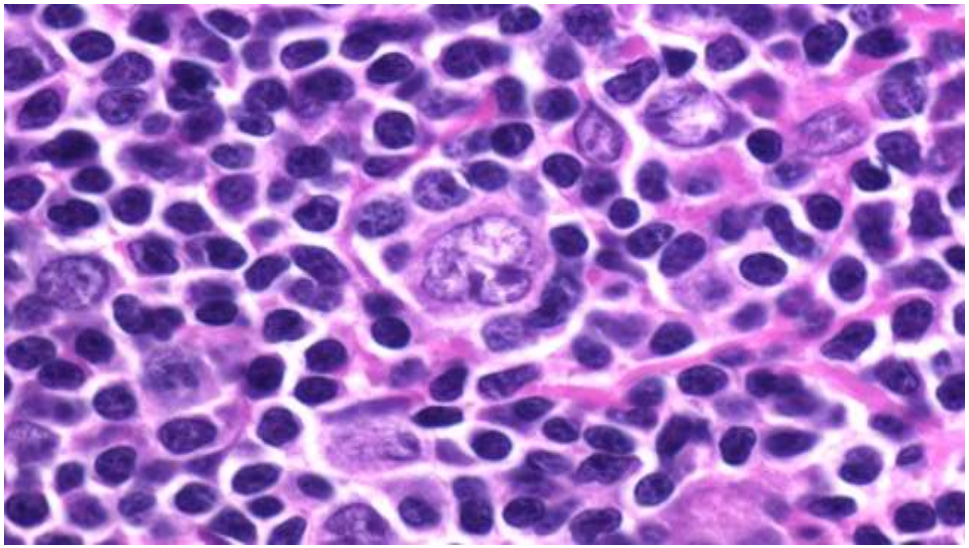
popcorn cell

(lymphocyte predominance)

Nodular lymphocyte-predominant Hodgkin lymphoma

Nodular lymphocyte-predominant Hodgkin lymphoma

- These cells have also been referred to as “popcorn” cells, but the WHO classification of 2008 recommended the use of the term “LP cell.”
- In comparison with classical HRS cells, the nucleoli of the LP cells are smaller, multiple, and basophilic.



A close-up of L&H cell (popcorn cell) in a case of Nodular Lymphocyte-predominant Hodgkin Lymphoma. It has a large, multilobed, folded nucleus and is surrounded by small lymphocytes. L&H cells are of B-cell lineage and express pan-B-cell markers.

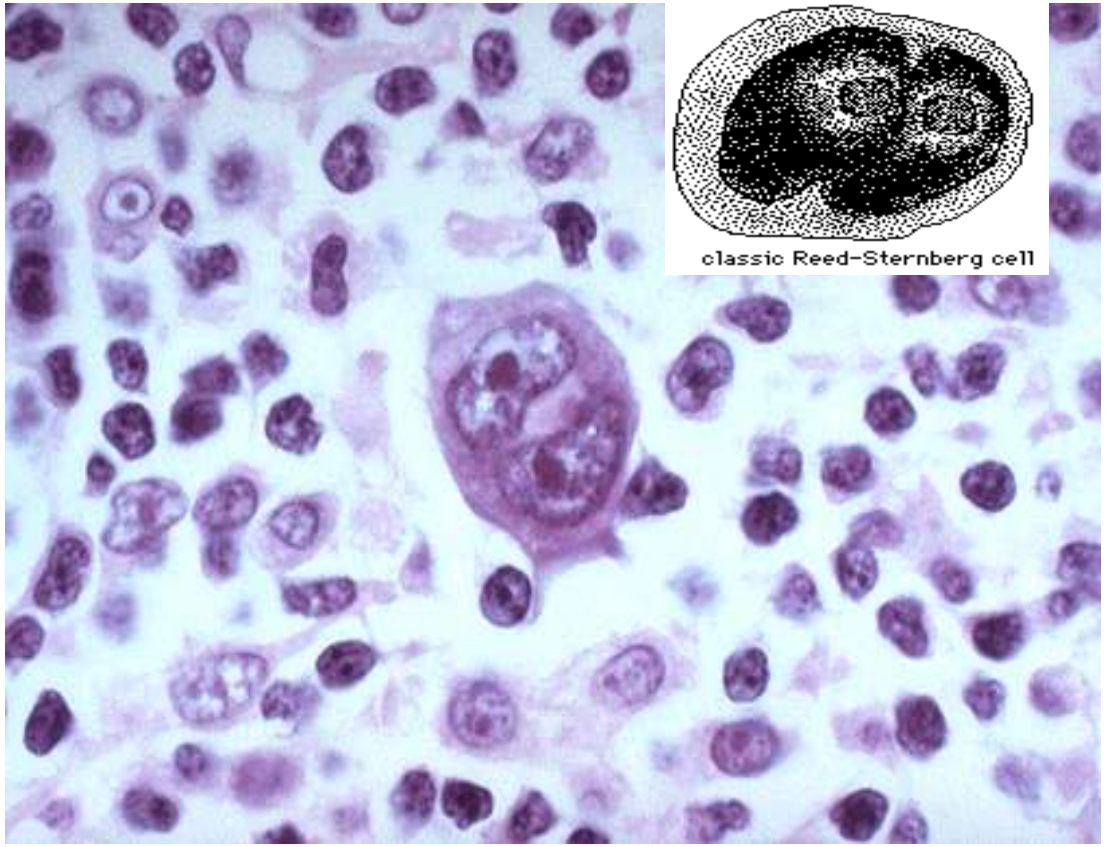
http://www.webpathology.com/image.asp?case=388&n=16

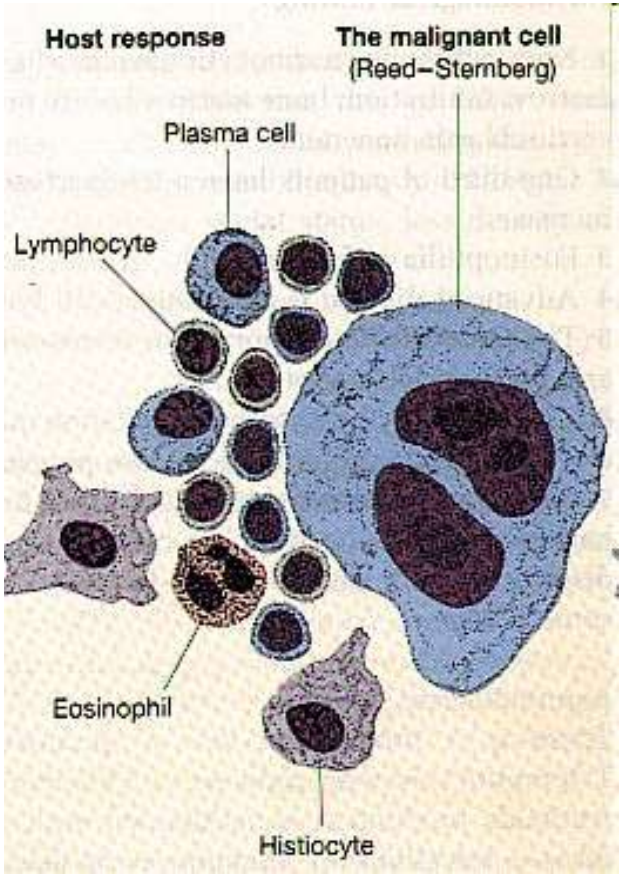
Classical Hodgkin lymphomas

Reed-Sternberg cell

- Diagnostic RS-cells are large cells (20-50 Mm) in diameter or more with abundant weakly acidophilic or amphophilic cytoplasm, which may appear homogenous or granular and lacks a pale zone in the Golgi area , The nucleus is bilobed or polylobed .
- The nuclear membrane is thick and sharply defined. The nuclear pattern is usually vesicular but with some coarse chromatin clumps scattered throughout .There is very large ,variously shaped, but usually rounded, highly acidophilic central inclusion like nucleolus surrounded by a clear halo. When the two lobes face each other (mirror image) owl eye appearance results.
- Cells with this set of features but lacking nuclear lobation are referred to as mononuclear variant of RS cells or H-cells (Hodgkin's cells).

Reed-Sternberg cell

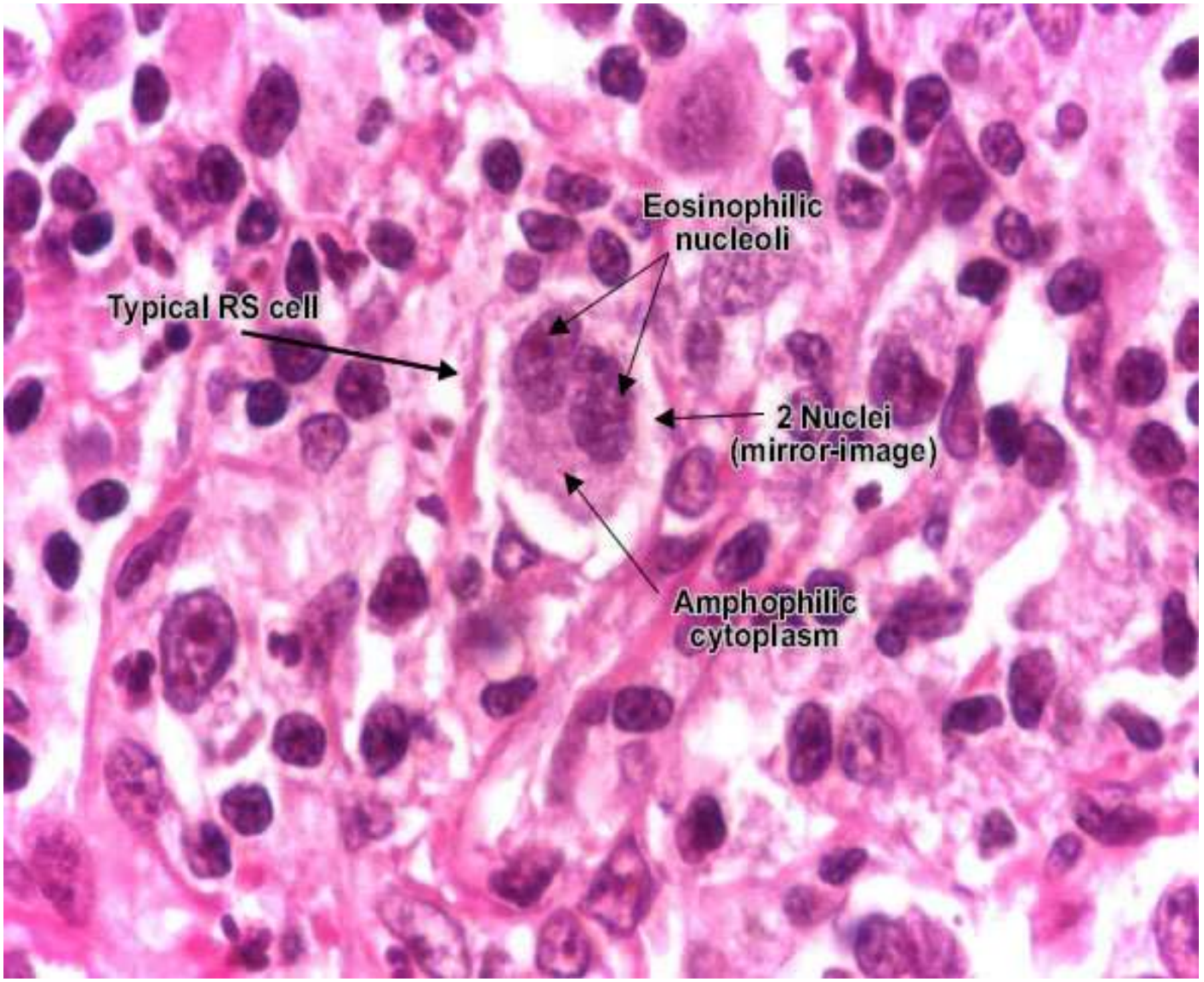


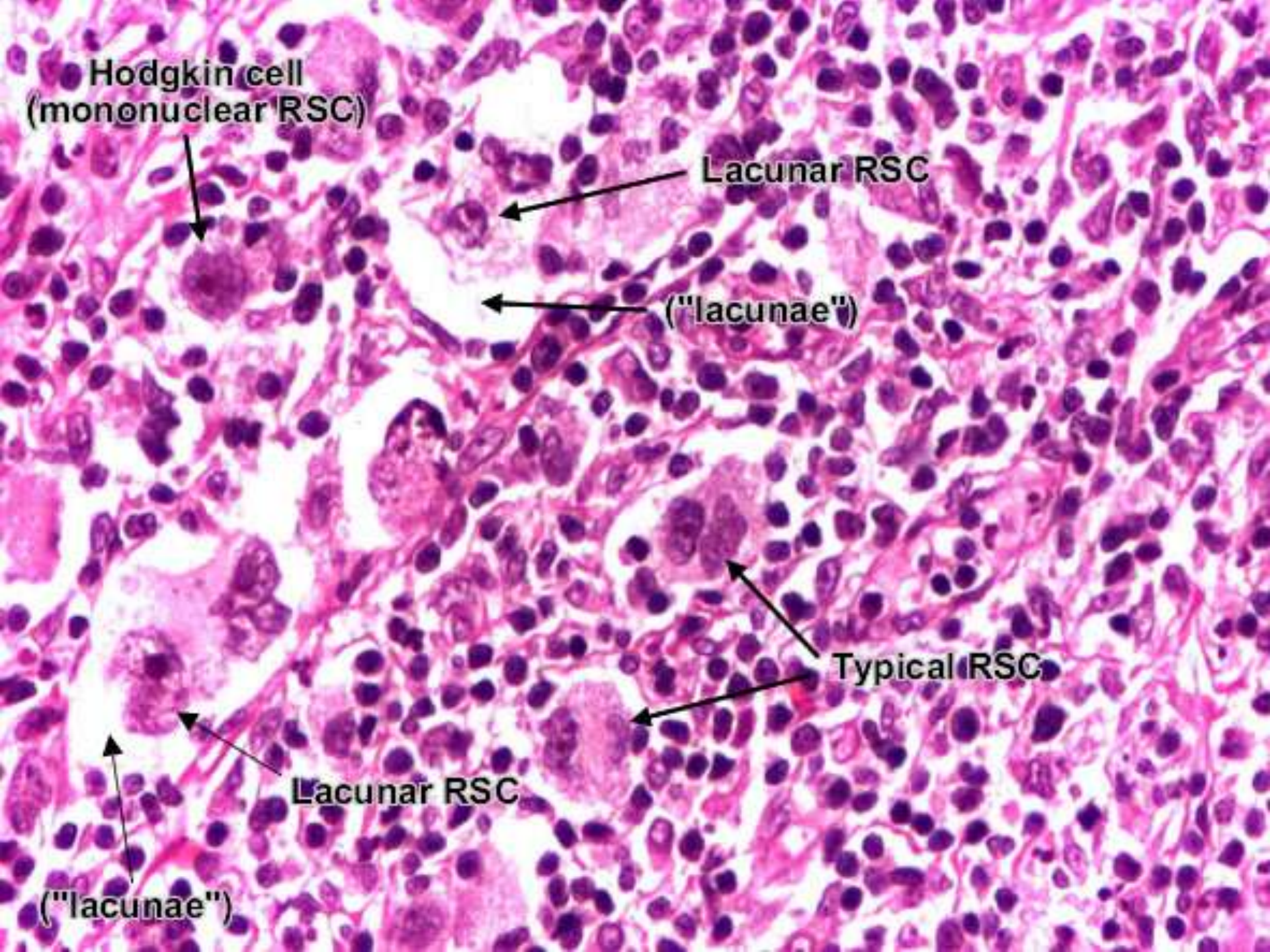


Malignant REED-STERNBERG (RS) Cell: Bi-nucleate cell with a prominent nucleolus. Derived from B cell, at an early stage of differentiation.

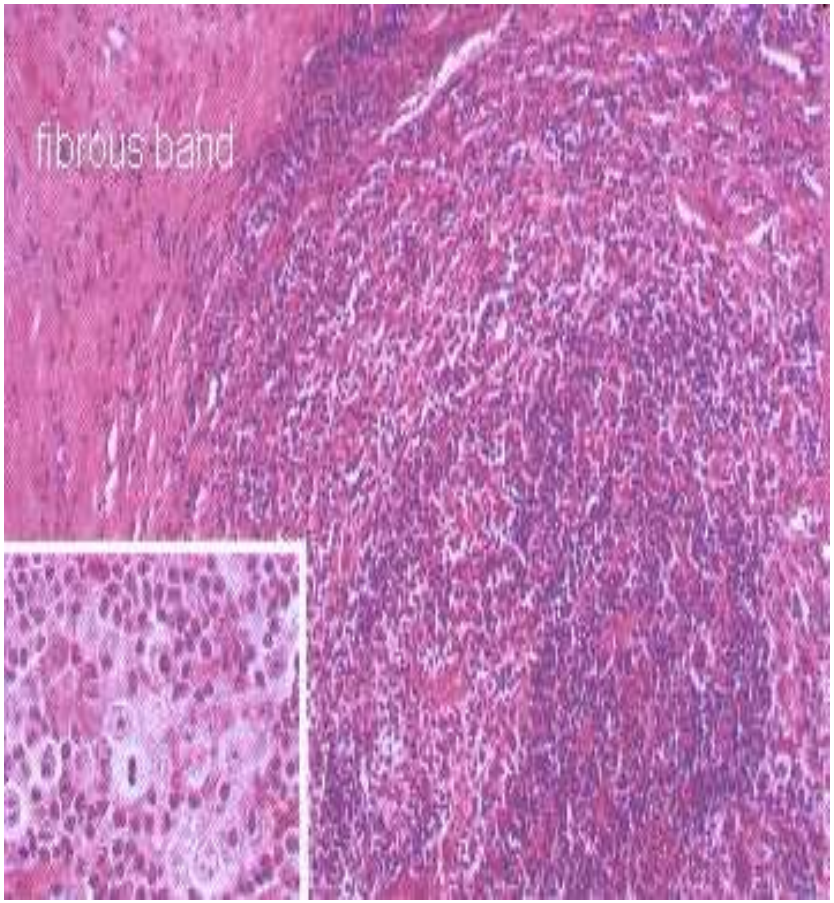
pical membrane and paranuclear dot-like staining of a

Classical RS cells


Eosinophilic nucleoli
Typical RS cell
2 Nuclei (mirror-image)
Amphophilic cytoplasm


Hodgkin cell
(mononuclear RSC)
Lacunar RSC
("lacunae")
Typical RSC
Lacunar RSC
("lacunae")

Nodular sclerosis



- 70% of all CHL - is the most frequent subtype
- In most cases, NSHL has at least a partially nodular pattern, with fibrosious bands separating the nodules.
- The disease affects primarily young adults and is less often observed in the elderly.
- Female predominance.
- In 80% of patients with NSCHL the mediastinum is involved and 50% of patients with NSCHL present with bulky disease.

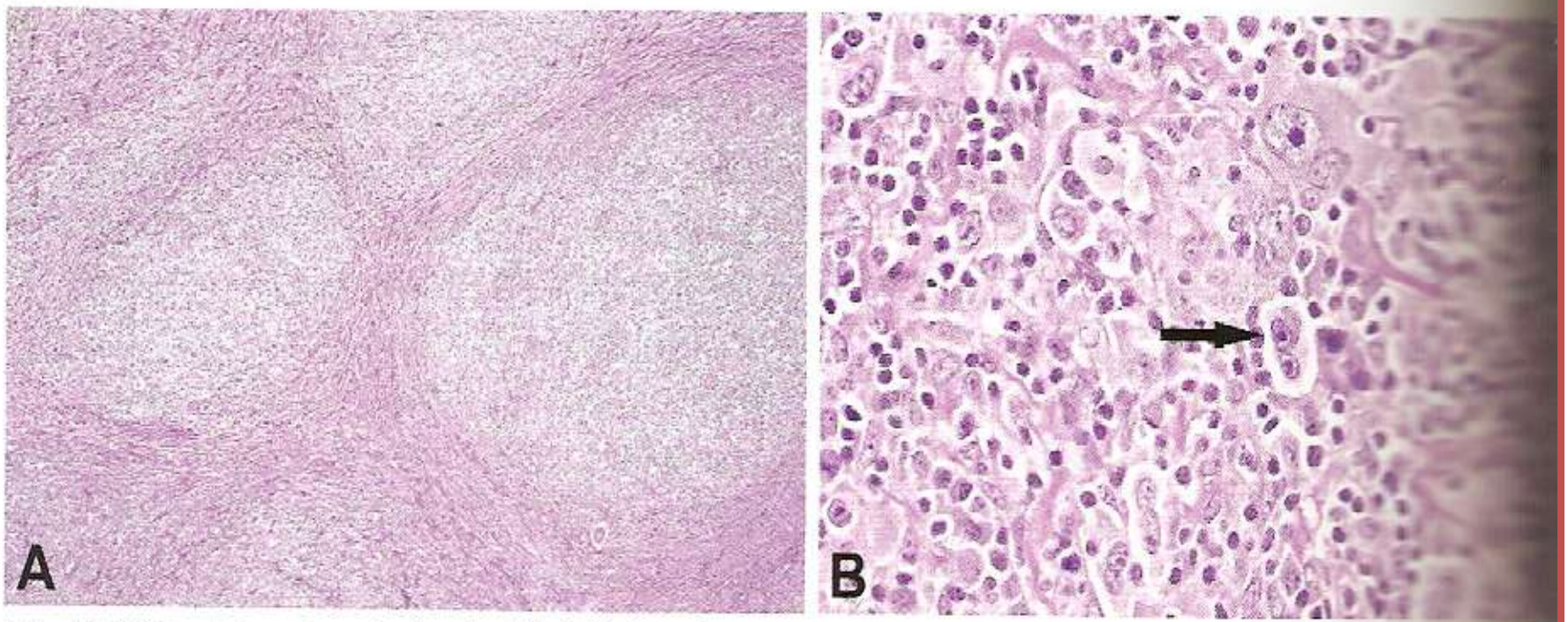
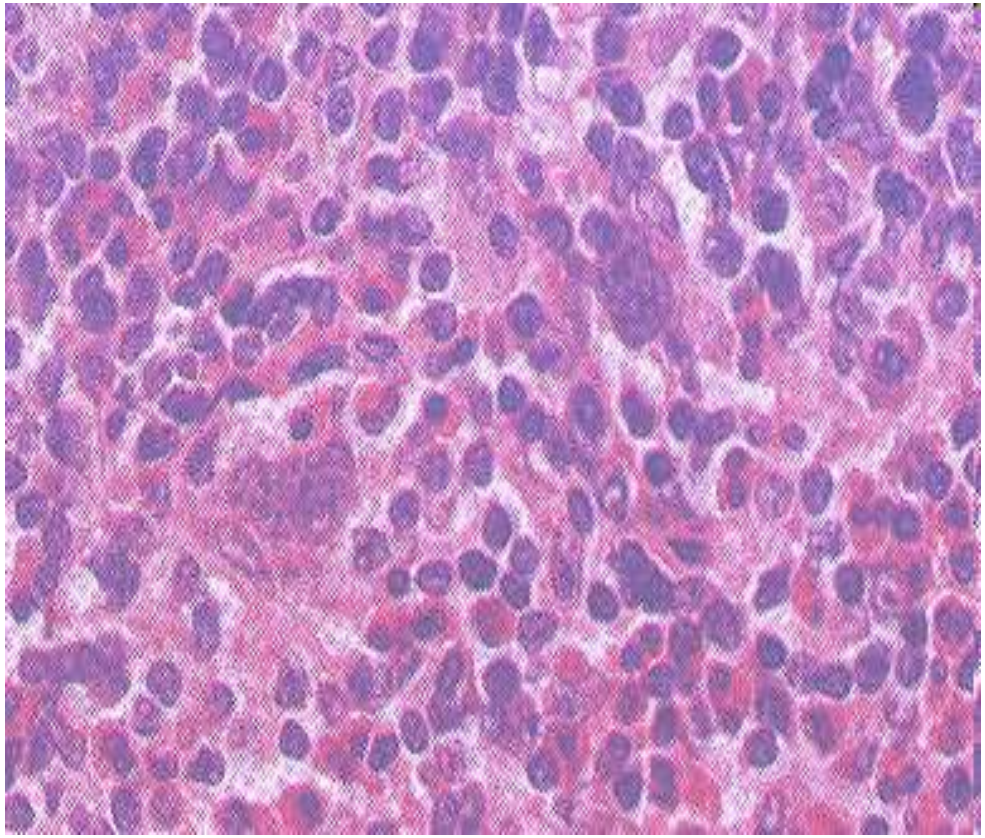
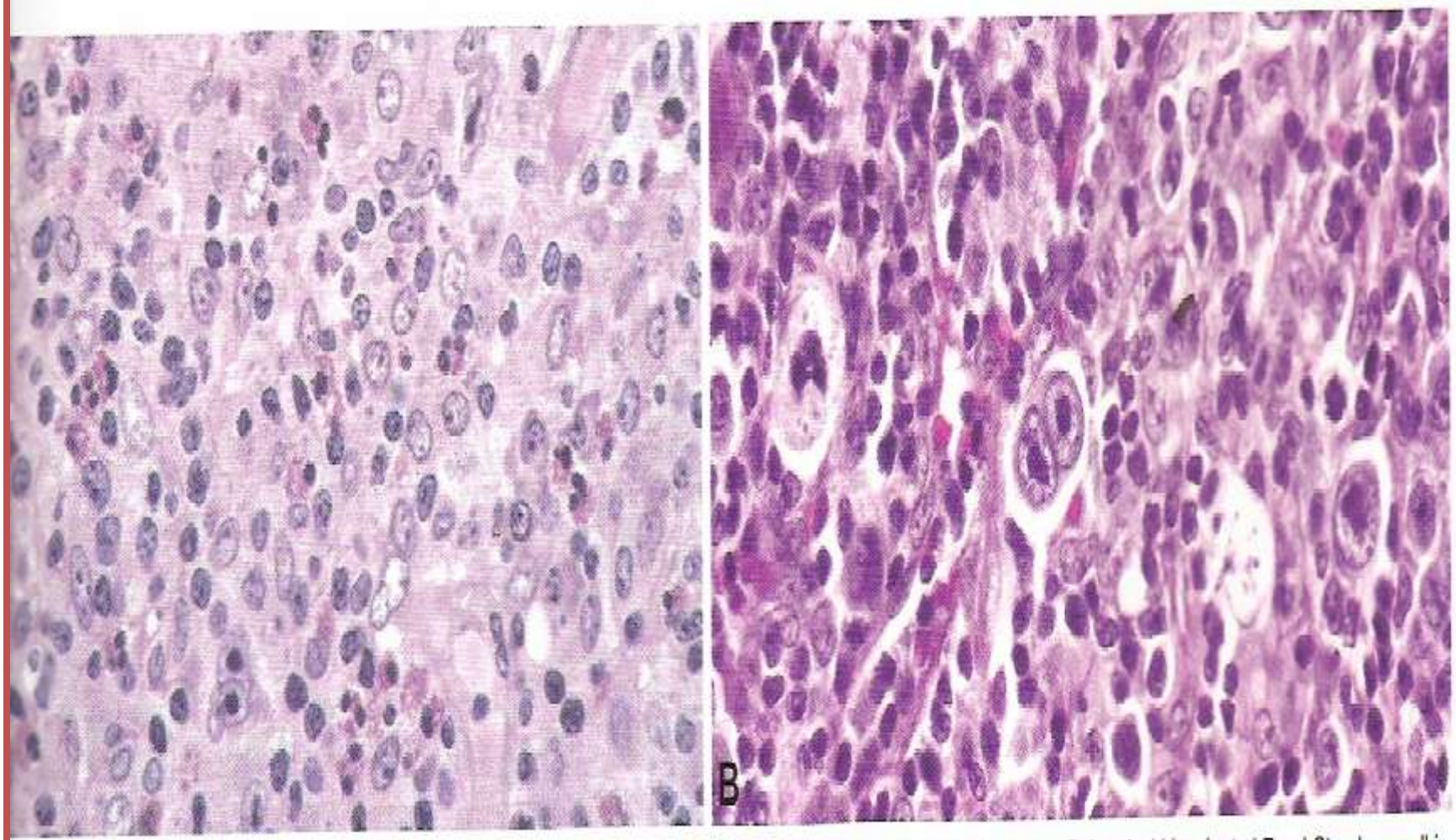


Fig. 12.16 Nodular sclerosis classical Hodgkin lymphoma. **A** Fibrous collagen bands divide the lymph node into nodules. **B** Several lacunar cells (arrowed) are present.

Mixed cellularity Hodgkin's disease

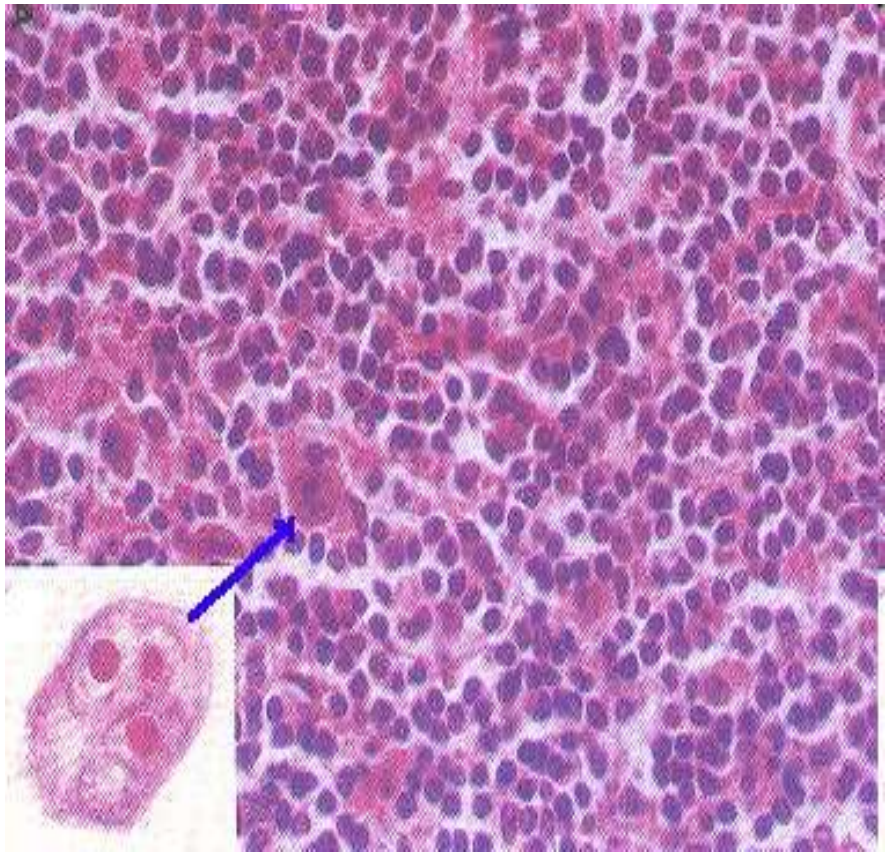


- The appearance is usually diffuse or vaguely nodular, without bands forming sclerosis.
- The overall prognosis is also worse than in LP or NS HD but varies with stage, and the disease can be cured in many patients.
- At low power, the involved tissue appears diffusely effaced by a mixed cellular infiltrate consisting of scattered diagnostic RS cells and varying proportions of mature small lymphocytes, large lymphocytes, histiocytes, eosinophils, and plasma cells



2.18 Mixed cellularity subtype of classical Hodgkin lymphoma. **A** The mixed cellular infiltrate does not contain fibrotic bands. **B** A typical binucleated Reed-Sternberg cell in ed cellular infiltrate with lymphocytes, macrophages and eosinophils is visible.

Lymphocyte Rich



- Some cases of the CHL with RS-cells of the classical type or lacunar type may have a background infiltrate that consist predominantly of lymphocytes, with rare or no eosinophils, the term lymphocyte rich CHL was proposed.
- The frequency of <10%
- It is more common in young men
- Usually found in stage I and progresses slowly
- The **prognosis** is very good

Lymphocyte depleted

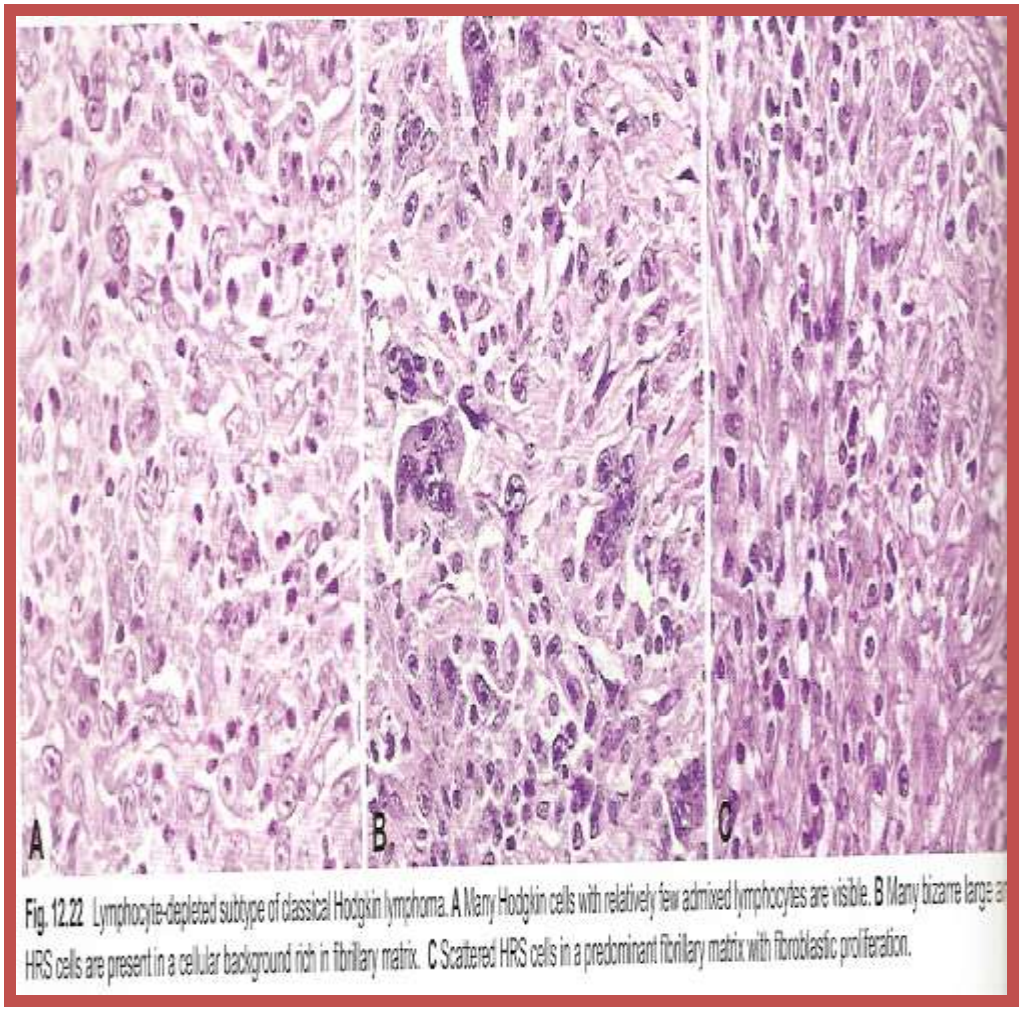


Fig. 12.22 Lymphocyte-depleted subtype of classical Hodgkin lymphoma. **A** Many Hodgkin cells with relatively few admixed lymphocytes are visible. **B** Many bizarre large a HRS cells are present in a cellular background rich in fibrillary matrix. **C** Scattered HRS cells in a predominant fibrillary matrix with fibroblastic proliferation.

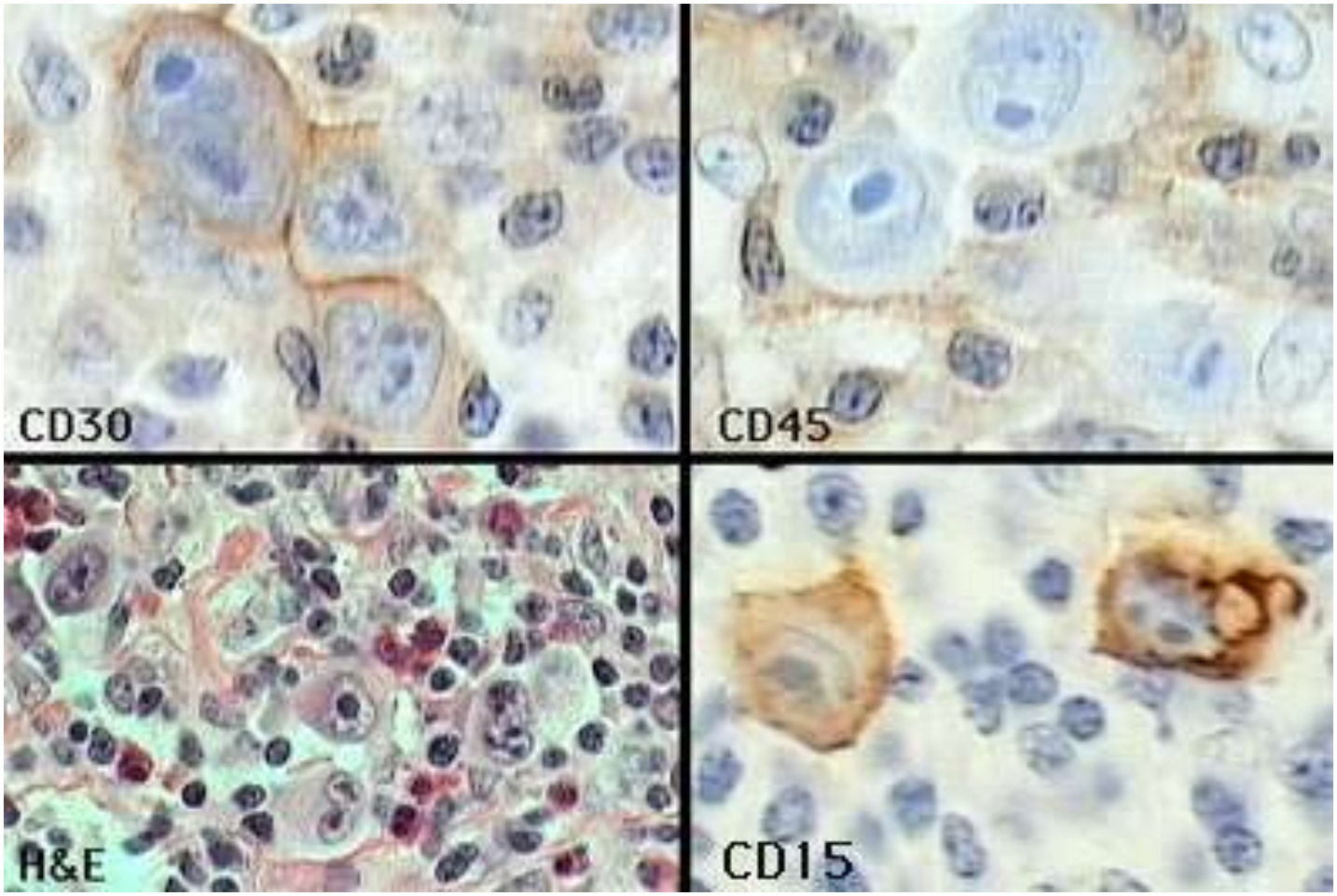
- Is the least common subtype of CHL
- The pattern in LDHL is diffuse and often appears hypocellular ,due to the presence of fibrosis , necrosis, and a paucity of inflammatory cells.
- Large number of classical RS-cells are present with a bizarre pleomorphic sarcomatous variants.
- Approximately 70% of patients present at an advanced stage and most (80%) have B symptoms.

IMMUNOHISTOCHEMISTRY OF HODGKIN'S LYMPHOMA

- The diagnosis of Hodgkin's lymphoma is primarily based on the recognition of the typical tumor cells, either HRS cells or LP cells, in the appropriate environment.
- In addition immunophenotypic and molecular markers help to classify the disease into the various tumor subtypes.
- In nearly all cases of CHL, HRS cells are positive for CD30. In addition, the majority of HRS cells (85%) also express CD15
- LP cells are usually negative for both CD15 and CD30. The B-cell markers CD20 and CD79a are positive in nearly all cases of NLPHL.

	LP Cells NLPHL	HRS Cells CHL
Nonlineage antigens		
CD45	+	–
CD30	–	+
CD15	–	+/–
B cell-associated antigens		
CD20	+	–/+
CD79a	+	–/+
J chain	+/–	–
IgD	+/–	–
B cell-related transcription factors		
BOB.1	+	–/+
OCT 2	+	–/+
PU.1	+	–
PAX5	+	+ (weak)
EBV detection		
LMP-1	–	+/–*
EBER	–	+/–*

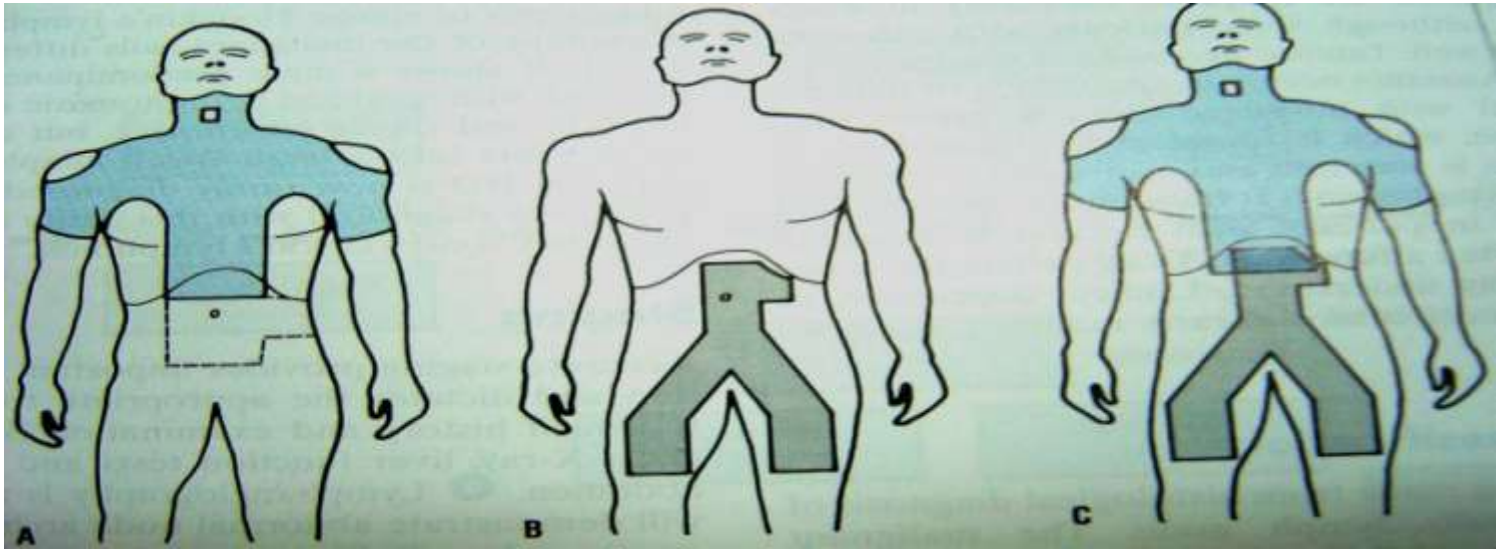
Reed-Sternberg cells and most Hodgkin variants express the monoclonal antigens

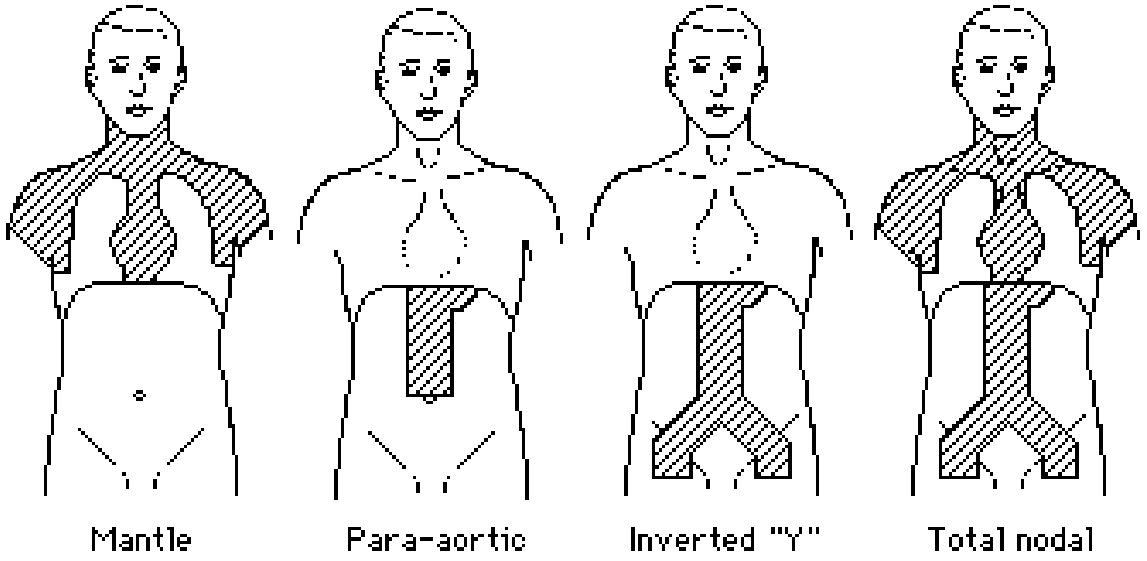


Treatment of Hodgkin Disesae

With appropriate treatment about 85% of patients with Hodgkin disease are curable

- **I A,B: radiation therapy**
- **II A : combination chemotherapy** (ABVD Adriamycin, Bleomycin, Vinblastine and Dacarbazine) **+ radiotherapy**
- **IIB IIIA,B IVA,B : combination chemotherapy (+/- radiotherapy)**





Irradiation fields used in Hodgkin's Lymphoma

Outcomes of HL

In assessing the long-term 20-year results of treatment it has been established:

1.During the first 5-8 years after the end of treatment, the patients mostly die from Hodgkin's disease progression.

2.After 15-20 years of follow-leading cause of death of patients are late complications of treatment:

- secondary tumors and leukemias (10-30%)
- myocardial infarction (7-16%)
- infection (4-10%)
- serious damage to the lung tissue after mediastinal irradiation, particularly when combined with bleomycin (6-7%)

Causes of Death among 2733 Patients with Hodgkin's Disease/Lymphoma

Hodgkin lymphoma	383	41.2%
Secondary cancers	200	21.5%
Cardiovascular	148	15.9%
Pulmonary	41	4.4%
Infection	35	3.8%
Trauma/Suicide	16	1.7%
MDS	11	1.2%
Other/Unknown	96	10.3%
Total	930	100.0%

Stanford, Hoppe et al

Prognosis

- Hodgkin' s disease is considered one of the most curable forms of cancer, especially if it is diagnosed and treated early.
- Unlike other cancers, Hodgkin's disease is even potentially curable in late stages
- Five-year survival rates for patients diagnosed with stage I or stage II Hodgkin' s disease are 90 - 95%.
- With advances in treatment, recent studies have indicated that even patients with advanced Hodgkin' s disease have 5-year survival rates of 90%, although it is not yet certain if their cancer will return. Patients who survive 15 years after treatment are more likely to later die from other causes than Hodgkin' s disease.

Non-Hodgkin lymphomas

Definition

- **Non-Hodgkin's lymphoma (NHL) is a heterogeneous group of lymphoproliferative malignancies. More than 30 different subtypes of NHL have been identified and categorized according to several prognostic factors, including size, growth rate, and anatomic site.**

Epidemiology:

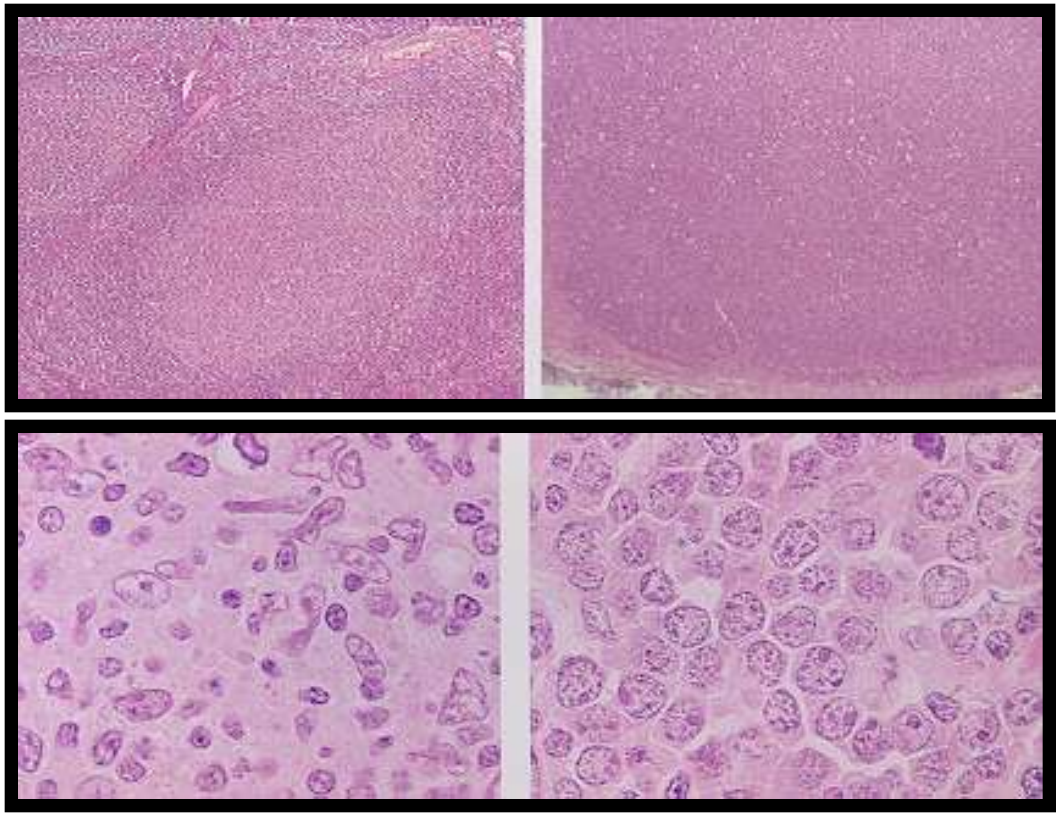
- **annual incidence: 5-10 new cases per 100 000 persons,**
- **age distribution: middle-age patients and the elderly,**
- **males are affected more often than females (1.5:1.0).**

Risk Factors

- Most cases of NHL occur in patients who are 60 years of age or older.
- NHL occurs more frequently in men than in women.
- Exposure to chemicals such as benzene and herbicides has been linked to an increased risk of NHL.
- People with a weakened immune system and certain infections, such as HIV, are also at an increased risk for NHL.

Non-Hodgkin's Lymphoma Rappaport Classification

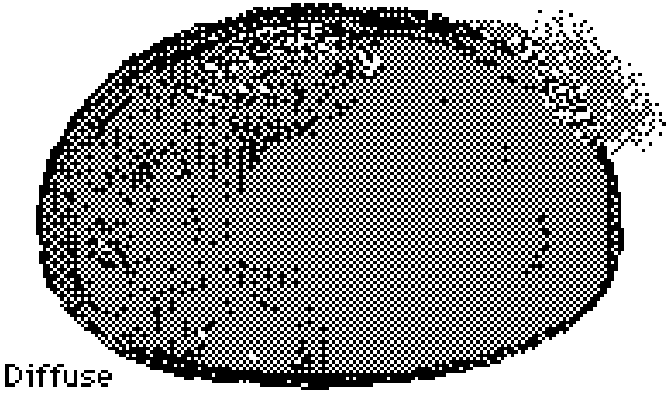
Nodular (follicular) Diffuse

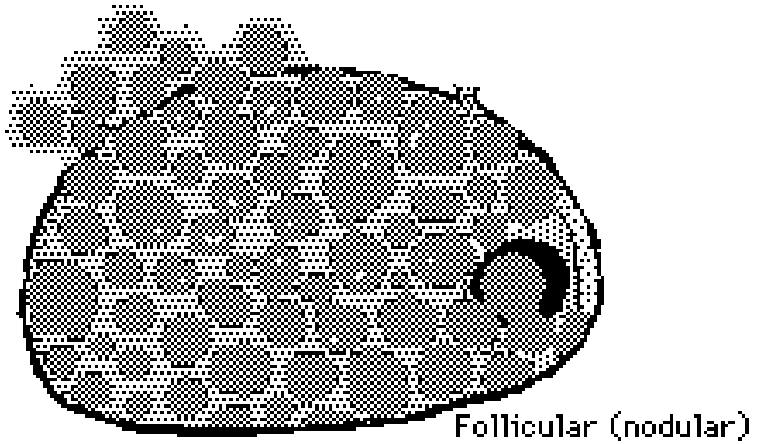


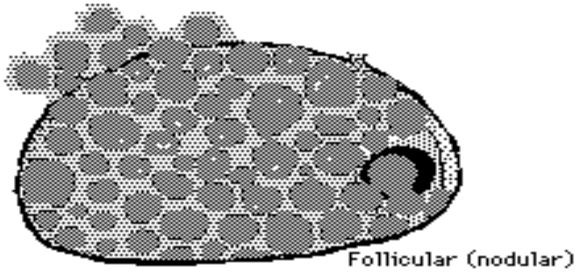
Indolent Aggressive

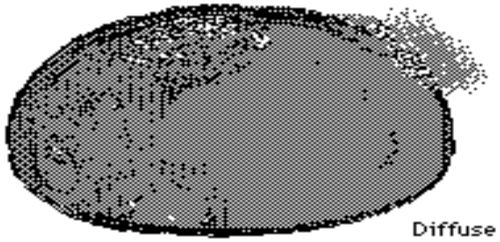
Small cell Large cell

The two most often encountered patterns of growth are 1) follicular (sometimes referred to as nodular) in which the lymphoma mimics follicular center structures and 2) diffuse in which the lymphoid cells proliferate in an apparently unorganized fashion. Occasionally lymphoma will be distributed within lymph node sinuses.

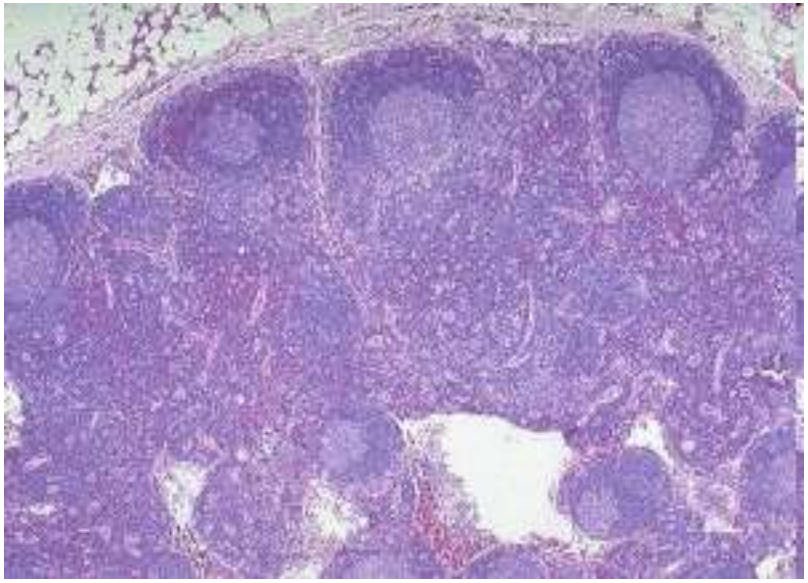




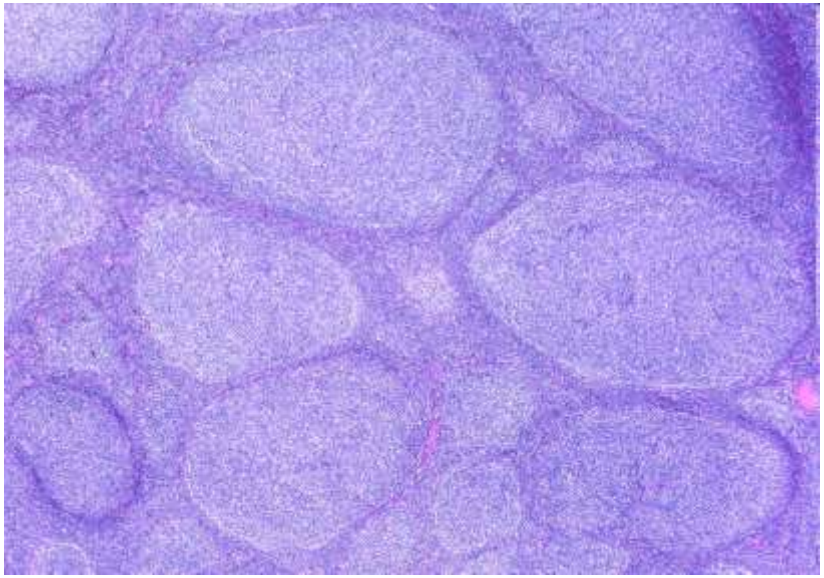




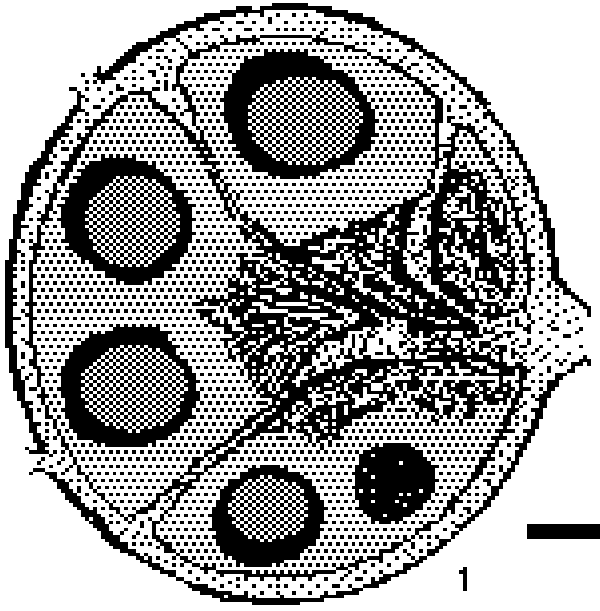
Histological comparison of normal lymph node and the lymph node affected by lymphoma



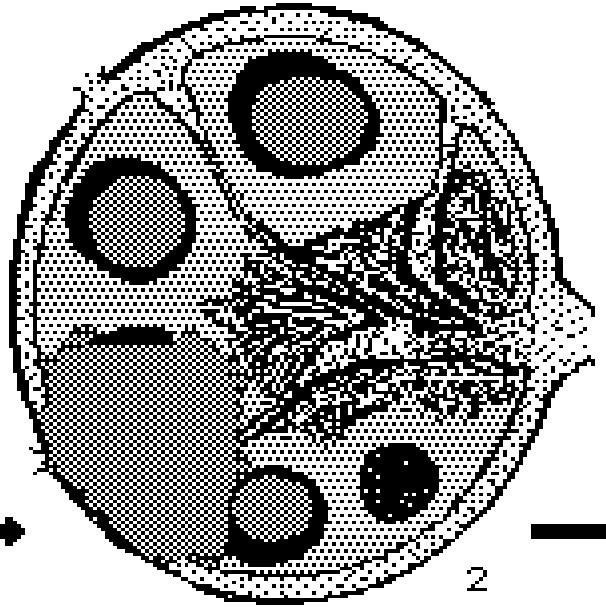
Normal lymph node



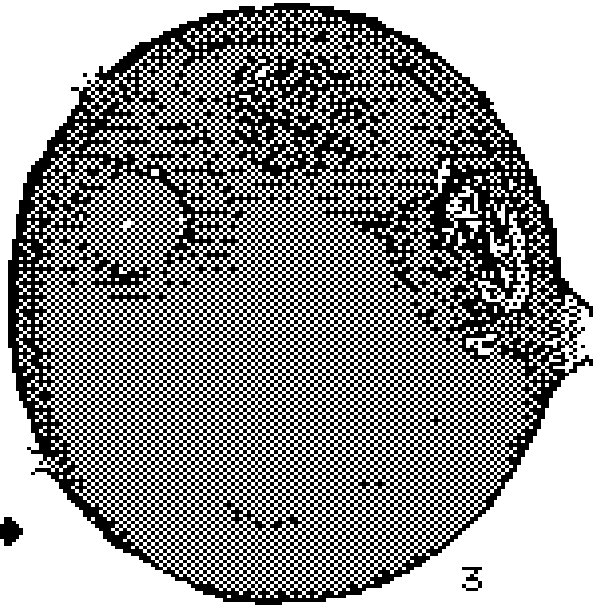
Follicular lymphoma



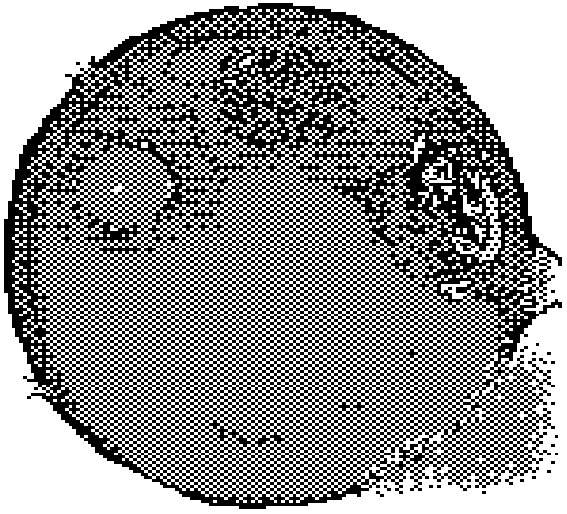
Normal Lymph Node



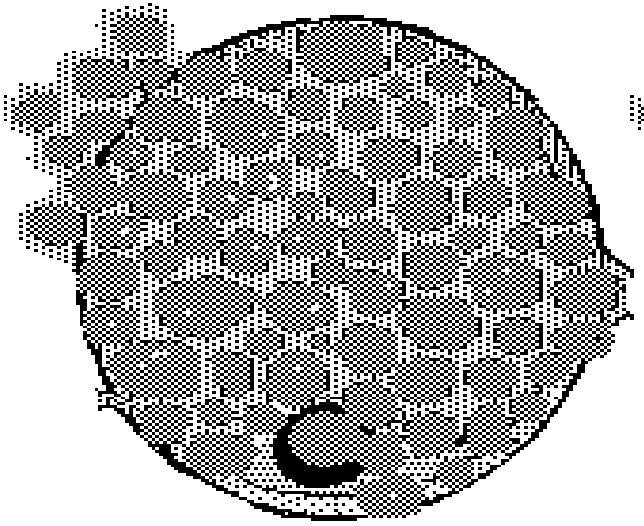
Partial Involvement
by Lymphoma



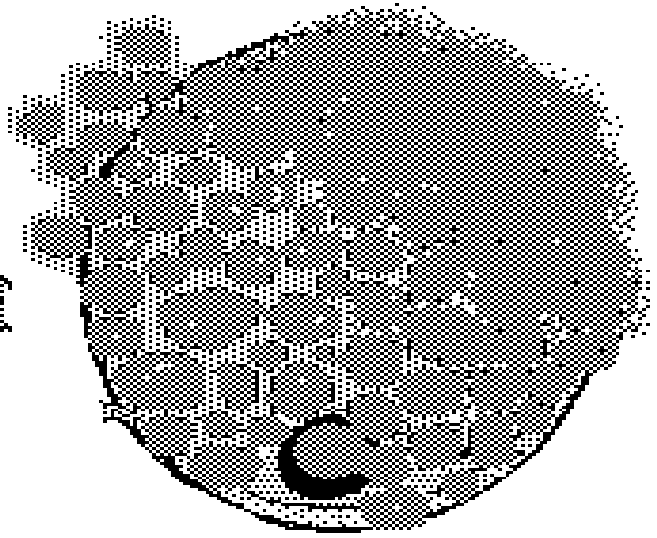
Extensive Lymphoma with
nearly complete effacement
of normal architecture



Diffuse



Follicular (nodular)



Follicular (nodular) and Diffuse

WHO Classification: B-Cell Malignancies

Precursor B-cell neoplasm

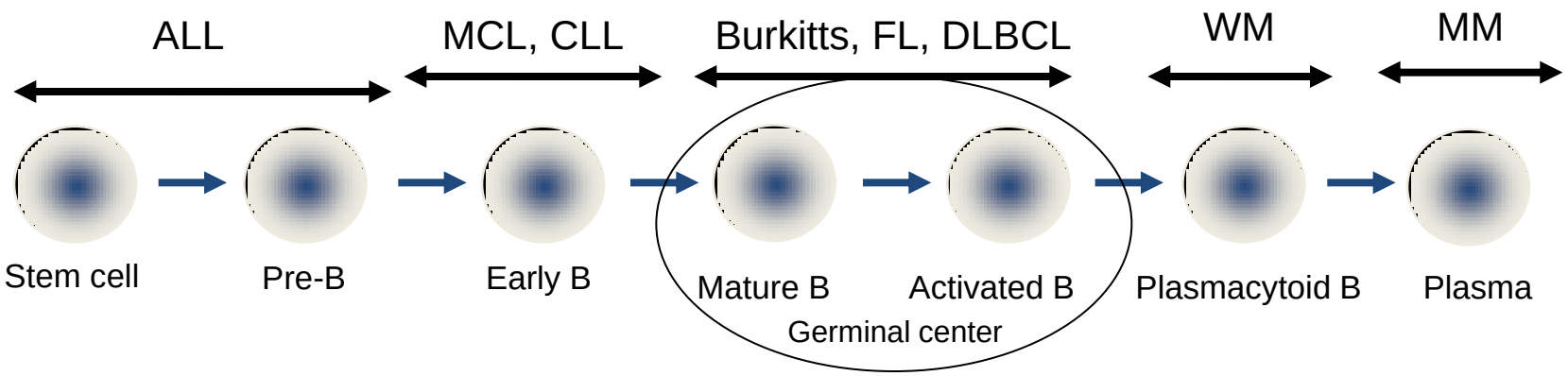
- Precursor B-lymphoblastic leukemia/lymphoma

Mature (peripheral) B-cell neoplasms

- B-cell chronic lymphocytic leukemia/ small lymphocytic lymphoma
- B-cell prolymphocytic leukemia
- Lymphoplasmacytic lymphoma
- Splenic marginal-zone B-cell lymphoma
- Nodal marginal-zone lymphoma
- Extranodal marginal-zone B-cell lymphoma, mucosa-associated lymphoid tissue (MALT) type
- Hairy cell leukemia
- Plasma-cell myeloma/ plasmacytoma
- Follicular lymphoma
- Mantle-cell lymphoma
- Diffuse large B-cell lymphoma (DLBCL)
- Burkitt's lymphoma/Burkitt's cell leukemia
- Blastic NK-cell leukemia

Harris NL et al. *J Clin Oncol*. 1999;17:3835-3849.

Antigen Expression in B-Cell Lineage



Type of B cell lymphoma is a function of:

1) Where the cell was in development/maturation when it went “bad”

2) What molecular derangement occurred

Jaffe. In: *Non-Hodgkin’s Lymphoma*. 1997:84.

WHO Classification: T-Cell Malignancies

Precursor T-cell neoplasm

- Precursor T-lymphoblastic leukemia/lymphoma

Mature (peripheral) T-cell neoplasms

- T-cell prolymphocytic leukemia
- T-cell granular lymphocytic leukemia
- Aggressive NK-cell leukemia
- Adult T-cell lymphoma/leukemia (HTLV1+)
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy-type T-cell lymphoma
- Hepatosplenic gamma-delta T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides/Sézary syndrome
- Primary cutaneous anaplastic large cell lymphoma, T/null cell
- Peripheral T-cell lymphoma, unspecified
- Angioimmunoblastic T-cell lymphoma
- Primary systemic anaplastic large cell lymphoma, T/null cell
- Blastic NK lymphoma

Harris NL et al. *J Clin Oncol*. 1999;17:3835-3849.

Table 11.1 World Health Organization classification (major categories) of lymphoma

Classification	Frequency (%)	5-year survival (%)
B lineage		
• Diffuse large B-cell lymphoma	30.6	40 (15 to >90)
• Follicular lymphoma	22.0	60 (20 to >90)
• Marginal zone B-cell lymphoma/mucosa-associated lymphoid tissue	7.6	70 (60 to >90)
• Chronic lymphocytic leukaemia/small lymphocytic lymphoma	6.7	>50 (20 to >90)
• Mantle cell lymphoma	6.0	25
• Primary mediastinal large B-cell lymphoma	2.4	70
• Burkitt's/Burkitt-like lymphoma	2.5	85
T lineage		
• Peripheral T-cell lymphoma	7.0	25
• Anaplastic large cell lymphoma	2.4	70 (15 to >90)
• Lymphoblastic lymphoma	1.7	30

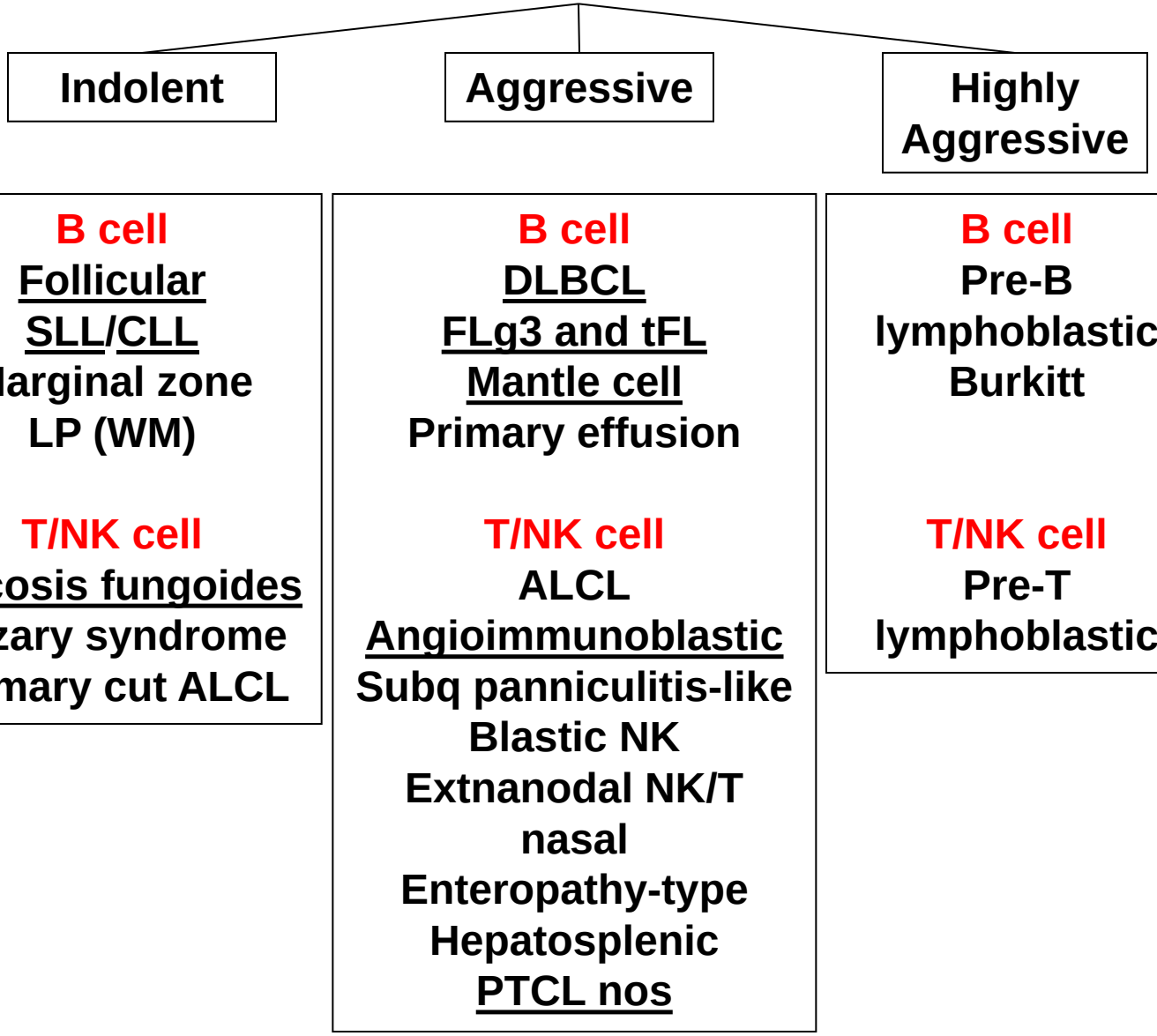
Non-Hodgkin's Lymphoma Working Classification

- Low Grade
  - Small Lymphocytic
  - Follicular small-cleaved cell
  - Follicular mixed small-cleaved and large cell
- Intermediate Grade
  - Follicular large cell
  - Diffuse small cleaved cell
  - Diffuse mixed small and large cell
  - Diffuse large cell
- High Grade
  - Large cell immunoblastic
  - Lymphoblastic
  - Small non-cleaved cell (Burkitt's and non-Burkitt's type)

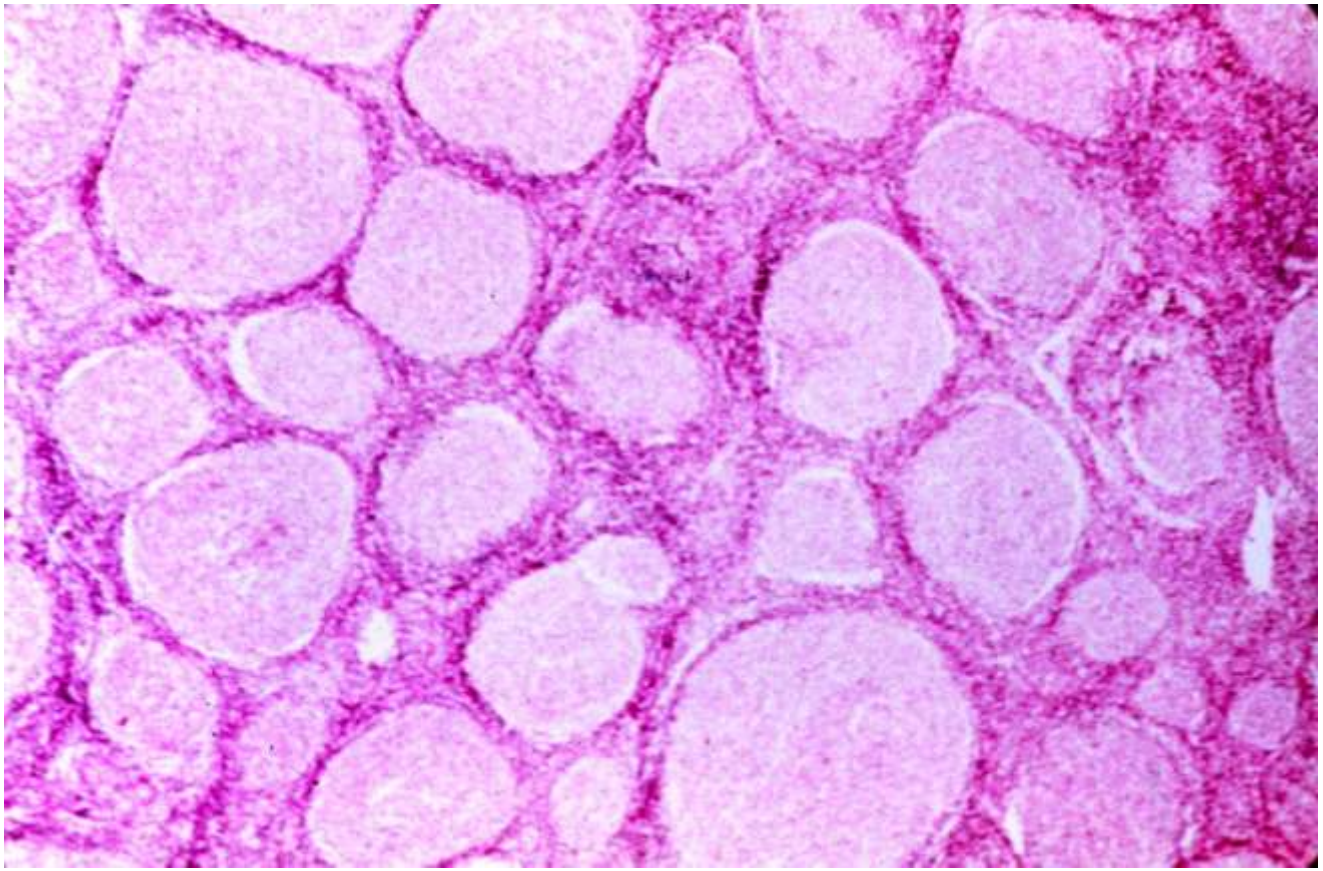
Lymphoma Biology

- Aggressive NHL
  - short natural history (patients die within months if untreated)
  - disease of rapid cellular proliferation
  - Potentially curable with chemotherapy
- Indolent NHL
  - long natural history (patients can live for many years untreated)
  - disease of slow cellular accumulation
  - Generally incurable with chemotherapy

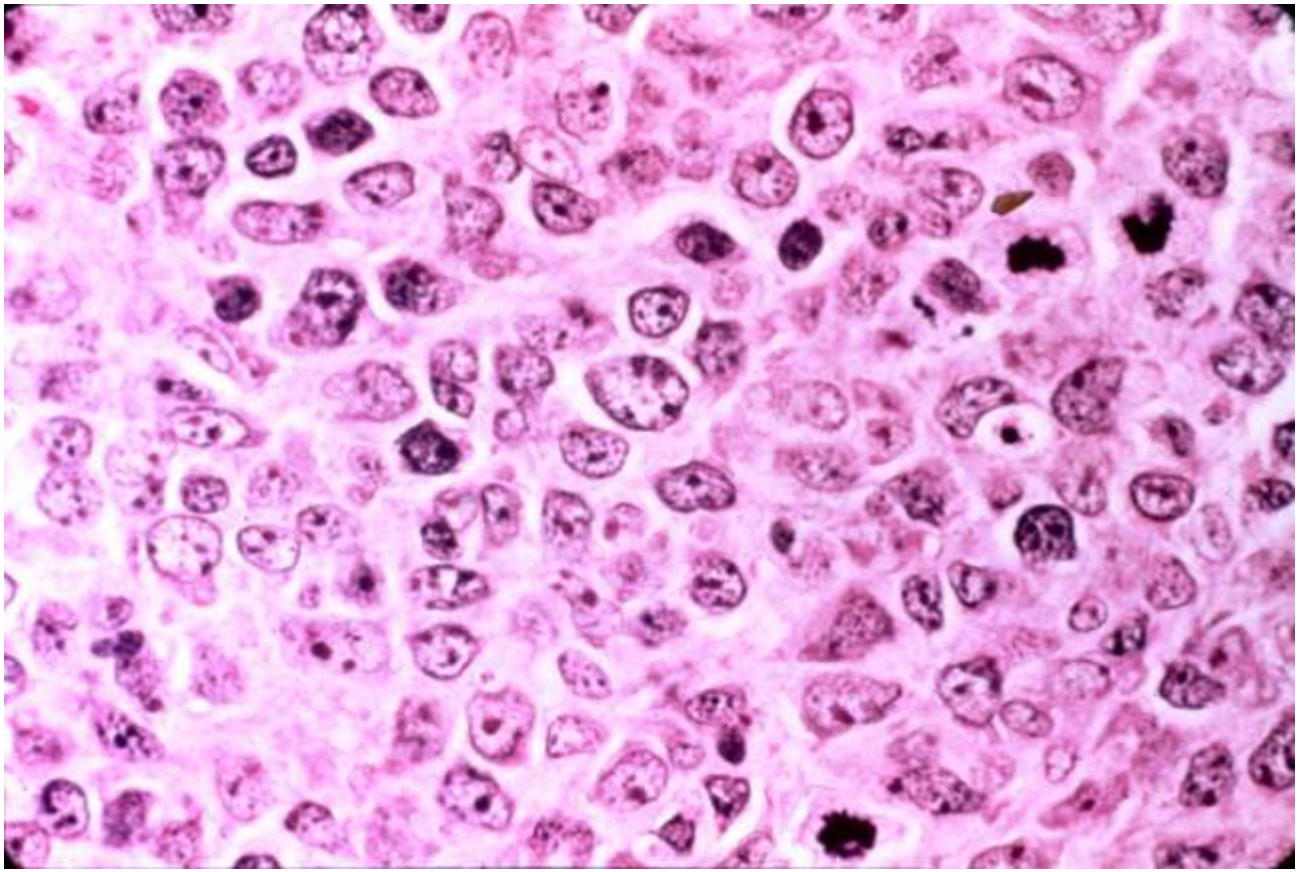
Non Hodgkin Lymphoma



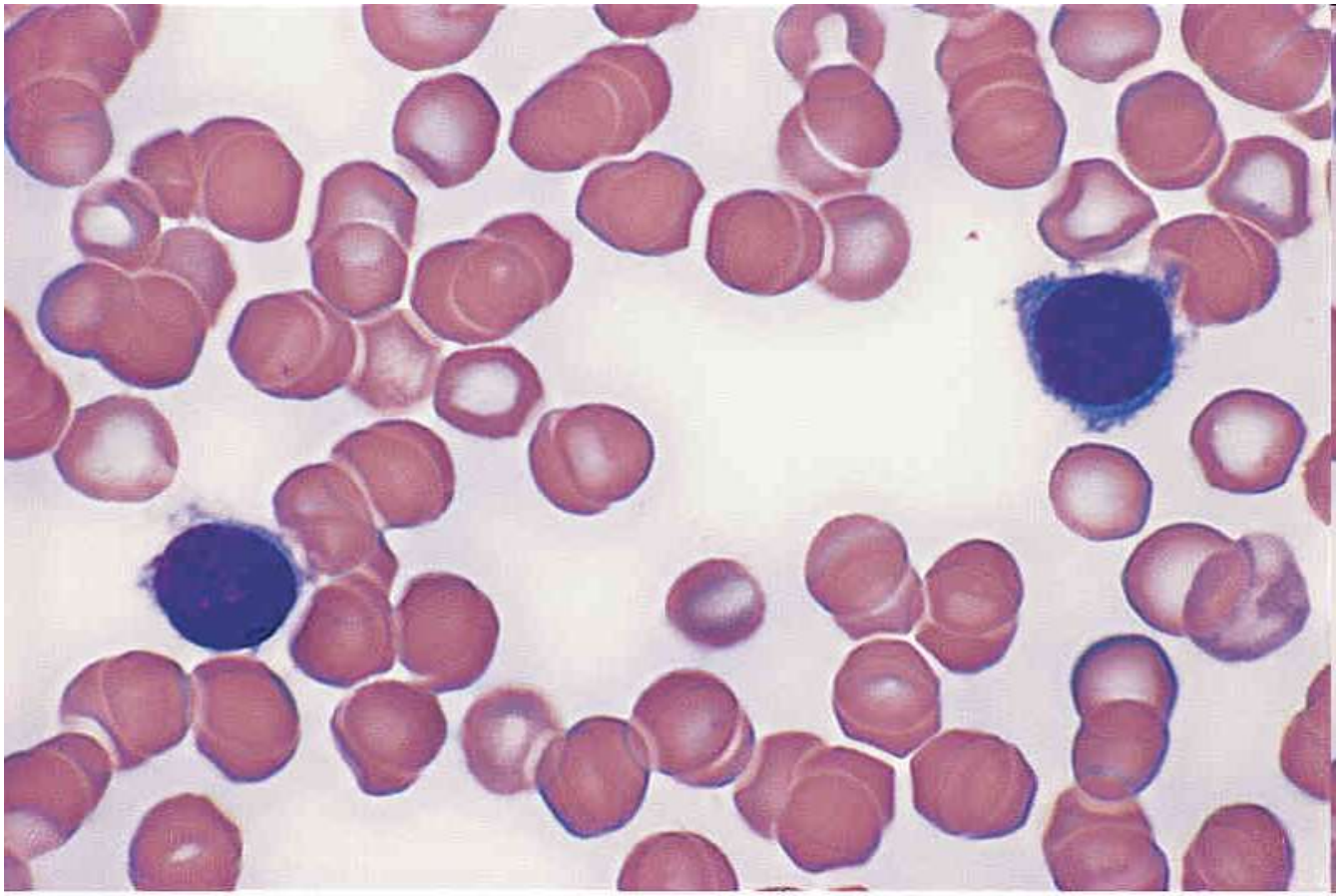
Follicular Lymphoma



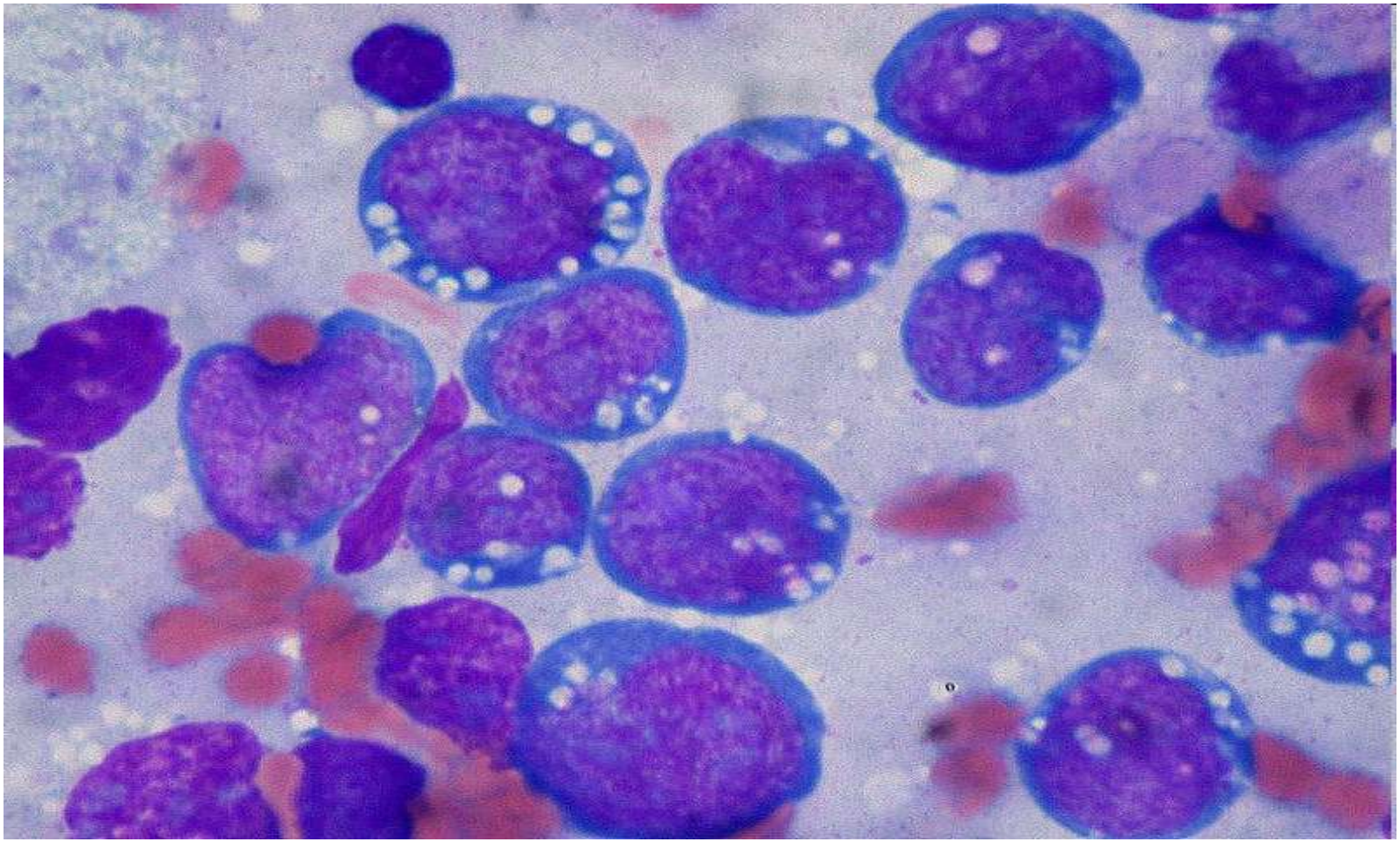
Diffuse Large B Cell Lymphoma



Non-Hodgkin's Lymphoma
Splenic Lymphoma



Burkitt's Lymhoma
Starry, Starry Night



Clinical Presentation

- Patients with lymphoma may present with the following symptoms:

- Lympadenopathy similar to tuberculosis
- Mediastinal mass
- Pleural effusion
- Splenomegaly
- Maxillary mass (Burkitt lymphoma)
- Right iliac fossa mass
- Intussusception
- Bowel obstruction
- Bowel perforation
- Fever, weight loss, night sweats

- Aggressive NHL
  - Patients likely to present with symptoms
- Indolent NHL
  - Patients likely to present with painless adenopathy

Denis Parsons Burkitt (28 February 1911 – 23 March 1993)

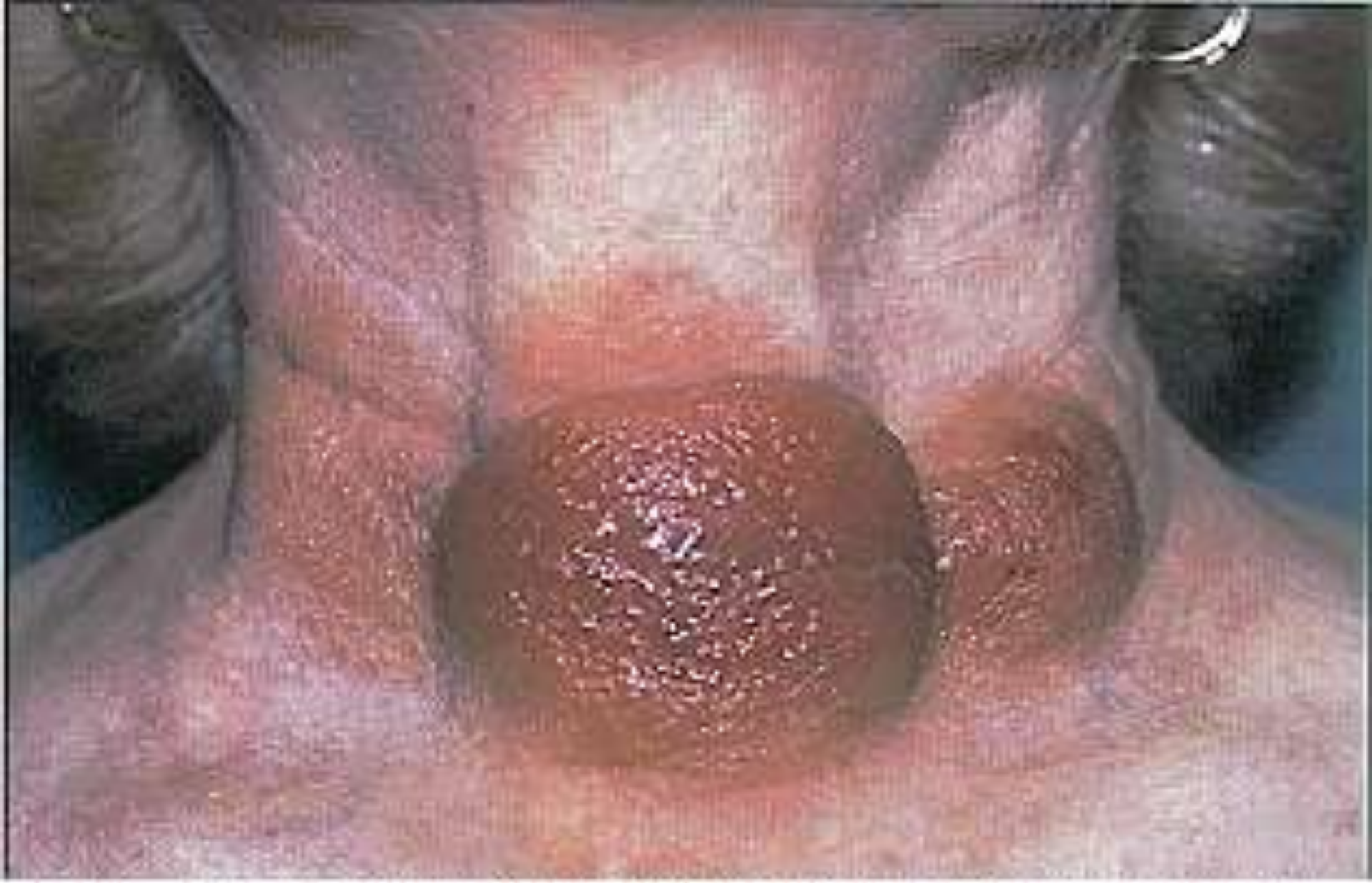
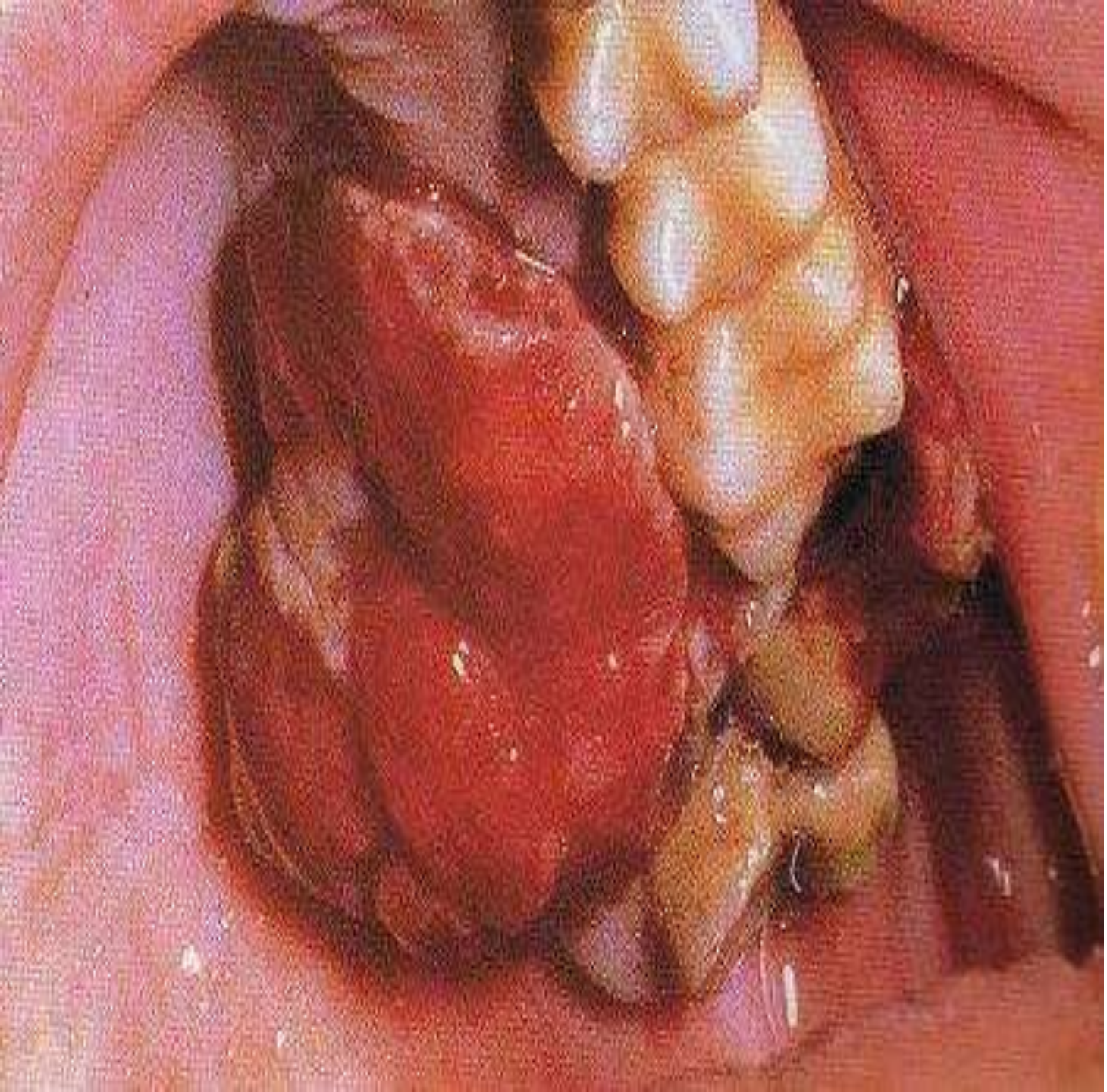
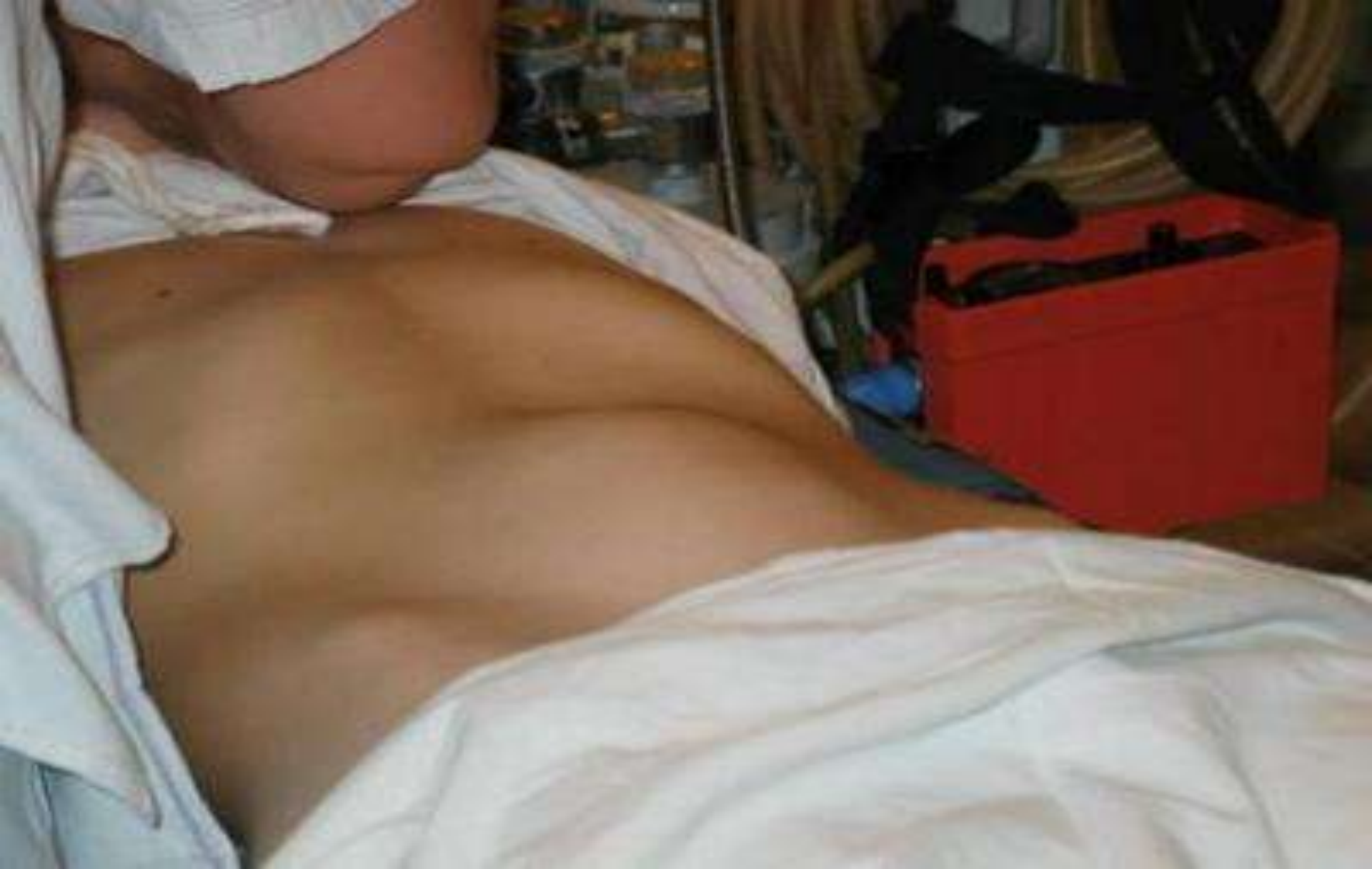


Fig 3. -- Tumor stage of mycosis fungoides. Lesions are deeply indurated, large, and often ulcerated.



Nodular non-Hodgkin's lymphoma in a patient with AIDS

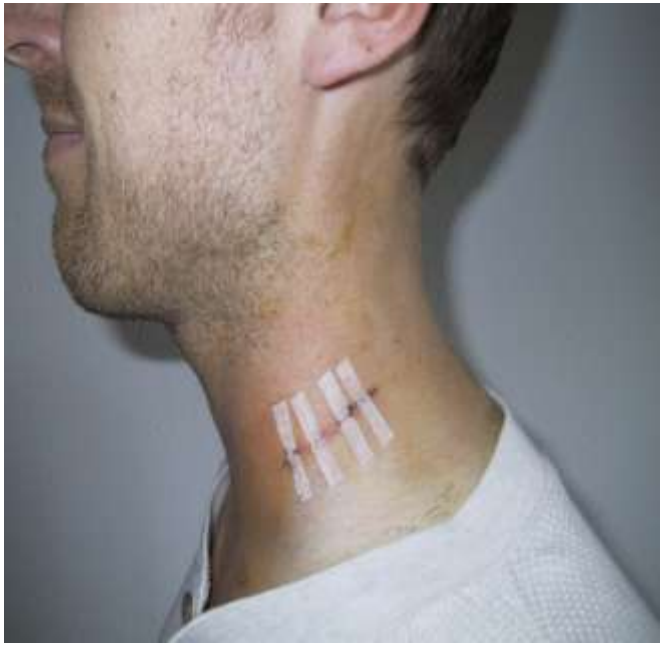


В-клеточная неходжкинская лимфома с поражением илеоцекального угла.

Non-Hodgkin Lymphoma Diagnosis

Lymph node biopsy

- **Biopsy of lymph node is the main method of diagnosis of lymphoma.**
- **Material for morphological study lymph node can be obtained by using:**
- **aspiration biopsy (suspension cells)**
- **needle biopsy (tissue column)**
- **open incisional biopsy (a fragment of the lymph nodes)**
- **open excisional biopsy (the entire lymph node or conglomerate lymph nodes).**

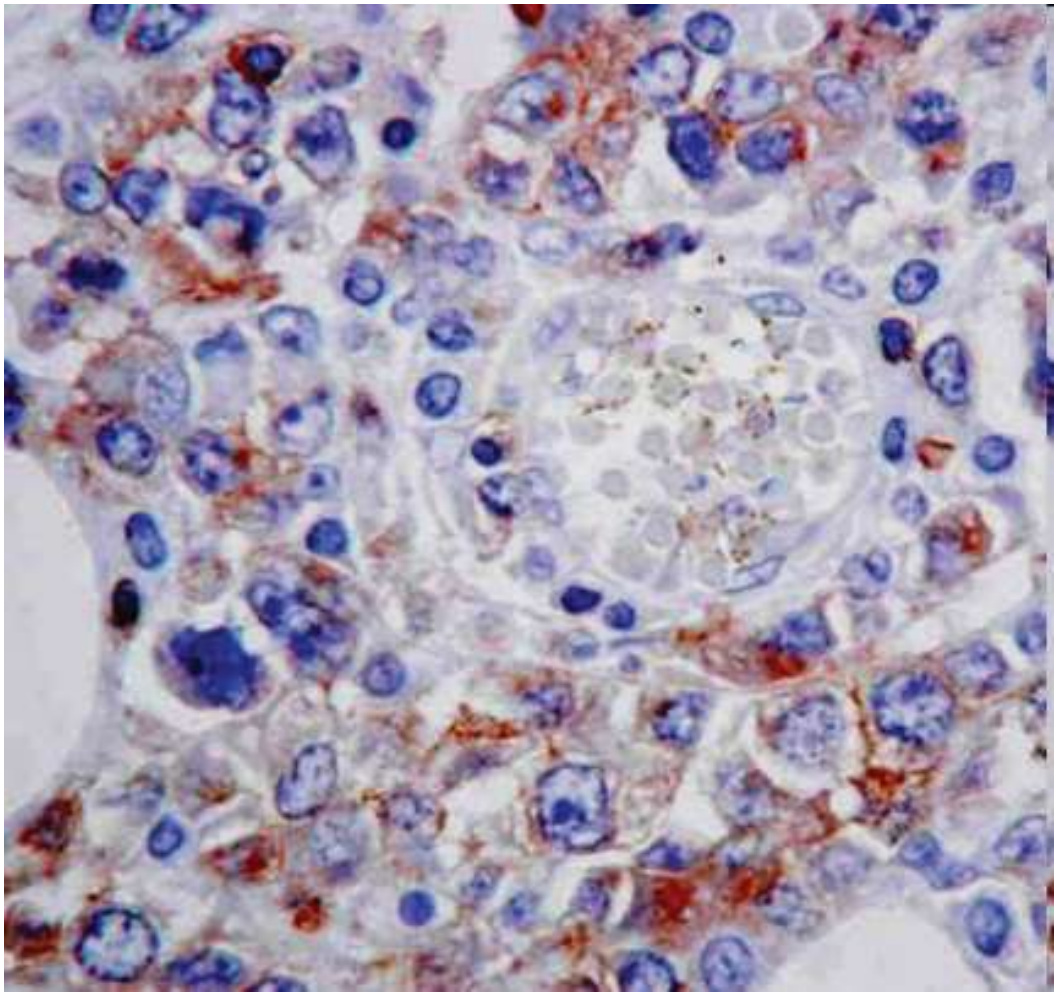


Non-Hodgkin's Lymphoma Immunophenotyping

- Immunohistochemistry
- Immunofluorescence
- Flow cytometry

- Identification of CD's (cluster determinants)
  - CD5 = T cell type
  - CD20 = B cell type

Immunohistochemistry



Extranodal NK / T-cell lymphoma, nasal type
stain on CD3

Treatment approach

- Approach dictated mainly by histology
  - reliable hematopathology crucial
- Aggressive NHL
  - Cure is often the goal
- Indolent NHL
  - Cure is rarely the goal
  - Control is the goal