Hodgkin Lymphoma

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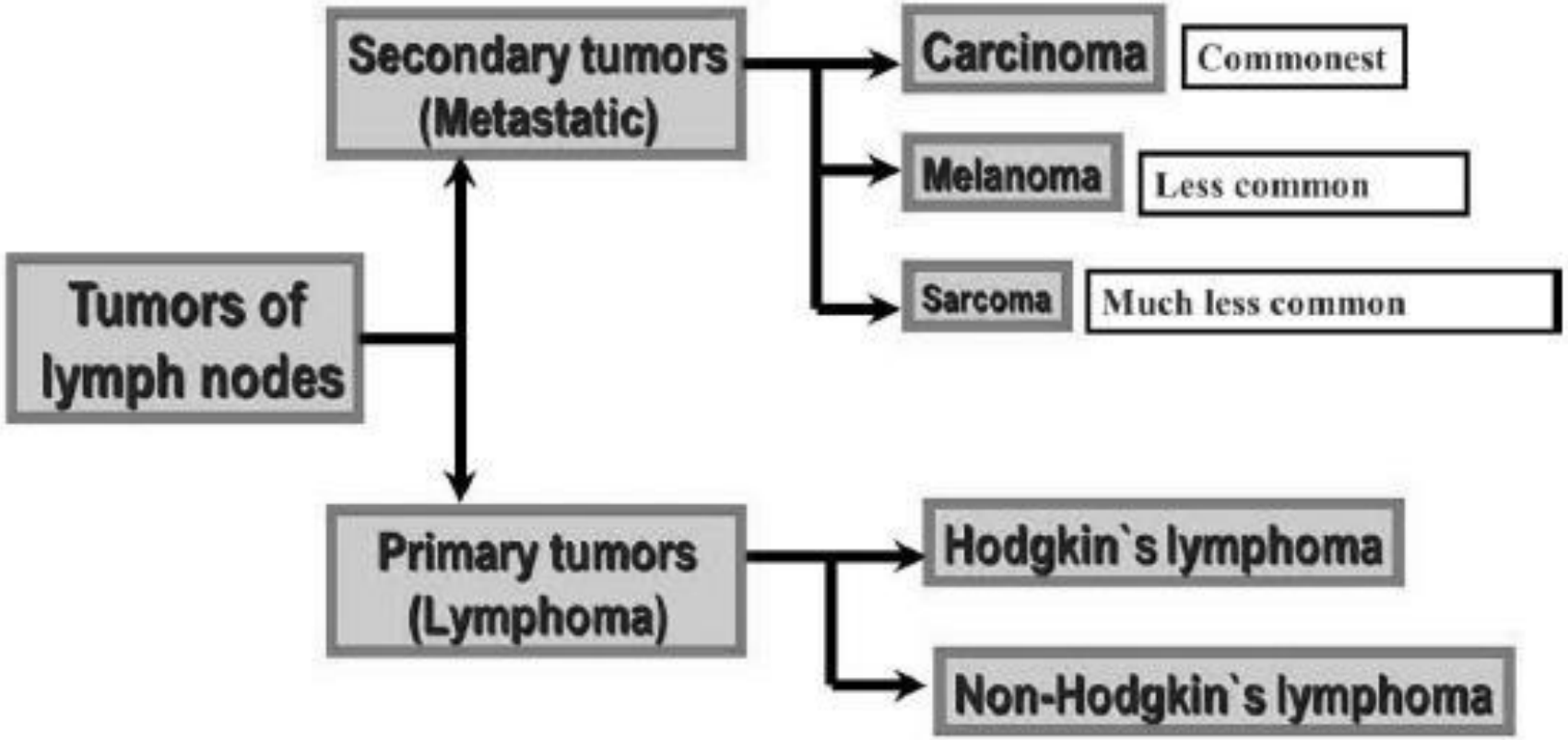
ILOs

- - Describe the different types of Hodgkin lymphoma
- - Emphasis on clinical presentation
- - Emphasis on histopathologic features
- - Emphasis on immunophenotyping of Hodgkin giant cells
- - Emphasis on prognosis of Hodgkin lymphoma
- Non-Hodgkin’s Lymphoma
- - Describe clinically important NHL subsets:
- - Small lymphocytic lymphoma/CLL
- - Follicular lymphoma
- - Mantle cell lymphoma
- - MALT lymphoma
- - Diffuse large B cell lymphoma
- - Burkitt lymphoma

TUMORS OF LYMPH NODES

Classification of tumors of lymph nodes

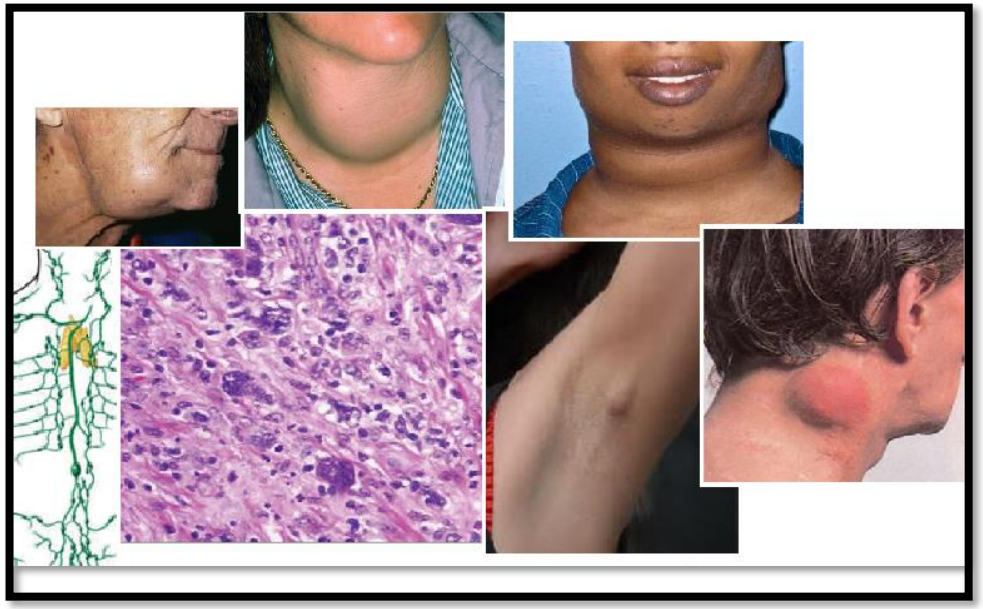


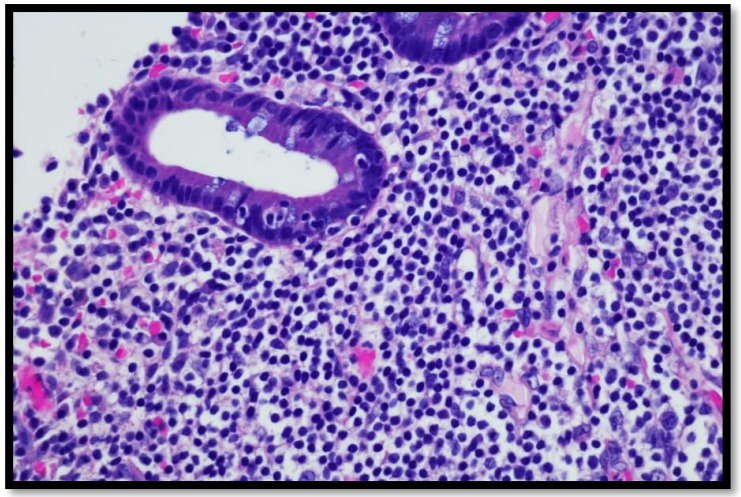
Lymphoma

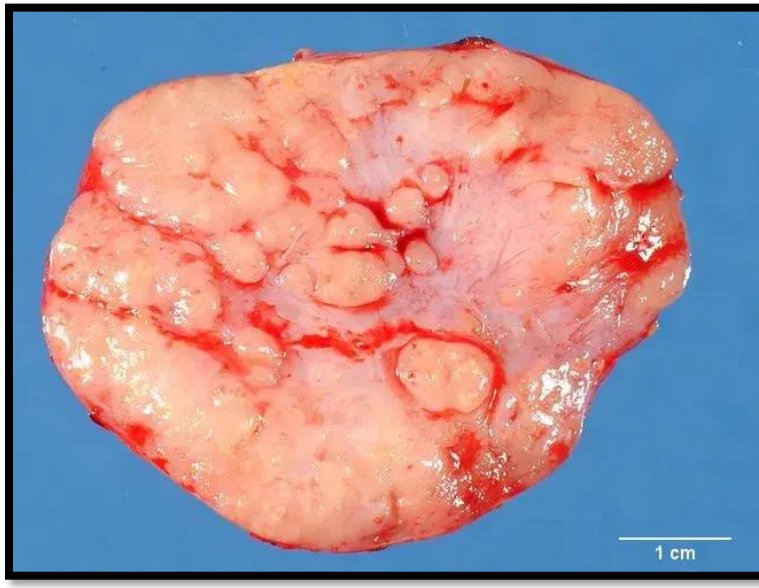
- Definition: Malignant tumors of lymphoid tissue
- - Organs affected: lymphomas could arise from
- - A. Nodal lymphoid tissue (nodal lymphoma)
- - B. Extra-nodal lymphoid tissue (tonsils, GIT, etc.)
- - Involves one group → spreads to others
- - Can infiltrate organs if untreated

Gross & Microscopic Features

- - Grossly/Clinically: Painless LN enlargement
- - Usually involves multiple LN groups
- - Microscopically: Effacement of normal nodal architecture
- - Other features vary by lymphoma type







Hodgkin Lymphoma

- - Malignant tumor of lymphoid tissue
- - Characterized by large neoplastic cells (Reed-Sternberg/Hodgkin's cells)
- - Polymorphic cellular background
- - Reactive inflammatory cells present
- Incidence & Spread~30% of all lymphomas
- - Bimodal age distribution (young & old)
- - Most types affect men > women (except nodular sclerosing)
- - Spread is contiguous
- - ~50% linked to EBV

Clinical Features – LN Enlargement

- - Painless lymphadenopathy
- - Commonly cervical & supraclavicular LNs
- - May involve splenomegaly
- - Tends to involve one group then another
- - More frequent axial LN groups
-
- Systemic Manifestation:
- - In ~25% of cases
- - Non-specific symptoms:
- - Intermittent low-grade fever
- - Night sweats
- - Progressive weight loss

- Gross Features
- - LNs:
- early = enlarged, firm, discrete
- Later: fusion into irregular fixed mass
- - Cut surface: nodular, grayish-pink
- - Spleen: enlarged, firm, grayish nodules
- - Extra-nodal sites: less common (liver, BM)

Microscopic Features

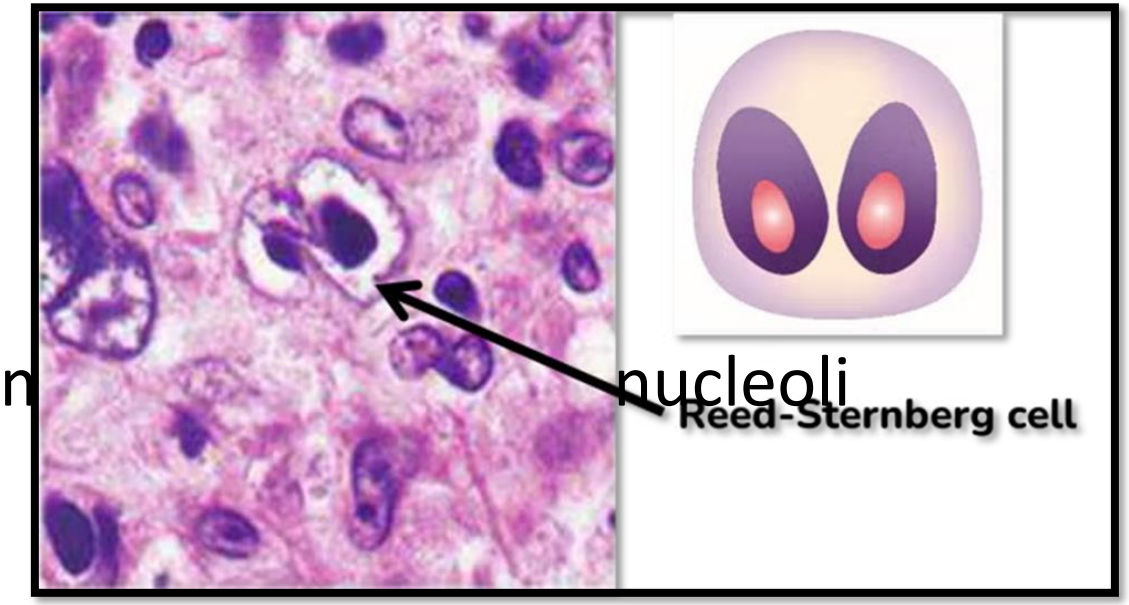
- - Partial/complete loss of normal LN architecture
- - Infiltration by RS cells or variants
- - Many reactive inflammatory cells

Types of RS CELLS

1-Classic RS Cells

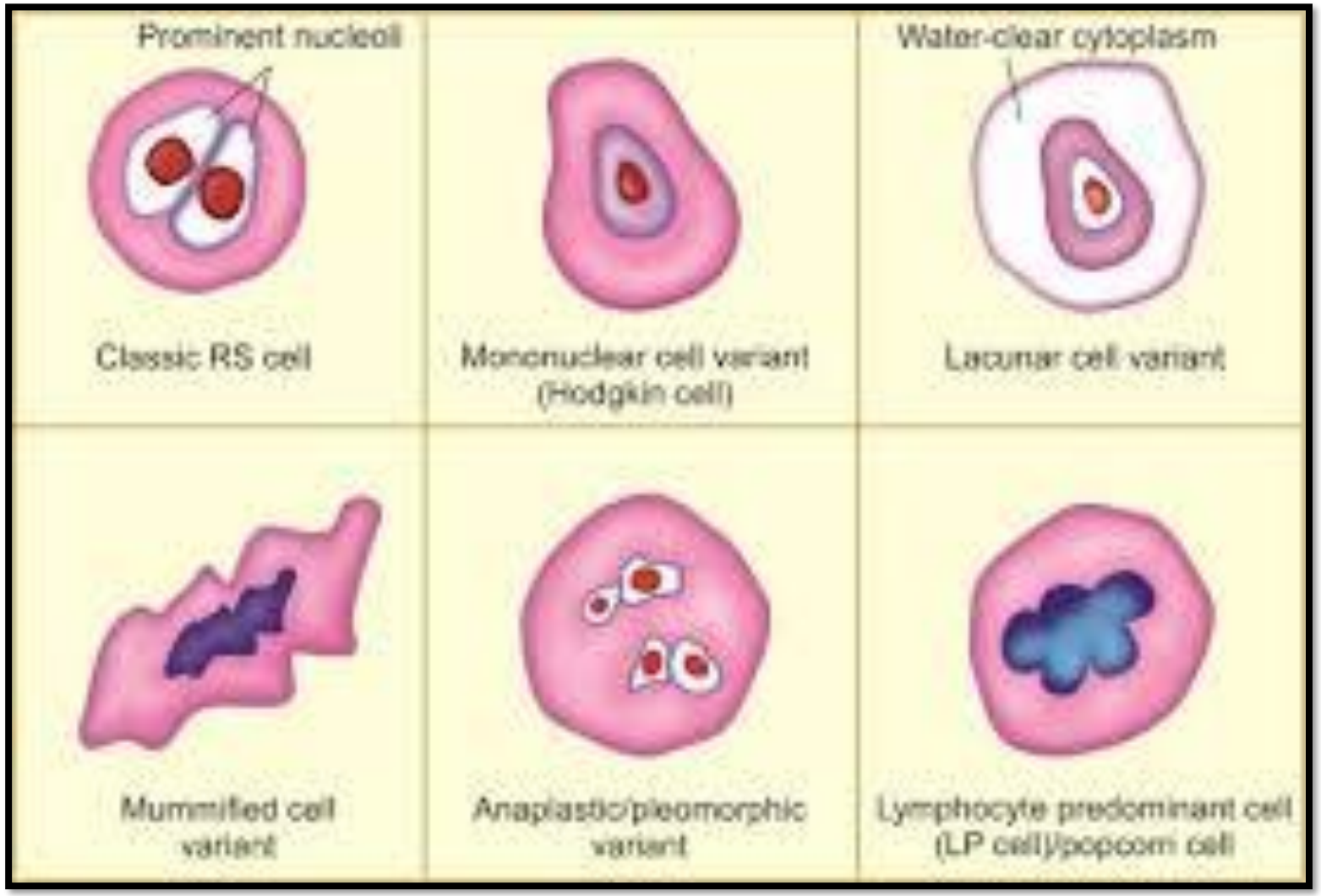
- Also called Hodgkin's/Dorothy Reed cells
- - Giant cells (30–60 µm)
- - Abundant pale eosinophilic cytoplasm
- - Two nuclei (mirror image/owl eye)

- - Pron nucleoli



2-RS Cell Variants

- Mononuclear variant:
- single nucleus
- Lacunar cell:
- shrunken cytoplasm
- (clear space)
- Popcorn cell: lobed nuclei,
- small nucleoli

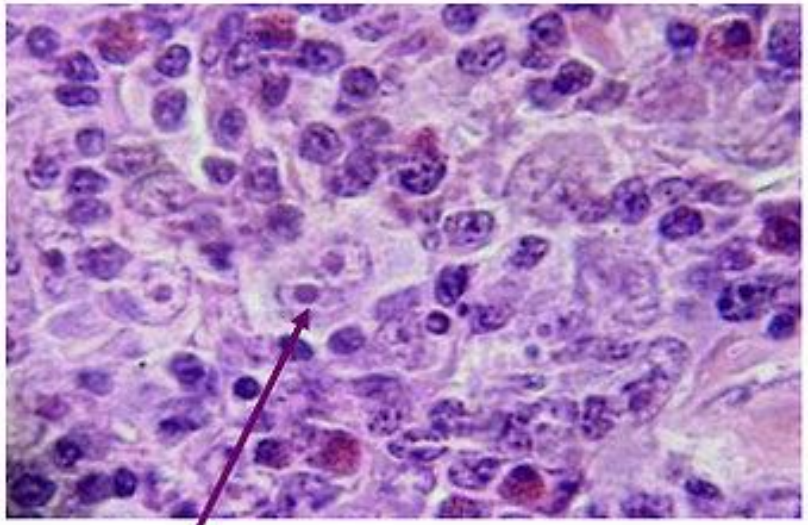


Types of Hodgkin Lymphoma

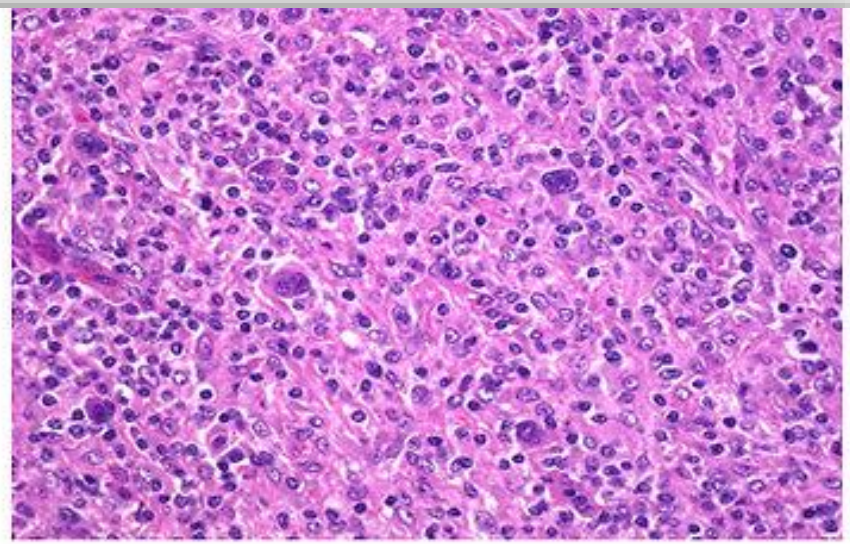
- - Classified by RS cell frequency, background cells, fibrosis
- Nodular Lymphocyte Predominant HL
- - ~5% of HL cases
- - Best prognosis
- - Nodular appearance with reactive cells (lymphocytes)
- - Popcorn variant RS cells
- - No classic RS cells

- Classic HL – Lymphocyte-Rich Type
- - ~5% of HL cases
- - Good prognosis
- - Reactive cells mainly lymphocytes
- - Mononuclear Hodgkin’s cells
- - Classic RS cells rare

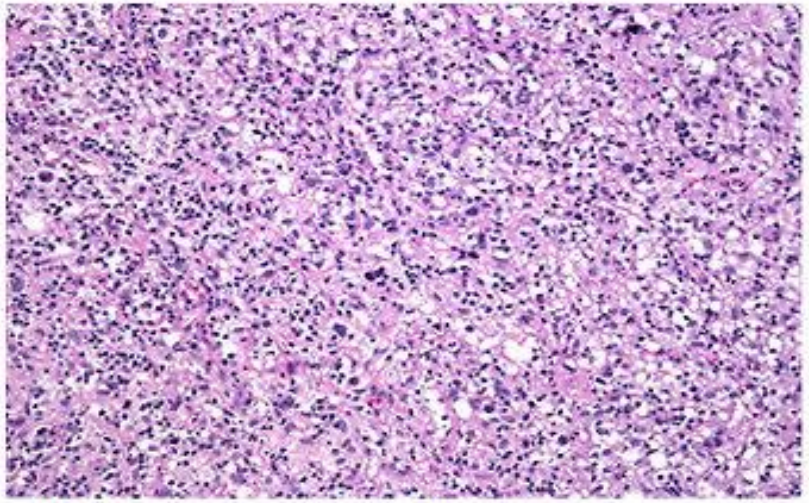
- Classic HL – Nodular Sclerosing Type
- - ~65% of HL cases
- - Good prognosis
- - LN divided into nodules by collagen bands
- - Nodules contain mixed reactive cells
- - Lacunar Hodgkin's cells
- - Classic RS cells rare
- Classic HL – Mixed Cellularity Type- ~20–25% of HL cases
- - Poor prognosis
- - Diffuse mixed inflammatory background
- - Numerous classic RS & mononuclear cells
- : Classic HL – Lymphocyte Depletion Type
- - 1–5% of HL cases
- - Worst prognosis
- - Few reactive cells & lymphocytes
- - Many classic RS & Hodgkin's cells
- - Frequent mitosis



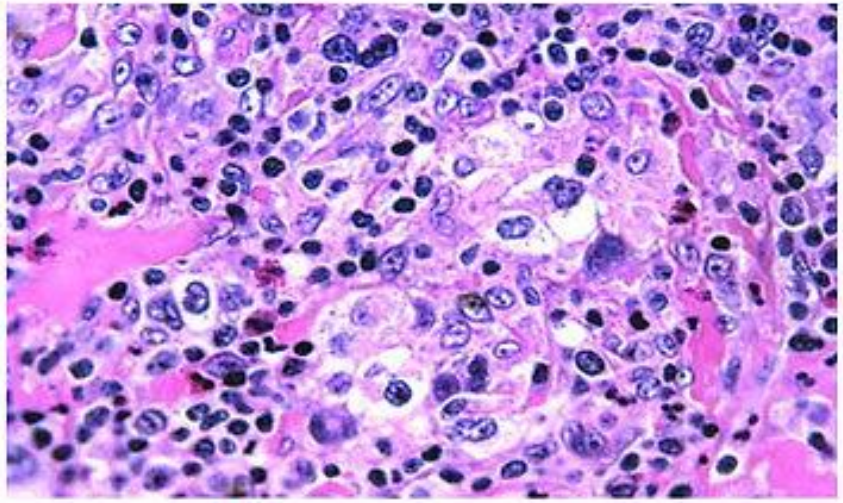
Typical Reed-Sternberg cell in Lymphocyte rich type of HL



HL, mixed cellularity



HL, lymphocyte depletion



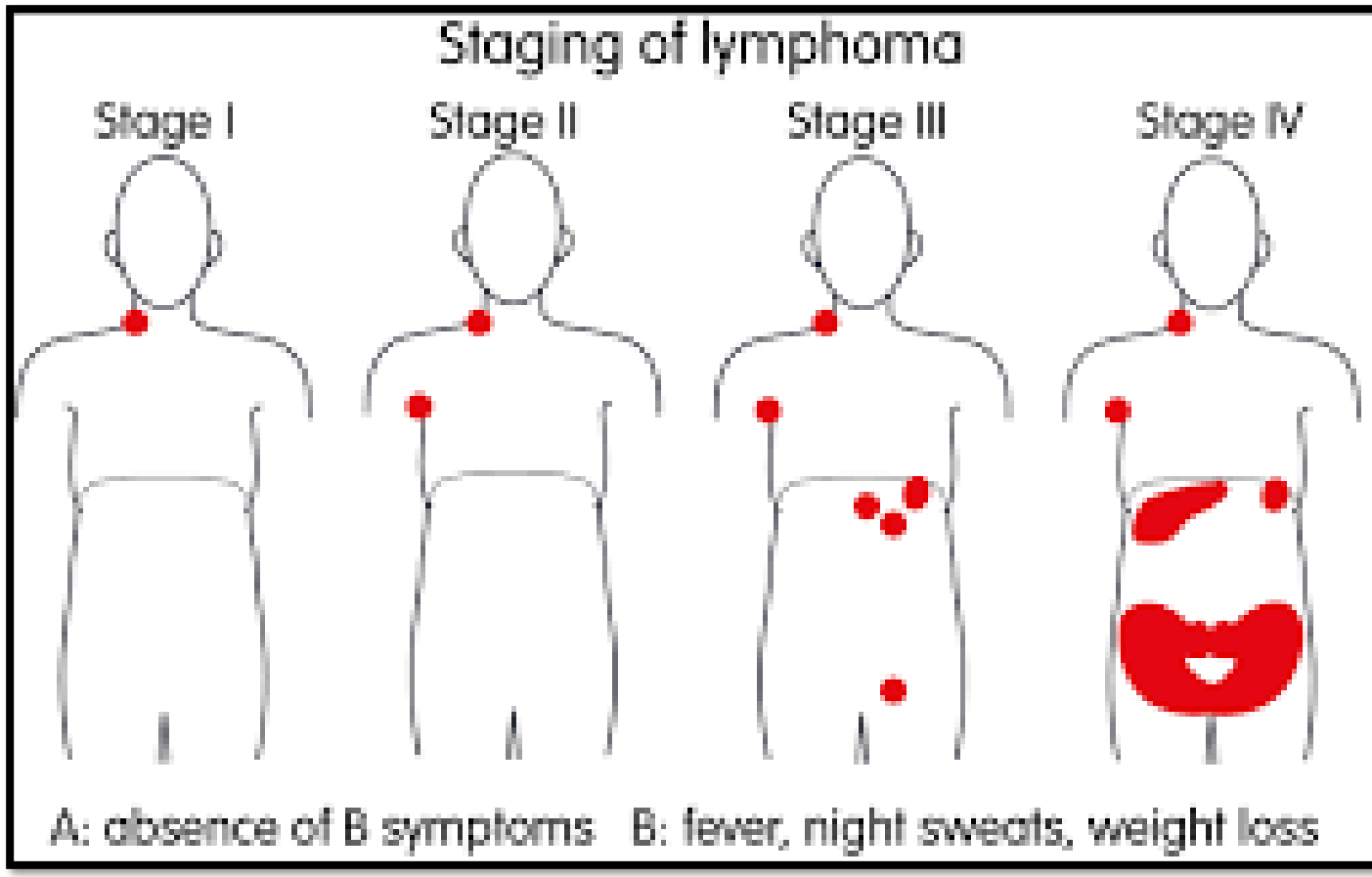
HL, nodular sclerosis

Prognosis of Hodgkin Lymphoma

- - Depends on histological subtype
- - Good: Nodular lymphocyte predominant & lymphocyte-rich
- - Relatively good: Nodular sclerosis
- - Poor: Mixed cellularity
- - Worse: Lymphocyte depletion
- - Clinical stage & organ infiltration more important

Staging of Hodgkin Lymphoma

- - Stage I: One LN group affected
- - Stage II: ≥2 LN groups, same side
- of diaphragm
- - Stage III: LN groups both sides of diaphragm
- - Stage IV: Spread to organs beyond LNs/spleen



Non-Hodgkin’s Lymphoma

- Definition- Malignant tumor of lymphoid tissue
- - Mostly from B or T lymphocytes
- - May arise in nodal or extra-nodal tissue
- Special Features of NHL
- - Multiple heterogeneous disorders
- - Peripheral LN affection
- - Non-contiguous spread
- - Common primary extra-nodal presentation

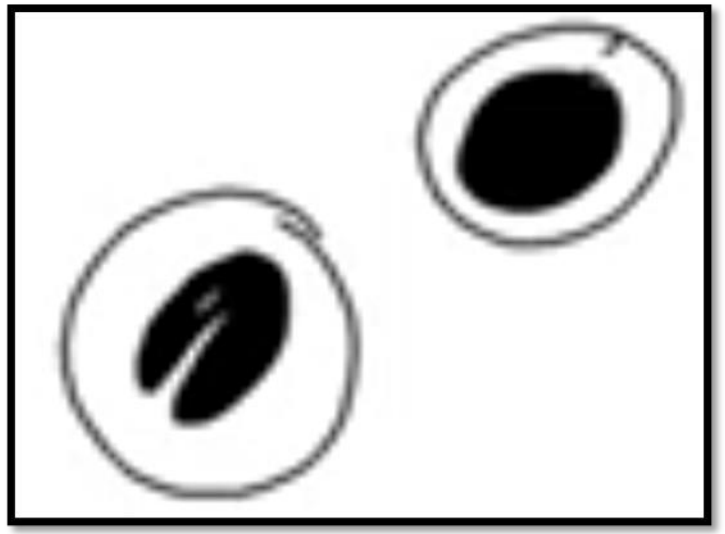
Comparison of HL &NHL

	HL	NHL
Cellular origin	B lymphocytes	B lymphocytes (90%), T lymphocytes (10%)
Extent of disease	Localized	Disseminated
B symptoms	common	40%
Extranodal involvement	rare	common

	HL	NHL
Incidence	+/- 30 % of all lymphomas	More common
Age incidence	Bimodal	Increase with age
Neoplastic cells	RS cells or its variants	B cells or T cells
Background cells	Numerous reactive cells	No or rare reactive cells
Progression	Often localized to a single group of LNs	Tend to involve more than one group of LNs
Spread	Usually contiguous spread.	Usually non-contiguous spread.
Peri-nodal extension	Less frequent peri-nodal extension	Frequent peri-nodal extension
Extra nodal extension	Extension of extra-nodal sites is uncommon.	Extension to extra-nodal sites is common.
Prognosis	Generally better than NHL (based on stage)	Generally worse than HL (based on stage)

- - Gross: Enlarged, soft LNs (fish flesh), pale gray
- - Microscopic: Replacement by monoclonal B/T cells
- - IHC: B cell = CD20+, T cell = CD3+
- Types of NHL Classifications
- - Working formulation**: based on histology & grade**
- - WHO classification: **based on cell of origin (B/T)**

- - Most recent: WHO classification
- Working Formulation of NHL
- - Based solely on morphology
- - Therapeutic & prognostic validity
- - Depends on architectural & cytological features



Working Formulation Grades

- - Low grade: SLL, follicular small cell, mixed
- - Intermediate: Follicular large cell, diffuse mixed
- - High grade: Immunoblastic, lymphoblastic, Burkitt's
- Real/WHO Classification
- - Based on cell of origin (B or T)
- - Determined by IHC (immunohistochemistry), not histology
- Pathological Features
- - Effacement of LN architecture
- - Proliferation of small lymphocytes
- - Small, uniform, hyperchromatic nuclei
- - IHC: CD5+, B-cell markers+

Working Formulation Grades

- Based solely on morphology in histological sections.
- Has therapeutic and prognostic validity.
- Depends on:
  - **Architectural features (low magnification):**
    - Follicle (nodule) formation
    - Diffuse proliferation
  - **Cytological features (high magnification):**

Cell size

- small
- large
- mixed small and large

Nuclear outline

- cleaved (indented)
- non-cleaved

Examples for B cell lymphoma

- Small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL / CLL)

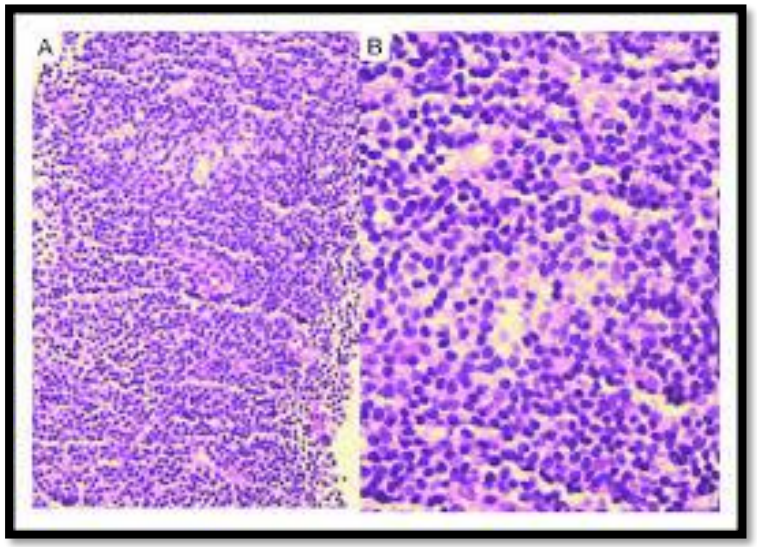
Clinical features:

–Affects old age (~ 60 years)

–Generalized lymphadenopathy

–Hepatosplenomegaly is common.

–May be accompanied with chronic lymphocytic leukemia



•Pathological features:

–Effacement of normal nodal architecture

–Proliferation of small lymphocytes

–The lymphocytes have Small size, Uniform shape, Scanty cytoplasm, hyperchromatic nuclei and rare mitosis

•IHC

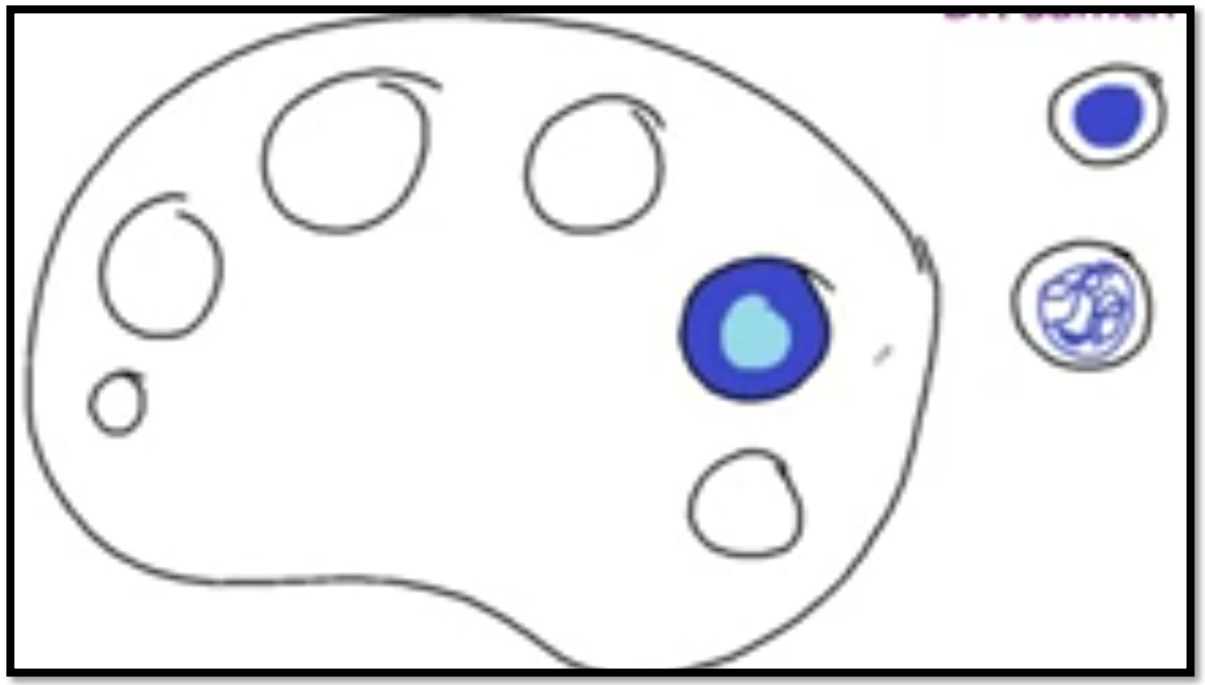
–Typically positive for CD5

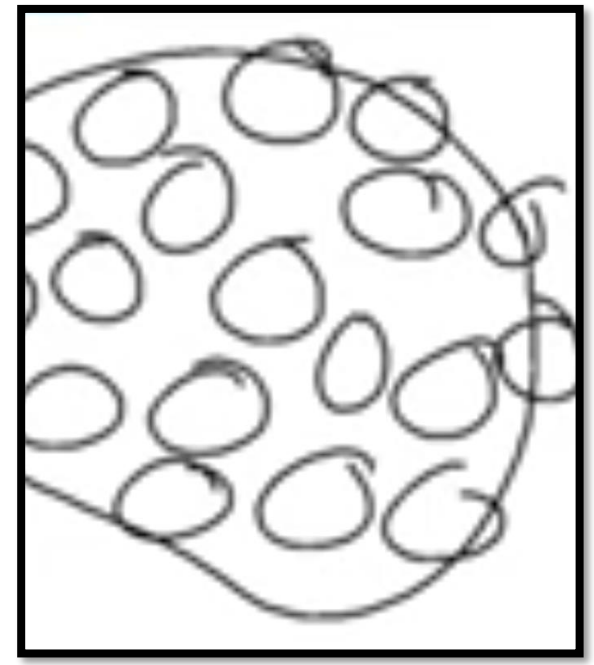
–Positive for other B- cell markers

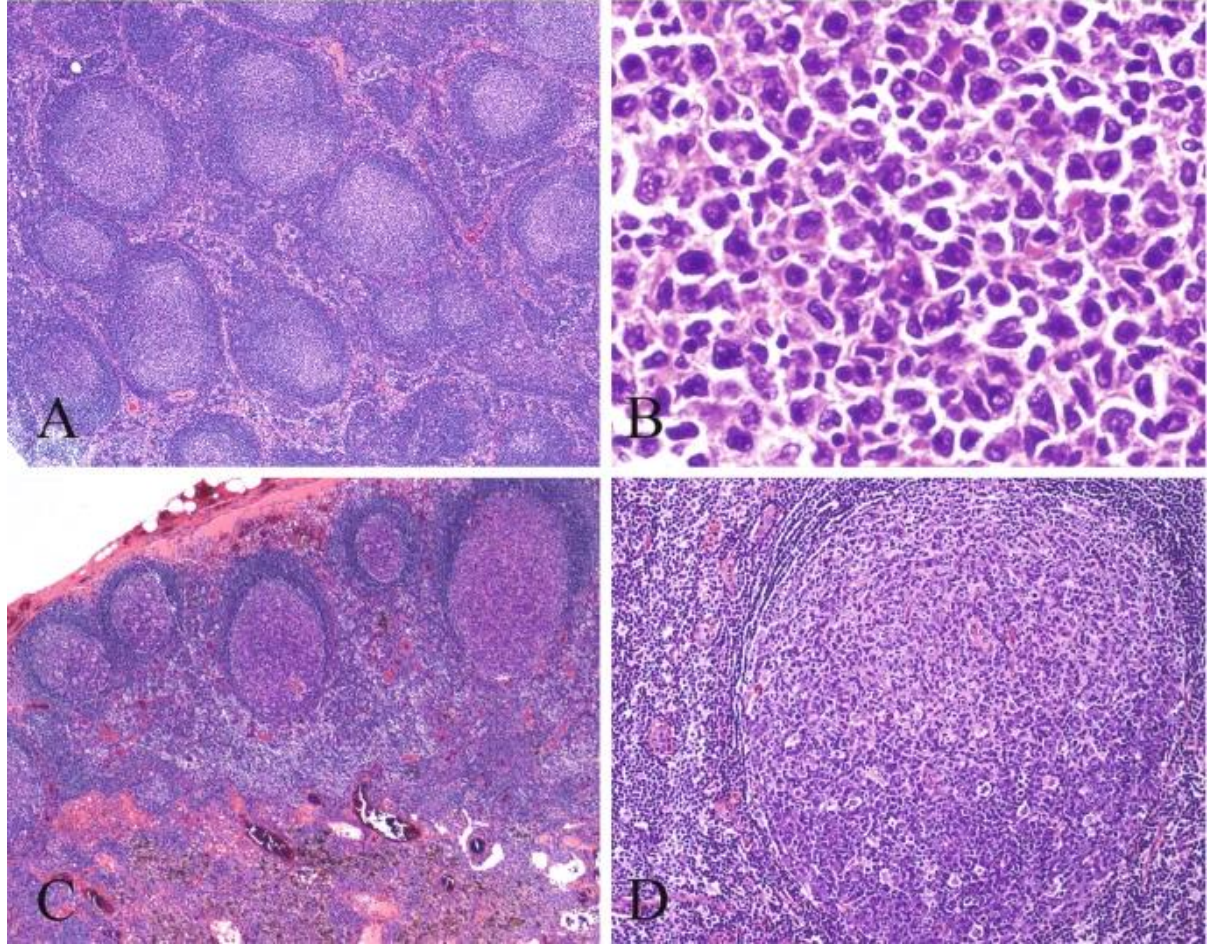
Follicular Lymphoma Clinical

- - Old age (~60 years)
- - Generalized lymphadenopathy & splenomegaly
- - May involve extra-nodal sites (e.g., intestine)
- Pathological feature
- - Effacement of LN architecture
- - Tumor cells form nodules
- - Nodules resemble follicles but:
- - Crowded follicles, absent mantle zones
- - No tingible-body macrophages
- - Monoclonal by IHC
- : IHC of Follicular Lymphoma
- - Positive for CD19 & CD20
- - Positive for BCL2

	Follicular hyperplasia	Follicular lymphoma
Low power	•Loosely packed follicles •Polymorphic follicles •Prominent mantle zone •Polarized follicles •Prominent germinal center •Preserved patent sinuses •No capsular invasion	•Tightly packed follicles •Monomorphic follicles •Absent mantle zone •Non polarized follicles •No detected germinal center •Compressed sinuses •Extension to peri-nodal tissue
H. power	•High mitotic rate in germ center •Tingible body macrophages •Paracortical lymphoid cells between follicles	•Lower mitotic rate •No tingible body macrophages •Atypical lymphoid cells between follicles
IHC	•Polyclonal light chain expression •No reactivity to Bcl-2 expression	•Monoclonal light chain expression •85% positive for bcl-2 expression







Follicular lymphoma and follicular lymphoid hyperplasia. (**a**) Low magnification shows numerous neoplastic follicles with a uniform cell population, lack of polarity, and blurry interface between mantle zone and germinal centers. (**b**) High magnification shows a predominance of small centrocytes and scattered large centroblasts. (**c**) Low magnification of lymph node with follicular lymphoid hyperplasia shows widely spaced lymphoid follicles with polarity, surrounded by distinct mantle zones with polarity, being wider toward the capsule and thinner toward the medullary region. (**d**) High magnification of hyperplastic germinal center with polarity of germinal center cells, dark with a starry sky at the bottom, clear and uniform at the top

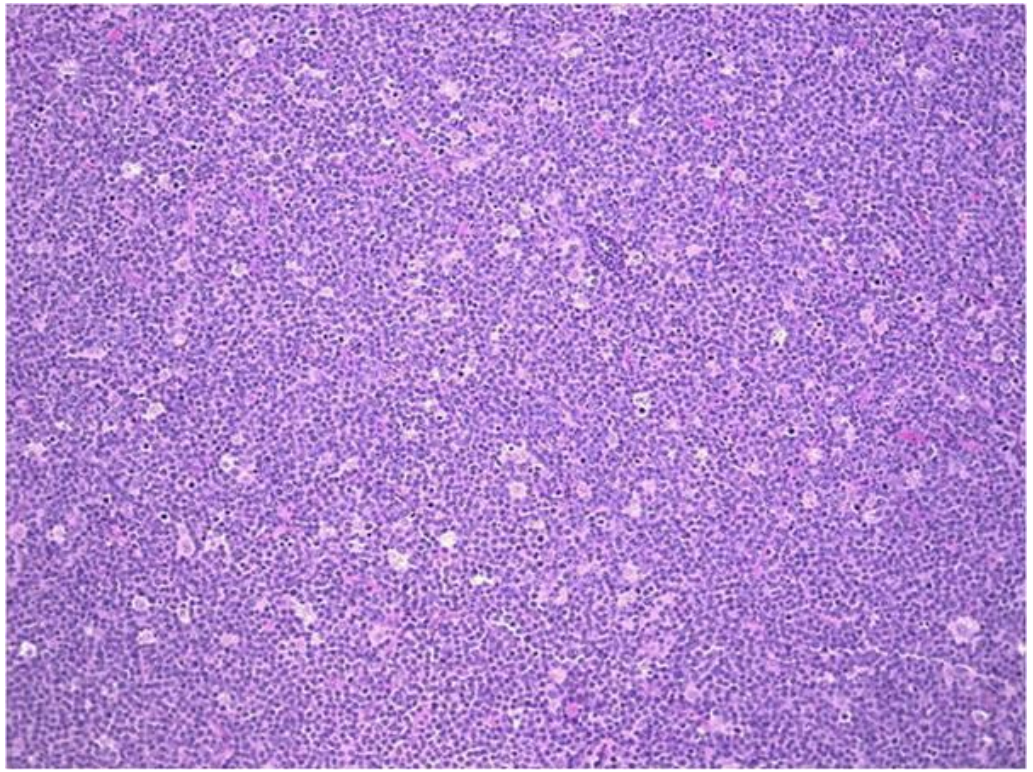
Mantle Cell Lymphoma Clinical

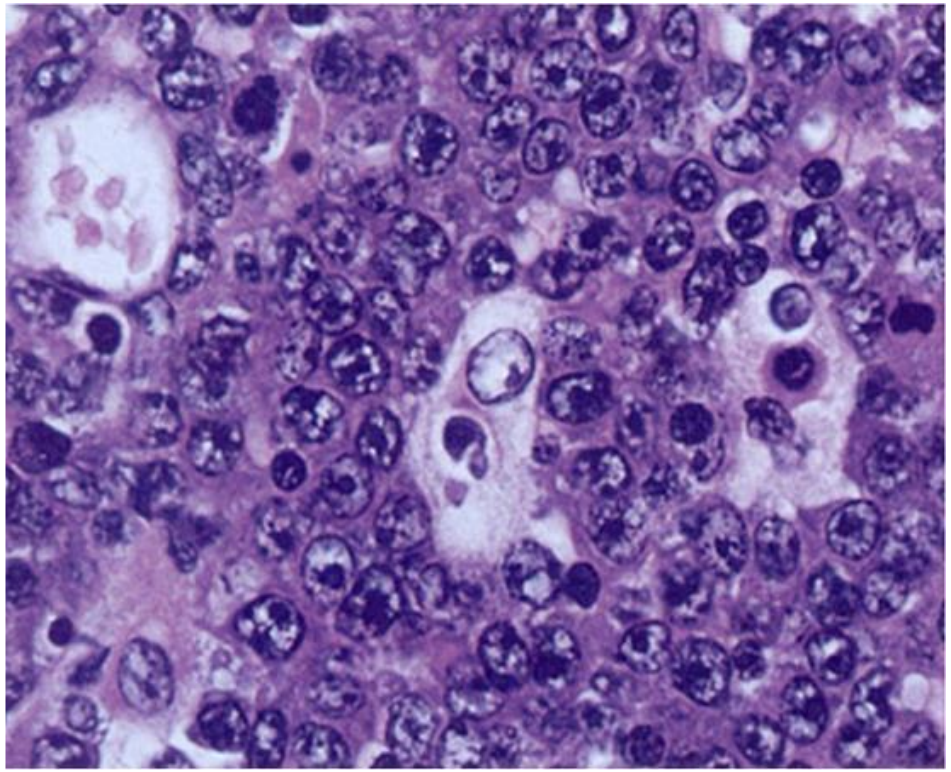
- - ~8% of NHLs
- - Old age
- **- Extra-nodal sites** involved (BM, spleen, liver)
- Mantle Cell Pathological & IHC- Arises from mantle zone B-cells
- - Diffuse or nodular pattern
- - Small/intermediate irregular lymphocytes
- - IHC: CD5+

Burkitt Lymphoma Clinical

- Aggressive B cell lymphoma
- - Also called small non-cleaved cell lymphoma
- - **Types:** Endemic (Africa), Sporadic, HIV-associated
- Burkitt Pathological Features-
- Masses in jaws or abdomen
- - Small lymphocytes, high mitosis
- - Starry-sky appearance from macrophages

Starry-sky appearance



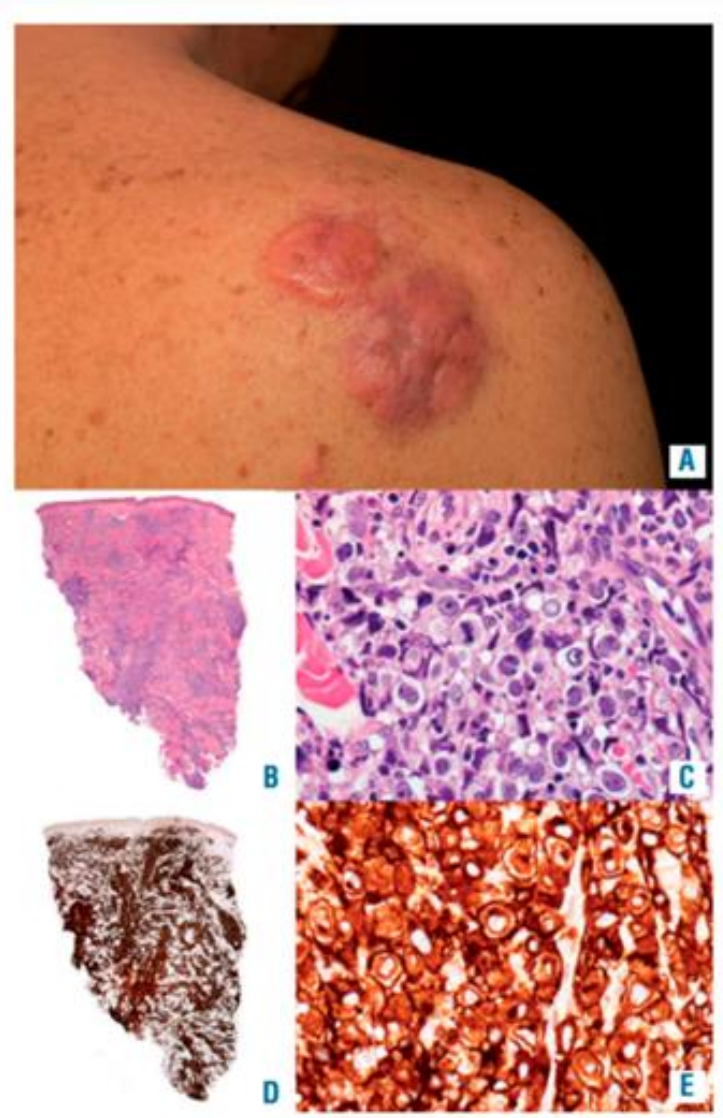


T Cell Lymphoma Example

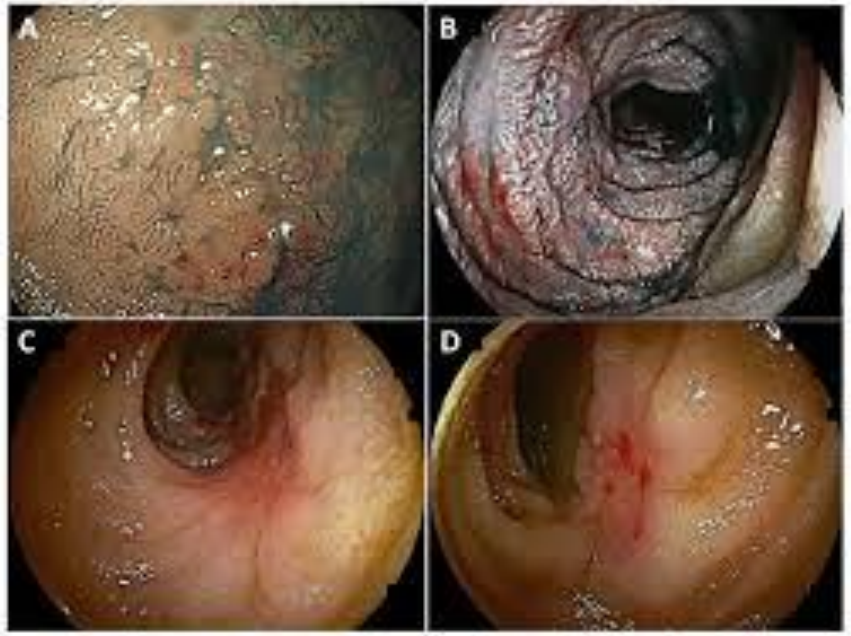
- - Anaplastic large T cell lymphoma (ALTCL)
- - Middle age, generalized lymphadenopathy
- - Aggressive type
- ALTCL Pathological Features
- Effacement of normal nodal architecture
- -Proliferation of atypical (neoplastic) lymphoid

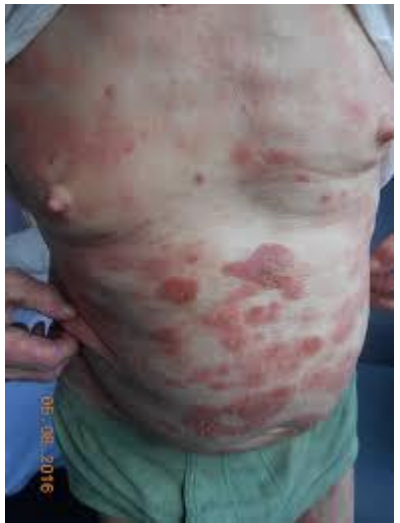
cells with following features:

- Cells are large in size
- Cells have abundant cytoplasm
- Cells have large lobulated nuclei
- Cells are CD30 positive



- Extra-Nodal Lymphoma Example
- B cell Extra-Nodal Lymphoma (NHL)
- Gastric MALT lymphoma
- - B cell, low grade, excellent prognosis
- - Common sites: gastric, salivary, lacrimal glands
- Gastric MALT Pathological
- - Diffuse infiltration of gastric mucosa
- - Small, uniform lymphocytes
- - Lymphoepithelial lesions (destroy glands)
- T cell Extra-Nodal Lymphoma (NHL)
- mycosis fungoides





Diagnosis of Lymphoma

- - Clinical: Generalized LN not responding to treatment
- - Histological: Loss of architecture + atypical cells
- - IHC: Tissue markers for diagnosis & subtyping
- Importance of Subtyping-
- Treatment: Specific target therapy available
- - Prognosis: Indolent vs aggressive subtypes
- - Histology alone not conclusive for separation
- : IHC for Lymphoma Subtypes
- - B cell lymphomas: CD20+
- - T cell lymphomas: CD3+
- - Burkitt: CD10+
- - Follicular: Bcl-2+
- - Anaplastic large cell: CD30+
- - Hodgkin: CD15+ & CD30+

Clinical Staging of Lymphoma

- - Four stages based on LN groups & diaphragm
- - Similar to Hodgkin staging system
- Metastatic Carcinoma in LNs
- Definition: Epithelial malignant deposits in LNs
- - Gross: Enlarged, discrete/fused, grayish-white
- - Microscopic: Replacement by epithelial tumor
- Clinical Importance of LN Metastasis
- Essential for TNM staging
- - Guides treatment & prognosis
-

Lymphadenopathy

- Definition & Types - Enlargement of ≥1 LN groups
- - Localized: One group
- - Generalized: >1 group
- Causes of Lymphadenopathy- Inflammatory: Acute/chronic lymphadenitis
- - Autoimmune: RA, SLE, Sjögren’s
- - Neoplastic: Metastasis, lymphoma, leukemia
- - Drug-induced, reactive hyperplasia