

Lymphoma Diagnostic Work-up from a Lab Perspective

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Lymphoproliferative Disorders

- **Malignant lymphoma**
 1. Non-Hodgkin lymphoma (NHL)
 2. Hodgkin (disease) lymphoma
 3. Multiple myeloma

Basic concepts

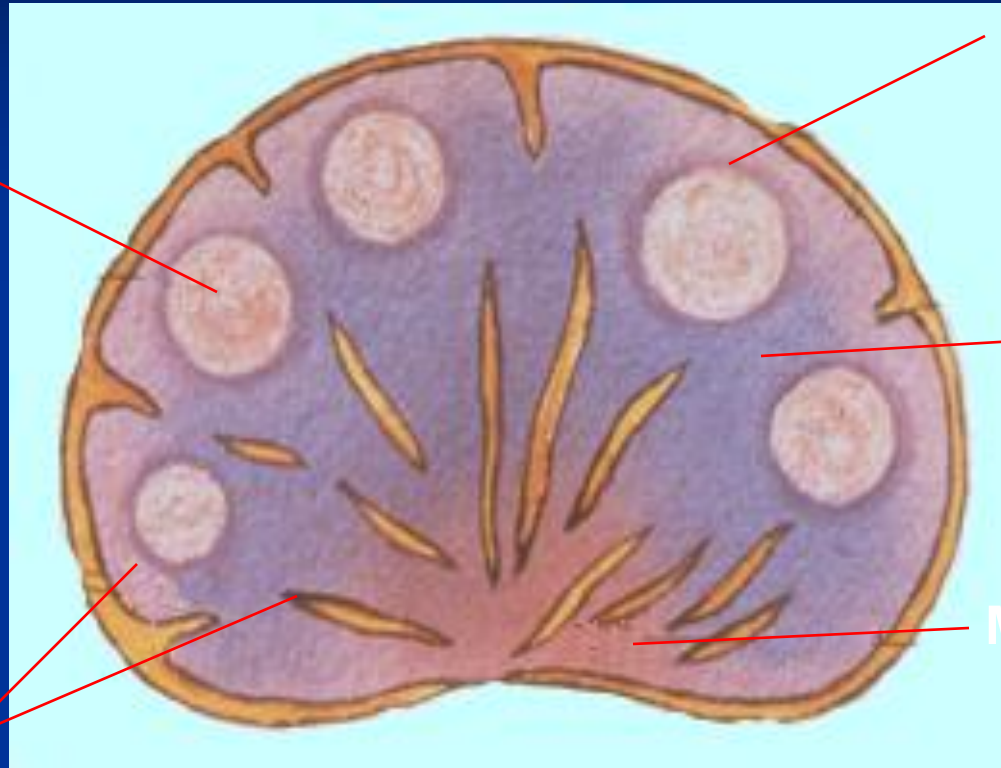
- Lymphomas are solid tumors of the hematopoietic system. Neoplasms of lymphoid origin, typically causing lymphadenopathy
- leukemia vs. lymphoma
 - Leukemias as systemically distributed neoplasms of white cells

Very important concept.....

☞ lymphomas and leukemias are clonal expansions of cells at certain developmental stages



Follicle / germinal
center (B cell)



Mantle zone
(B-cell)

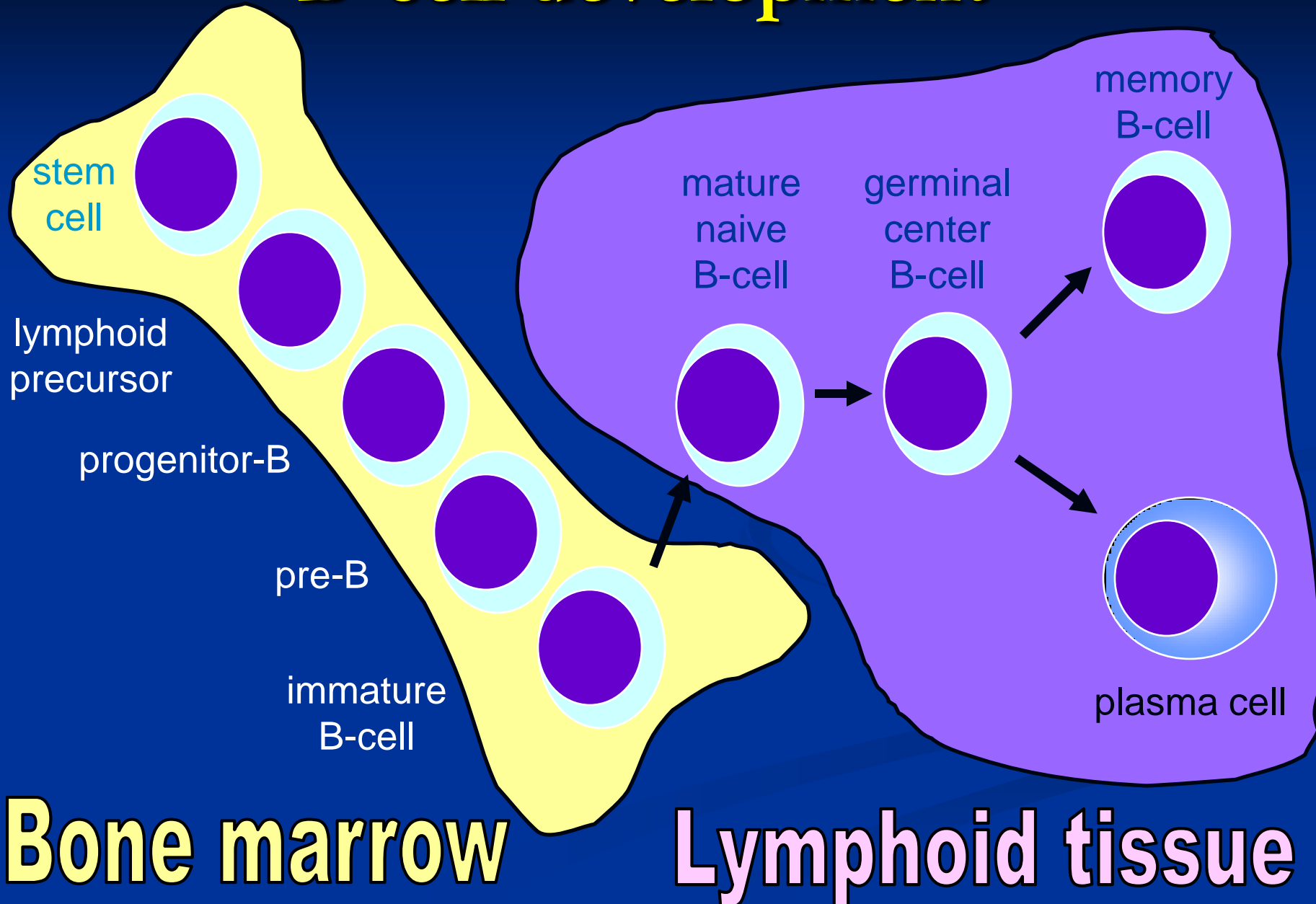
Paracortex
(T-cell)

Medullary cord
(B-cell)

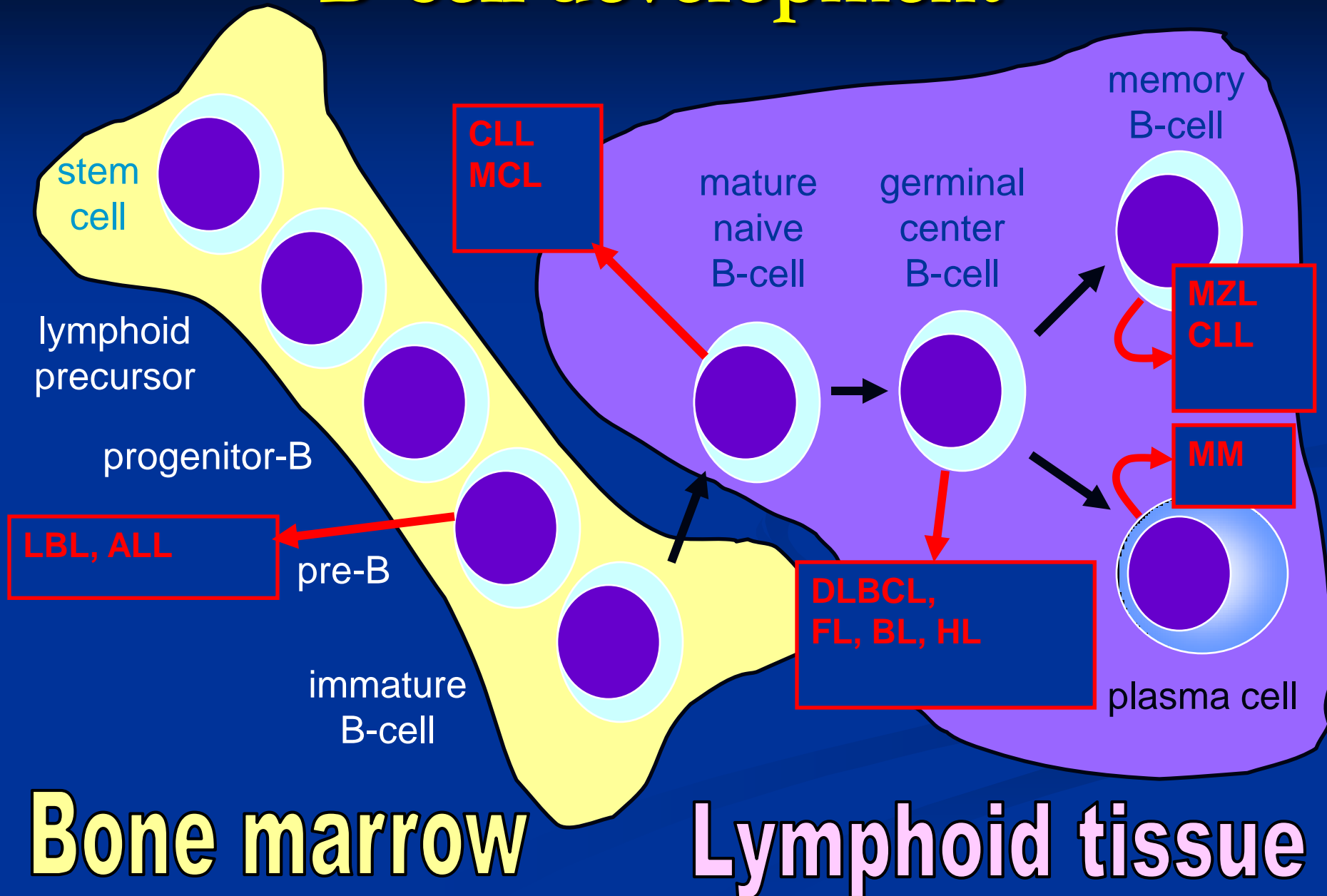
Lymphatic sinus

NORMAL LYMPH NODE

B-cell development



B-cell development



A practical way to think of lymphoma

Category		Survival of untreated patients	Curability	To treat or not to treat
Non-Hodgkin lymphoma	Indolent	Years	Generally not curable	Generally defer Rx if asymptomatic
	Aggressive	Months	Curable in some	Treat
	Very aggressive	Weeks	Curable in some	Treat
Hodgkin lymphoma	All types	Variable – months to years	Curable in most	Treat

Non-Hodgkin Lymphomas

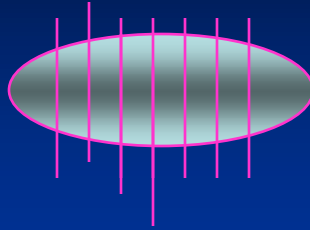
How do we diagnose and classify these types of lymphoproliferative disorders?

- ♦ Architectural pattern
- ♦ Cytologic (cellular) morphologic appearance
- ♦ Immunophenotypic (antigenic) characteristics
- ♦ Molecular / genetic characteristics

Diagnosis requires an adequate biopsy

- Diagnosis should be biopsy-proven before treatment is initiated
- Need enough tissue to assess cells and architecture
 - open bx vs core needle bx vs FNA

Lymph Node Protocol



Permanent sections
Morphologic evaluation

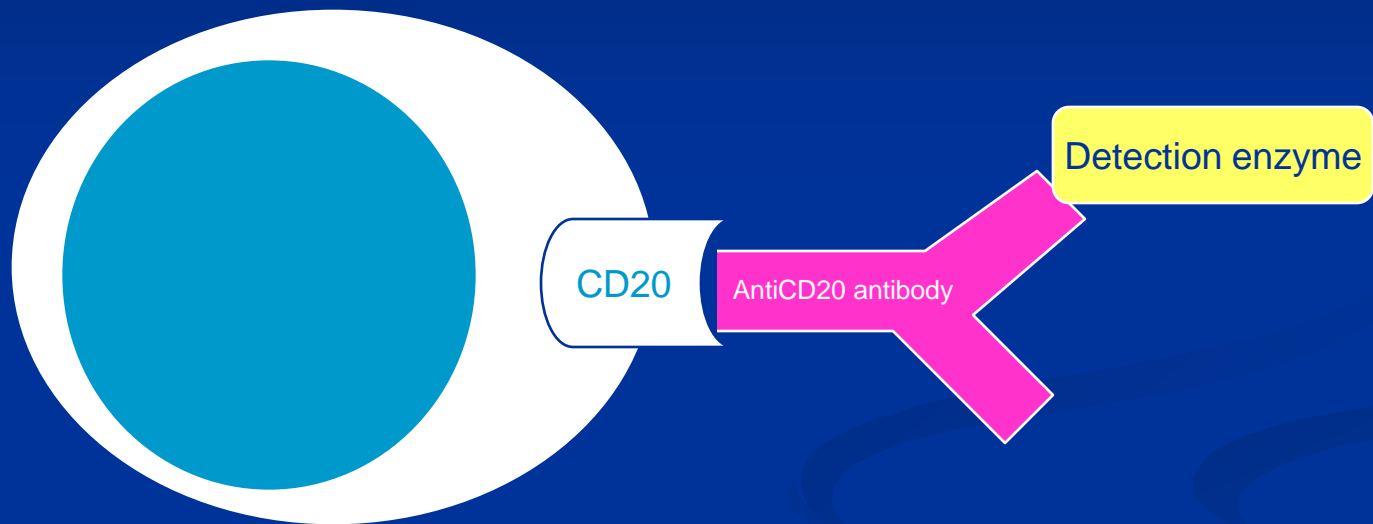


Flowcytometry

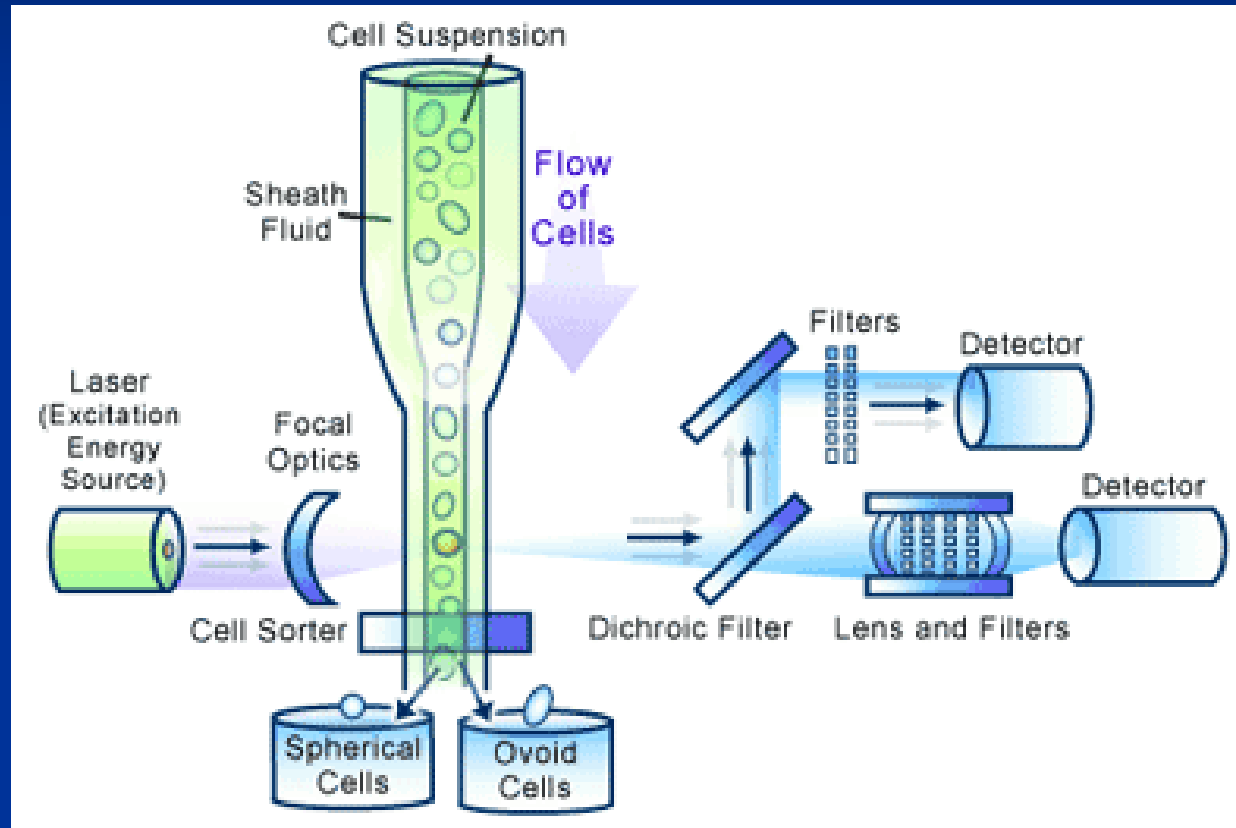
Immunostains

Cytogenetics

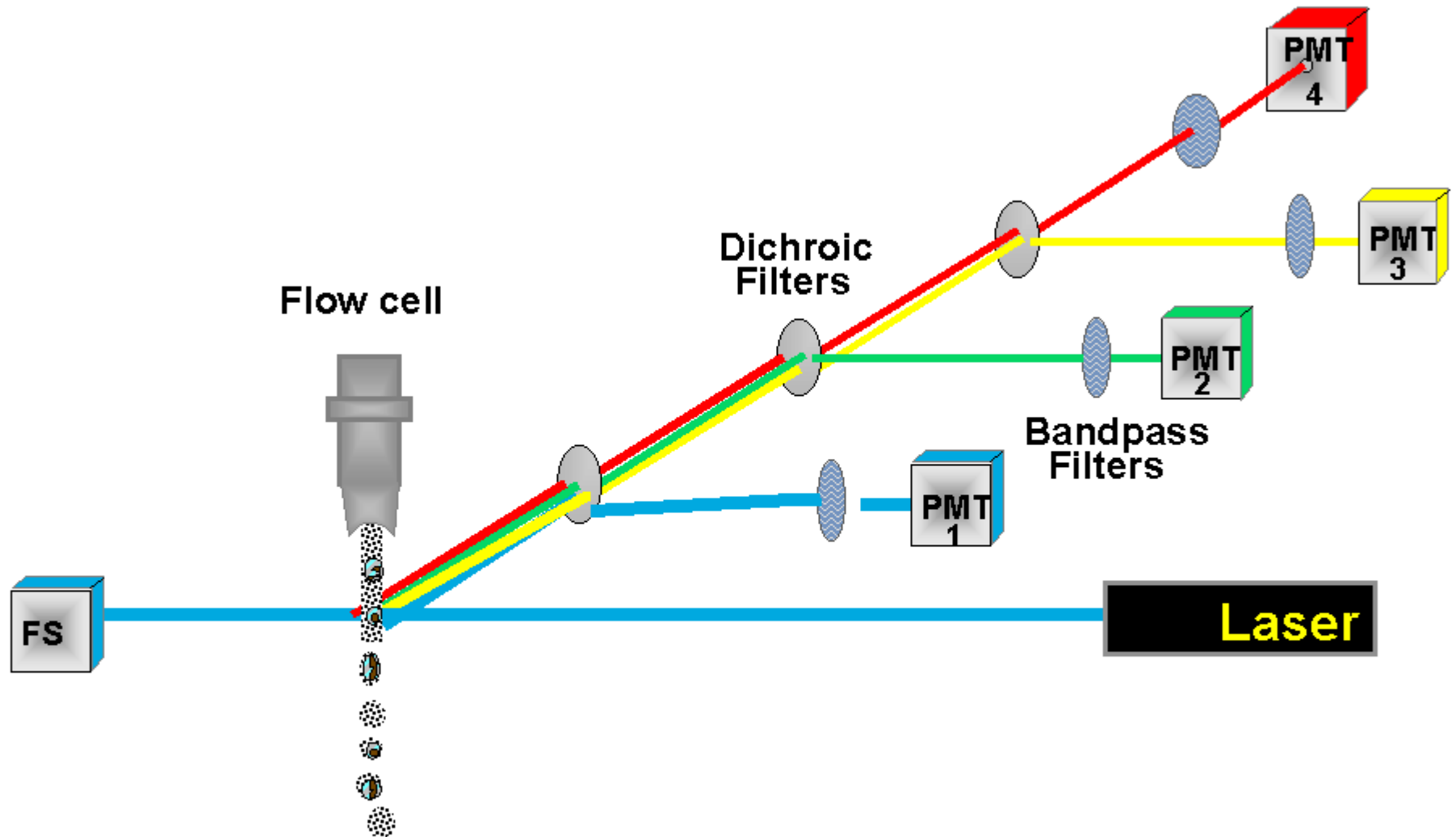
Molecular



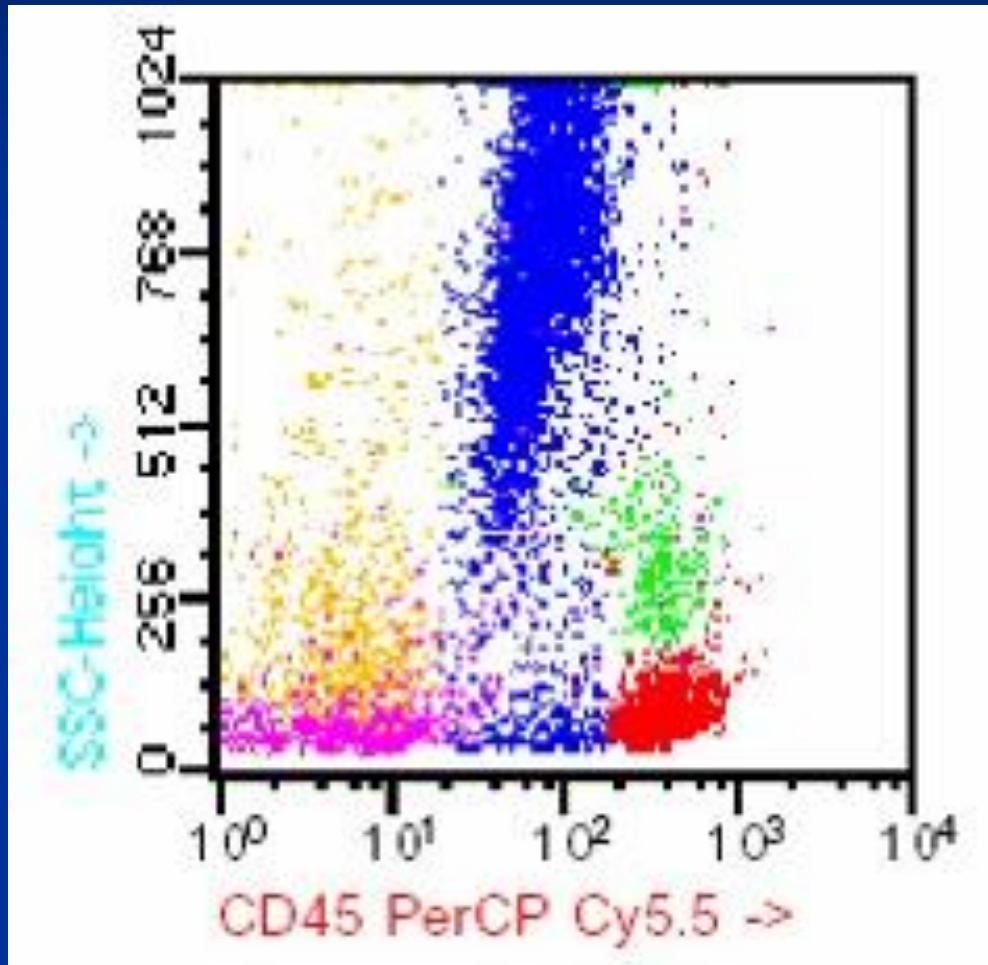
Flow-cytometry

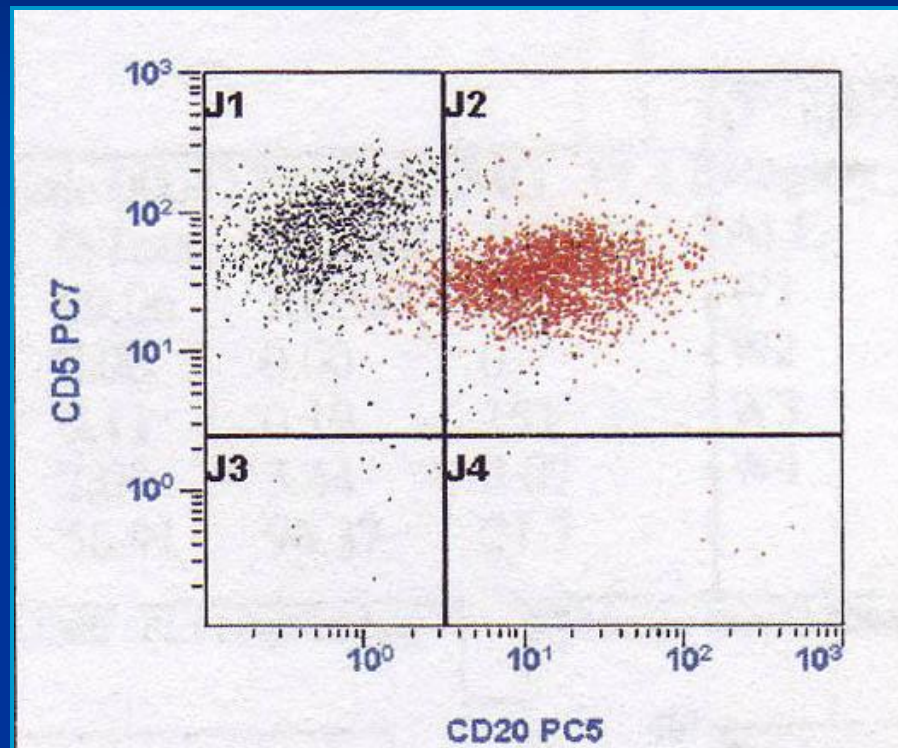


Flow-cytometry

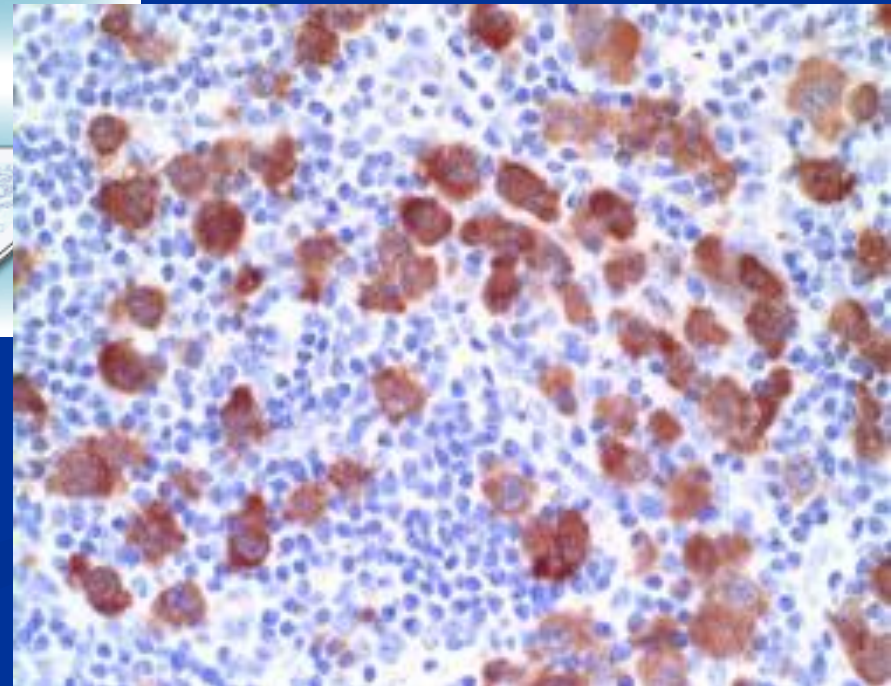
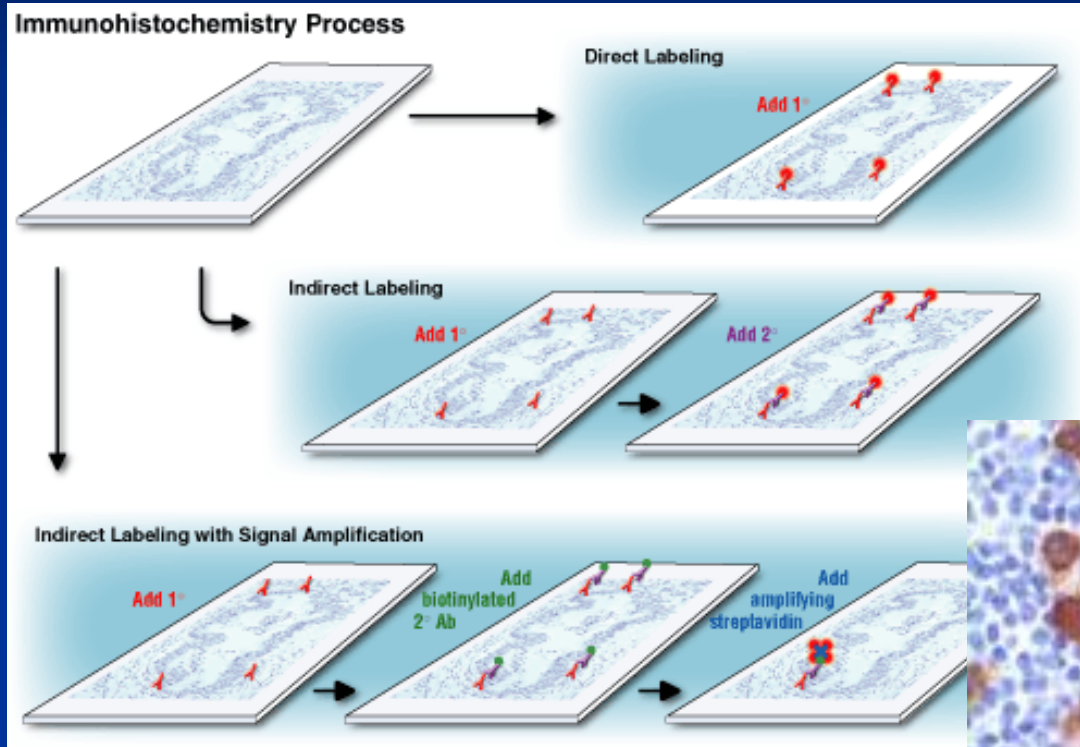


Flow-cytometry





Immunostains



Non-Hodgkin Lymphomas

- Neoplasm of the immune system
- B-cells, T-cells, histiocytes
- Usually begin in the lymph nodes, but may arise in other lymphoid tissues such as spleen, bone marrow, or extranodal sites

Clinical Findings

- Enlarged, painless lymphadenopathy
- B-symptoms-fever, weight loss
- Impingement or obstruction of other structures

Subtypes of Non-Hodgkin Lymphoma

	Frequency	%
I Diffuse Large B cell Lymphoma	422	31
L Follicular Lymphoma	306	22
L Chronic Lymphocytic Leukemia	88	6
I Mantle Cell Lymphoma	83	6
L Marginal Zone B-cell Lymphoma,MALT-type	72	5
L Marginal Zone B-cell Lymphoma,Nodal	20	1
L Lymphoplasmacytic Lymphoma	15	1
H Burkitt Lymphoma	10	<1
H Burkitt-like Lymphoma	29	2
H Lymphoblastic Lymphoma T/B	26	2
I Peripheral T cell Lymphoma	76	6
I Anaplastic Large T-/Null cell Lymphoma	33	2

Most common types of lymphoma

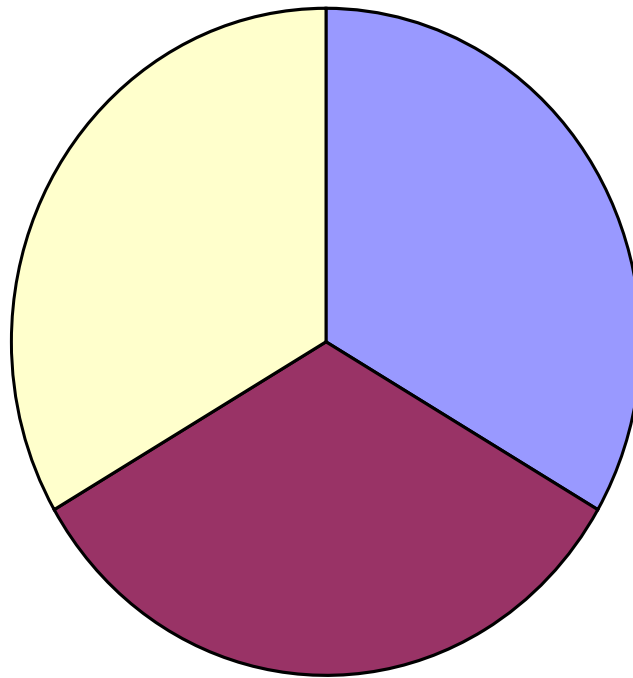
1. Non-Hodgkin lymphoma (NHL)
 - SLL/CLL
 - Follicular lymphoma
 - Diffuse large B cell lymphoma
 - Burkitt's lymphoma
2. Hodgkin lymphoma (HL)

Non-Hodgkin lymphoma

Incidence

Diffuse
large B-cell
lymphoma

Follicular
lymphoma



Other NHL

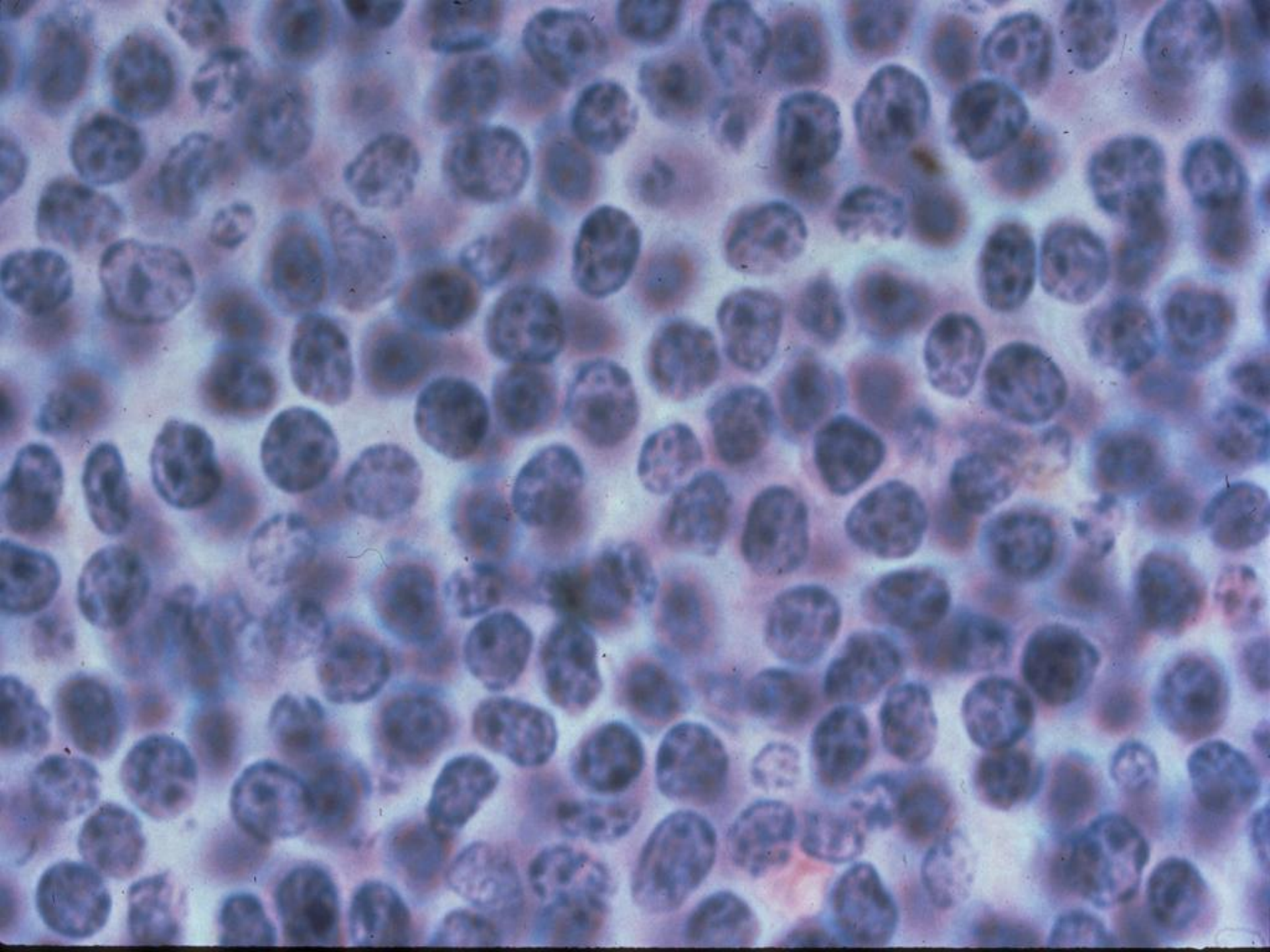
General Features

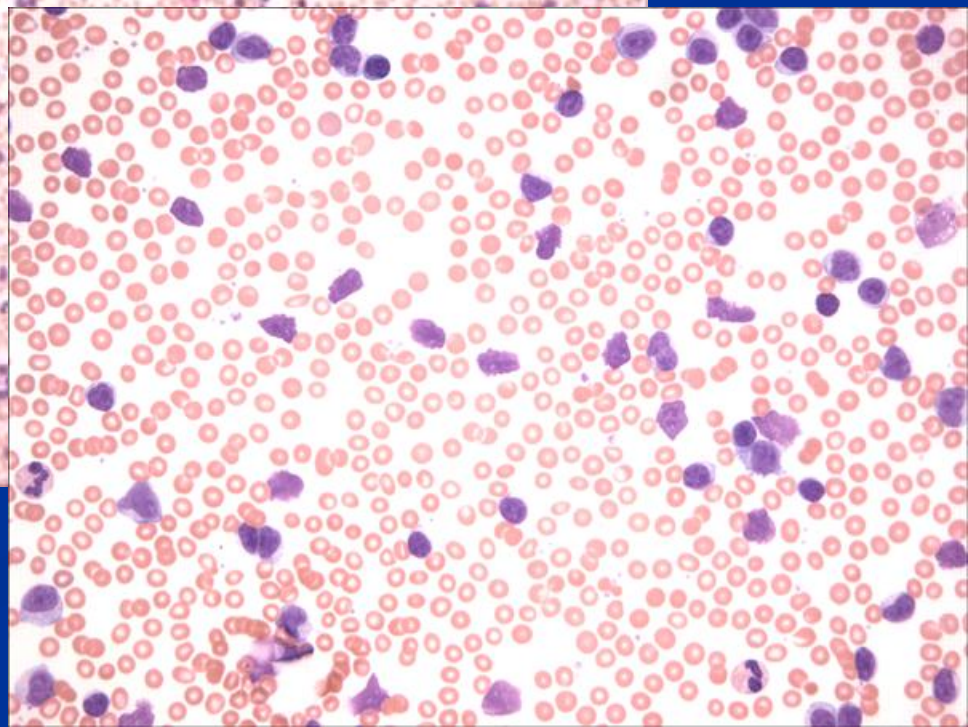
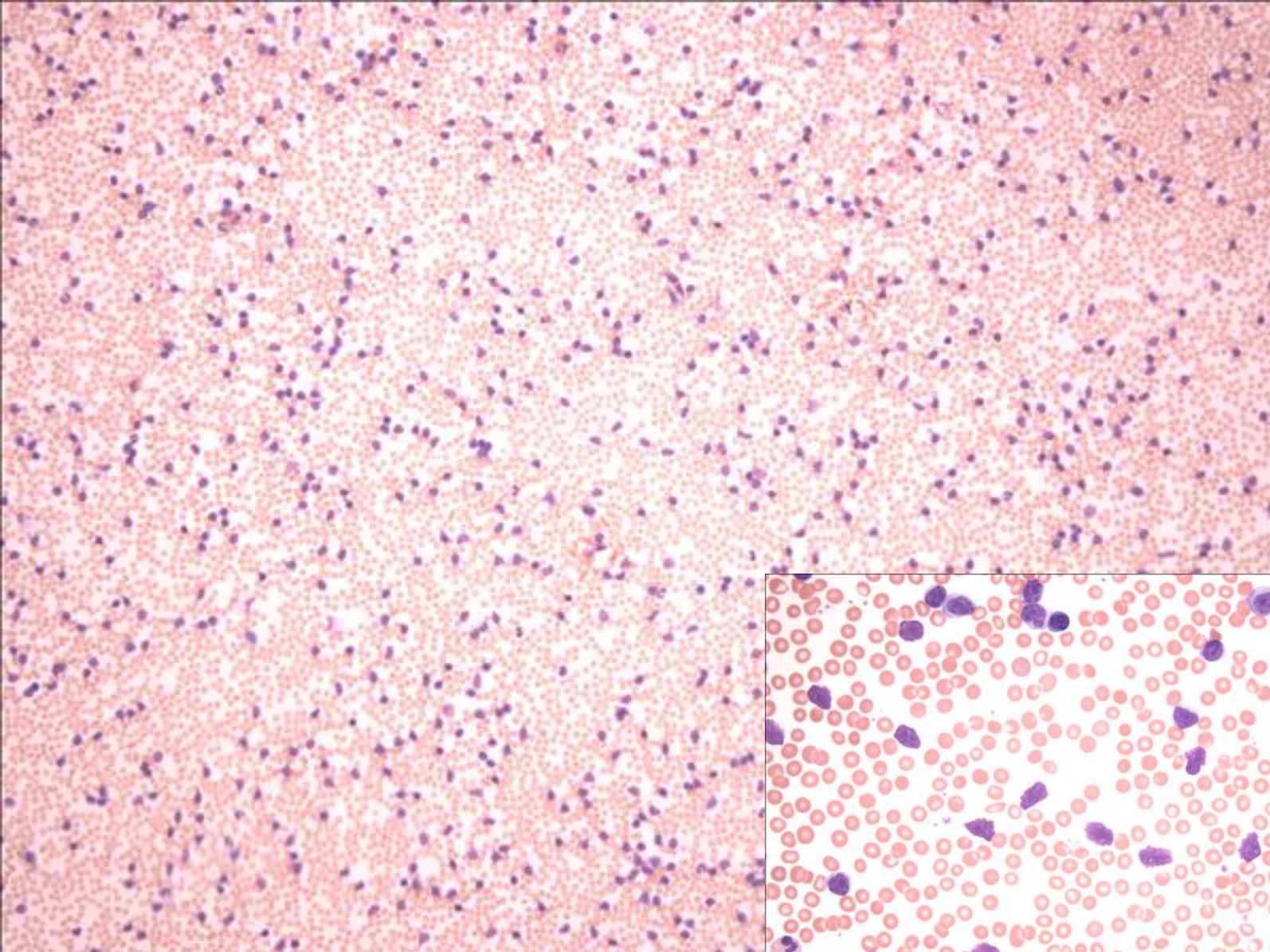
Low Grade Lymphomas

- Adult population affected (median age, 50-70 years)
- Rare in children
- High stage disease (III/IV) is most common
- Indolent course with relatively long survival
- Generally incurable
- Transformation to higher grade NHL may occur

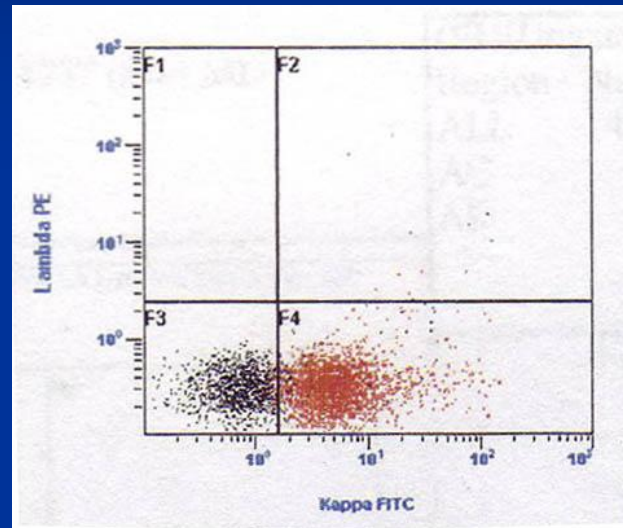
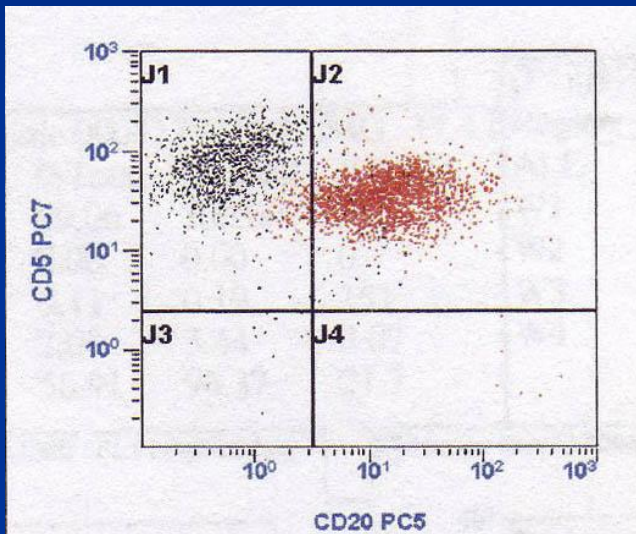
Small Lymphocytic Lymphoma

- Low grade B-cell malignancy
- Similar to chronic lymphocytic leukemia (CLL)
- Frequency - $\sim 4\%$ of NHL
- Older age group (median, 60.5 years)
- Bone marrow involvement: Common
- Indolent course





Flow cytometry



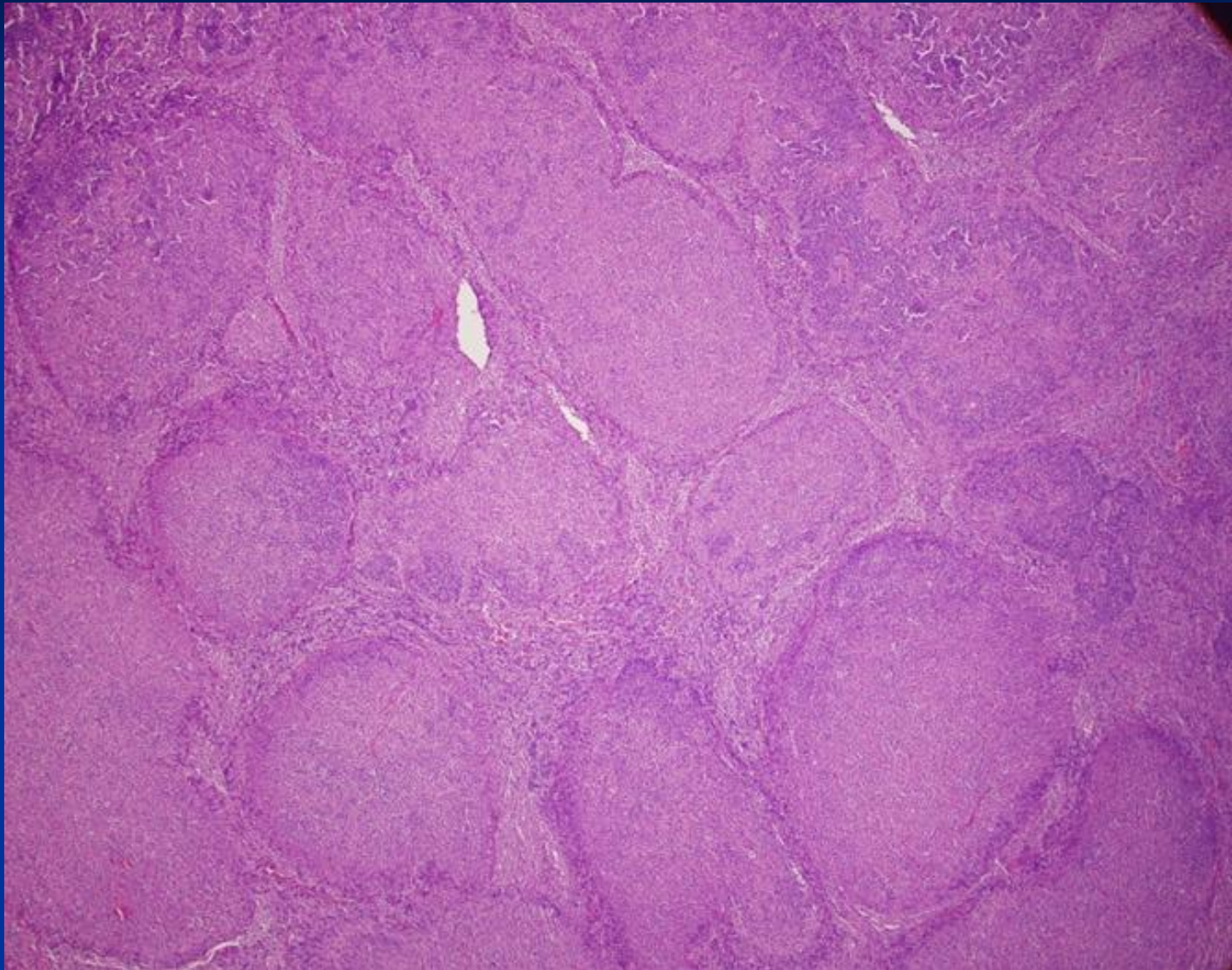
Follicular Lymphomas

- Frequency - ~40% of NHL (most common)
- Older age group (median, 55 years)
- Often asymptomatic
- Bone marrow involvement: Common
- Indolent Course
- Chromosomal translocation, t(14;18)

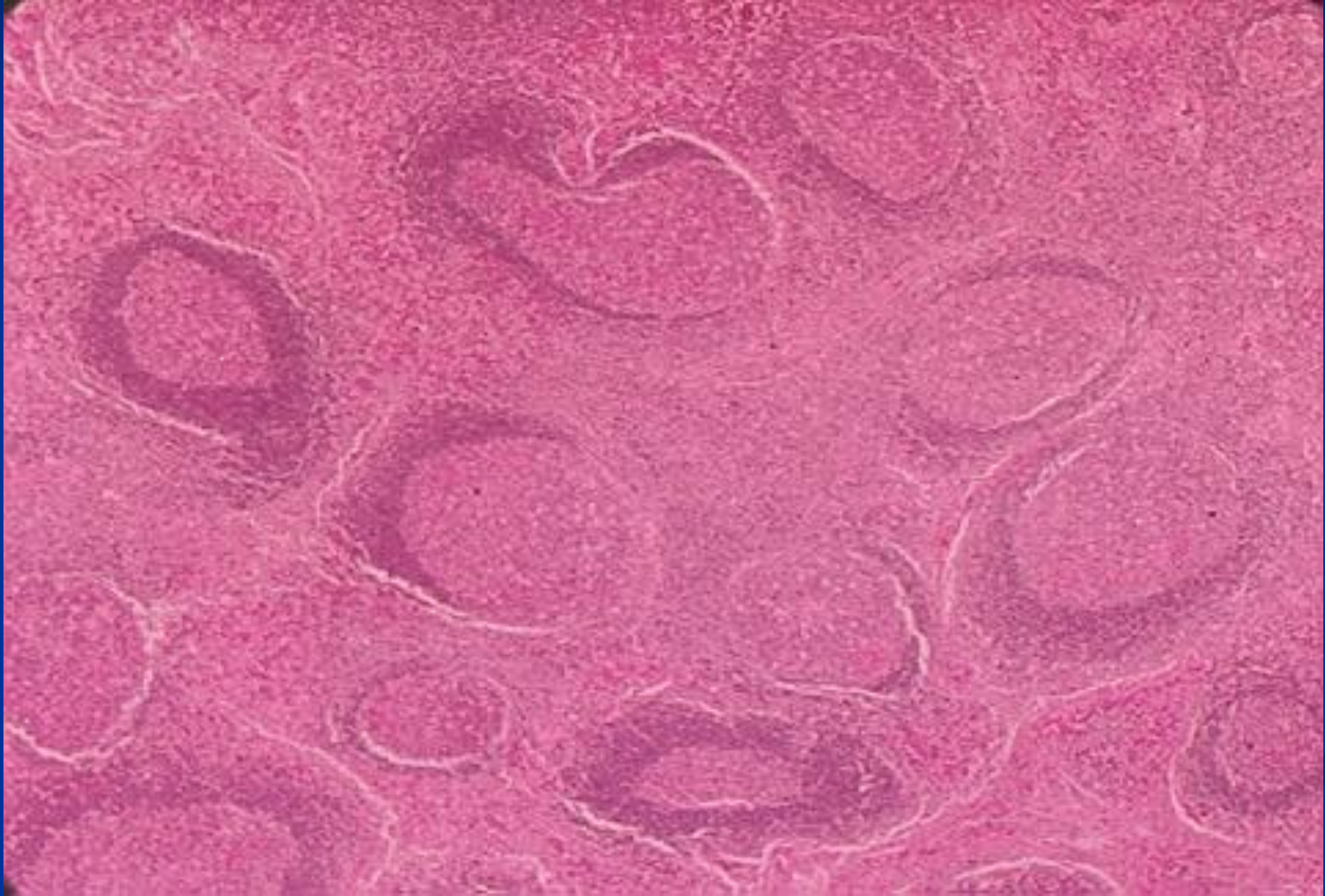
Follicular Lymphomas

- Several chemotherapy options if symptomatic
- Median survival: years
- Transformation to more aggressive B-cell lymphoma

Follicular Lymphoma



Reactive Follicular Hyperplasia



Architectural Features

Distinguishing Reactive Follicular Hyperplasia and Follicular NHL

	Reactive Follicular Hyperplasia	Follicular NHL
Nodal Architecture	Preserved	Effaced
Germinal Center Size & Shape	Marked variation	Slight to moderate variation
Capsular infiltration	None or minimal	Invasion with extension into pericapsular fat
Density of follicles	Low, with intervening lymphoid tissue	High, with back to back follicles
Morphology of follicles	Sharply defined, mantle zone	Ill defined, no mantle zone

Intermediate Grade/Aggressive

Mantle cell lymphoma

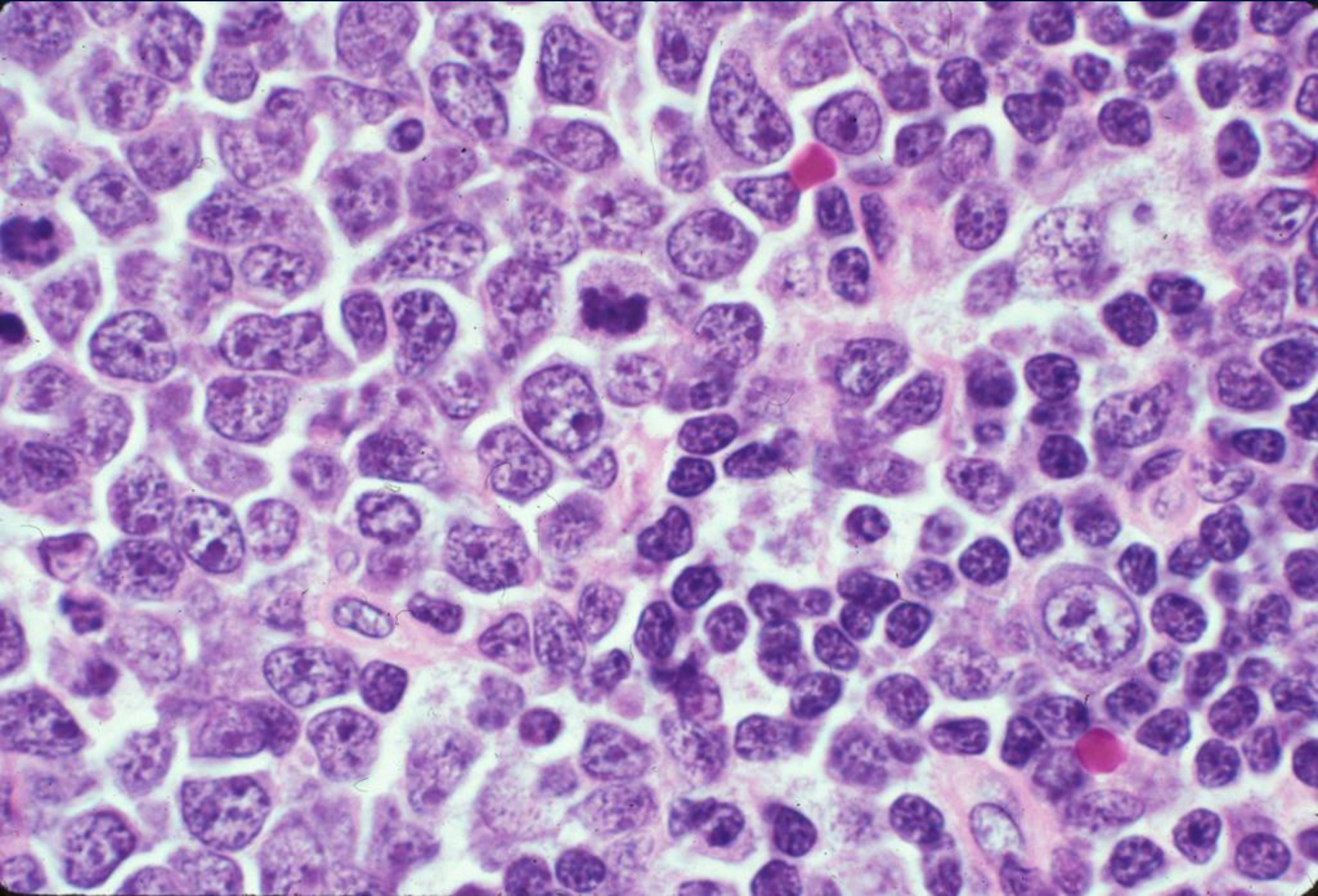
t(11;14) translocation results in
over- expression of cyclin D1 protein

Diffuse large cell lymphoma

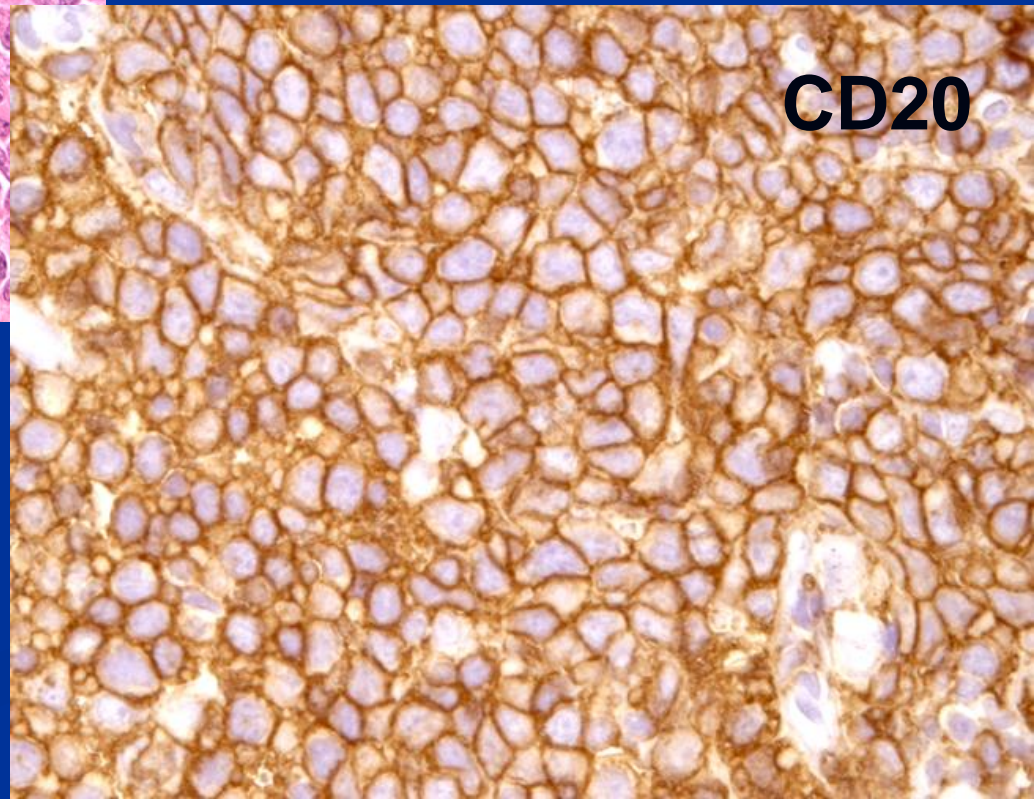
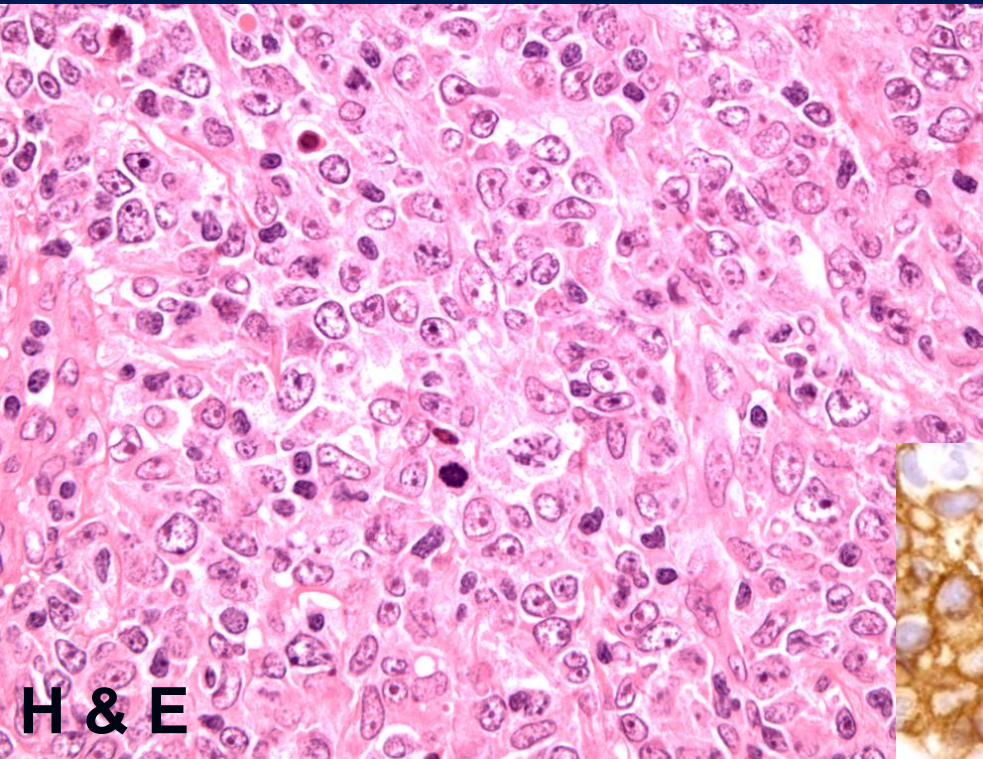
Diffuse Large Cell

- 60-70% derived from B-cells
- Often stage I or II at diagnosis
- More likely to have extranodal sites
- Peripheral blood involvement is rare

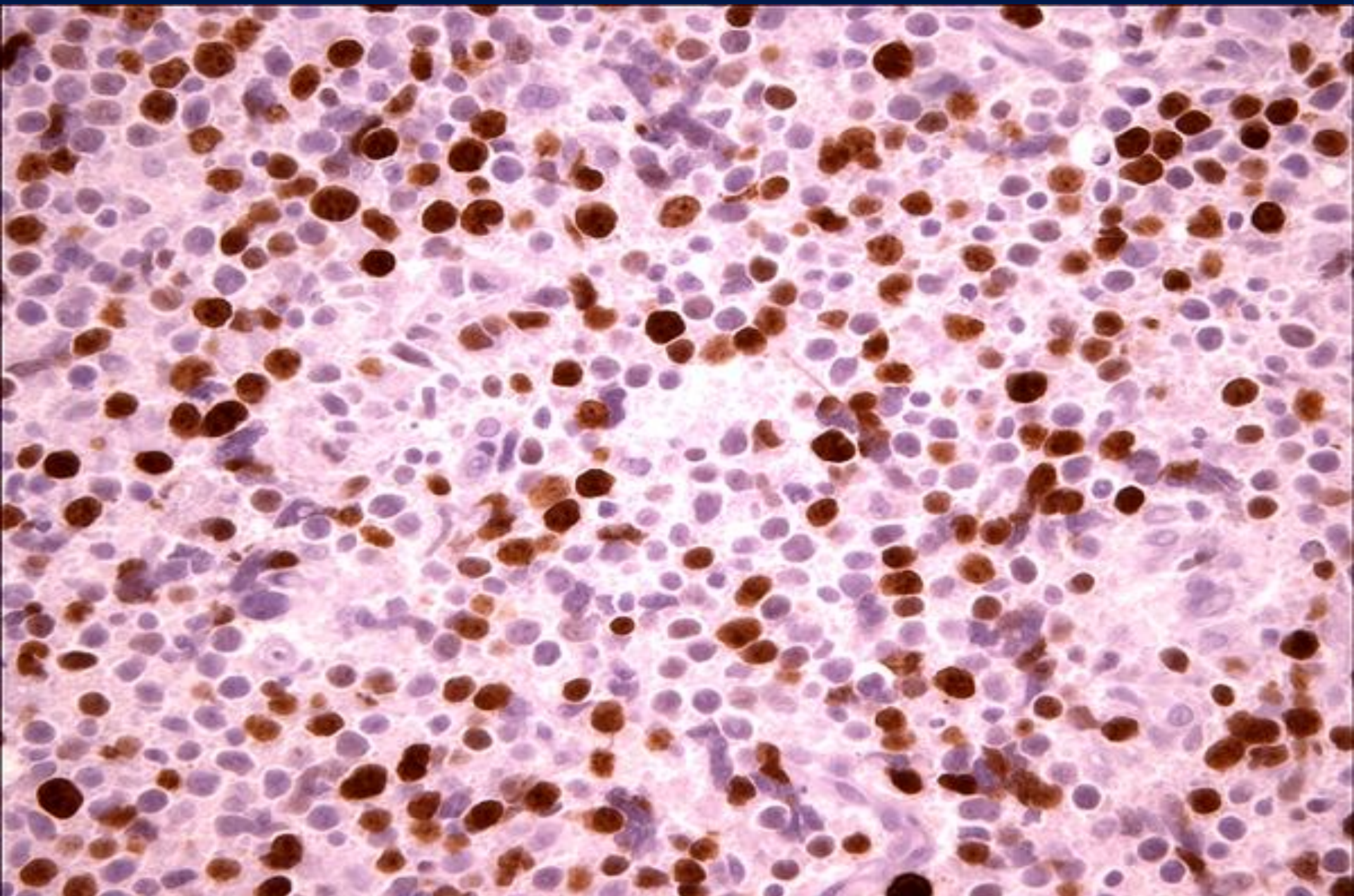
Diffuse large B-cell lymphoma



Diffuse Large B-cell Lymphoma



MIB-1



High Grade (small non-cleaved)

Burkitt lymphoma

- Endemic in Africa
- Seen in children and related to Epstein-Barr virus
- Usually extranodal

AIDS associated lymphoma

Clinical Findings

- Enlarged painless lymphadenopathy
- B-symptoms, fever, sweats, weight loss
- Impingement or obstruction of adjacent structures (mass effect)
- Extranodal presentation (30% of cases)
GI tract, spleen, salivary gland

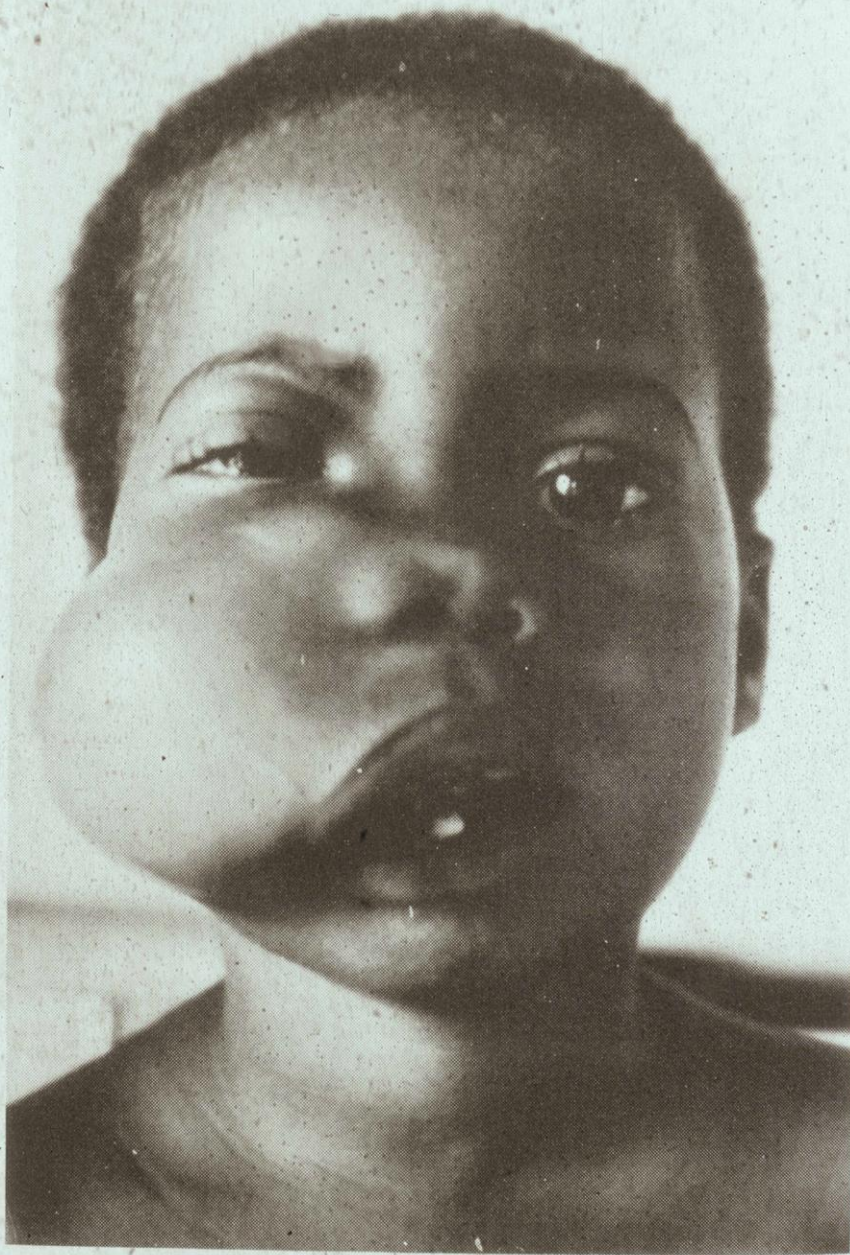
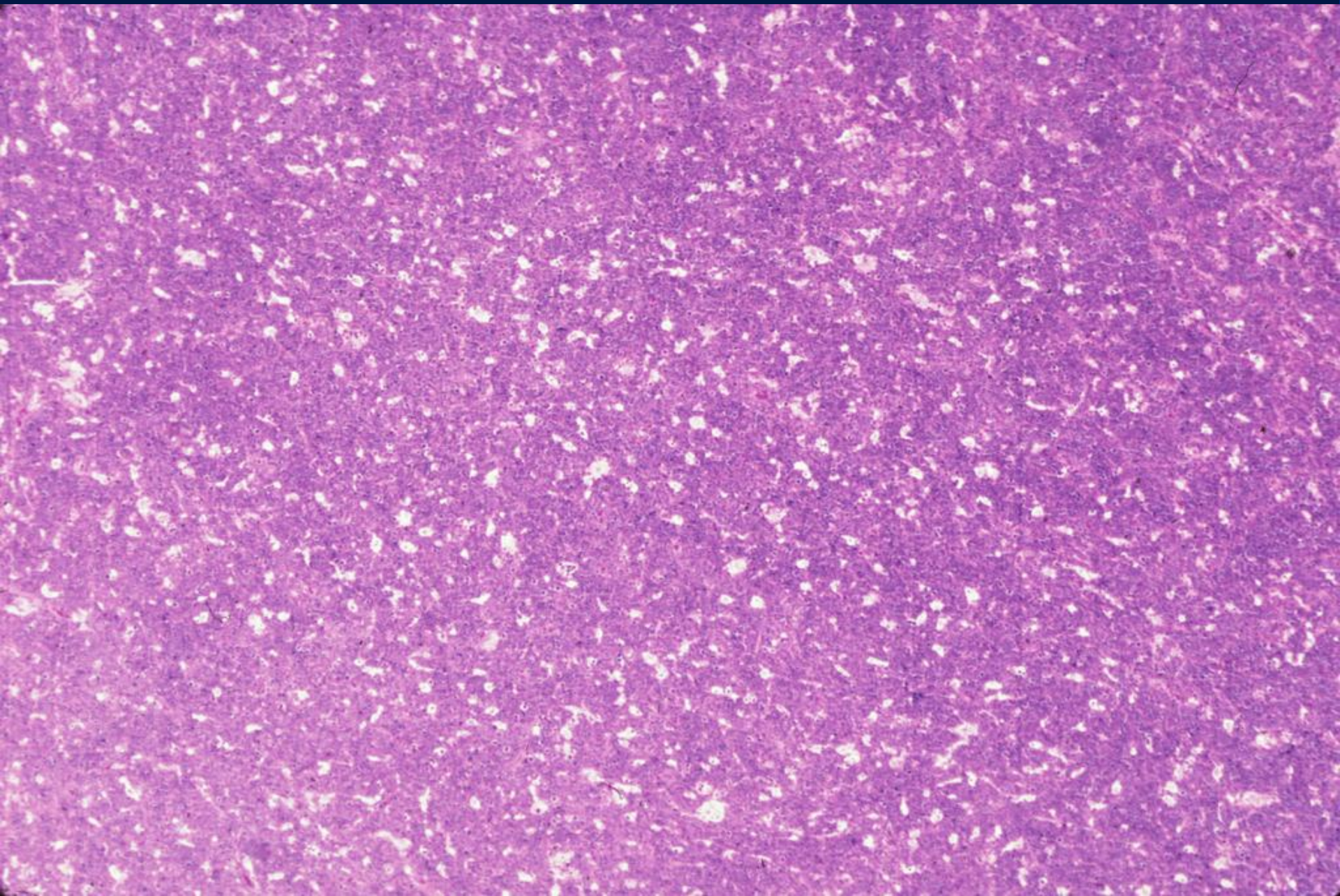


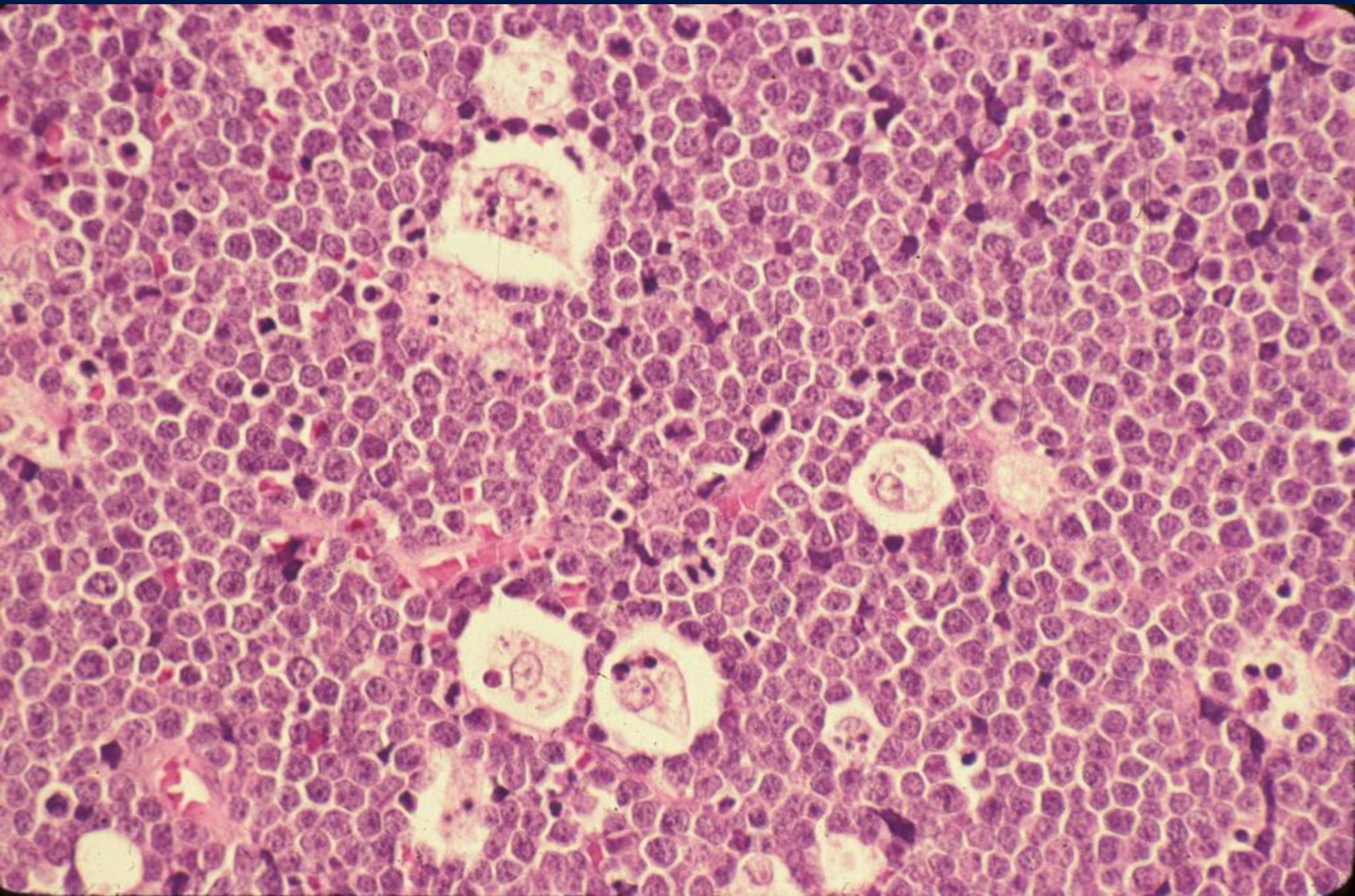
FIGURE 10-6. Burkitt's lymphoma in a nine-year-old child. The maxillary tumor mass is a characteristic presentation of this disease.

Burkitt lymphoma involving jaw

Burkitt lymphoma - Starry-sky pattern



Burkitt lymphoma tingible-body macrophages



High grade

❑ Burkitt lymphoma

- Endemic in Africa
- Seen in children and related to Epstein-Barr virus
- B-cell phenotype
- t(8:14) MYC/IgH
- Usually extranodal
- High mitotic rate (starry-sky)

❑ Lymphoblastic lymphoma

Sum...

■ Indolent Lymphomas

- Very slow growing, over years.
- Follicular lymphoma, grades I/II is prototype.
- If can't cure, goal is to control disease/symptoms.
- Decision of WHEN to treat is important.

■ Aggressive Lymphomas

- Rapidly growing, over days, months.
- Diffuse large B cell lymphoma is prototype.
- Cure is possible.
- About 50% with multi-agent chemotherapy.