

# 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

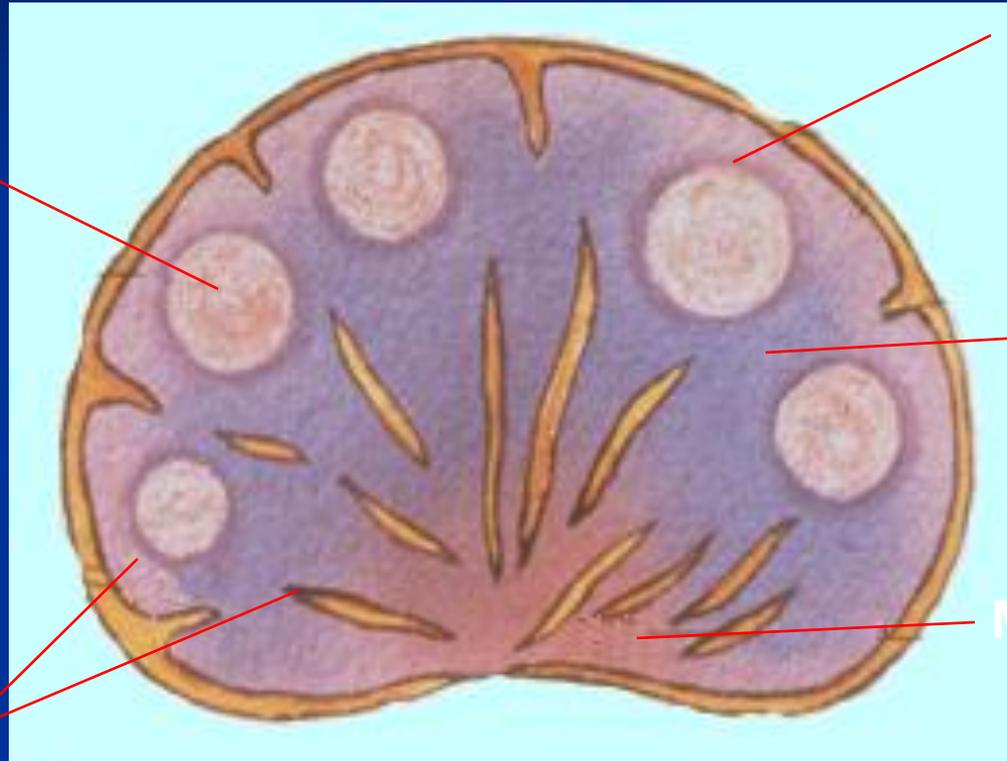
- Lymphomas are solid tumors of the hematopoietic system. Neoplasms of lymphoid origin, typically causing lymphadenopathy
- leukemia vs. lymphoma
  - Leukemias as systemically distributed neoplasms of white cells

Very important concept.....

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



Follicle / germinal center (B cell)



Mantle zone  
(B-cell)

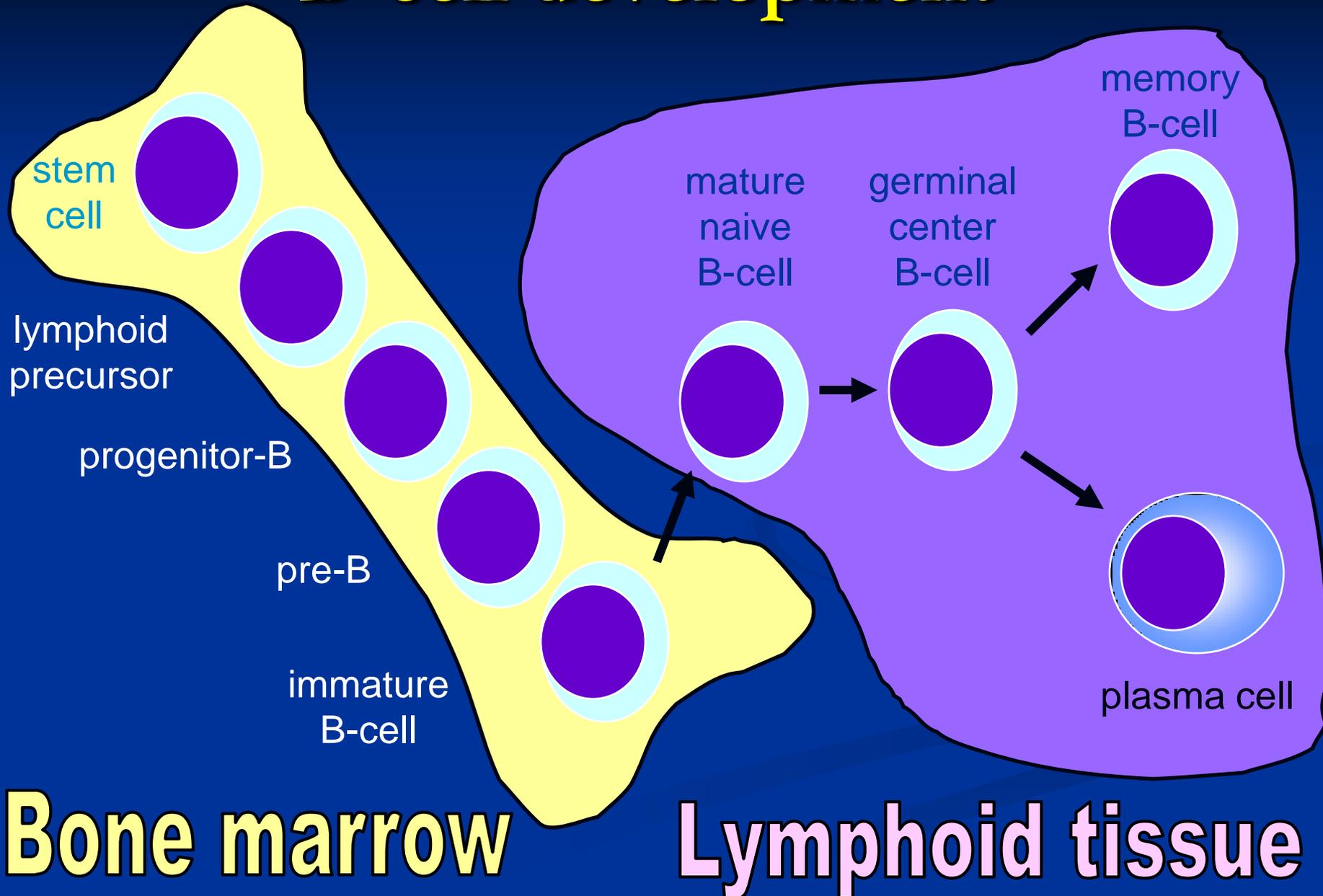
Paracortex  
(T-cell)

Medullary cord  
(B-cell)

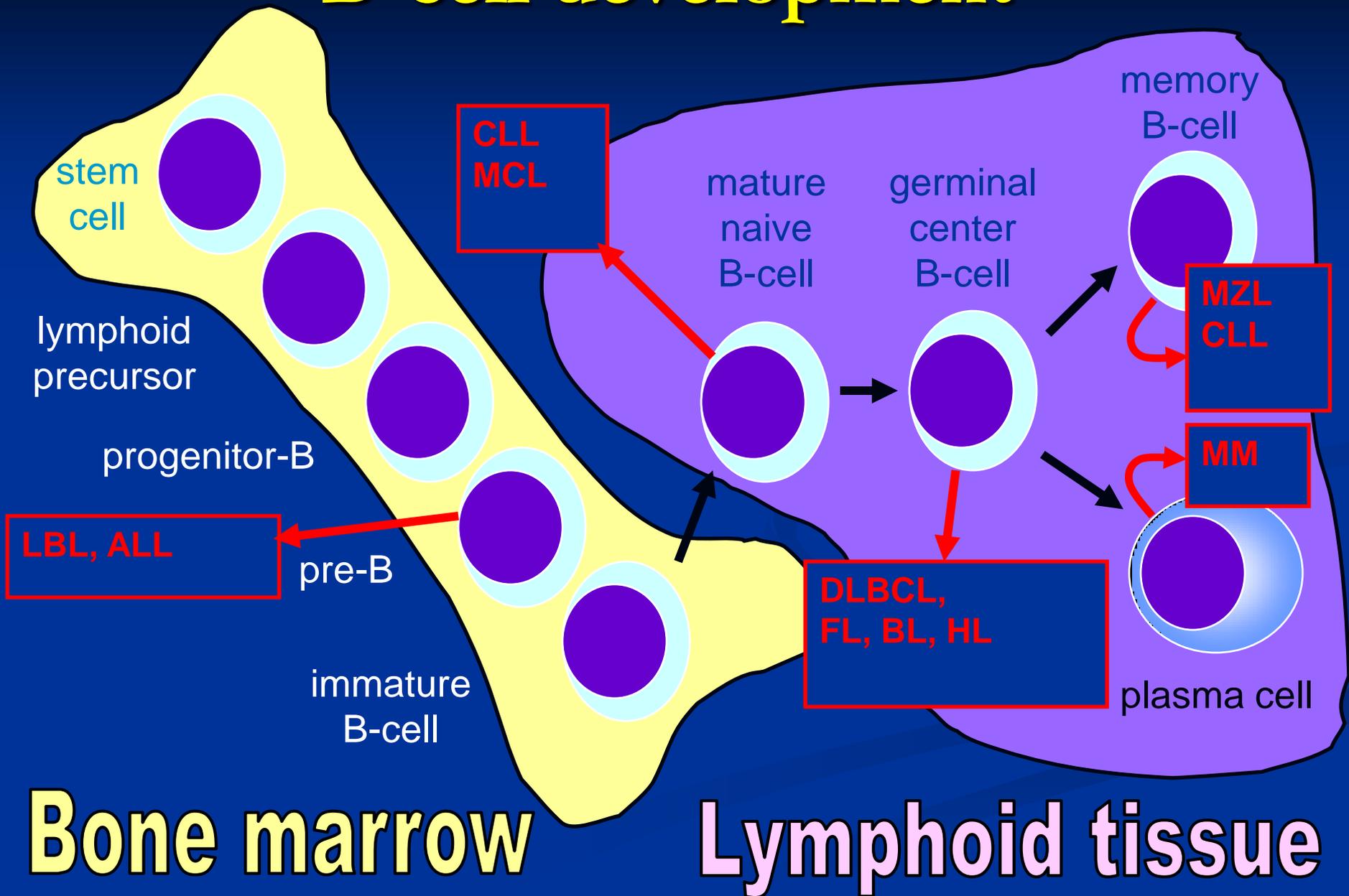
Lymphatic sinus

## **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

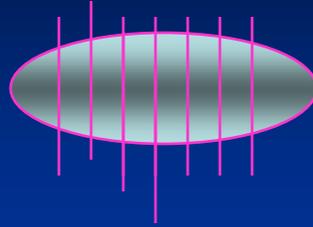
How do we diagnose and classify these types of lymphoproliferative disorders?

- ♦ **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

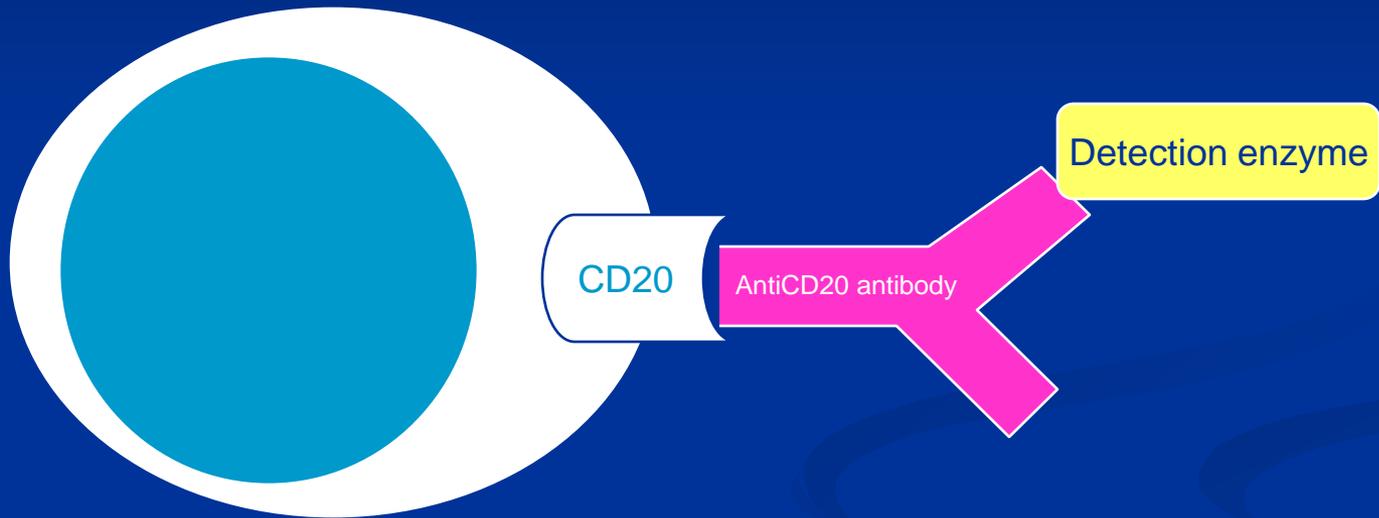


Flowcytometry

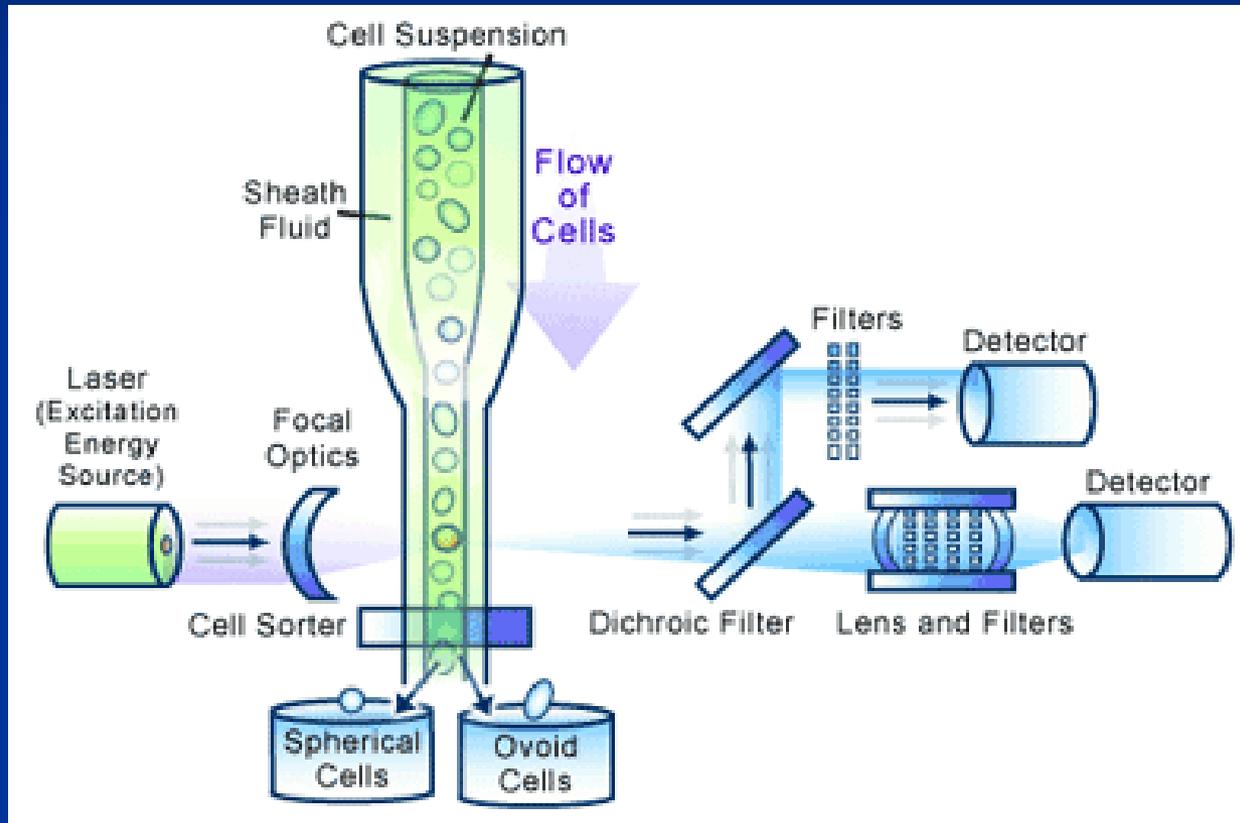
Immunostains

Cytogenetics

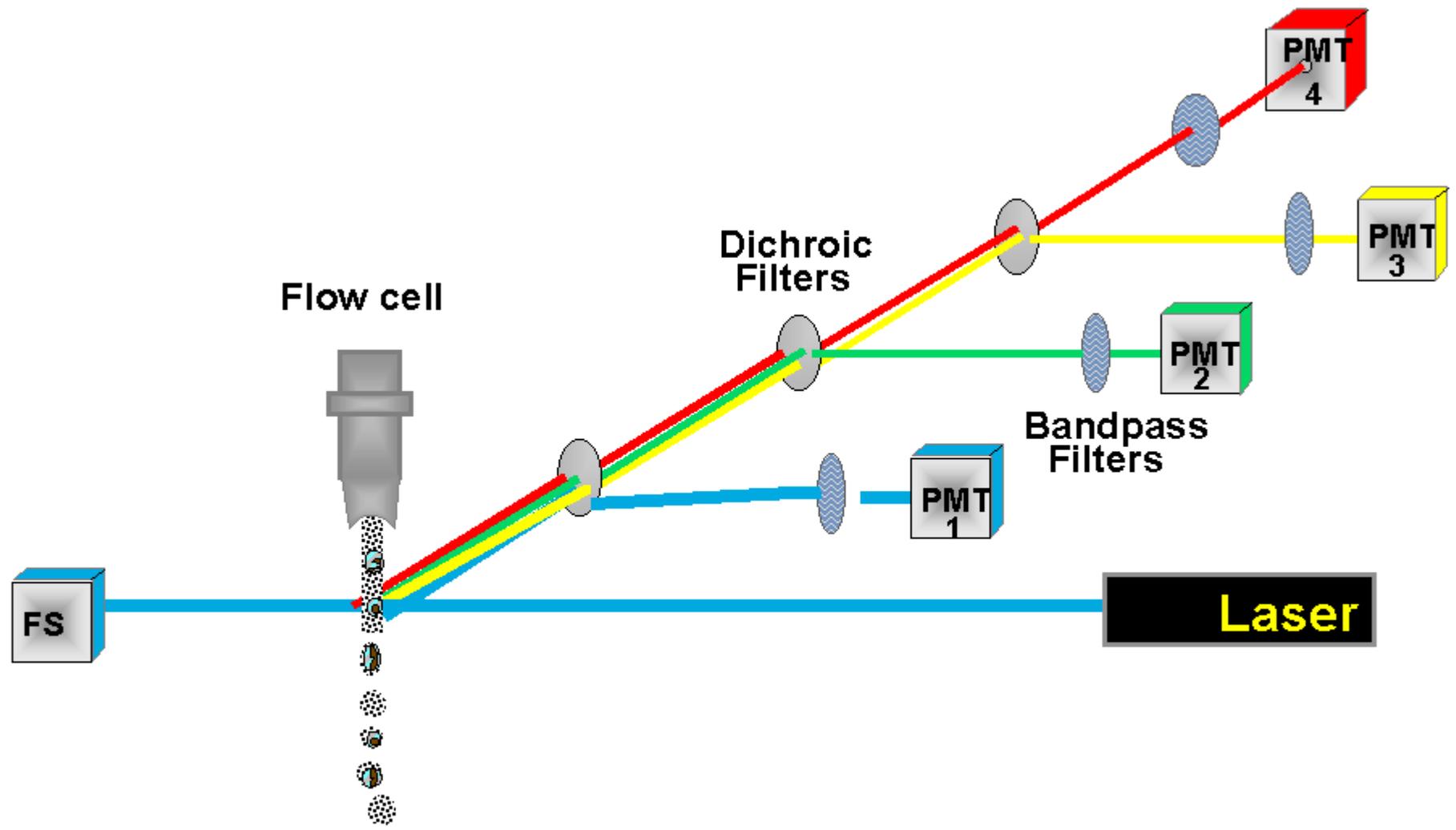
Molecular



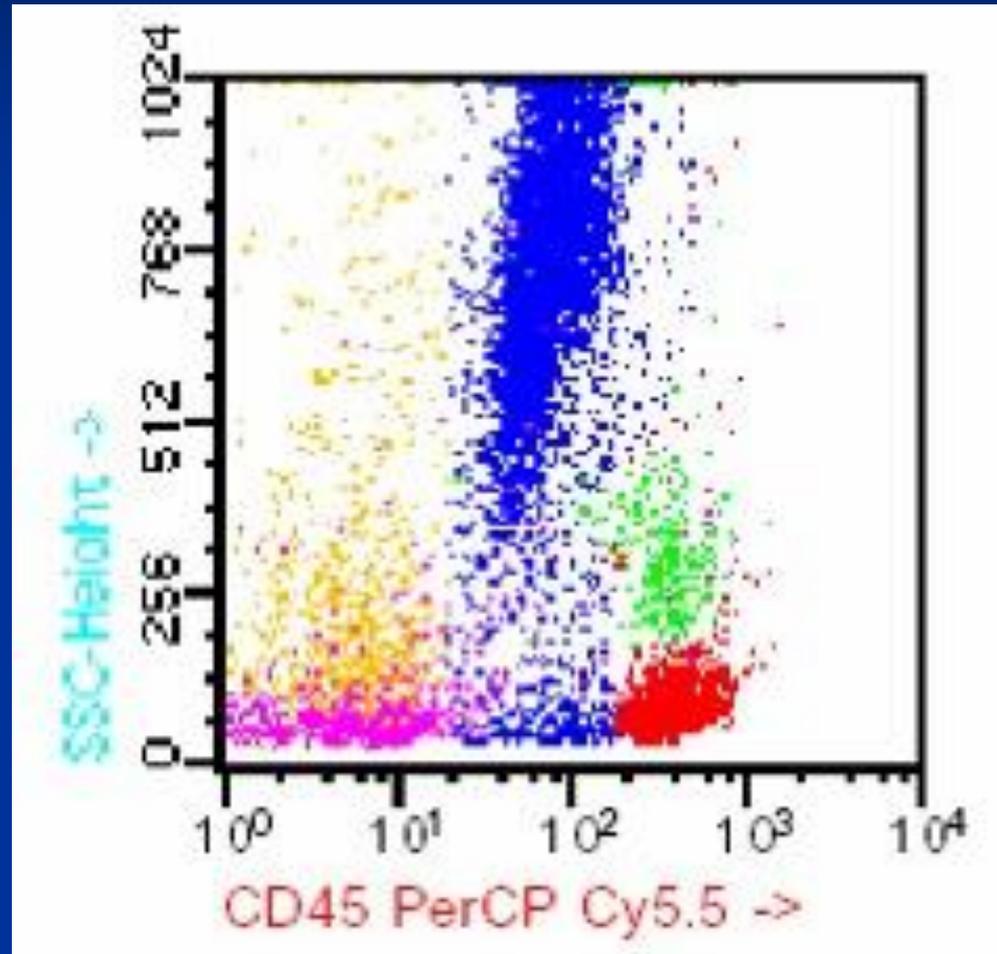
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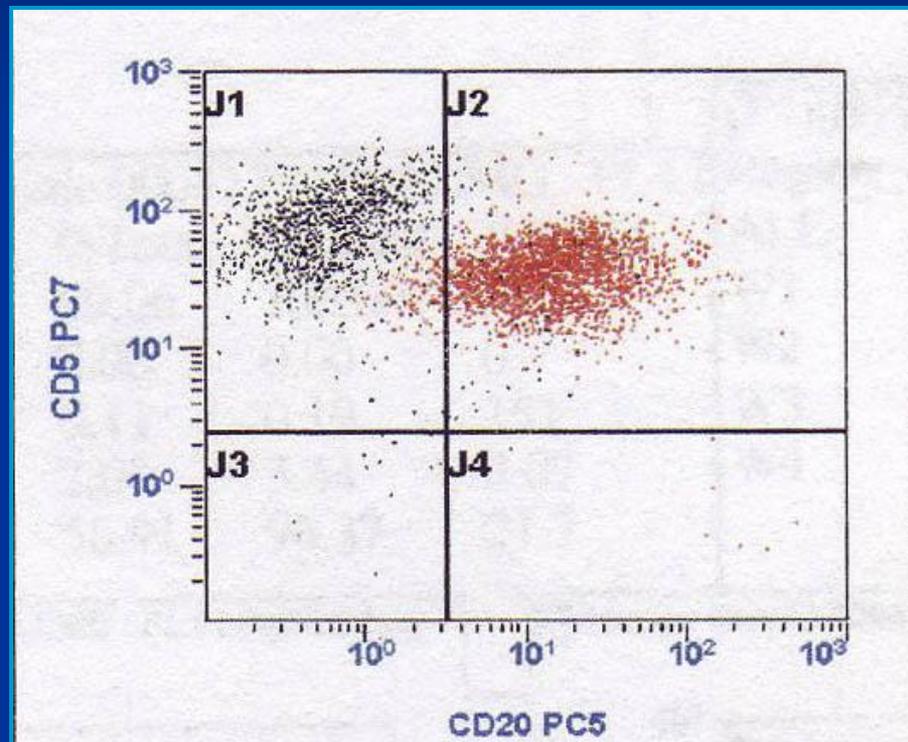


Flow-cytometry



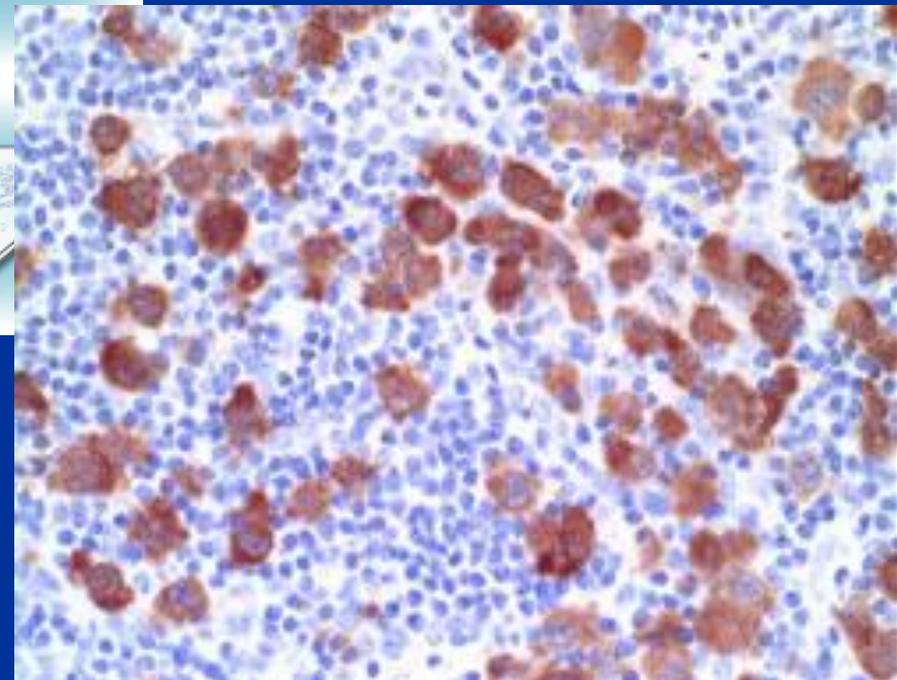
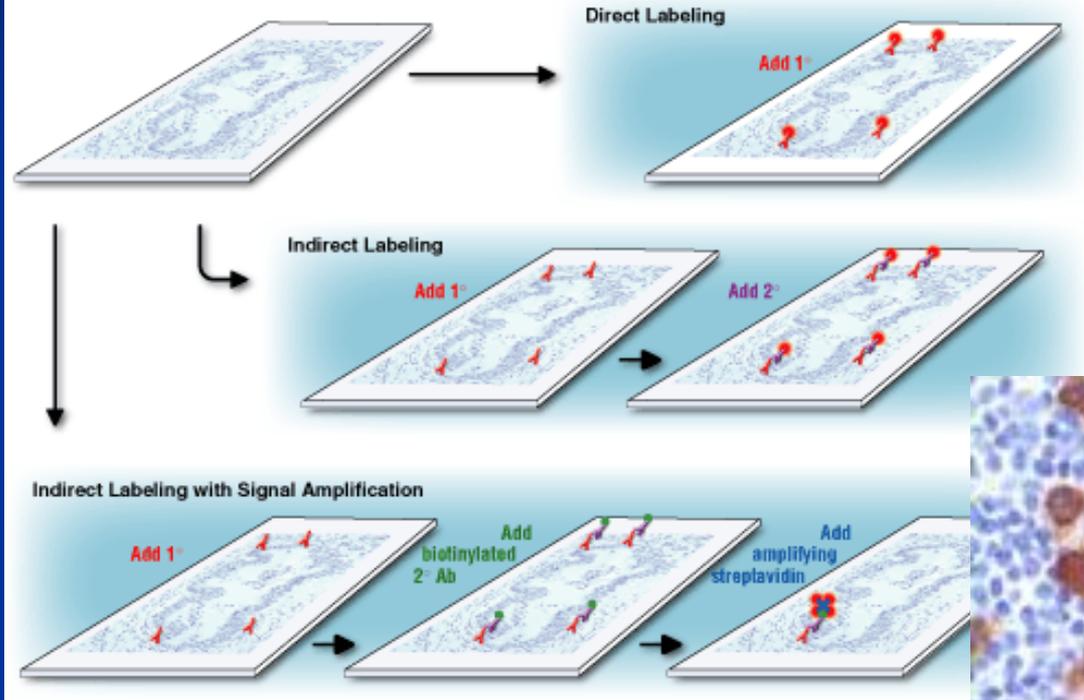
# Flow-cytometry





# Immunostains

## Immunohistochemistry Process



# *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*

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

# Most common types of lymphoma

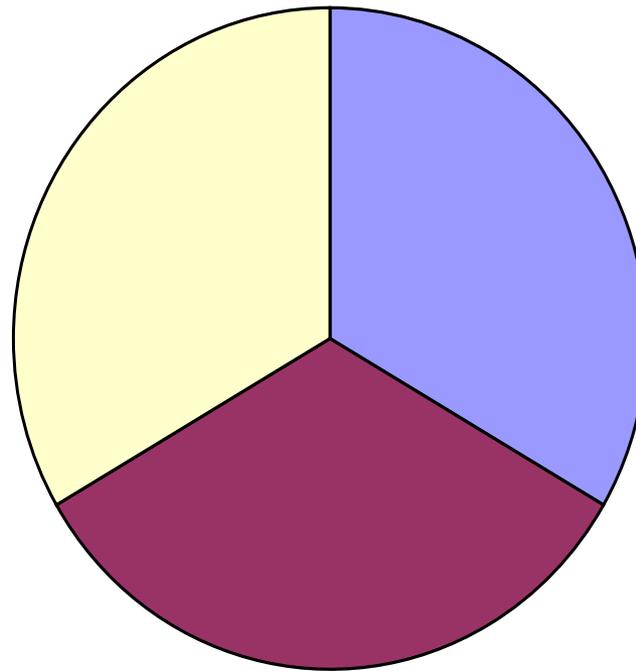
1. Non-Hodgkin lymphoma (NHL)
  - SLL/CLL
  - Follicular lymphoma
  - Diffuse large B cell lymphoma
  - Burkitt's lymphoma
2. Hodgkin lymphoma (HL)

# Non-Hodgkin lymphoma

Incidence

Diffuse  
large B-cell  
lymphoma

Follicular  
lymphoma



Other NHL

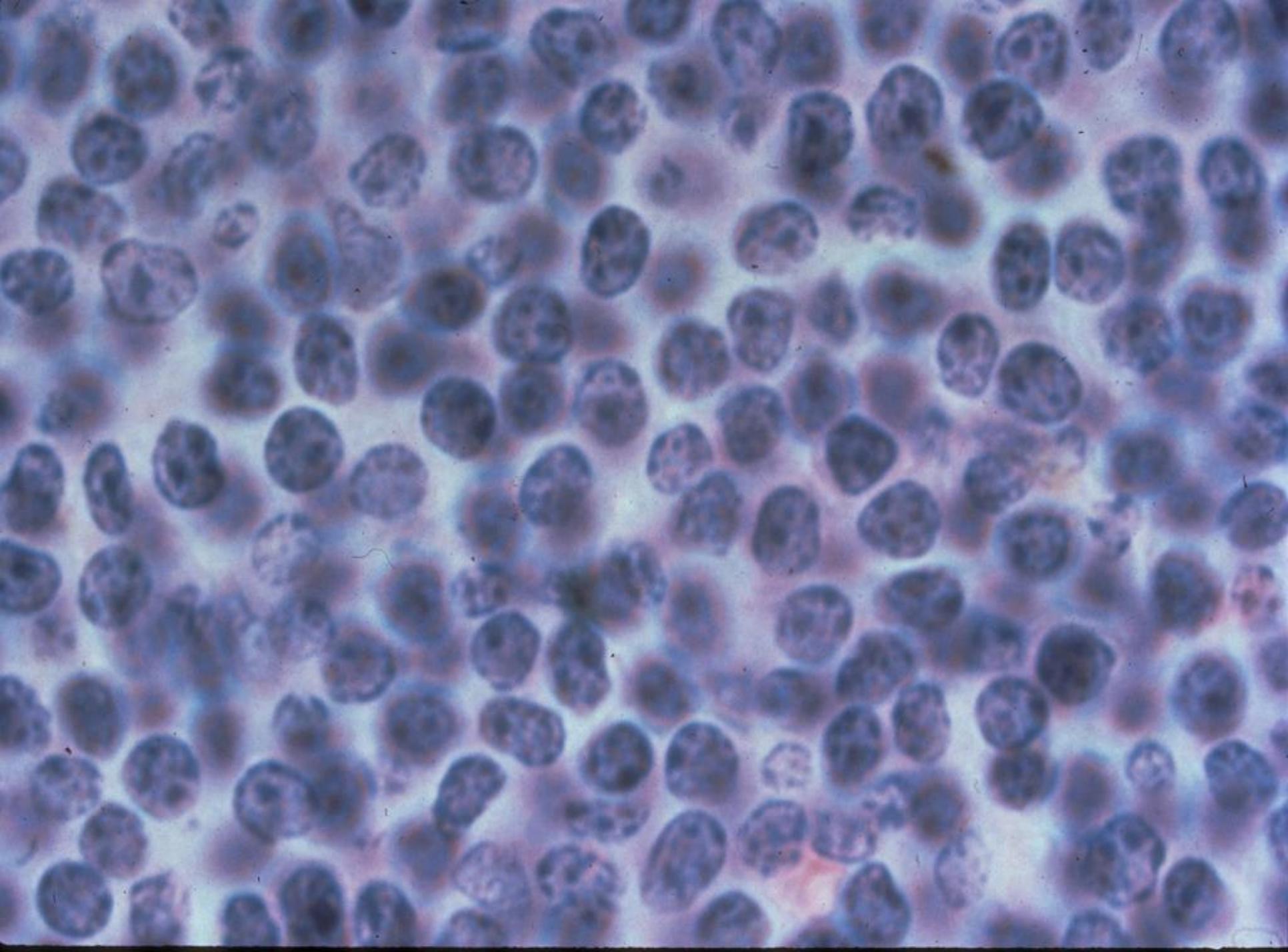
# *General Features*

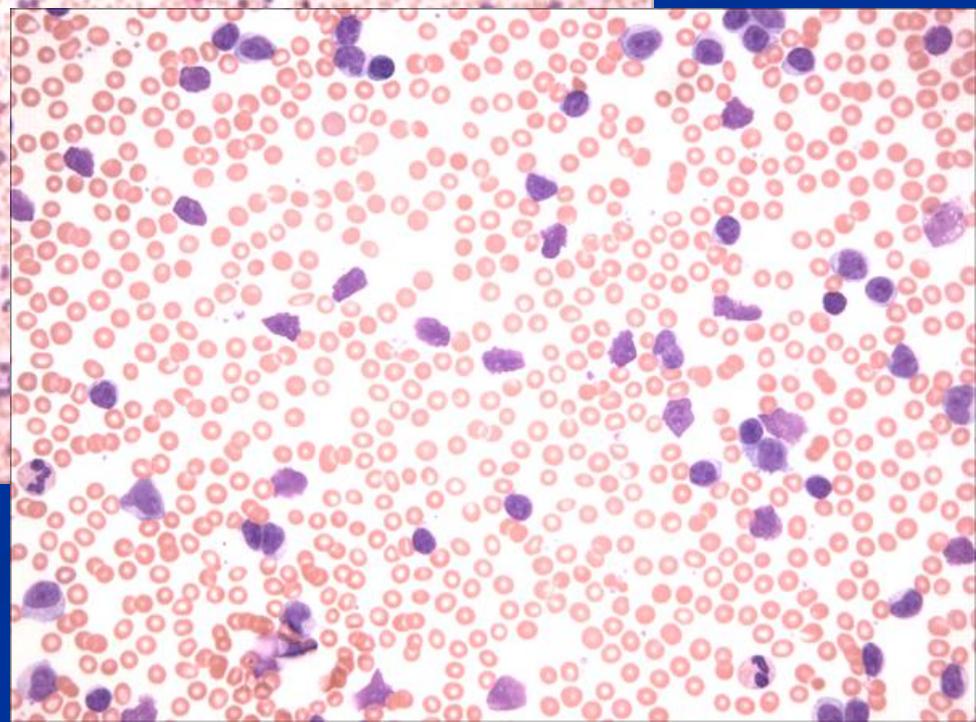
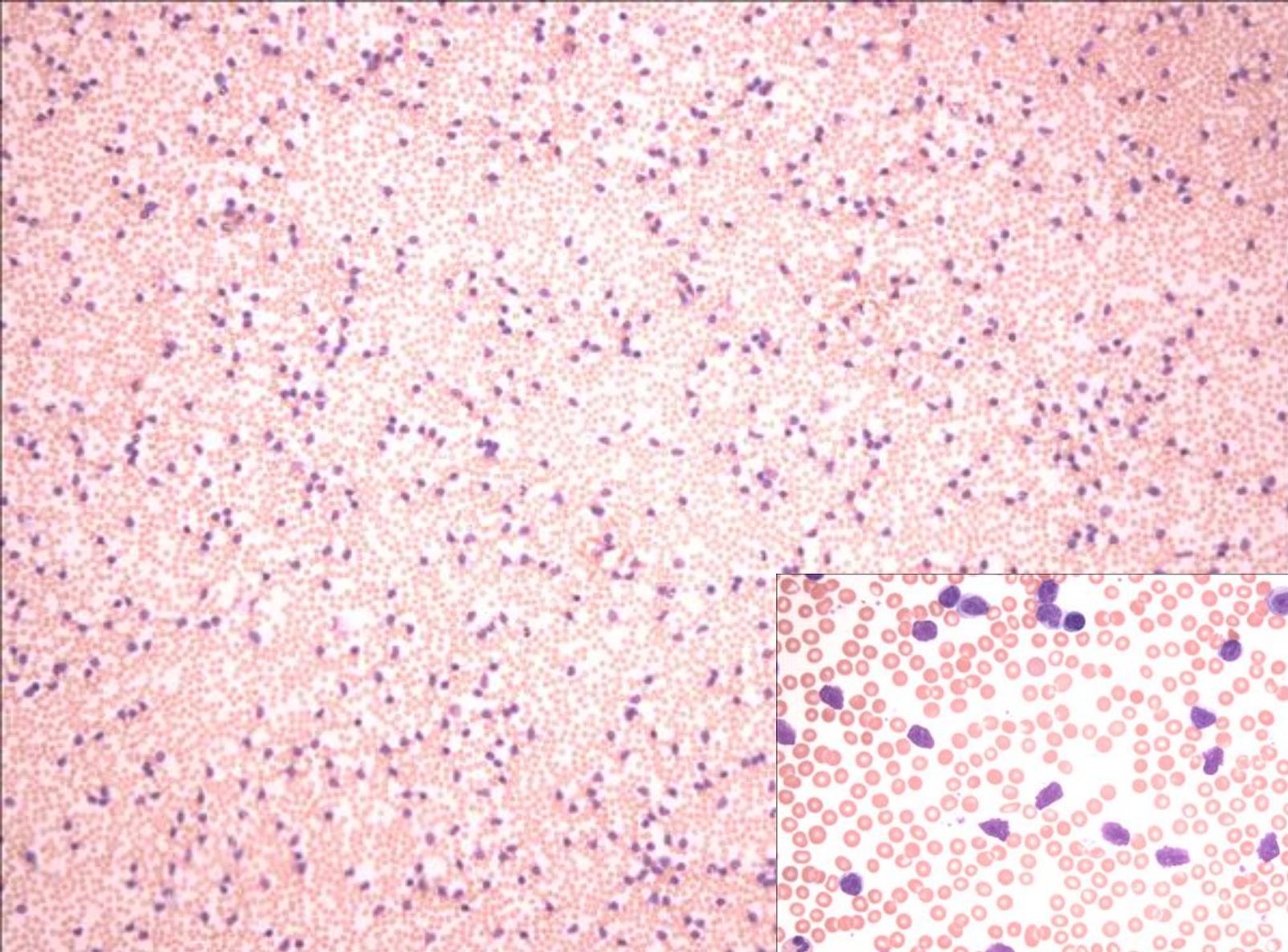
## *Low Grade Lymphomas*

- 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

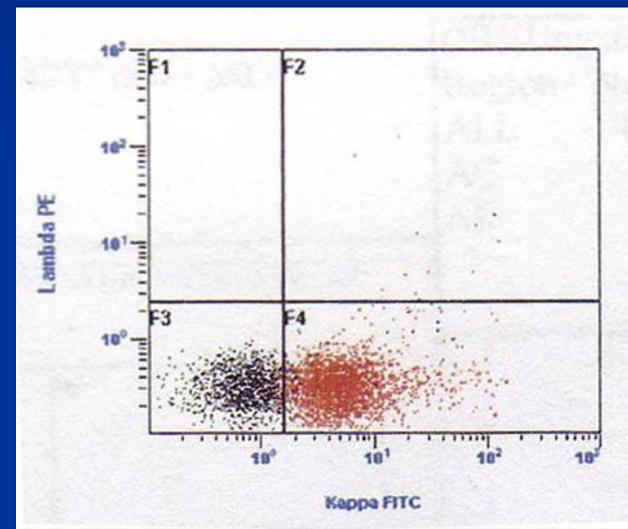
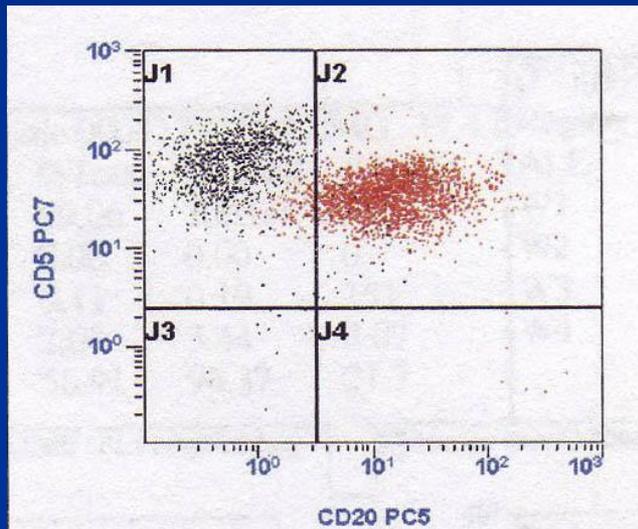
# *Small Lymphocytic Lymphoma*

- 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



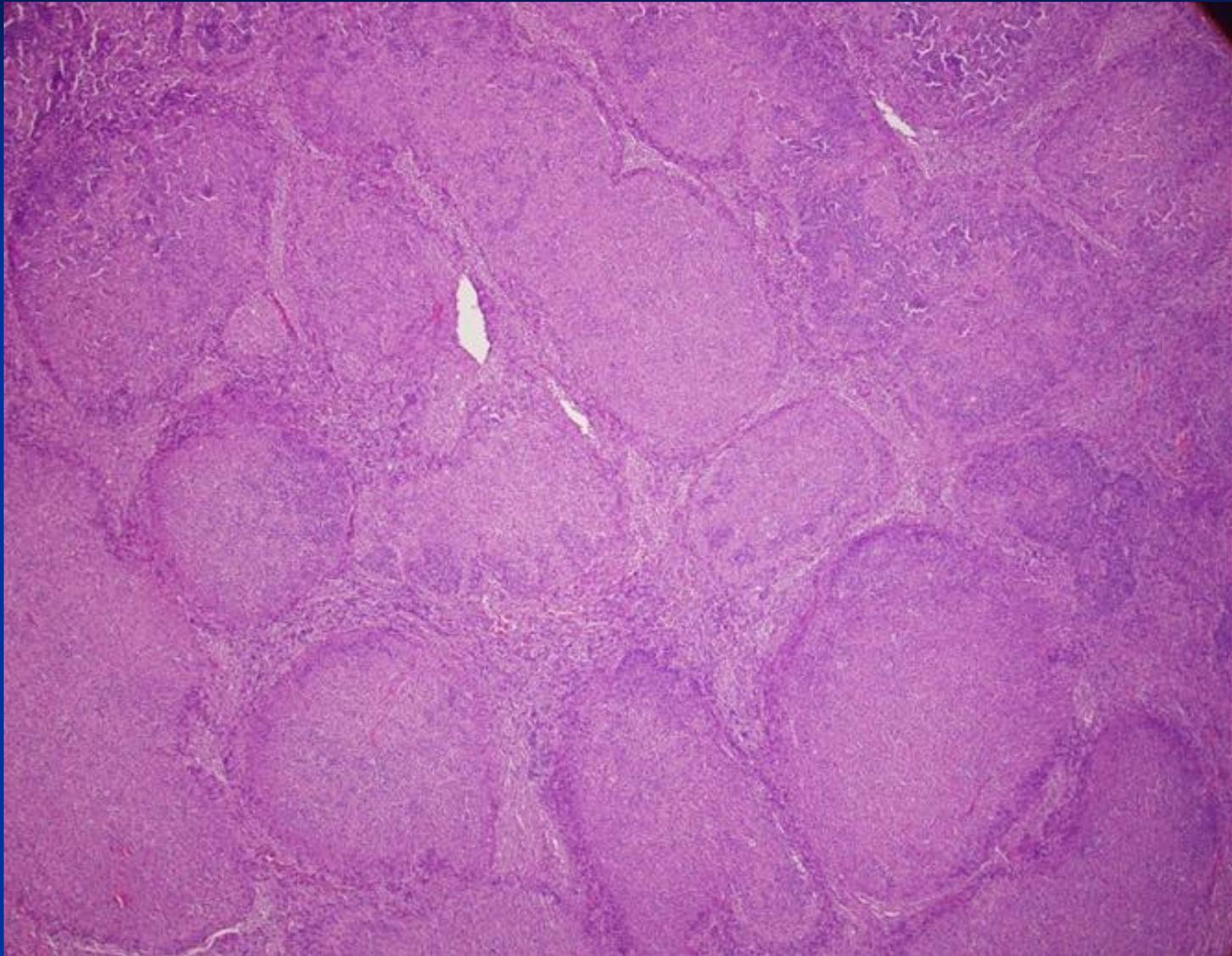
# Follicular Lymphomas

- 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*

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

*Intermediate  
Grade/Aggressive*

Mantle cell lymphoma

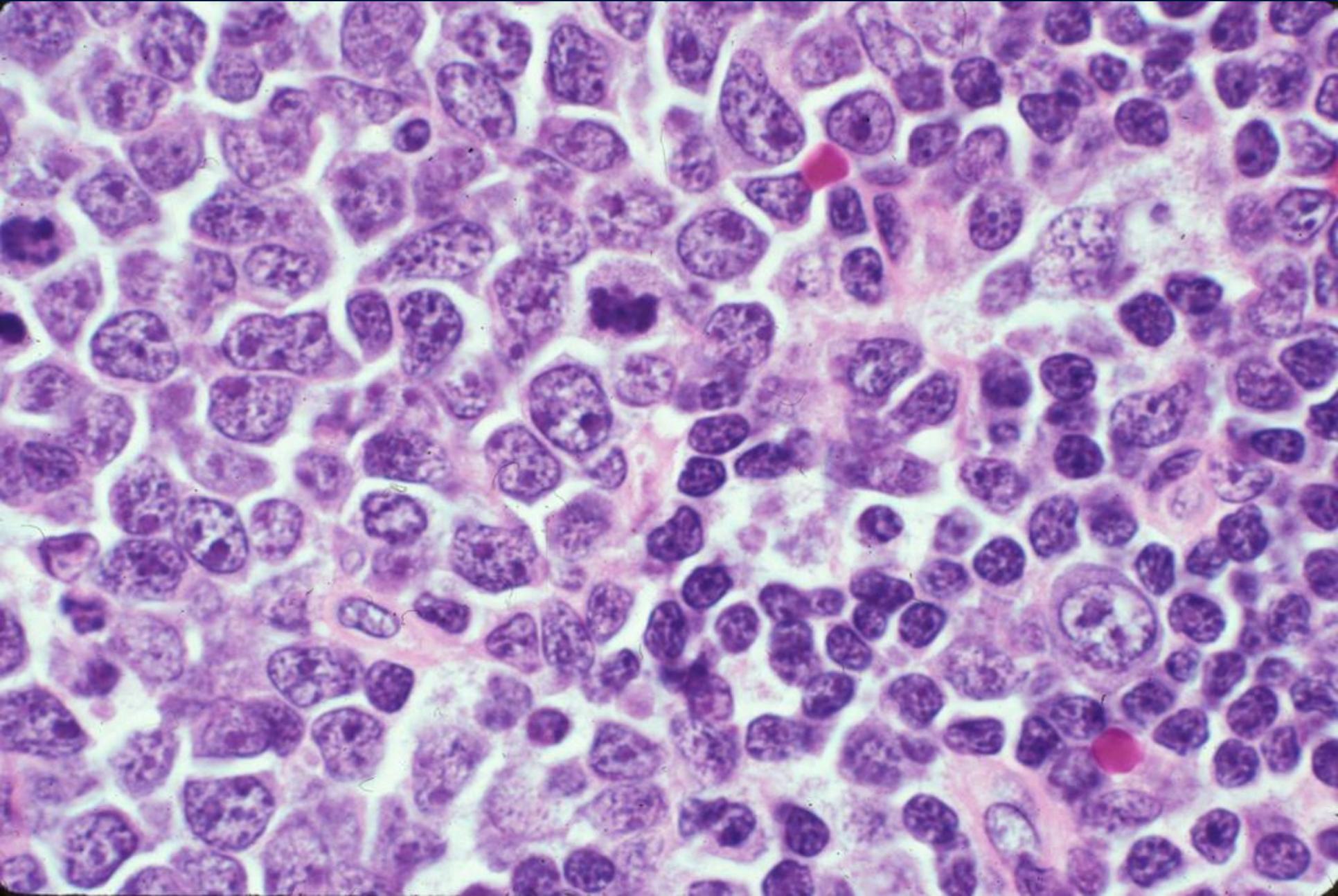
t(11;14) translocation results in  
over- expression of cyclin D1 protein

Diffuse large cell lymphoma

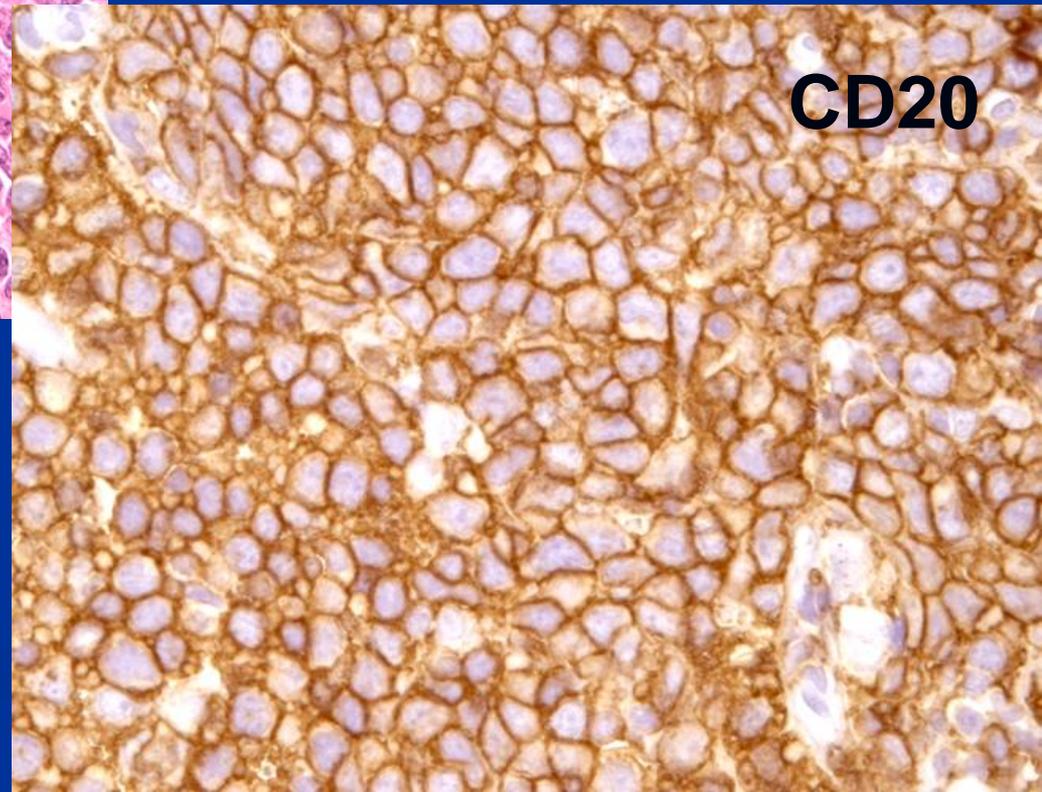
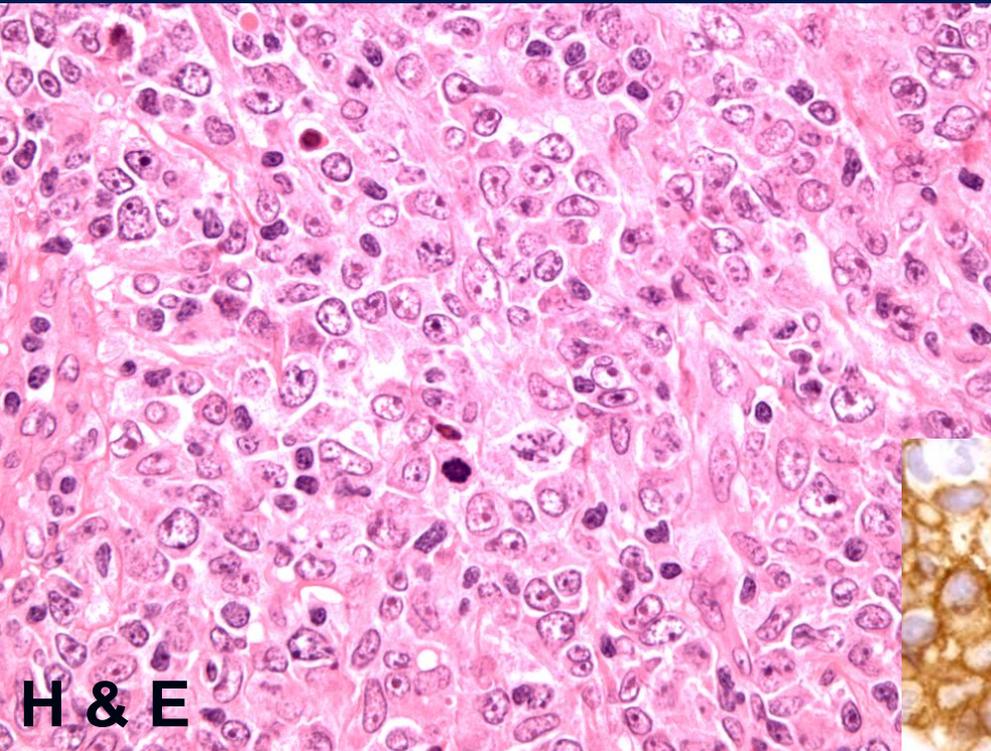
# *Diffuse Large Cell*

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

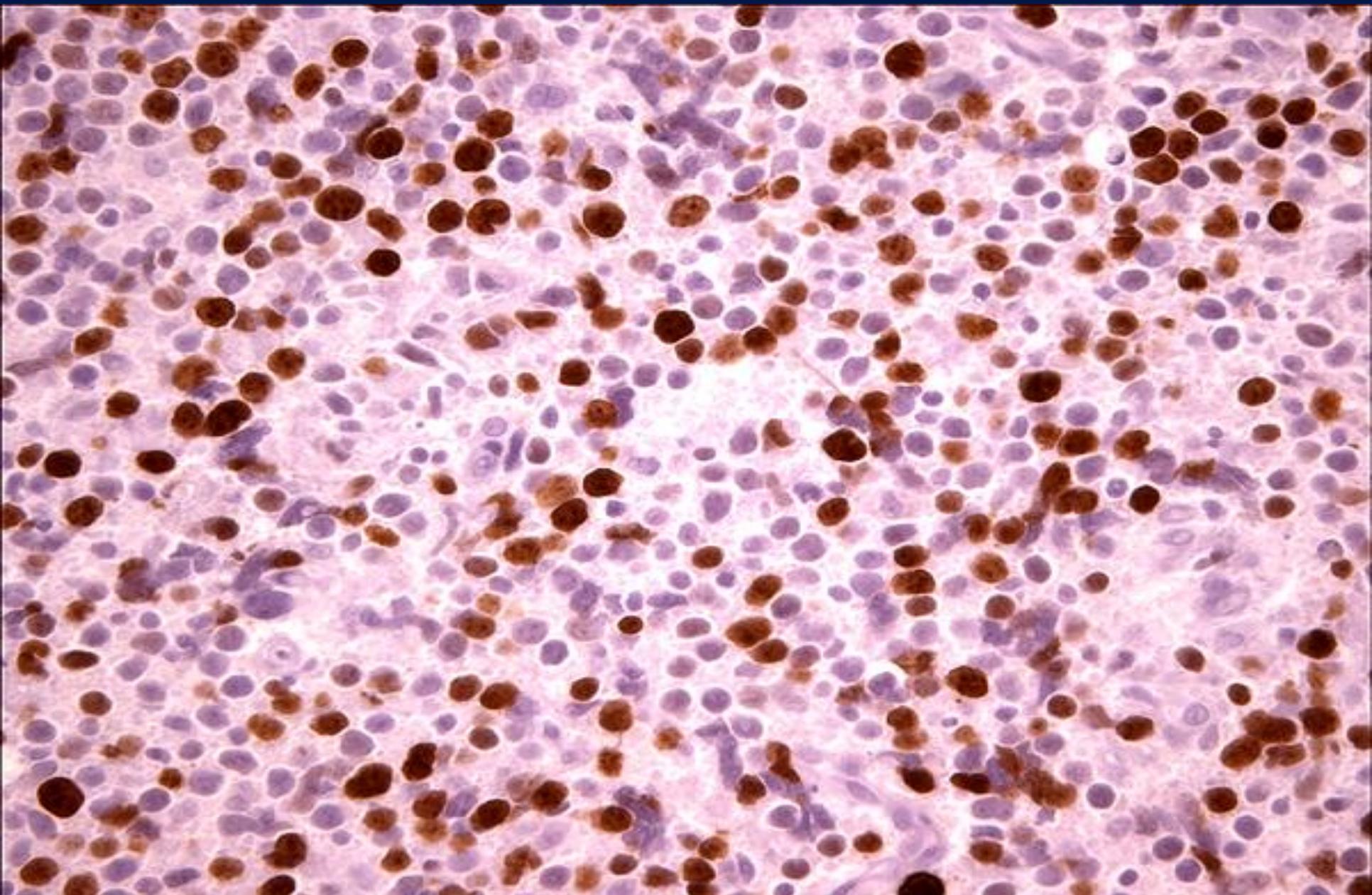
*Diffuse large B-cell lymphoma*



# *Diffuse Large B-cell Lymphoma*



# *MIB-1*



# *High Grade (small non-cleaved)*

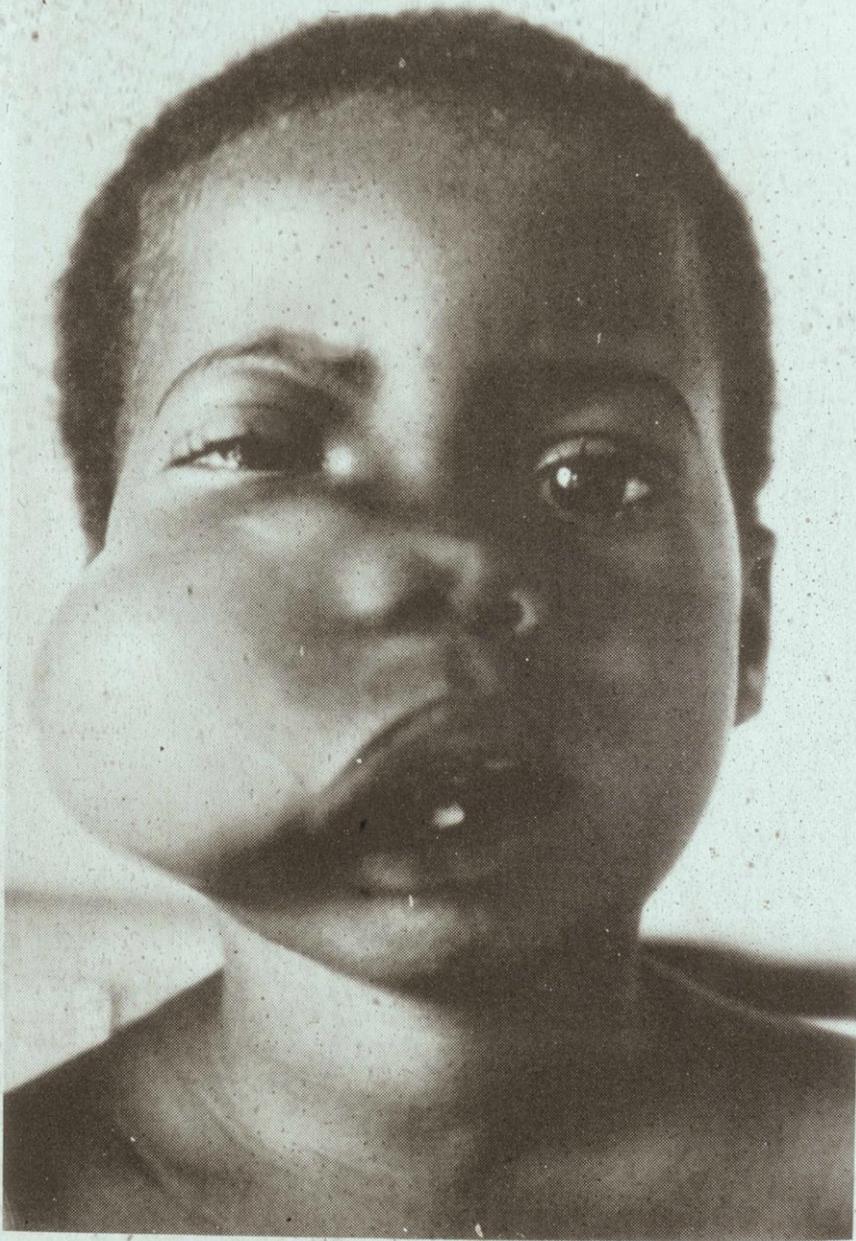
## **Burkitt lymphoma**

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

## **AIDS associated lymphoma**

# *Clinical Findings*

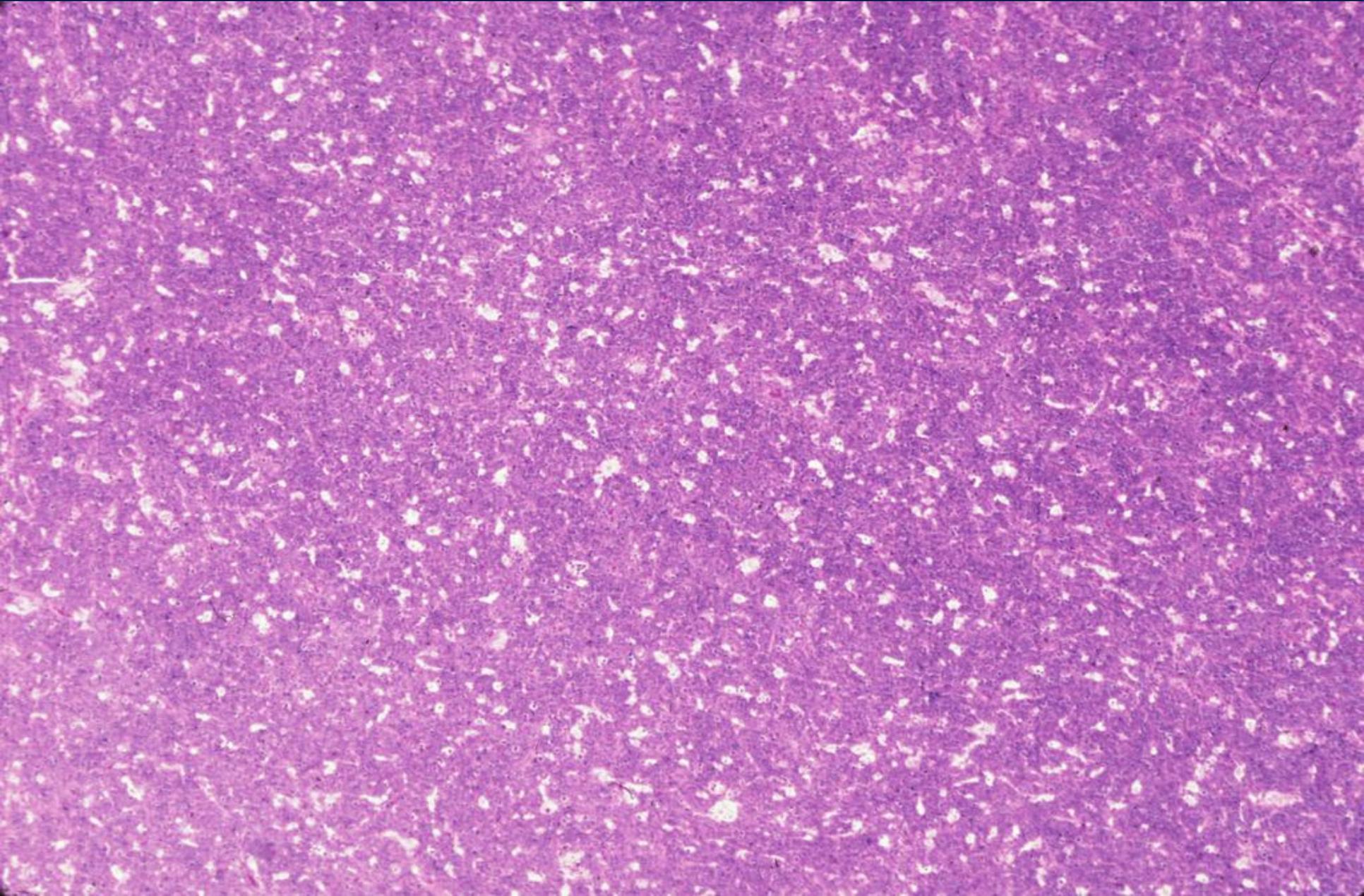
- Enlarged painless lymphadenopathy
- B-symptoms, fever, sweats, weight loss
- Impingement or obstruction of adjacent structures (mass effect)
- Extranodal presentation (30% of cases)  
GI tract, spleen, salivary gland



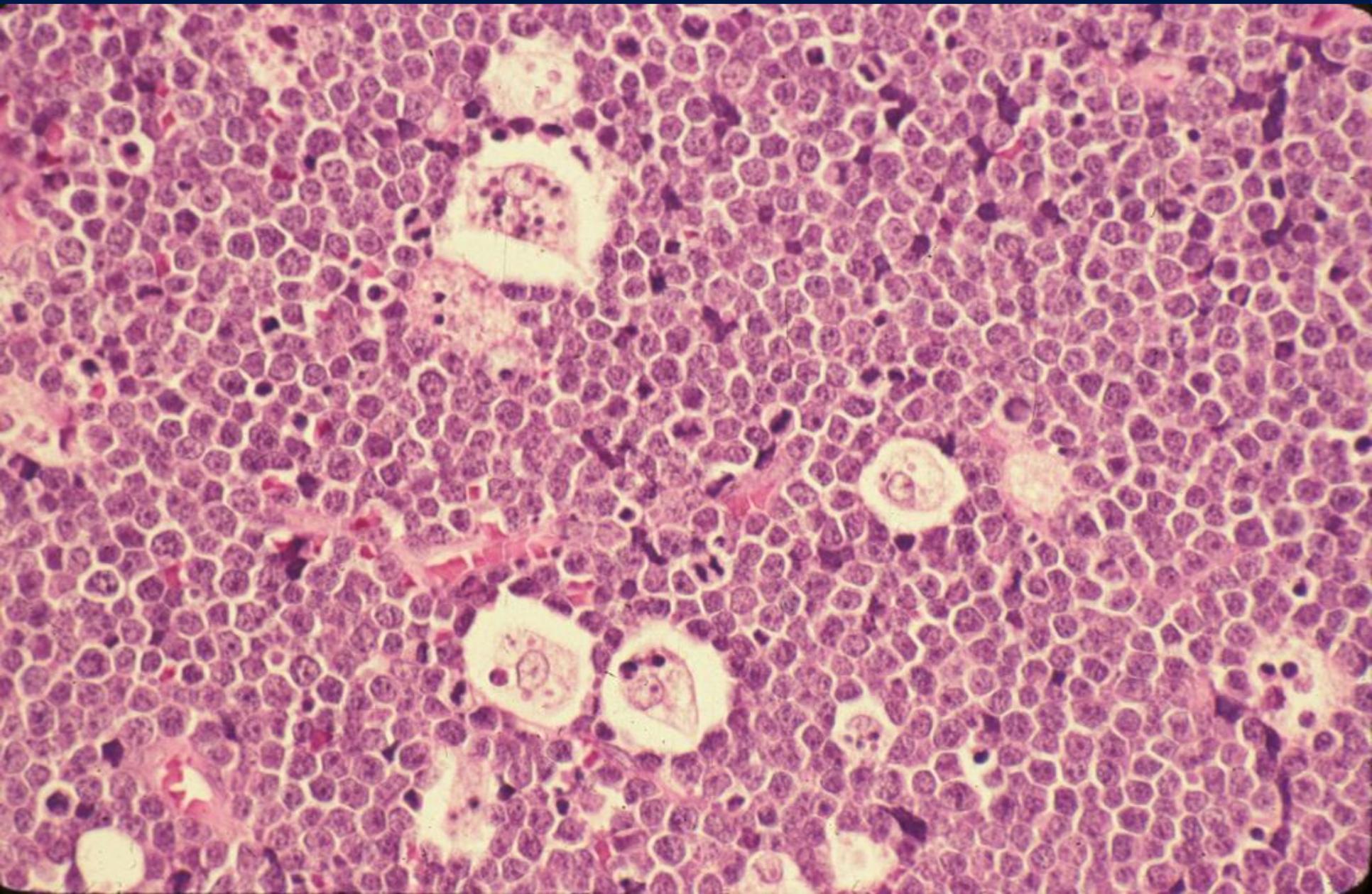
## Burkitt lymphoma involving jaw

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 - 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.