

# **LYMPHOPROLIFERATIVE DISORDERS**

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# Definition

## Lymphoproliferative disorders

Several clinical conditions in which lymphocytes are produced in excessive quantities ( Lymphocytosis)

## Lymphoma

Malignant lymphoid mass involving the lymphoid tissues ( $\pm$  other tissues e.g : skin ,GIT ,CNS ...)

## Lymphoid leukemia

Malignant proliferation of lymphoid cells in Bone marrow and peripheral blood ( $\pm$  other tissues e.g : lymph nods ,spleen , skin ,GIT ,CNS ...)

# Lymphoproliferative disorders

**Autoimmune**

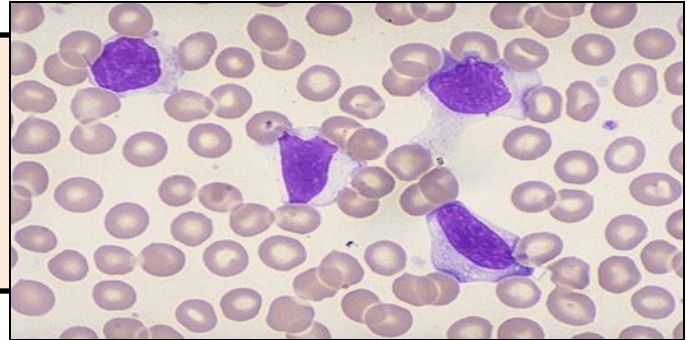
**Infection**

**Malignant**

# Lymphocytosis

## 1- Viral infection :

• *Infectious mononucleosis* , cytomegalovirus , rubella, hepatitis, adenoviruses, varicella....

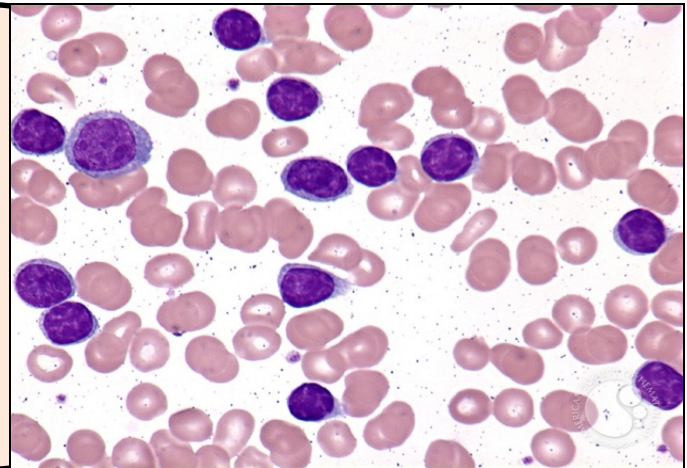


## 2- Some bacterial infection:

(Pertussis ,brucellosis ...)

## 3-Immune : SLE , Allergic drug reactions

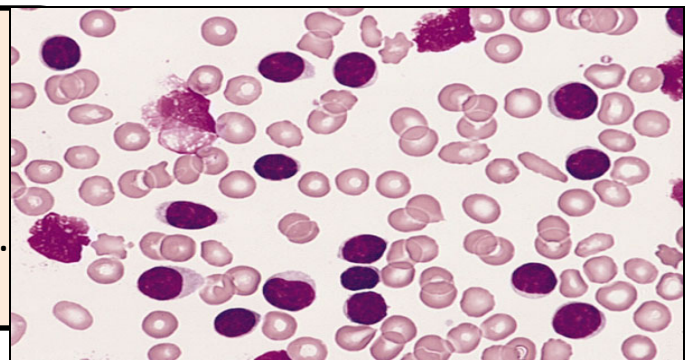
4- Other conditions:, splenectomy, dermatitis ,hyperthyroidism metastatic carcinoma....)



## 5- Chronic lymphocytic leukemia (CLL)

## 6-Other lymphomas:

Mantle cell lymphoma ,Hodgkin lymphoma...

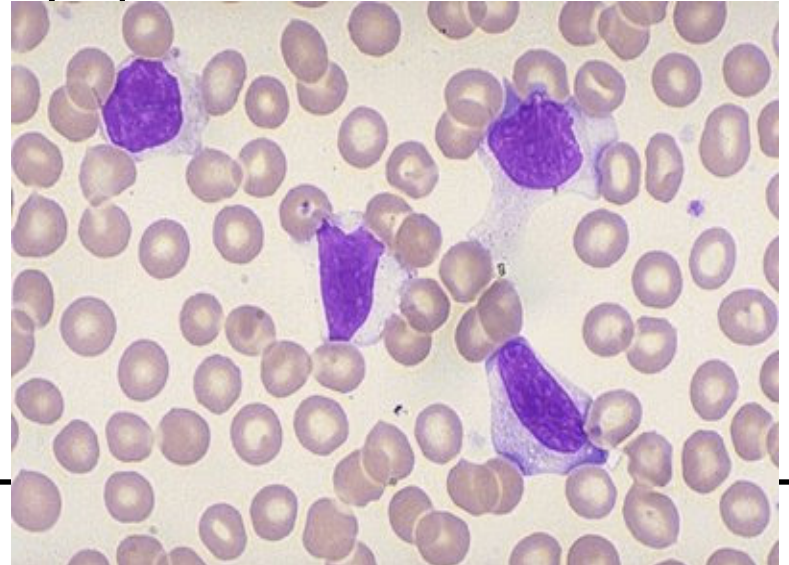




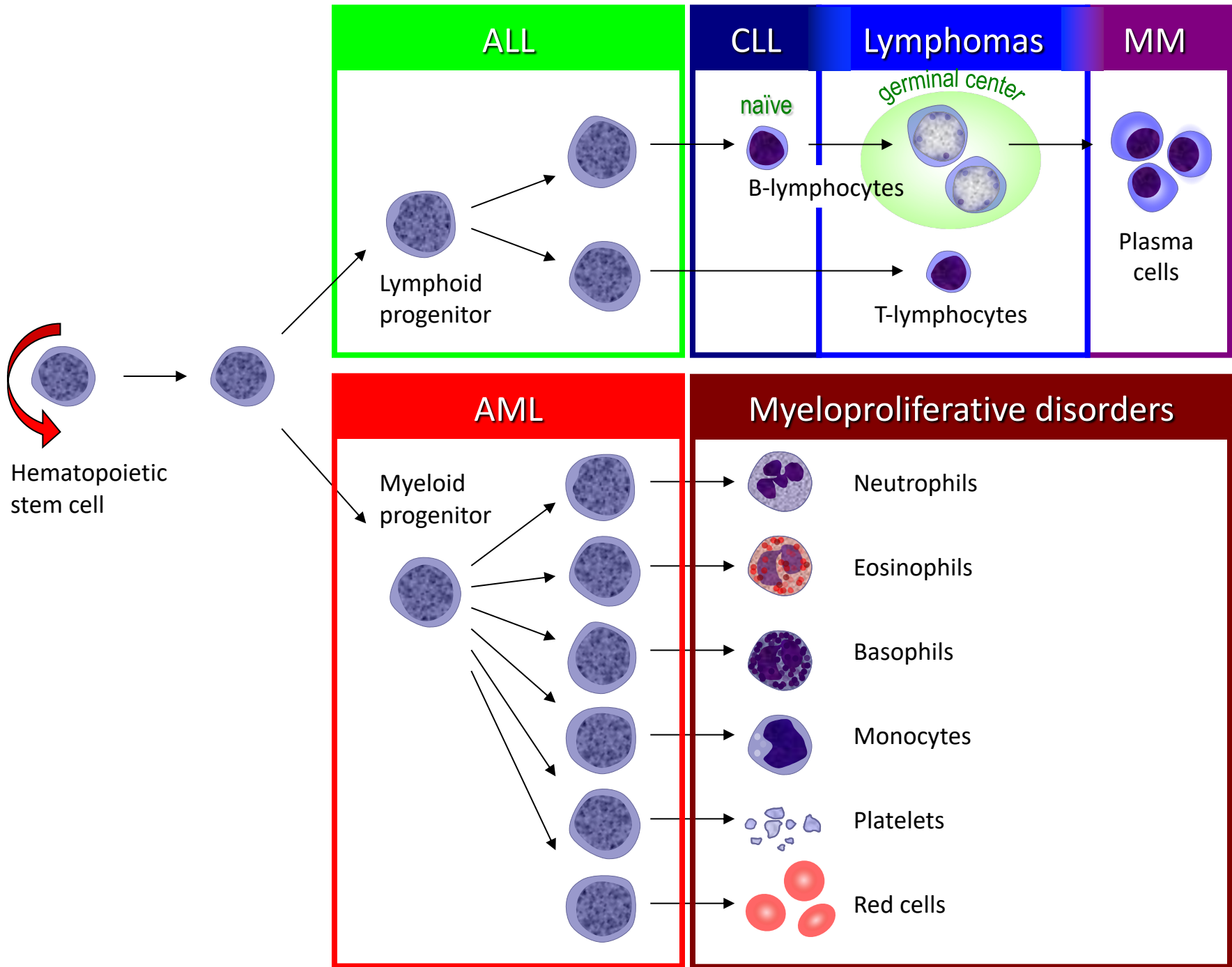
# Infectious mononucleosis

An acute, infectious disease, caused by Epstein-Barr virus and characterized by

- fever
- swollen lymph nodes (painful)
- Sore throat,
- atypical lymphocyte
- Affect young people ( usually)



# **Malignant Lymphoproliferative Disorders**



# Malignant Lymphoproliferative disorders

**Immature**

**ALL**

**Mature**

**Lymphoma**

**Non Hodgkin lymphoma**

**Hodgkin lymphoma**

**90%**

**B- cell neoplasm**

**T- cell neoplasm**

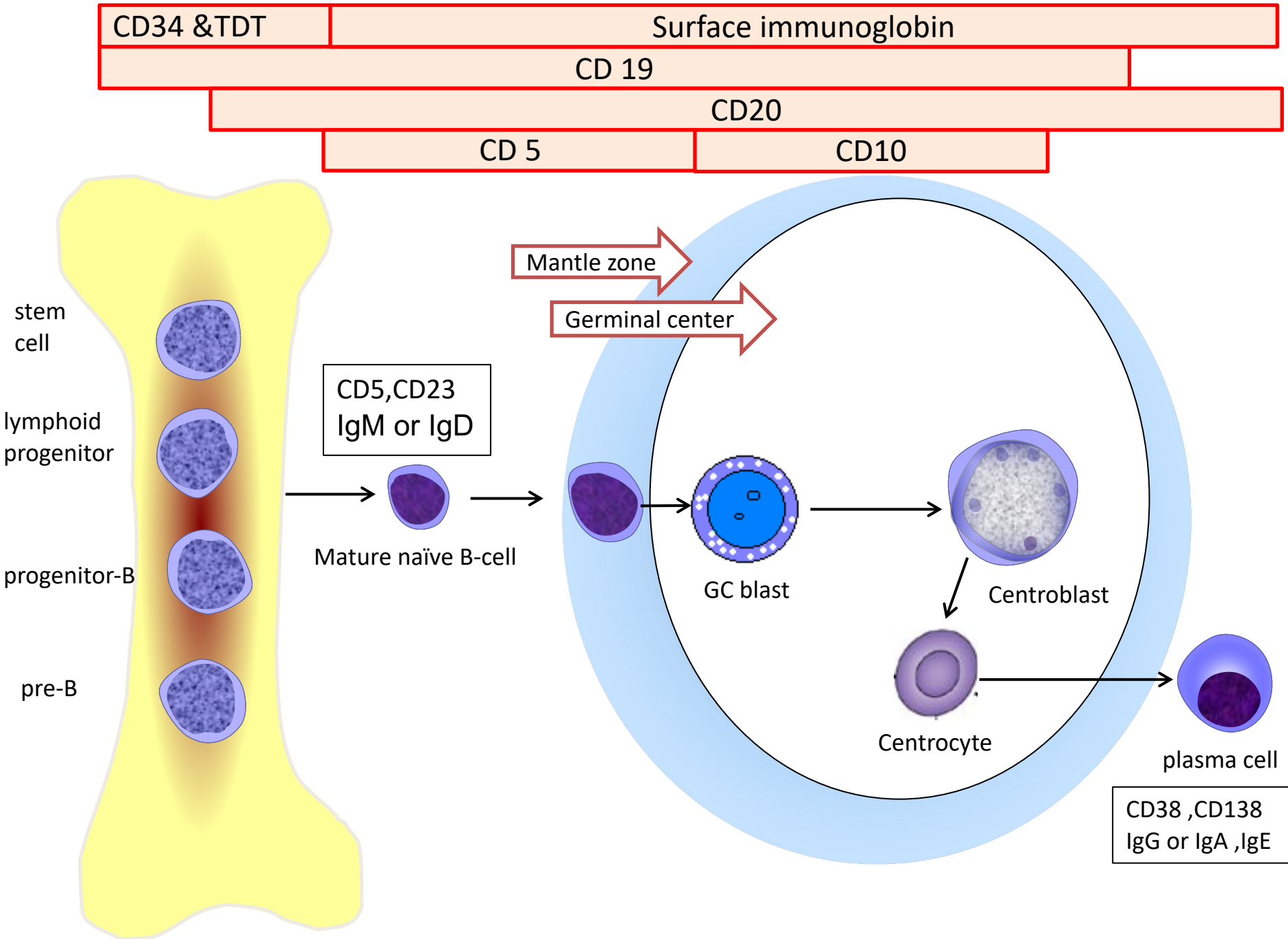
**10%**

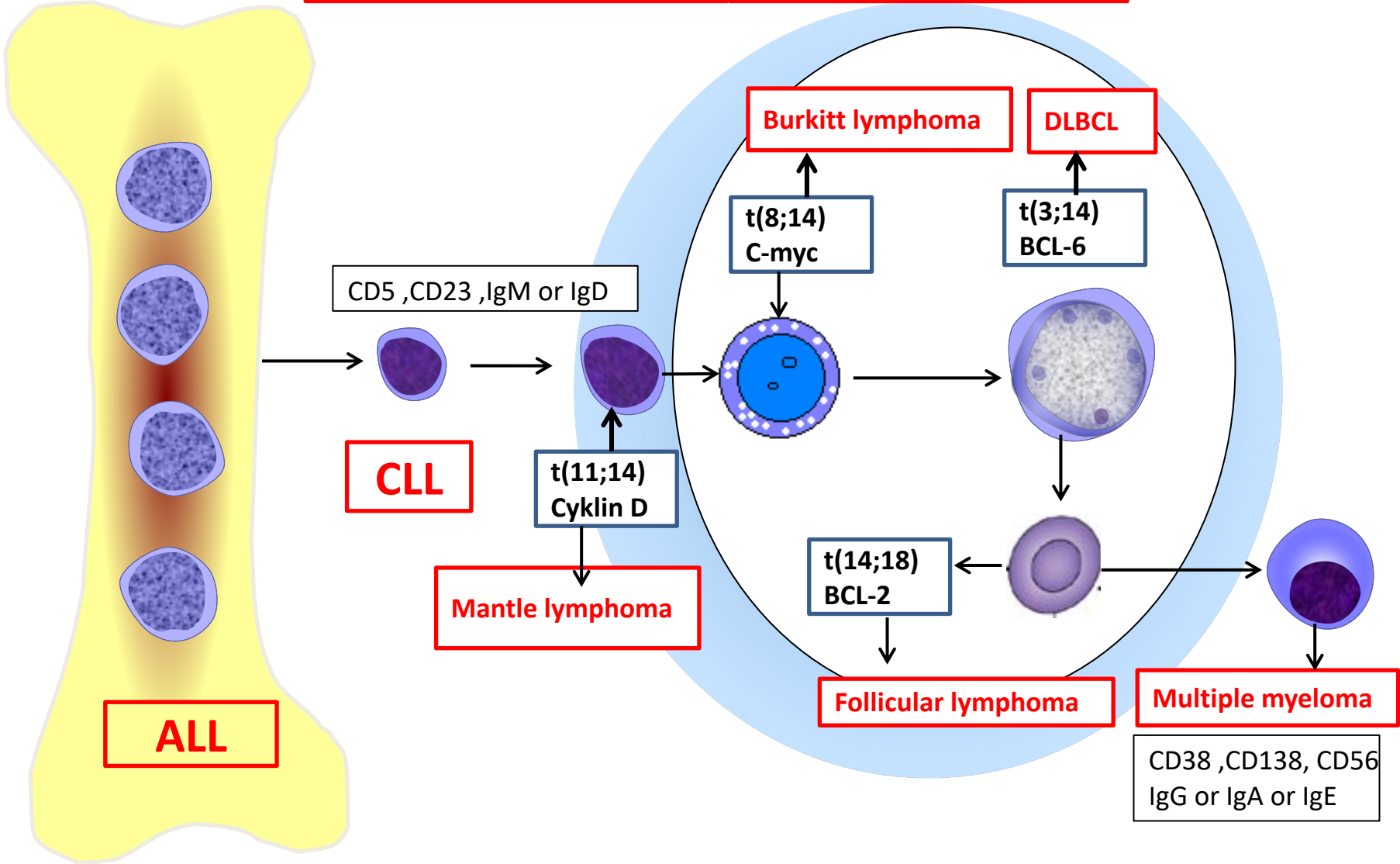
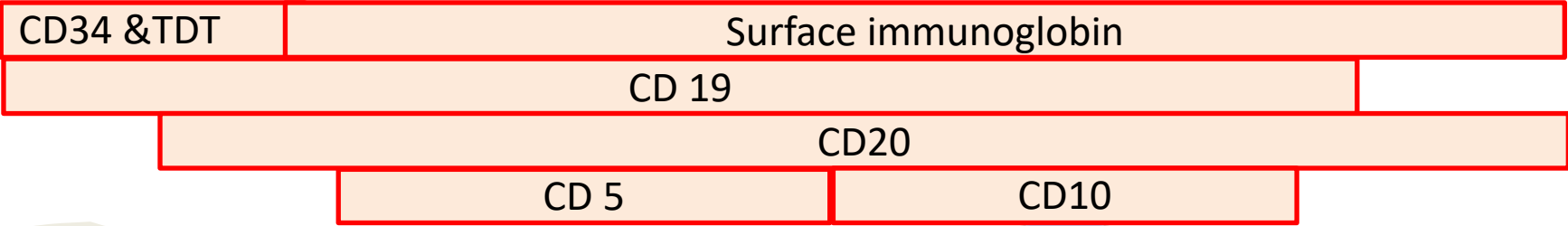
Burkitt lymphoma  
Diffuse large B lymphoma  
Follicular lymphoma  
Multiple myeloma

Adult T leukemia lymphoma  
Sezary syndrome  
Large anaplastic T lymphoma

**Lymphoid leukemia**

CLL  
Hairy cell leukemia  
T- prolymphocytic leukemia  
Leukemic phase of lymphoma





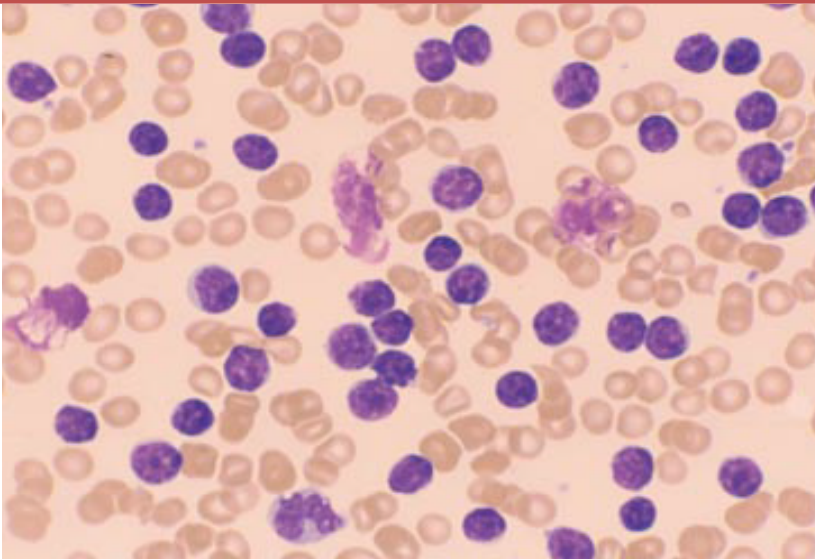
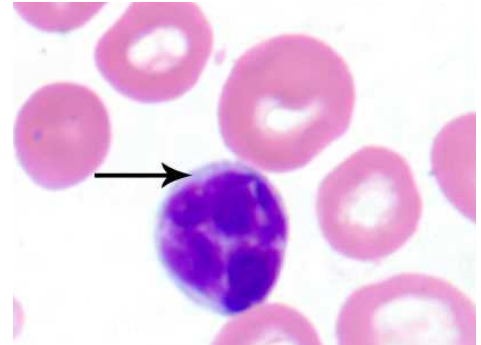
## **Chronic Lymphocytic Leukemia**

- **Malignant neoplasim characterized by an increased number of small, mature lymphocytes in the blood (>5,000 ) and bone marrow (± spleen and lymph node)**
- **The most common adult leukemia (~25% of adult leukemias)**
- **The median age is ~55 to 65 years. ( rare < 40 years).**
- **1.5 to 2 times more common in men than women.**



## Features of CLL

- ❑ 40% of patients are asymptomatic at diagnosis.
- ❑ Moderate lymphadenopathy and splenomegaly
- ❑ Lymphocytosis (>5,000):
  - **Small mature-appearing lymphocytes**
  - **Condensed (“soccer ball”) nuclear chromatin**
  - **Numerous “smudge cells”**
- ❑ Predisposition to infection
- ❑ Autoimmune phenomena (autoimmune hemolytic anemia)
- ❑ Transformation to large cell lymphoma (Richter’s syndrome)





# CLL Staging

Rai Staging	Prognosis
Stage 0: Lymphocytosis only (blood and marrow)	Low risk <b>Watch &amp; wait</b>
Stage I: Lymphocytosis plus enlarged nodes	<b>Watch &amp; wait</b>
Stage II: Lymphocytosis plus enlarged spleen and/or liver, ± nodes	Intermediate <b>±chemo</b>
Stage III: Lymphocytosis plus anemia (Hgb <11 g/dL), ± above	<b>±chemo</b>
Stage IV: Lymphocytosis plus thrombocytopenia ( $<100 \times 10^9/L$ ) ± above	High risk <b>FCR</b>

# Burkitt's lymphoma

High-grade non-Hodgkin's B-cell lymphoma which is rapidly growing and highly aggressive with extremely short doubling time (24 hrs)

## Types of Burkitt's lymphoma

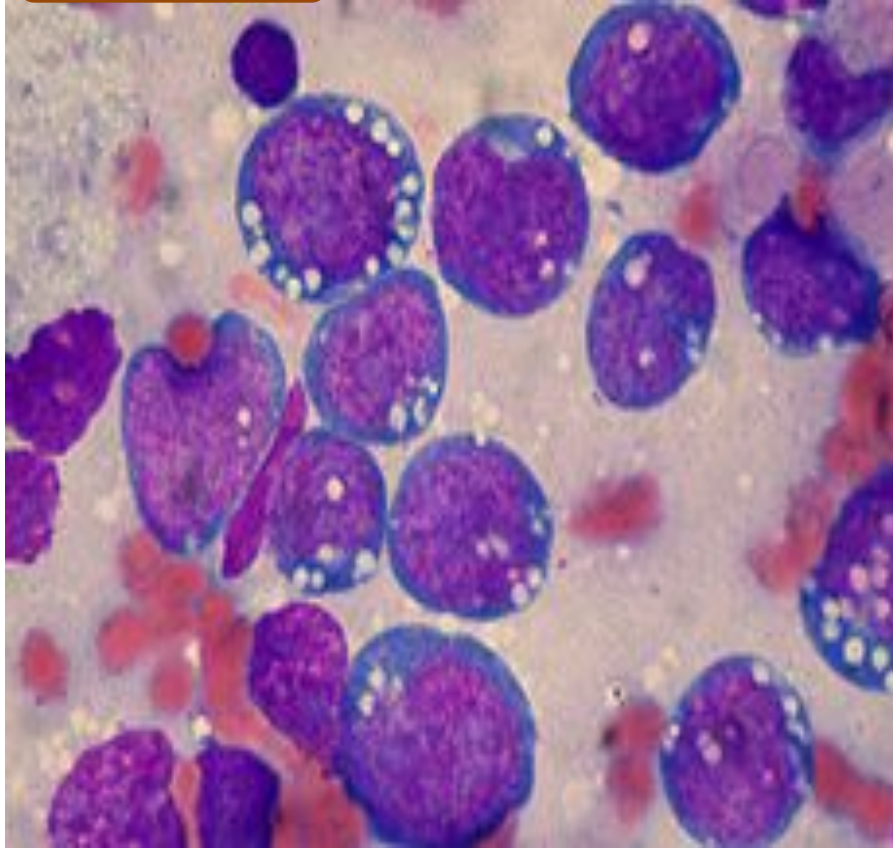
***1-Endemic:*** associated with chronic malaria and EBV In equatorial Africa . It particularly affects the jaw, other facial bone and breast.

**Sporadic:** occurs throughout the world and affects GIT.

**Immunodeficiency-associated:** associated with HIV infection or the use of immunosuppressive drugs

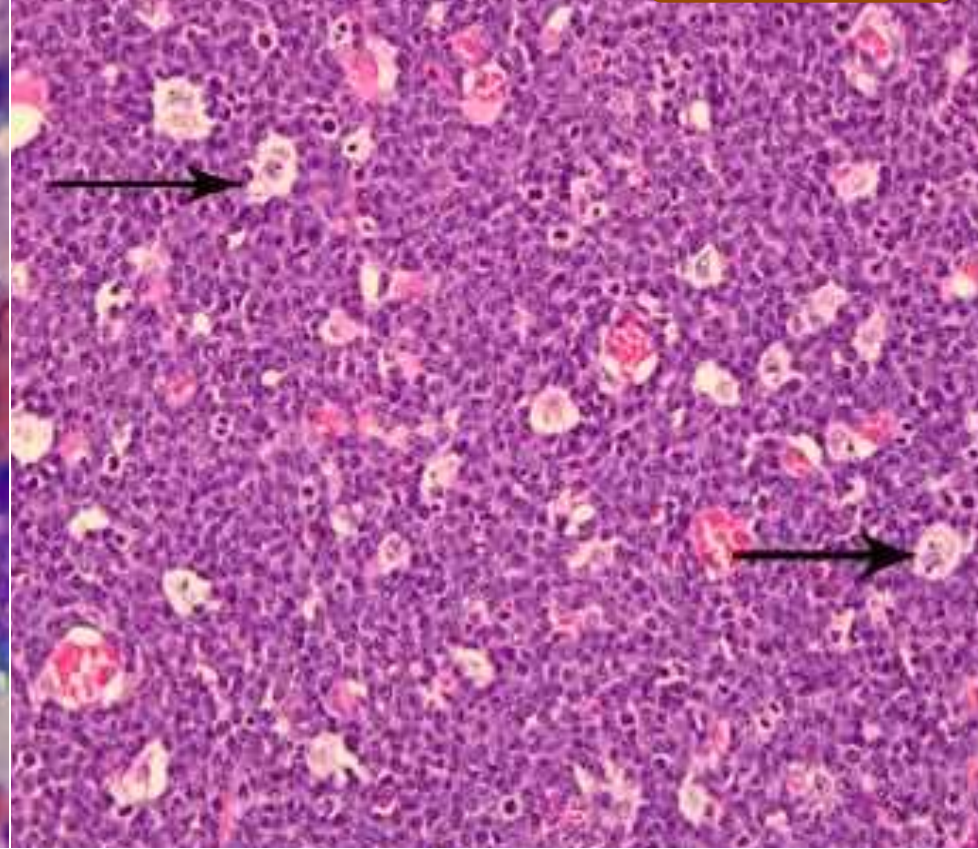
# Morphology

**BMA**



**Homogenous medium size cells with round nuclei and deeply basophilic and vacuolated cytoplasm**

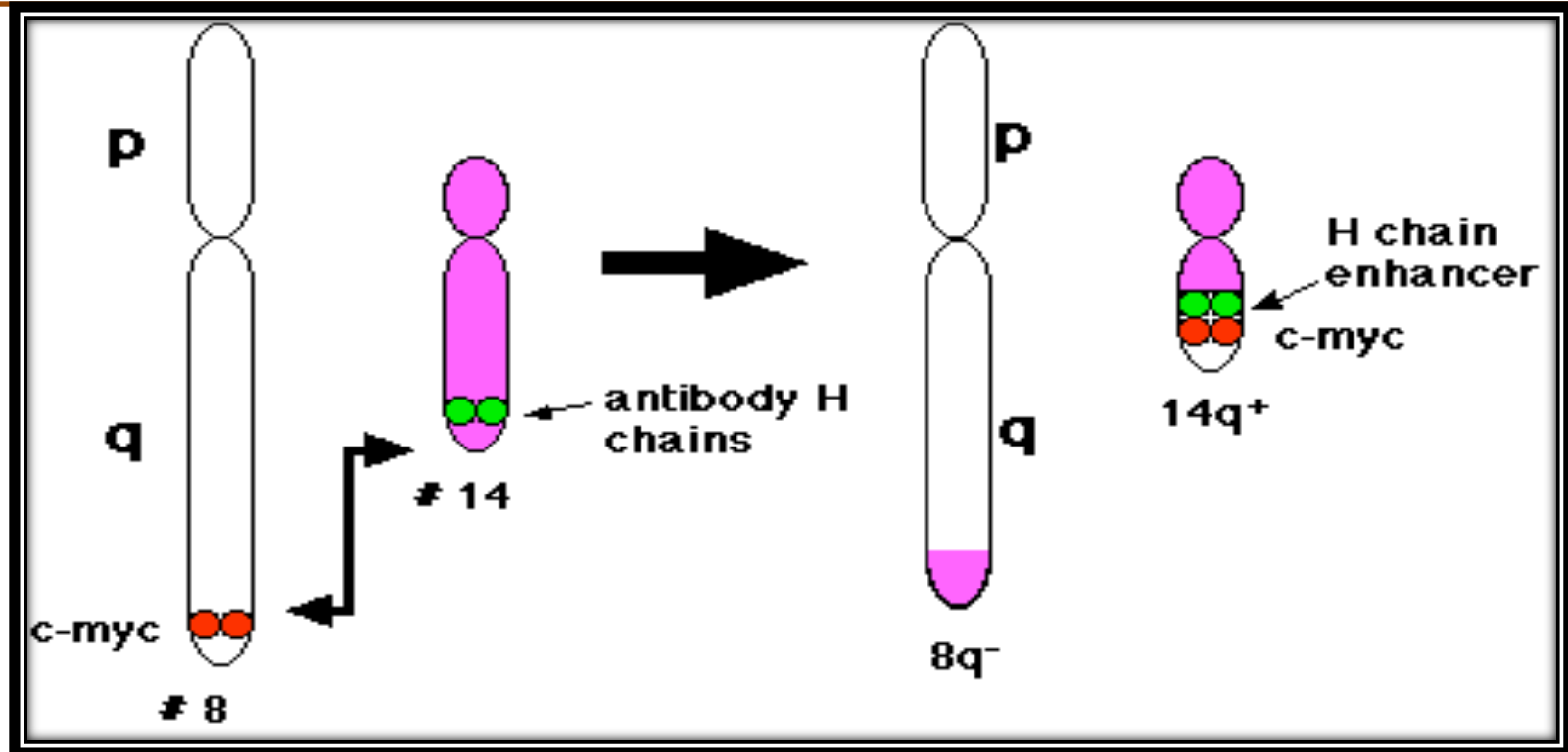
**Biopsy**



**Diffuse infiltration with "starry sky" (Macrophages engulfing the apoptotic cells)**

# Genetics of BL

- ❑ Highly associated with t(8;14):  
Translocation of the c-MYC proto-oncogene at chromosome 8 to immunoglobulin gene at chromosome 14
- ❑ The c-MYC is nuclear transcription factor .
- ❑ Burkitt's lymphoma is the fastest growing tumor in humans.





# Clinical Presentation



After 25 D  
of intensive  
chemotherapy



## Cure rate:

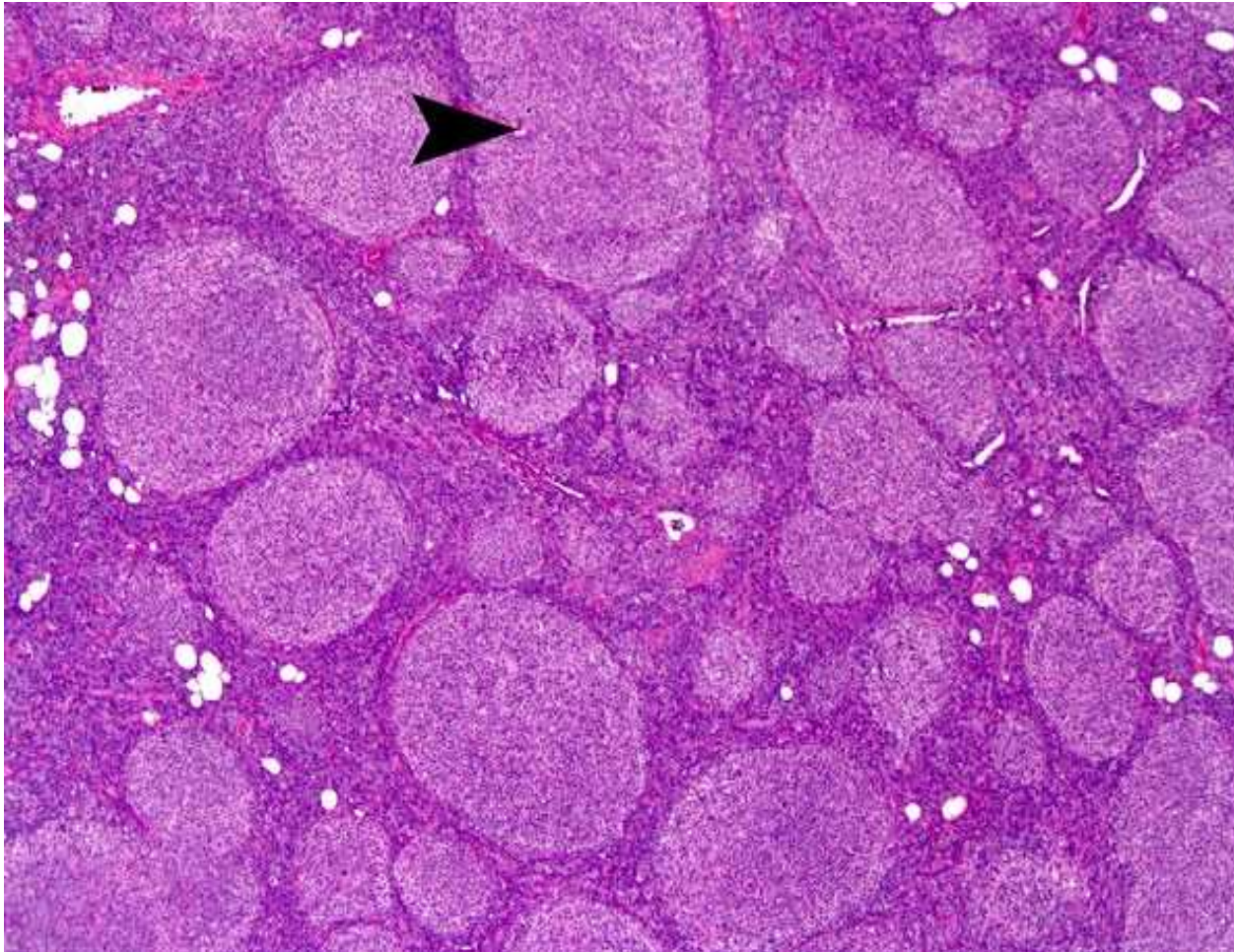
- 90% at early phase
- 70% at advance disease

# Follicular lymphoma

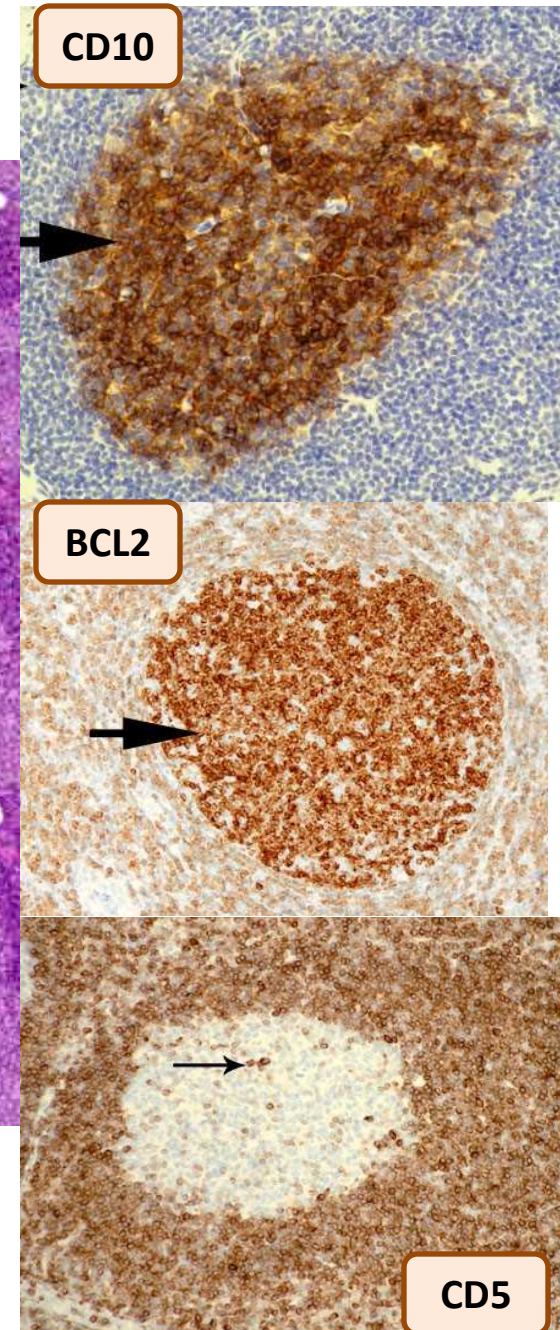
- **FL is malignant proliferation of germinal center B cells centrocyte which has at least a partially follicular pattern.**
- **Due to overexpression of Bcl2 caused by t(14;18) .**
- **Most common type of “indolent” lymphoma (25% ).**
- **Presented as:**
  - Lymphadenopathy (100%)
  - splenomegaly (80%)
  - BM involvement (60%)
  - blood involvement (40%).
- **Indolent but incurable (some exceptions)**



# Diagnosis



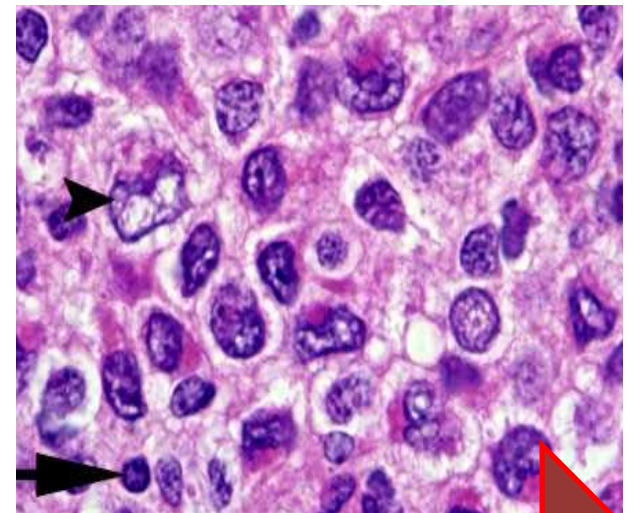
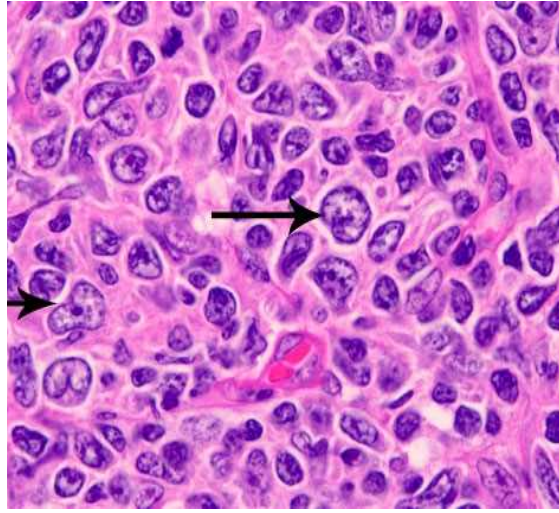
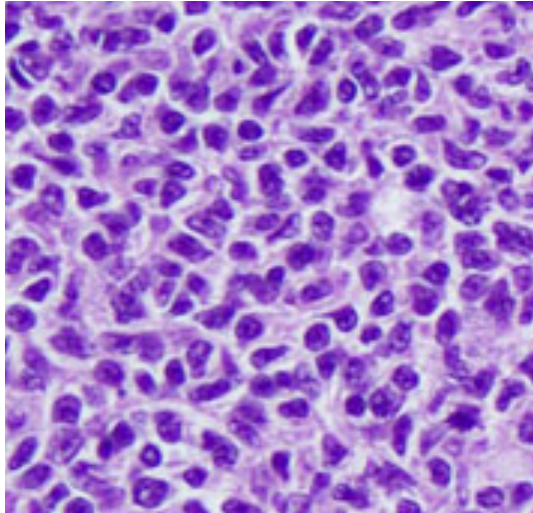
**Immunophenotyping:  
Positive for CD10,CD20 and Bcl2  
Negative for CD5 ( in most cases)**





# Management

- Median survival is around 10 years.
- Transformation to aggressive lymphoma (DLBCL) can occur.



Low grade FL

FL in transformation

Aggressive transformation (DLBCL)

Watch and weight  
(most often)

Chemotherapy

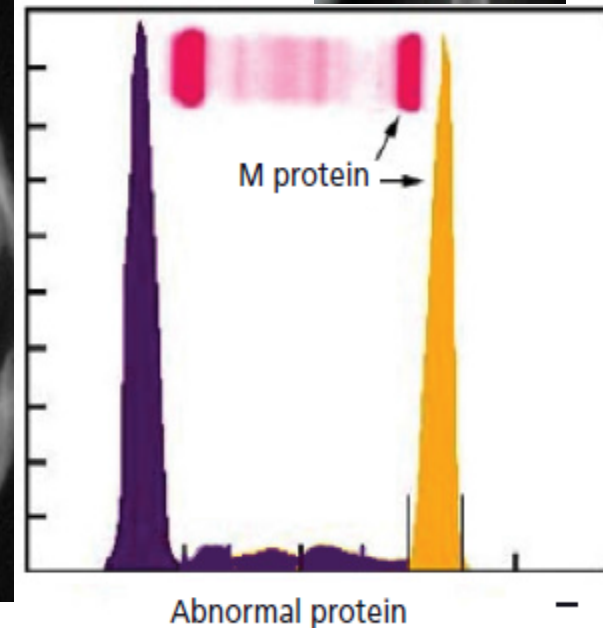
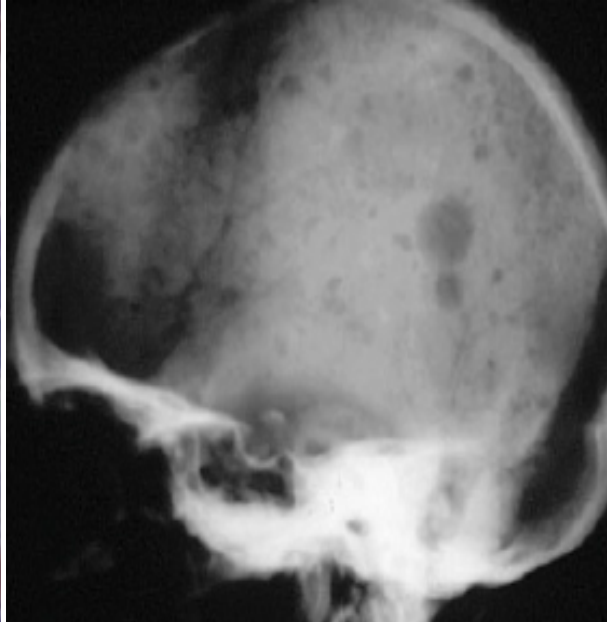
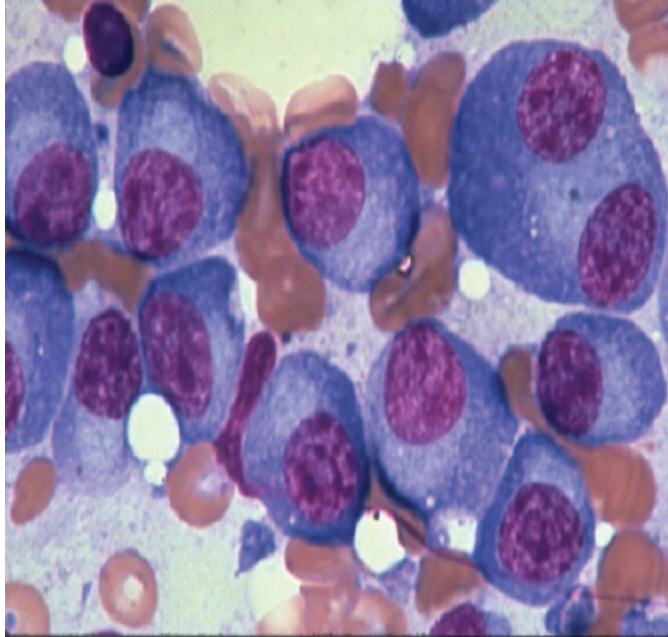
Aggressive  
Chemotherapy (± SCT)



# Multiple Myeloma

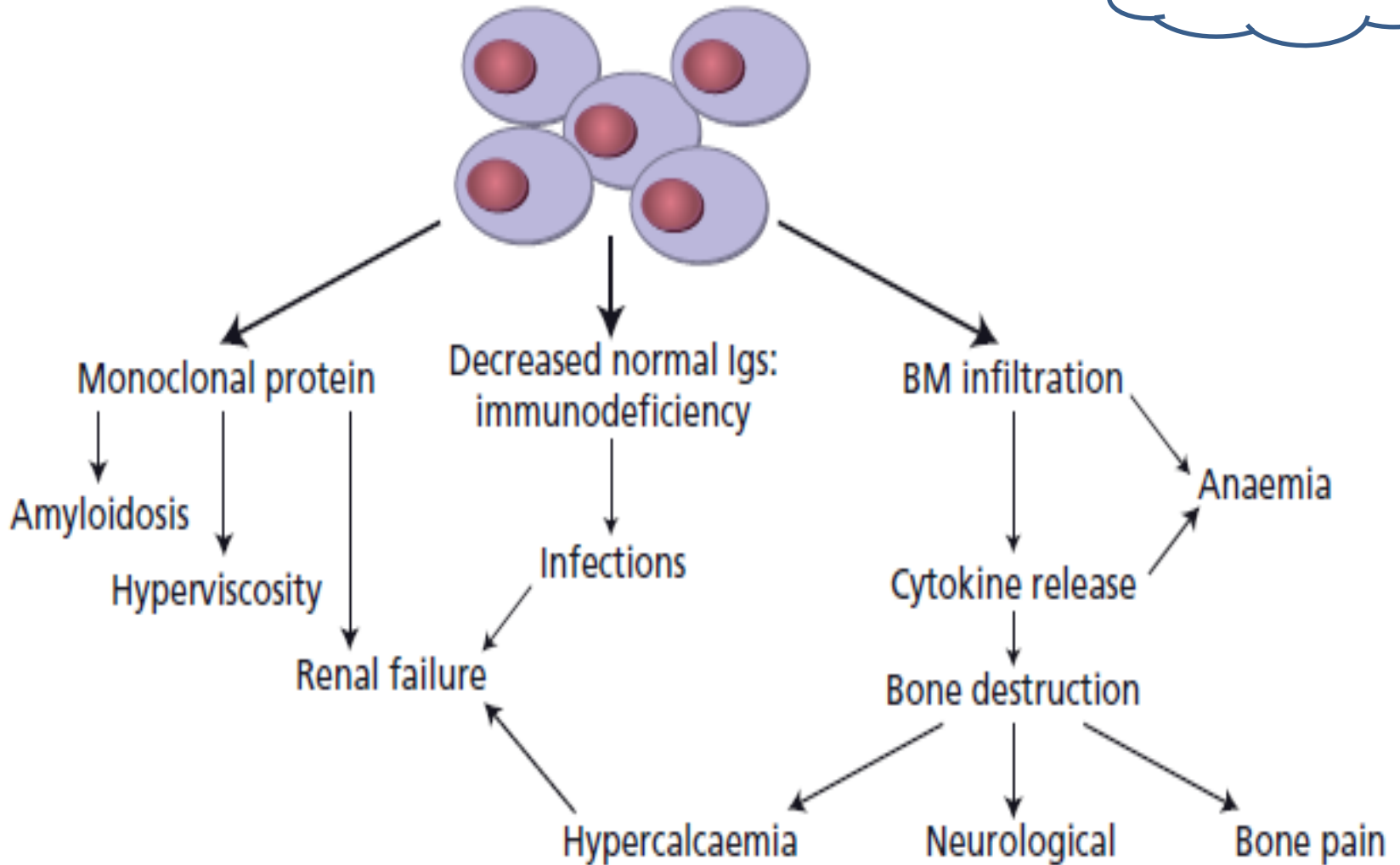
**Malignant B neoplasm characterized by a triad of abnormalities:**

- Accumulation of plasma cells in the bone marrow
- Lytic Bone lesions
- Production of a monoclonal immunoglobulin (Ig) or Ig fragments



# Pathogenesis of MM

For reading



# Hodgkin lymphoma

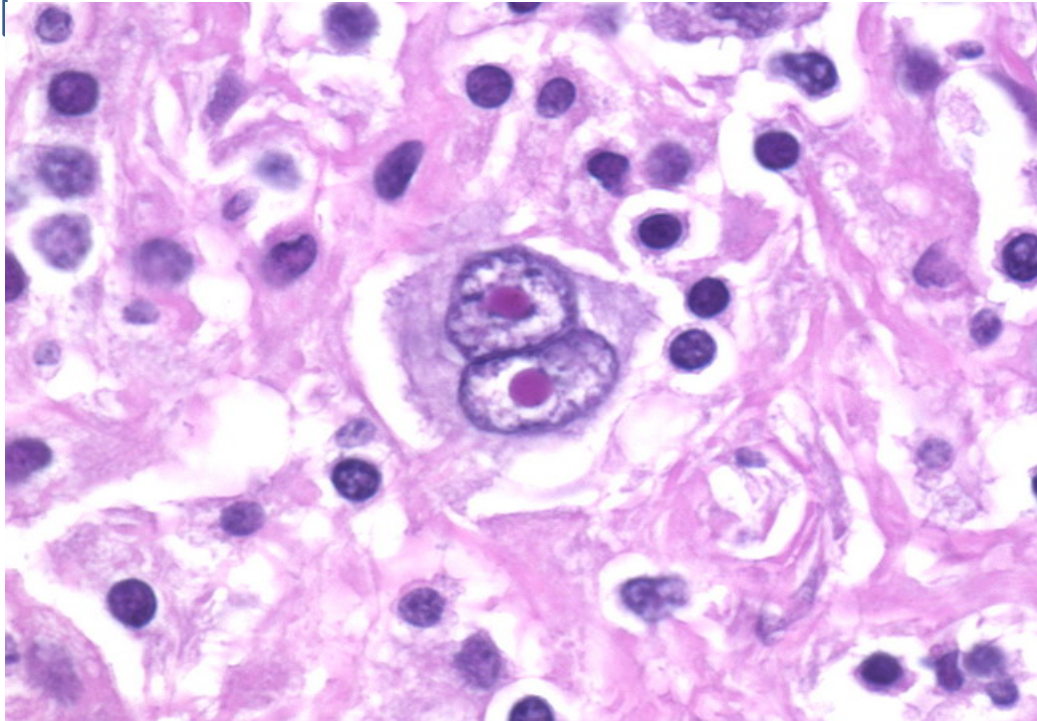


Thomas Hodgkin  
(1798-1866)

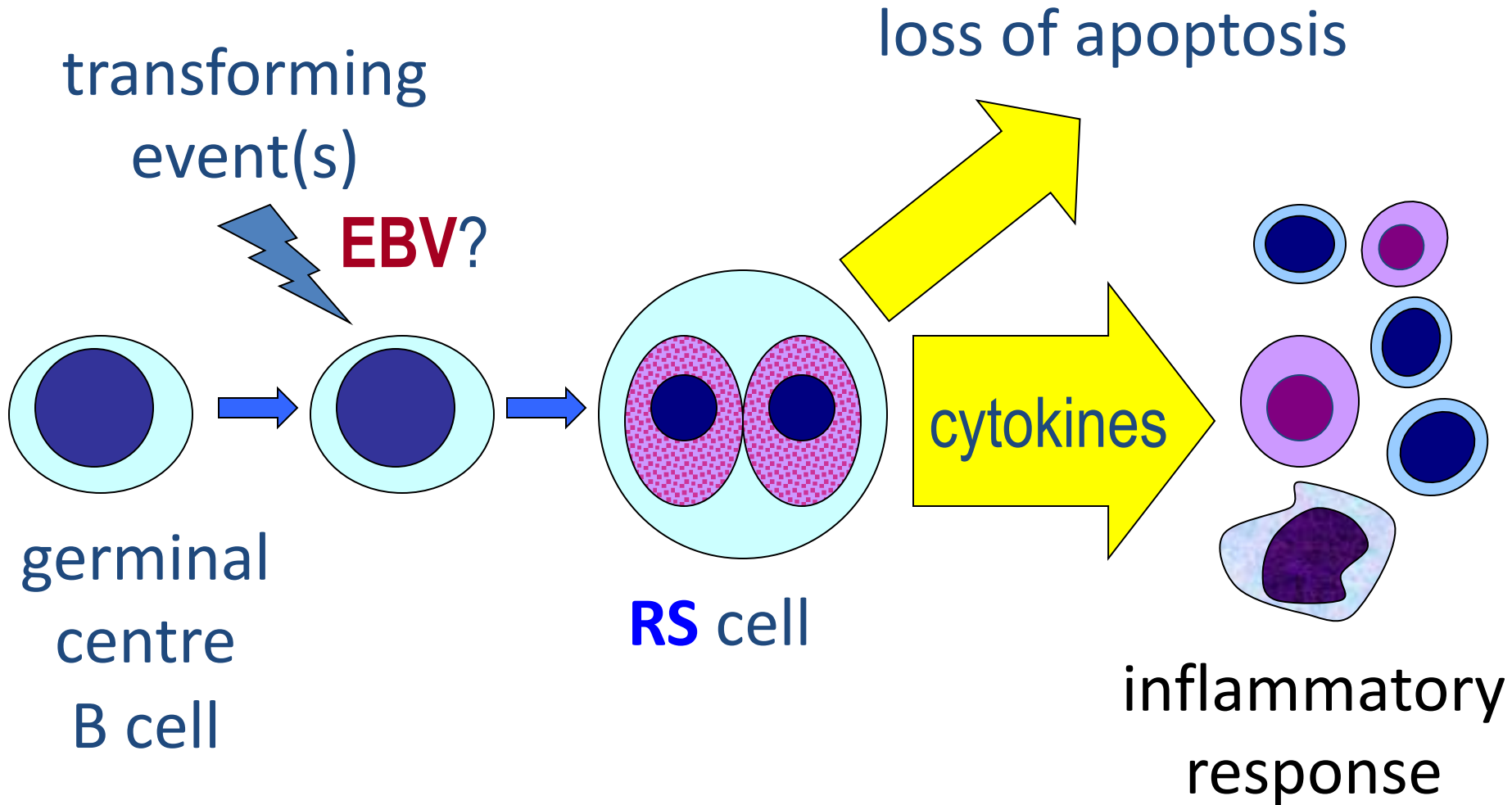
# Classical Hodgkin Lymphoma

Indolent malignant lymphoma characterized by :

- 1- presence of few large binucleated cells (Reed-Sternberg ) surrounded by reactive cells (lymphocytes, plasma cells ,eosinophils)
- 2- Involving cervical lymph nodes in young adults (most often )



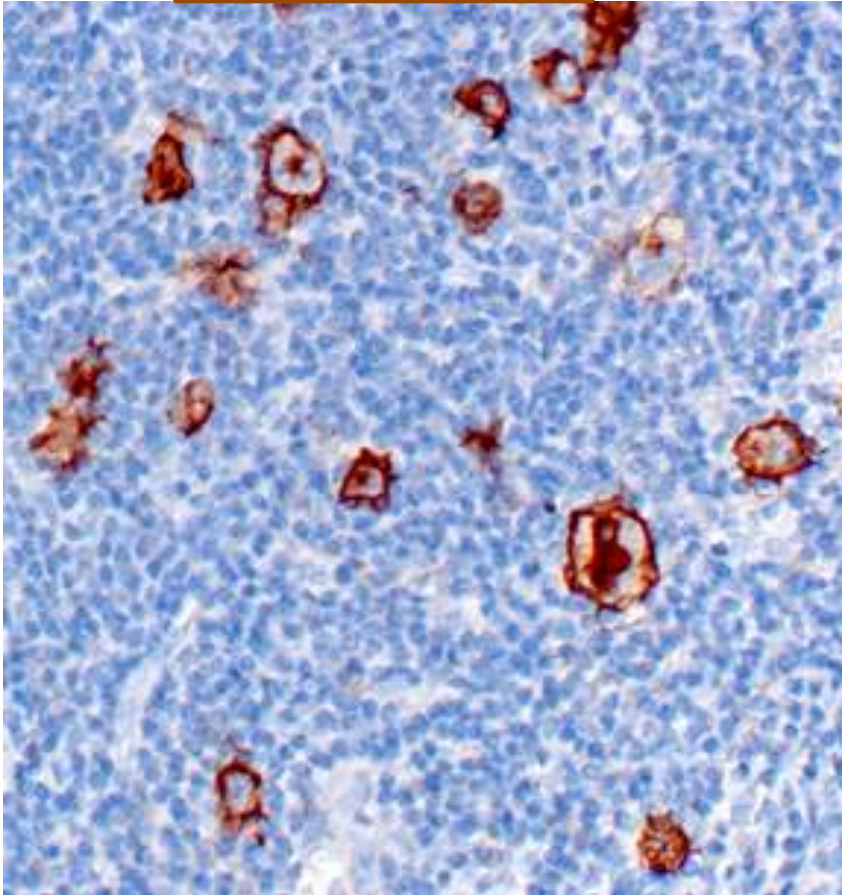
# A possible model of pathogenesis



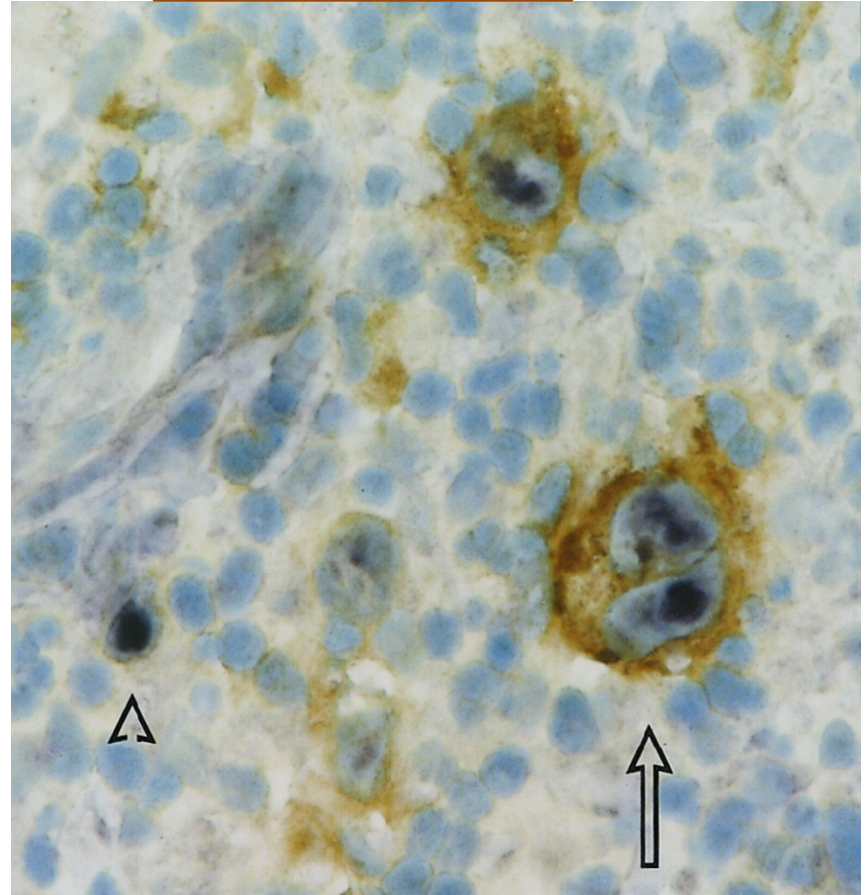


# Diagnosis of Hodgkin Lymphoma

CD 30



CD 15



For reading

## Immunophenotype of Small B-Cell Neoplasms

Marker	CLL/ SLL	Mantle Cell Lymphoma	Follicular Lymphoma	Hairy Cell Leukemia	Marginal Zone Lymphoma
CD5	+	+	-	-	-
CD10 (cALLA)	-	-	+	-	-
CD20	Dim	+	+	+	+
CD23	+	-	+/-	+/-	-
FMC-7	-	+	+	+/-	+
Surface Ig*	Dim	Moderate or bright	+	+	+
Other				CD11c, CD25, and CD103	