

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

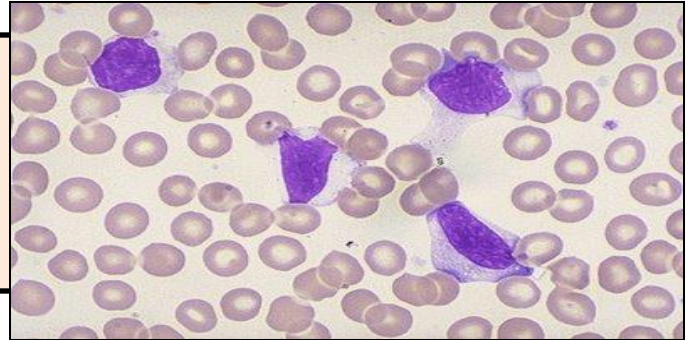
Infection

Malignant

Lymphocytosis

1- Viral infection :

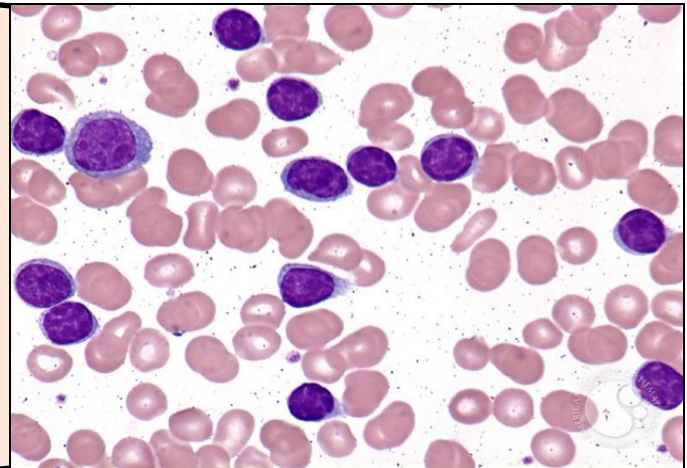
• Infectious mononucleosis , cytomegalovirus , rubella, hepatitis, adenoviruses, varicella....



2- Some bacterial infection: (Pertussis ,brucellosis ...)

3-Immune : SLE , Allergic drug reactions

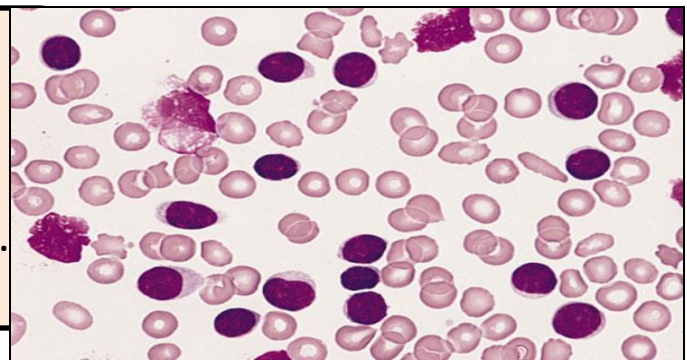
4- Other conditions:, splenectomy,
dermatitis ,hyperthyroidism metastatic
carcinoma....)



5- Chronic lymphocytic leukemia (CLL)

6-Other lymphomas:

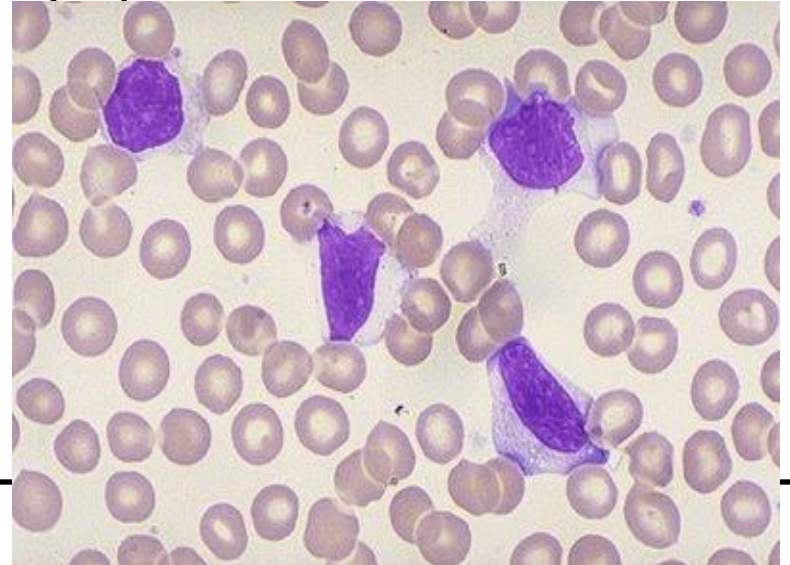
Mantle cell lymphoma ,Hodgkin lymphoma...



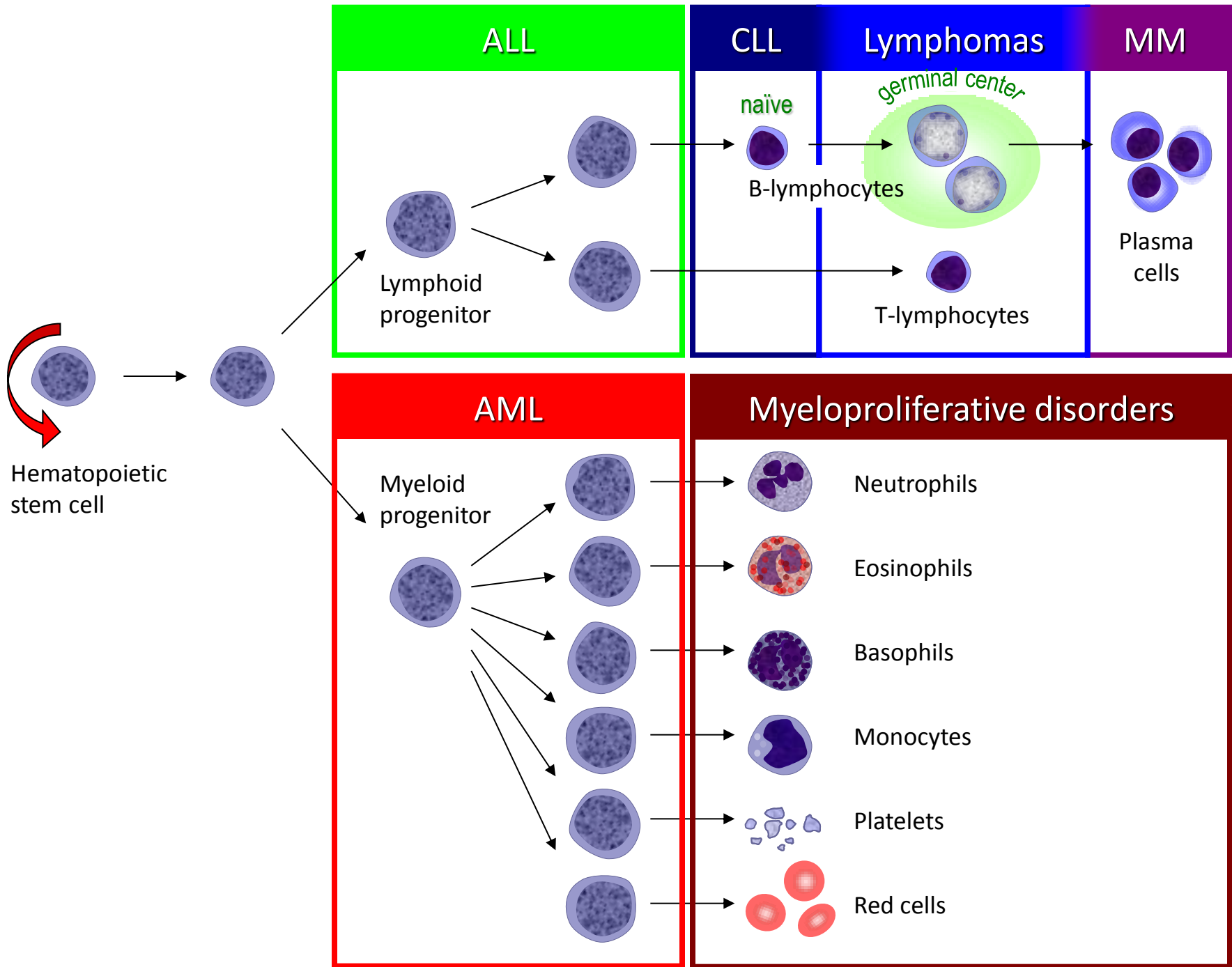
Infectious mononucleosis

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

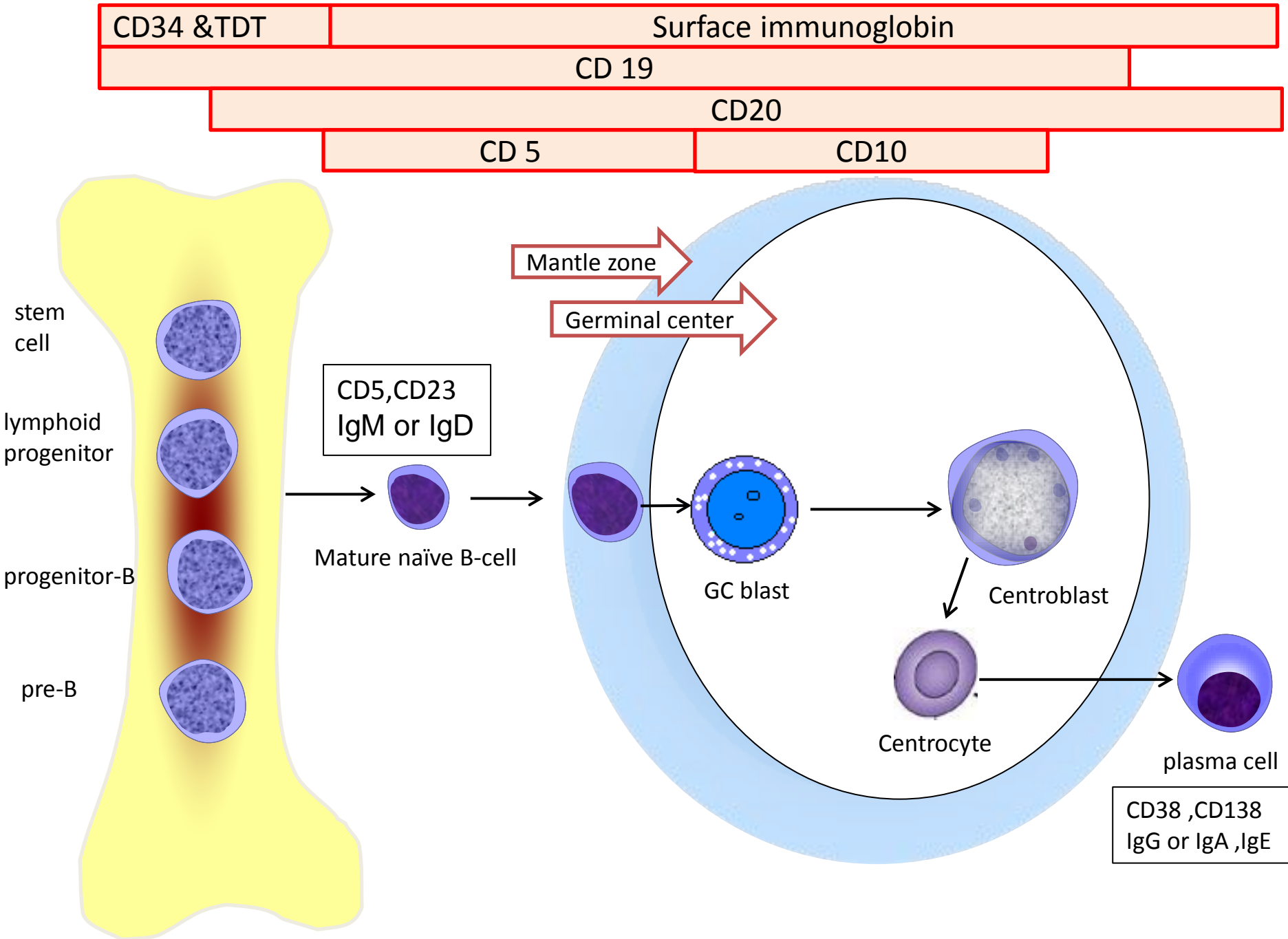
10%

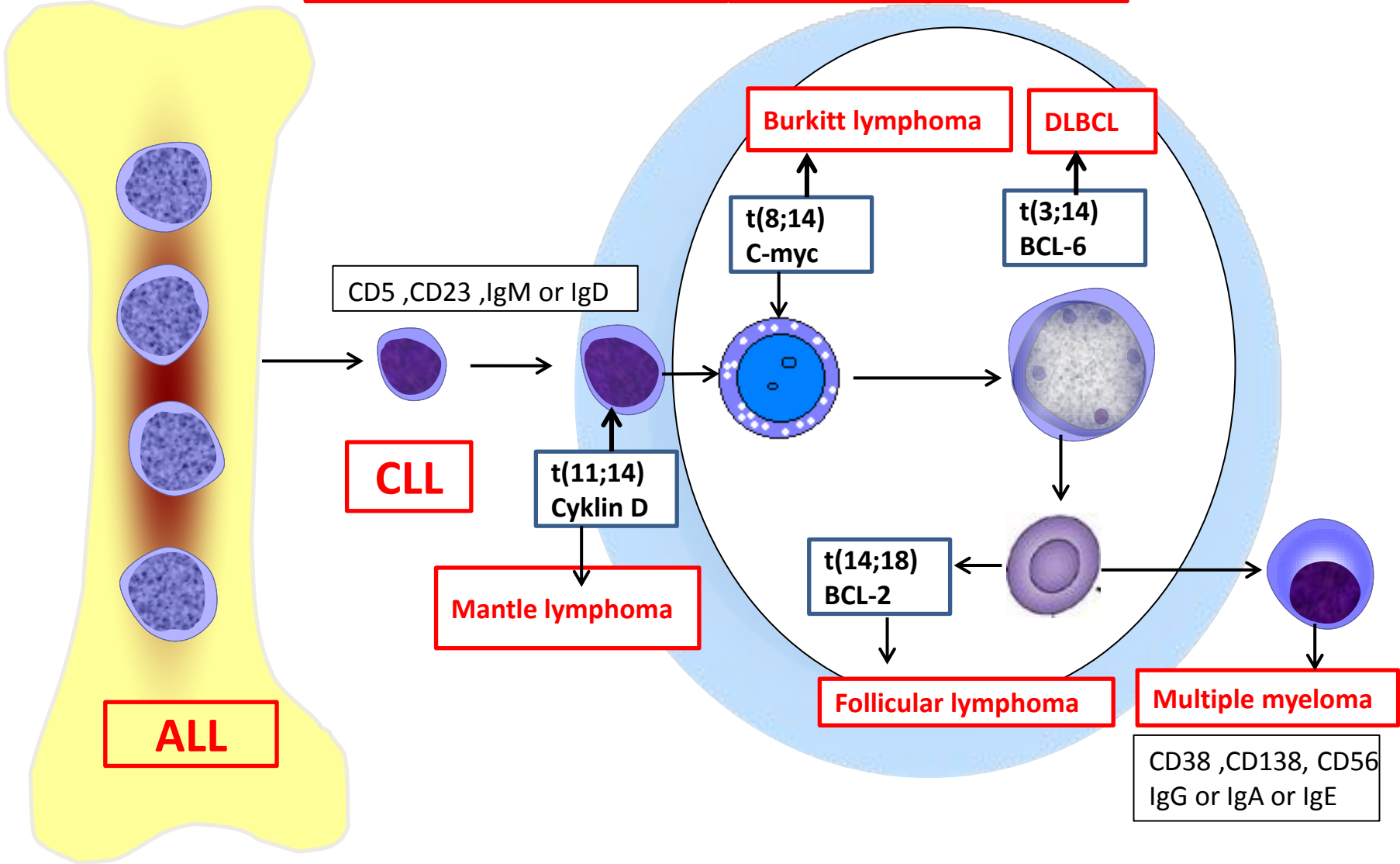
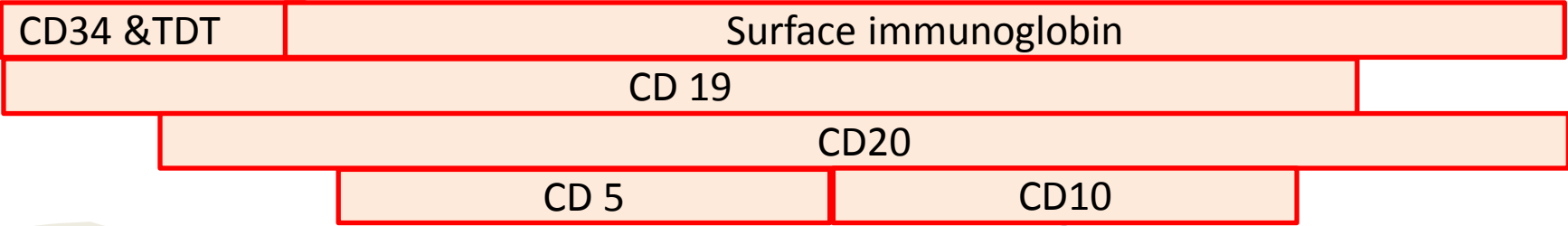
Burkitt lymphoma
Diffuse large B lymphoma
Follicular lymphoma
Multiple myeloma

Adult T leukemia lymphoma
Sezary syndrome
Large anaplastic T lymphoma

Lymphoid leukemia

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



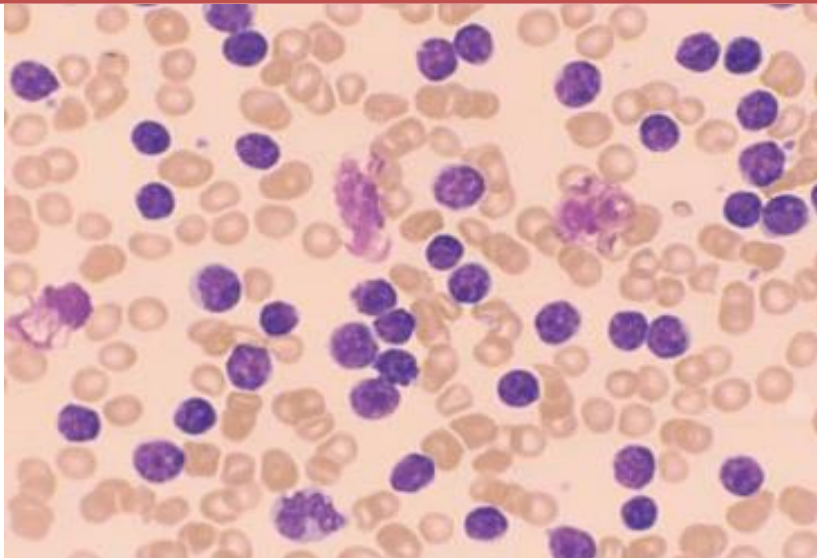
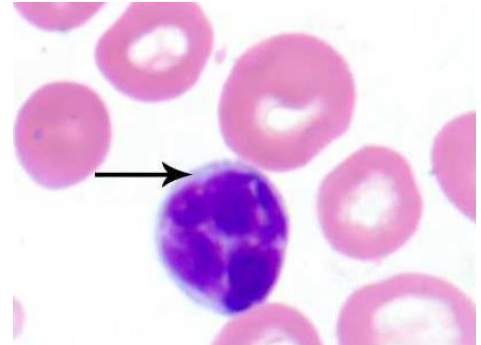


Chronic Lymphocytic Leukemia

- **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 Watch & wait
Stage I: Lymphocytosis plus enlarged nodes	Watch & wait
Stage II: Lymphocytosis plus enlarged spleen and/or liver, ± nodes	Intermediate ±chemo
Stage III: Lymphocytosis plus anemia (Hgb <11 g/dL), ± above	±chemo
Stage IV: Lymphocytosis plus thrombocytopenia ($<100 \times 10^9/L$) ± above	High risk FCR

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

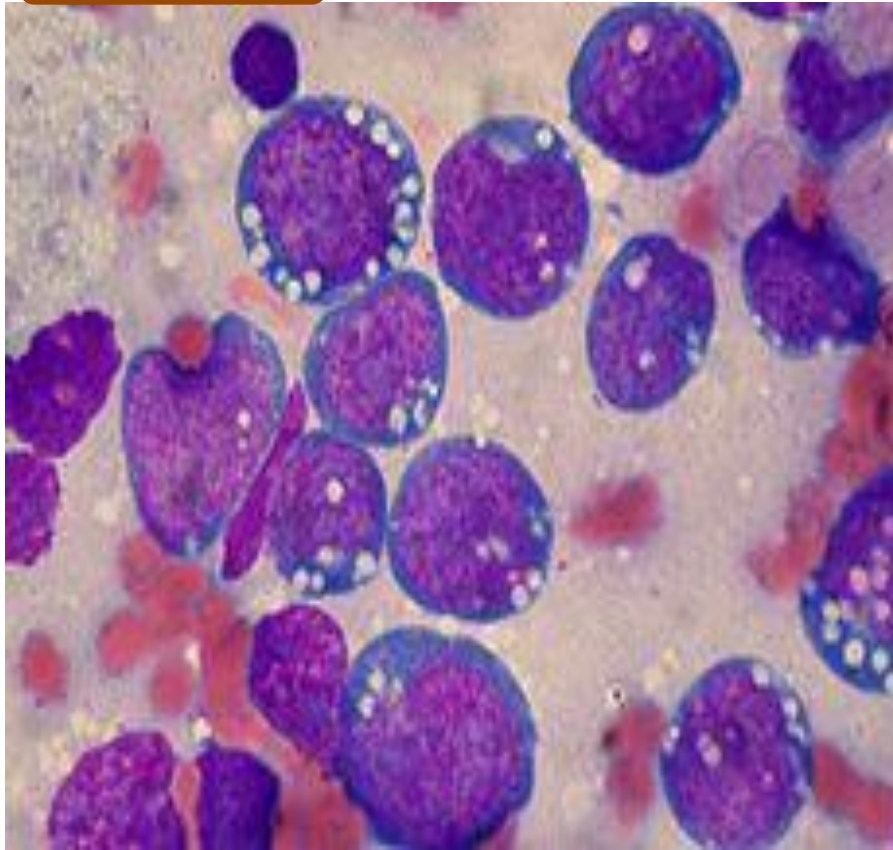
1-Endemic: associated with chronic malaria and EBV In equatorial Africa . It particularly affects the jaw, other facial bone and breast.

Sporadic: occurs throughout the world and affects GIT.

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

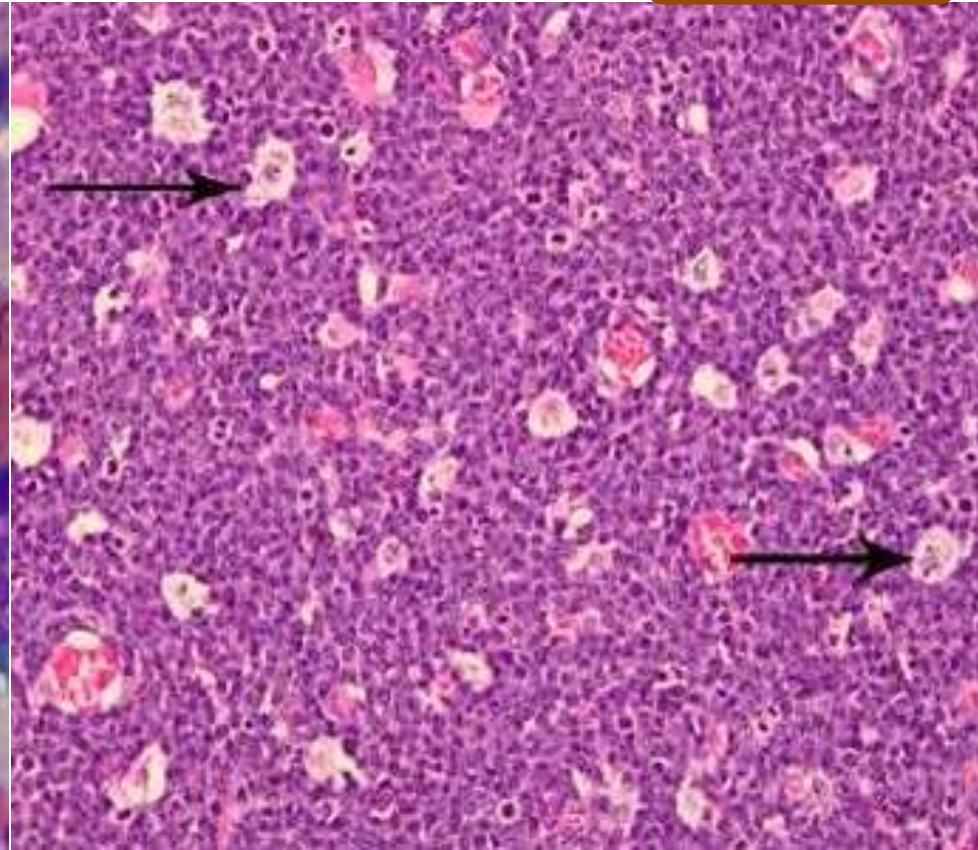
Morphology

BMA



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

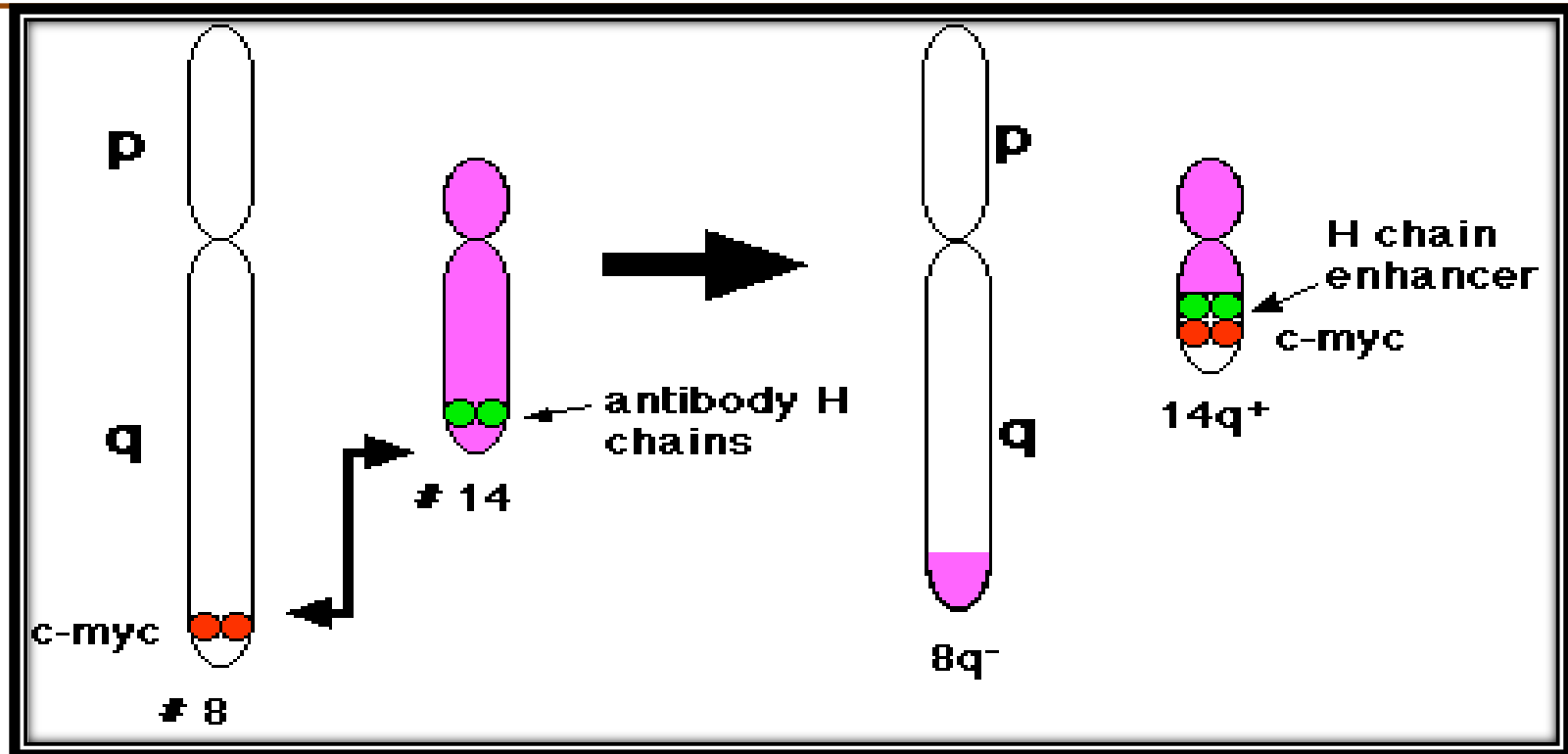
Biopsy



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



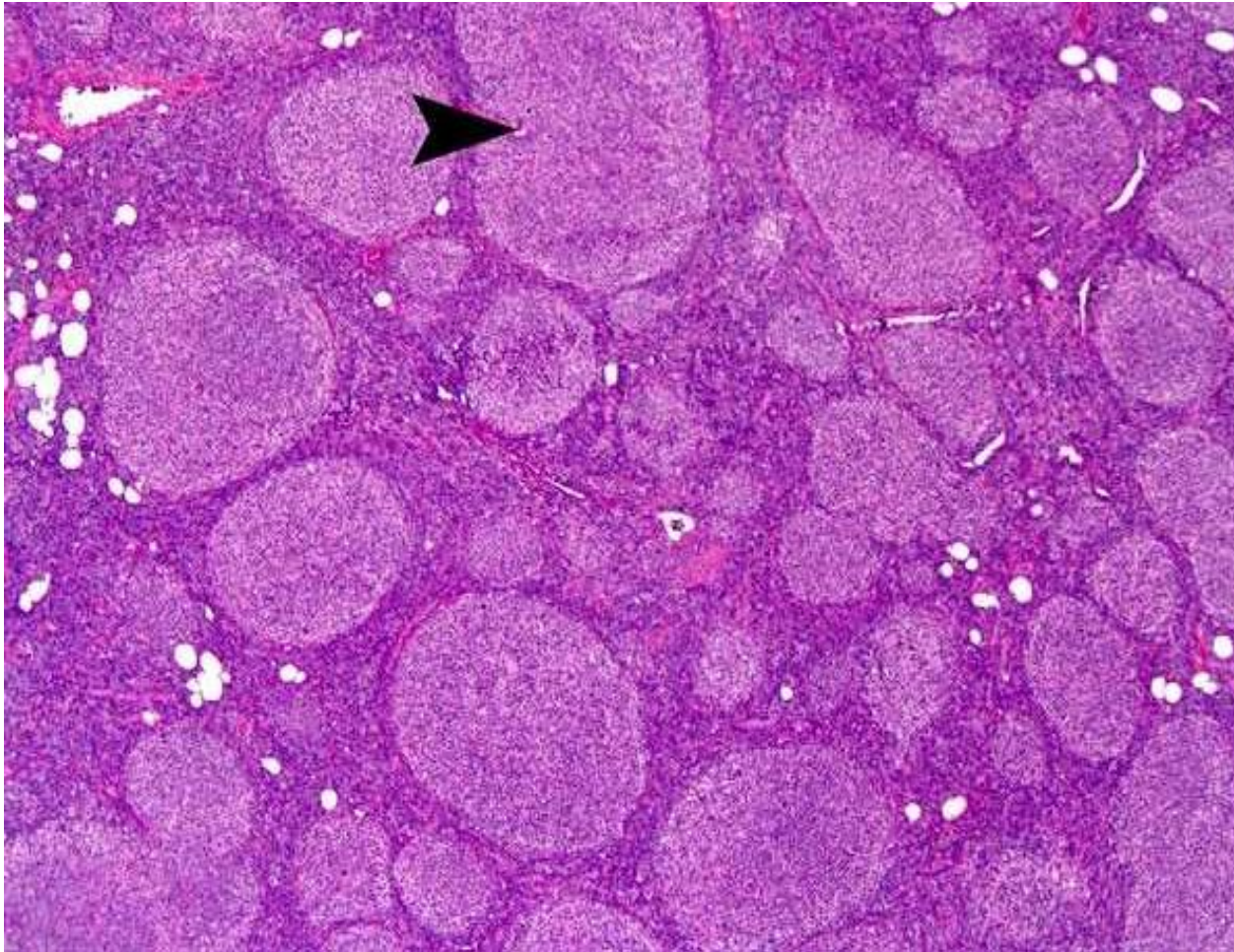
Cure rate:

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

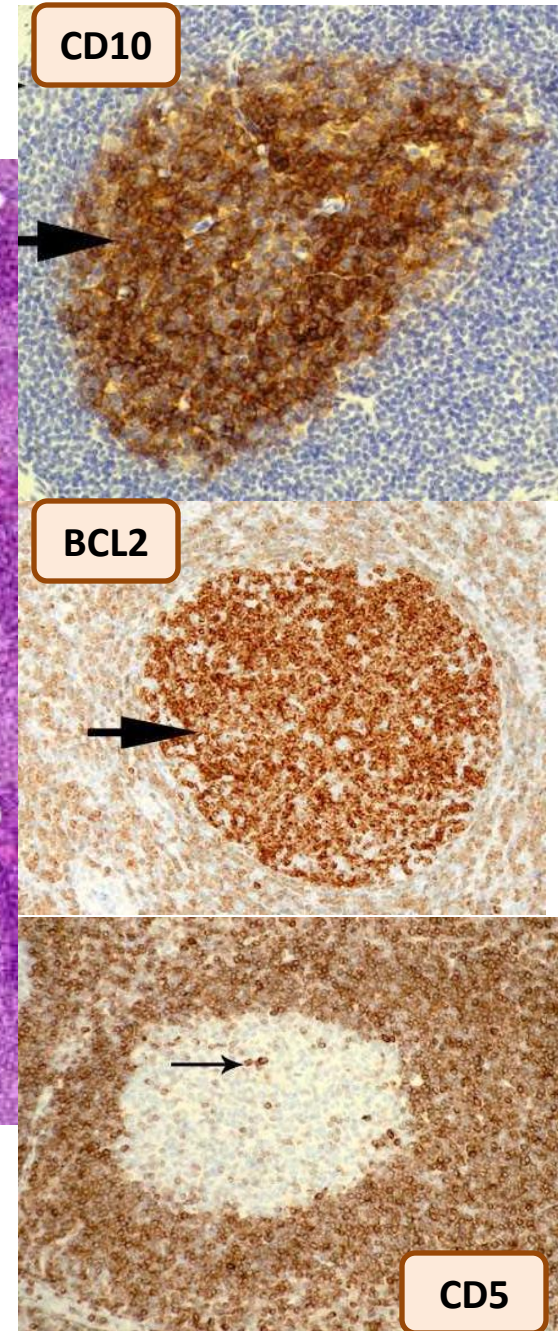
Follicular lymphoma

- **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

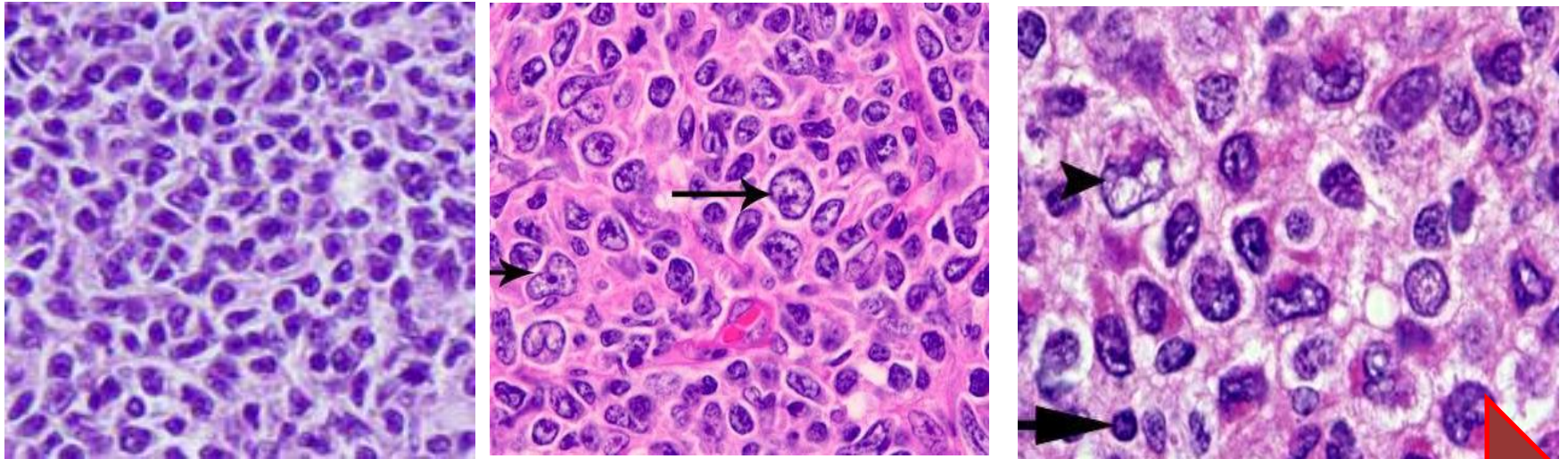


**Immunophenotyping:
Positive for CD10,CD20 and Bcl2
Negative for CD5 (in most cases)**



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)

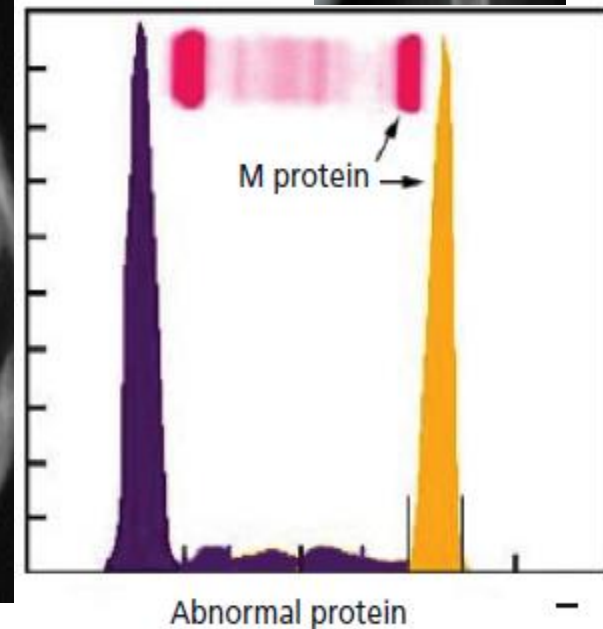
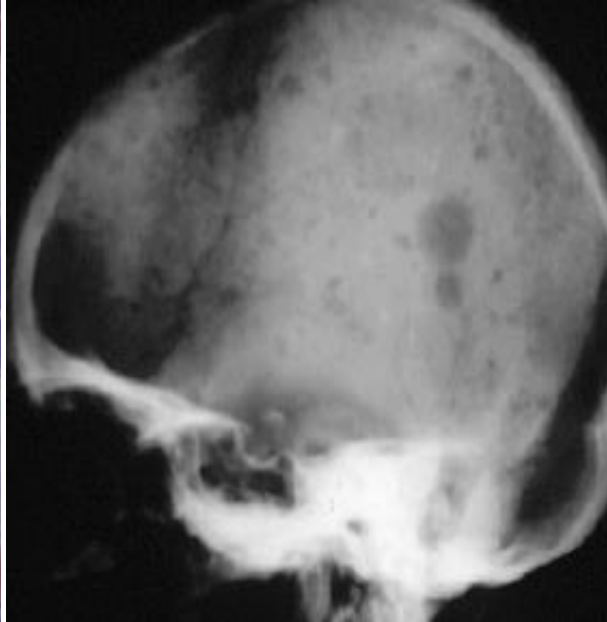
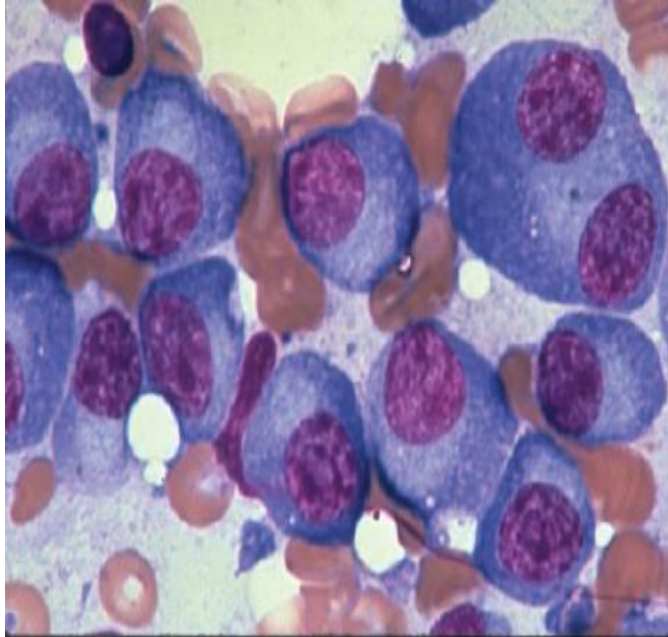
Chemotherapy

Aggressive
Chemotherapy(± SCT)

Multiple Myeloma

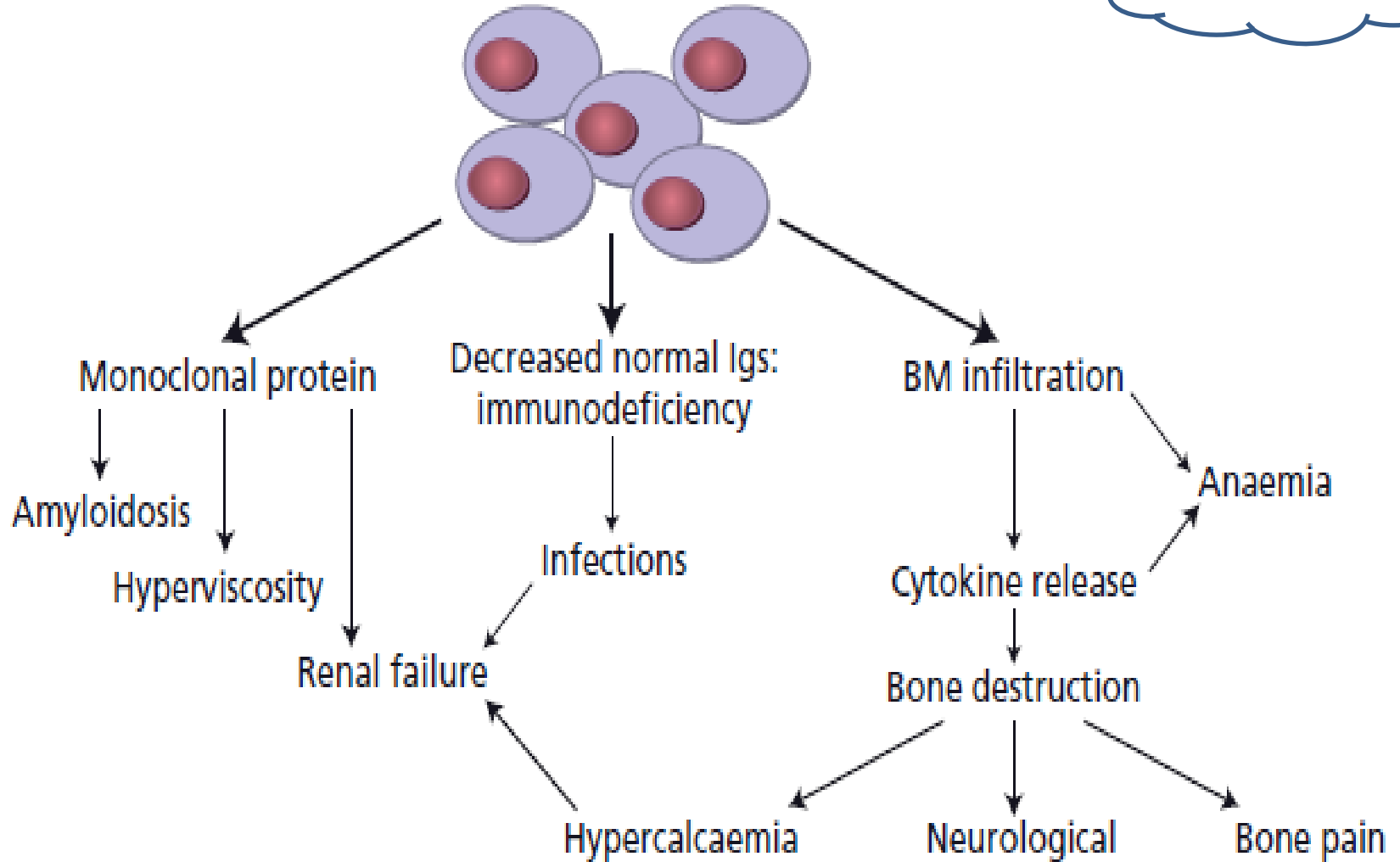
Malignant B neoplasm characterized by a triad of abnormalities:

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

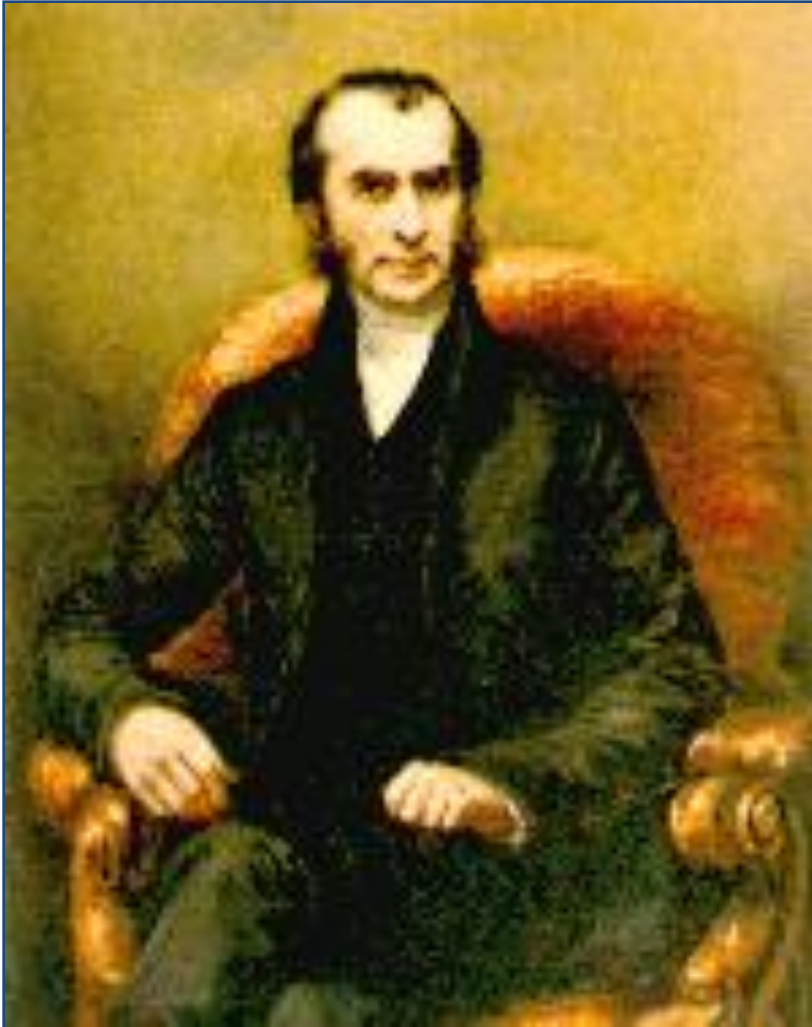


Pathogenesis of MM

For reading



Hodgkin lymphoma

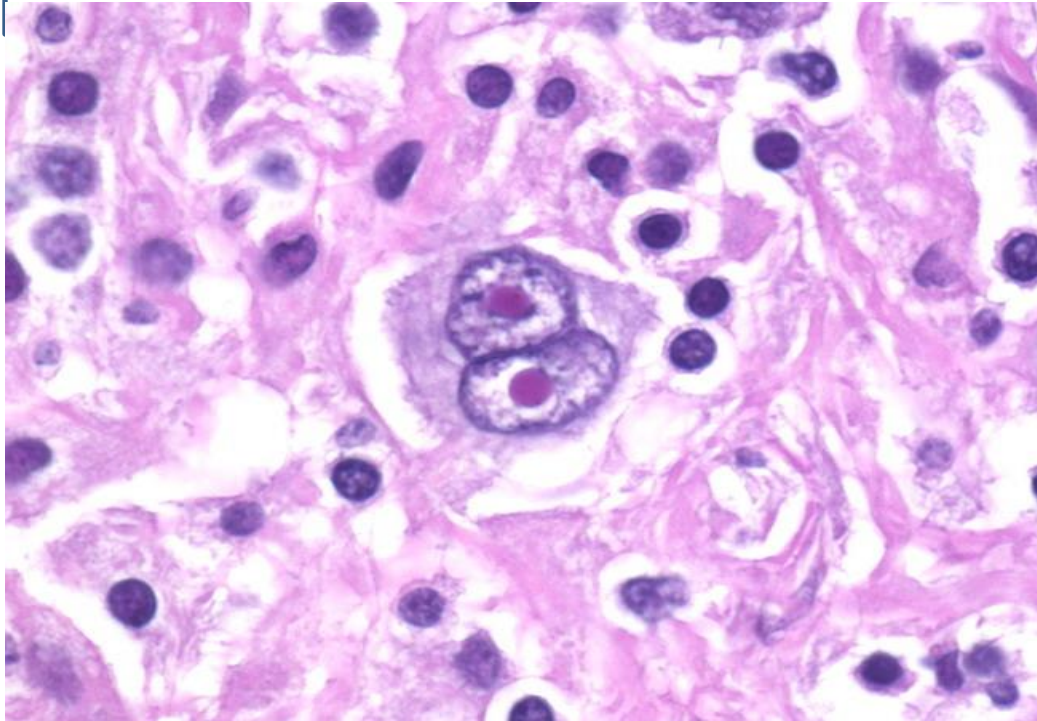


Thomas Hodgkin
(1798-1866)

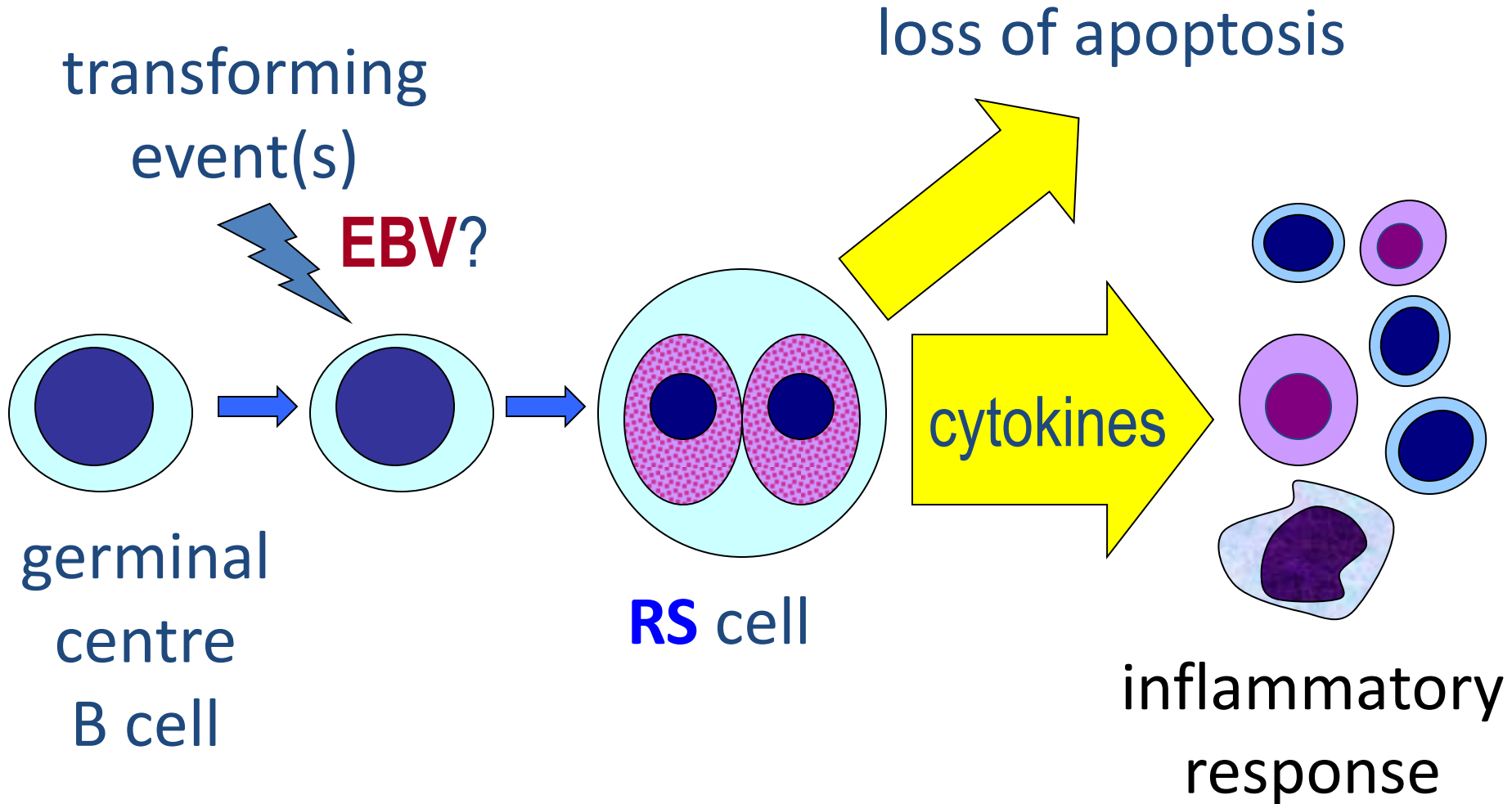
Classical Hodgkin Lymphoma

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)

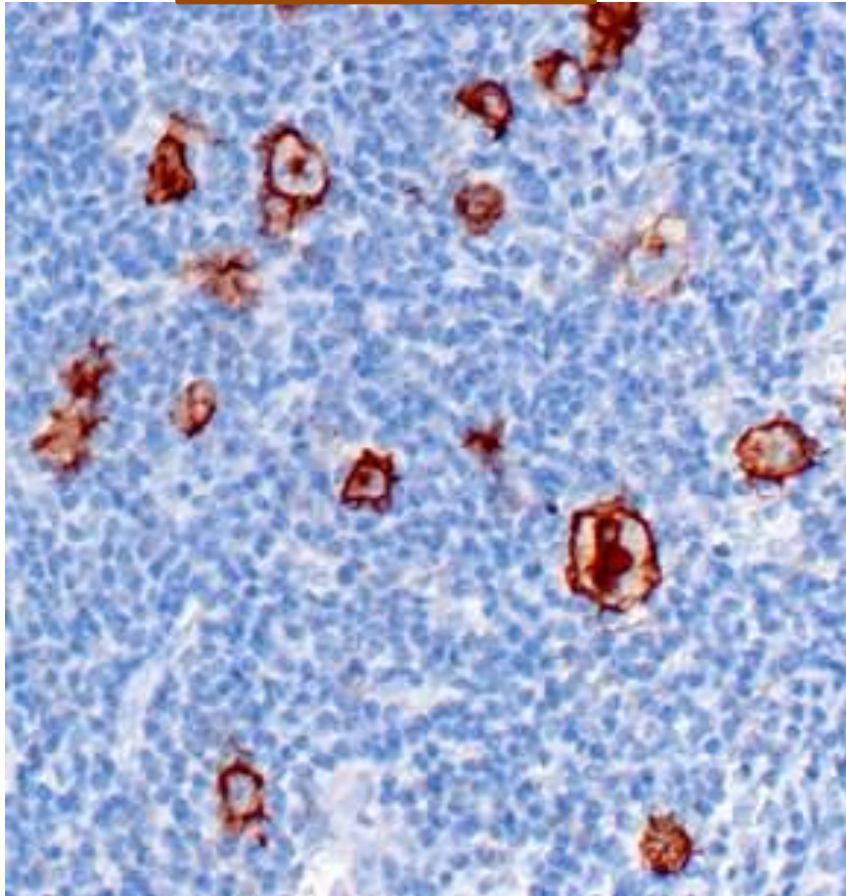


A possible model of pathogenesis

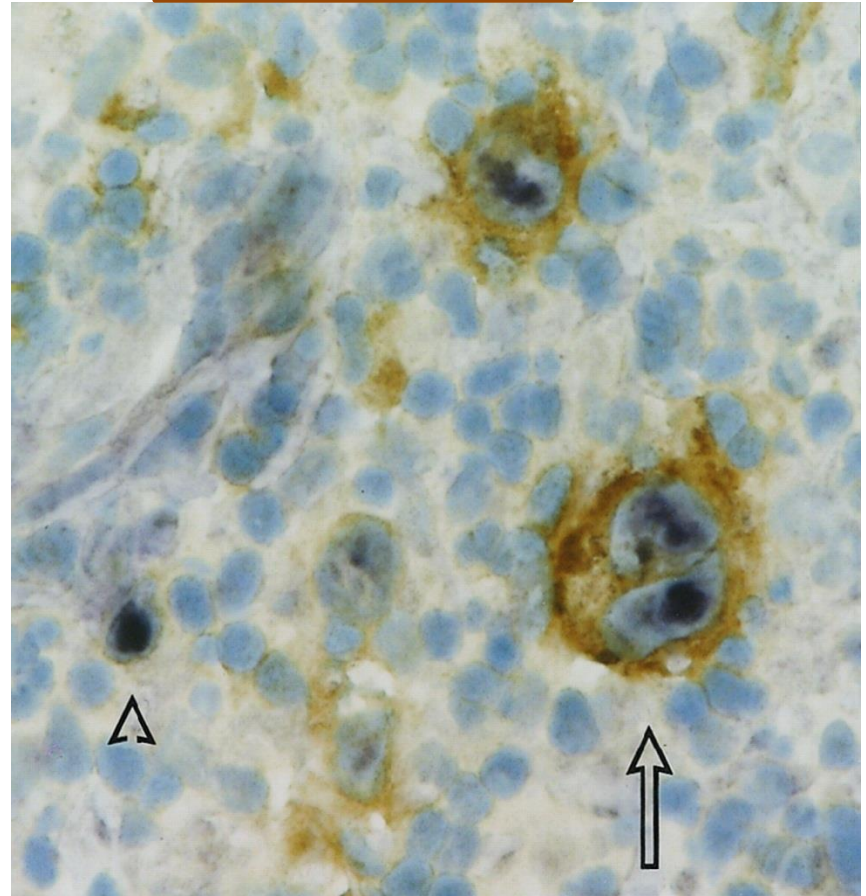


Diagnosis of Hodgkin Lymphoma

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	