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 (± other tissues e.g : skin ,GIT ,CNS …)

Lymphoid leukemia

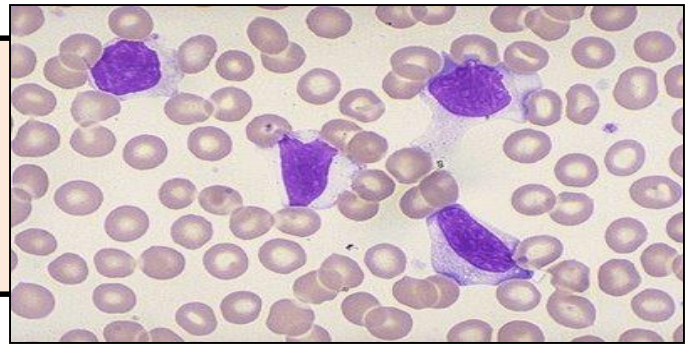
Malignant proliferation of lymphoid cells in Bone marrow and peripheral blood (± other tissues e.g : lymph nods ,spleen , skin ,GIT ,CNS …)

Lymphoproliferative disorders

Lymphocytosis

1- Viral infection :

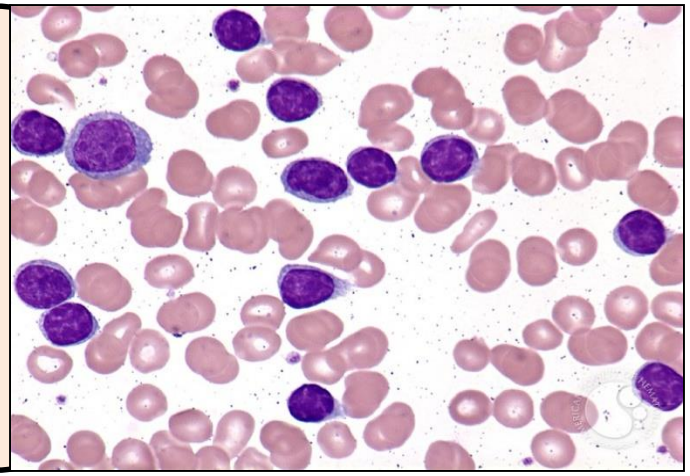
•*Infectious mononucleosis* ,cytomegalovirus ,rubella, hepatitis, adenoviruses, varicella….



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

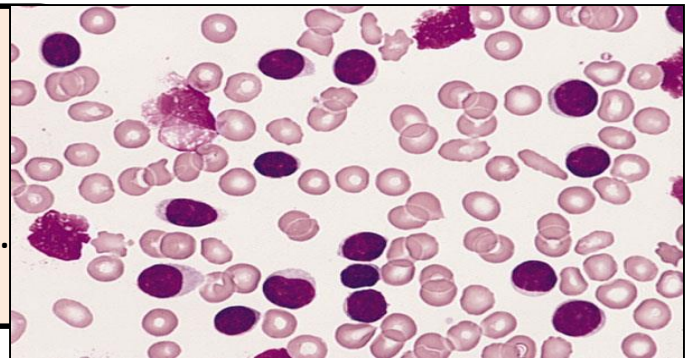
3-Immune : SLE , Allergic drug reactions

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



5- Chronic lymphocytic leukemia (CLL)

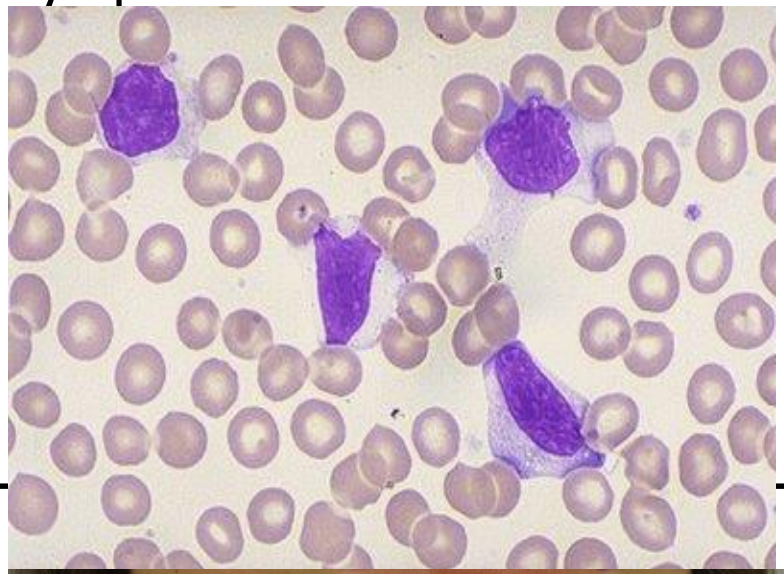
6-Other lymphomas:
Mantle cell lymphoma ,Hodgkin lymphoma…

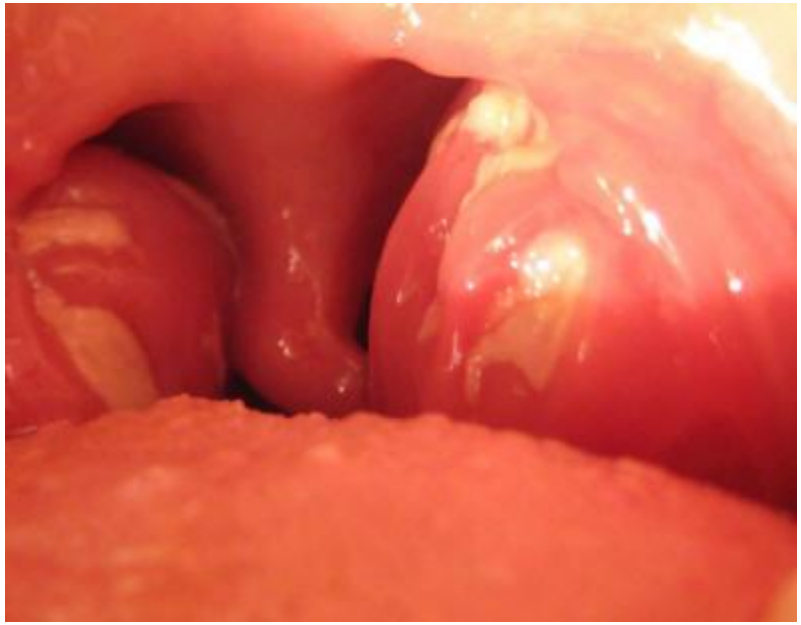


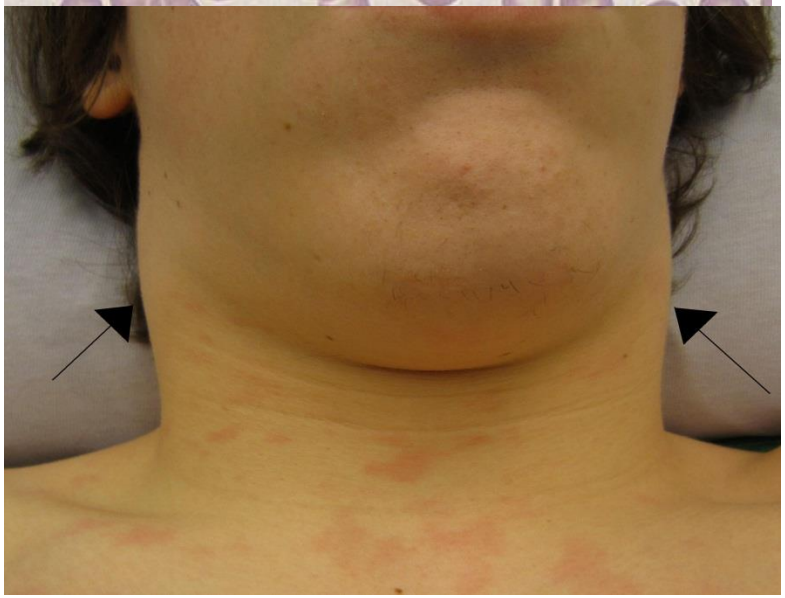
Infectious mononucleosis

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

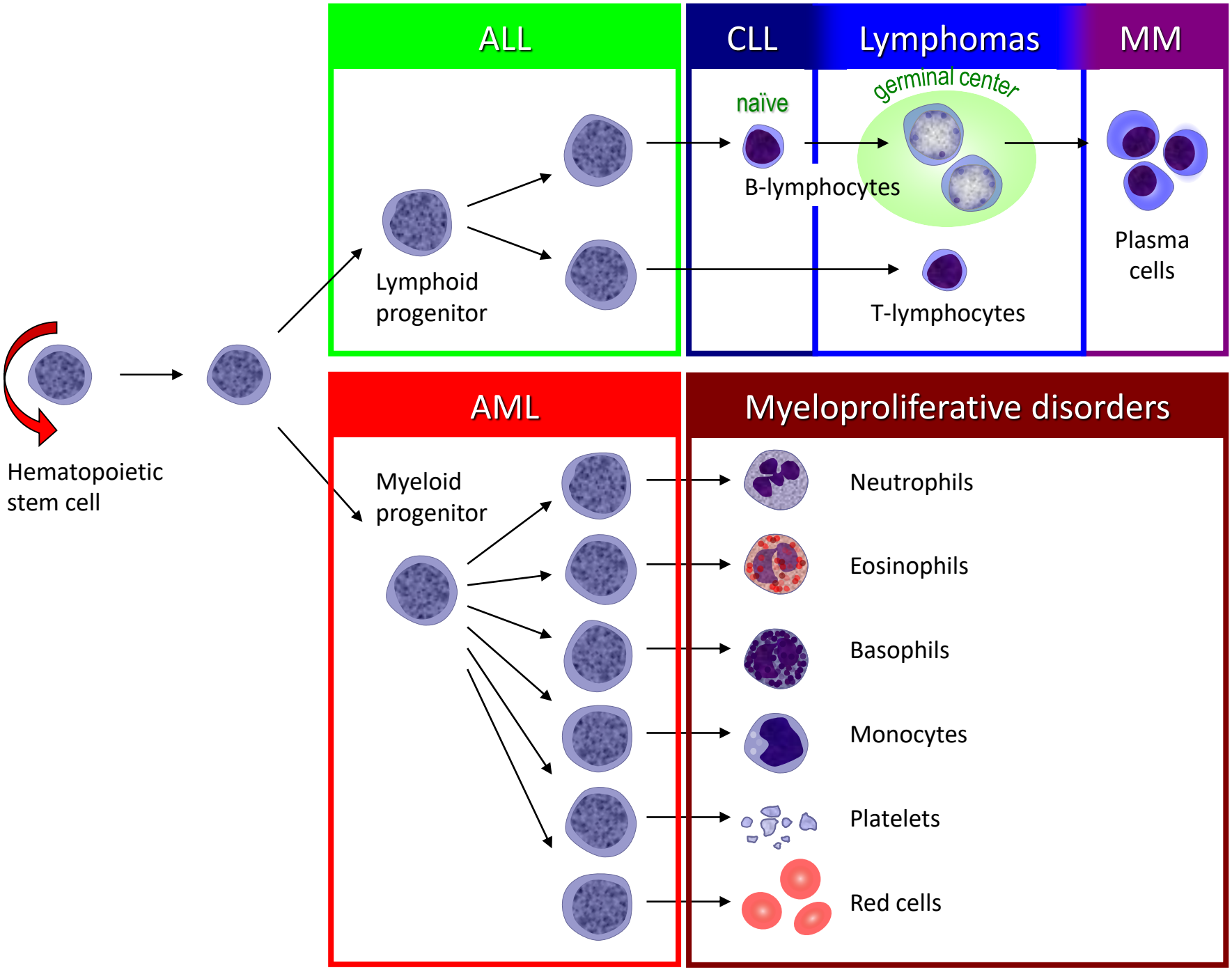
- fever
- swollen lymph nodes (painful)
- Sore throat,
- atypical lymphocyte
- Affect young people (usually)

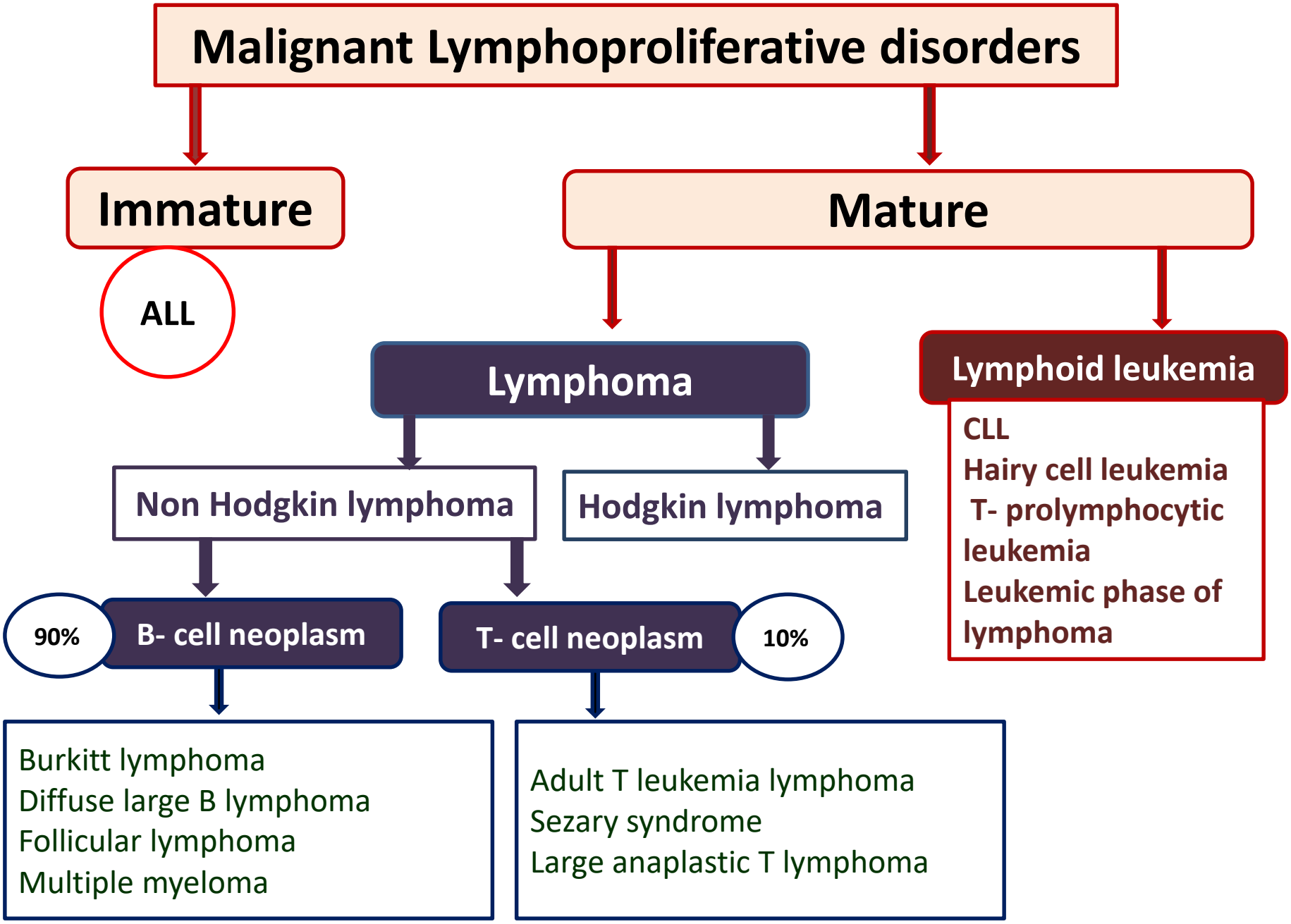


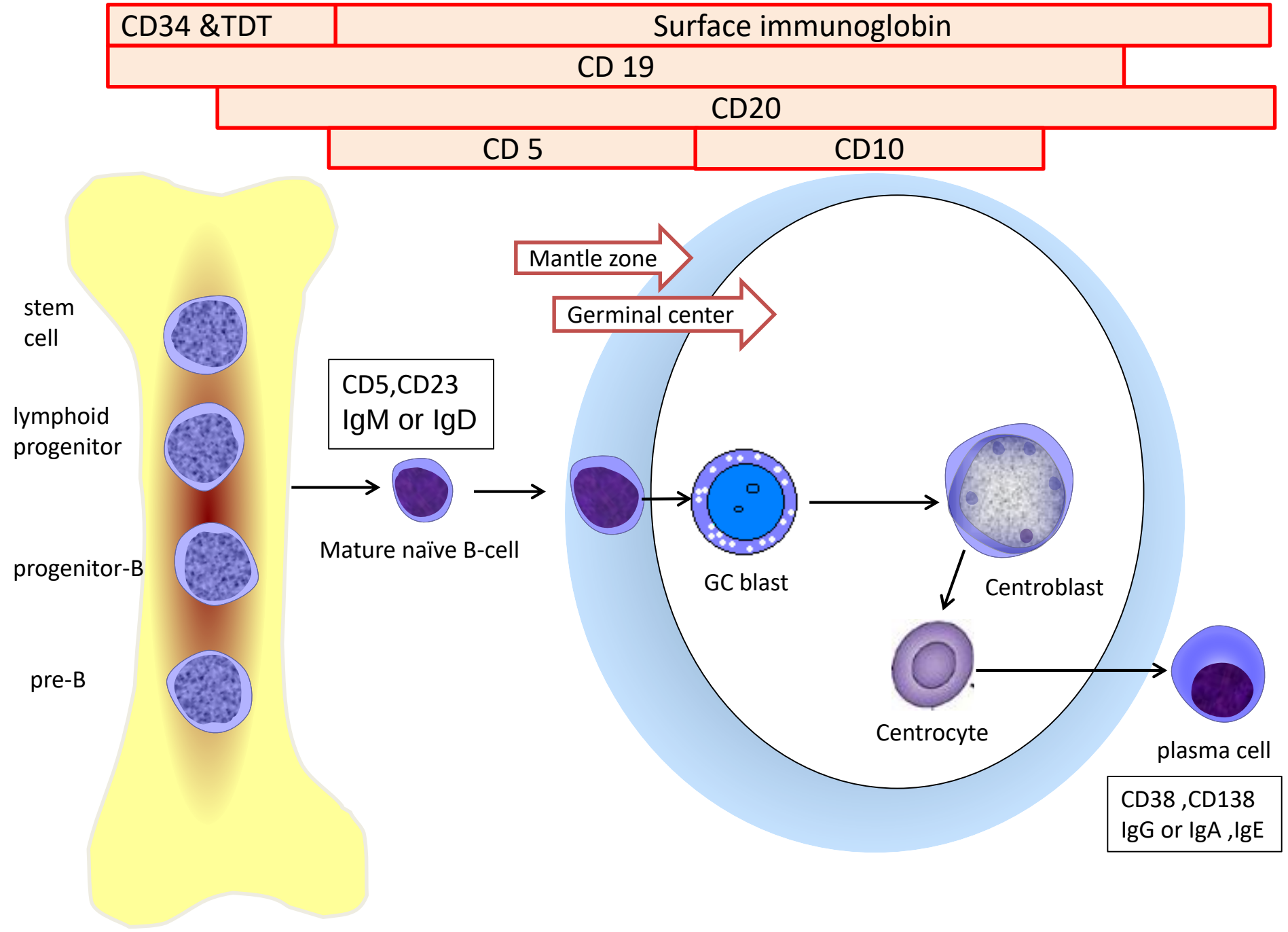


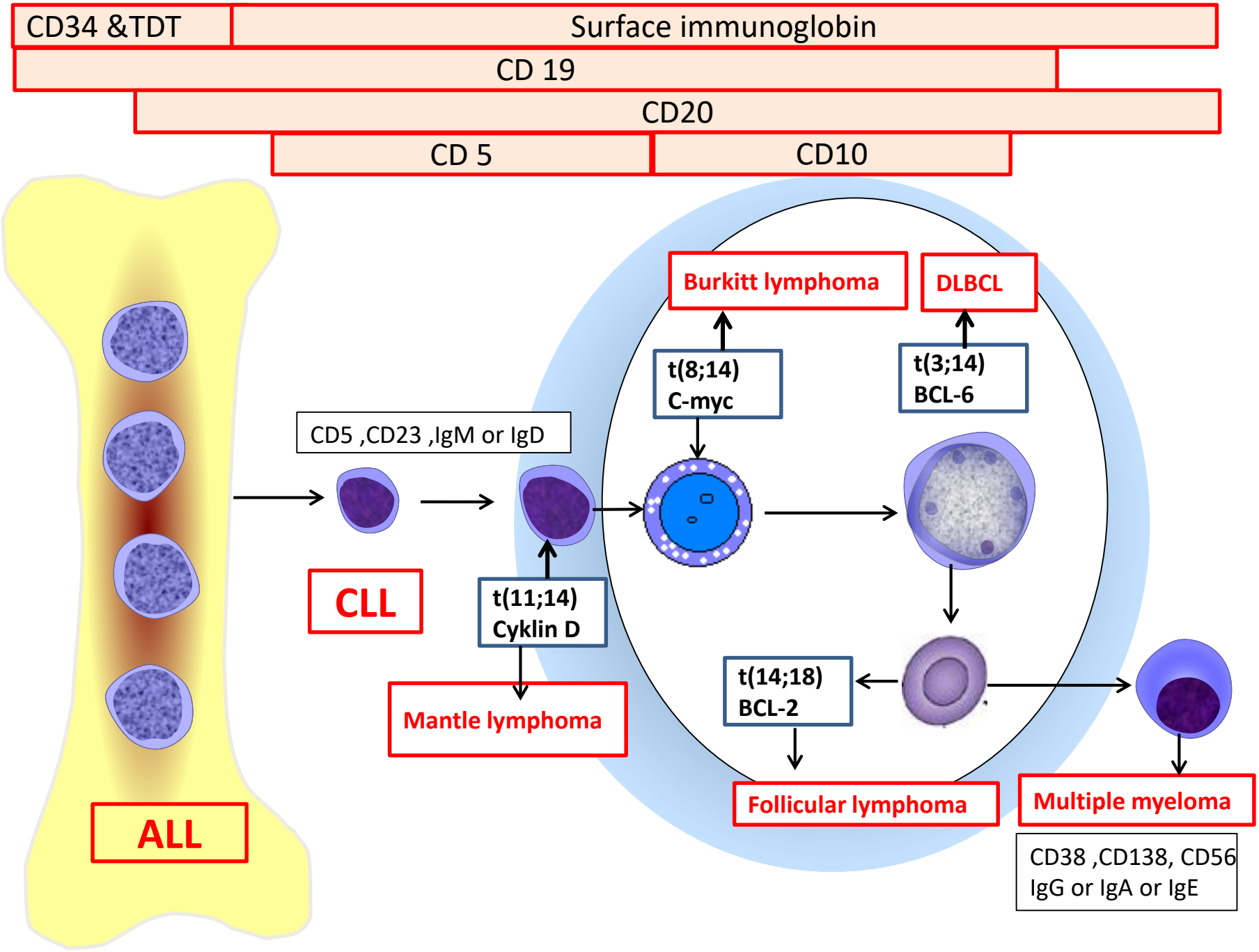


Malignant Lymphoproliferative Disorders


ALL
CLL
Lymphomas
MM
naïve
germinal center
B-lymphocytes
Plasma cells
Lymphoid progenitor
T-lymphocytes
Hematopoietic stem cell
AML
Myeloproliferative disorders
Myeloid progenitor
Neutrophils
Eosinophils
Basophils
Monocytes
Platelets
Red cells


Malignant Lymphoproliferative disorders
Immature
ALL
Mature
Lymphoma
Lymphoid leukemia
CLL
Hairy cell leukemia
T- prolymphocytic leukemia
Leukemic phase of 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


CD34 &TDT
Surface immunoglobin
CD 19
CD20
CD 5
CD10
stem cell
lymphoid progenitor
progenitor-B
pre-B
Mantle zone
Germinal center
CD5,CD23
IgM or IgD
Mature naïve B-cell
GC blast
Centroblast
Centrocyte
plasma cell
CD38 ,CD138
IgG or IgA ,IgE

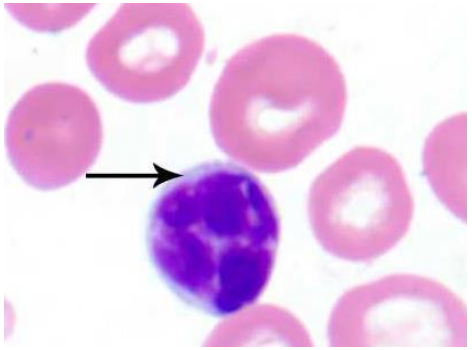

CD34 &TDT
Surface immunoglobin
CD 19
CD20
CD 5
CD10
ALL
CD5 ,CD23 ,IgM or IgD
CLL
t(11;14)
Cyklin D
Mantle lymphoma
Burkitt lymphoma
DLBCL
t(8;14)
C-myc
t(3;14)
BCL-6
t(14;18)
BCL-2
Follicular lymphoma
Multiple myeloma
CD38 ,CD138, CD56
IgG or IgA or IgE

Chronic Lymphocytic Leukemia

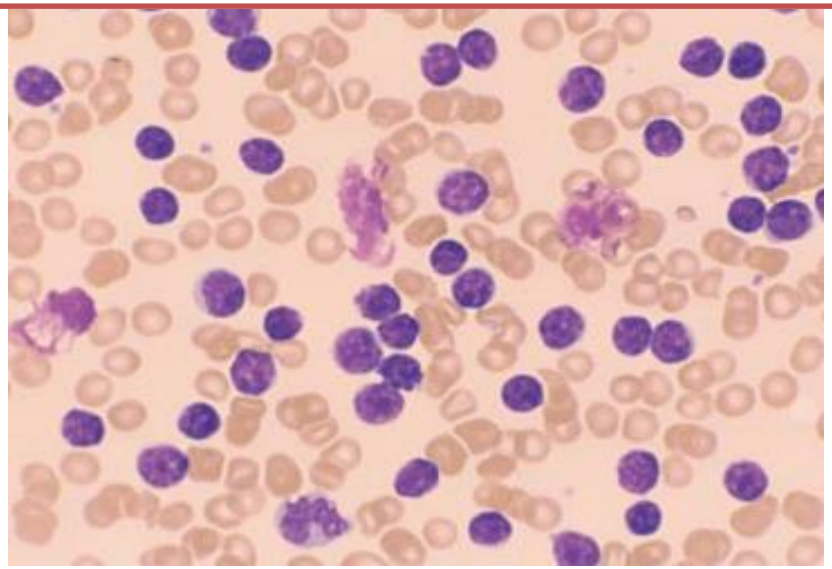
- Malignant neoplasim characterized by an increased number of small, mature lymphocytes in the blood (>5,000) and bone marrow (± spleen and lymph node)
- The most common adult leukemia (~25% of adult leukemias)
- The median age is ~55 to 65 years. (rare < 40 years).
- 1.5 to 2 times more common in men 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	
Stage II:	Lymphocytosis plus enlarged spleen and/or liver, ± nodes	Intermediate **±chemo**
Stage III:	Lymphocytosis plus anemia (Hgb <11 g/dL), ± above	
Stage IV:	Lymphocytosis plus thrombocytopenia (<100 × 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

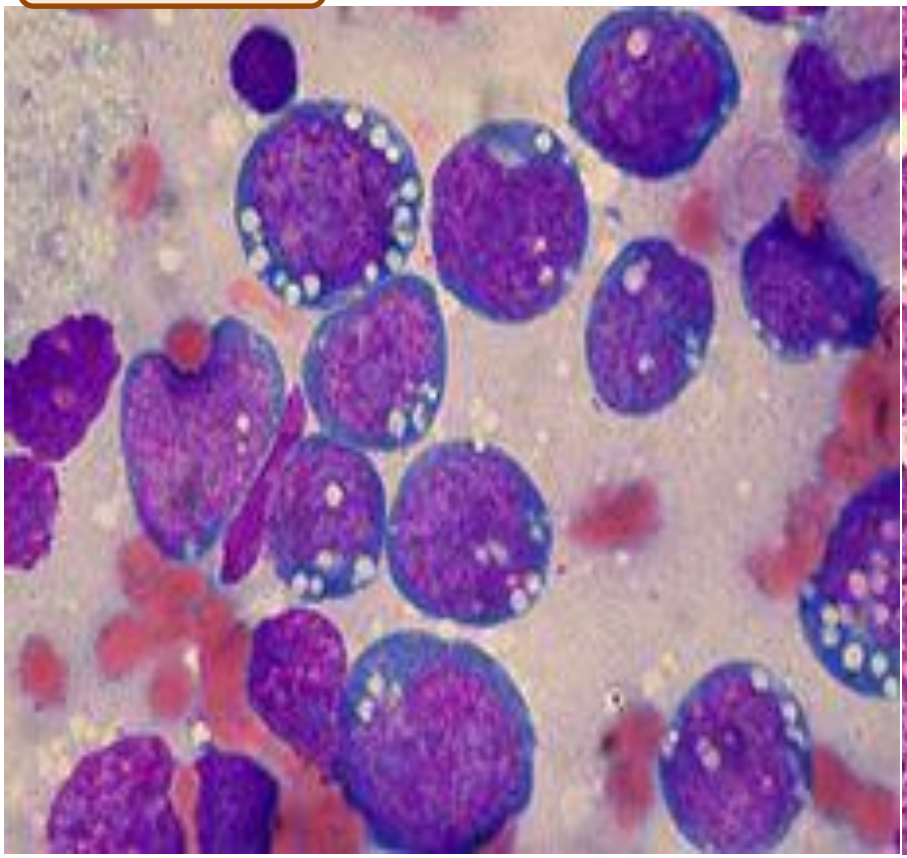
1-Endemic: associated with chronic malaria and EBV In equatorial Africa . It particularly affects the jaw, other facial bone and breast.

Sporadic: occurs throughout the world and affects GIT.

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

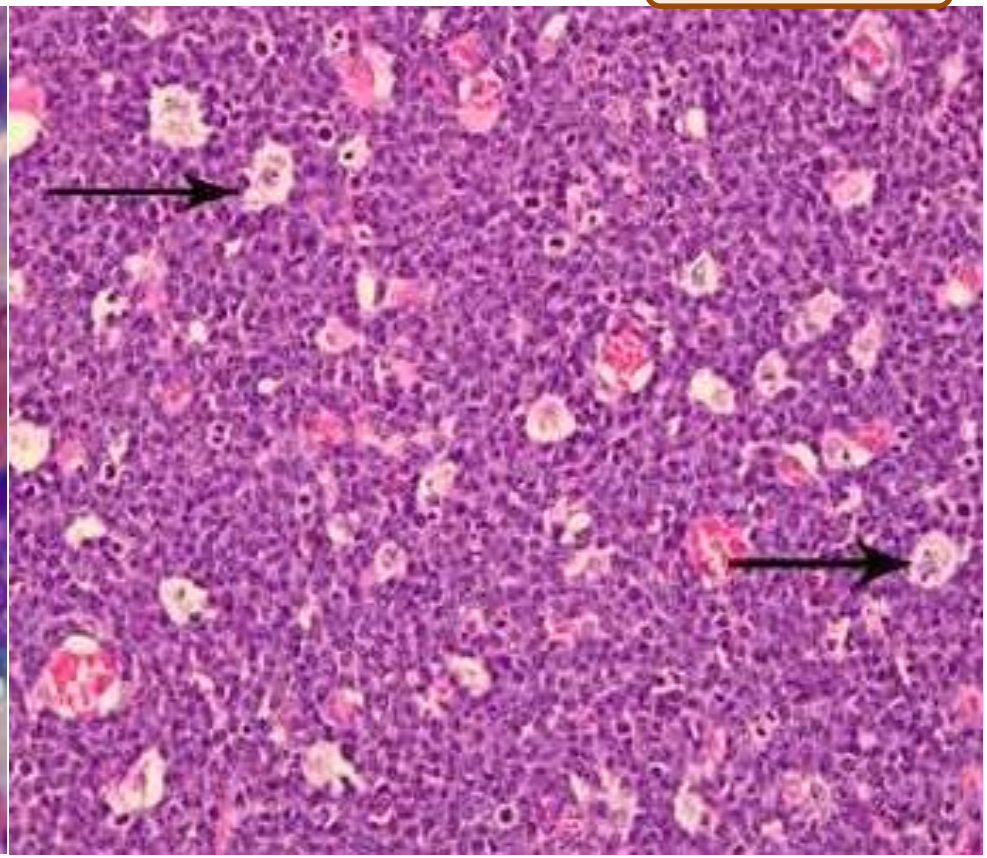
Morphology

BMA



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

Biobsy



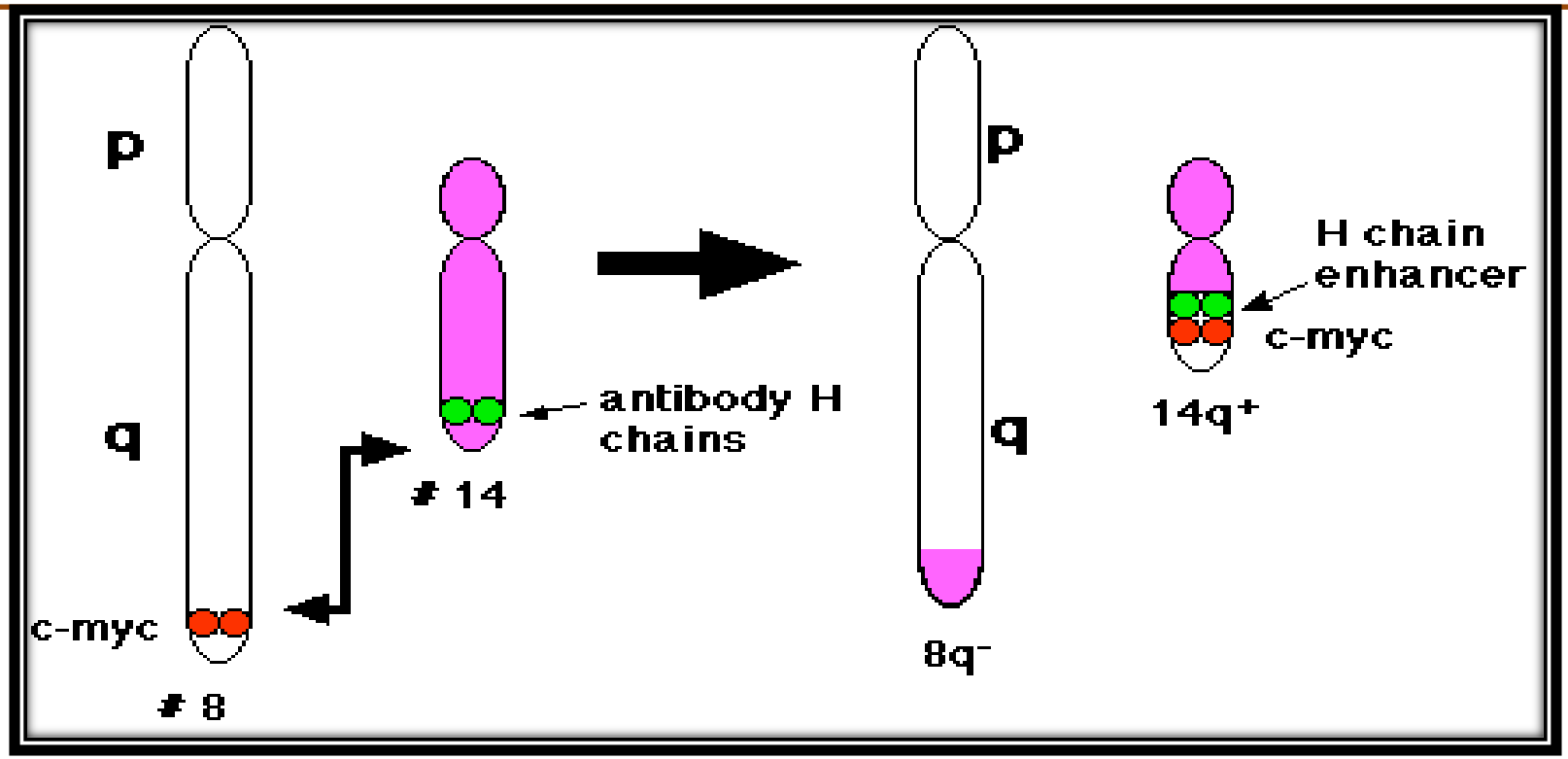
Diffuse infiltration with "starry sky" (Macrophages engulfing the apoptotic cells)

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

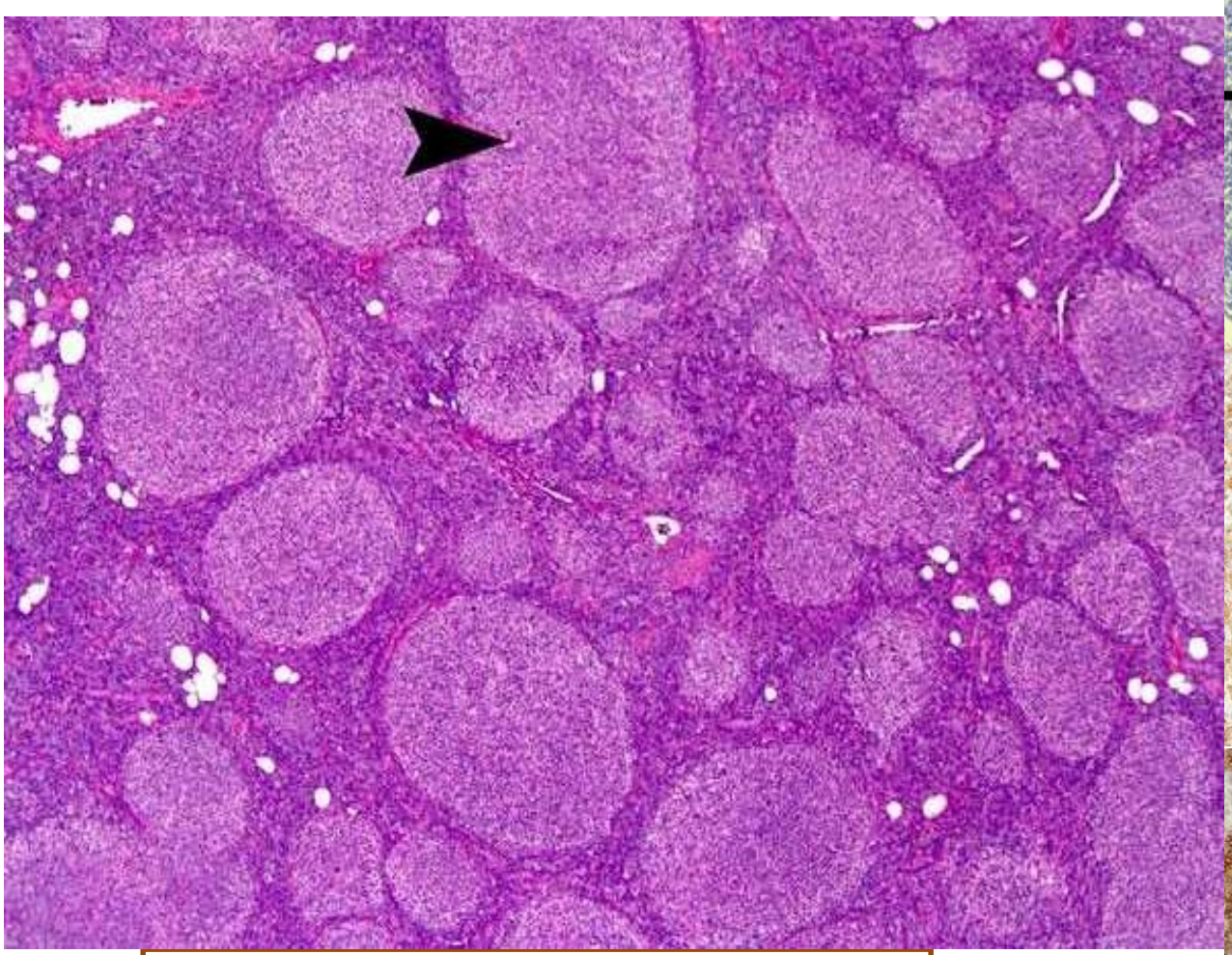
Cure rate:

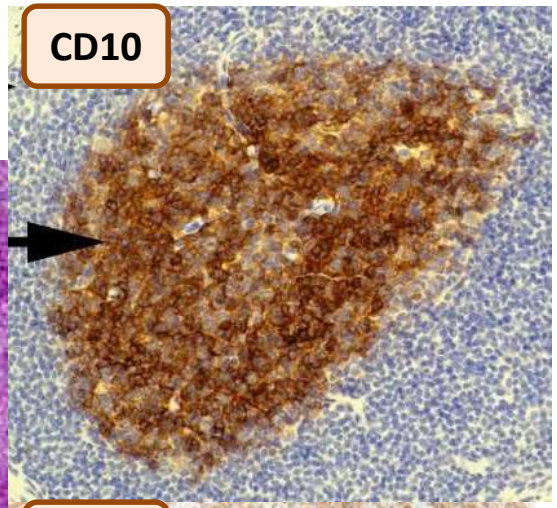
- **90% at early phase**
- **70% at advance disease**

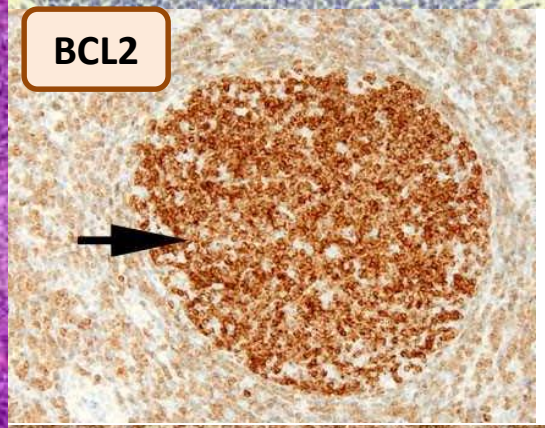
Follicular lymphoma

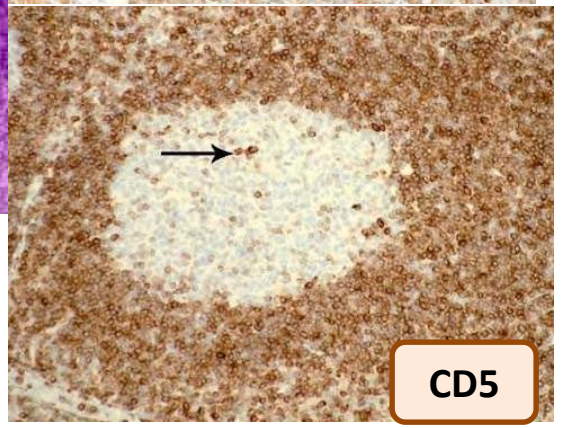
- **FL is malignant proliferation of germinal center B cells centrocyte which has at least a partially follicular pattern.**
- **Due to overexpression o f Bcl2 caused by t(14;18) .**
- **Most common type of “indolent” lymphoma (25%).**
- **Presented as:**
- Lymphadenopathy (100%)
- splenomegaly (80%)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

Diagnosis





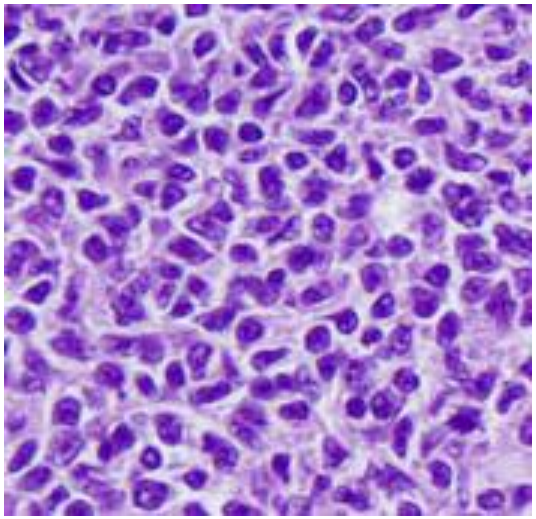


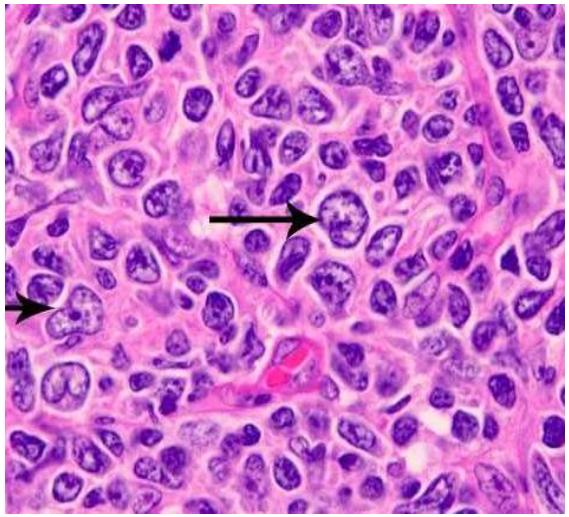


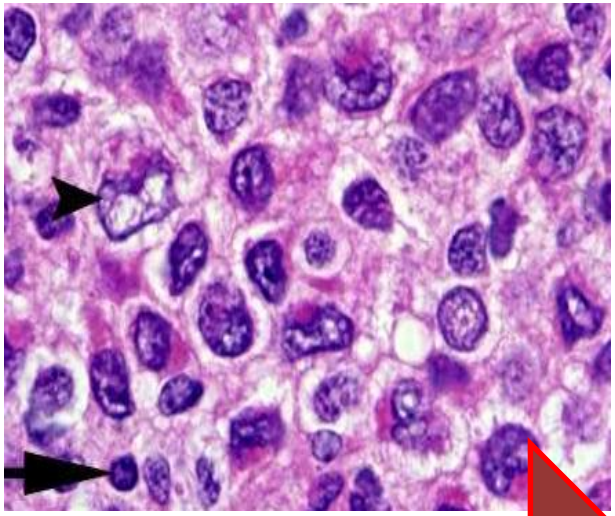
Immunophenotyping:
Positive for CD10,CD20 and Bcl2
Negative for CD5 (in most cases)

Management

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





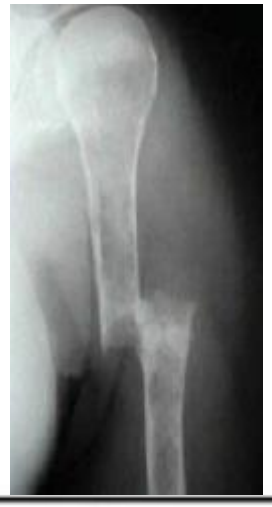


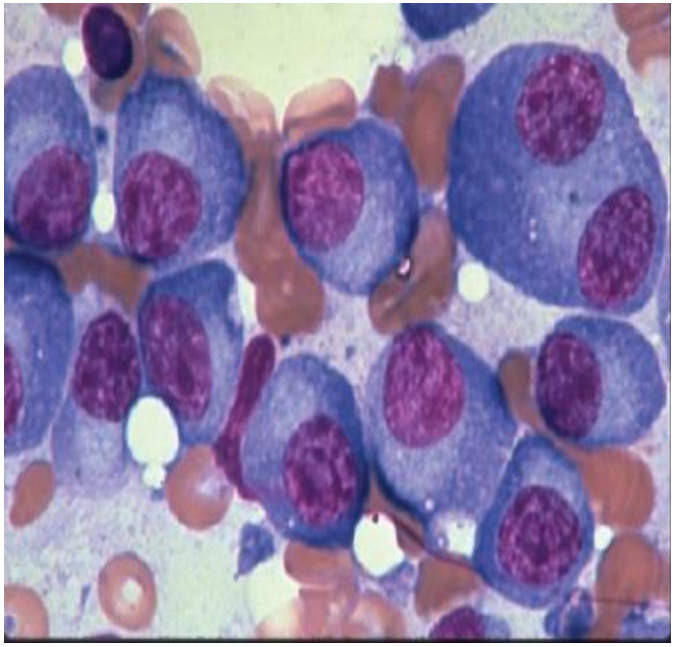
Low grade FL	FL in transformation	Aggressive transformation (DLBCL)
Watch and weight (most often)	Chemotherapy	Aggressive Chemotherapy(± SCT)

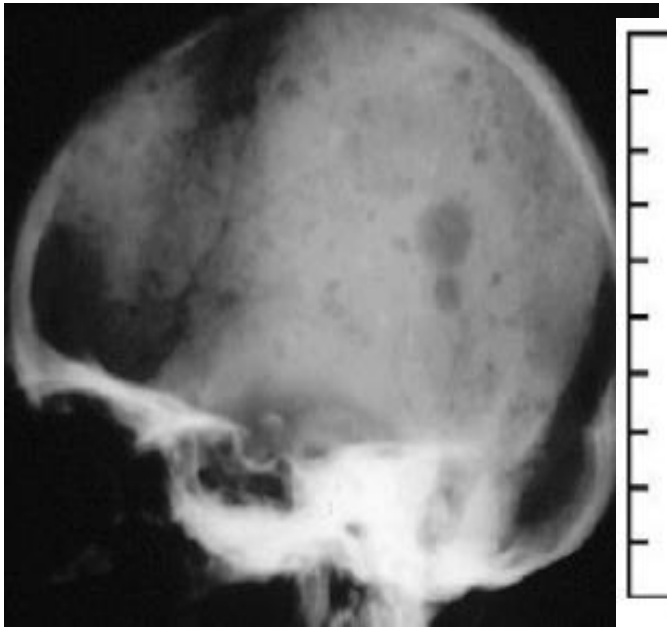
Multiple Myeloma

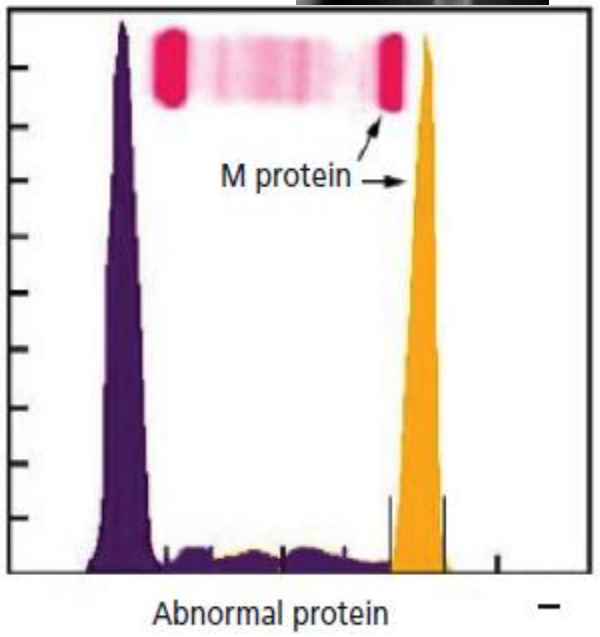
Malignant B neoplasm characterized by a triad of abnormalities:

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



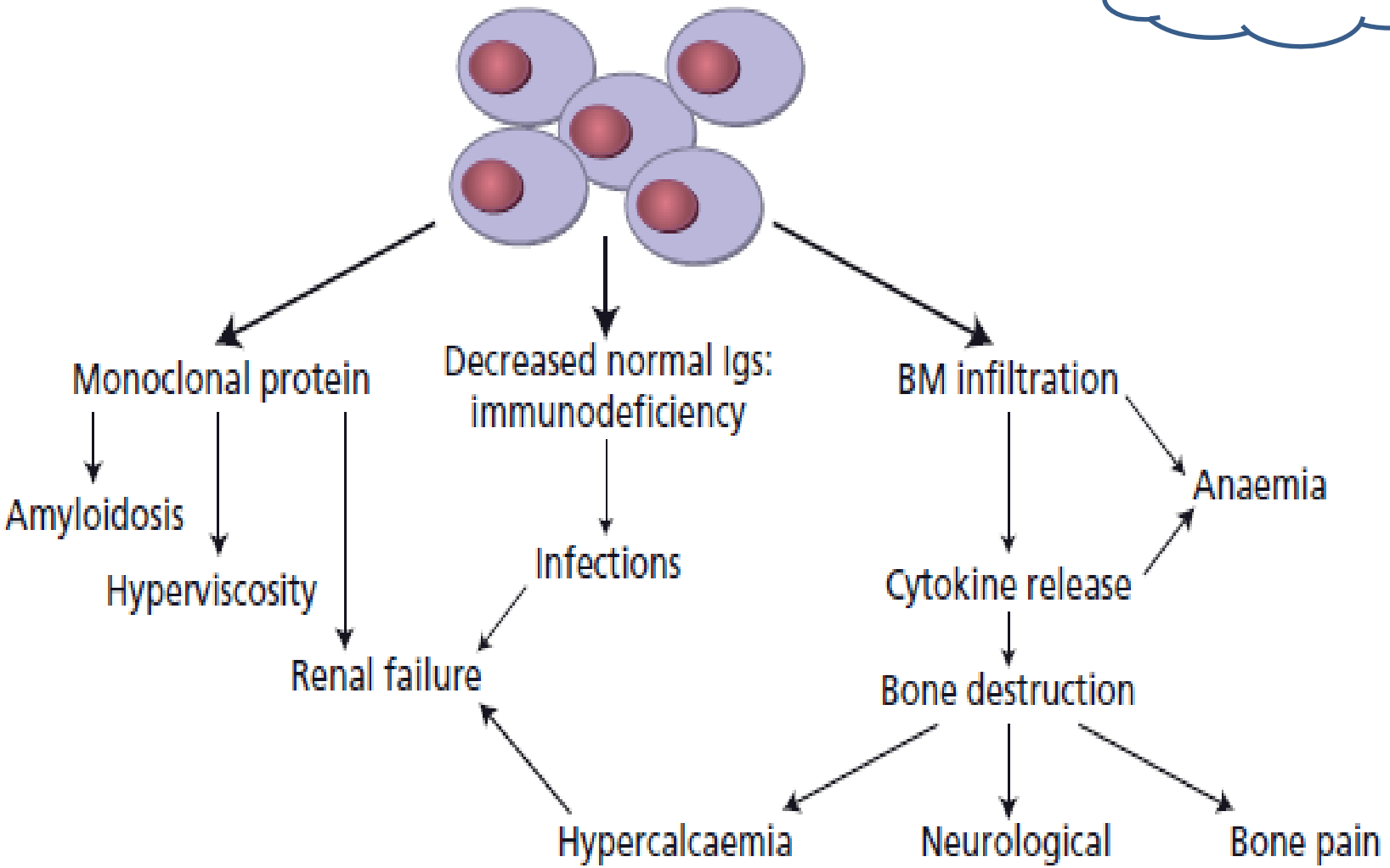




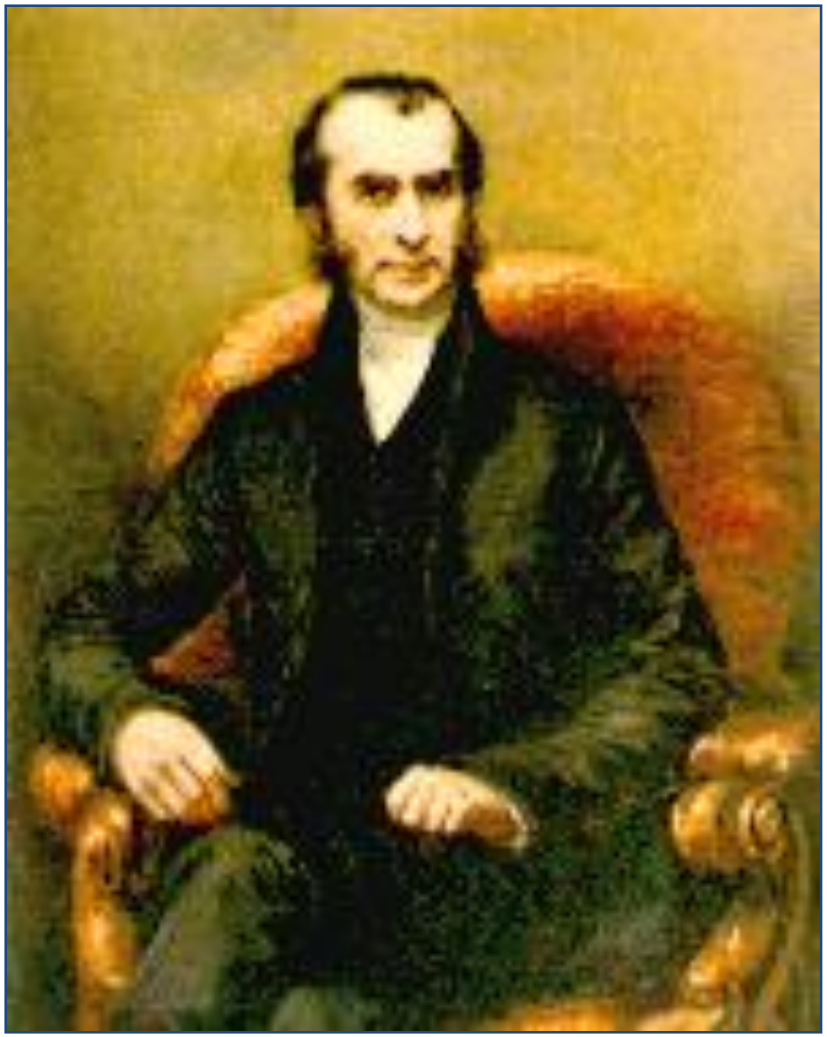


Pathogenesis of MM

For reading



Hodgkin lymphoma



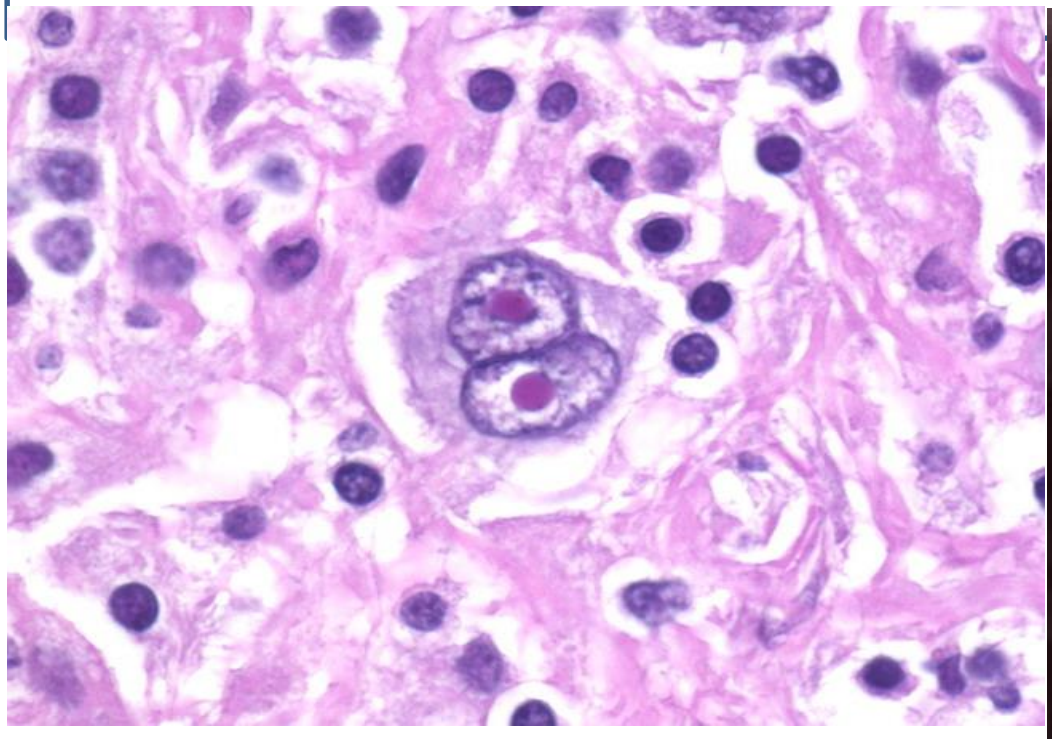
Thomas Hodgkin
(1798-1866)

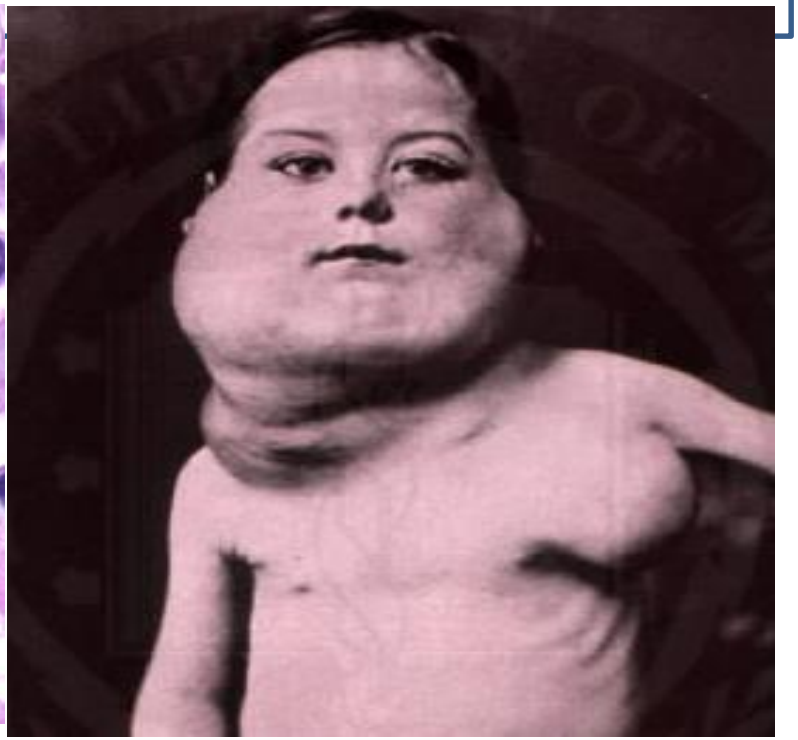
Classical Hodgkin Lymphoma

Indolent malignant lymphoma characterized by :

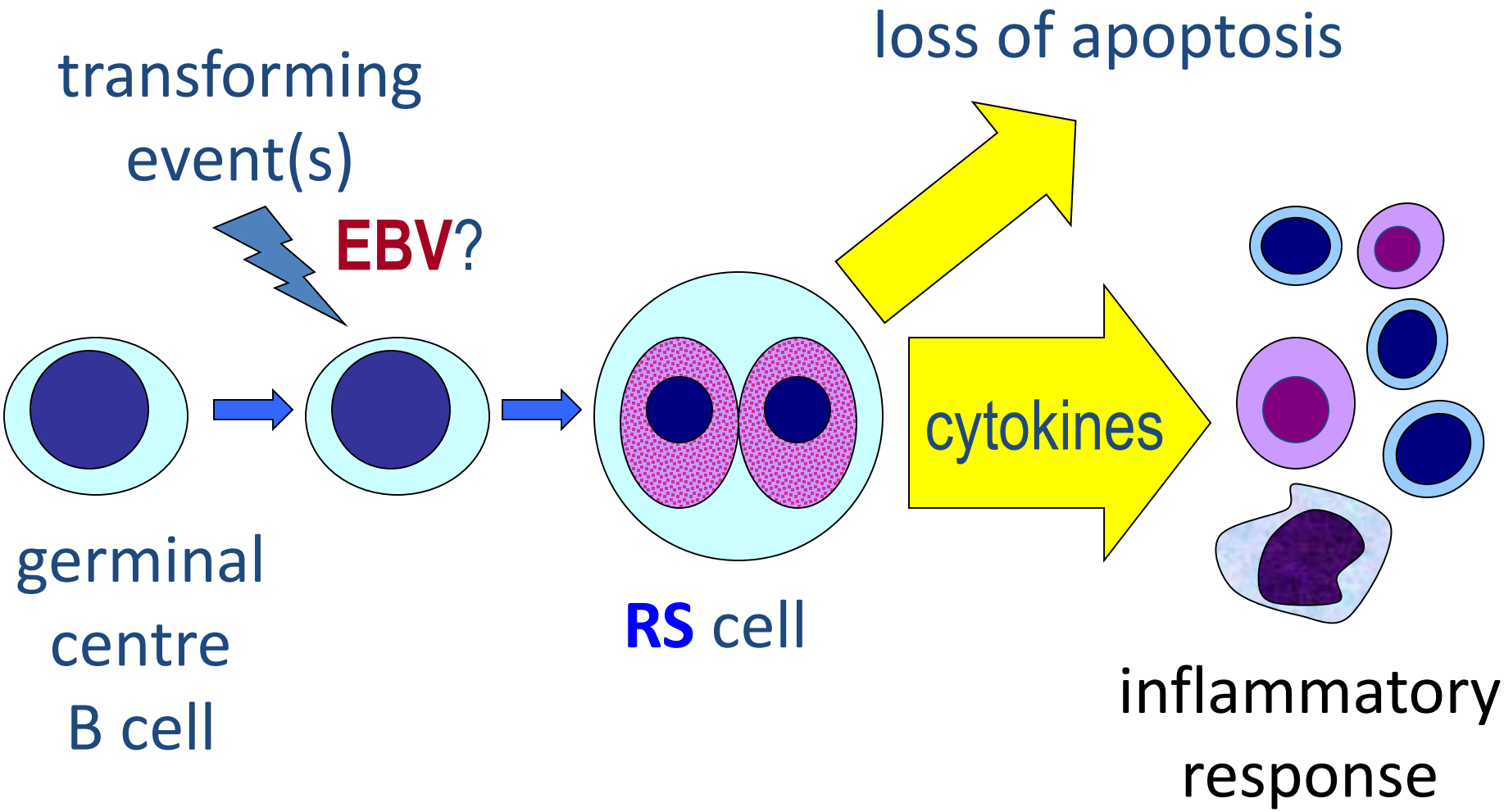
1- presence of few large binucleated cells (Reed-Sternberg) surrounded by reactive cells (lymphocytes, plasma cells ,eosinophils)

2- Involving cervical lymph nodes in young adults (most often)



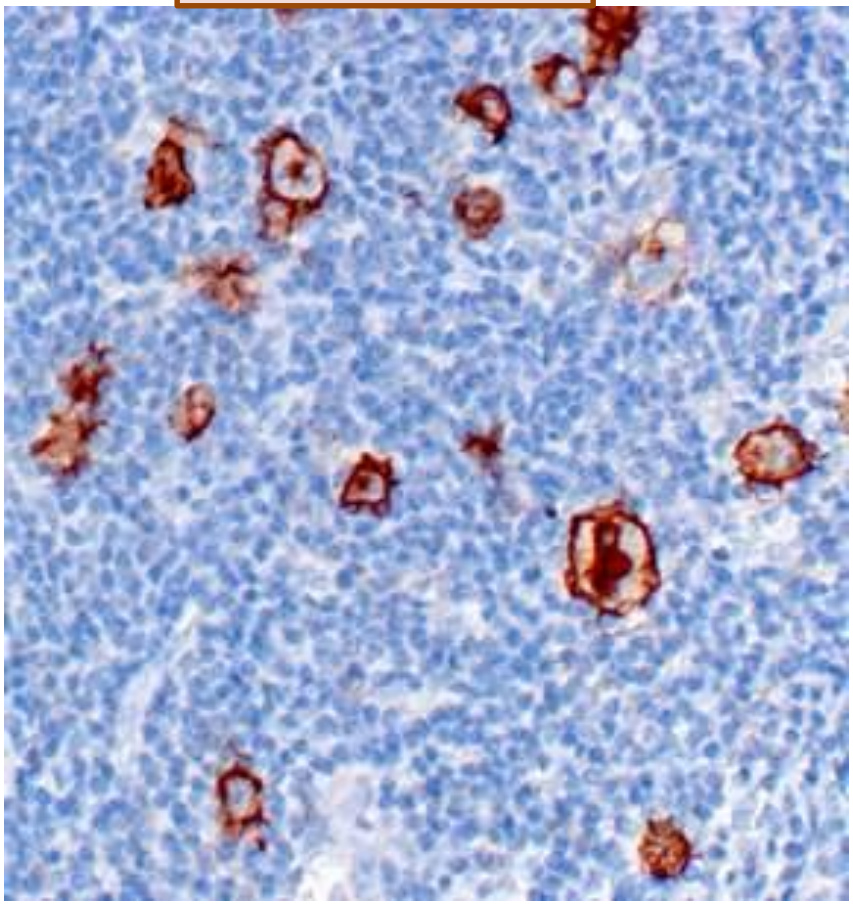


A possible model of pathogenesis

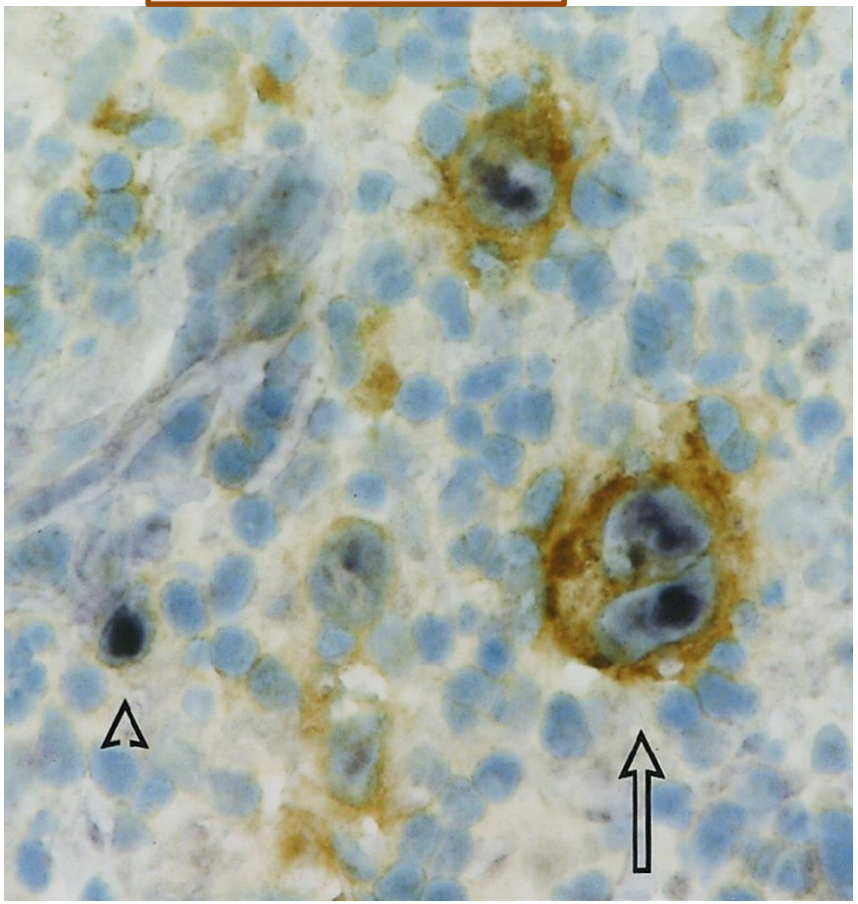


Diagnosis of Hodgkin Lymphoma

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	