LYMPHOID TISSUE DISORDERS

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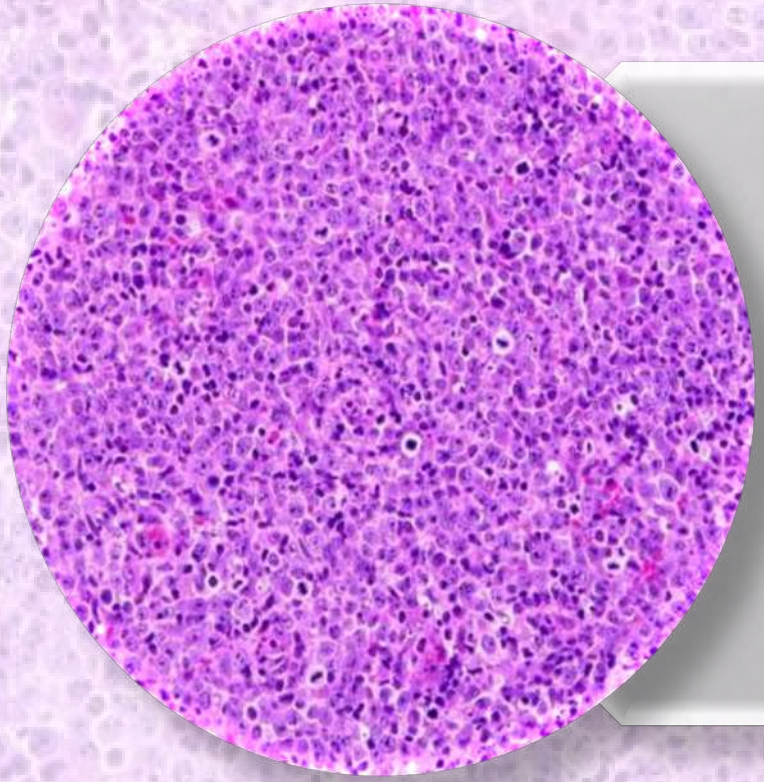


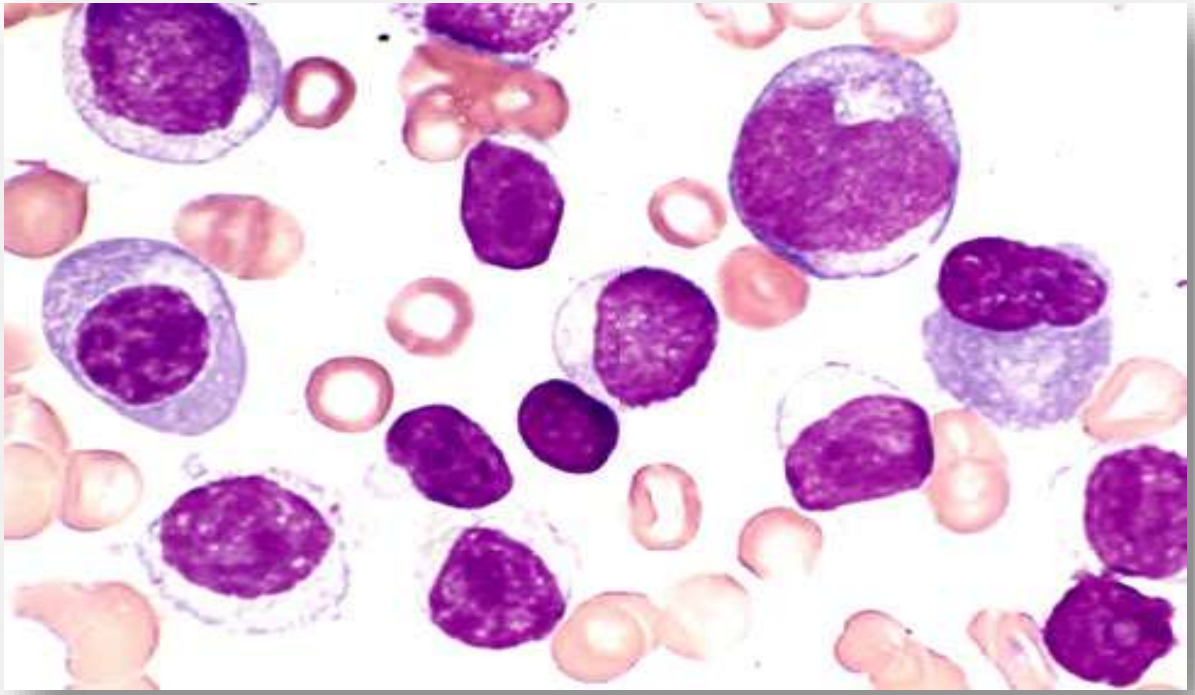
NON-HODGKIN LYMPHOMA Cont'd

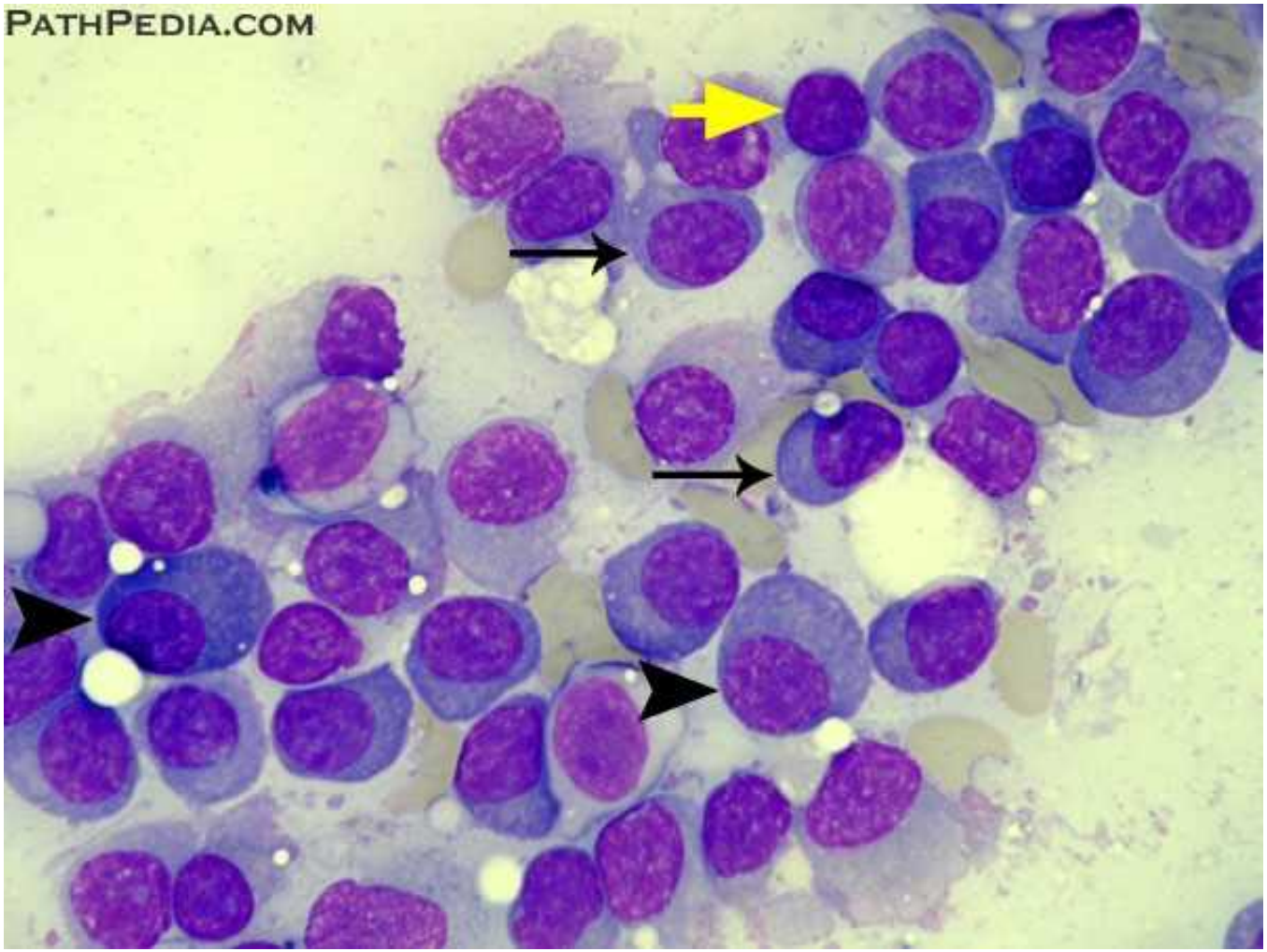
3- Lymphoplasmacytoid Lymphoma (Waldenström's Macroglobulinemia)

Most frequently in men over 50 years of age.

- Diagnosis is made by the finding of a **monoclonal serum IgM** together with bone marrow or lymph node infiltration with lymphoplasmacytoid cells (resembles plasma cells).

- The erythrocyte sedimentation rate (ESR) is raised and there may be a peripheral blood lymphocytosis.





BMA for WM shows the characteristic cell population. The yellow arrow at the top highlights a small lymphocyte, the two arrowheads show two plasma cells. The two long arrows indicate two plasmacytoid lymphocytes, are so named because of their appearance. They have more eccentric cytoplasm than a small lymphocyte but less so than that of a typical plasma cell

4- Marginal Zone Lymphomas:

According the anatomical site at which they arise in spleen, lymph node (nodal) or mucosa (MALT) (Mucosa Associated Lymphoid Tissue, usually arise in the stomach, after *H.pylori* or respiratory tract, skin and salivary glands.

5- Mantle Cell Lymphoma

- Can have nodular or diffuse growth pattern.

- The proliferation consists of a monotonous population of small lymphocytes with irregular (cleaved) nuclear contours.

6- Diffuse Large Cell Lymphoma

As a group, this is one of the most important type of NHL lymphoma in adults (50% of adult NHL), and is the most common form of NHL in USA.

- Diffuse growth pattern with aggressive forms.

- 30% extranodal presentation: Usually involves one sites, common tissues involved are; GIT, skin and brain.

- Involvement of BM, liver and spleen is rare at time of diagnosis.

- Rapidly fatal if not treated. However; complete remission can be achieved in 60-80% of the patients, and 50% are cured.

- Immunotherapy with anti-CD20 antibody seems to improve both them initial response and the overall outcome.

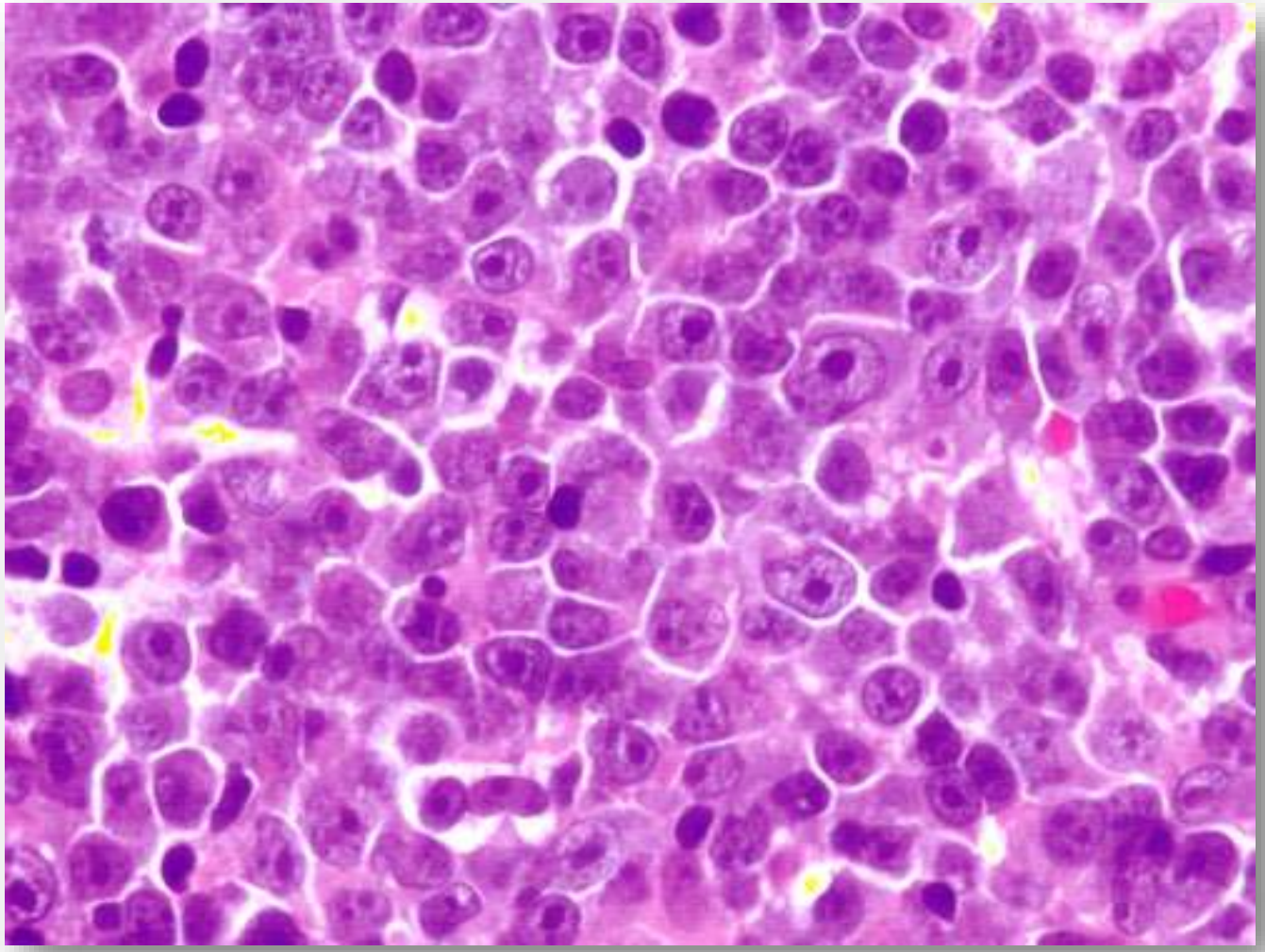
Microscopic features;

- The nuclei of the neoplastic B cells are large (3-4 times the size of resting lymphocytes).
- There are two morphologic variants of DLBCLs:

1. ***Centroblastic:*** The tumor cells have a round or oval vesicular nucleus with multiple nucleoli located adjacent to the nuclear membrane.

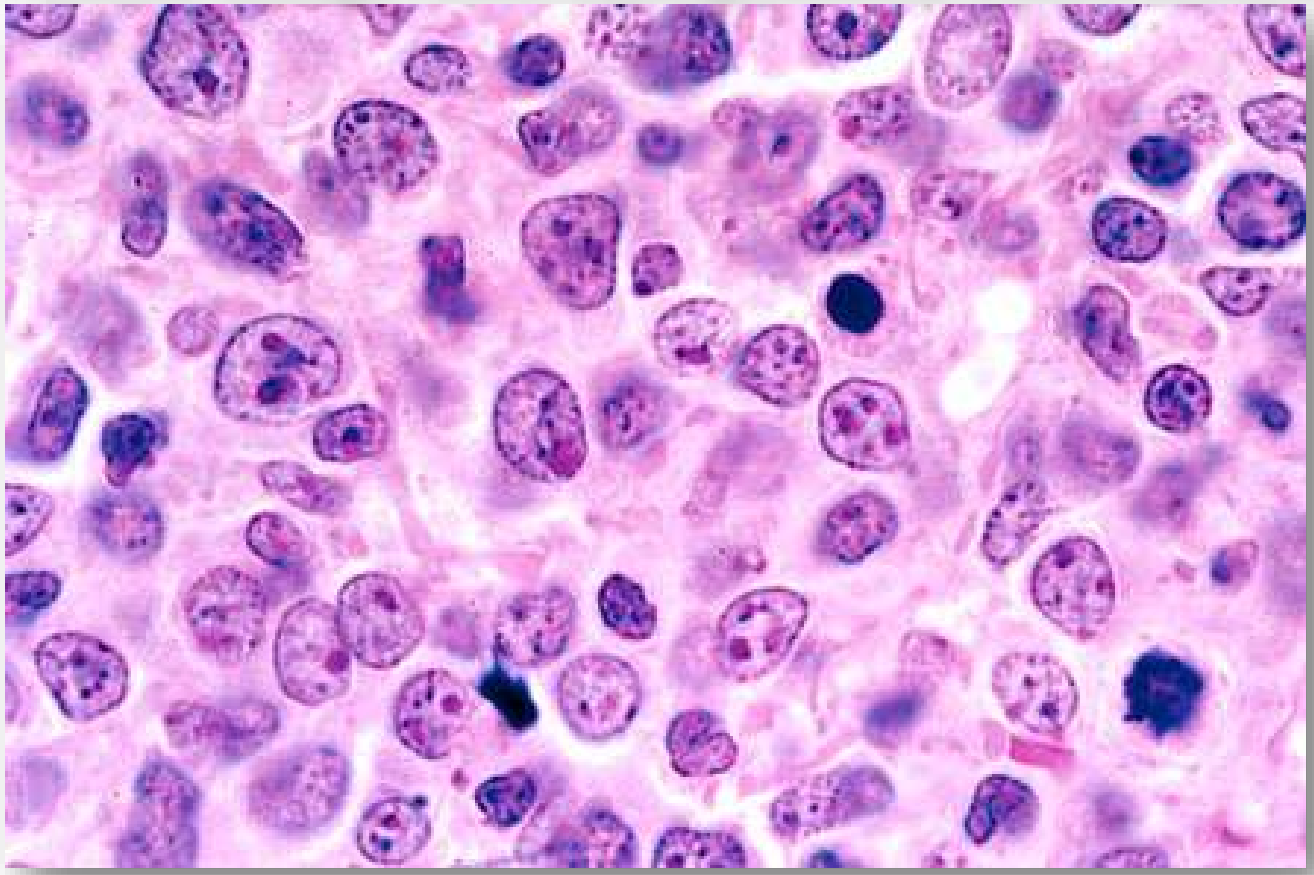
2. Immunoblastic: have a large round or multilobulated nucleus, one or two centrally placed prominent nucleoli, and abundant cytoplasm.

Diffuse Large Cell Lymphoma; Immunoblastic

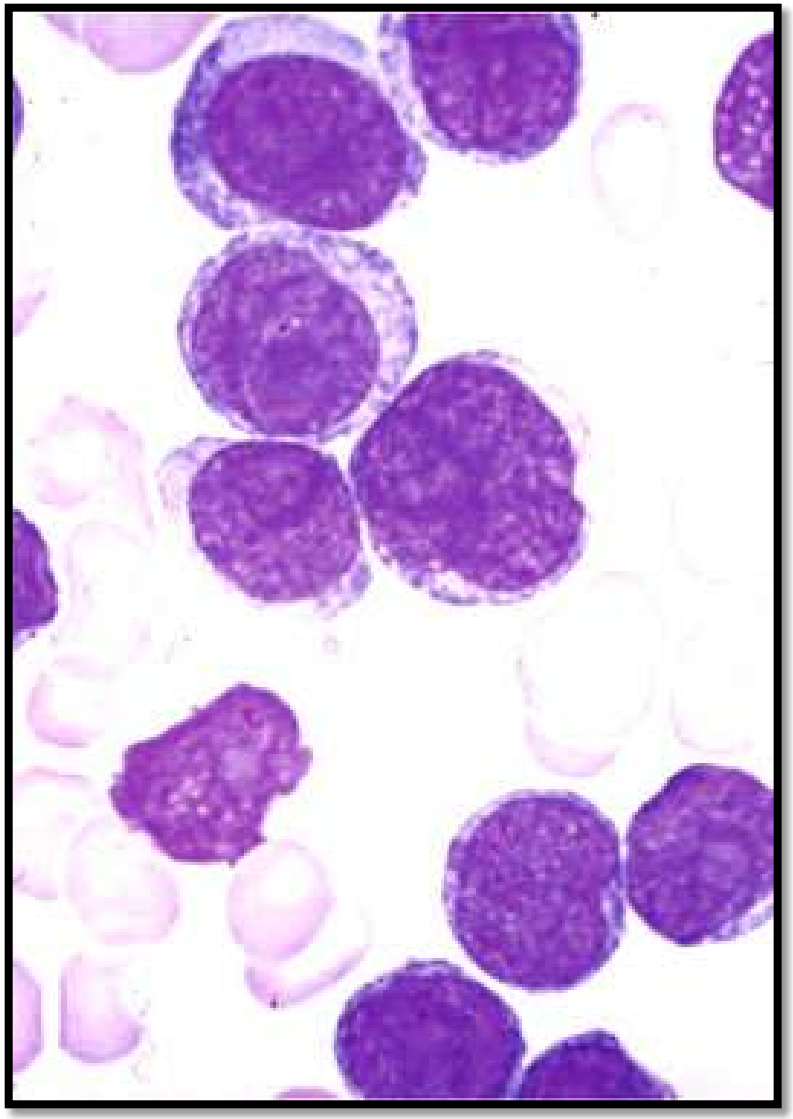


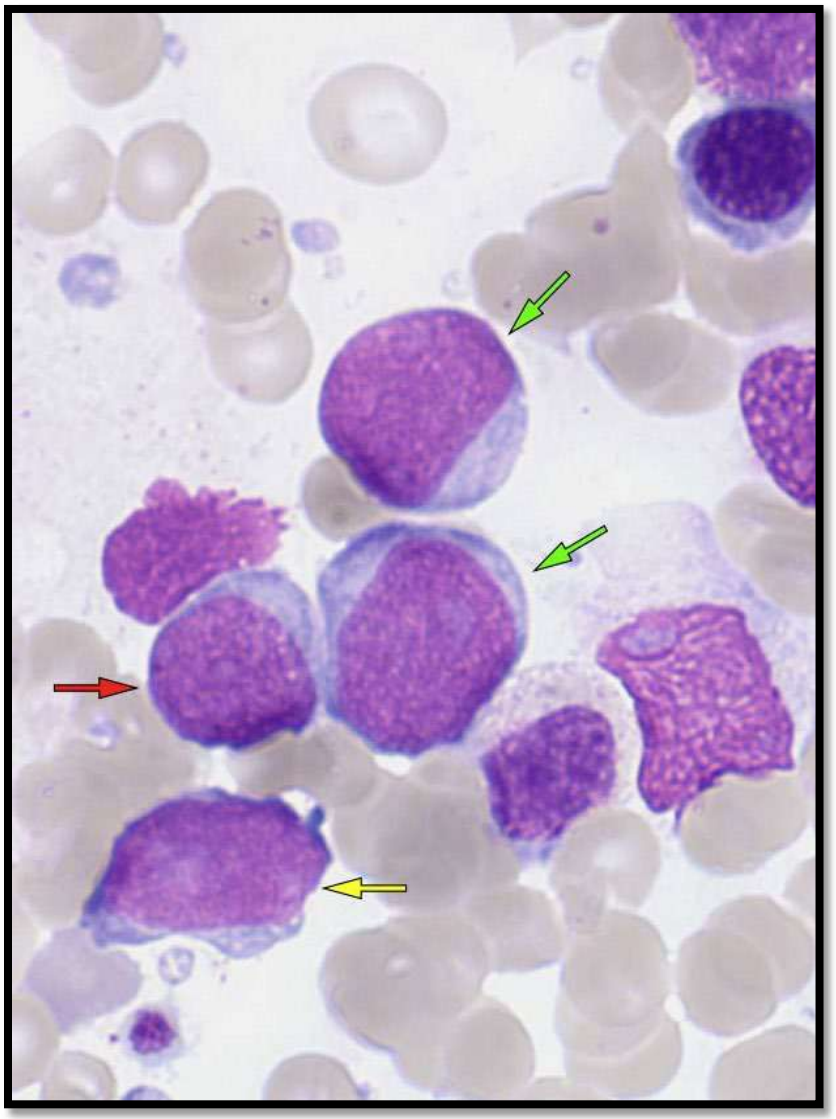
Tumor cells have large nuclei, open chromatin, and prominent centrally located nucleoli.

Diffuse Large Cell Lymphoma; Centroblastic



Heterogeneous cells, but predominantly large cells with vesicular chromatin and prominent nucleoli adjacent to the nuclear membrane.





large B-cell lymphoma (rarely seen in BM or peripheral blood); large cells with variable appearance of large cells, irregular nuclear outline and prominent nucleoli

7- Burkitt Lymphoma:

- Three major types exist:

1- African (endemic). often involves the **mandible**.

2- Sporadic (non-endemic). mostly **intraabdominal** (ileocecal).

3- HIV associated.

- In all type there is a relation to EBV infection.

- Endemic and sporadic forming ~30% of child / young NHL.

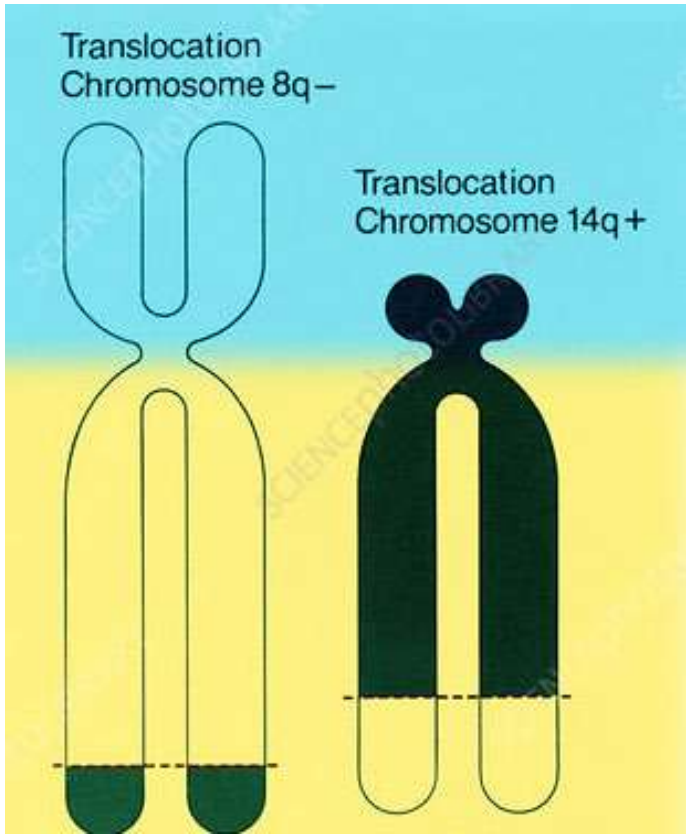
- Pathologically, both the African and nonendemic forms are identical, although there are clinical and virologic differences.

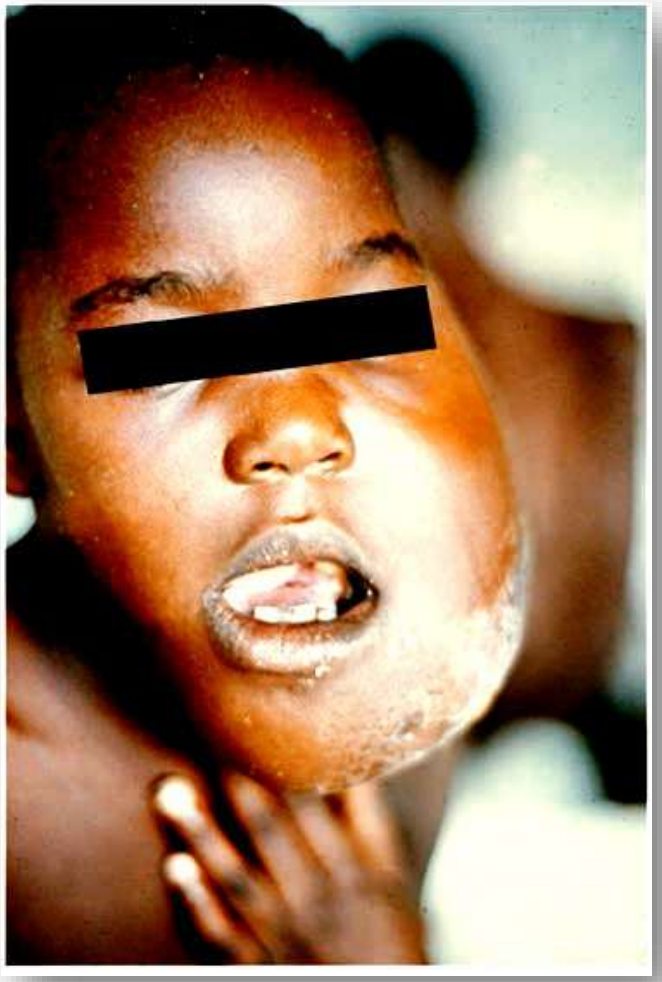
In both forms, the disease usually arises at extranodal sites.

- In **African patients**, involvement of the maxilla or mandible is the common mode of presentation, whereas in **nonendemic**; abdominal tumors involving the bowel, retroperitoneum, and ovaries are more common areas.

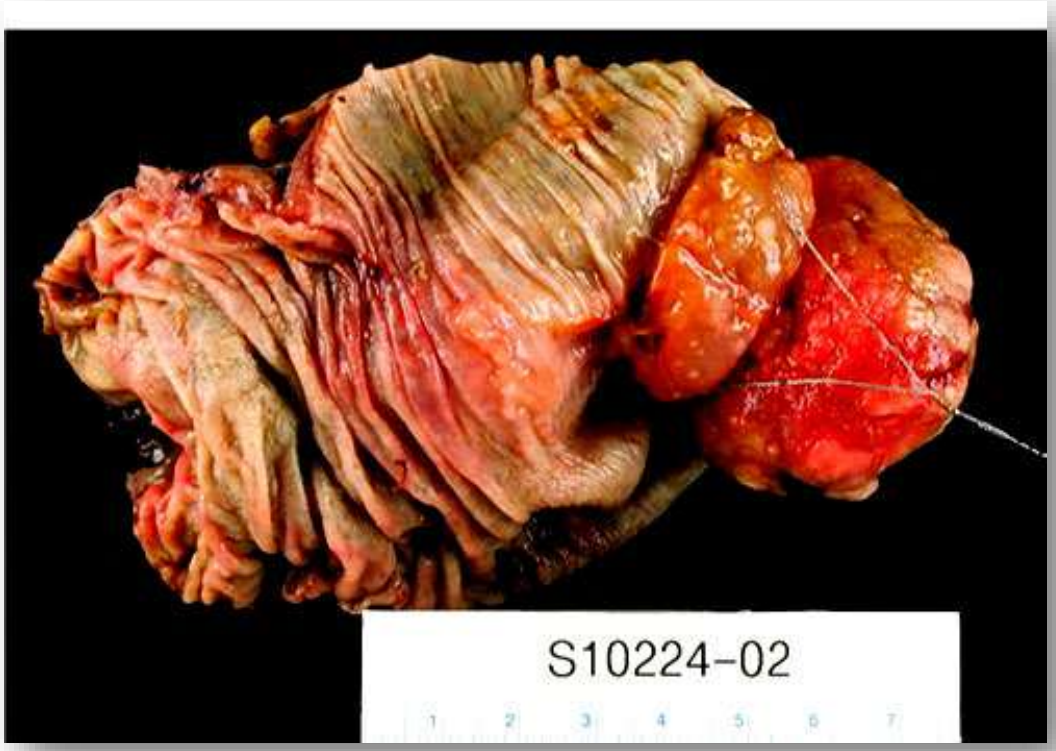
- Burkitt lymphoma is a **high-grade tumor** that is among the fastest growing human neoplasms; however, with very aggressive chemotherapy regimens, the majority of patients can be cured.

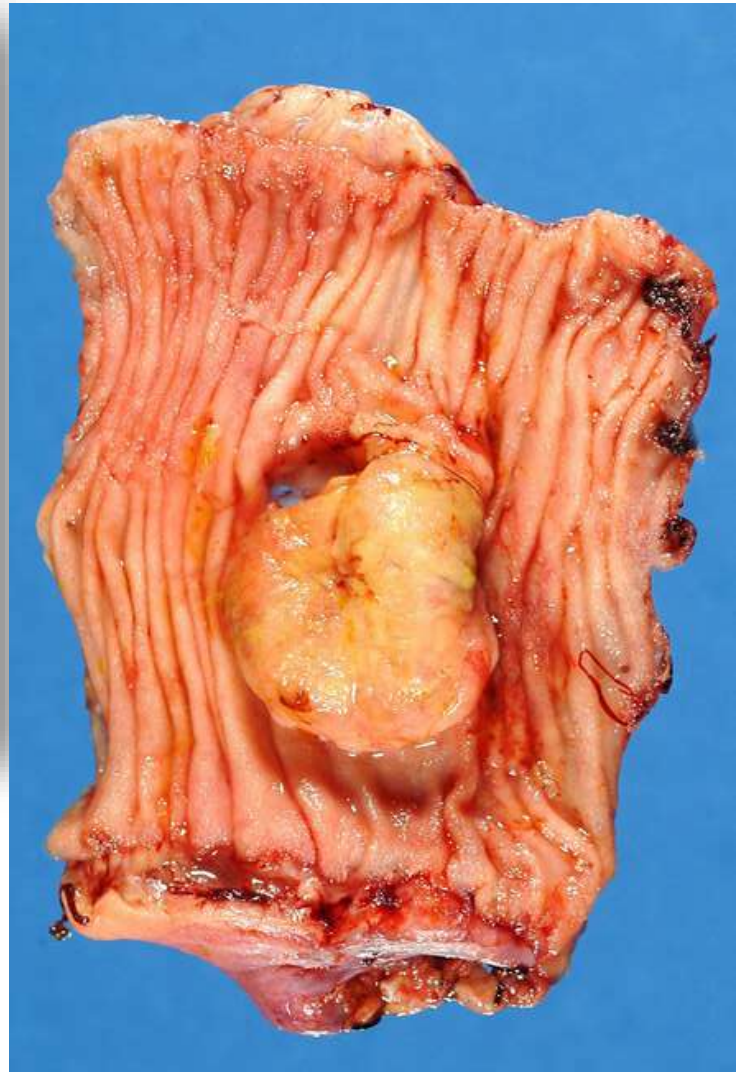
- Lymphoma cells emerge only when additional mutations, such as the ***t(8;14)*** translocation.





Most cases of the **endemic type** arise in children present as facial swelling caused by extensive tumour involvement of the mandible and surrounding soft tissues including the **jaws**





Sporadic type (nonendemic); presenting as a large polypoid mass of the intestine.

Microscopic Features:

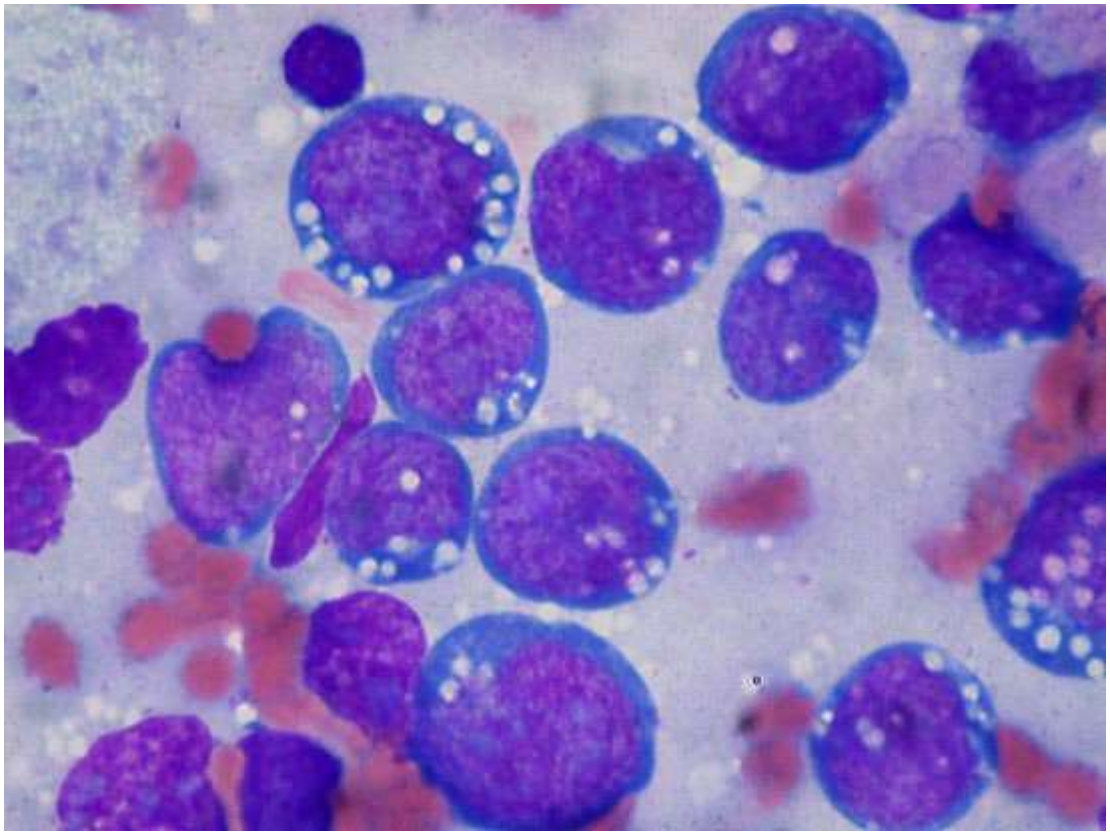
- The tumor cells are uniform and intermediate in size with round nuclei containing 2 to 5 prominent nucleoli.

- There is a moderate amount of basophilic cytoplasm, which on cytological smears often contains small lipid vacuoles.

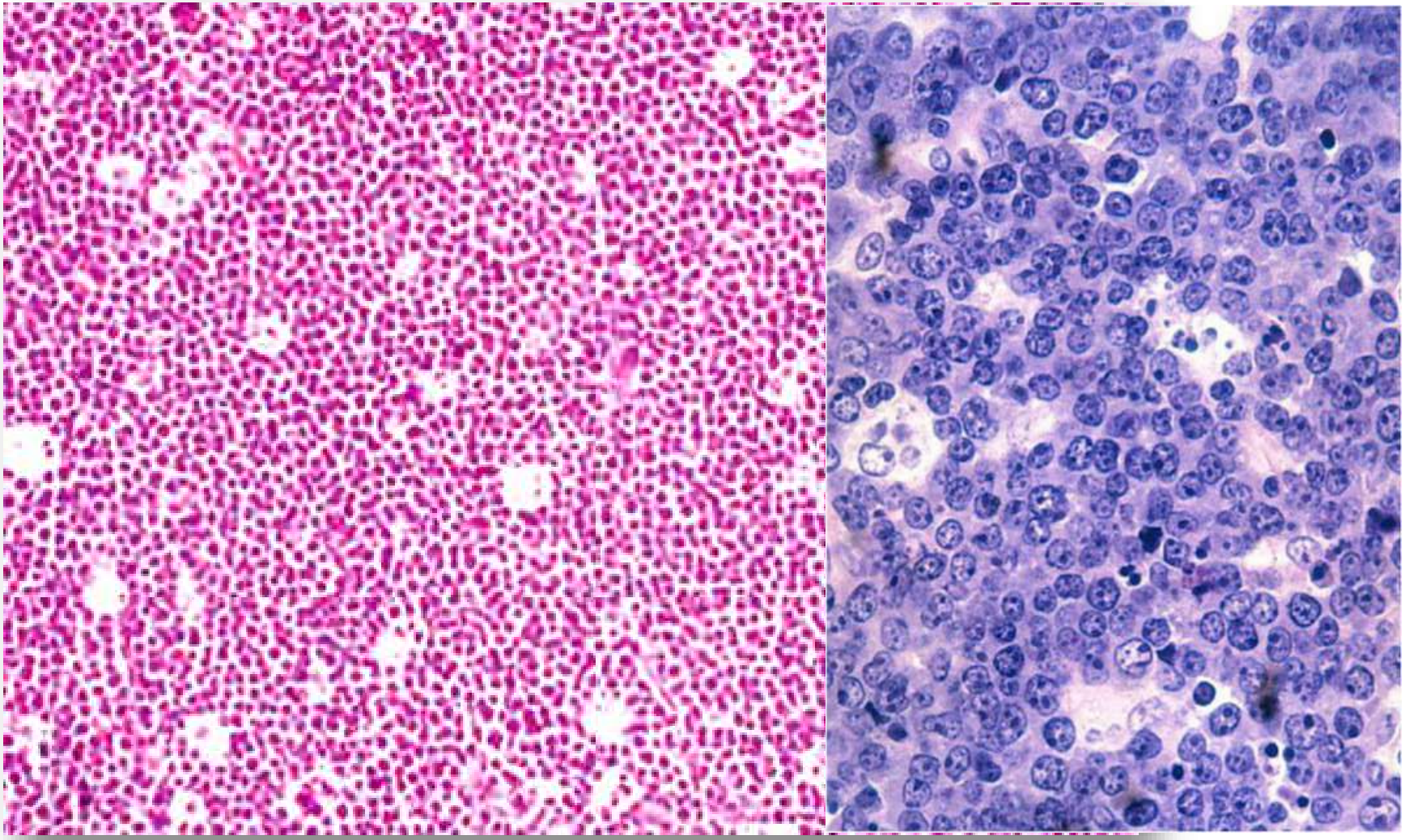
- A high mitotic rate is very characteristic of this tumor, as is cell death. The latter accounts for the presence of numerous tissue macrophages containing ingested nuclear debris.

- Because the tumor cells of B lymphoblasts which are large rounded nucleus and the nucleoli with the basophilic cytoplasm are closely apposed to each other forming a dark blue background (the 'sky'). The surrounding macrophages with abundant pale foamy cytoplasm scattered among the tumour cells (the stars) giving rise to "**starry sky**" pattern is thus created.

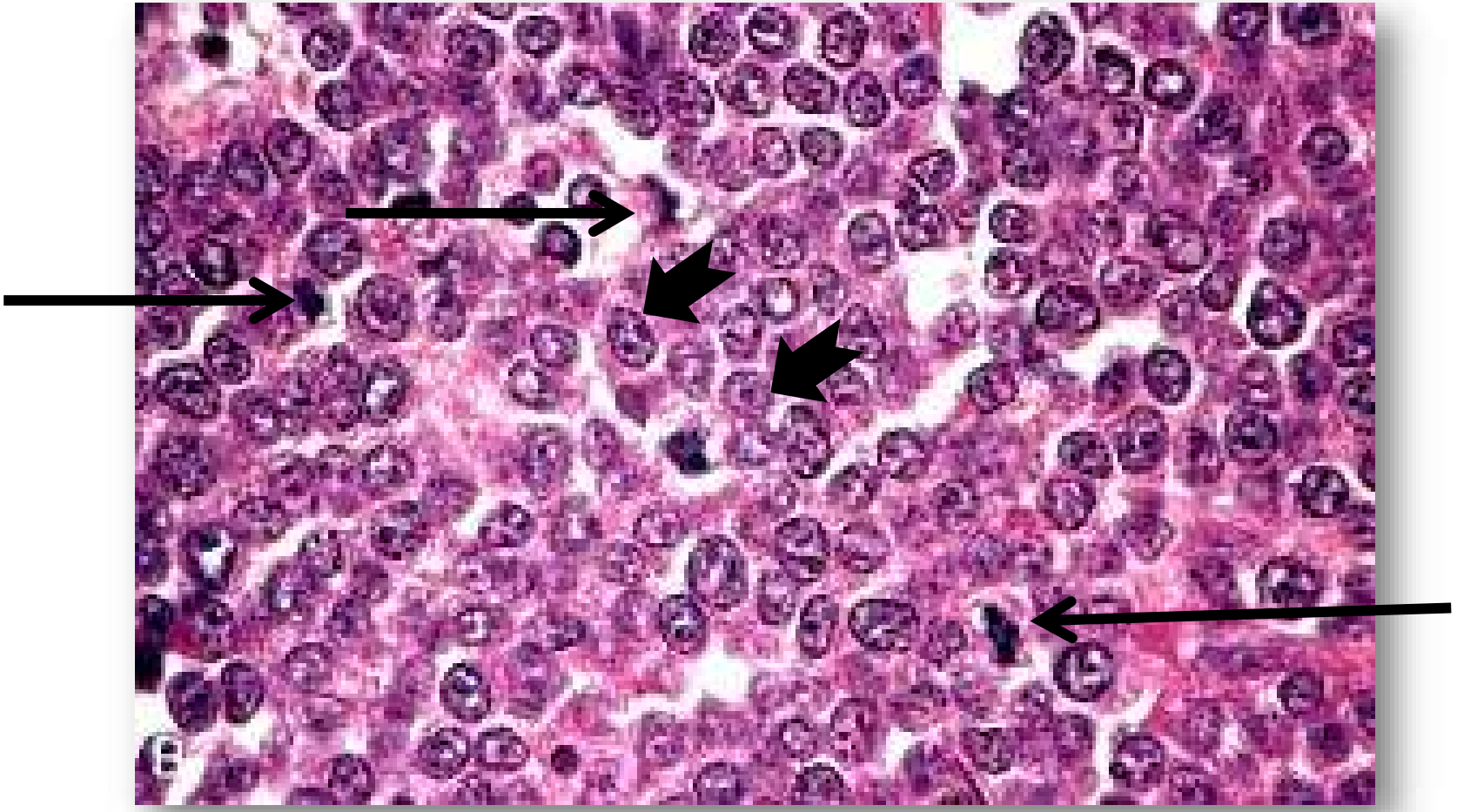
Burkitt Lymphoma Cytological Smear



The tumor cells are uniform of intermediate size with round nuclei containing 2 to 5 **prominent nucleoli**. There is a moderate amount of basophilic cytoplasm, which on cytological smears often contains small lipid **vacuoles** as seen in **L3 Acute Lymphoblastic Leukemia**



Burkitt lymphoma: histological section of lymph node, low (left) and high (right) power, showing sheets of monotonous cells and blue cytoplasm with apoptotic bodies (tangible macrophages) giving **'starry sky'** appearance.

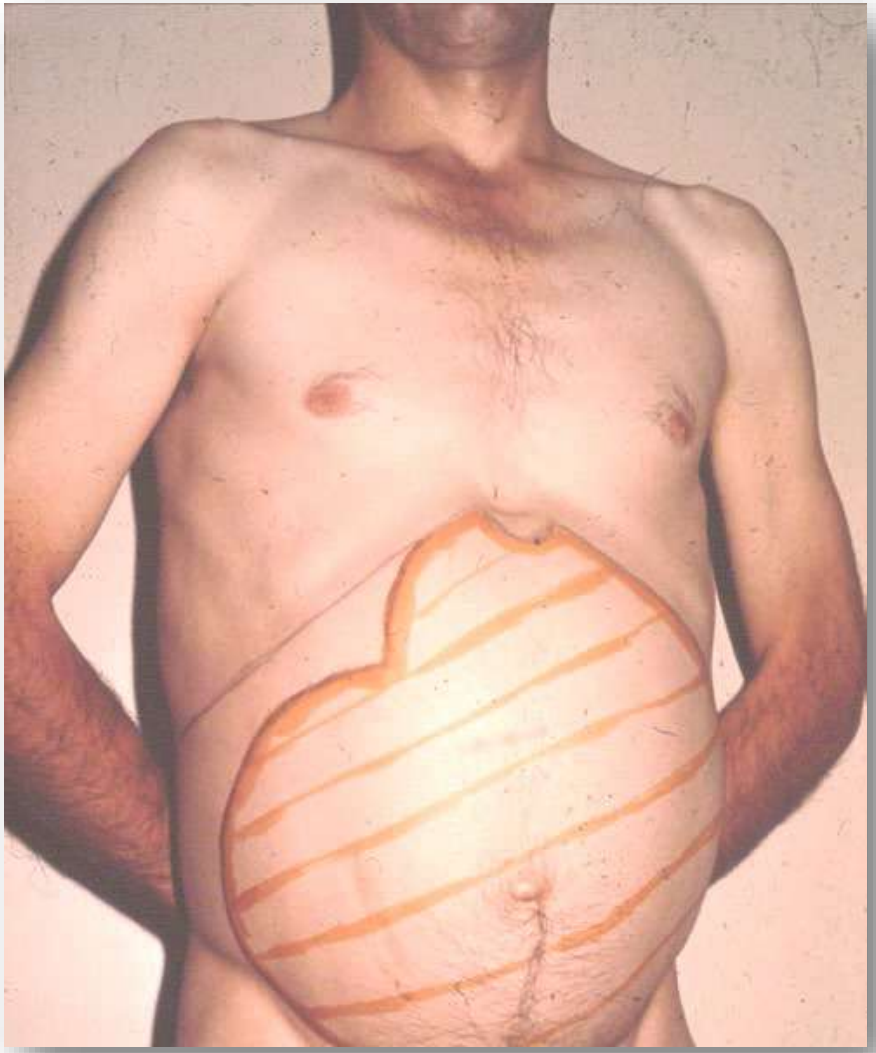


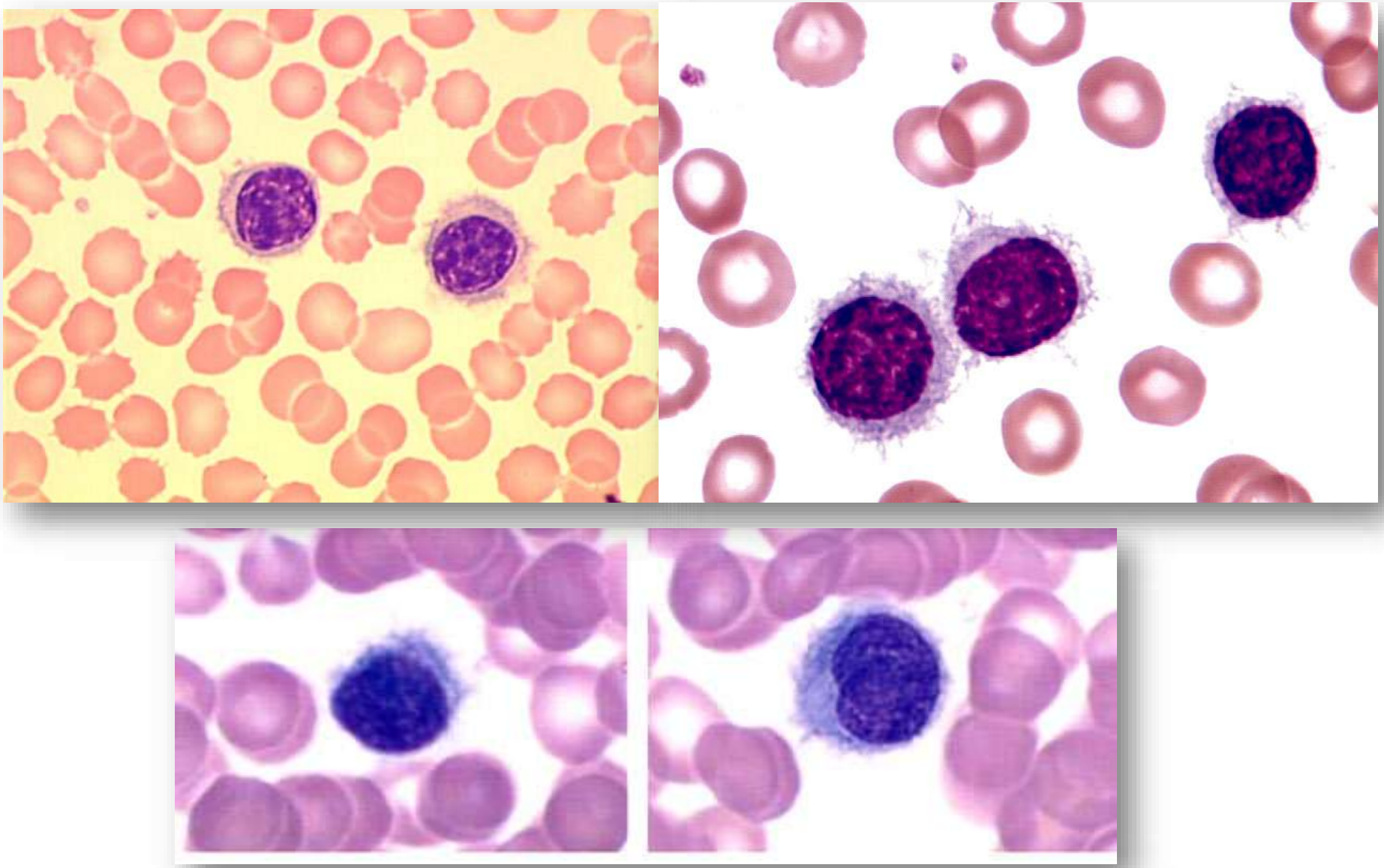
Burkitt lymphoma; high power, tumor cells have multiple small nucleoli (thick arrows) and high mitotic index (narrow arrows). The lack of significant variation in nuclear shape and size lends a monotonous appearance.

8- Hairy Cell Leukemia:

Usually affect older males. Presented as **pancytopenia** and **massive splenomegaly**. Its course usually indolent.

Characterized by presence of cells with fine irregular cytoplasmic projections (**hairy cells**)





Hairy cells; showing irregular fine cytoplasmic projections

9- Plasma Cell Dyscrasias

Heterogeneous group of disorders caused by the monoclonal proliferation of lymphoplasmacytic cells in the bone marrow with the presence of a monoclonal immunoglobulin in the serum (called monoclonal gammopathies), and the associated immunoglobulin is referred to as an M protein.

- Plasma cell dyscrasias are most common in middle-aged and elderly persons. a peak incidence between 65 and 70 years

- M components are fairly common in otherwise normal elderly persons and in a condition called monoclonal gammopathy of undetermined significance (MGUS).

The plasma cell dyscrasias can be divided into six major variants:

1- Multiple myeloma.

2- Localized plasmacytoma (solitary myeloma).

3- Lymphoplasmacytic lymphoma.

4- Heavy-chain disease.

5- Primary or immunocyte-associated amyloidosis.

6- Monoclonal gammopathy of undetermined significance (MGUS).

Multiple Myeloma (MM)

It is the most common of the malignant plasma cell dyscrasias.

It is a clonal proliferation of neoplastic plasma cells in the bone marrow that is usually associated with **multifocal lytic** lesions throughout the skeletal system.

- The most common M component is IgG (60%). Usually produce **κ or λ light chains**.

- Because of their low molecular weight, the free light chains are rapidly excreted in the urine, where they are termed **Bence-Jones proteins**.

Clinical Manifestations;

The main features are due to;

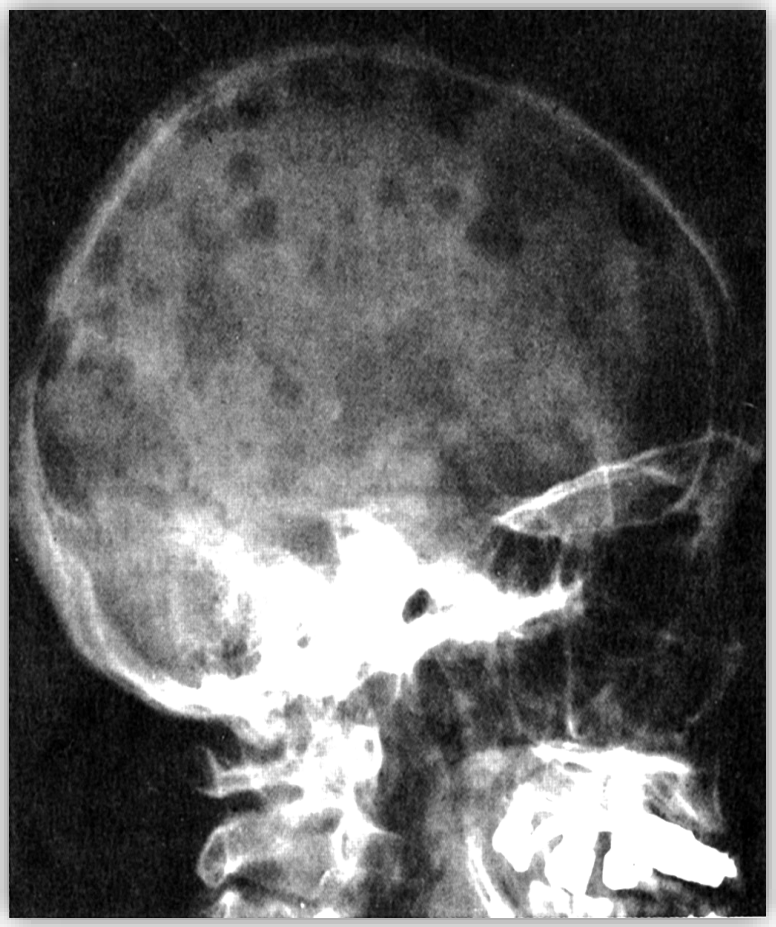
1- The destructive effect of the infiltrating neoplastic cells in various tissues.

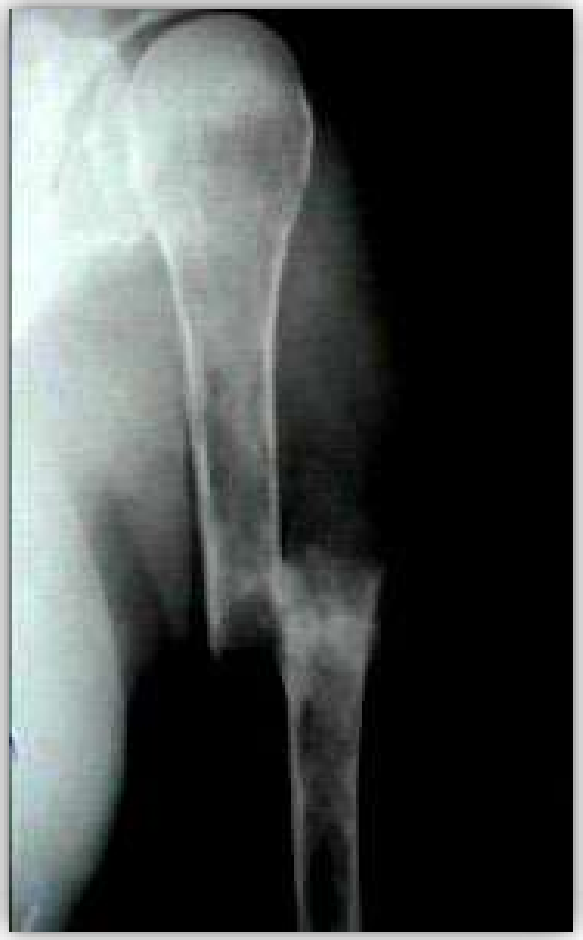
2- The abnormal immunoglobulins secreted by the tumors.

- A useful acronym for tissue damage is **BARC** (CRAB); **B**one disease, **A**nemia, **R**enal impairment and **Hyperc**alcemia.

- Amyloid, hyperviscosity, recurrent infections, peripheral neuropathy and deep vein thrombosis are other clinical complications which are less frequently presenting features

- Bones pain and mostly show multifocal destructive bone lesions as punched-out defects throughout the skeletal system, result from the secretion of certain cytokines.
- There are often pathologic fractures, which occur most frequently in the vertebral column.





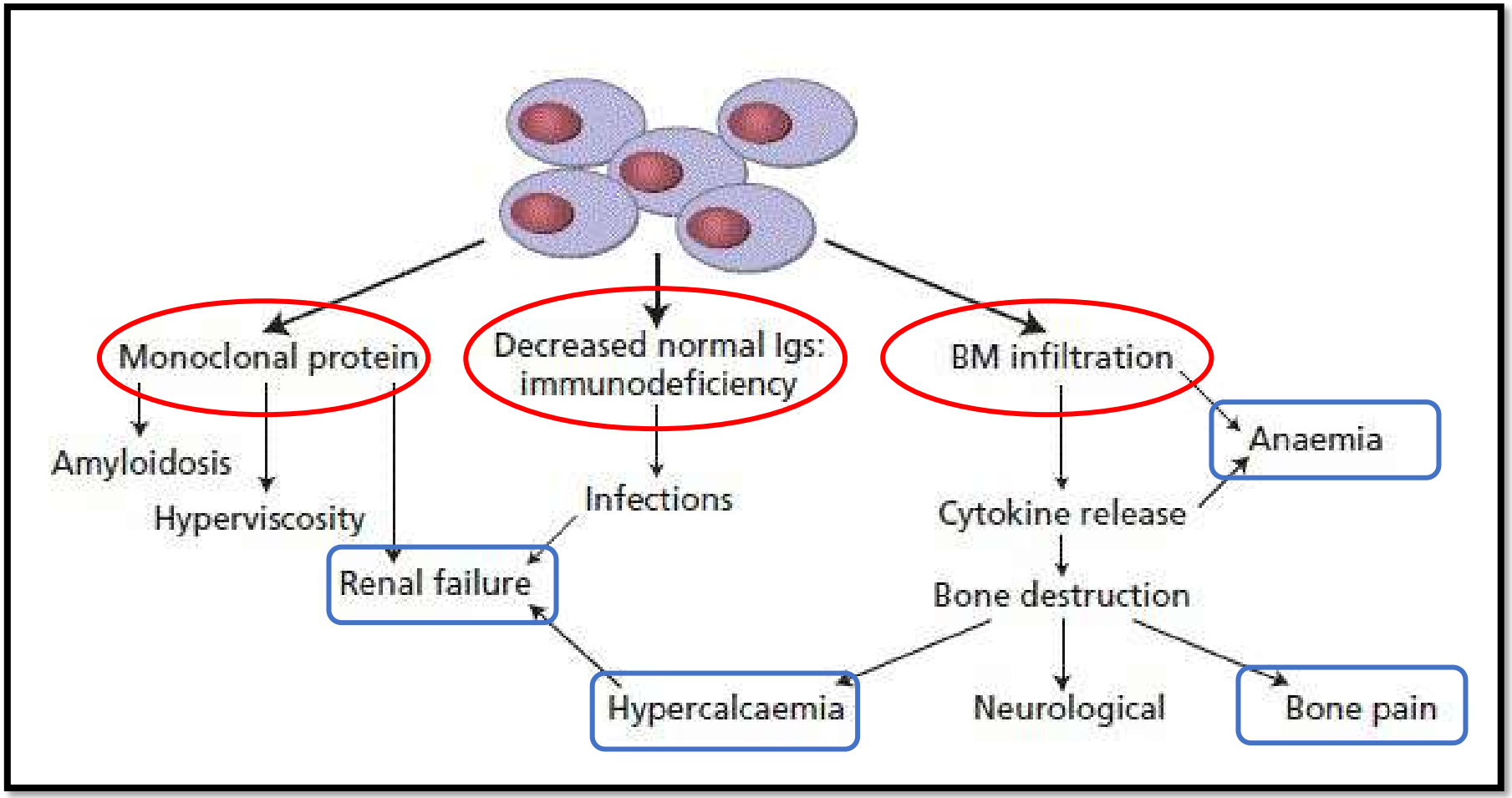
- Anemia; results from marrow suppression and cytokines effects.

- Renal insufficiency occurs in as many as 50% of patients. It results from the toxic effects of Bence-Jones proteins on cells lining the tubules, recurrent bacterial infections and hypercalcemia.

- Recurrent infections with bacteria are serious clinical problems. They result from severe suppression of normal immunoglobulin secretion.

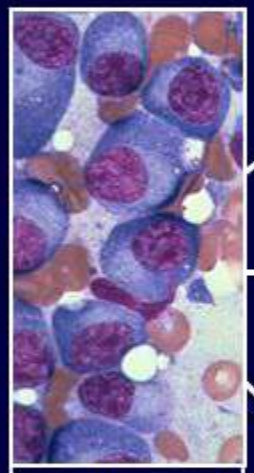
- Hyperviscosity syndrome may occur due to excessive production and aggregation of myeloma proteins.

- Amyloidosis develops in 5% to 10% of patients.

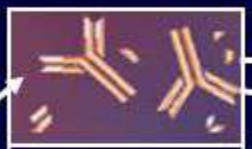


The pathophysiology of the main clinical manifestations in MM

Myeloma Can Result in a Broad Spectrum of Clinical Manifestations



Multiple myeloma cells



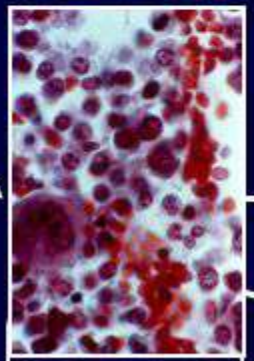
M-protein

Renal compromise (30%)

Neuropathy (33%)
Hyperviscosity
Amyloidosis

Immune deficiency

Infection (15%)



Marrow infiltration

Destruction of bone

Hypercalcemia (15% to 20%)

Bone pain

Lytic lesions (70%)

Anemia (10% to 35%)

Hoffman R. Hematology: basic principles and practice, 5th edition; 2008. Ropper AH, et al. N Engl J Med. 1998;338:1601-1607.

Diagnostic Features of MM:

- There is usually a normochromic normocytic or macrocytic anemia. Rouleaux formation is marked in most cases.

- High erythrocyte sedimentation rate (ESR).

- Bone marrow; shows increased plasma cells (usually more than 20%) with normal plasma cell, but often with abnormal forms.

- Terminally, a leukemic picture may emerge (Plasma cell Leukemia).

- Presence of a paraprotein: In 99% of cases a monoclonal spike of complete immunoglobulin or immunoglobulin light chains, which can be detected in the serum, urine, or in both.

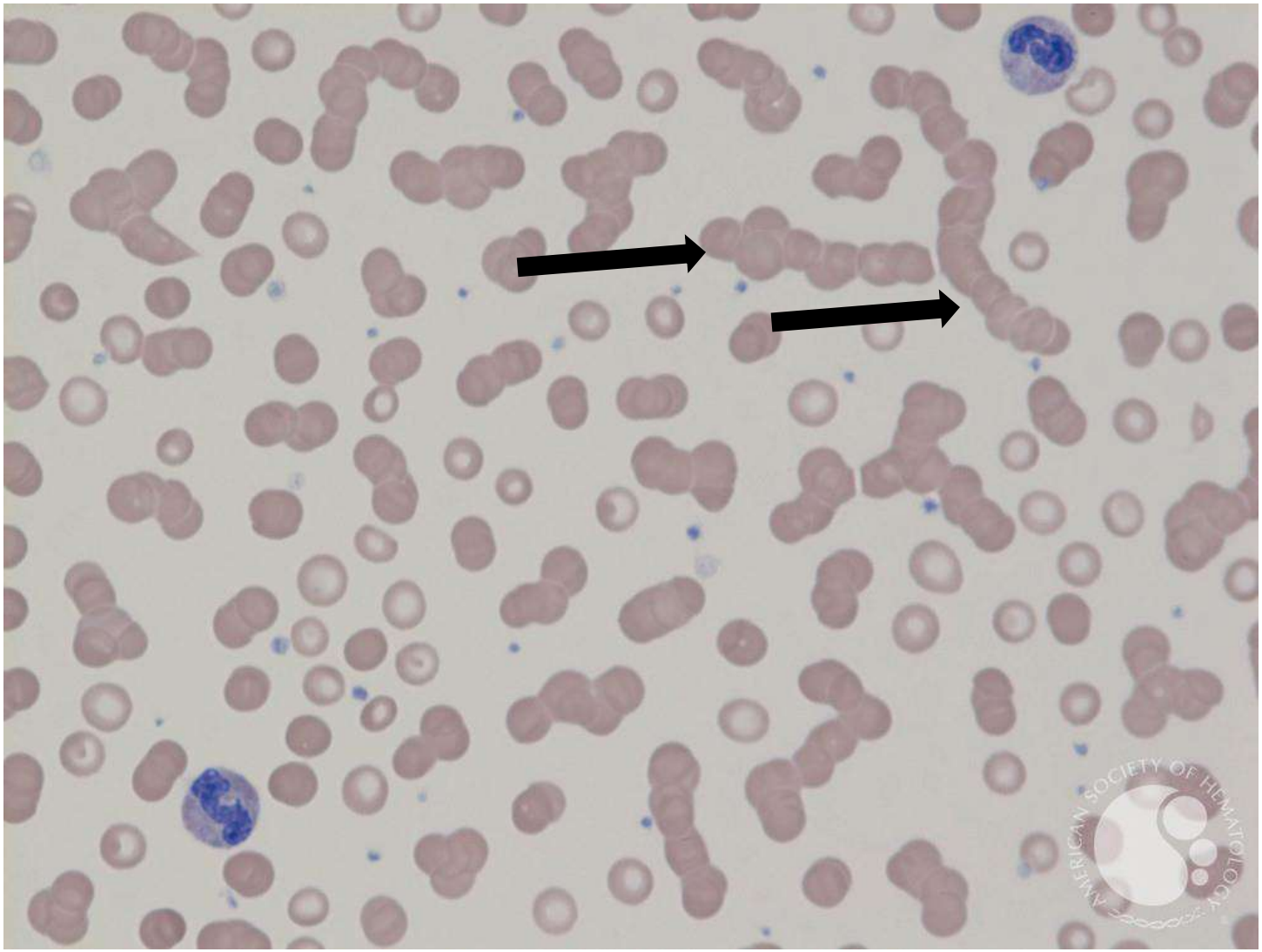
- Reduced normal serum immunoglobulin levels (IgG, IgA and IgM) and elevated serum immunoglobulin-free light chains: typically in myeloma there is an increase in either the κ or λ serum free light chain value.

- Serum calcium and serum creatinine are elevated.

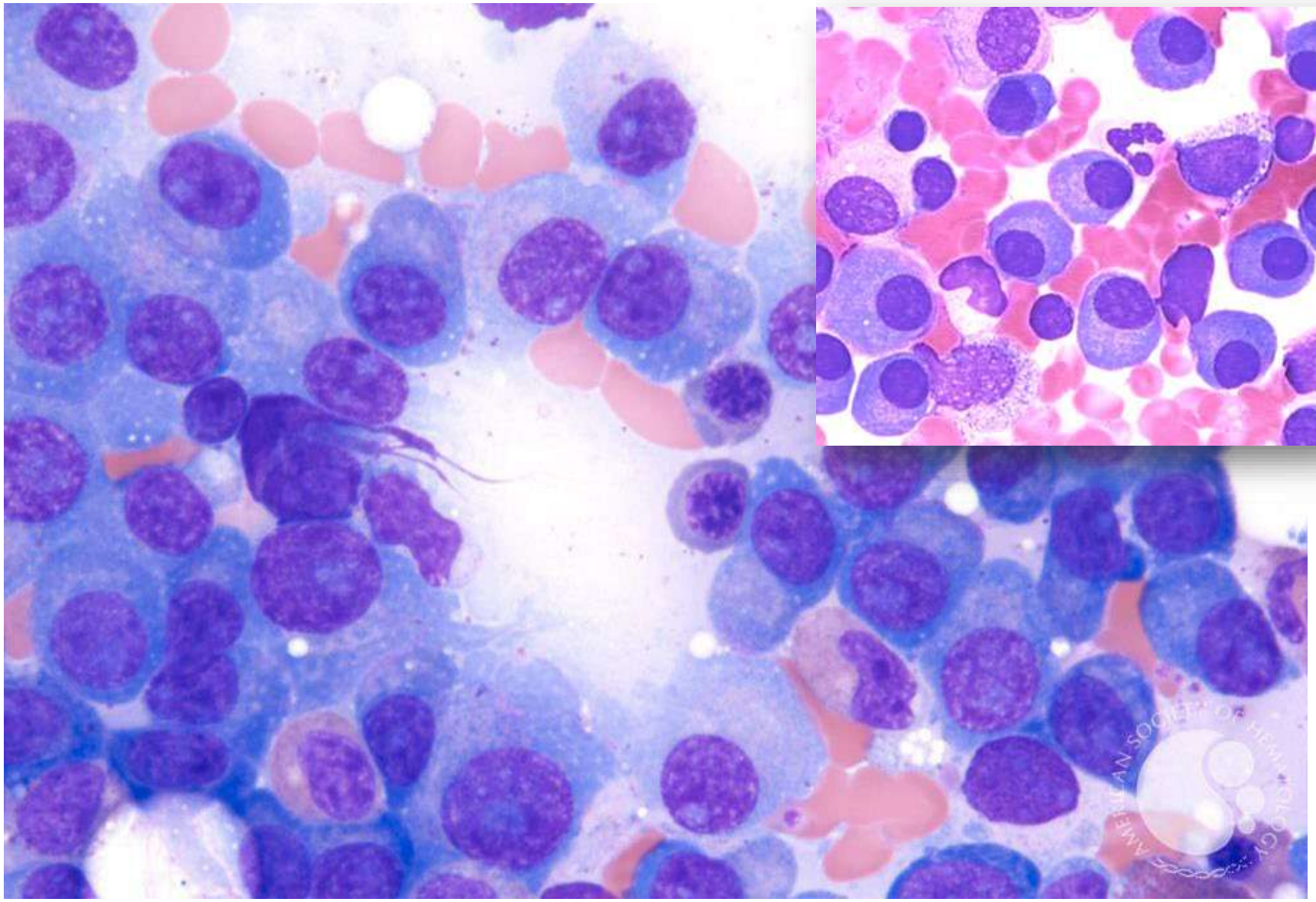
- The urine contains free light chains, Bence–Jones protein, in two thirds of cases.

- Radiological investigation of the skeleton reveals bone lesions such as osteolytic areas without evidence of surrounding osteoblastic reaction or sclerosis. MRI of the spine and PET scan are sensitive imaging technique to detect bone damage

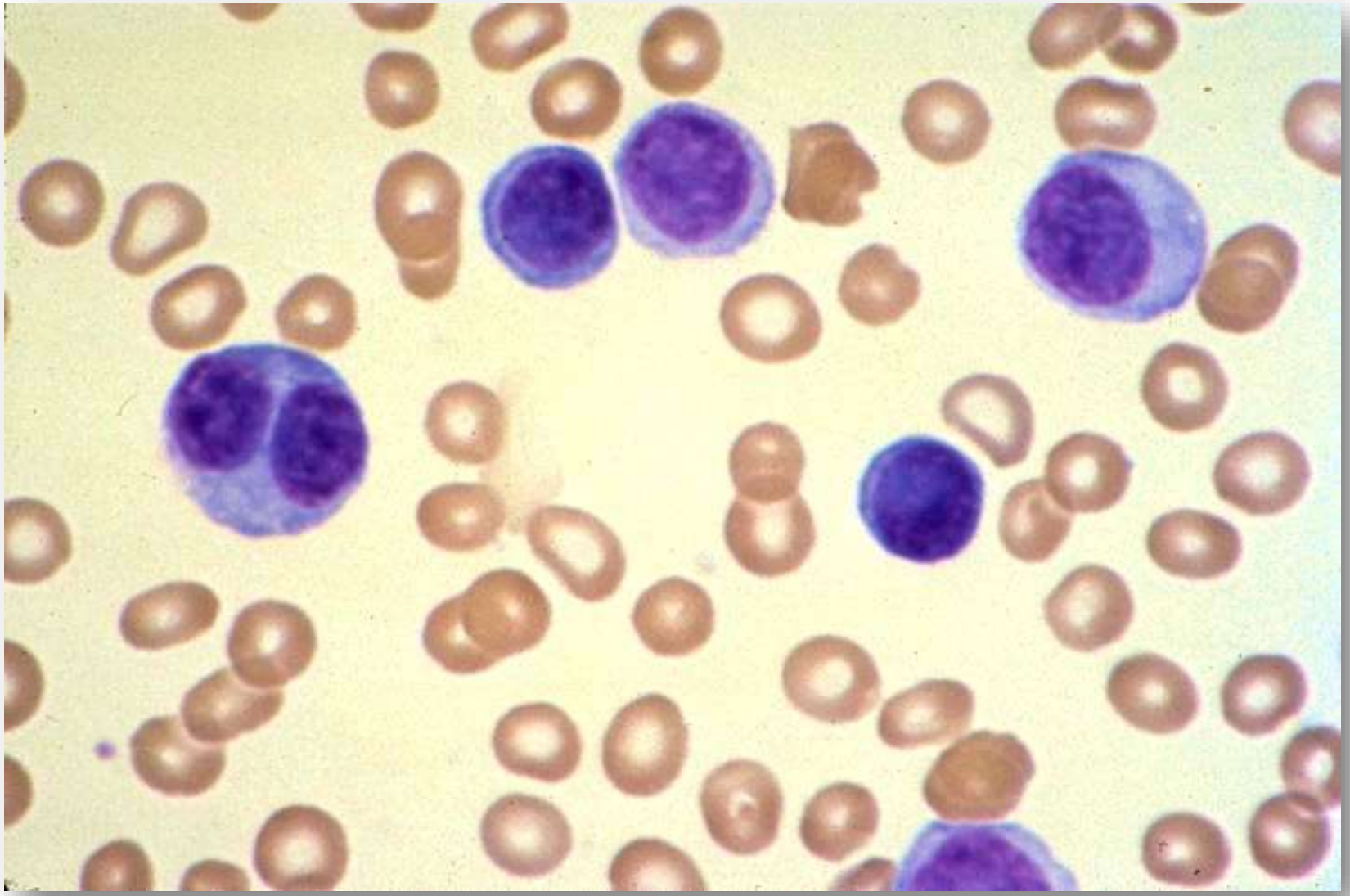
- The molecular and cytogenetic changes are important for diagnosis and prognosis.



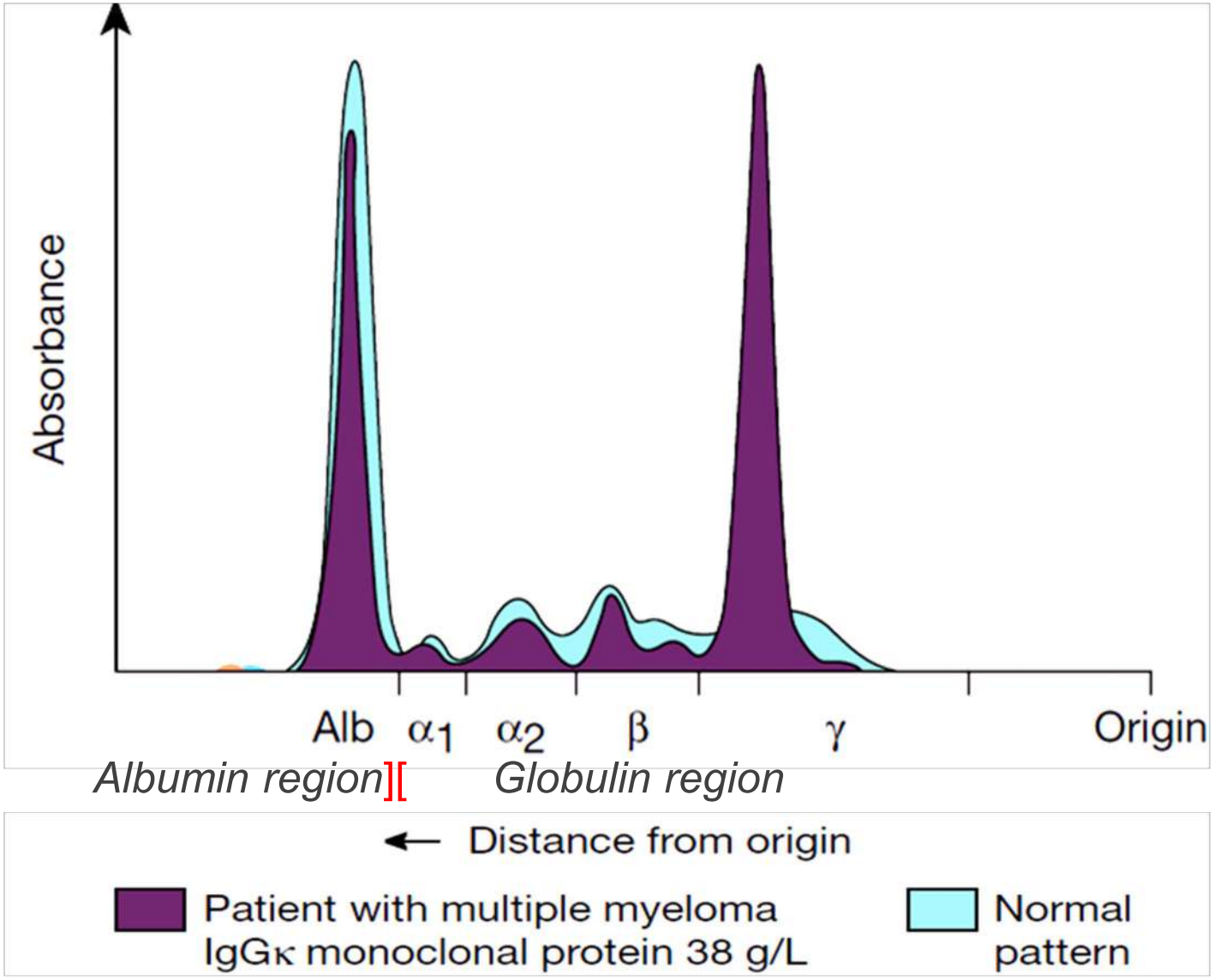
Blood film of MM; erythrocytes are grouped in "rouleaux," a "stack-of-coins" pattern most often associated with elevated levels of immunoglobulin



Bone marrow shows most of the cells are plasma cells



Plasma Cell Leukemia; plasma cells in the blood film



Serum protein electrophoresis in MM; showing an abnormal paraprotein in the γ-globulin region with reduced levels of background β- and γ-globulins.

Diagnostic Criteria of MM:

Clonal bone marrow plasma cells >10% + any one or more of the following BARC (CRAB) features:

Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:

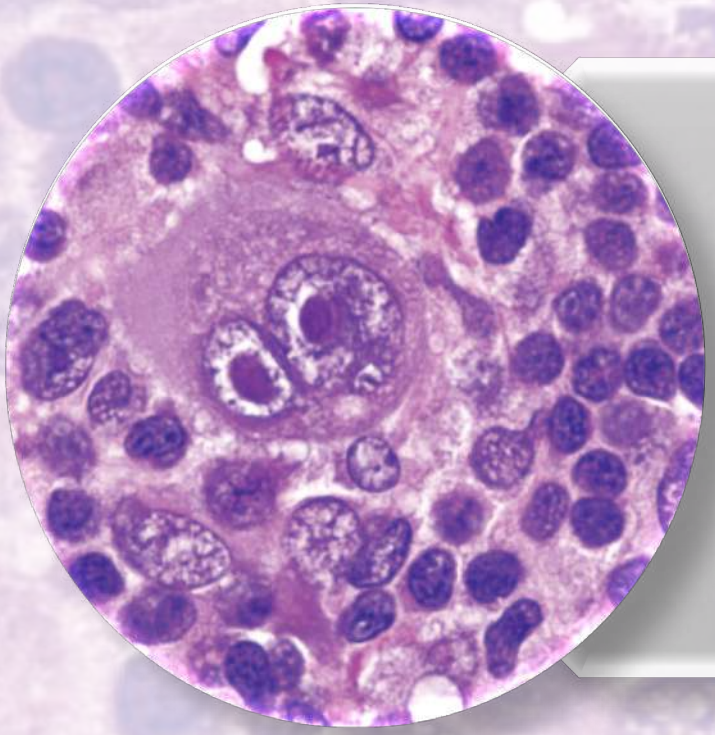
- **Hypercalcemia**: serum **c**alcium >2.75 mmol/L (>11mg/dL)
- **Renal** insufficiency: serum creatinine >2mg/dL or creatinine clearance <40 mL per minute.
- **Anemia**: low hemoglobin value.
- **Bone** lesions: one or more osteolytic lesion on skeletal radiography, CT, or PET/CT. If bone marrow has <10% clonal plasma cells, more than one bone lesion is required to distinguish from **solitary plasmacytoma** with minimal marrow involvement.

III. Precursor T-cell Neoplasms; (T-cell acute lymphoblastic leukemia/lymphoma (T-ALL)

IV- Neoplasms of Mature T Cells and NK cells

Diagnosis	Cell Origin	Genotype	Salient Clinical Features
1-Adult T-cell leukemia/ lymphoma	Helper T cell	HTLV-1 provirus present in tumor cells	Adults with cutaneous lesions, marrow involvement, and hypercalcemia; occurs mainly in Japan, West Africa, and the Caribbean; aggressive
2- Peripheral T-cell lymphoma, unspecified	Helper or cytotoxic T cell	No specific chromosomal abnormality	Mainly older adults; usually presents with lymphadenopathy; aggressive
3- Anaplastic large-cell lymphoma	Cytotoxic T cell	Rearrangements of ALK	Children and young adults, usually with lymph node and soft-tissue disease; aggressive

Diagnosis	Cell Origin	Genotype	Salient Clinical Features
4-Extranodal NK/T-cell lymphoma	NK-cell (common) or cytotoxic T cell (rare)	EBV-associated; no specific chromosomal abnormality	Adults with destructive extranodal masses, most commonly sinonasal; aggressive
5- Mycosis fungoides/ Sézary syndrome	Helper T cell	No specific chromosomal abnormality	Adult patients with cutaneous patches, plaques, nodules, or generalized erythema; indolent
6- Large granular lymphocytic leukemia	Two types: cytotoxic T cell and NK cell	No specific chromosomal abnormality	Adult patients with splenomegaly, neutropenia, and anemia, sometimes, accompanied by autoimmune disease



HODGKIN LYMPHOMA

Hodgkin Lymphoma (Disease)

A primary malignant neoplasm of the lymphoid system, which is characterized by the presence of **giant multinucleated giant** cells (Reed-Sternberg) and their mononuclear analogues (Hodgkin cells).

- Its an aggressive B-cell lymphoma and in minority of T cell origin. Its is one of the most curable of all hematological malignancies.

- Age and sex: Bimodal age distribution with median age of 31 years, the first peak at 20-35 years and the second is above 50. There is a slight male excess.

- The Epstein-Barr virus (EBV) genome is present in the Hodgkin Reed-Sternberg cells (HRS) cells, the characteristic cells of Hodgkin's Lymphoma - in up to 70%, thus suggests that the virus contributes to the development of Hodgkin's disease in some cases.

Classification of Hodgkin lymphoma

- **Rye Classification (1966)**

1- Nodular sclerosis.
2- Mixed cellularity.
3- Lymphocyte depleted.
4- Lymphocyte predominant.

- **REAL/WHO Classification;**

A- Classical HL (95%)

1- Nodular sclerosis.
2- Mixed cellularity.
3- Lymphocyte predominance.
4- Lymphocyte depleted.

B- Nodular lymphocyte predominant. (5%)

Clinical Presentations:

- Painless peripheral lymphadenopathy, mostly cervical and supraclavicular.

- B-symptoms (systemic symptoms, according to Ann Arbor staging): Fever, drenching sweats (at night) and weight loss (10% of body weight).

- Splenomegaly in 16% of the cases.

- Anemia due to bone marrow involvement in 5% of the cases.

Investigations

- Blood count; may be normal, but presence of anemia or lymphopenia reflect poor prognosis.

- Eosinophilia or a neutrophilia may be present.

- ESR may be raised.

- Liver function if abnormal may reflect hepatic infiltration.

- Chest X-ray for presence of mediastinal mass.

- PET (Positron Emission Tomography)/CT of thorax, abdomen, chest and pelvis

- MRI

- Histology of the lymph node; biopsy may be undertaken surgically or by percutaneous needle biopsy under radiological guidance .

Histopathology of Hodgkin Lymphoma:

Three factors which are important in diagnosis of HL and can be differentiated from NHL:

1- Neoplastic cells; which constitute a minority (1- 5%) of tumor mass, either;

A- Classical Hodgkin Reed-Sternberg cells (RS-cells)

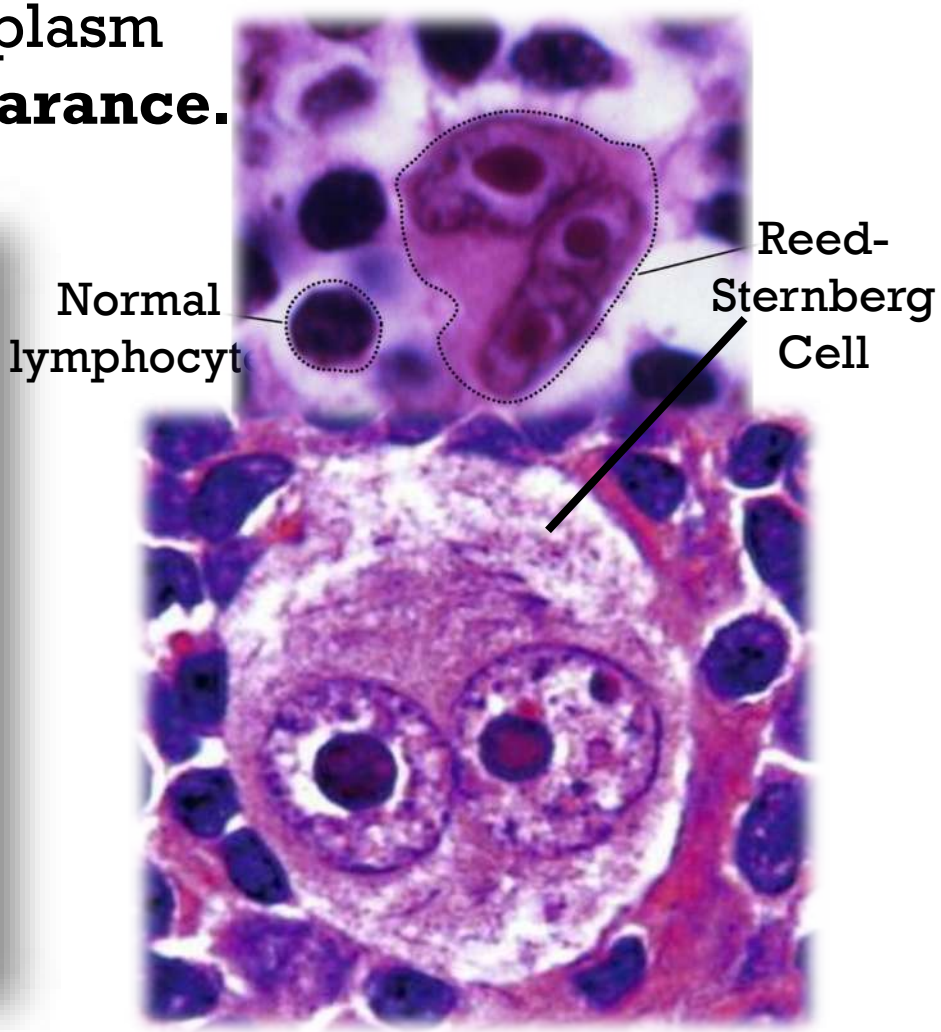
B- RS- cell Variants;

2- Non-neoplastic "reactive" background; include lymphocytes, neutrophils, Plasma cells, Eosinophils, Histiocytes, Fibroblasts and fibrous tissue.

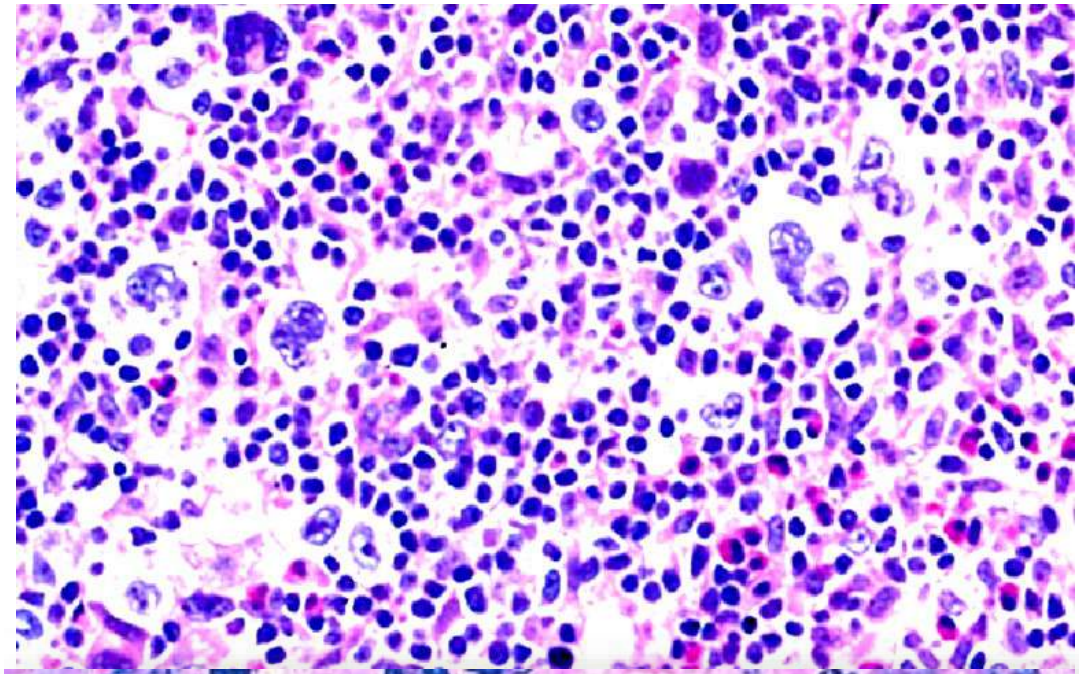
3- Characteristic Immunostains of RS-cells.

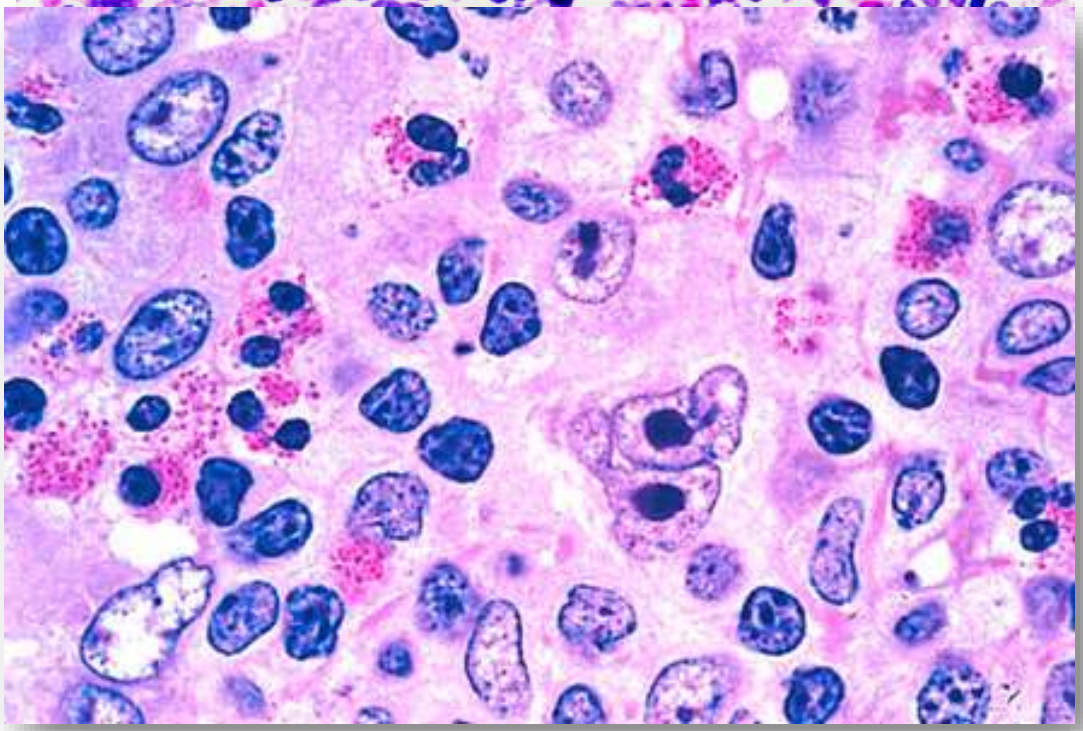
A- Hodgkin Reed-Sternberg (HRS), Classical;

A large binucleated cell with large eosinophilic (inclusion-like) nucleoli (mirror- image) surrounded by slightly eosinophilic cytoplasm giving an **owl's eye appearance.**



HRS cell surrounded by reactive cells, including pleomorphic neutrophils, eosinophils (bright red cytoplasm), lymphocytes, and histiocytes.





B- Reed-Sternberg Cells (RS-cells) Variants;

1- Hodgkin cells (Mononuclear variant): Insufficient for diagnosis but can be used for diagnosing extranodal sites in known cases.

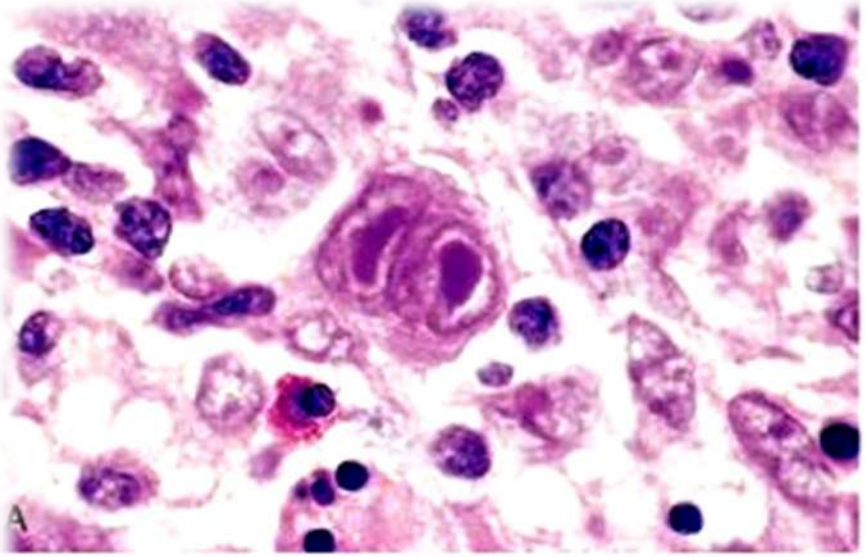
2- Mummified cells: Dark smudge degenerating cells with pyknotic nuclei and eosinophilic cytoplasm.

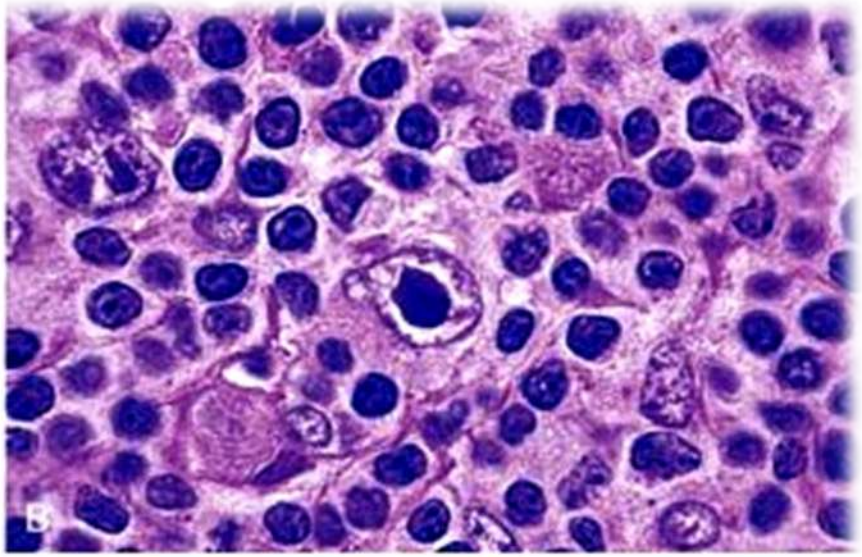
3- Lacunar cells: has a folded or multilobated nucleus and lies within an open space, which is an artifact created by disruption of the cytoplasm during tissue sectioning.

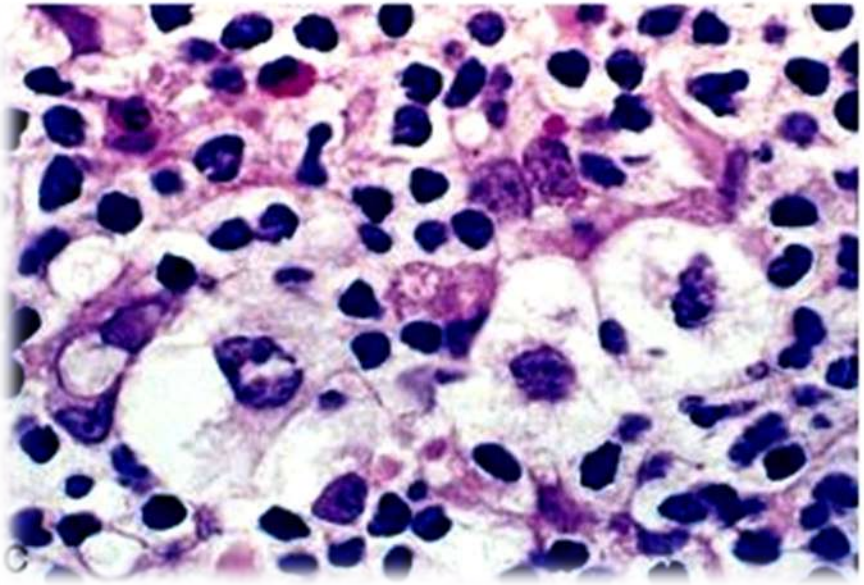
4- Lymphohistiocytic cells (popcorn cells): Cells with hyperlobated nuclei, finely granular chromatin and inconspicuous small nucleoli.

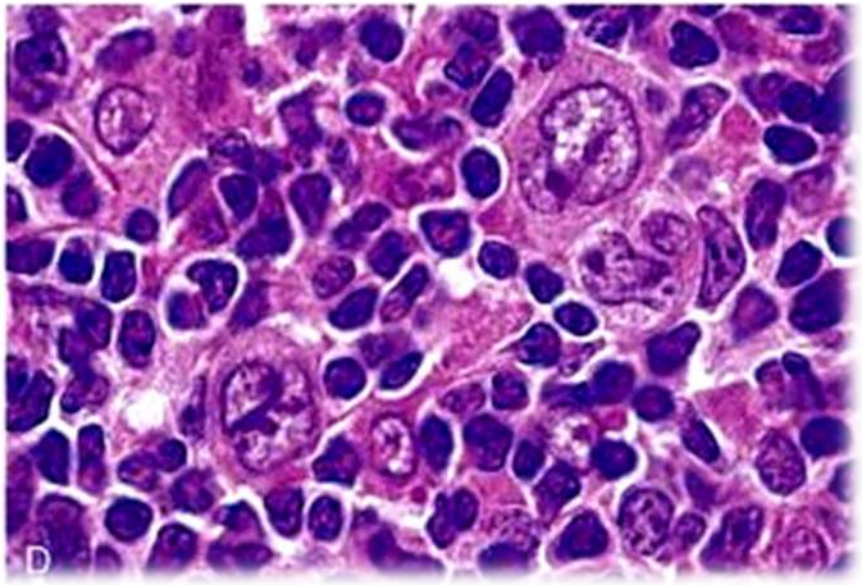
Classical RS

Mononuclear variant









Lacunar variant

Lymphohistiocytic

Staging System (Ann Arbor Staging System) for Hodgkin's Disease

Staging involves:

1- physical examination,

2- Radiologic imaging of the abdomen, pelvis and chest.

3- Biopsy of the bone marrow

With current treatment protocols, tumor stage rather than histologic type is the most important prognostic variable. The cure rate of patients with stages I and IIA is close to 90%. Even with advanced disease (stages IVA and IVB), disease-free survival at 5 years is 60% to 70%.

HL Ann Arbor Staging System

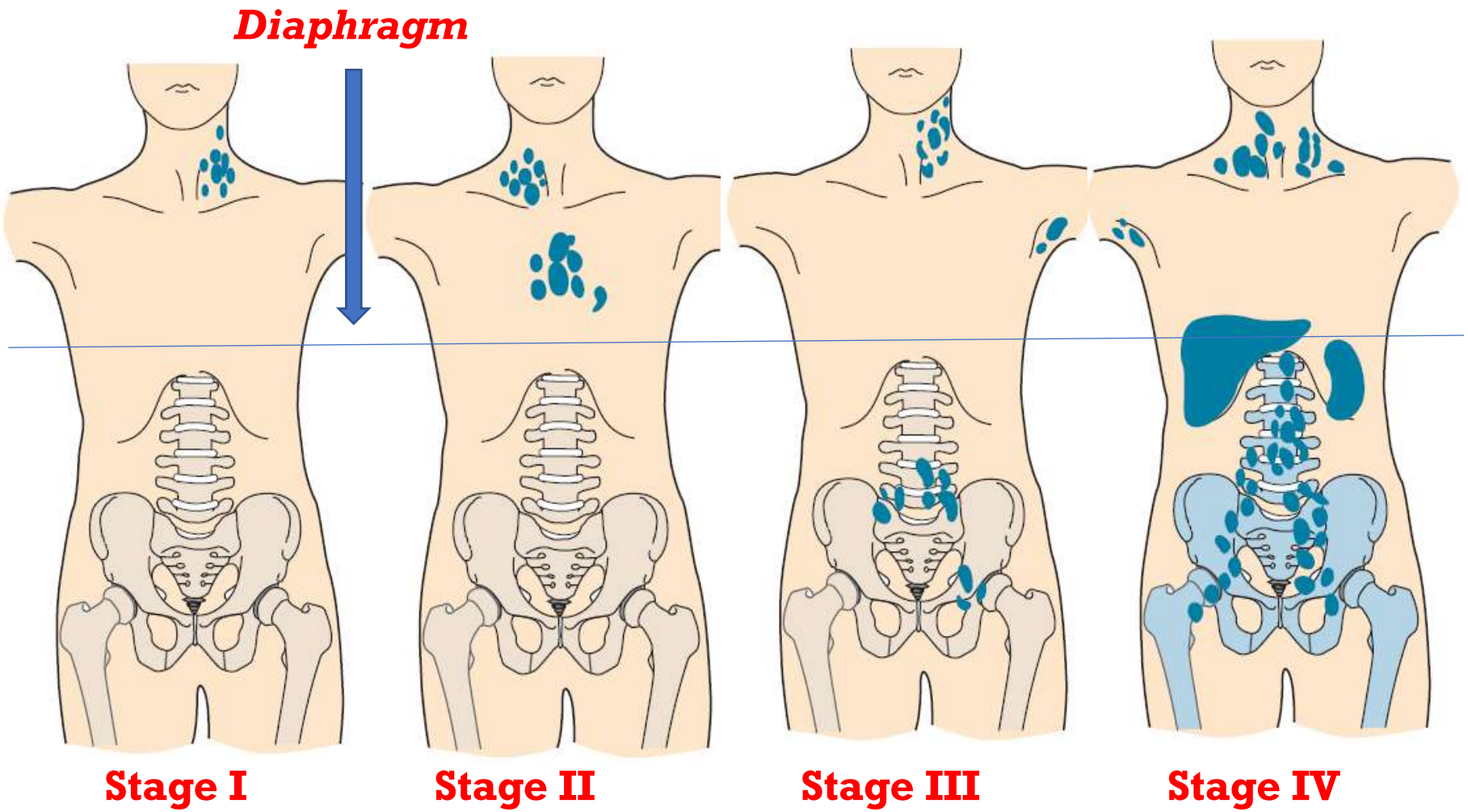
Stage I	Involvement of a single lymph node region (I) or extralymphatic site (IE)
Stage II	Involvement of two or more lymph node regions (II) or an extralymphatic site and lymph node regions on the same side of (above or below) the diaphragm (IIE)
Stage III	Involvement of lymph node regions on both sides of the diaphragm with (IIIE) or without (III) localized extralymphatic involvement or involvement of the spleen (IIIS) or both (IIISE)
Stage IV	Diffuse involvement of one or more extralymphatic tissues, e.g. liver or bone marrow

Each stage is subclassified:

A; No systemic symptoms

B; Weight loss, drenching sweats

E; The lymphatic structures are defined as the lymph nodes, spleen, thymus, Waldeyer's ring, appendix and Peyer's patches.



Ann Arbor Staging System

Types of Hodgkin Lymphoma;

According to the WHO HL classified into;

A- Classical Hodgkin lymphoma (95% of cases);

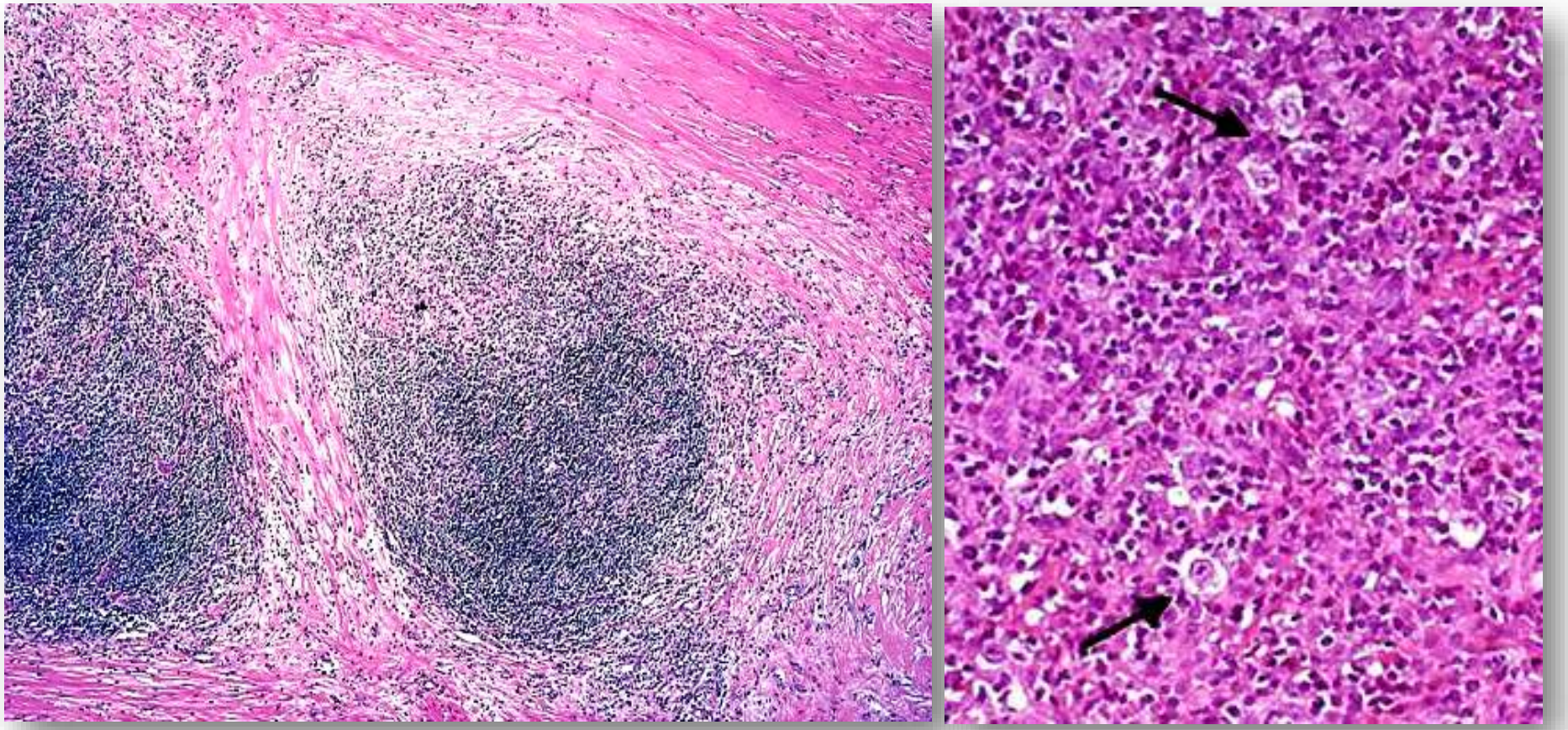
1- Nodular sclerosis; it's the most common type (≈70%) characterized by collagen (fibrotic) bands extend from the node capsule to encircle nodules of abnormal tissue. A characteristic lacunar cell variant of the RS-cell is often found.

2-Mixed cellularity; The second common type (≈25%). There is prominence of RS-cells, frequent mononuclear variants with cellular background of lymphocytes, eosinophils, macrophages, plasma cells and neutrophils.

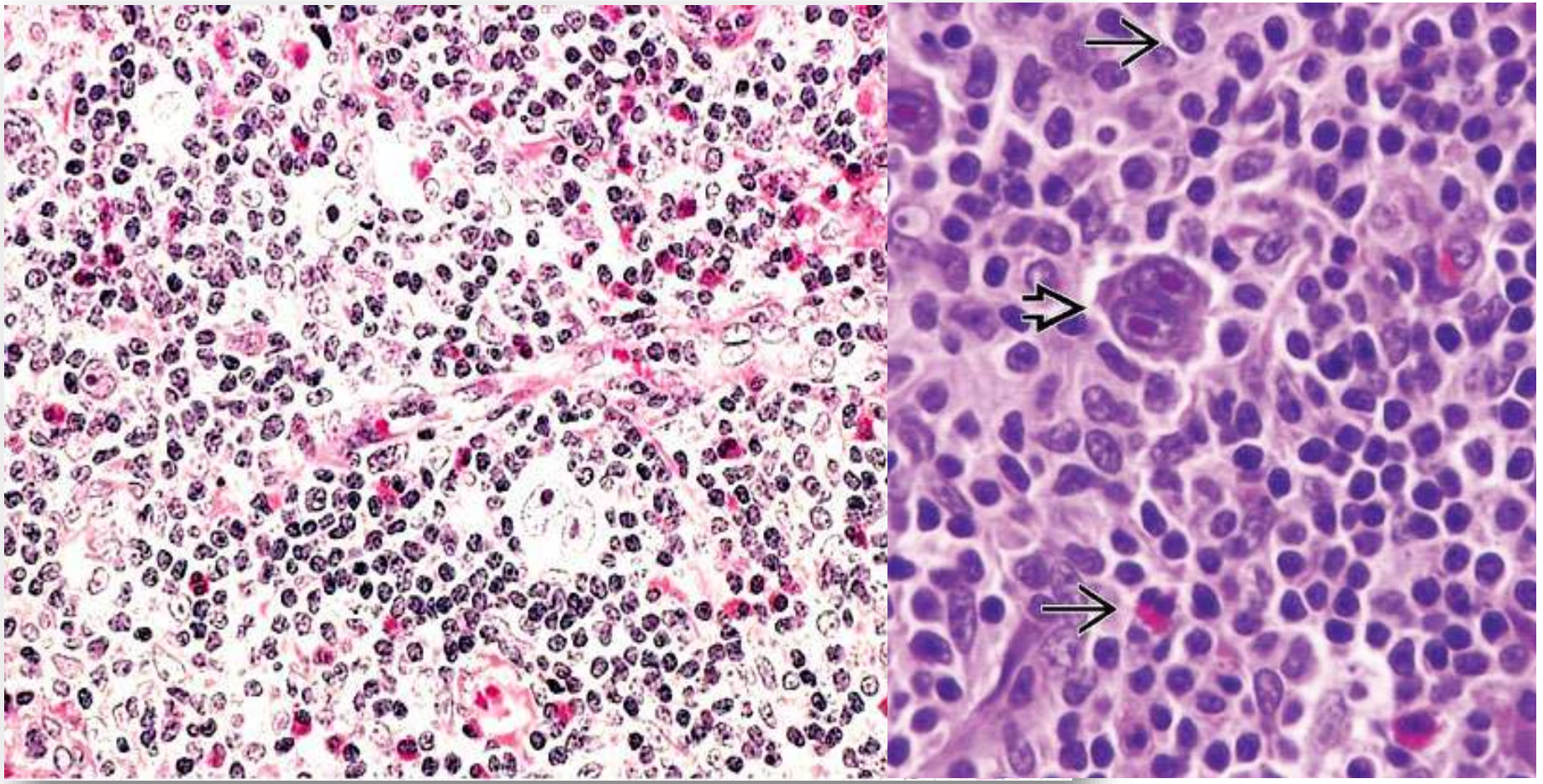
3- Lymphocyte predominance (rich); Characterized by the vast majority of the cells those of reactive T-lymphocytes, and canty RS-cells usually of popcorn variant. Usually the lymph node is diffusely effaced.

4- Lymphocyte depleted; its uncommon type (5%), with a bad prognosis. Characterized by a low number of lymphocytes with variable numbers of RS-cells.

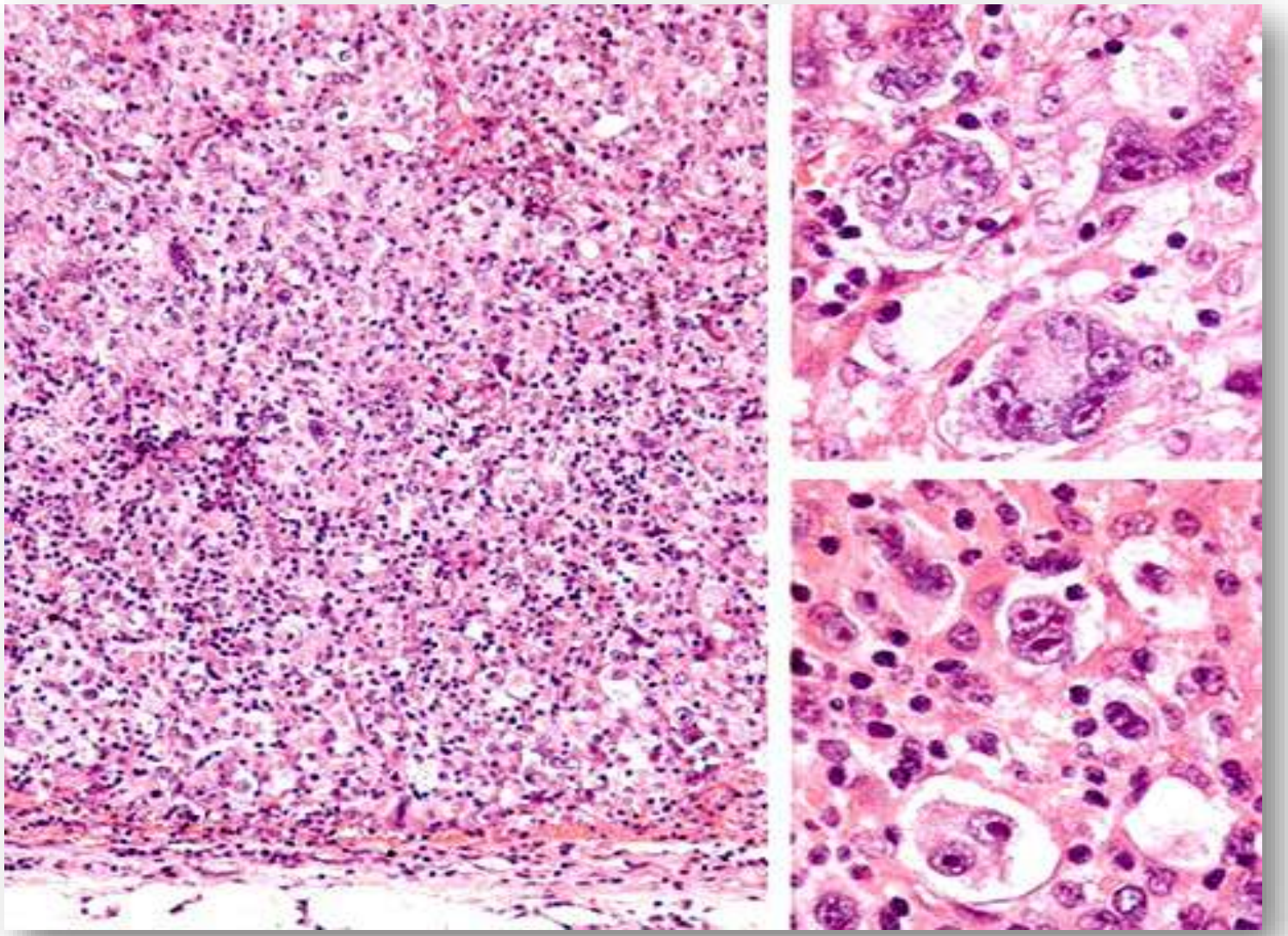
B- Nodular Lymphocyte-Predominant; (5% of cases), with a good prognosis. Its of a nodular form with prominence of lymphocyte and the lymphohistiocytic (popcorn) cells.



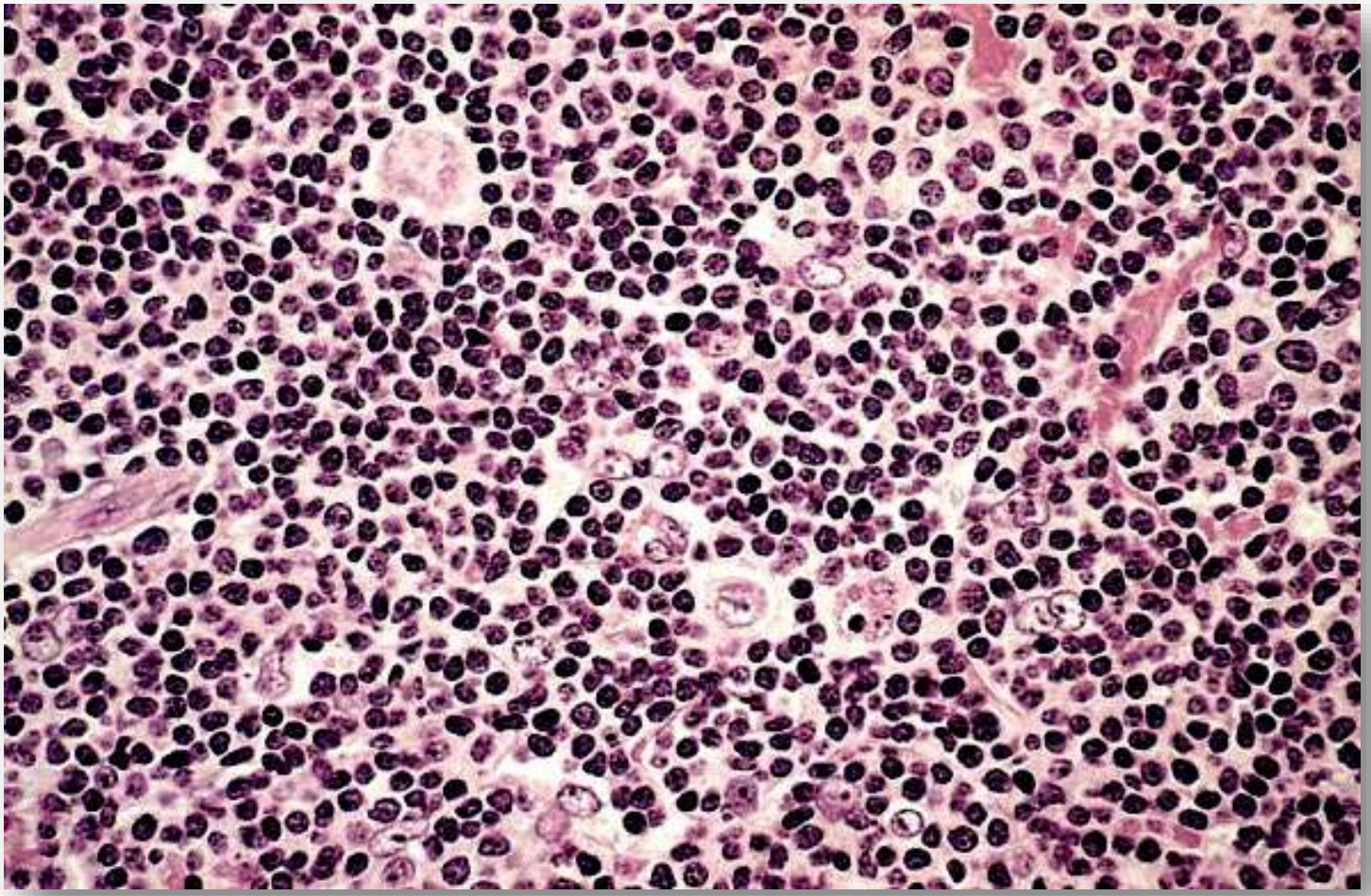
Nodular Sclerosis; left; low power shows nodular configuration created by sclerotic/fibrotic bands surrounding cellular clusters of cells. **Right**; high power shows lacunar cells (arrow), large cells with a surrounding prominent clear space.



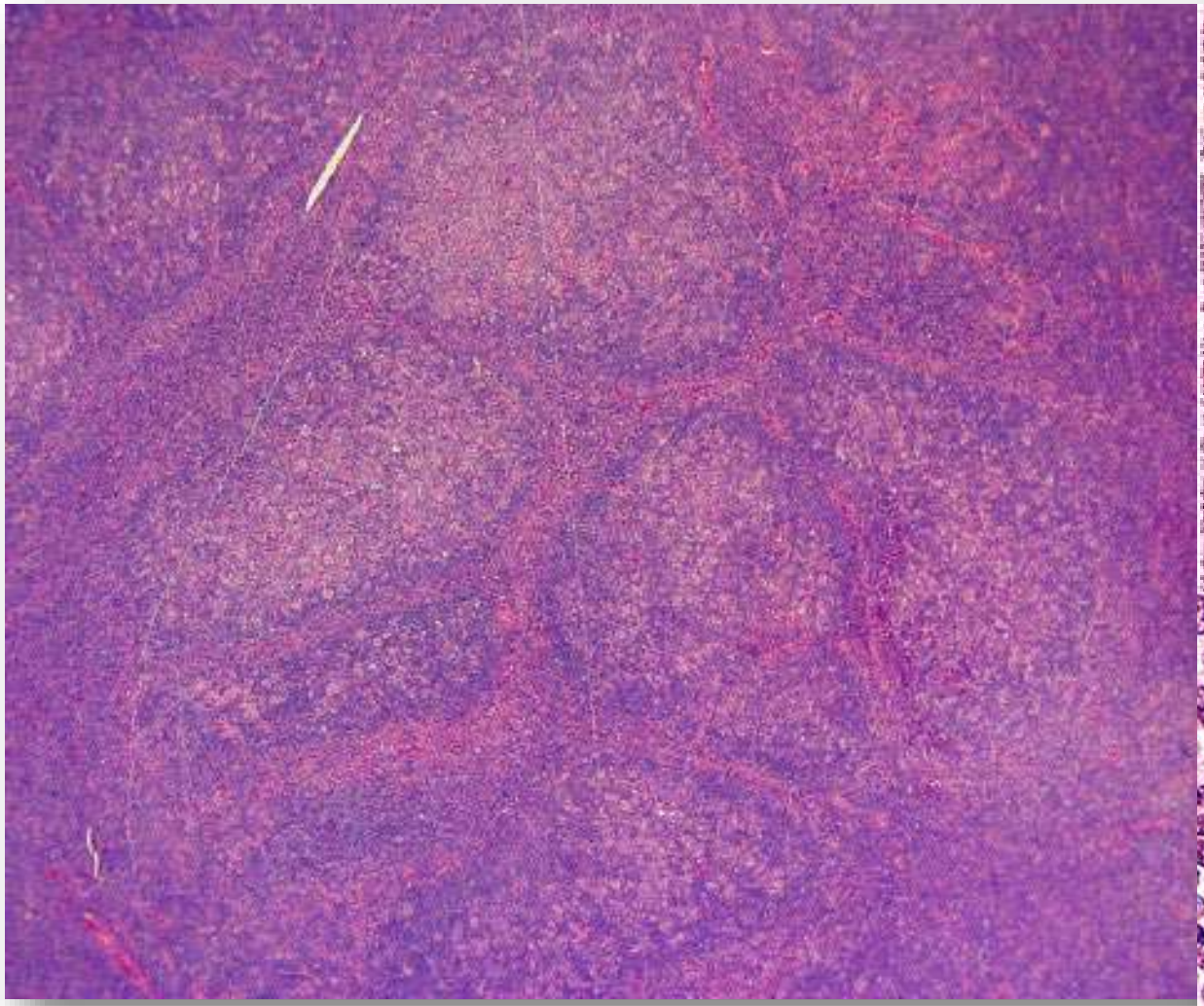
Mixed cellularity; low and high power, binucleated RS-cell (wide arrow), surrounded by reactive cells (narrow arrow), including eosinophils (bright red cytoplasm), lymphocytes, and histiocytes.

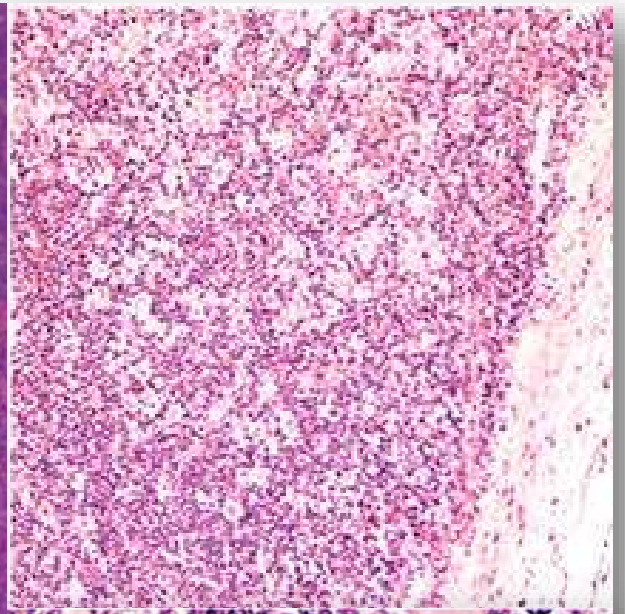


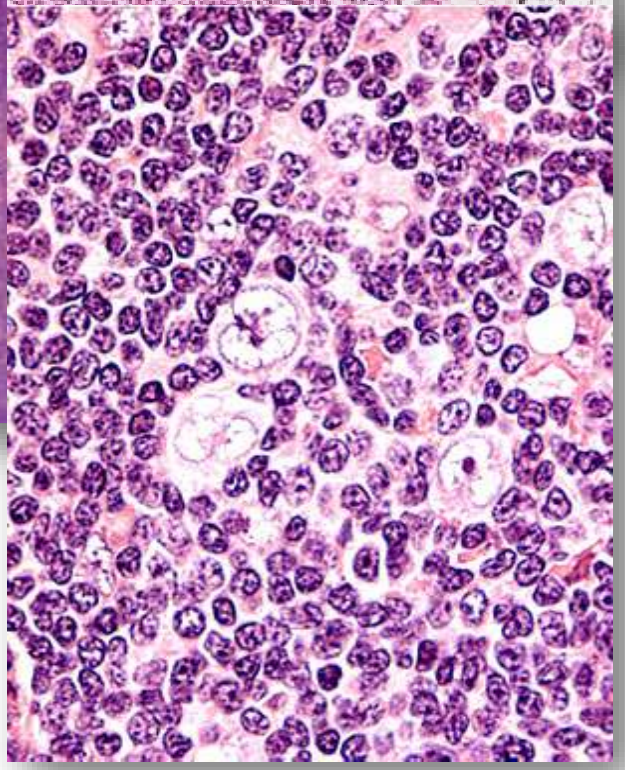
Lymphocyte Depleted; low number of the lymphocytes with numerous RS-cells.



Lymphocyte Predominance; numerous mature-looking lymphocytes surround scattered, large, pale-staining lymphohistiocytic variants (“popcorn” cells).

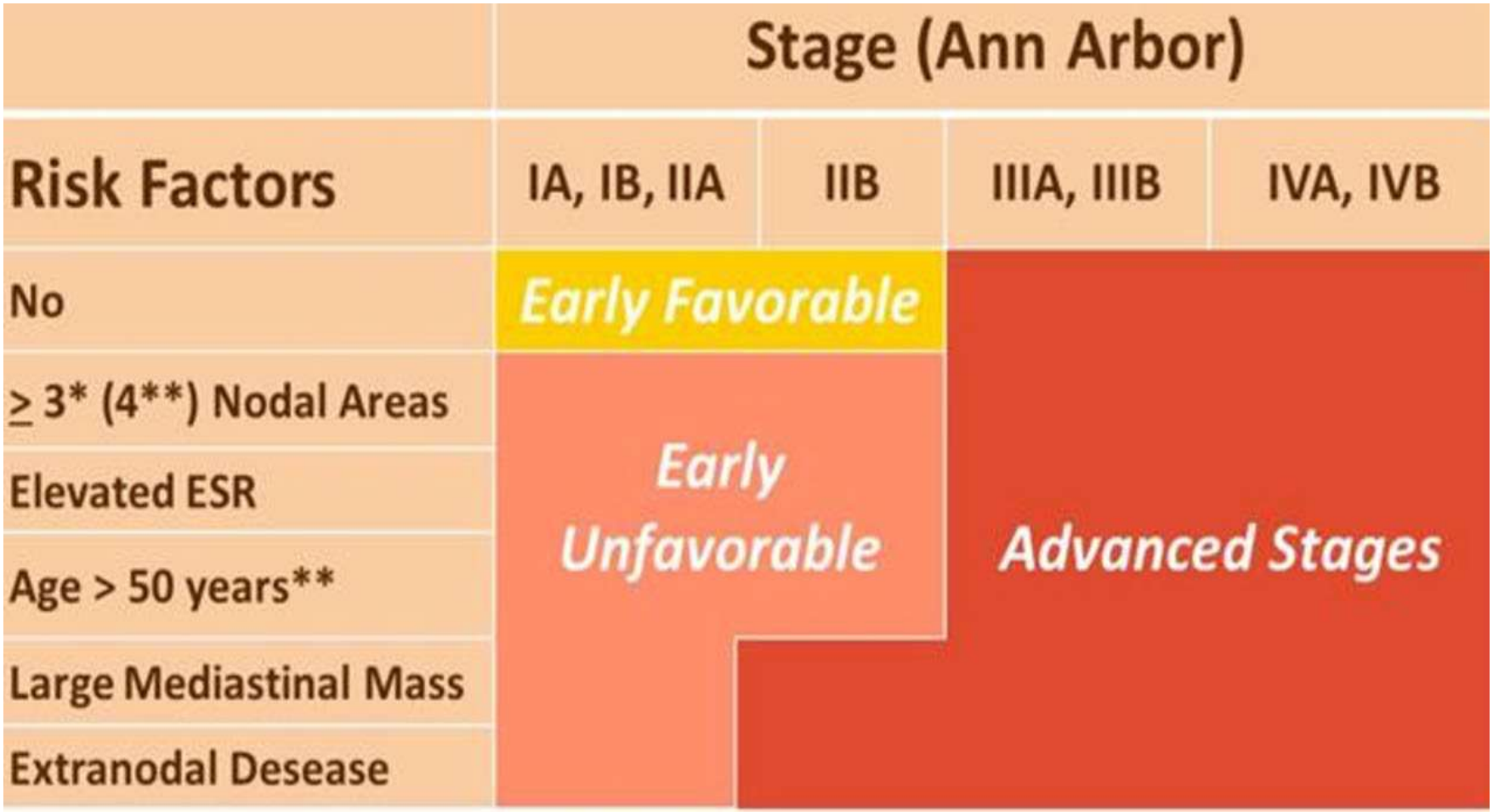






Nodular lymphocyte-predominant; showing nodular features and prominent lymphocytes and scattered Popcorn RS variant cells

Prognostic Factors in HL

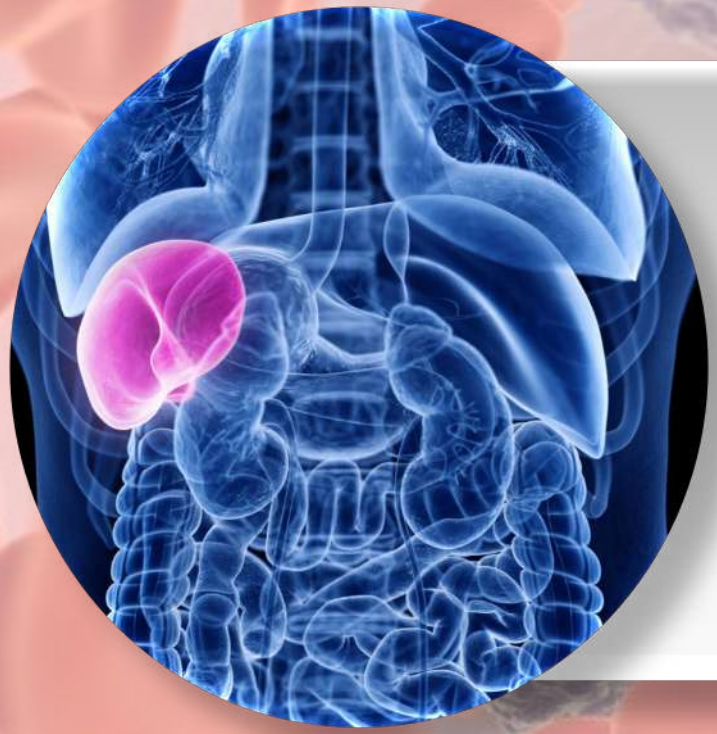


*EORTC; European Organization for Research and Treatment of Cancer

**GSHG; German Hodgkin Study Group

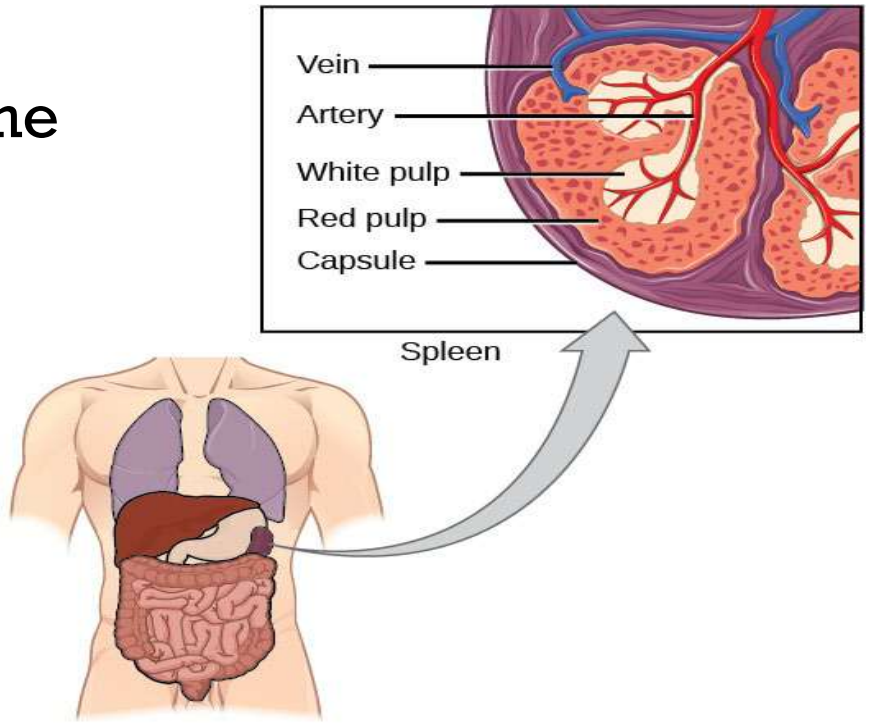
Differences Between HL and NHL

	Non-Hodgkin L.	Hodgkin Lymphoma
1-	More frequent involvement of **multiple peripheral nodes**	More often localized to a **single axial group** of nodes (cervical, mediastinal, para-aortic)
2-	**Noncontiguous** spread (not in contact or not adjacent)	**Contiguous** spread (directly adjacent)
3-	*Waldeyer's ring and mesenteric nodes* **commonly** involved	*Waldeyer's ring and mesenteric nodes* **rarely** involved
4-	*Extra-nodal presentation* **common**	*Extra-nodal presentation* **rare**



SPLEEN

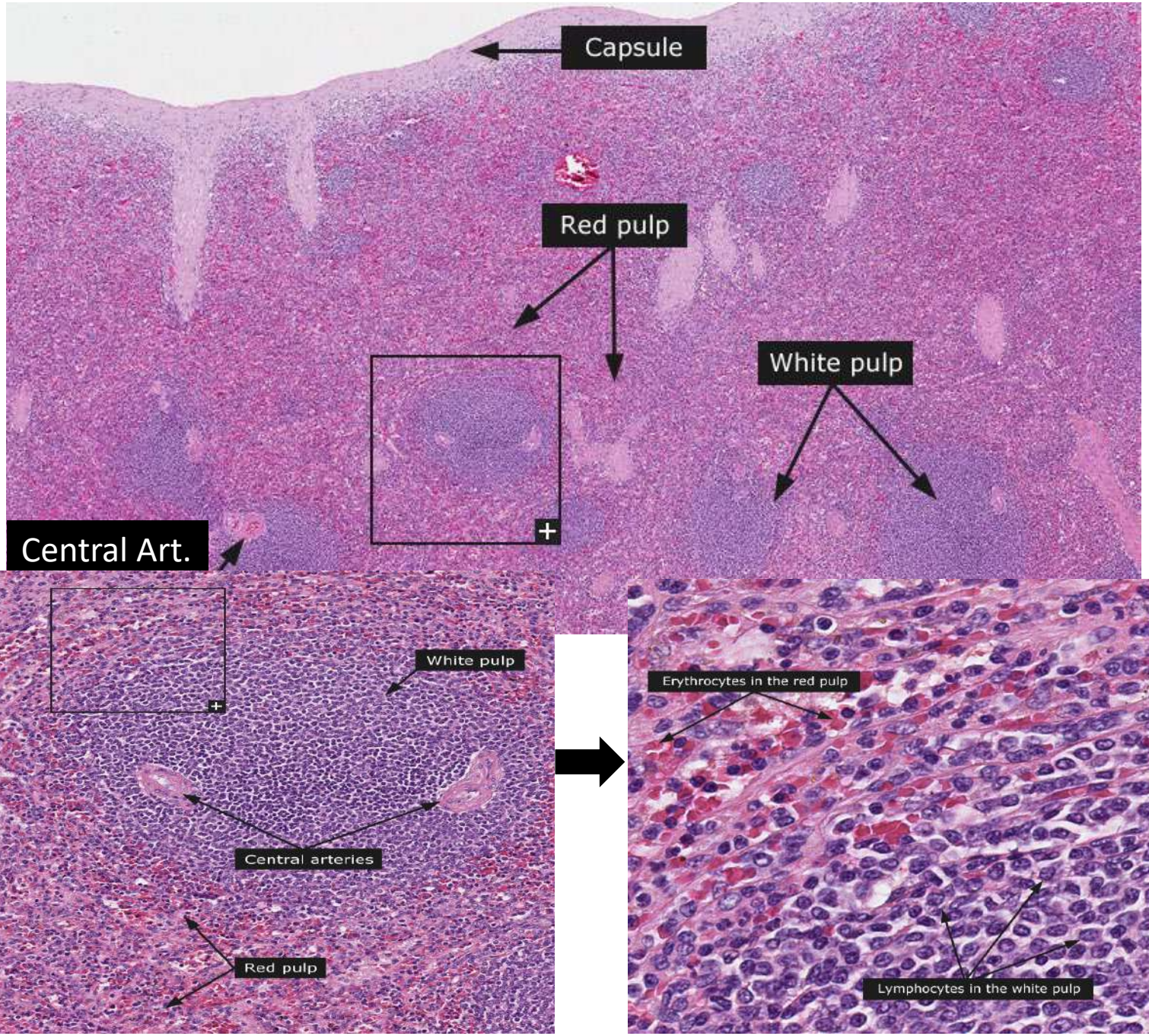
- It is the **largest single** accumulation of lymphoid tissue in the body, in the adult it weighs about 150gm.
- Contain the lymphocyte pool of both T and B cells.
- Has a unique role in acting as an immunological filter for the blood stream.
- The small lymphocytes centered on the splenic arteriole at the center, forming the white pulp. Around this is the red pulp composed of many splenic sinusoids .
- A reservoir of granulocytes and It represents 30-50% of the total marginating pool.
- 20-40% of the total platelet mass is pooled in the spleen and the platelets spend up to 1/3 of their lifespan there.



- The **red pulp** occupies the majority of the stromal tissue of the spleen. The red pulp functions as a blood filter for various toxins, destroying them before they enter systemic circulation.

- The **white pulp** composed of inner layer, is mainly composed of T lymphocytes which is why it is also called the T-zone. The outer layer has a more diverse cellular morphology, containing T and B lymphocytes.

- The spleen is covered by a **capsule**, which consists of dense irregular fibroelastic tissue, contains contractile cells called myofibroblasts. By producing weak contraction of the capsule, these cells help to discharge the blood stored within the spleen into the circulation. Also allows the spleen to significantly increase in size when necessary.


Capsule
Red pulp
White pulp
Central Art.
White pulp
Central arteries
Red pulp
Erythrocytes in the red pulp
Lymphocytes in the white pulp

- The spleen, a key part of the **immune** system, has dendritic cells in periarterial lymphatic sheaths that trap antigens and present them to T-lymphocytes , where T- and B-cells interact at the edges of white pulp follicles , generating antibody-secreting plasma cells found mainly within the sinuses of red pulp.
- It provides a **first** line of immune defense against bacterial sepsis, especially from *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*. The spleen also appears to act as a defense against viral infections and intraerythrocyte parasitic infections such as *Plasmodium* and *Babesia* .
- The lack of splenic function from splenectomy or with autoinfarction (sickle cell disease) leads to susceptibility to disseminated infection with encapsulated bacteria , such as pneumococcus, meningococcus, and *Haemophilus influenzae*.

Pathological Basis of Splenomegaly

In the adult, an enlarged spleen is usually palpable when its length exceeds 14 cm. However, the measurement of spleen size by means of a physical examination of the abdomen is unreliable, as minor enlargement is often undetected by palpation and even a grossly enlarged spleen may be missed in an obese person.

Following mechanisms may be the cause;

1- Reactive increase due to inflammation and infection.
2- Congestive expansion of the red pulp compartment.
3- Increased blood pool.
4- Increased macrophage function.
5- Proliferative cellular infiltration.
6- Extramedullary hemopoiesis.
7- Storage disease.
8- Solid tumors and cysts.

Splenomegaly:

- The spleen is **frequently** secondarily involved in a wide variety of systemic diseases.
- In all instances, the response of the spleen causes its enlargement (splenomegaly)
- Evaluation of splenomegaly is a common clinical problem.
- As an aid to diagnosis, splenomegaly is classified according to the degree of its enlargement (mild, moderate and massive).

- An enlarged spleen often removes excessive numbers of one or more of the formed elements of blood, resulting in anemia, leukopenia, or thrombocytopenia. This is referred to as **hypersplenism**, a state that can be associated with many of the diseases affecting the spleen.

- It can be in a one form of enlargement;

1- Mild splenomegaly (weight < 500 gm)

a. Acute splenitis and splenic congestion.

b. Infectious mononucleosis.

c. Miscellaneous acute febrile disorders, including; septicemia, SLE, and intra-abdominal infections.

2- Moderate splenomegaly (weight 500-1000gm)

a. Chronic congestive splenomegaly.
b. Acute leukemia.
c. Hemolysis (hereditary spherocytosis and thalassemia.
d. Autoimmune hemolytic anemia.

3- Massive splenomegaly (weight more than 1000gm)

a. Chronic myeloproliferative disorders (chronic myeloid leukemia and myelofibrosis)
b. Chronic lymphocytic leukemia and Lymphomas.
c. Hairy cell leukemia.
d. Leishmaniasis.
e. Malaria.

Hypersplenism

Hypersplenism is a clinical syndrome and does not imply a specific causal mechanism.

It has the following characteristics; features:

1- Splenomegaly.

2- Reduction in one or more of the cell lines in the peripheral blood.

3- Normal or hyperplastic cellularity of the bone marrow.

4- Premature release of cells into peripheral blood (normoblastemia and/or granulocyte left shift), resulting in reticulocytosis and/or large immature platelets.

5- Increased splenic red cell pool, decreased red cell survival and increased splenic pooling of platelets with shortening of their lifespan.


thank you
danke
謝謝
gracias
merci
obrigado
dziękuję
bedankt
hvala
mauruuru
go raibh maith agat
sukriya
kop khun krap
terima kasih
grazie
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