# “Hematopoietic And Lymphoid System (HLS)”

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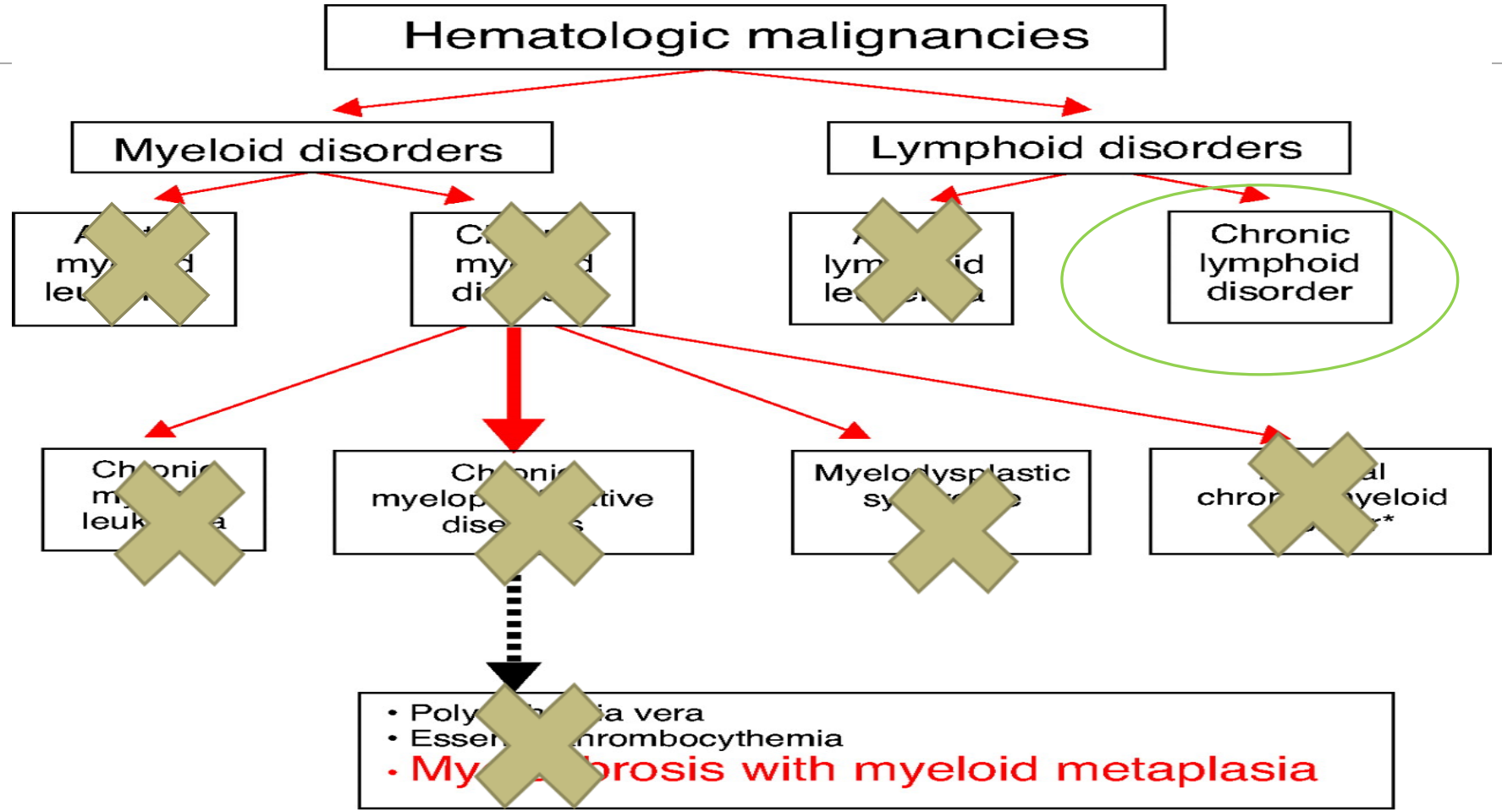
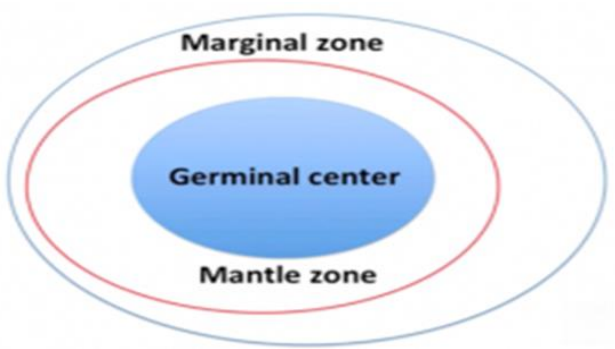
# Neoplastic Proliferations Of White Cells



# Normal Lymph Node Morphology

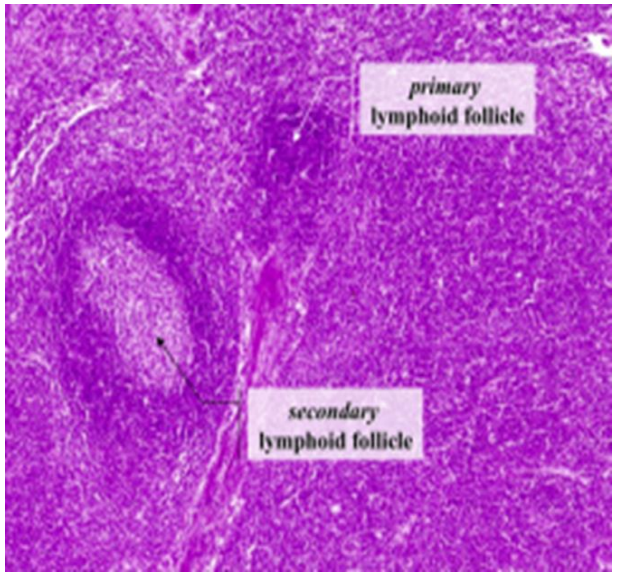
## Gross Description:

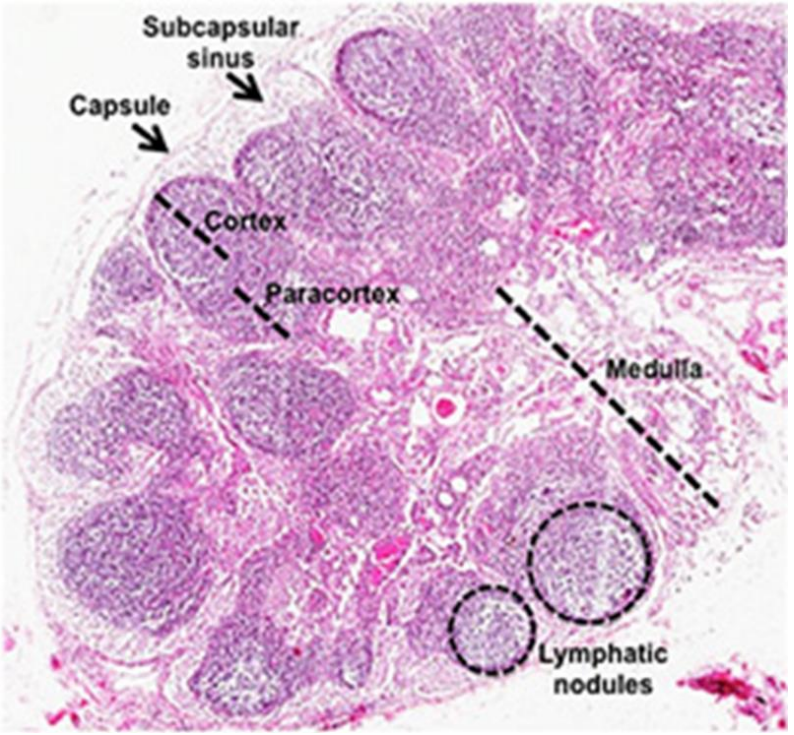
- Ovoid with gray-tan cut surface.



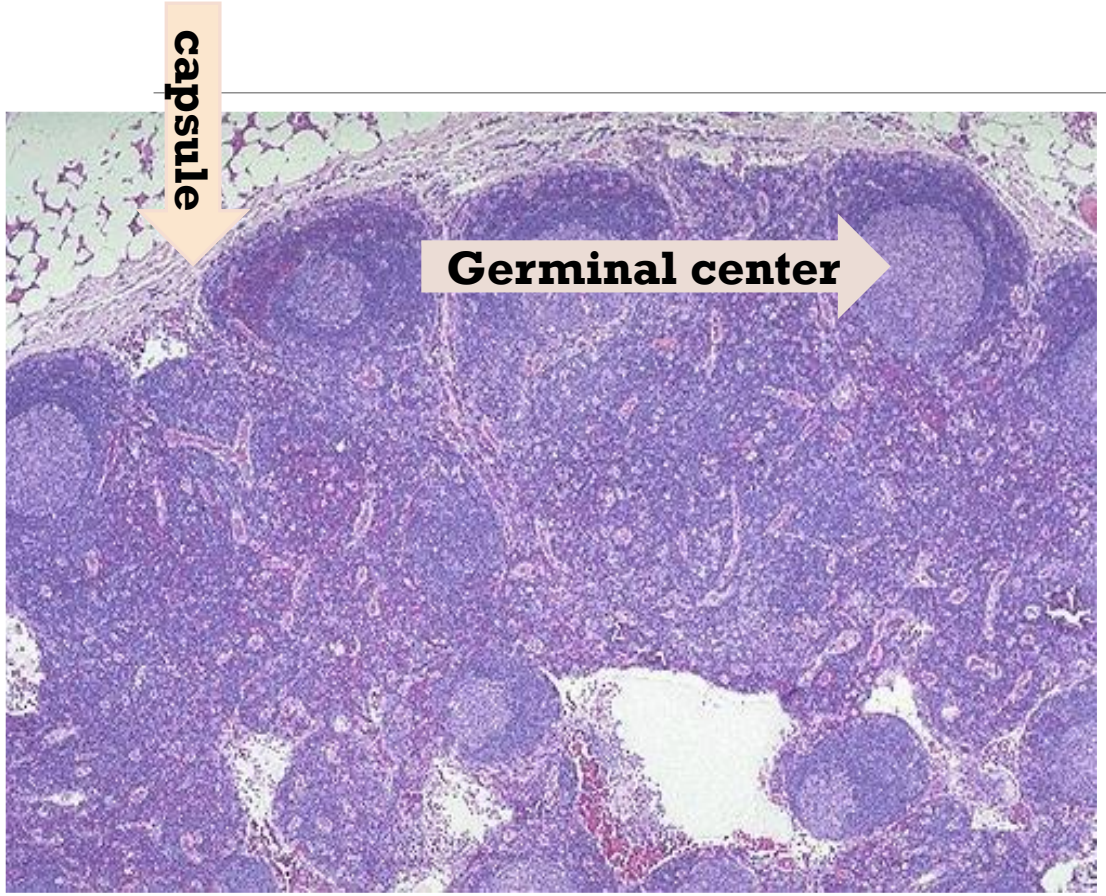

## Microscopically:

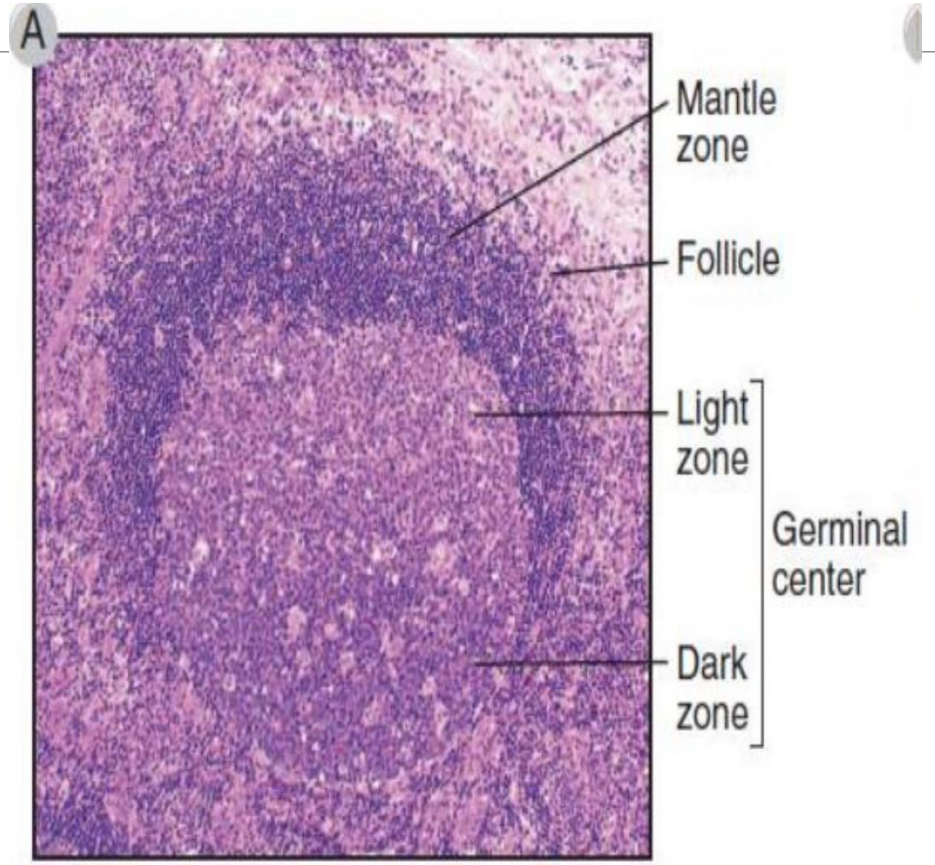
1. Cortex
2. Paracortex
3. Medulla



# Normal Reactive LN



# ❑Reactive Lymphadenitis

## ❖ Acute Nonspecific Lymphadenitis:

### Morphology:

- Inflamed nodes are swollen, gray-red,  engorged, and **tender.**

- Large germinal centers with numerous mitotic figures.
- Macrophages often contain debris derived from dead bacteria or necrotic cells.
- A neutrophilic infiltrate is seen around the follicles and in the sinuses.
- An abscess can occur.

- With control of the infection, the lymph nodes may revert to a normal appearance or, if damaged, undergo scarring.

## ❖ Chronic Nonspecific Lymphadenitis

- Enlarged, **painless, nontender** lymph nodes.
- Occurs **slowly**

## 1. Follicular Hyperplasia:

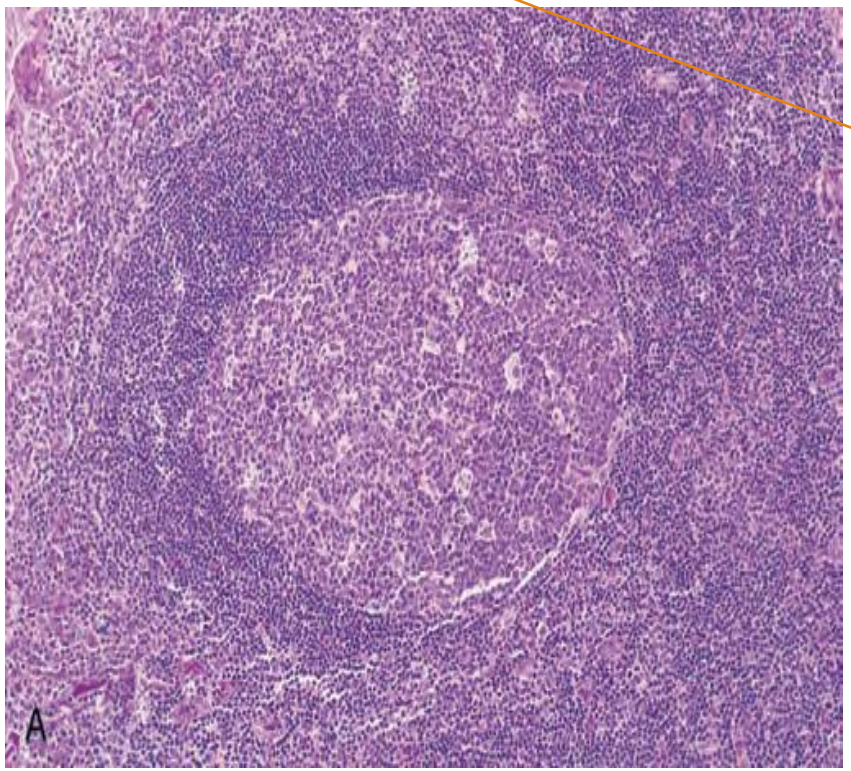
- Large germinal centers (secondary follicles) contain numerous activated B cells, scattered T cells, tingible body macrophages, and a meshwork of follicular dendritic cells.

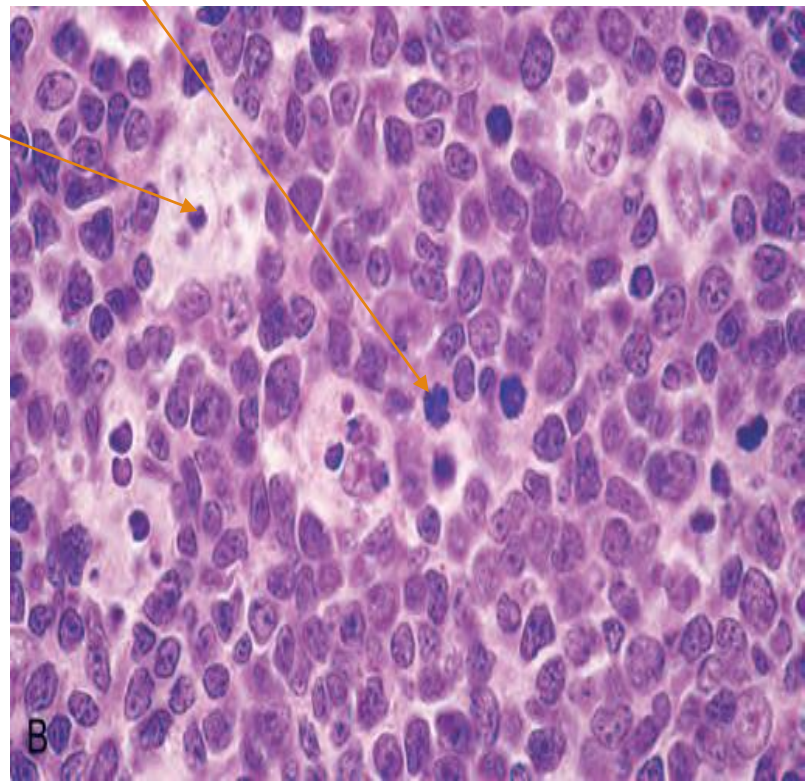
❑ **Findings that favor follicular hyperplasia over follicular lymphoma are:**

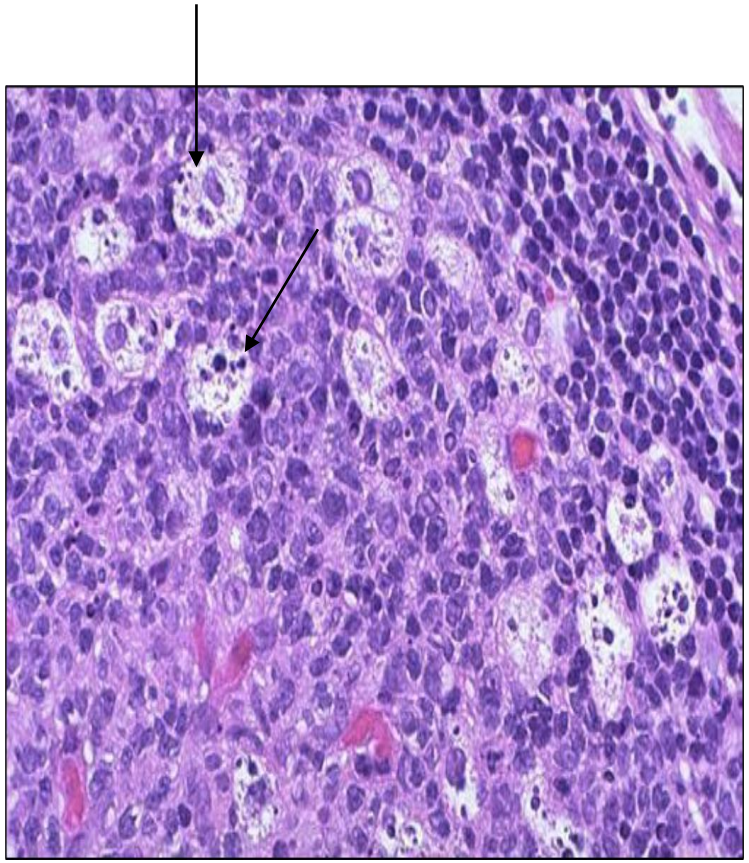
(1) The preservation of the lymph node architecture
(2) Variation in the shape and size of the germinal centers
(3) Prominent phagocytic and mitotic activity in germinal centers
(4) The follicles, mainly in the cortex
(5) No Infiltration of the lymph node capsule and surrounding fat

## Follicular hyperplasia

**A** Low-power view showing a reactive follicle and surrounding mantle zone.
**B** High-power view shows several mitotic figures and numerous macrophages containing phagocytosed apoptotic cells (tingible bodies).



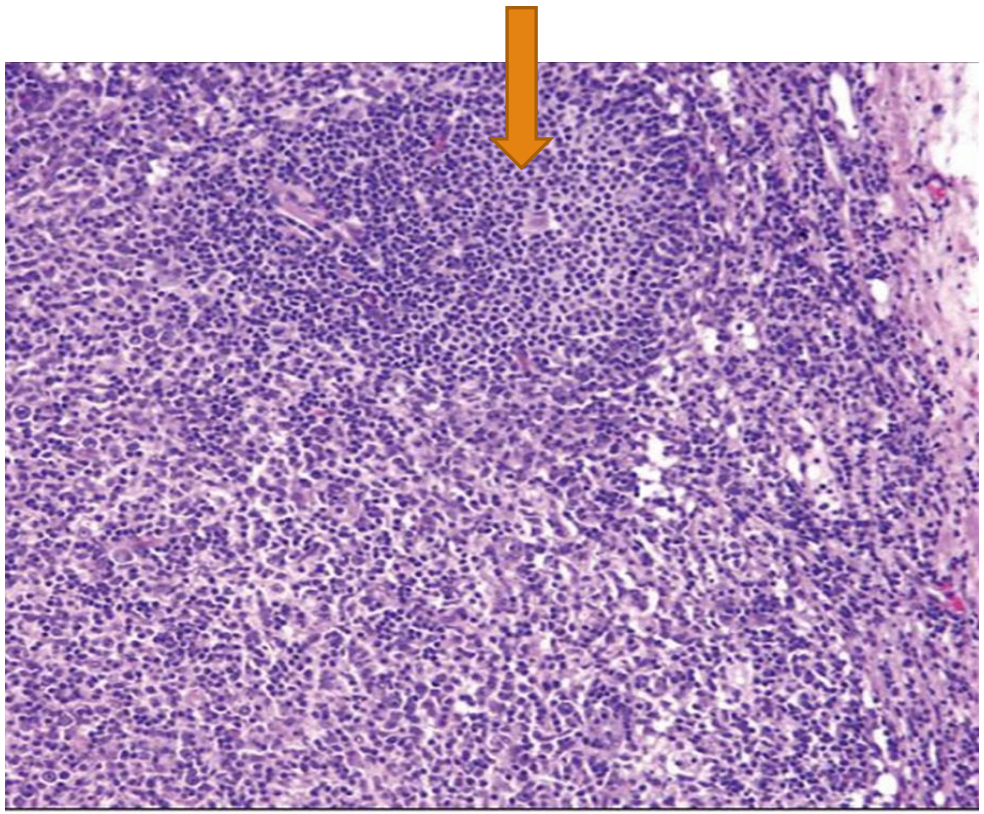
## 2. Paracortical Hyperplasia:

- When activated, parafollicular T cells transform into large immunoblasts that can efface the B cell follicles.

-Seen in:

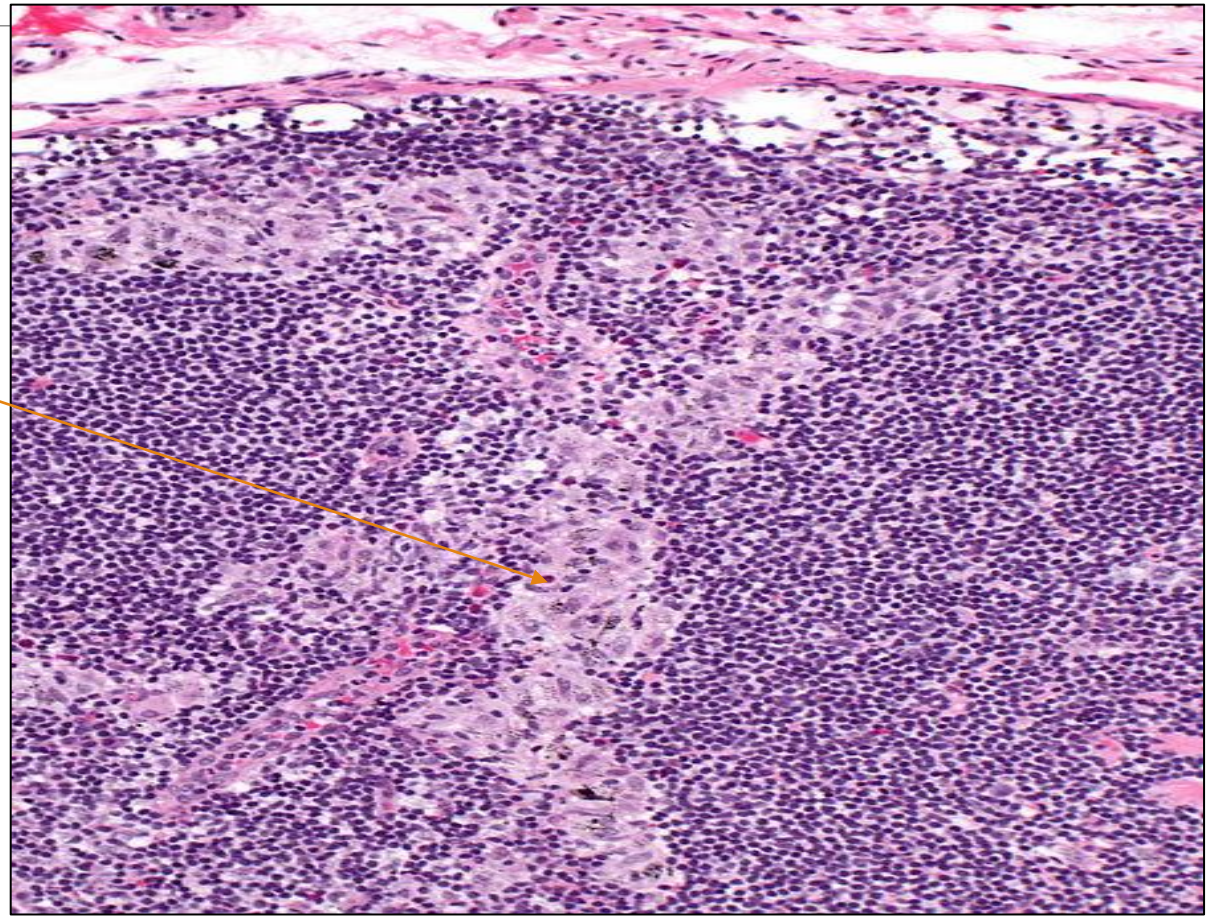
- **Viral infections.**
- After certain **vaccinations** (e.g., smallpox)
- In immune reactions induced by **drugs.**

- A residual follicle is at the top of the field.



# 3.Sinus Histiocytosis:

**-D**istention of the lymphatic sinusoids, due to a marked hypertrophy of lining endothelial cells and an infiltrate of macrophages (histiocytes).

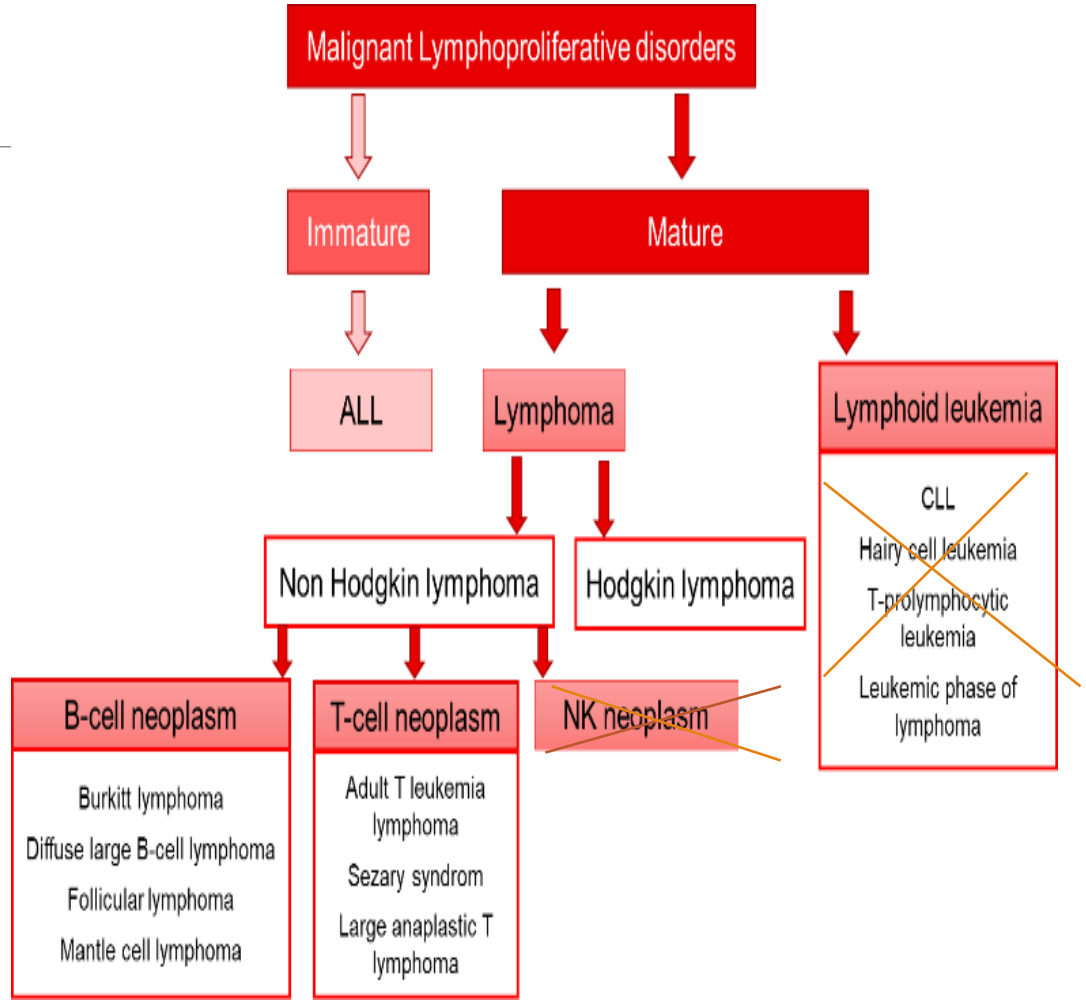


# Lymphoid Neoplasms

**Definition:**

- Malignant tumors of lymphoid tissue, characterized by the abnormal proliferation of B or T cells in the lymphoid tissue.

- Classified according to the **cell of origin** and the **degree of maturation.**
- The cell of origin **can't be determined by morphology alone** and IHC or flowcytometry.



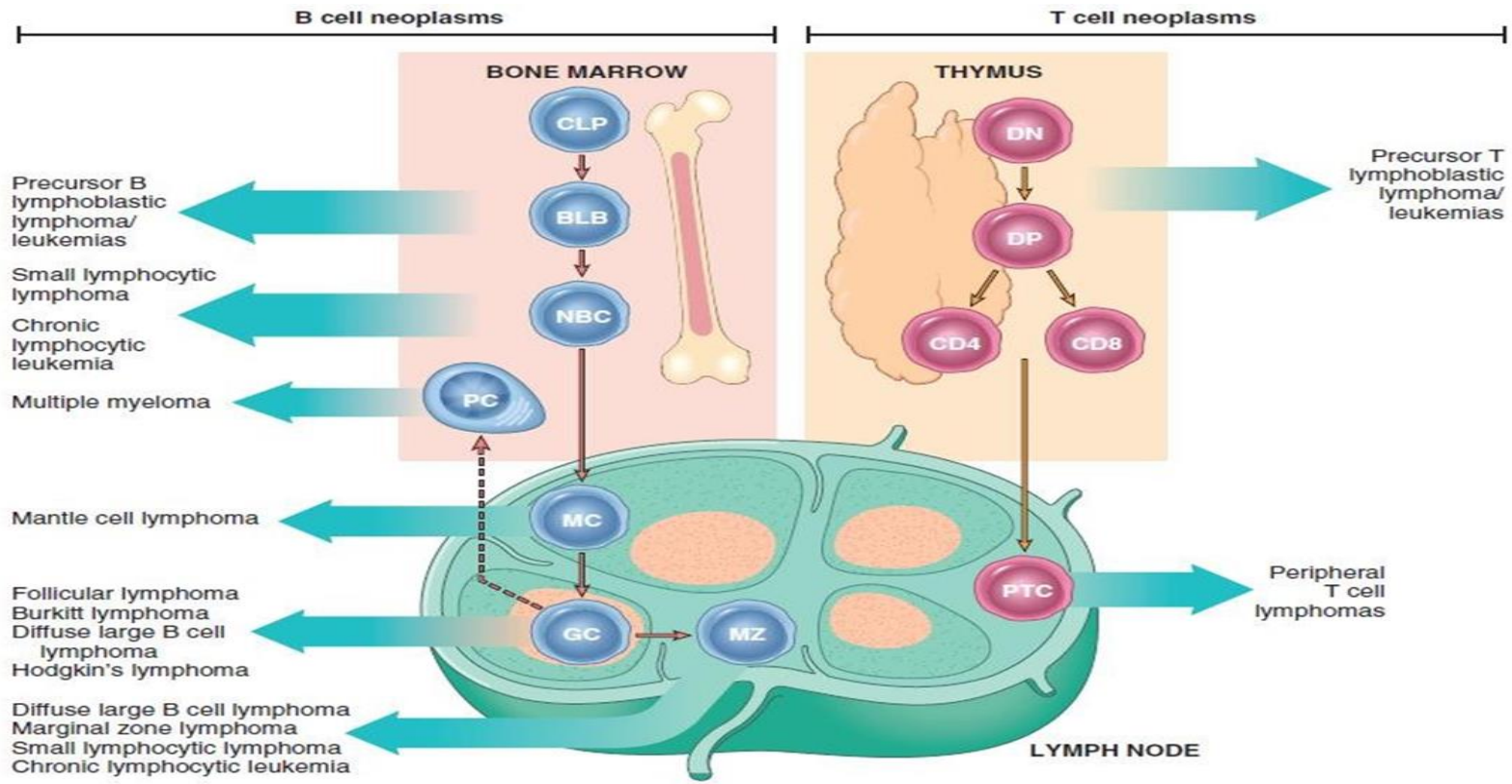



Fig. 12.13 Origin of lymphoid neoplasms. Stages of B and T cell differentiation from which specific lymphoid and tumors emerge are shown. *BLB*, Pre-B lymphoblast; *CLP*, common lymphoid progenitor; *DN*, CD4–/CD8– (double-negative) pro-T cell; *DP*, CD4+/CD8+ (double-positive) pre-T cell; *GC*, germinal center B cell; *MC*, mantle zone B cell; *MZ*, marginal zone B cell; *NBC*, naive B cell; *PC*, plasma cell; *PTC*, peripheral T cell.

- **Leukemia**: Tumors that involve the **bone marrow and peripheral blood** predominantly.
- **Lymphoma**: Tumors that involve **lymph nodes or other organs** predominantly.
- **Plasma cell myeloma** is confined to the **bones** as discrete masses or **bone marrow** with **no** lymph node or peripheral blood involvement.

- **Lymphoid neoplasms often disrupt normal immune function.** Both **immunodeficiency and autoimmunity** may be seen.

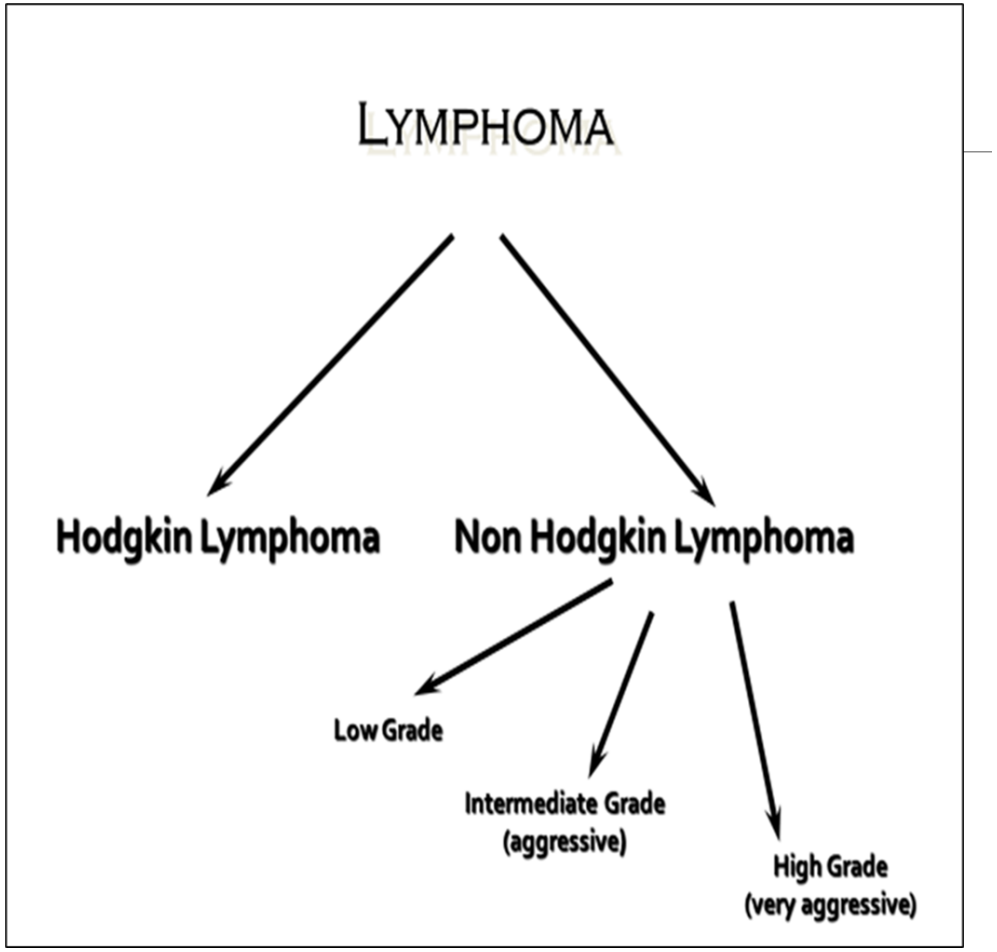



**Table 12.7 WHO Classification of Lymphoid Neoplasms**[a]

| |
|---|
| **Precursor B Cell Neoplasms** |
| *Precursor B cell leukemia/lymphoma (B-ALL)* |
| **Peripheral B Cell Neoplasms** |
| *B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)* |
| B cell prolymphocytic leukemia |
| Lymphoplasmacytic lymphoma |
| *Mantle cell lymphoma* |
| Follicular lymphoma |
| Extranodal marginal zone lymphoma |
| Splenic and nodal marginal zone lymphoma |
| Hairy cell leukemia |
| Plasmacytoma/plasma cell myeloma |
| Diffuse large B cell lymphoma (multiple subtypes) |
| Burkitt lymphoma |
| **Precursor T Cell Neoplasms** |
| *Precursor T cell leukemia/lymphoma (T-ALL)* |
| **Peripheral T/NK Cell Neoplasms** |
| T cell prolymphocytic leukemia |
| T cell granular lymphocytic leukemia |
| *Mycosis fungoides/Sézary syndrome* |
| *Peripheral T cell lymphoma, unspecified* |
| Angioimmunoblastic T cell lymphoma |
| Anaplastic large cell lymphoma |
| Enteropathy-type T cell lymphoma |
| Panniculitis-like T cell lymphoma |
| Hepatosplenic γδ T cell lymphoma |
| Adult T cell lymphoma/leukemia |
| Extranodal NK/T cell lymphoma |
| Aggressive NK cell leukemia |
| **Hodgkin Lymphoma** |
| *Nodular sclerosis* |
| *Mixed cellularity* |
| Lymphocyte-rich |
| Lymphocyte-depleted |
| Lymphocyte predominant |

*NK*, Natural killer; *WHO*, World Health Organization.
[a]Entries in *italics* are among the most common lymphoid tumors.

# Non-Hodgkin's Lymphoma

## B-Cell Neoplasms:

- Precursor B-cell neoplasms (ALL)
- **Mature B-cell neoplasms** ➡

# Low grade B-cell NHL

## Small Lymphocytic Lymphoma (SLL)/Chronic Lymphocytic Leukemia (CLL)

- Indolent malignant proliferation of small mature B-lymphocytes.
- These two disorders are morphologically & genotypically identical, differing only in the extent of peripheral blood involvement.
- If the peripheral blood lymphocytes **>5000** cell/microliter with or without nodal or extra-nodal involvement, the patient is diagnosed as CLL, if **<5000** with nodal or extra-nodal involvement the diagnosis is SLL.
- CLL is the most common leukemia in **adults** (median age **70 y**).
- By contrast, SLL constitutes only 4% of NHLs.

## ❑ Clinical Features

- Often asymptomatic
- Easy fatigability, weight loss & anorexia.
- Generalized lymphadenopathy, hepatosplenomegaly.
- Less commonly autoimmune hemolytic anemia and thrombocytopenia.
- **Hypo**gammaglobulinemia with increased risk for bacterial infections.
- Median survival is 4 to 6 years (variable).
- About 5% to 10% of SLL cases **transform to diffuse large B-cell lymphoma** (**DLBCL; Richter syndrome**).
- Prolymphocytoid transformation – 10%

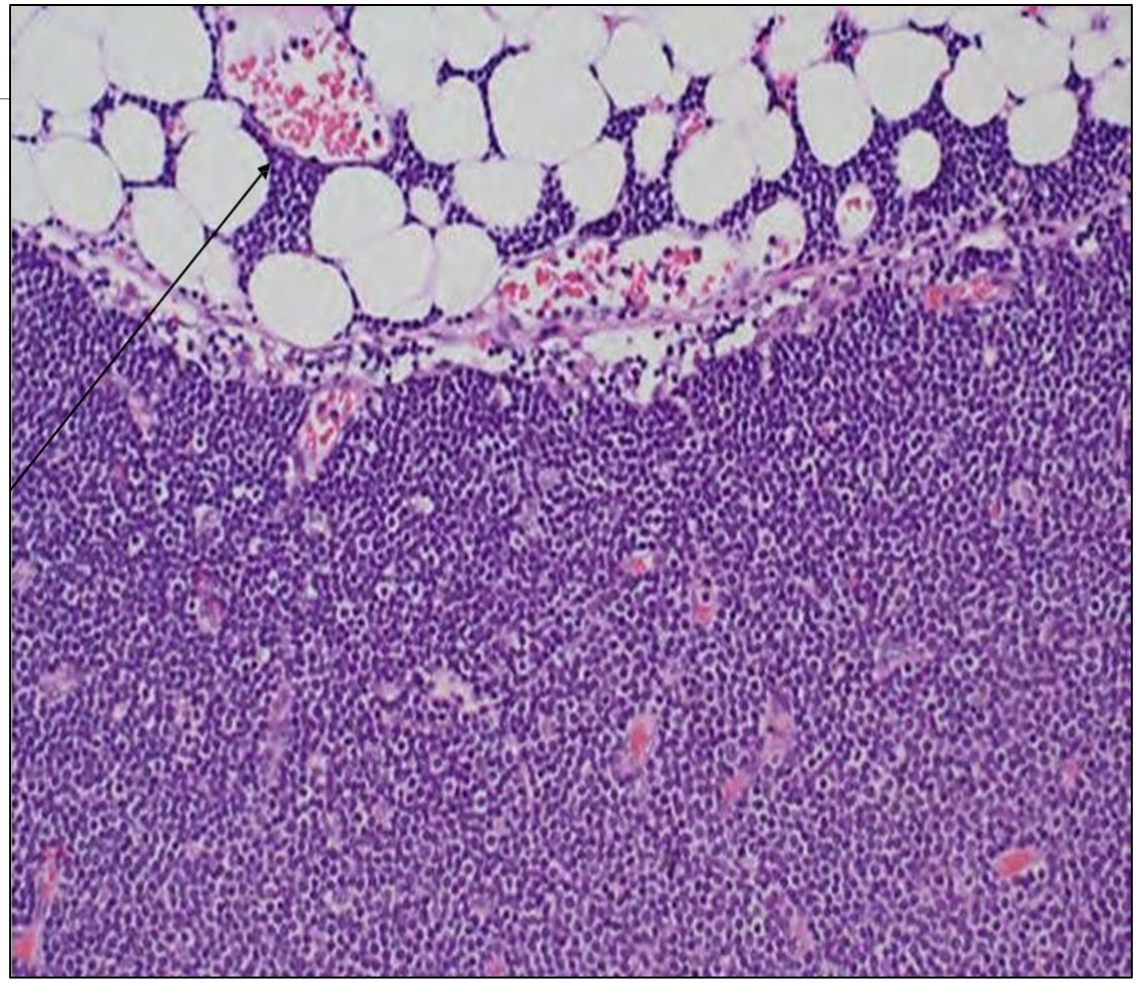
# ❑ Morphology

- Lymph nodes are effaced by **diffuse** sheets of **small, resting lymphocytes** with scant cytoplasm and dark, round nuclei with clumped chromatin reminiscence of a **soccer ball**.

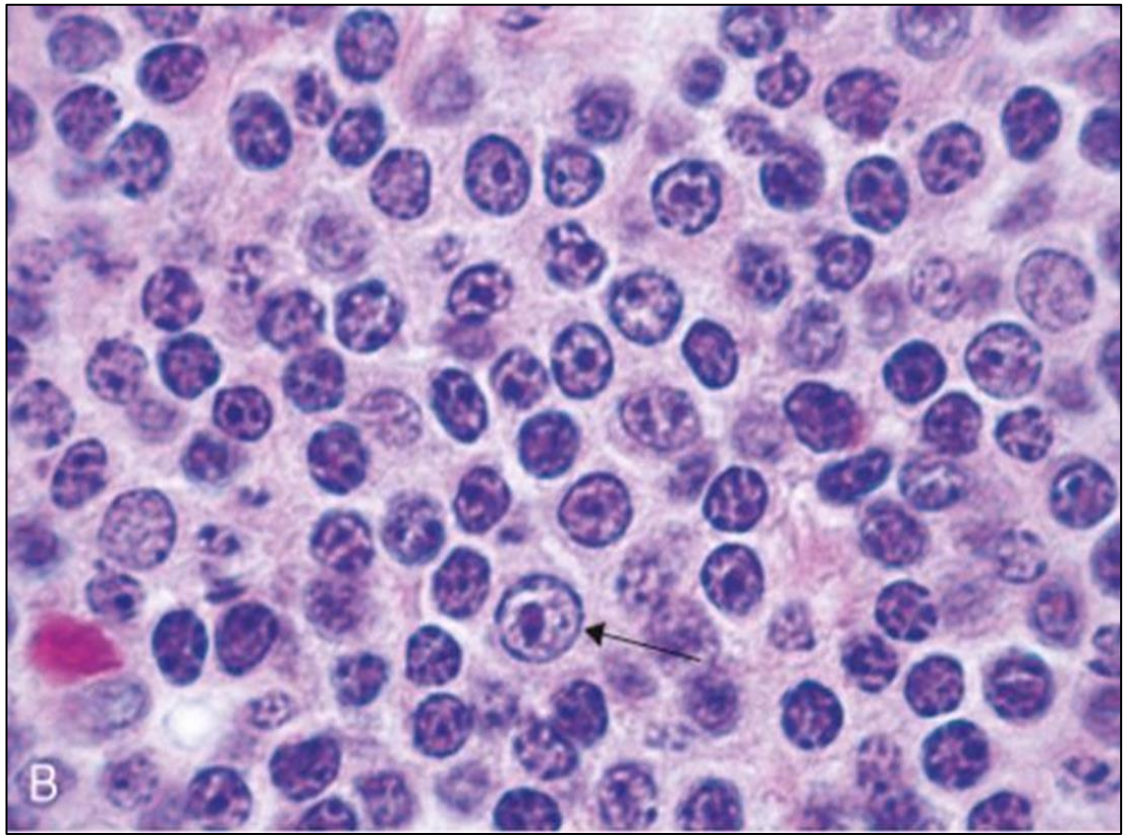
- The infiltrate extends through the capsule into the adipose tissue.

- There are scattered ill-defined foci of larger, actively dividing cells **(prolymphocytes): proliferation centers**

- The bone marrow, spleen, and liver are involved in **ALMOST ALL CASES (**Small lymphocytic infiltrate)

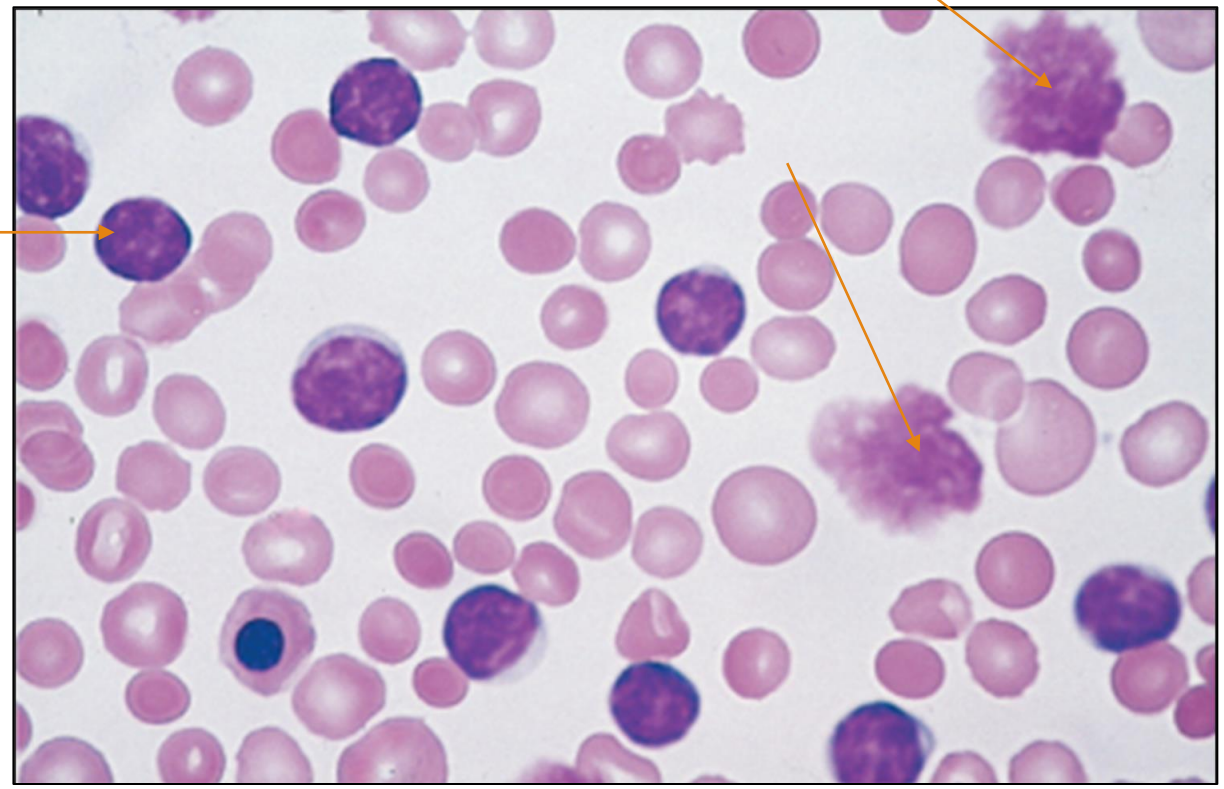


- Most tumor cells are small, round lymphocytes.
- A “prolymphocyte,” a larger cell with a centrally placed nucleolus is also present in this field (arrow).



**<u>Peripheral blood</u>**:
In most patients, there is an absolute lymphocytosis featuring small, mature-looking lymphocytes.

These cells are fragile, and during the preparation of smears, many are disrupted, producing characteristic **smudge cells**. (arrows)

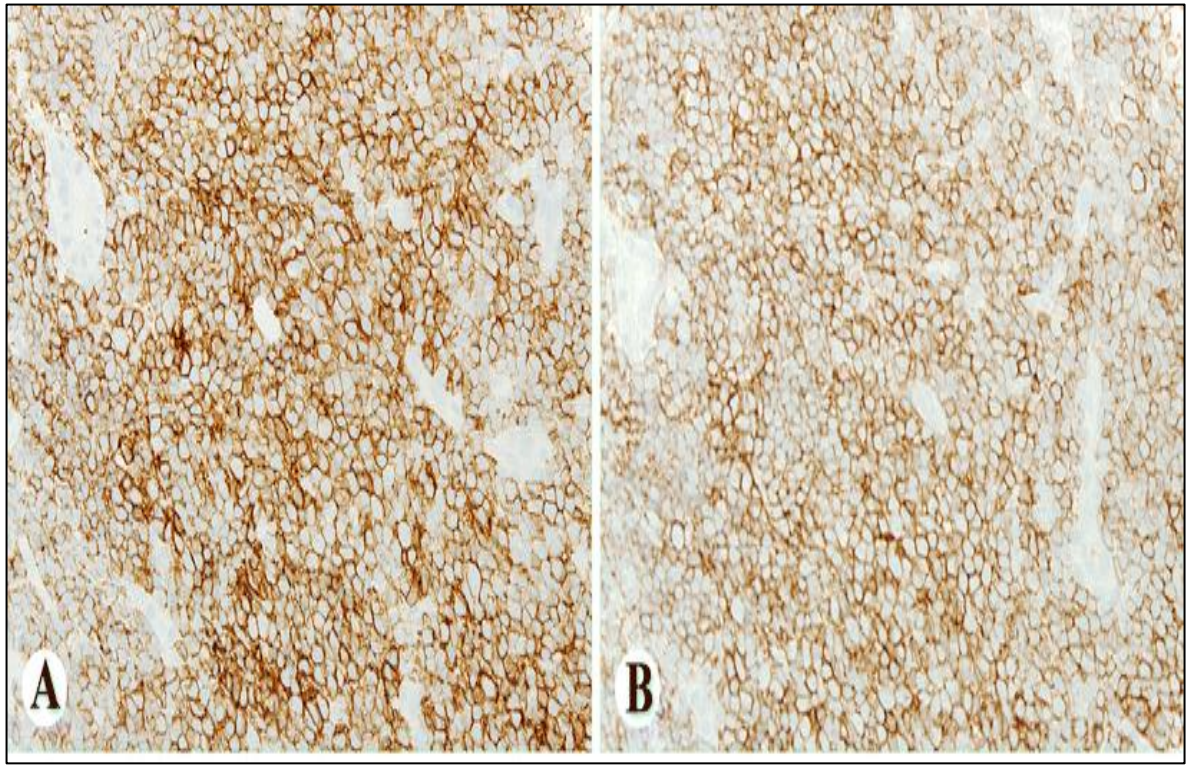


## ❑ Immunophenotyping

CD20 (a), CD23 (b)

Positive expression of:

- B cell markers as: **CD19, CD20**, and **CD23**
- K or L light chain
- **CD5** (which is a T-cell marker), and it is imp. to make the Dx.



# Follicular Lymphoma

- 40% of the adult NHLs.
- Older persons (>50), M=F.
- It presents as painless generalized lymphadenopathy.
- **The bone marrow is involved at diagnosis in 80% of cases**
- Extra-nodal sites are rare.
- 85% of cases are associated with a **t(14;18) translocation** ⟶ increased expression of the anti-apoptotic protein **BCL2**.
- The disease is **incurable** but follows an indolent course (median survival 7-9 years).
- In 30-40% of follicular lymphomas **progress to DLBCL**.

## Microscopically:

- Lymph nodes are effaced by **nodular follicular** appearance.
- The follicles have **two** types of neoplastic cells:

❖ **Centrocytes:** Slightly larger than lymphocytes, with angular "**cleaved**" nuclei, coarse chromatin, and indistinct nucleoli.

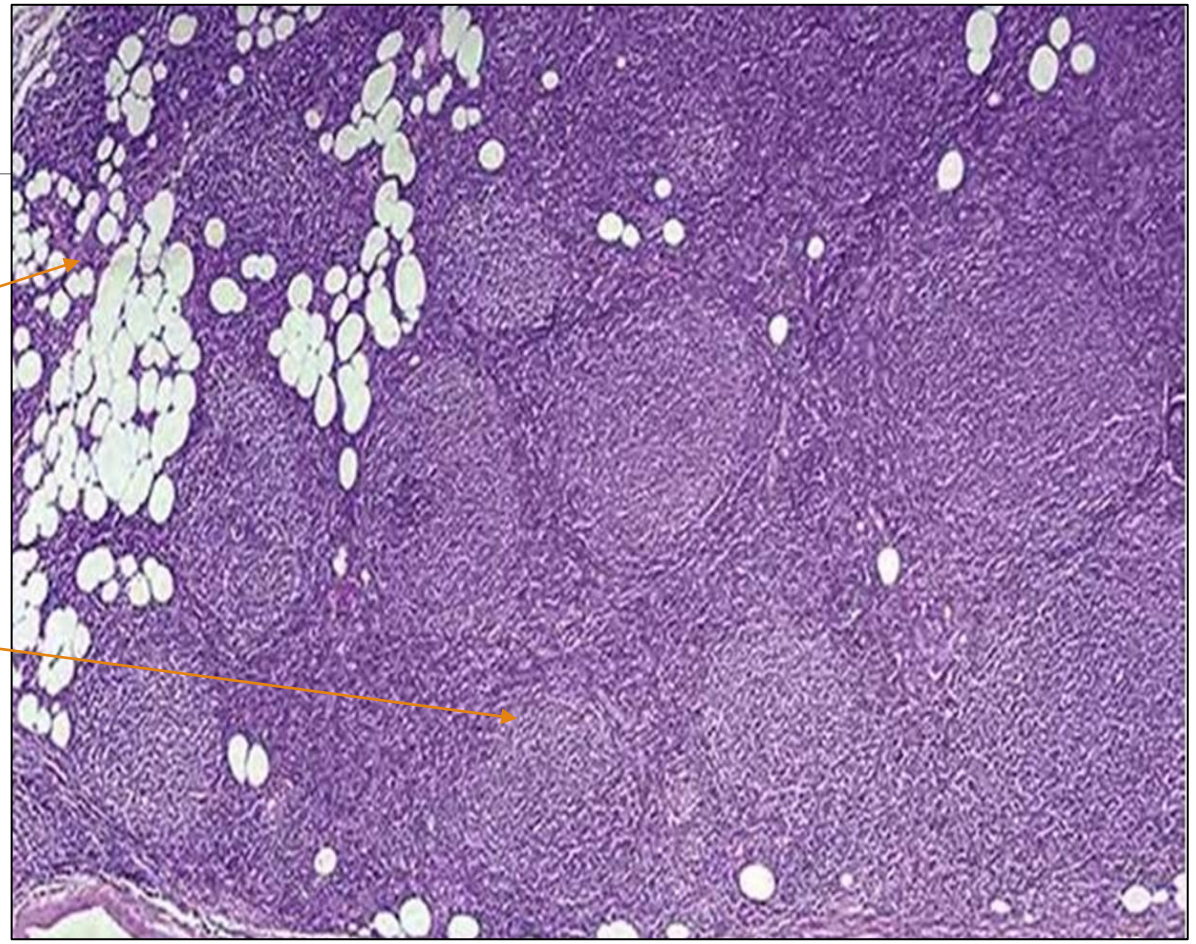
❖ **Centroblasts: L**arge cells with fine chromatin, prominent nucleoli, and modest amounts of cytoplasm.

- Mitosis is infrequent.
- Single necrotic cells are not seen.
- These findings help distinguish neoplastic from **reactive follicles**, in which **mitoses and apoptosis are prominent.**
- Immunophenotyping:

**- Bcl2 +** **- B cell markers** **- CD10**

# FL, Microscopic

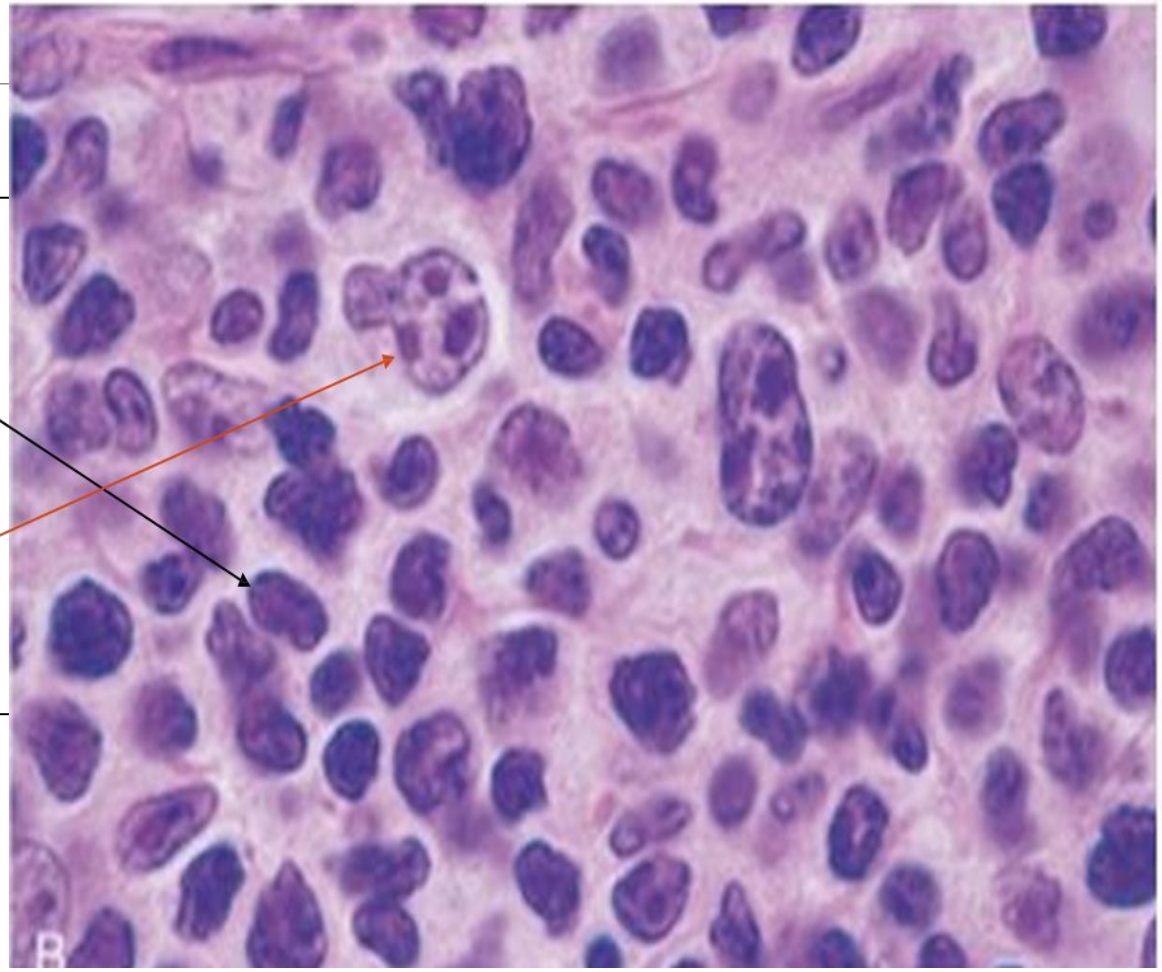
- The capsule of this lymph node has been invaded, and cells extend into the adipose tissue.
- The **follicles** are numerous, and present **throughout** giving the **nodular appearance.**



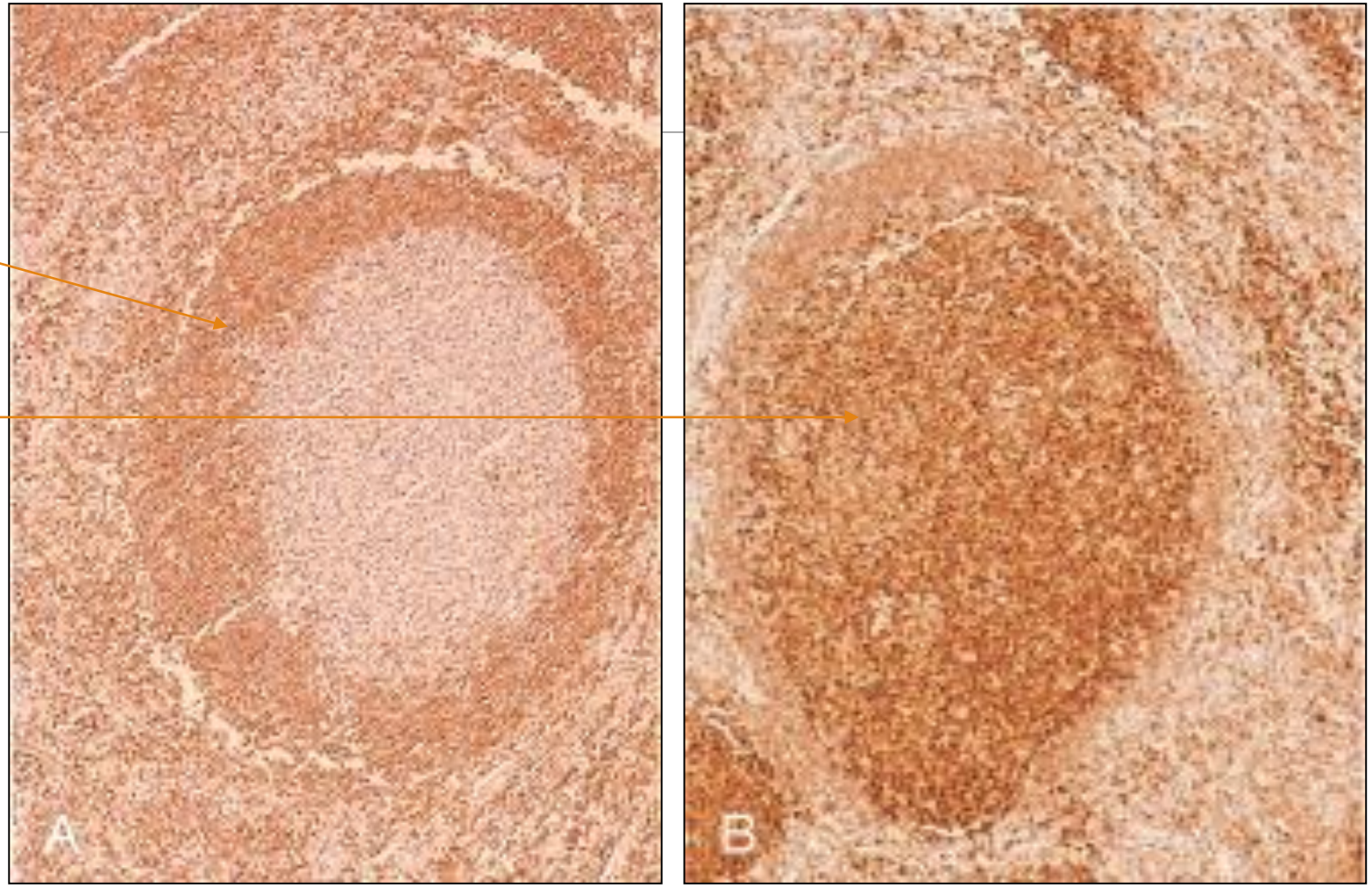
- 2 types of cells:

1. Centrocytes

1. Centroblasts



- In reactive follicles (A), BCL2 is present in the mantle zone cells but not follicular-center B cells
- whereas follicular lymphoma cells (B) show strong BCL2 staining in the center

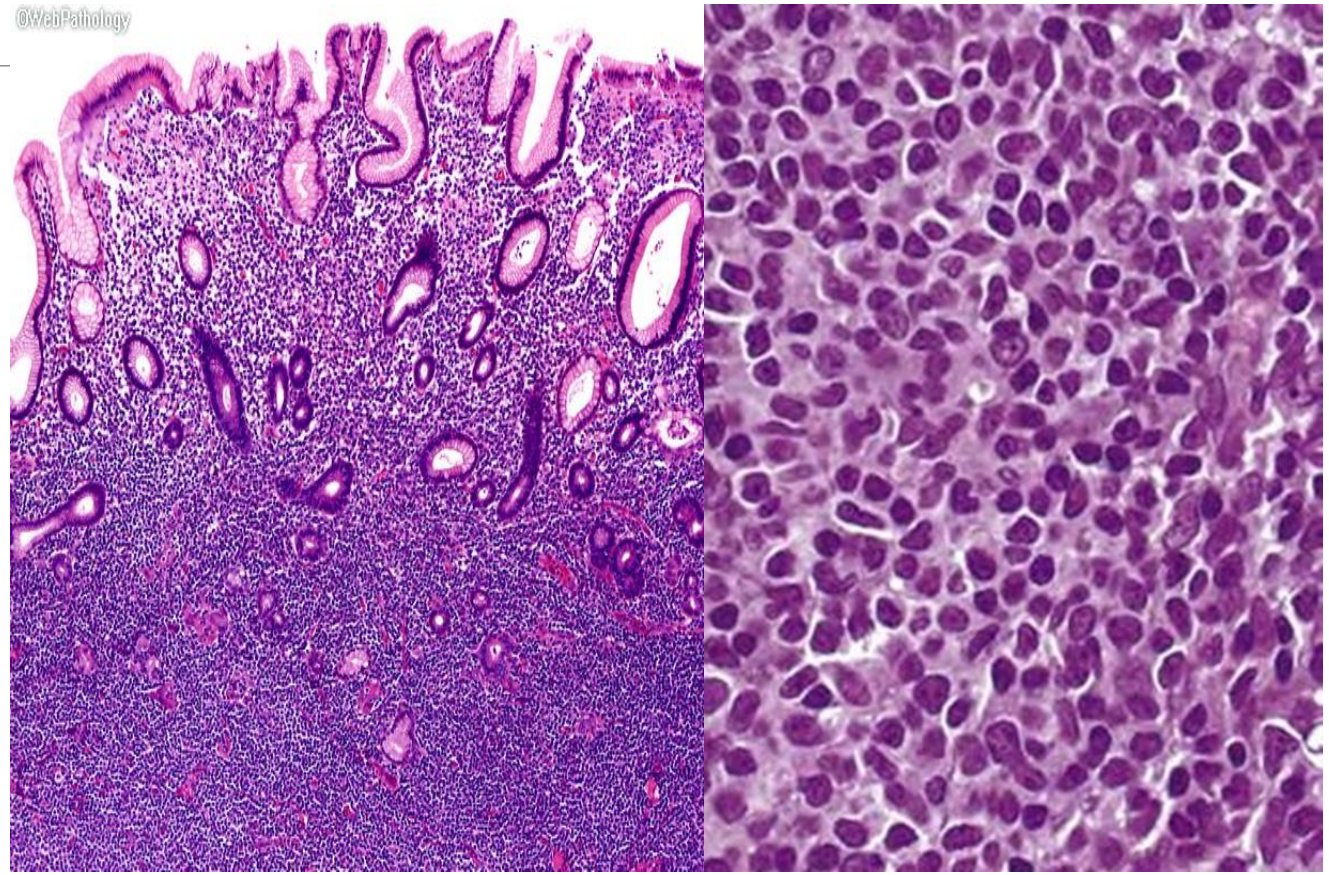


# MALT-Type Lymphoma (Extranodal Marginal Zone Lymphoma)

- Preceded by and may be associated with chronic inflammation or autoimmune disorders such as:
  - Helicobacter gastritis in the stomach.
  - Sialadenitis in salivary glands.
  - Hashimoto thyroiditis in the thyroid gland.
- Tendency to remain localized at the site of origin for a prolonged time.
- In the early stages, withdrawal of the cause of the inflammation leads to tumor regression (e.g. Eradication of H. Pylori by antibiotic treatment).

# Morphology

- **Small** round to irregular cells, resembling cells in the marginal zone) infiltrate the epithelium of involved tissues, often collecting in small aggregates that are called **lymphoepithelial lesions.**
- In some tumors, the tumor cells exhibit **plasma cell differentiation**



# Intermediate Grade B-cell NHL

## Mantle Cell Lymphoma

- Cells resembling the naive B cells found in the mantle zones.
- Mainly in **men**, > 50 years.
- The bone marrow is involved in most cases, and about 20% of patients have peripheral blood involvement.
- Most present with **fatigue and lymphadenopathy** and are found to have the generalized disease.
- Sometimes arises in GIT, submucosal nodules that resemble polyps (**lymphomatoid polyposis**)
- **Almost all** cases have a specific translocation **t(11;14)** that results in over expression of **cyclin D1**.
- These tumors are **aggressive and incurable, and** the median survival is 4 - 6 years.

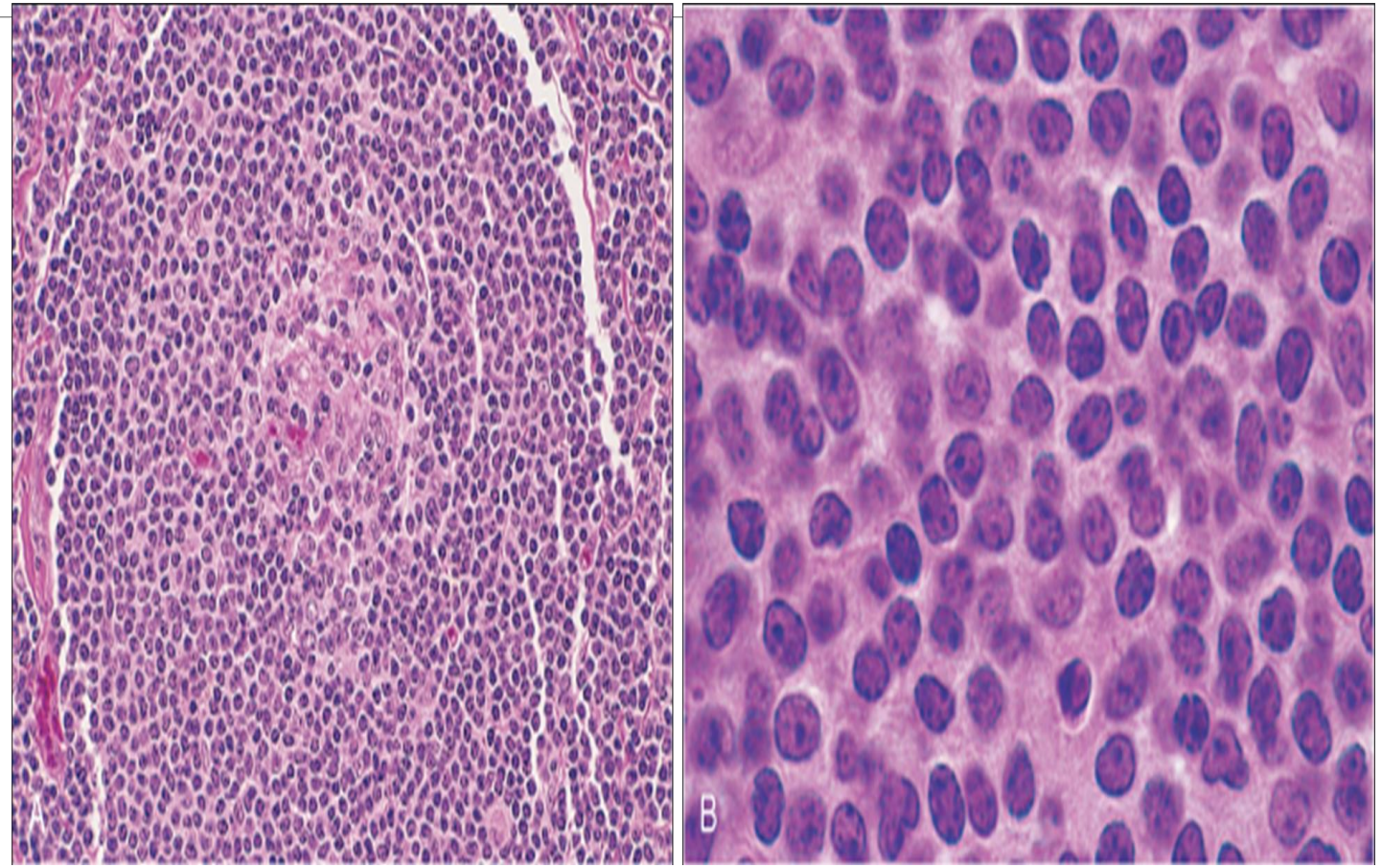
## ➢ Morphology

-D**iffuse** or vaguely **nodular** pattern.

- The cells are slightly larger than normal lymphocytes and have an irregular nucleus(cleaved), inconspicuous nucleoli, and scant cytoplasm.

**Neoplastic cells are positive for:**
CD19
**CD20**
**CD5**

**But lack CD23 (-)**.



# HIGH GRADE B CELL NHL

## 1.Diffuse Large B-cell Lymphoma (DLBL)

- **The most common type of lymphoma in adults.**
- The median age is **60 years** (but it occurs at any age).
- Present with a rapidly enlarging, often **symptomatic mass at one or several sites.**
- **Extranodal** presentations are **common** (The **GIT** is the **most common** extranodal site).
- Involvement of the liver, spleen, and bone marrow is **NOT common** at diagnosis.

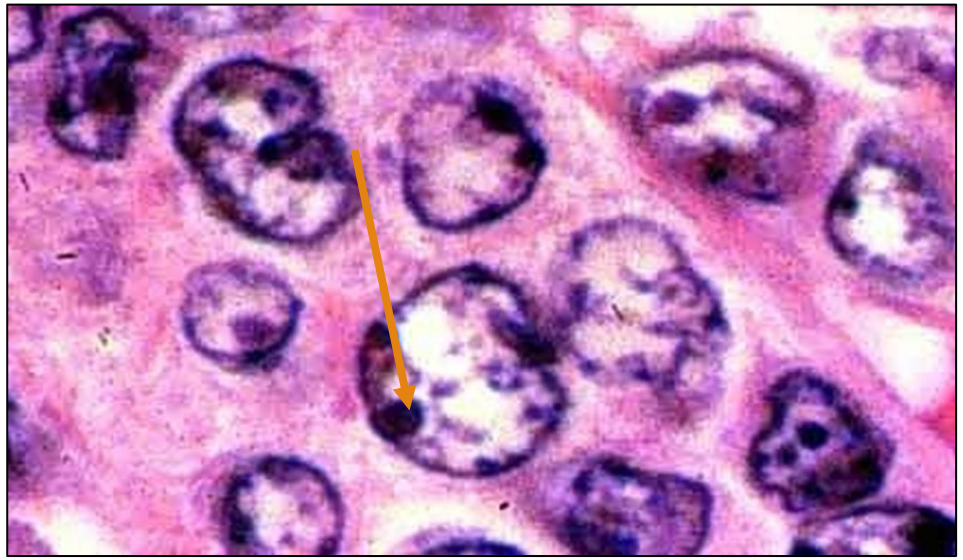
**This tumor is highly associated with rearrangements or mutations of BCL6 gene**; one-third arise from follicular lymphomas and carry t(14;18) translocation.

# ❖ Morphology:

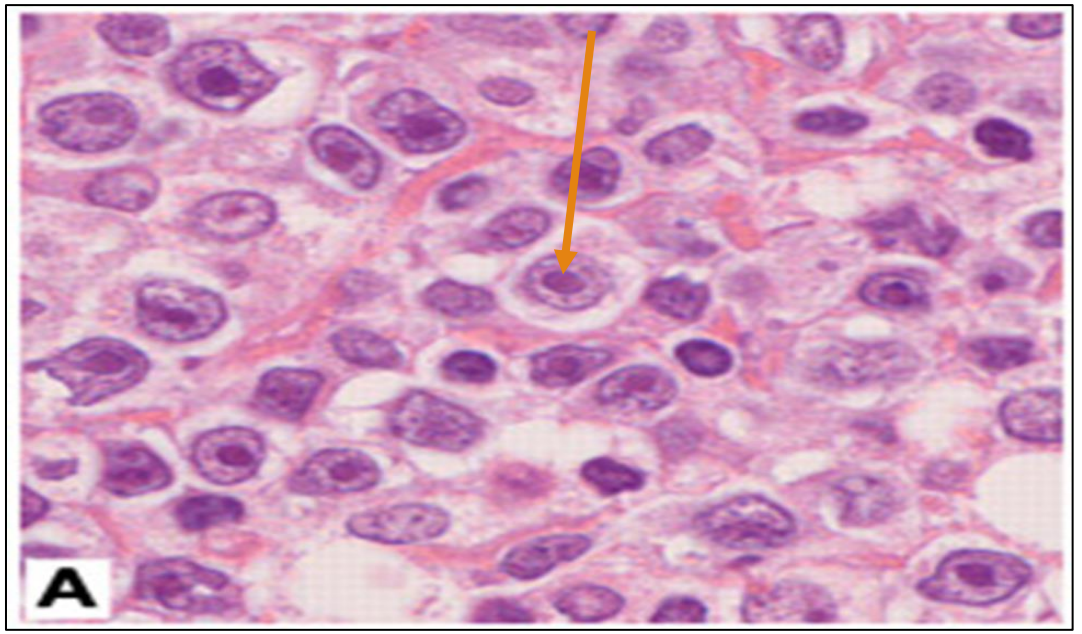
- **Diffuse** growth pattern.

- The cells are **large** (at least 3-4 times the size of resting lymphocytes) and vary in appearance from tumor to tumor:

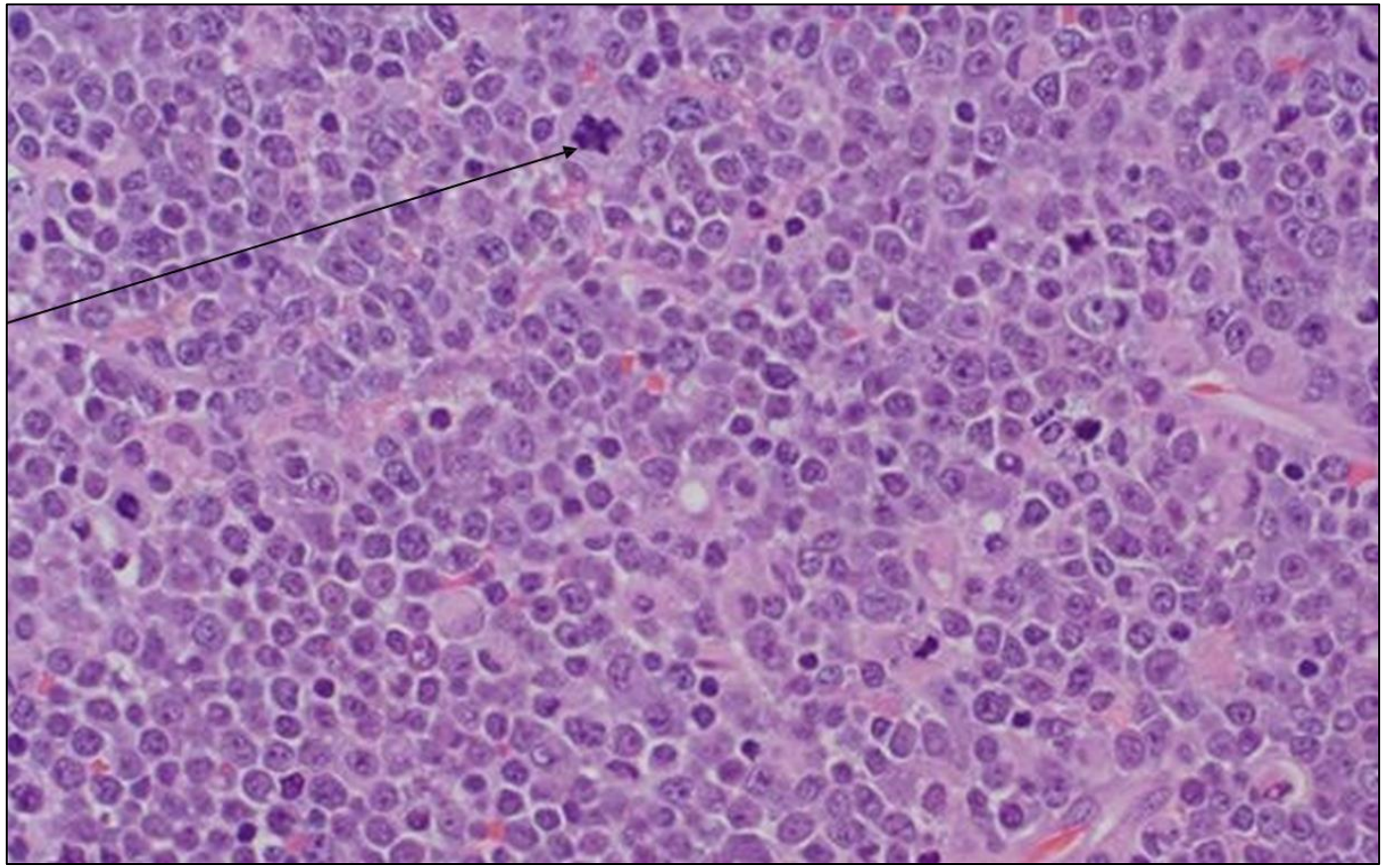
❑ **Centroblasts**: cells with round or oval nuclei, dispersed chromatin, several distinct nucleoli, and modest amounts of cytoplasm



❑ **Immunoblasts**: large round vesicular nucleus, one or two centrally placed prominent nucleoli, and abundant cytoplasm.



- Mitoses are frequent.
- Immunophenotyping:
  - The cells often mark with **CD10, and CD20**.



## ❖ Prognosis

- Without treatment, are aggressive and rapidly fatal.

- With intensive therapy, complete remissions or cure rate can be achieved.

## ❖ Subtypes Of Diffuse Large B Cell Lymphoma

1. **EBV-associated:** in AIDS, iatrogenic immunosuppression (in transplant recipient) and elderly.
2. **Kaposi sarcoma herpes virus** (HHV-8): associated with a rare primary effusion lymphoma in the pleura, pericardium & peritoneum.
3. **Mediastinal** Large B cell lymphoma occurs in young women with a predilection to involve viscera & CNS.

# 2. Burkitt Lymphoma

- It is a highly aggressive and rapidly proliferating lymphoma.

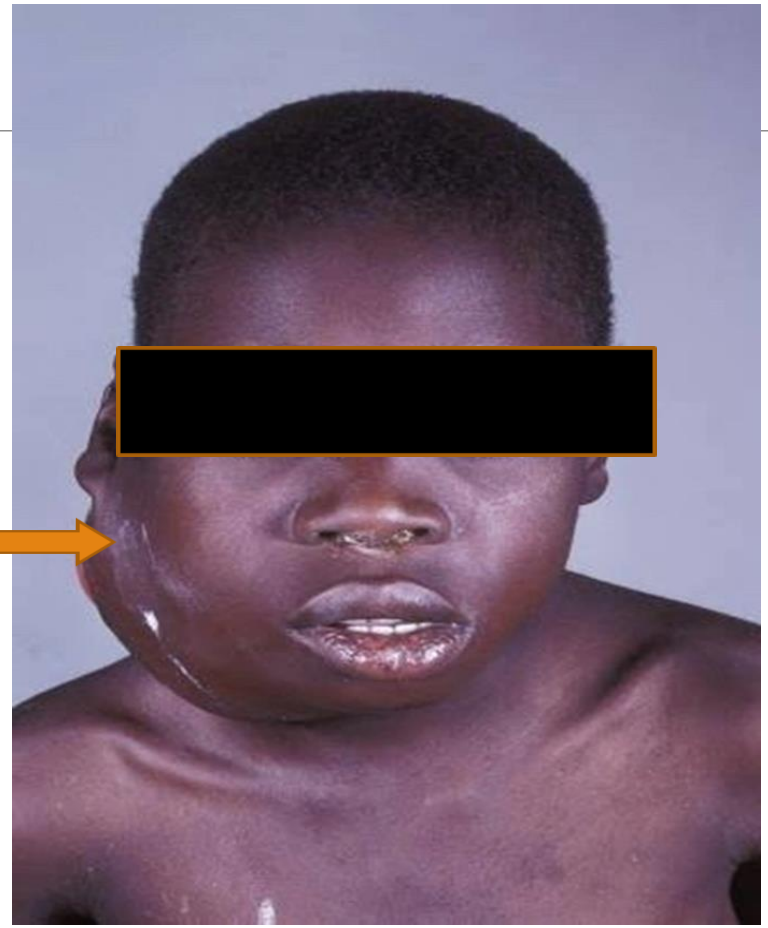
**Three major types exist:**

1. African (endemic).
2. Western (non-endemic, sporadic).
3. Immunodeficiency associated.

- Both the endemic and nonendemic forms affect mainly **children and young adults**.
- 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.
- In **North America, abdominal** tumors involving the bowel, retroperitoneum, and ovaries are more common

## ❑ Pathogenesis

- In most of African Burkitt's lymphoma, tumors carry the **EBV** genome.
- In ~20% of sporadic cases, the EBV genome is found in the tumor cells.
- Burkitt's lymphoma show **t(8;14)** chromosomal translocation( involves the **MYC** gene)



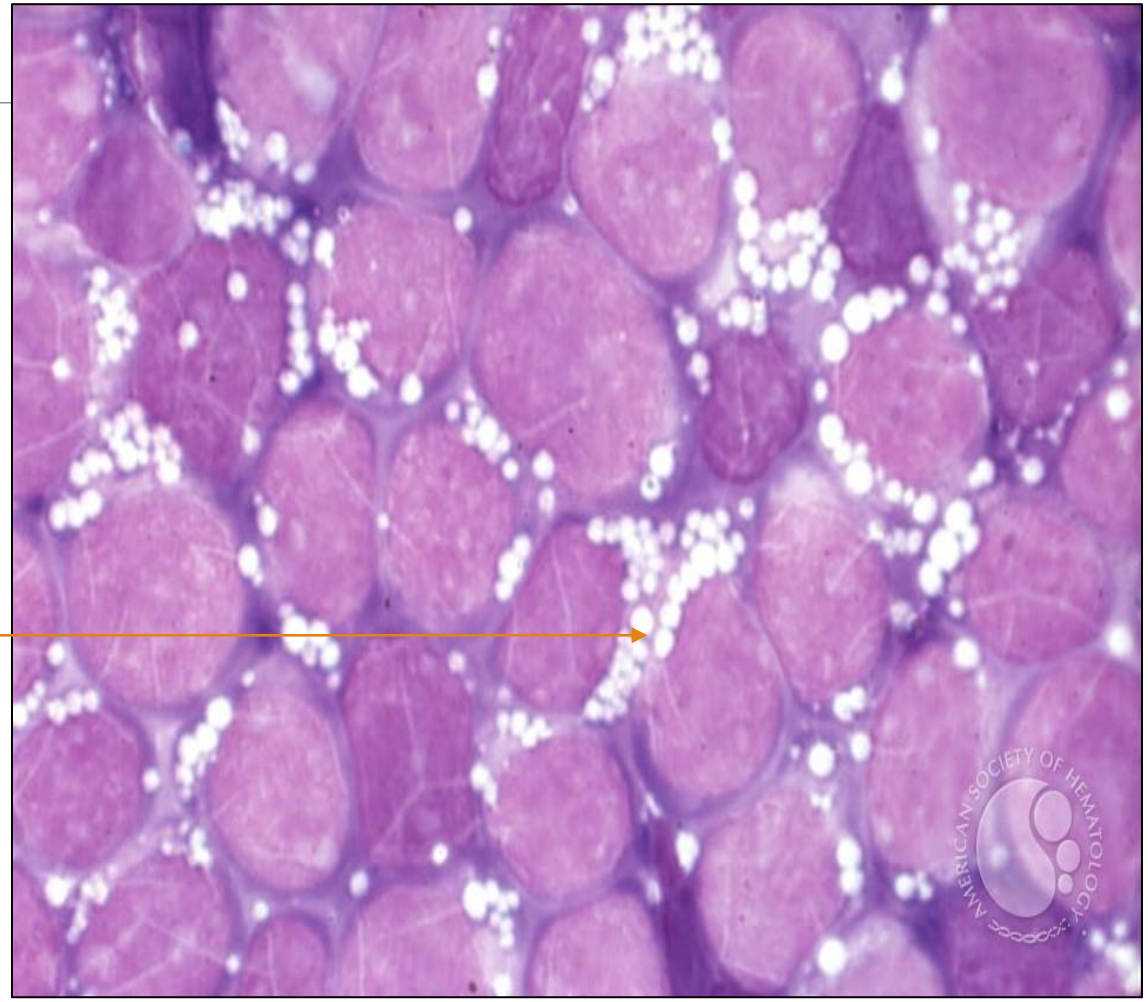
Endemic Burkitt Lymphoma in the jaw among African children.

## Morphology

- **Diffuse** growth pattern.

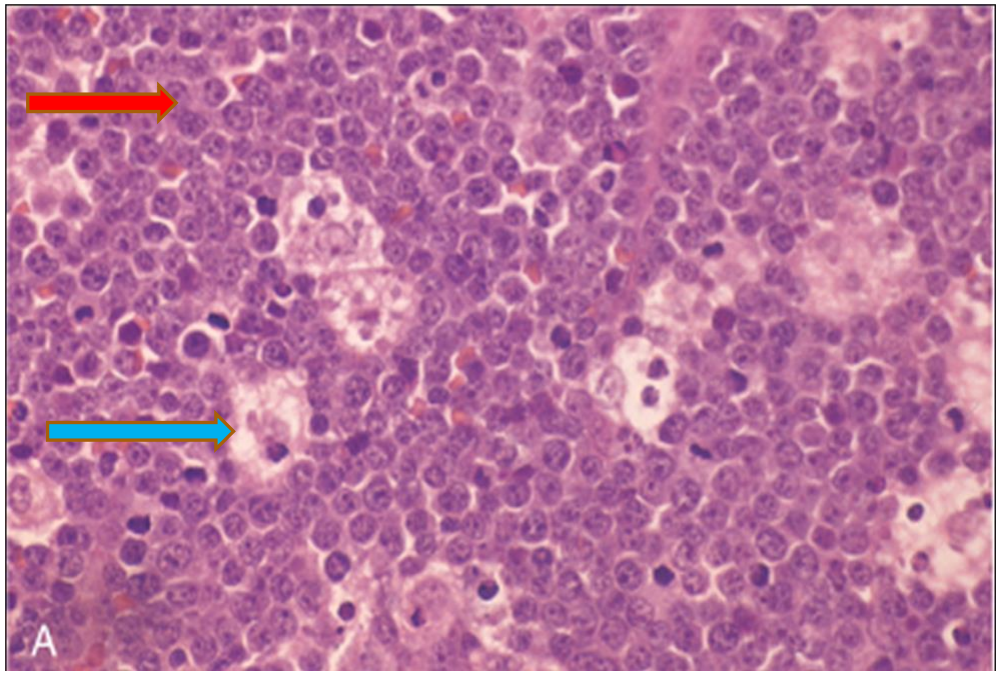
- The tumor cells are uniform and **intermediate** in size and typically have round or oval nuclei with 2-5 distinct **nucleoli**.

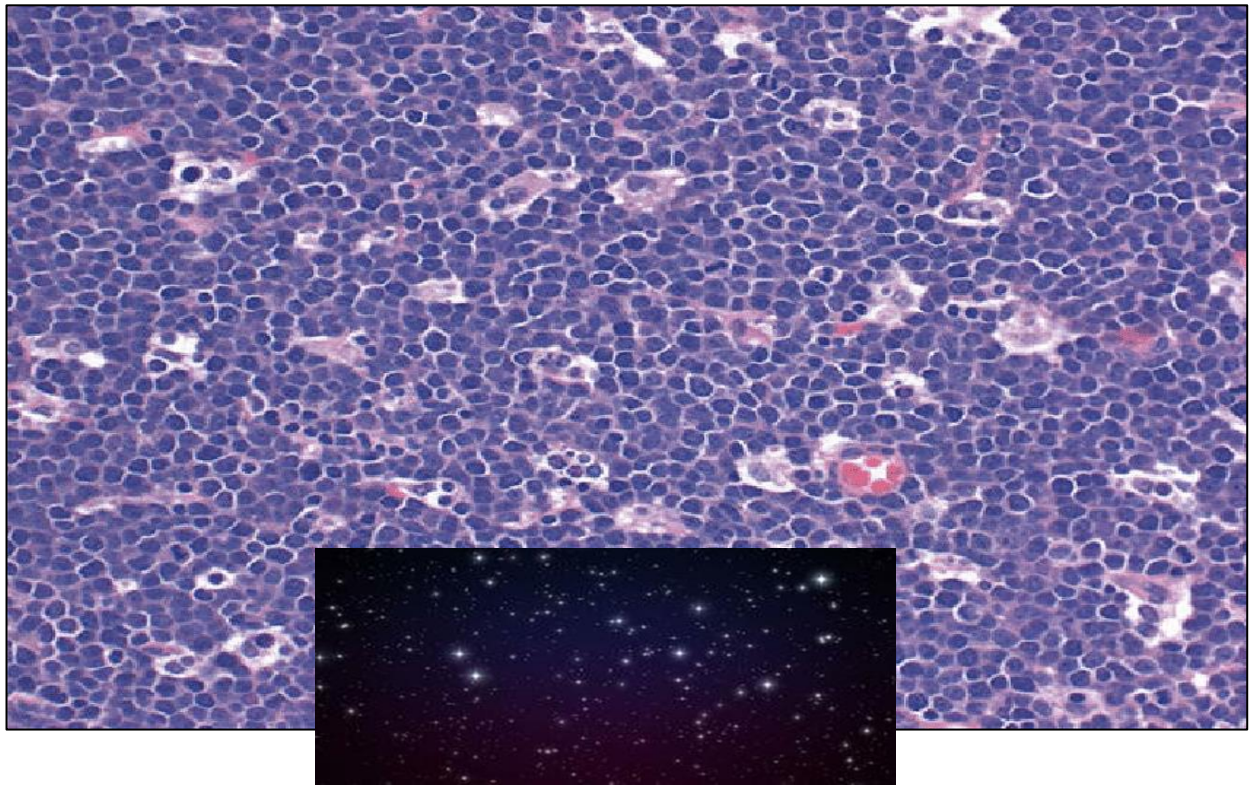
- There is a moderate amount of basophilic or amphophilic cytoplasm that often contains small, **lipid-filled vacuoles** (a feature appreciated on smears).



Diffuse sheets of medium sized neoplastic lymphocytes with abundant mitosis and apoptotic bodies, beside tingible body macrophages

- **A high mitotic rate** is very characteristic of this tumor, as is cell death accounting for the presence of numerous tissue **macrophages** containing ingested nuclear debris.
- Because these benign macrophages are often surrounded by a clear space, they create a" **starry sky**" pattern.



## ❑ Immunophenotype:

- These tumors express the B cell marker CD20.

## ❑ Prognosis

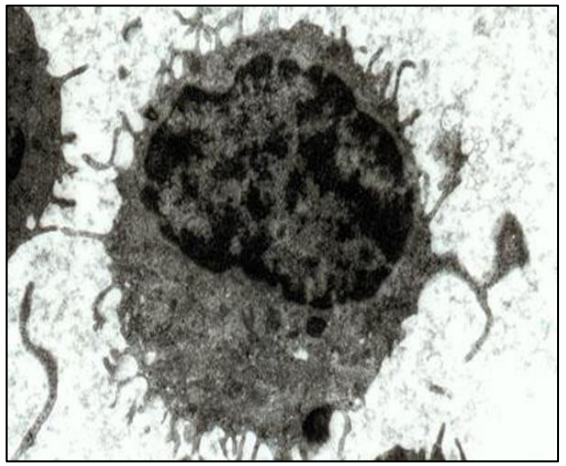
- Burkitt lymphoma is highly aggressive; however, with very intensive chemotherapy regimens, most patients can be cured.

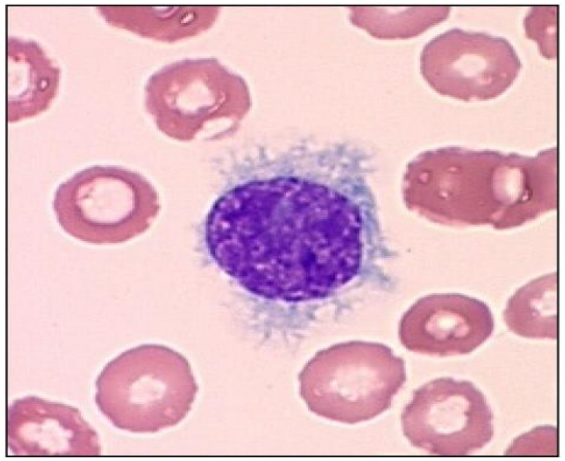
# Hairy Cell Leukemia

- It is a rare indolent B-cell neoplasm characterized by the presence of fine, hairlike cytoplasmic projections.

- Middle-aged males

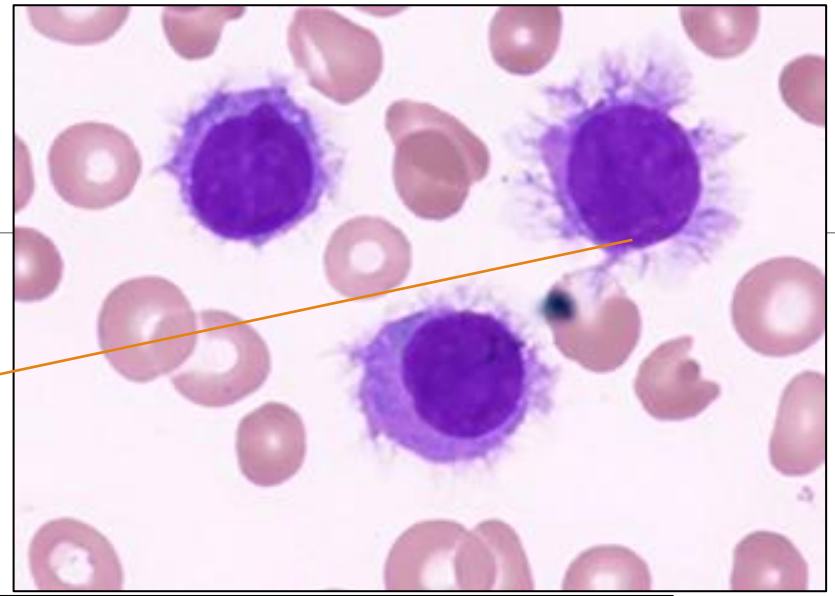
- **Massive splenomegaly.**
- **Pancytopenia** due to BM infiltration.
- **Lymph node** involvement is **rare**.
- **> 90%** have point mutations in the **BRAF** gene.
- Distinctive markers: B cell markers, **CD11c, CD25, CD103.**
- **Indolent course** with **excellent response** to chemotherapy

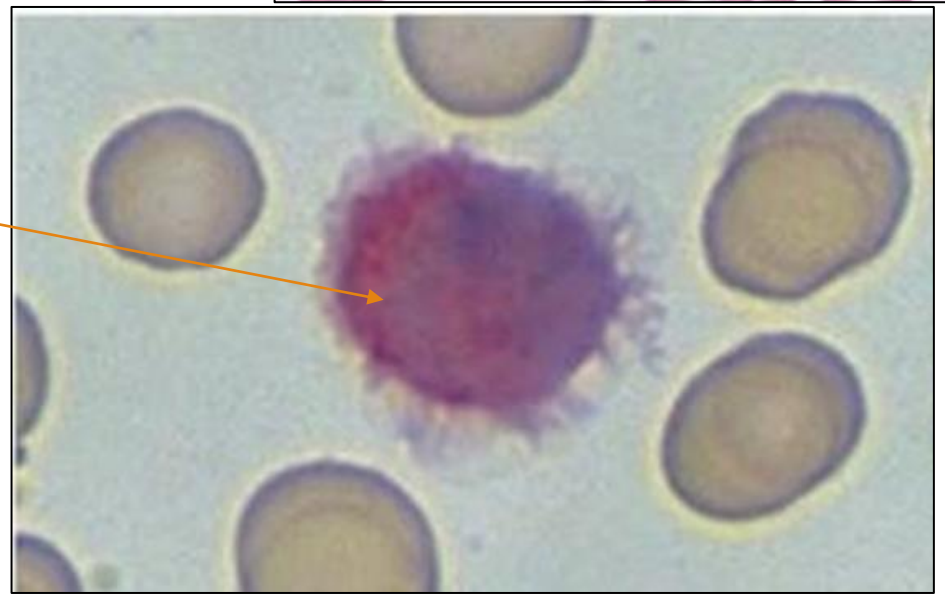




# Microscopic

- Peripheral blood smear shows abnormal lymphocytes with indistinct cytoplasmic borders and surface projections, giving the cells a "**hairy" appearance**.
- The red cytoplasmic staining seen at the lower right is **tartrate-resistant acid phosphatase (TRAP) positivity**





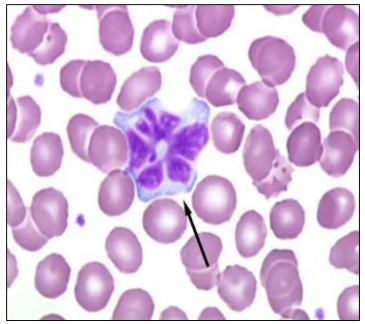
# T-cell lymphoma/Leukemia

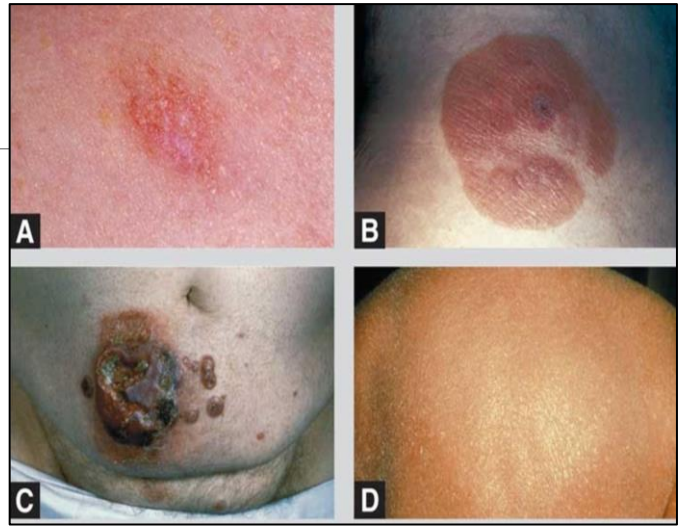
## ❖ Mycosis Fungoides

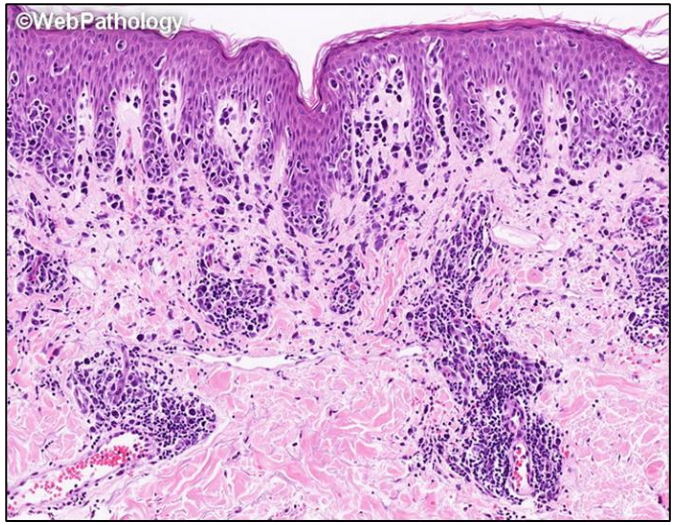
- Cutaneous T-cell lymphoma, usually CD4+

- Erythema, plaque, and tumor phases

- Epidermis and dermis infiltrated by cerebriform cells with marked infoldings of the nuclear membranes.





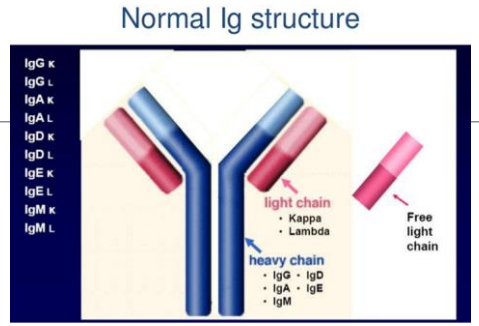
## ❖ Adult T-cell Leukemia/Lymphoma

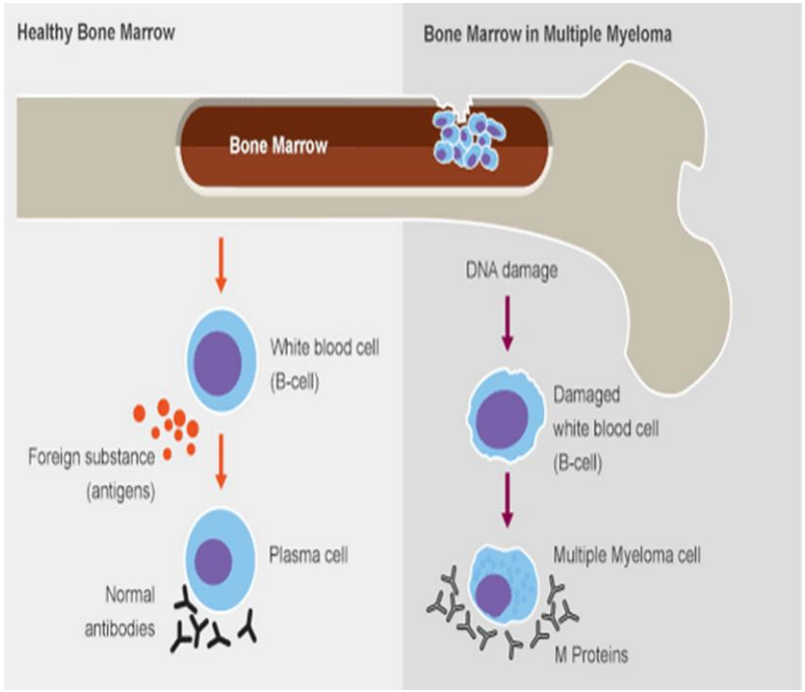
- Neoplasm of **CD4+** T cells
- Infection by **HTLV-1**
- Skin lesions, generalized Lymphadenopathy, hepatosplenomegaly, hypercalcemia.
- Very aggressive

# Plasma Cell Neoplasms

- Expansion of a single clone of immunoglobulin-secreting cells with serum increase of a **monoclonal Ig "M component," monoclonal gammopathy**

- B cell proliferations contain neoplastic plasma cells that secrete a monoclonal immunoglobulin or immunoglobulin fragment.



# Plasma cell neoplasm classification

| WHO CLASSIFICATION OF PLASMA CELL NEOPLASMS |
| --- |
| **Non-IgM monoclonal gammopathy of undetermined significance** (precursor lesion) |
| **Plasma cell Myeloma**<br>• Smouldering plasma cell myeloma<br>• Non-secretory myeloma<br>• Plasma cell leukemia |
| **Plasmacytoma**<br>• Solitary plasmacytoma of bone<br>• Extramedullary plasmacytoma |
| **Monoclonal immunoglobulin deposition diseases**<br>• Primary Amyloidosis<br>• Systemic light and heavy chain deposition diseases |
| **Plasma cell neoplasms with associated paraneoplastic syndrome**<br>• POEMS syndrome<br>• TEMPI syndrome (Provisional entity) |

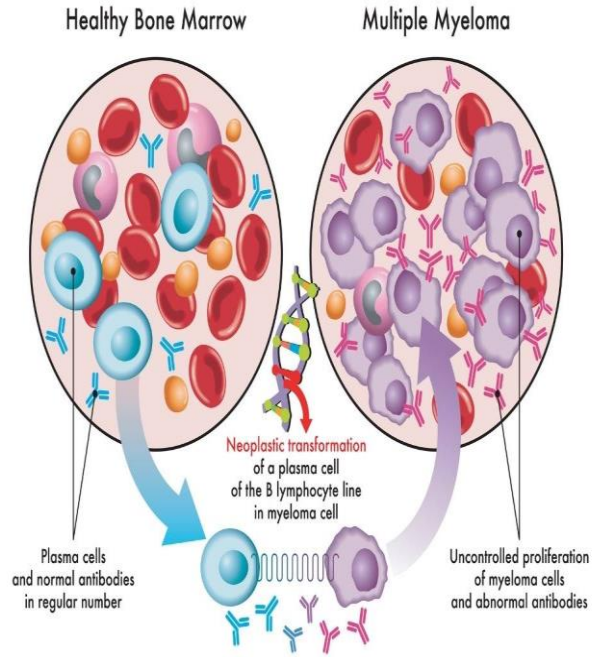
1. **Multiple myeloma (plasma cell myeloma).**
2. **Lymphoplasmacytic lymphoma (Waldenström macroglobulinemia).**
3. **Monoclonal gammopathy of undetermined significance (MGUS)**

# Multiple Myeloma

- The most common and deadly of these neoplasms.
- It is a B-cell neoplasm.
- It is a clonal proliferation of neoplastic plasma cells in the **bone marrow** that is usually associated with a **multifocal lytic lesions** throughout the skeletal system (commonly involve the **vertebral column**, ribs, skull, pelvis, femur, clavicle).
- The median age is 70 years, M >F
- Malignant plasma cells secrete complete immunoglobulin molecules called: M protein, which is IgG (60%), IgA (20% to 25%)and,
- In the remaining cases, the plasma cells produce only κ or λ light chains, the free light chains, because of their low molecular weight, are rapidly excreted in the urine called: Bence - Jones proteins.

# Pathogenesis

- Myelomas have chromosomal translocations involving the **IgH** locus(chr**14).**
- The fusion partners include the **cyclin D1**, **FGFR3**,and **cyclin D3** genes.
- Dysregulation of D cyclins is believed to contribute to increases in cell proliferation
- Plasma cells in multiple myeloma are supported by the cytokine **IL-6,** which is produced by fibroblasts and macrophages in the bone marrow stroma.



# Clinical features

- Bone pain and fractures: Resulting from bone resorption.
- Hypercalcemia: Resulting from bone resorption ⟶ neurological problems (confusion, weakness) and renal dysfunction
- Recurrent infections: due to marked suppression of normal humoral immunity.
- Anemia and bleeding: due to replacement by tumor cells with suppression of hematopoiesis.
- Renal insufficiency: result from the effects of **Bence Jones protein (**Obstructive proteinaceous casts),

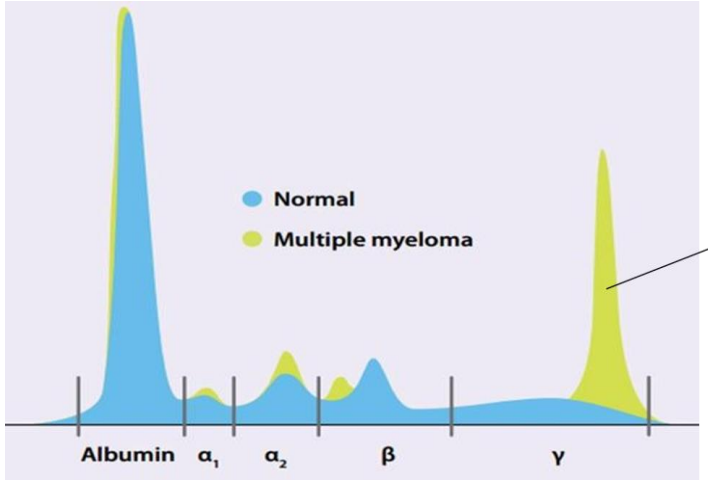
  Light chain deposition, as amyloid, renal stones, Bacterial pyelonephritis
- AL-type **amyloidosis**

# Diagnosis

1. Demonstration of monoclonal plasma cells in the bone marrow

   **(≥ 10%).**

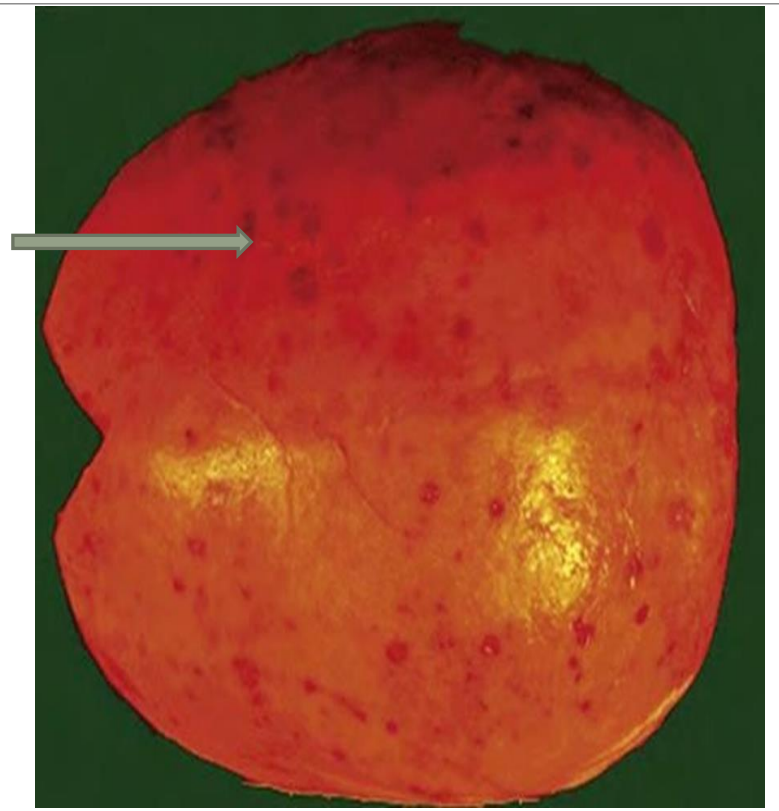
2. Monoclonal proteins in the serum.
3. End organ damage, defined as:
   i. HyperCalcemia
   ii. Renal dysfunction
   iii. Anemia (CBC)
   iv. Lytic Bone lesions (X-ray)



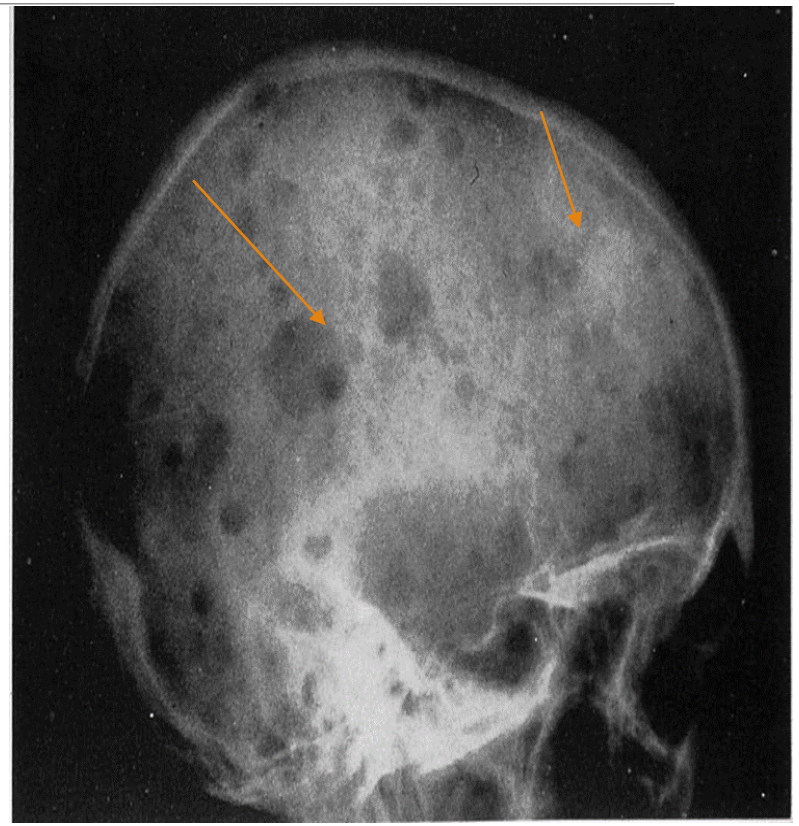

➢ Remember: CRAB (Calcium, Renal, Anemia, Bone)

## Grossly:

- This skull shows the characteristic rounded "punched-out" defects due to plasma cell proliferation resulting in bone lysis.

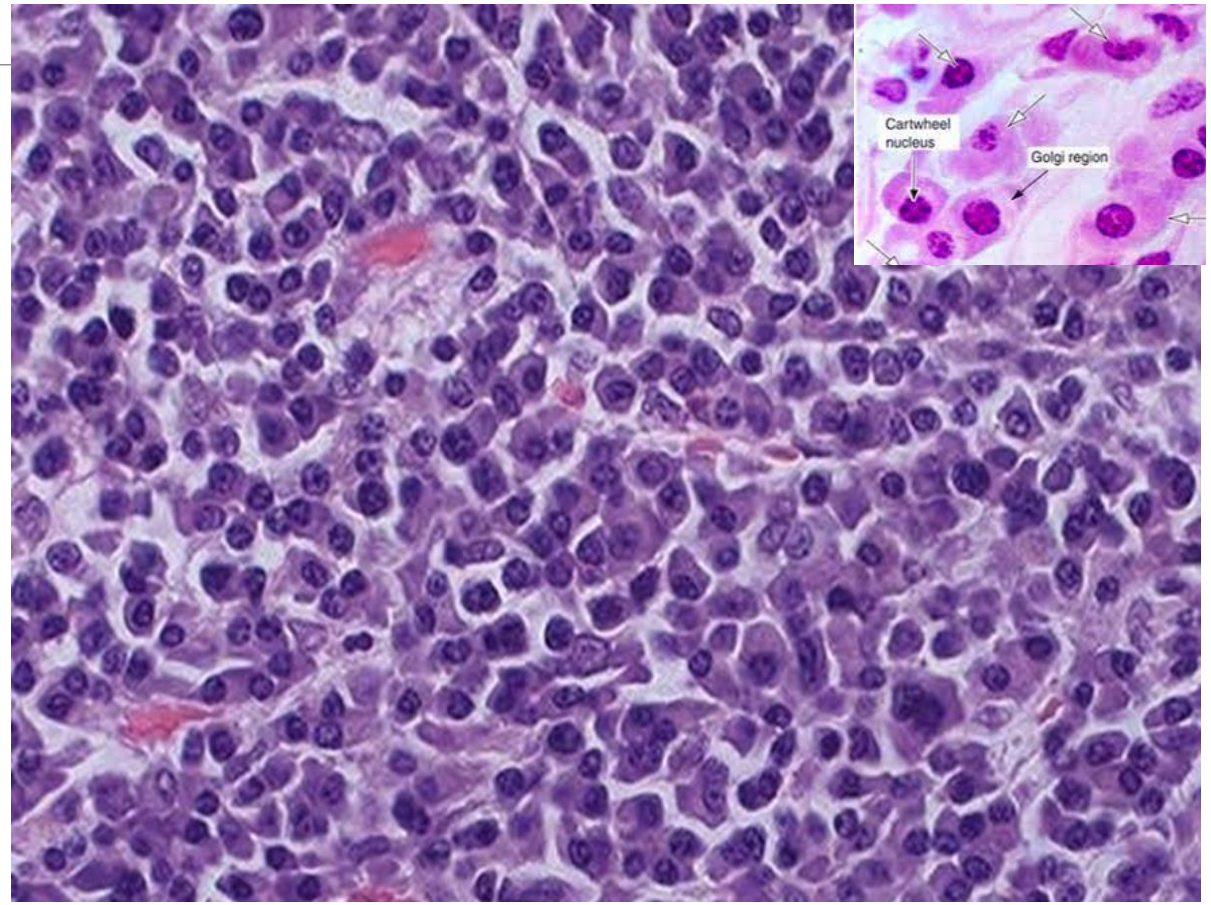


Skull X-ray showing multiple "punched out" osteolytic lesions

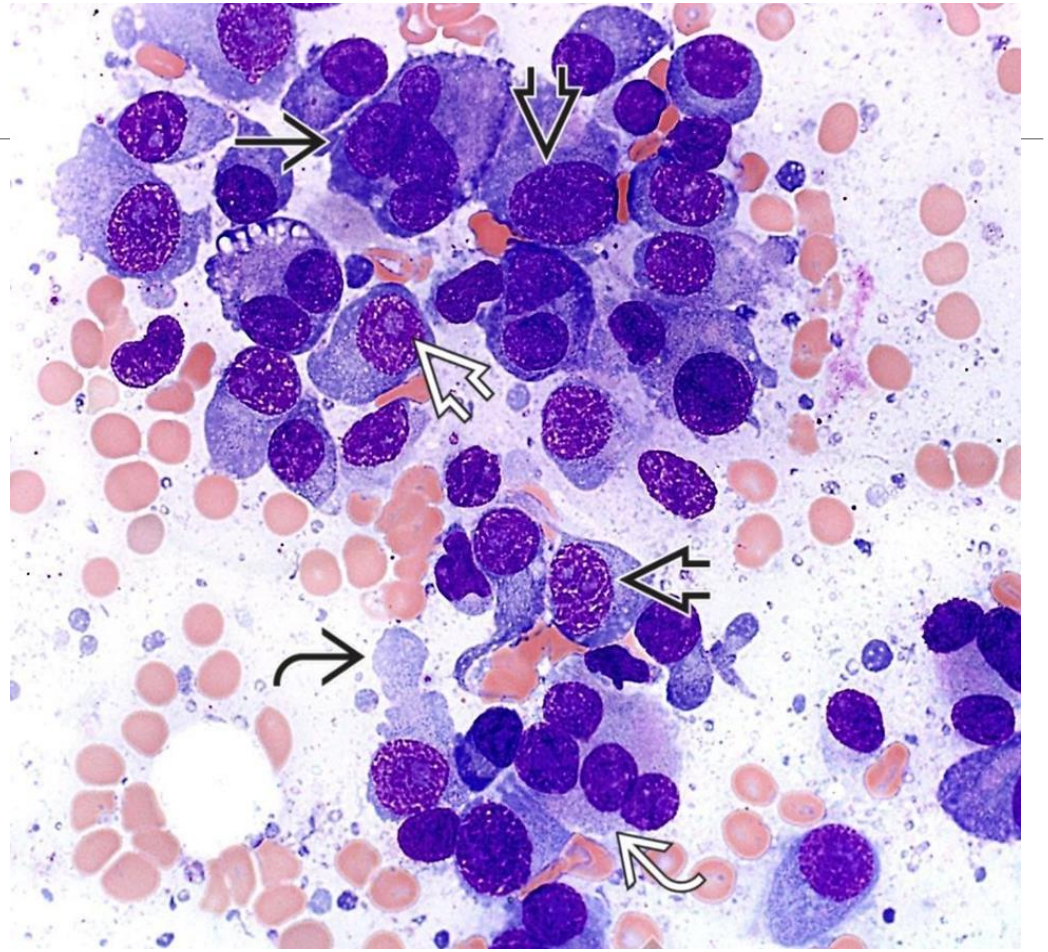


# Microscopically:

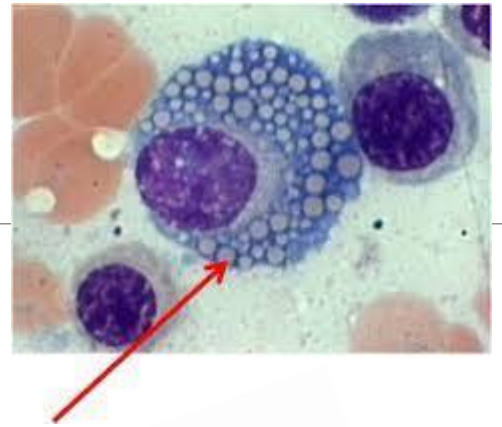
In the bone marrow biopsy section: there are sheets of plasma cells that are very similar to normal plasma cells, with eccentric nuclei and abundant pale purple cytoplasm resembling bike wheel.

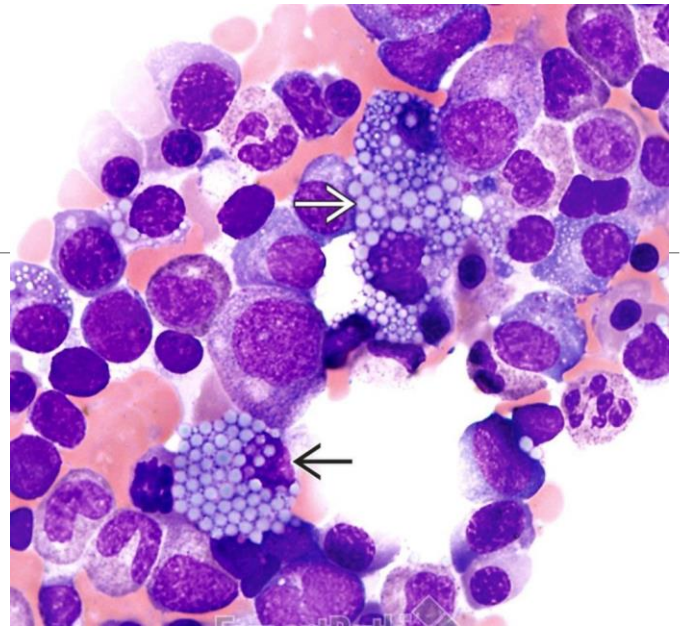


- Features of PC atypia are illustrated in this aspirate, including:
  - Cellular and nuclear enlargement, nuclear pleomorphism (black solid arrow),
  - Multinucleation (white curved arrow),
  - Dispersed nuclear chromatin (black open arrow),
  - Prominent nucleoli (white open arrow)
  - Cytoplasmic fraying or shedding(black curved arrow).

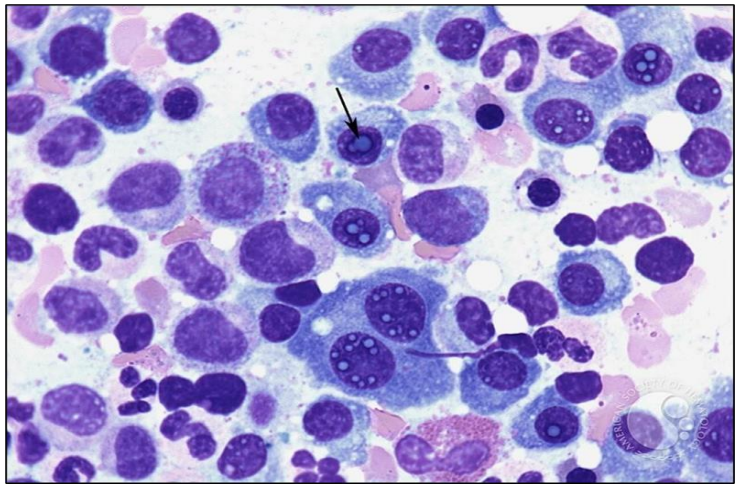


- Immunoglobulin accumulations appear as uniform, round, colorless globules called **Russell bodies** (white solid arrow) in the cytoplasm.
- When multiple Russell bodies are in the cytoplasm of cells, they are referred to as **Mott cells or morula cells, grape-like cells** (black solid arrow).



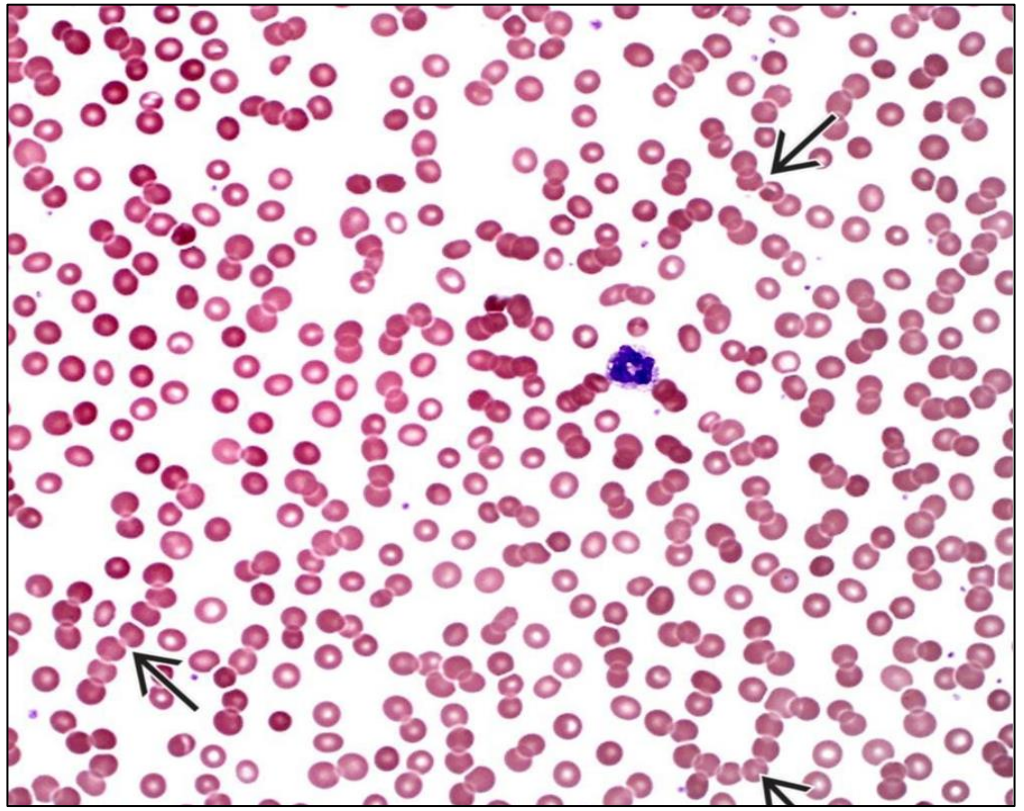


- If the inclusions are intranuclear they are called: **Dutcher bodies** (black arrow)



# Peripheral Blood

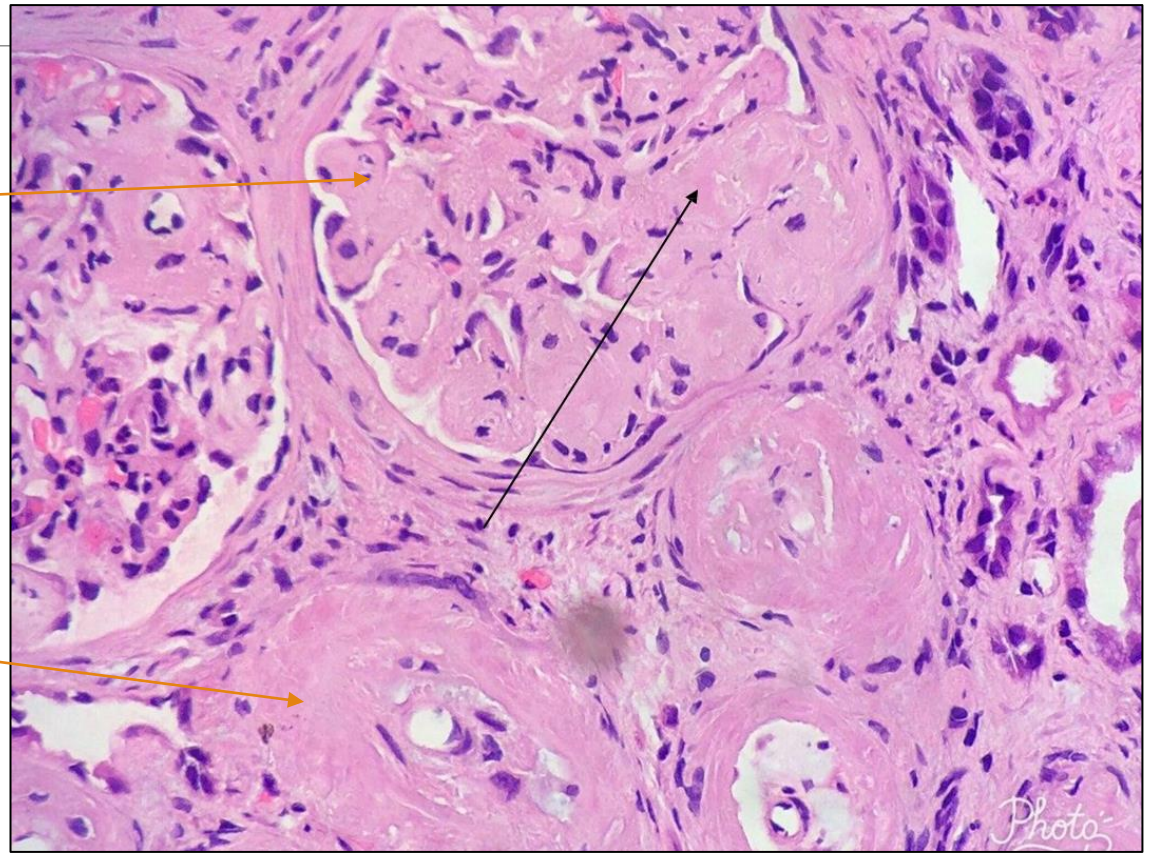
- **Rouleaux** formation (black solid arrow) is the linear arrangement of ≥ 4 red cells that resembles a stack of coins.
- It indicates increased proteins in the blood (i.e., Ig in myeloma)



# Renal Amyloidosis, Multiple Myeloma

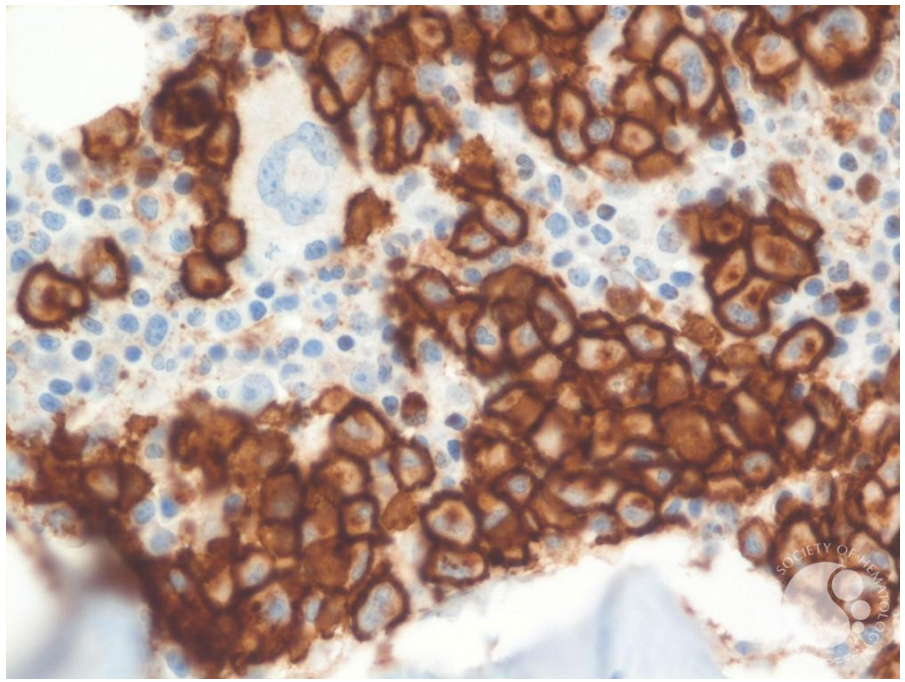
- In the renal cortex, pale pink amyloid deposits are visible within glomeruli.

- The **amorphous pink deposits of amyloid** may be found in and around arteries, in the interstitium, or in glomeruli.



# Immunophenotyping

- Despite it being a B-cell neoplasm, it does not express B-cell markers.
- It expresses CD138, and monoclonal kappa or lambda light chain.

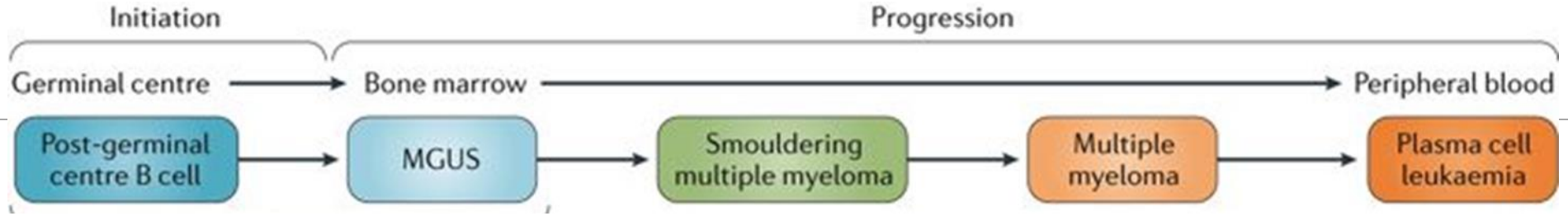


## Prognosis

- Variable.
- If untreated, patients rarely survive for more than 6 to 12 months
- The median survival is 4 to 7 years.

# Monoclonal Gammopathy Of Undetermined Significance (MGUS)

- M proteins are found in the serum of 1 % to 3 % of asymptomatic healthy persons older than age 50 years, making this the most common plasma cell proliferation.
- M-protein <3 gm/dl
- Clonal PC's in BM **<10%**
- No symptoms of myeloma present
- Risk of progression to myeloma is 1 % per year




**MGUS**

Monoclonal protein spike <3 g/dL

Plasma cells (PC) <10% of bone marrow

No CRAB features

**Smouldering multiple myeloma**

Monoclonal protein spike >3 g/dL

PC >10% of bone marrow

No CRAB features

**Multiple myeloma**

Monoclonal spike

PC >10% or plasmacytoma

CRAB features

Or PC >60% or SFLC ratio >100

Or more than one focal lesion on MRI

# Lymphoplasmacytic lymphoma

- B cell neoplasm,

- In $6^{th}$-$7^{th}$ decades.

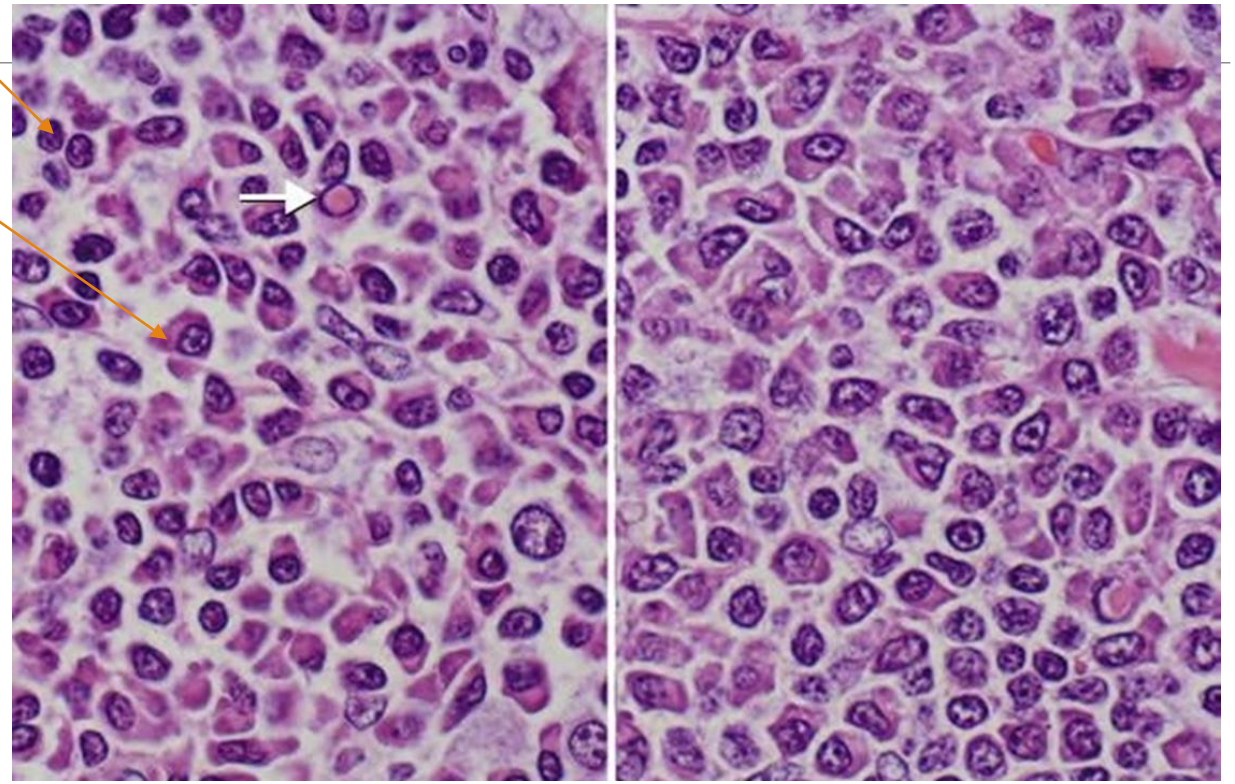
- A substantial fraction of the tumor cells undergo differentiation to plasma cells. Most commonly, the plasma cell component secretes monoclonal **IgM**, often in amounts sufficient to cause a hyperviscosity syndrome known as **Waldenström macroglobulinemia**.

- Acquired mutations in MYD88 encoding part of the NF-κB signaling pathway are nearly always present.

# Microscopically

The **marrow** contains an infiltrate of lymphocytes, plasma cells, and plasmacytoid lymphocytes in varying proportions.

PAS-positive inclusions containing immunoglobulin are frequently seen in the cytoplasm **(Russell bodies)** or the nucleus **(Dutcher bodies) (white arrow).**



# Clinical Symptoms

- Weakness, fatigue, and weight loss.

- Lymphadenopathy, hepatomegaly, and splenomegaly.

- Anemia caused by marrow infiltration is common.

- About 10% of patients have *autoimmune hemolysis* caused by IgM.

- Excess **IgM** secretion in the blood leads to a hyperviscosity syndrome (Because of its large size), with clinical features including:

  - Visual impairment
  - Neurologic problems: Headaches, dizziness, deafness
  - Bleeding.

- Lymphoplasmacytic lymphoma is an incurable, progressive disease
- Median survival is about 4 years.


Thank
You