



HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : Pathology

LEC NO. : 9

DONE BY : Hamza alsyouri

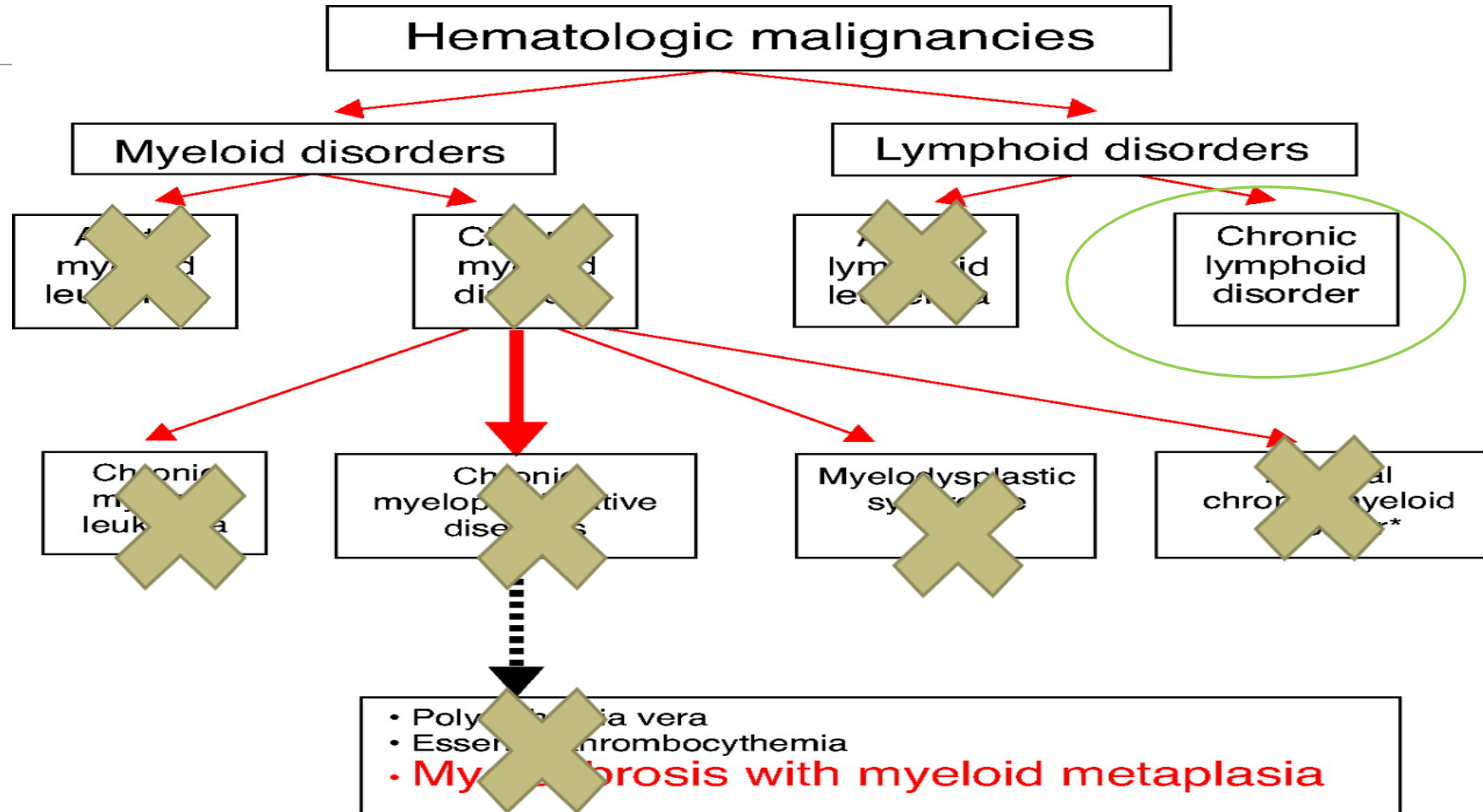
وَقُلْ رَبِّ زِدْنِي عِلْمًا



“Hematopoietic And Lymphoid System (HLS)”

Dr. Ola Abu Al Karsaneh

Neoplastic Proliferations Of White Cells



Normal Lymph Node Morphology

Gross Description:

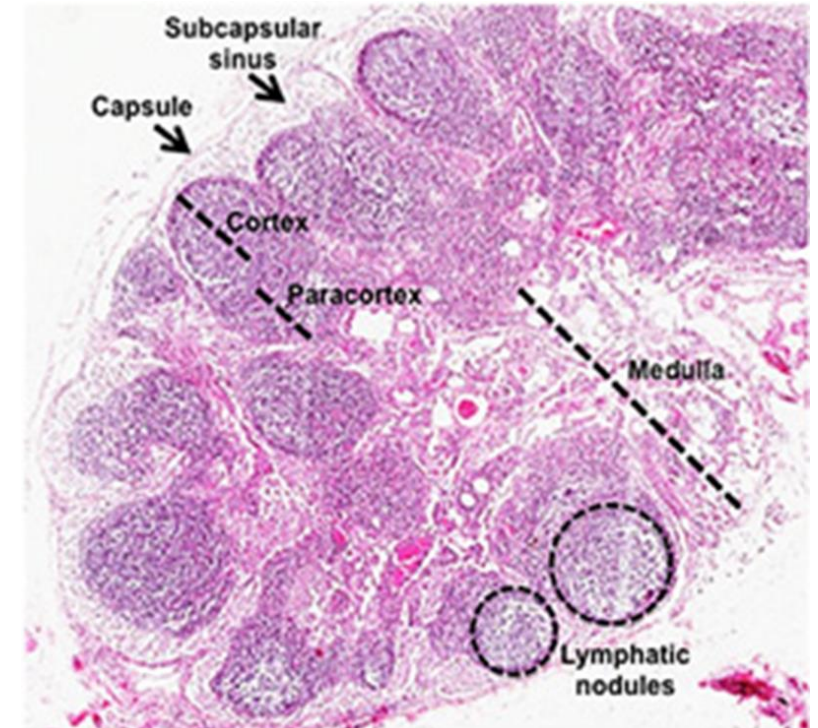
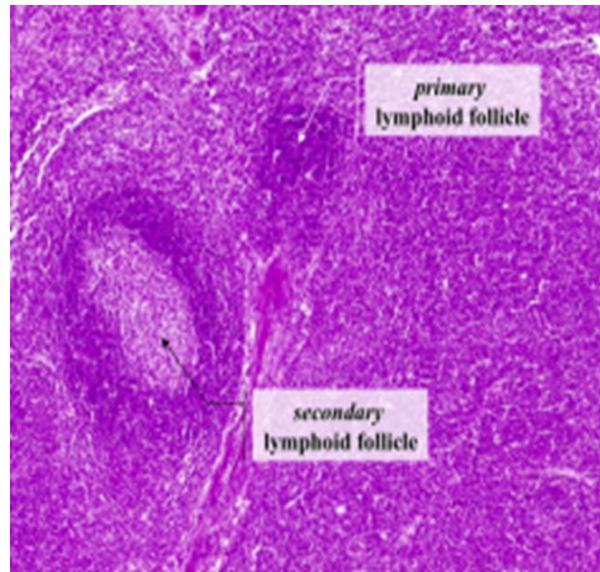
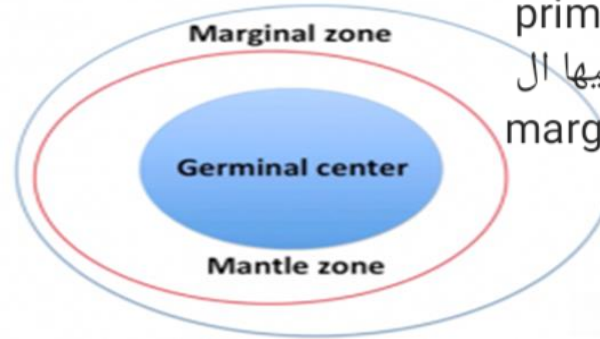
- Ovoid with gray-tan cut surface.

Microscopically:

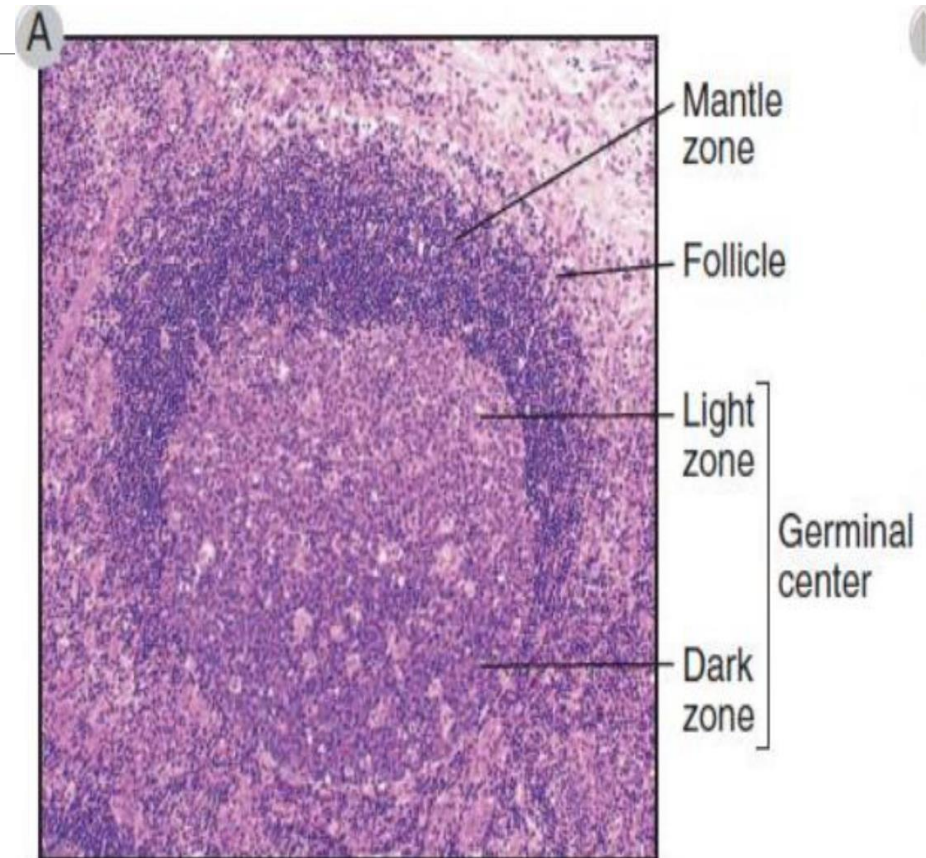
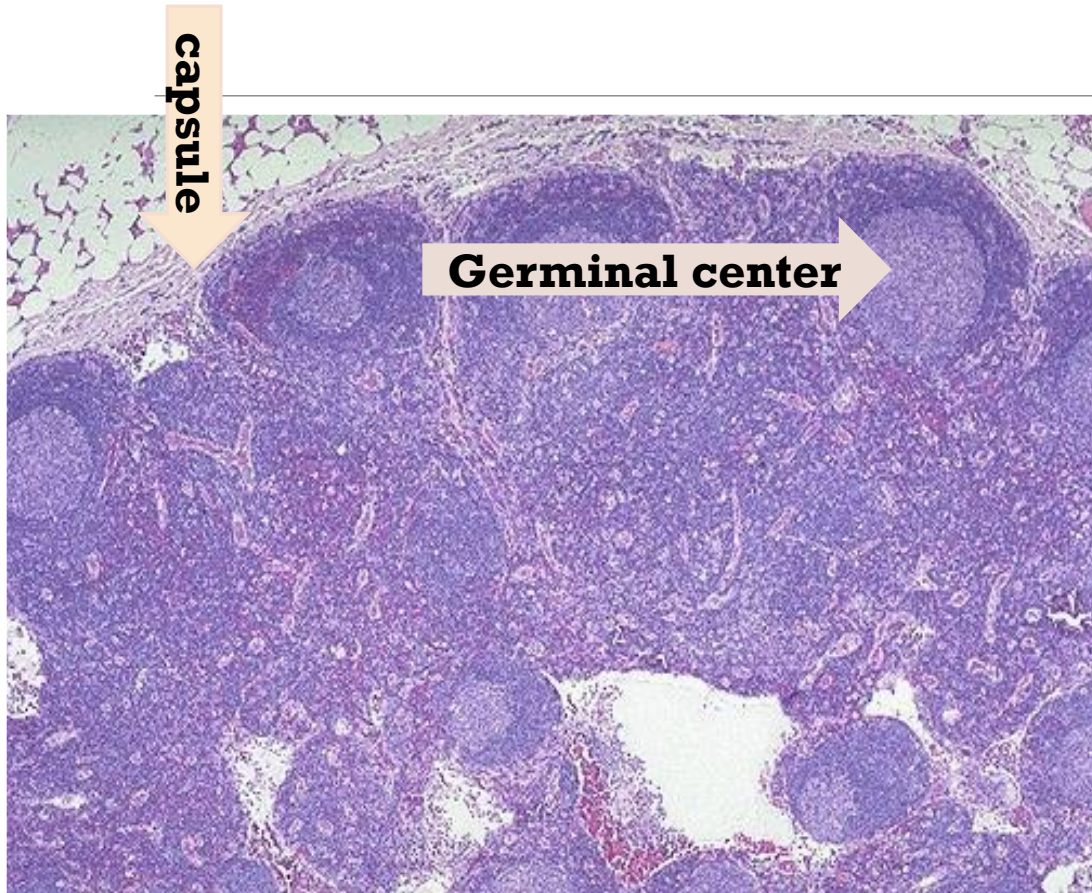
1. Cortex
2. Paracortex
3. Medulla

حكينا عن ال secondary لانه في بعض ال tumours بتطلع من ال Germinal center فبتكون مكونة من centrocyte and centroblast اللي هم اصلا نوع الخلايا اللي موجودين بال Germinal center وفي tumour بتطلع من ال mantle zone او بتشبهها وفي اخرى بتطلع من ال marginal

ال lymph node موجود داخل ال cortex و بتكون من نوعين ال primary and secondary ال secondary بكون بوسطها Germinal center وحولها ال mantle zone وبعديها ال marginal zone



Normal Reactive LN



□ Reactive Lymphadenitis

❖ Acute Nonspecific Lymphadenitis: هون بدنا نعرف انه مش كل واحد صار عنده enlargement في ال lymph node معناه انه عنده lymphoma احيانا ممكن يكون ال enlargement بكون reactive نتيجة infection, inflammation , او غيره فبالتالي عنا نوعين من ال acute or chronic inflammation في ال lymph node

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.

لو راح ال infection ممكن ترجع back to normal واذا ما راح ممكن يصير محله scar formation

❖ Chronic Nonspecific Lymphadenitis

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

عنا ٣ انواع من ال chronic حسب وين التغييرات صارت بأي lymph node في ال region

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

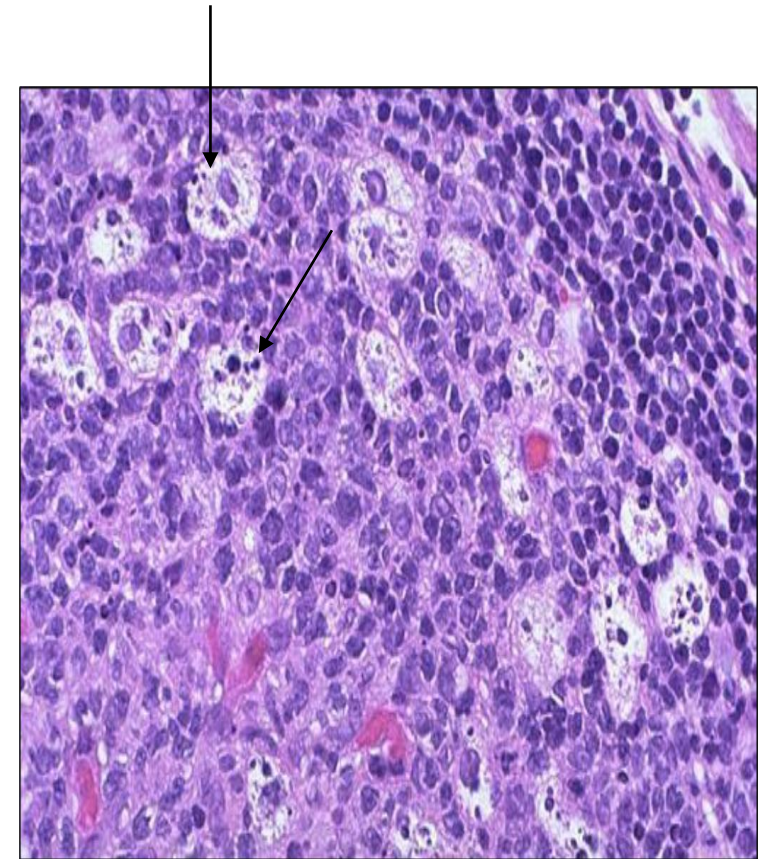
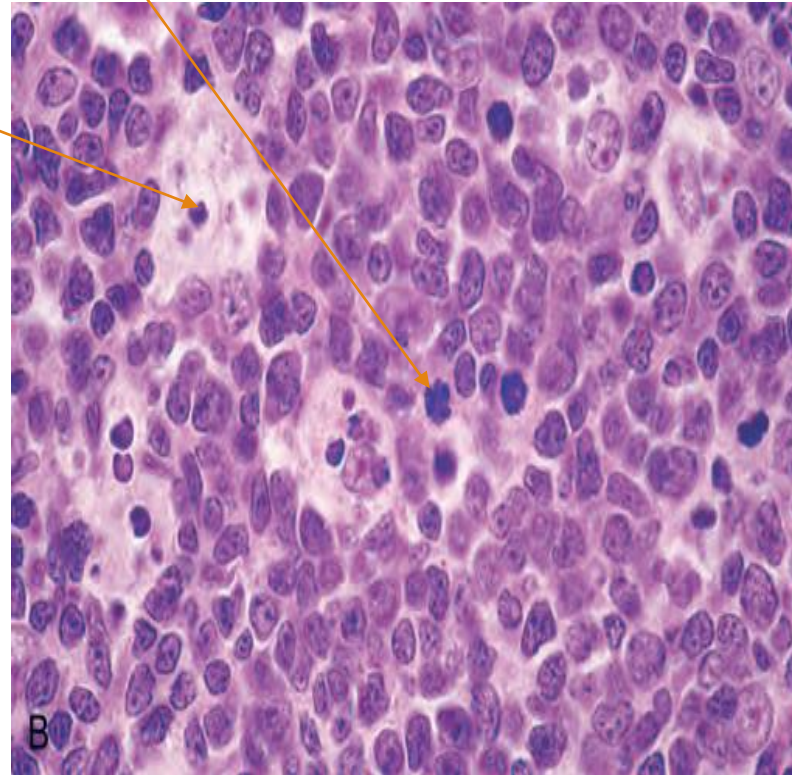
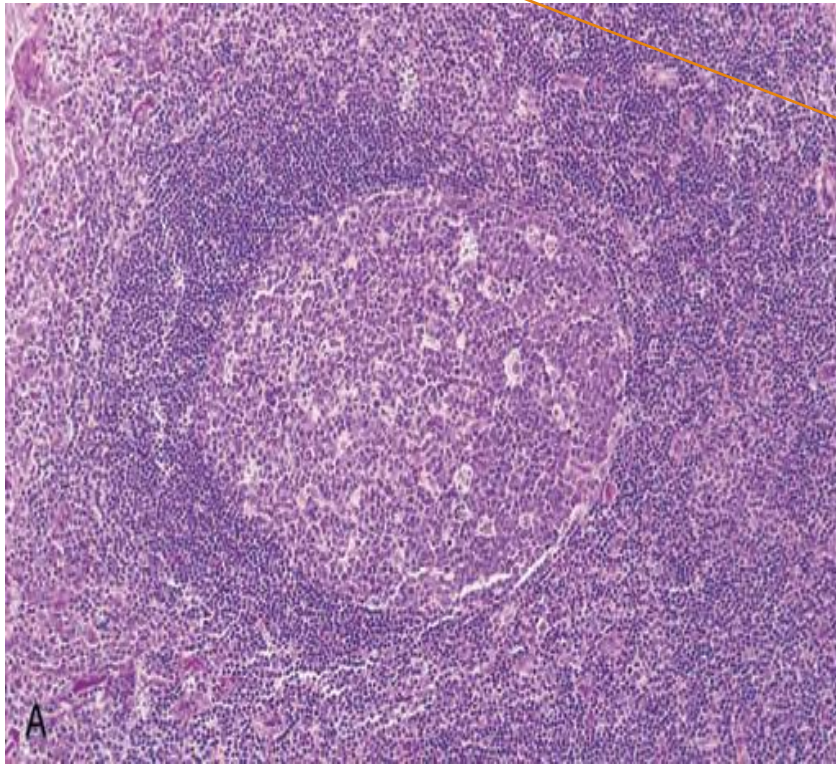
مهم نميز بين ال follicular hyperplasia and follicular lymphoma

ما بتطلع من ال lymph node و بضلها داخل ال cortex والاشي اللي بثبتلنا انها benign هو وجود ال tingible body macrophages

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**).



هي منطقة بين ال cortex وال medulla فبصير في
expansion زيادة بالخلايا الموجودة في منطقة
ال paracortex

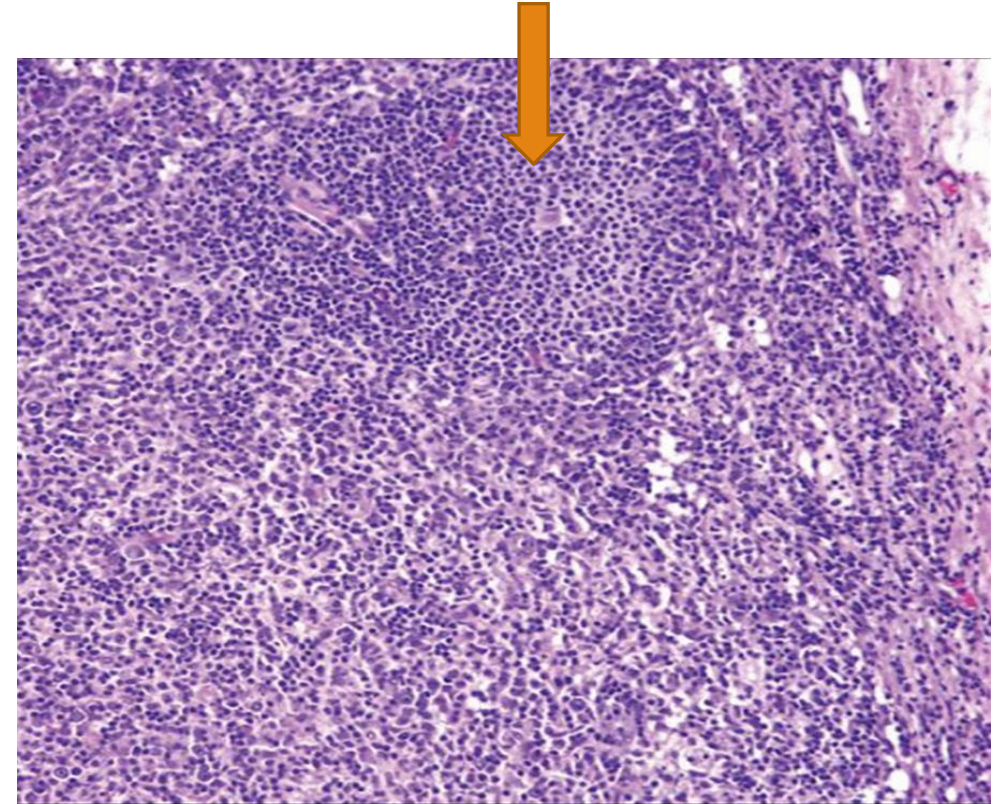
2. Paracortical Hyperplasia:

- 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.

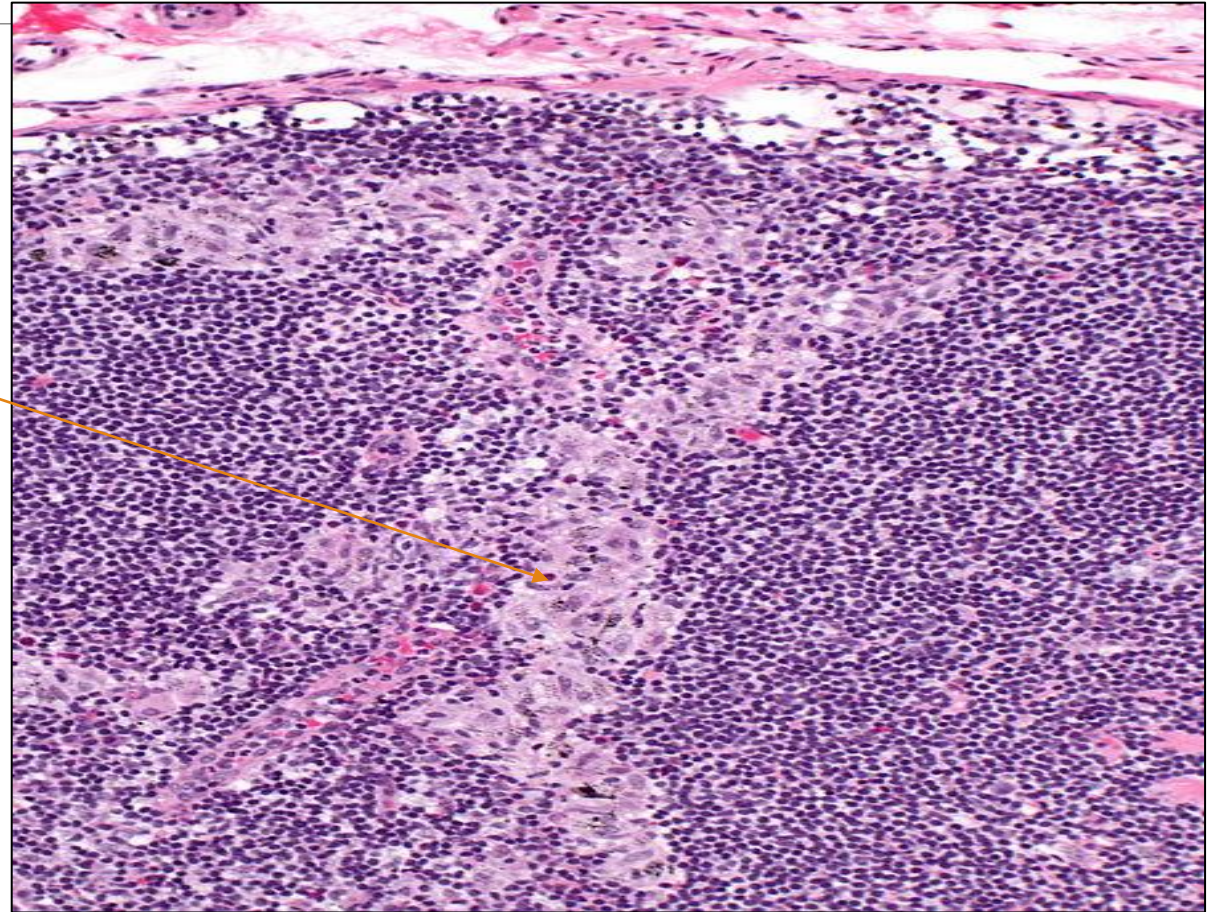


الدكتورة ما قرأت السلايد فاقرأوه احتياطاً

ال lymph node في الها subcapsular sinuses يعني subsinuses او lymphoid sinuses تحت
ال capsule وفي برضو lymphoid sinuses جوا لل lymph node نفسها فمرات بتصير تتوسع هاي
ال sinuses فبصير جواتها histiocytes او macrophages وهاد سبب تسميتها sinus histiocytosis

3. Sinus Histiocytosis:

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

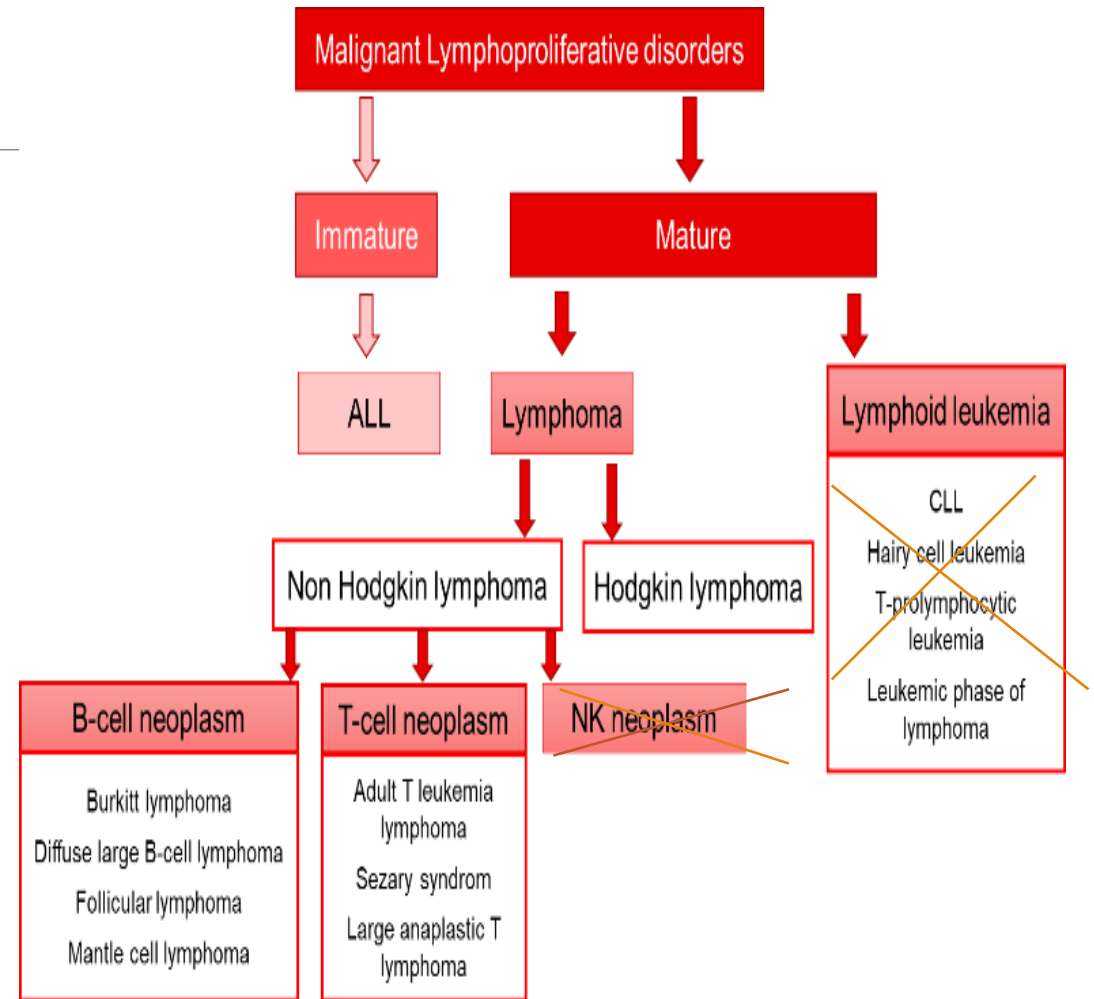


Lymphoid Neoplasms

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.



فمثلا لو كانت طالعة من ال Germenal center يمكن نسميها follicular

lymphoma لانها بتشبهها

لو طالعين من mantel cell او بشبهوها بنسميها mantel cell lymphoma

واذا طالعة من marginal zone بنسميها marginal zone lymphoma

احنا كمان بنصنف ال lymphoma حسب من وين طالعين

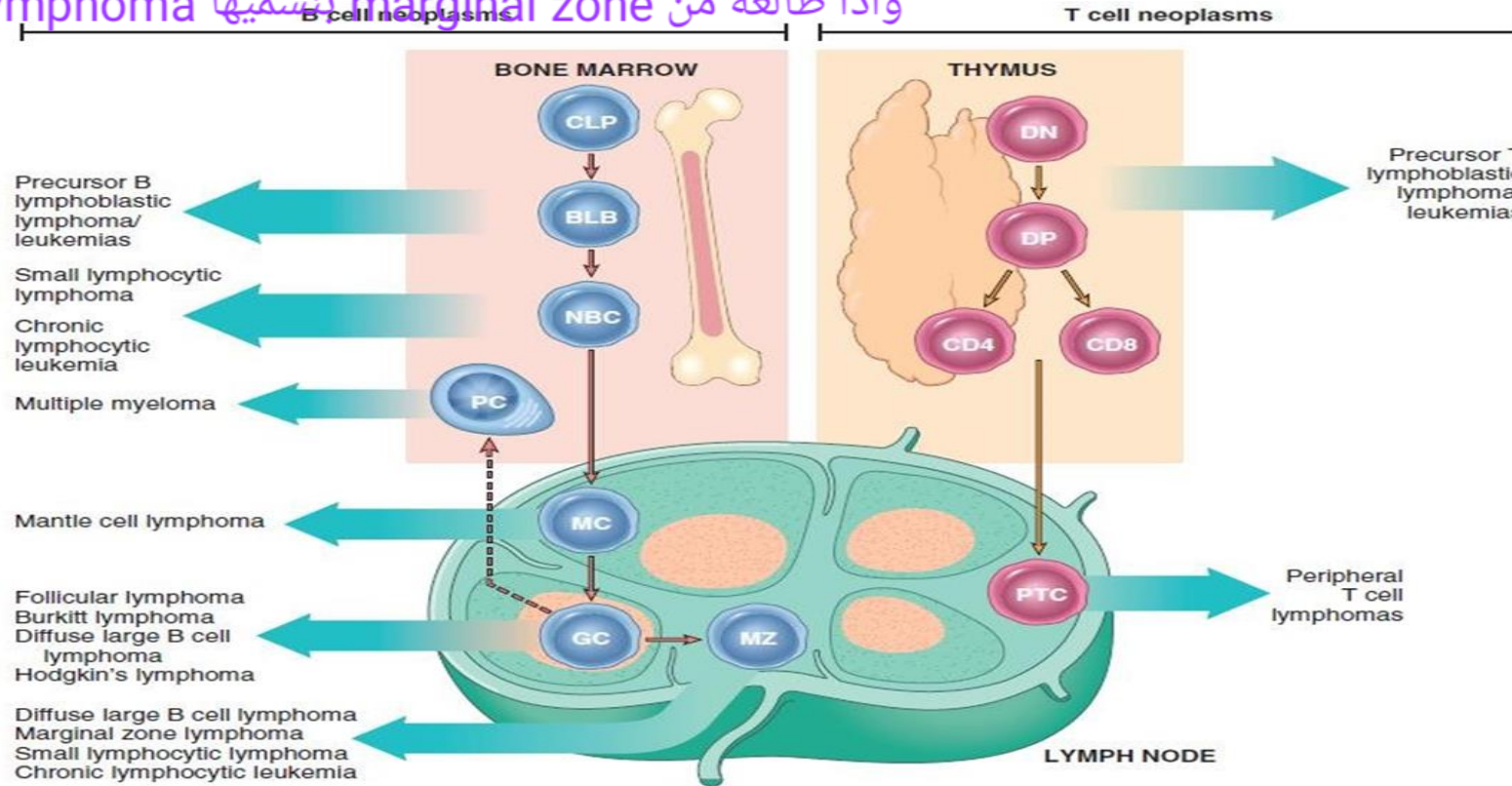


Fig. 12.13 Origin of lymphoid neoplasms. Stages of B and T cell differentiation from which specific lymphoid and tumors emerge are shown. BLB, Pre-B lymphoblast; CLP, common lymphoid progenitor; DN, CD4-/CD8- (double-negative) pro-T cell; DP, CD4+/CD8+ (double-positive) pre-T cell; GC, germinal center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



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- **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.

General idea صارت عند الناس

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

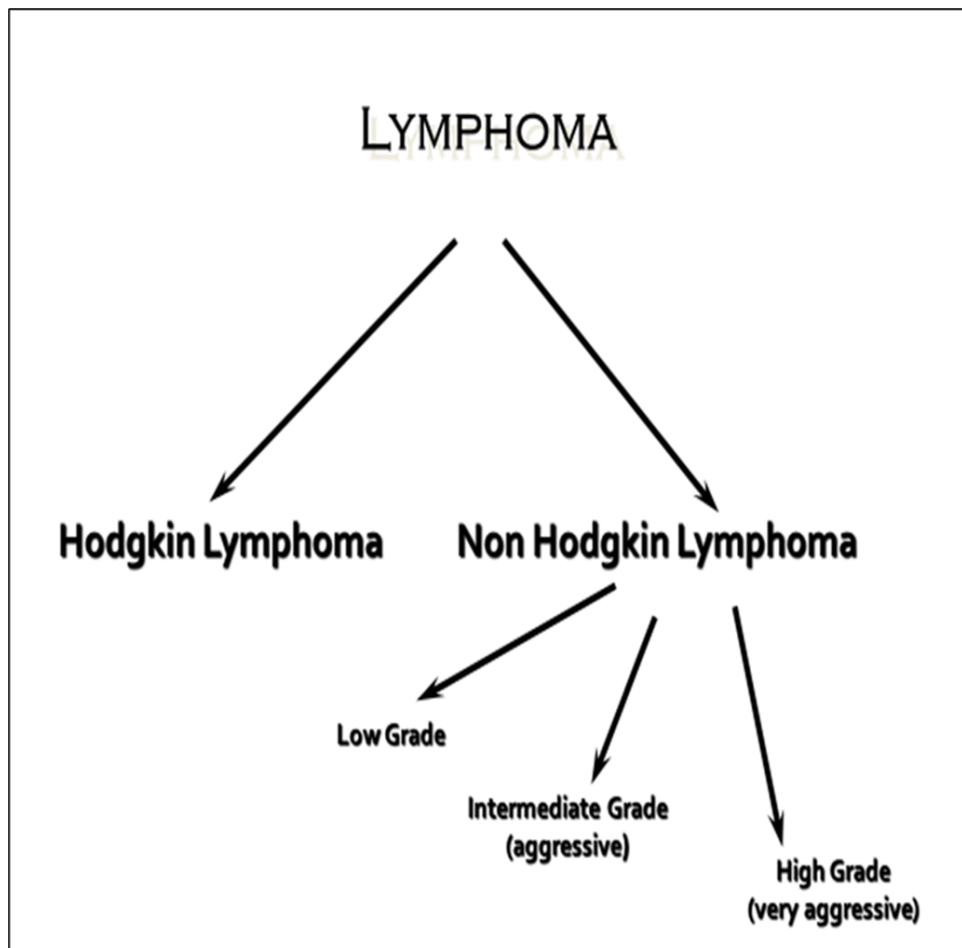


Table 12.7 WHO Classification of Lymphoid Neoplasms*

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

NK, Natural killer; WHO, World Health Organization.

*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 →

بدنا نحكي عن ال non Hodgkin's lymphoma
تحديدا عن ال B cell neoplasm
تحديدا عن الخلايا ال mature

Low grade B-cell NHL

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



والثانية lymphoma موجودة بال lymph node

بختلفو عن بعض لانه وحدة leukemia موجودة في
ال peripheral blood او bone marrow

- **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 معنا ال hypogammahlobulinemia يعني
- **Hypo**gammaglobulinemia with increased risk for bacterial infections. decreased بال immunoglobulin يعني
decreased بال antibody يعني نقص بالمناعة
- 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%

بالرغم من انه ال SLL صغيرة الحجم و low grade الا انها ممكن احيانا تتحول الى
diffuse large cell lymphoma اسمها higher grade lymphoma

□ Morphology

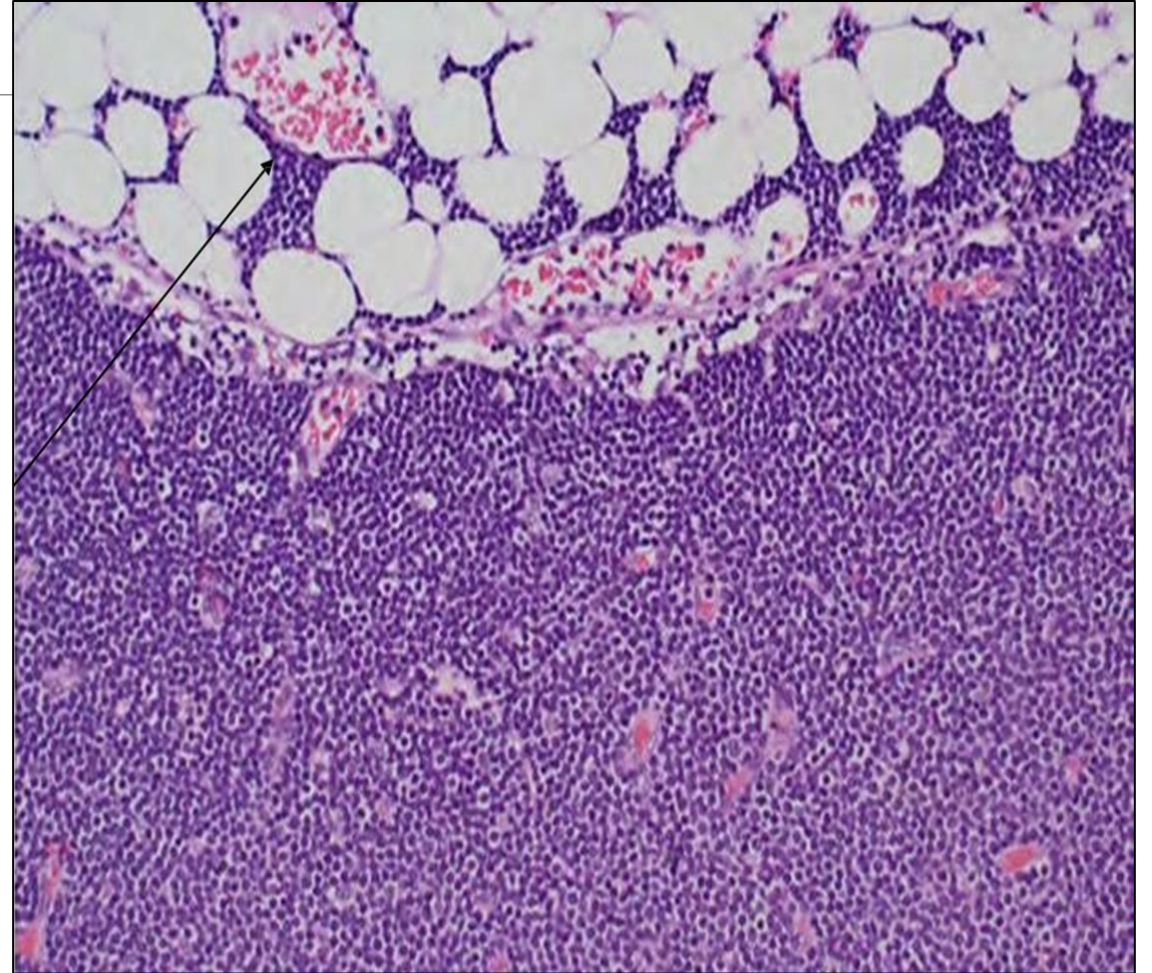
- Lymph nodes are effaced by **diffuse** sheets of **small, resting lymphocytes** with scant cytoplasm and dark, round nuclei with clumped chromatin reminiscent of a **soccer ball**.



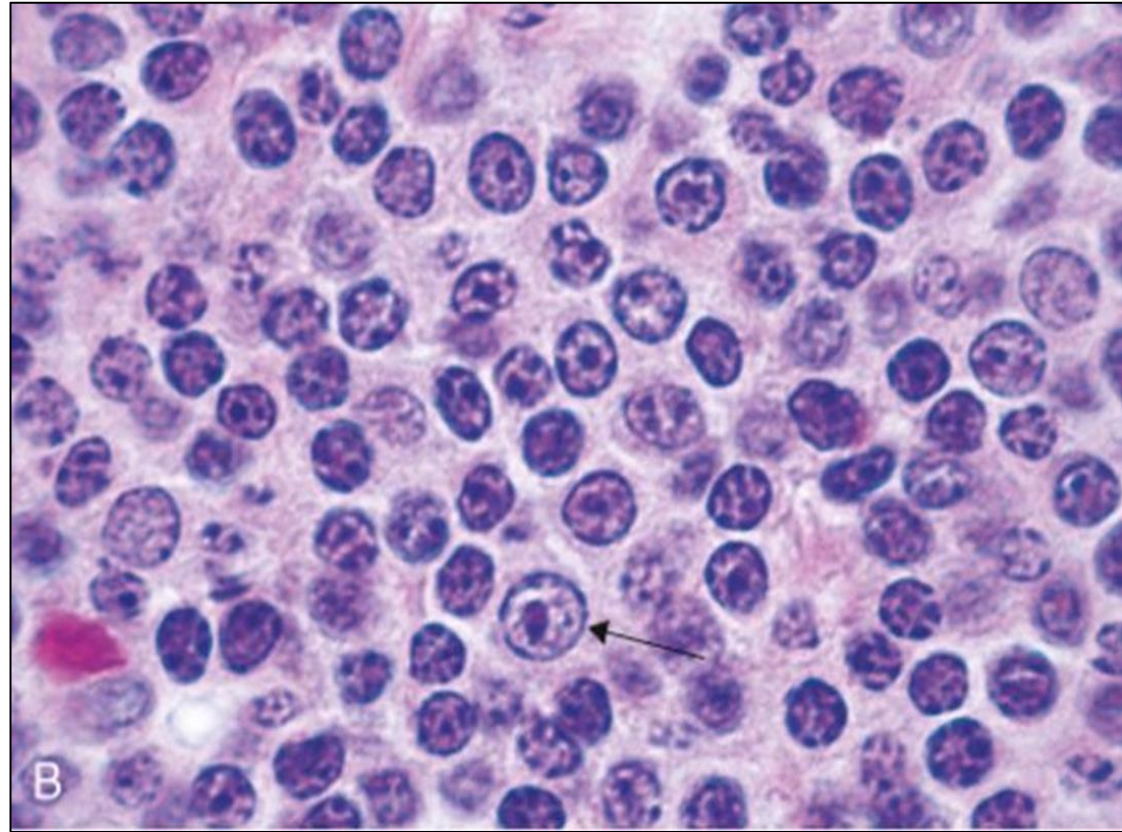
- The infiltrate extends through the capsule into the adipose tissue.
- There are scattered ill-defined foci of larger, actively dividing cells (**prolymphocytes**): **proliferation centers**
- The bone marrow, spleen, and liver are involved in **ALMOST ALL CASES** (Small lymphocytic infiltrate)

تقريباً كل المصابين بال SLL بوصول إلى
bone marrow ,spleen,and liver

والقاعدة العامة بتحكي كل ما كان ال tumour low grade كل ما
كانت احتمالية يآثر على ال bone marrow ,spleen ,liver أعلى



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



Peripheral blood:

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)

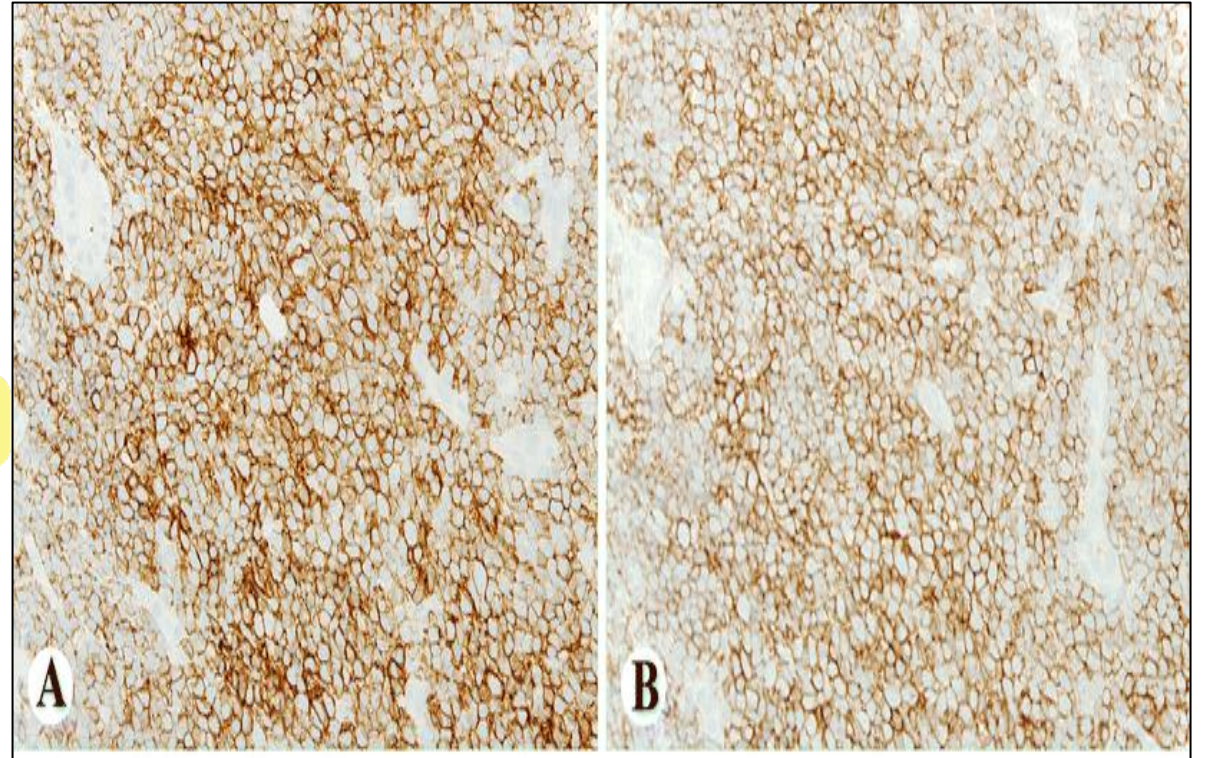


□ Immunophenotyping

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**.

بسبب هذه الزيادة بتبطل الخلايا تموت فبتكون المشكلة بهذا الtumour انه الخلايا ما بتموت اكثر من مشكلة انه بصيرلها proliferation

Microscopically:

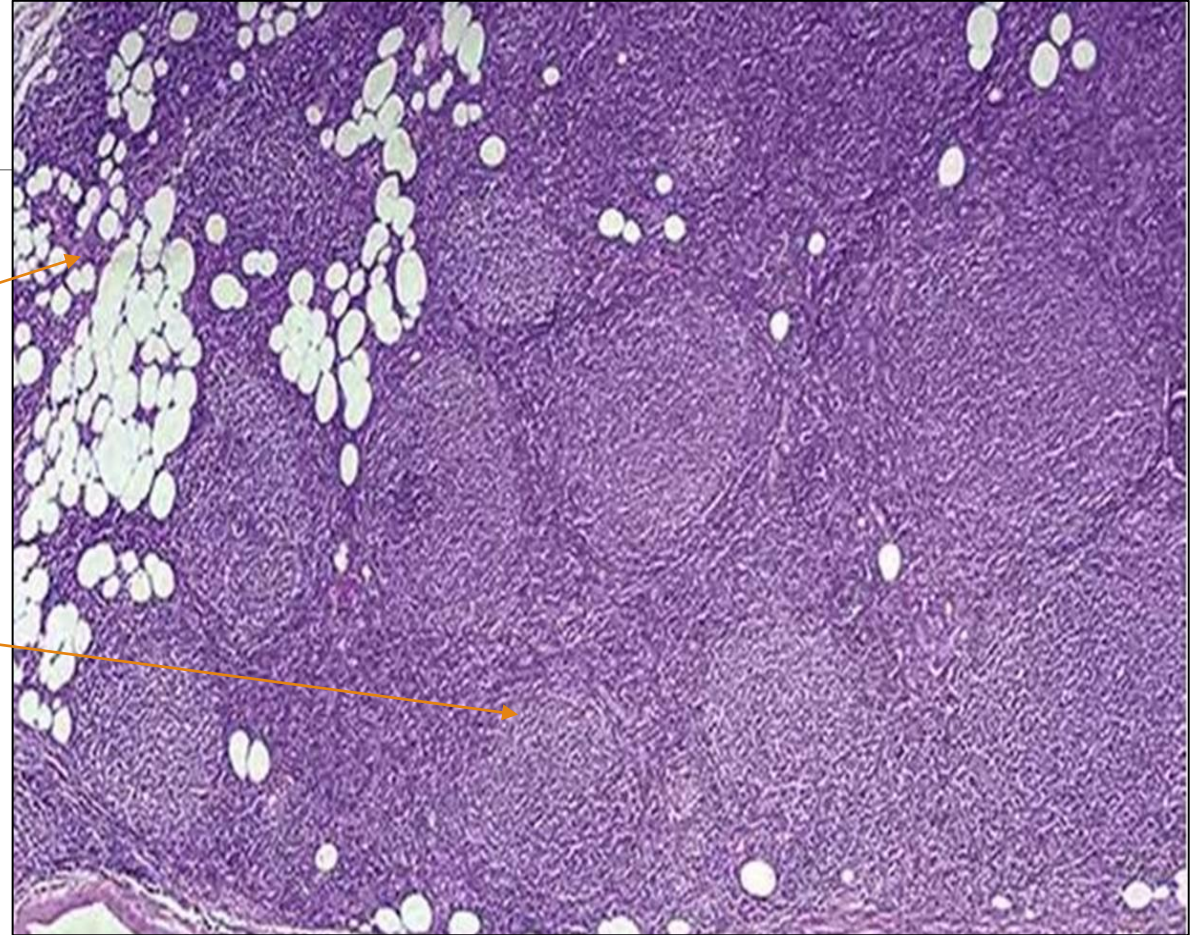
- Lymph nodes are effaced by **nodular follicular** appearance.
- The follicles have **two** types of neoplastic cells:
 - ❖ **Centrocytes:** Slightly larger than lymphocytes, with angular “**cleaved**” nuclei, coarse chromatin, and indistinct nucleoli.
 - ❖ **Centroblasts:** Large cells with fine chromatin, 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**

لانه الخلايا ما بتموت فبتكون ما فيها macrophages وما بنشوف tangible reactive follicular hyperplasia ال حالات ال bodies macrophages apoptosis فما بكون فيها كثير mitosis ولا

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**.

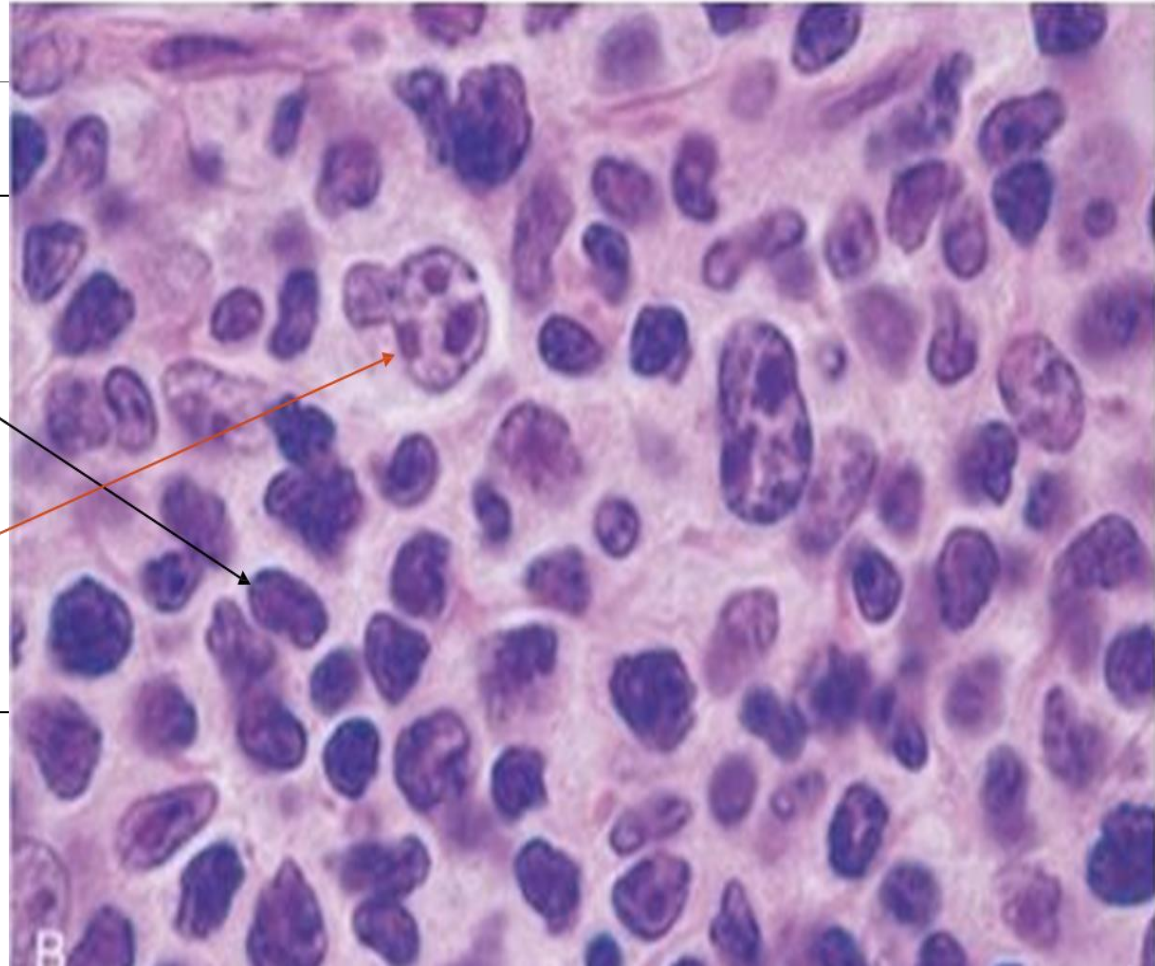
كلهم عاملين fat لل infiltration وهاد دليل على انها malignant



- 2 types of cells:

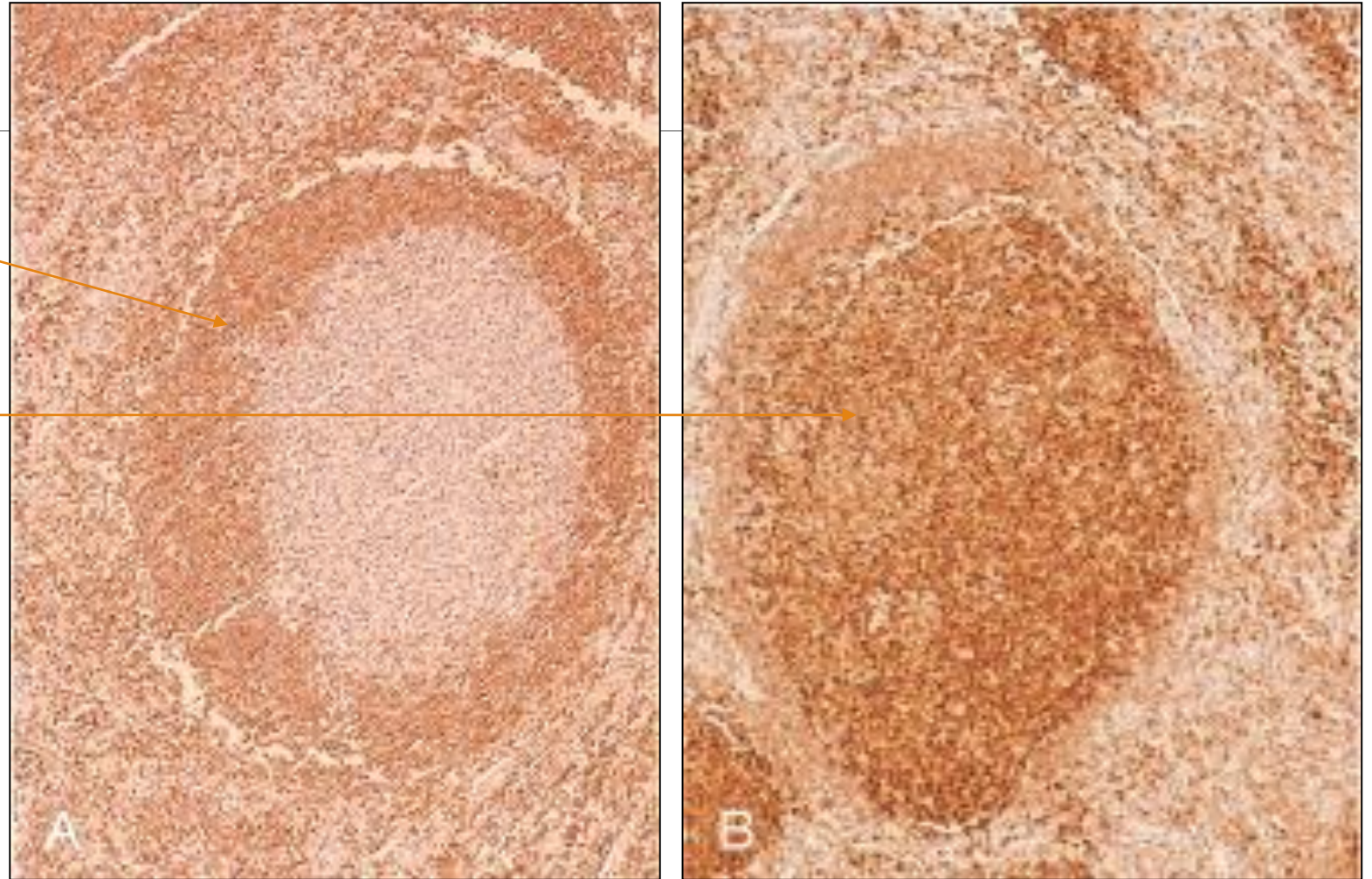
1. Centrocytes

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

ال BCL2 يكون POSITIVE بكل
ال follicle كاملة عشان هيك كلها ماخدة
positive يعني brown colour
لل BCL2 بينما لو كانت
ال center ما بياخد positive لل BCL2
و بضل لونه ابيض بضله negative



normal lymphoid tissue سميت malt lymphoma لأنها بتشبه ال
وجودة بجسمنا

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).

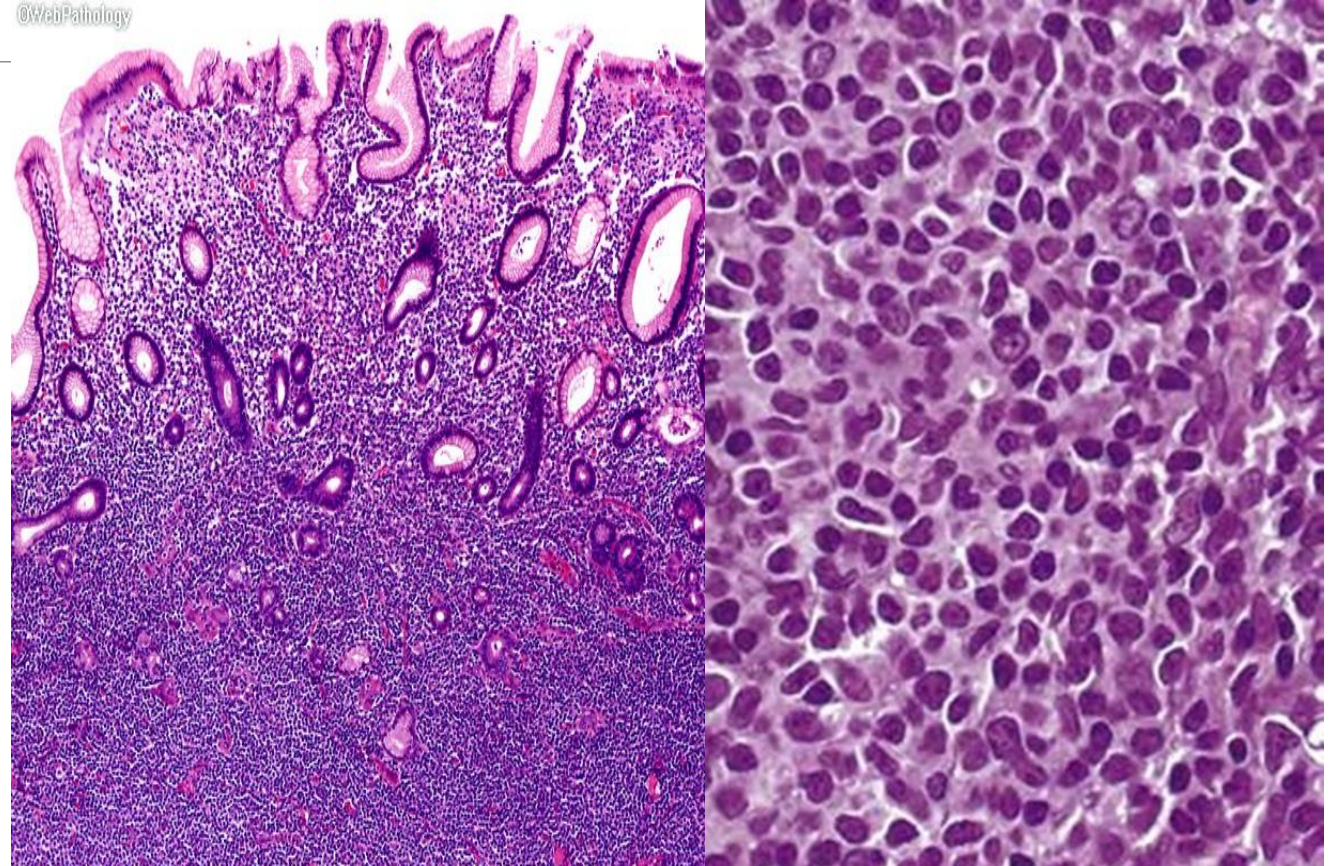
يعني لو عالجننا ال H.pylori بال antibiotic من البداية كان ممكن
يصير عنده regression بال lymphoma و يتحسن

فهي تعتبر low grade ونوعا ما كويسة لأنها ممكن علاجها و بضلها
localized

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**

@WebPathology



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.

ال cyclin D1 بحفز
ال proliferation في الخلايا

مهم: لازم تحفظو ال translocation

ال lymphoma فيهم بس 3 translocation لازم تحفظوهم وتعرفو كل واحد

بأي نوع من ال lymphoma بصير

➤ Morphology

ممکن تـجـي بالطريقتين لانها intermediate

-Diffuse or vaguely **nodular** pattern.

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

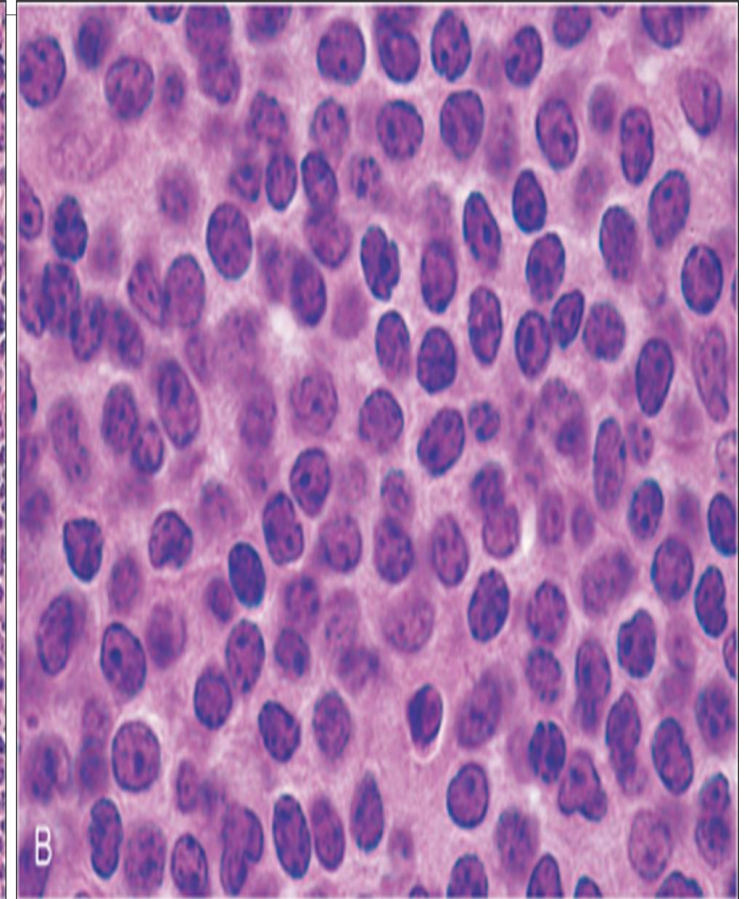
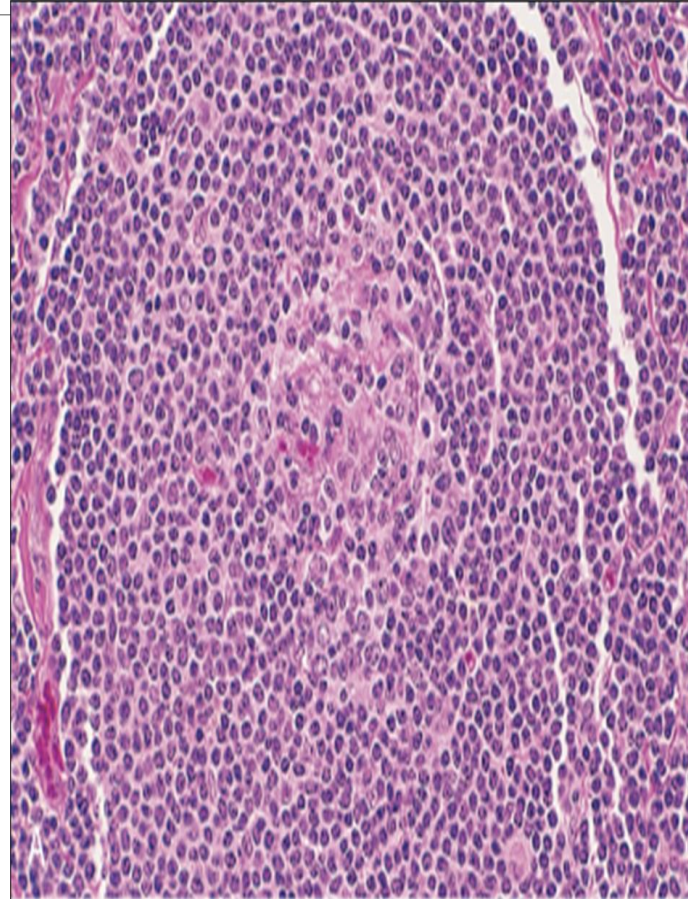
Neoplastic cells are positive for:

CD19

CD20

CD5

But lack CD23 (-).



هلا صار عندي ال CD5 بطلع positive بحالتين اما
ال SLL او ال mantel cell lymphoma
طيب هلا كيف بدنا نميز بيناتهم ؟
عن طريق يا اما بنثبت انو عندي
mantel cell lymphoma و بالتالي هاد
translocation(11;14) cyclin D1
بكون positive برضو لل
lymphoma او بنعمل CD23 بكون
positive in the SLL و لكن
negative في ال mantel cell lymphoma

HIGH GRADE B CELL NHL

In general بكونو aggressive tumour

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.

يعني كثير : Extranodal
ممکن تصیر برا ال

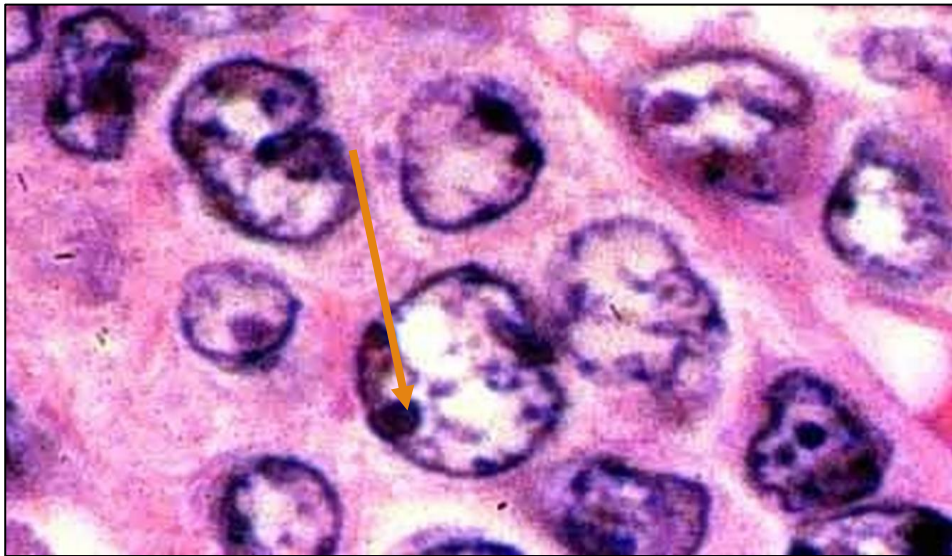
Lymph node
ممکن یجی المریرض بکتلة بأی مکان
diffuse large B وتكون بجسمه

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

حکینا انه المریرض الی عنده follicular lymphoma ممکن مع الزمن یتحول ل diffuse large B
فبتالی بهای الحالات بكون عند المریرض نفس ال translocation الی کان موجود بال follicular
lymphoma الی هو t(14;18)

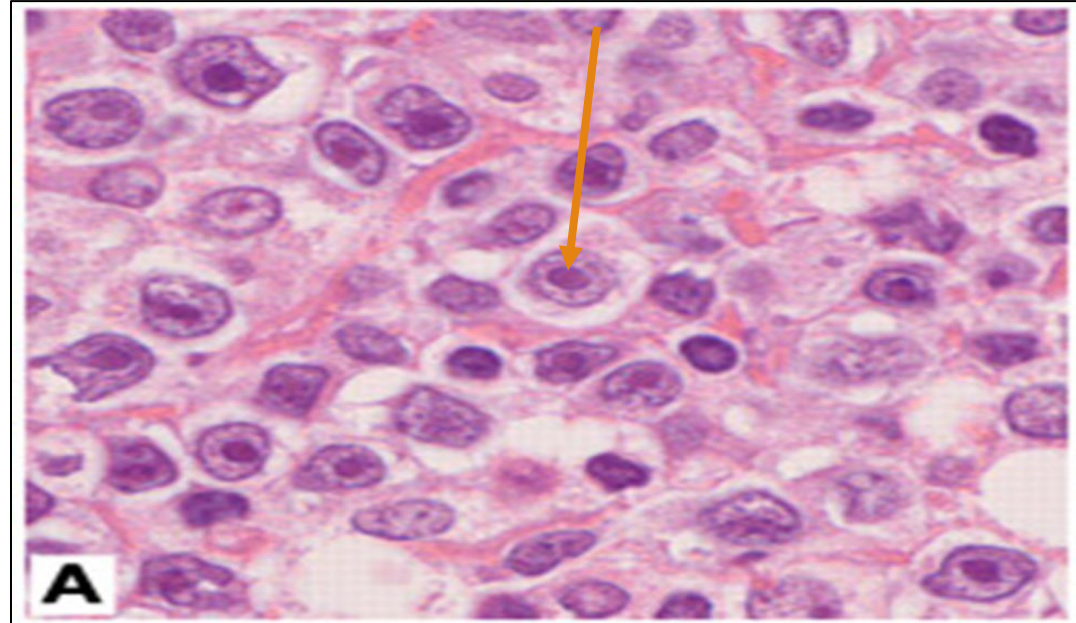
❖ Morphology:

- **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

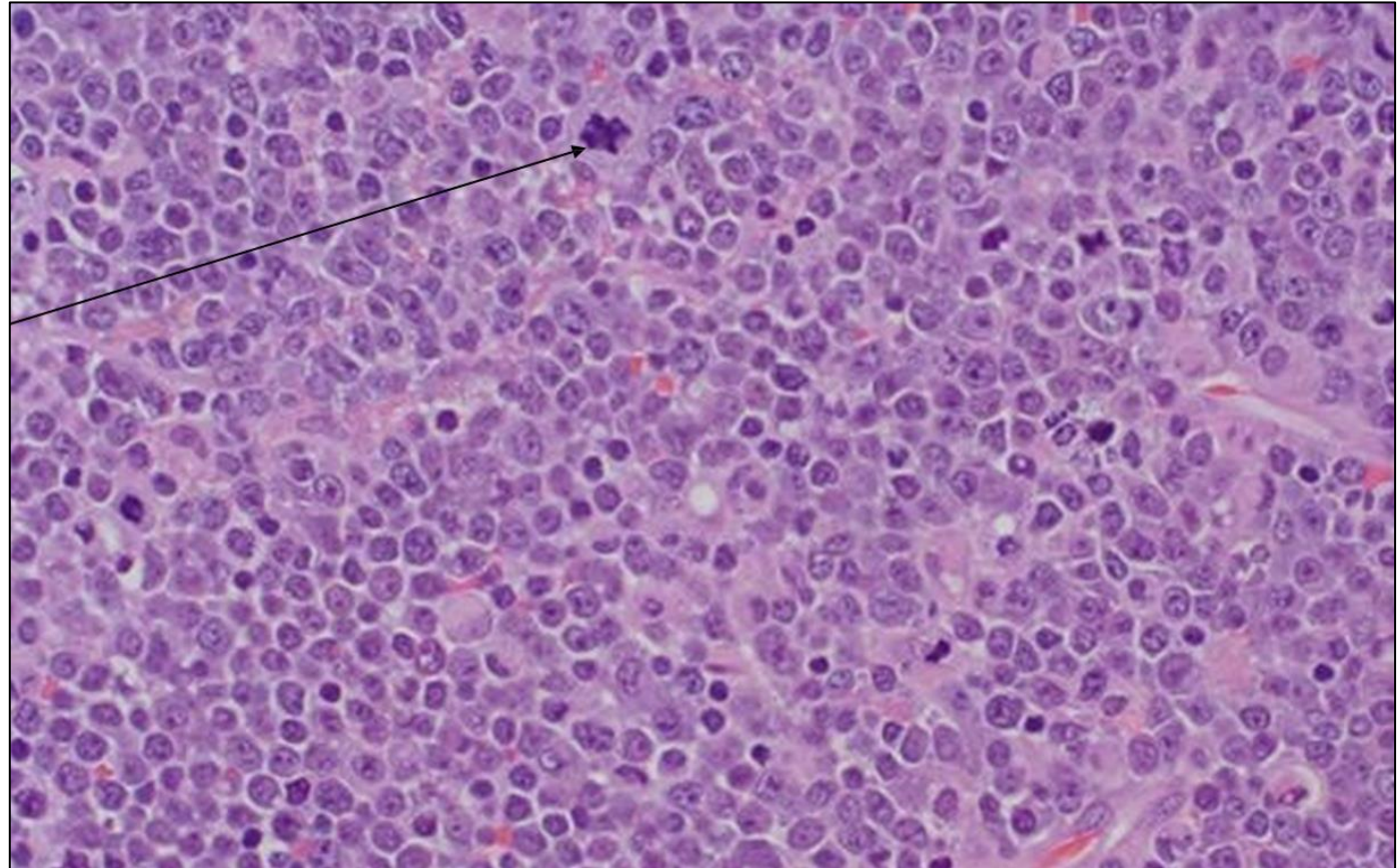


لون ال tissue كله صار بink بسبب كمية السيتوبلازم والا بالعادة كان لونها dark

- ❑ **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

With immunodeficiency

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.
يكون في تراكم للسوائل بالجسم
3. **Mediastinal** Large B cell lymphoma occurs in young women with a predilection to involve viscera & CNS.
بتصير بمنطقة الصدر وفي خطورة انه ينتشر