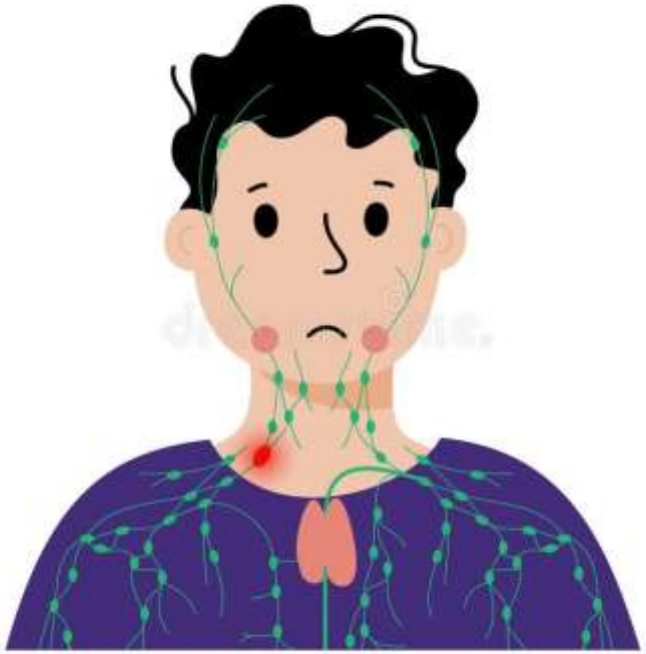
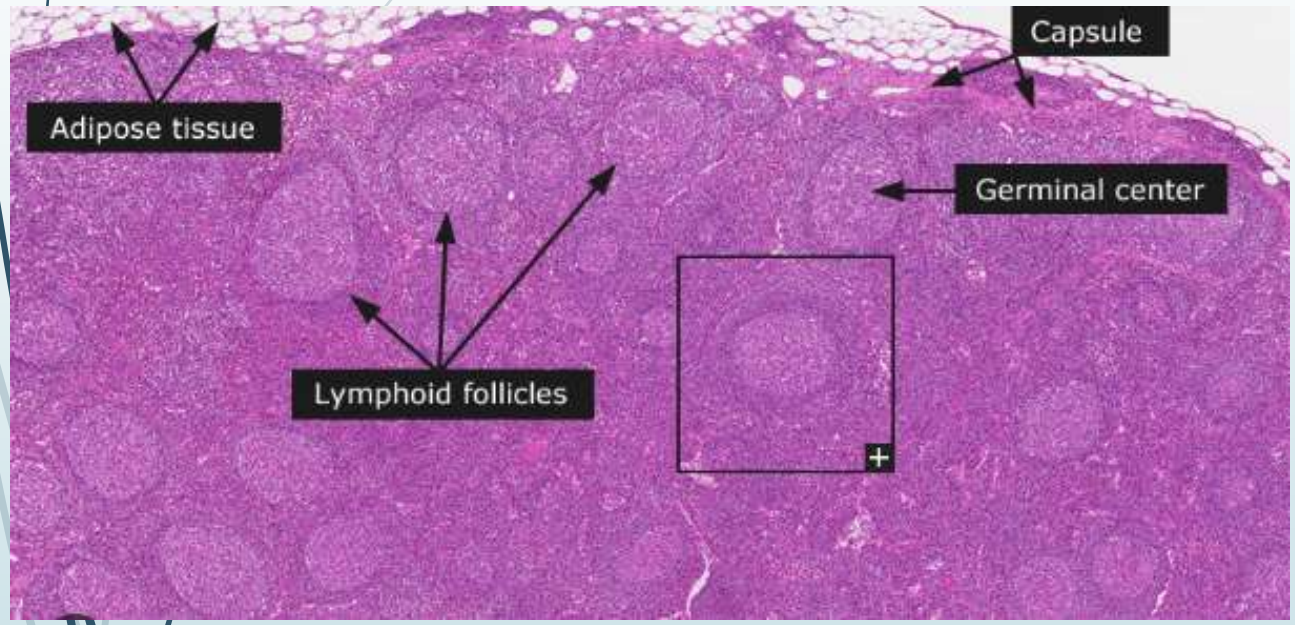
Lymphoma I.

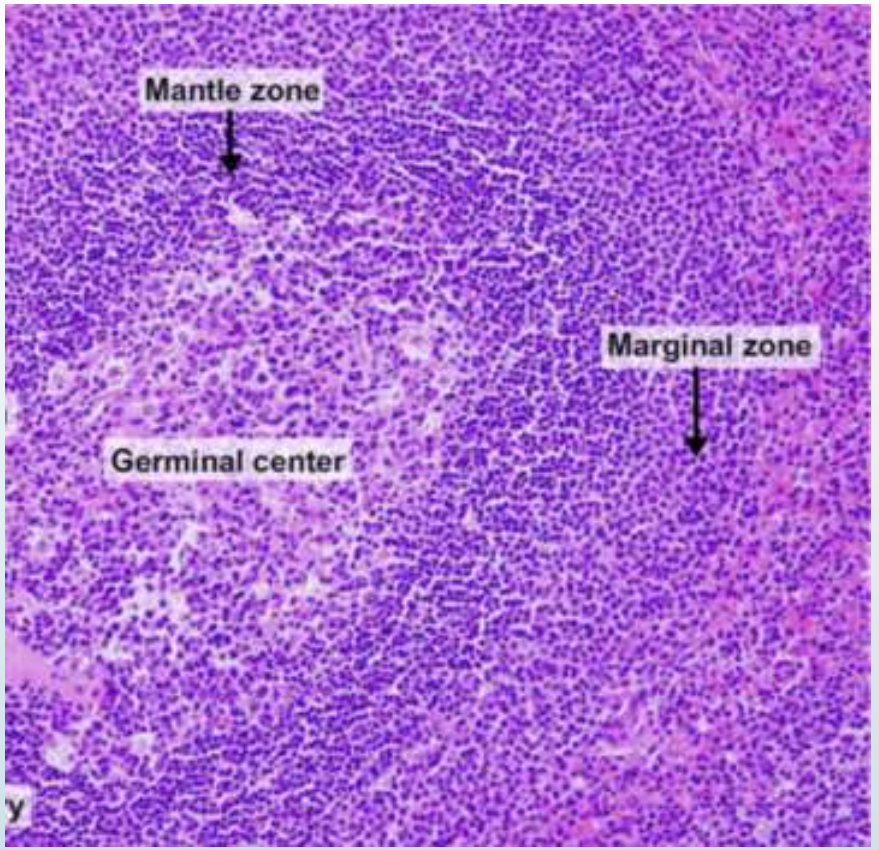


Dr. Eman Krieshan, M.D.

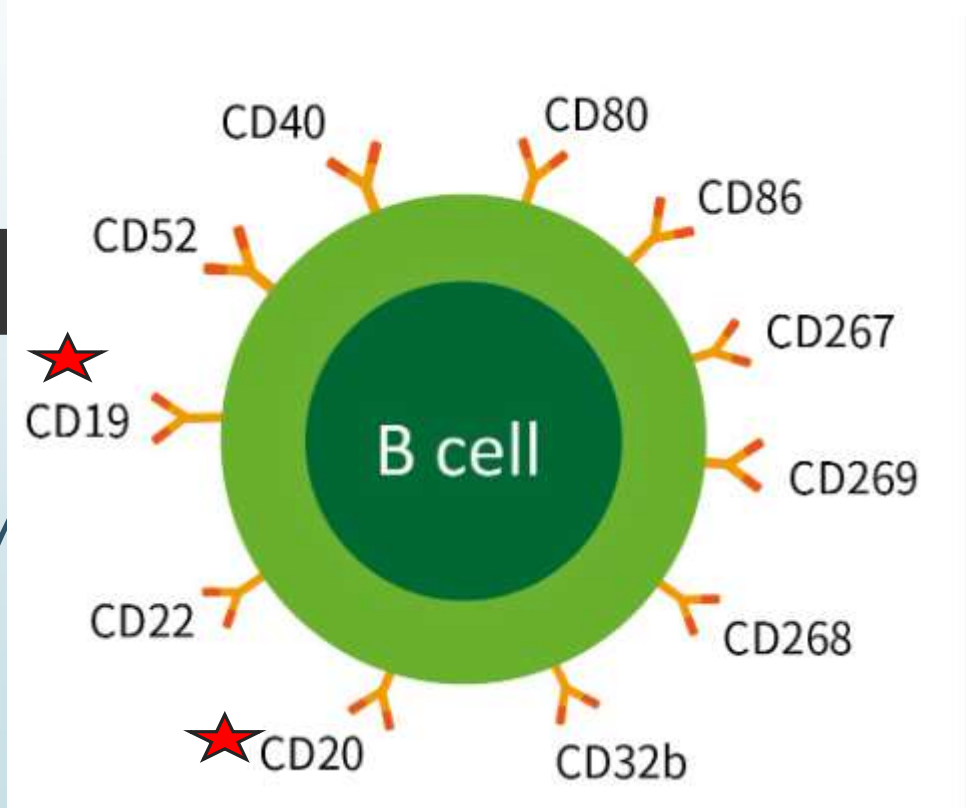
10/4/2023

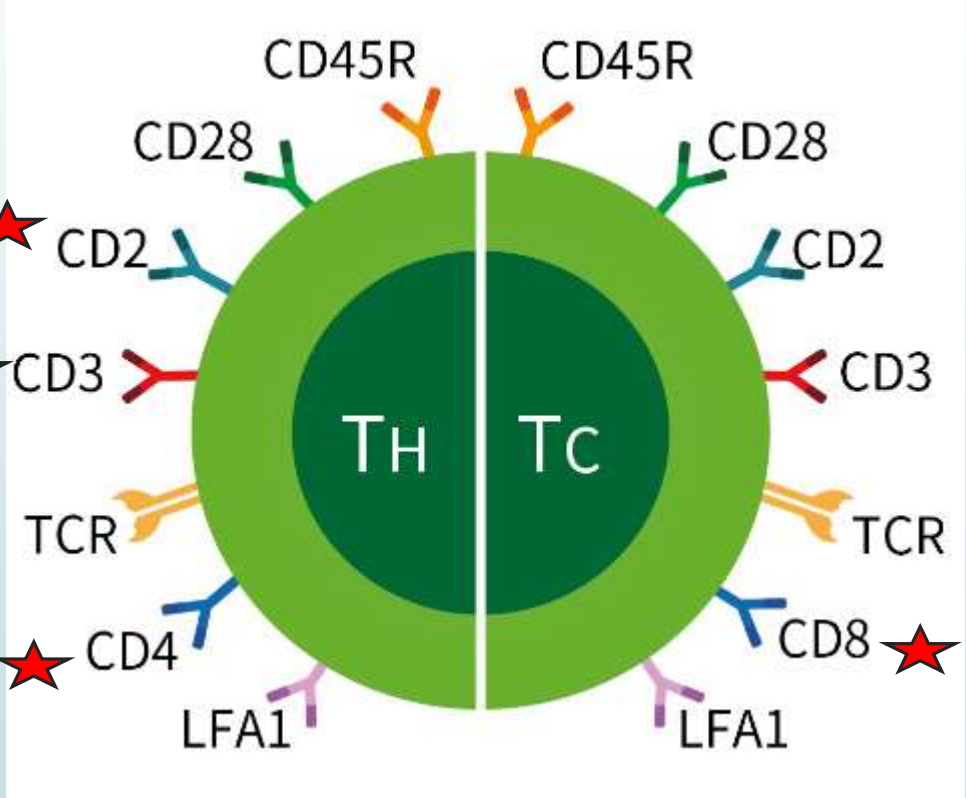
Histology


Capsule
Adipose tissue
Germinal center
Lymphoid follicles


Mantle zone
Marginal zone
Germinal center

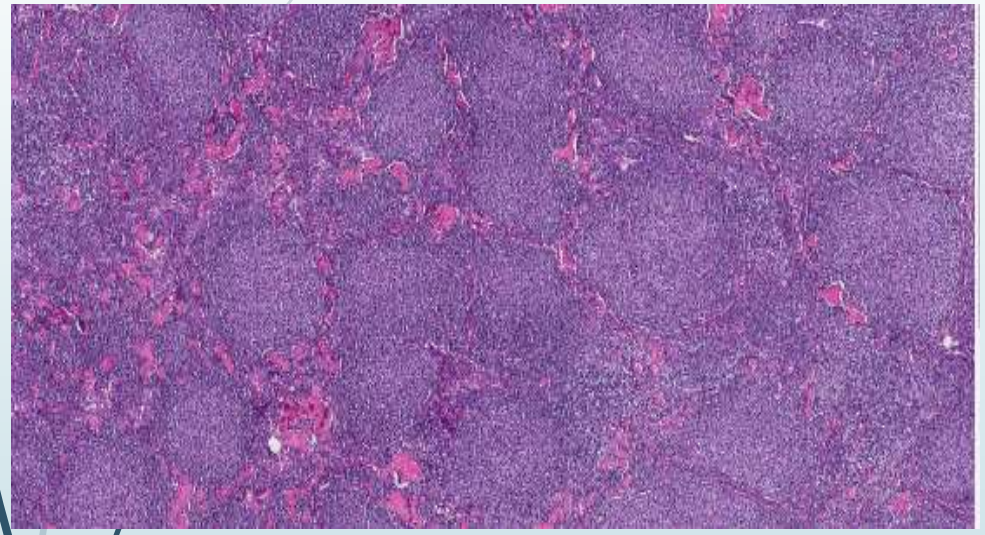
B VS T lymphocytes



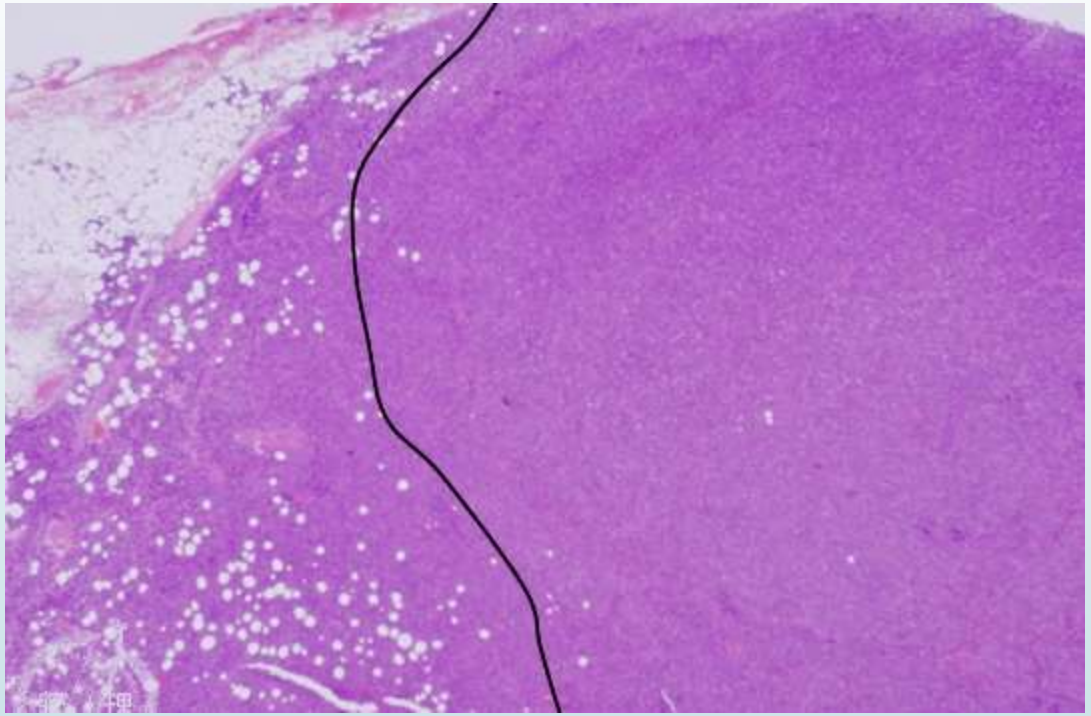


- Lymphoid neoplasms:
- NEOPLASTIC PROLIFERATIONS OF WHITE CELLS, if presented as:
  - tumors that produce masses in lymph nodes or other tissues :Lymphoma.
  - involvement of the bone marrow and the peripheral blood: Leukemia.

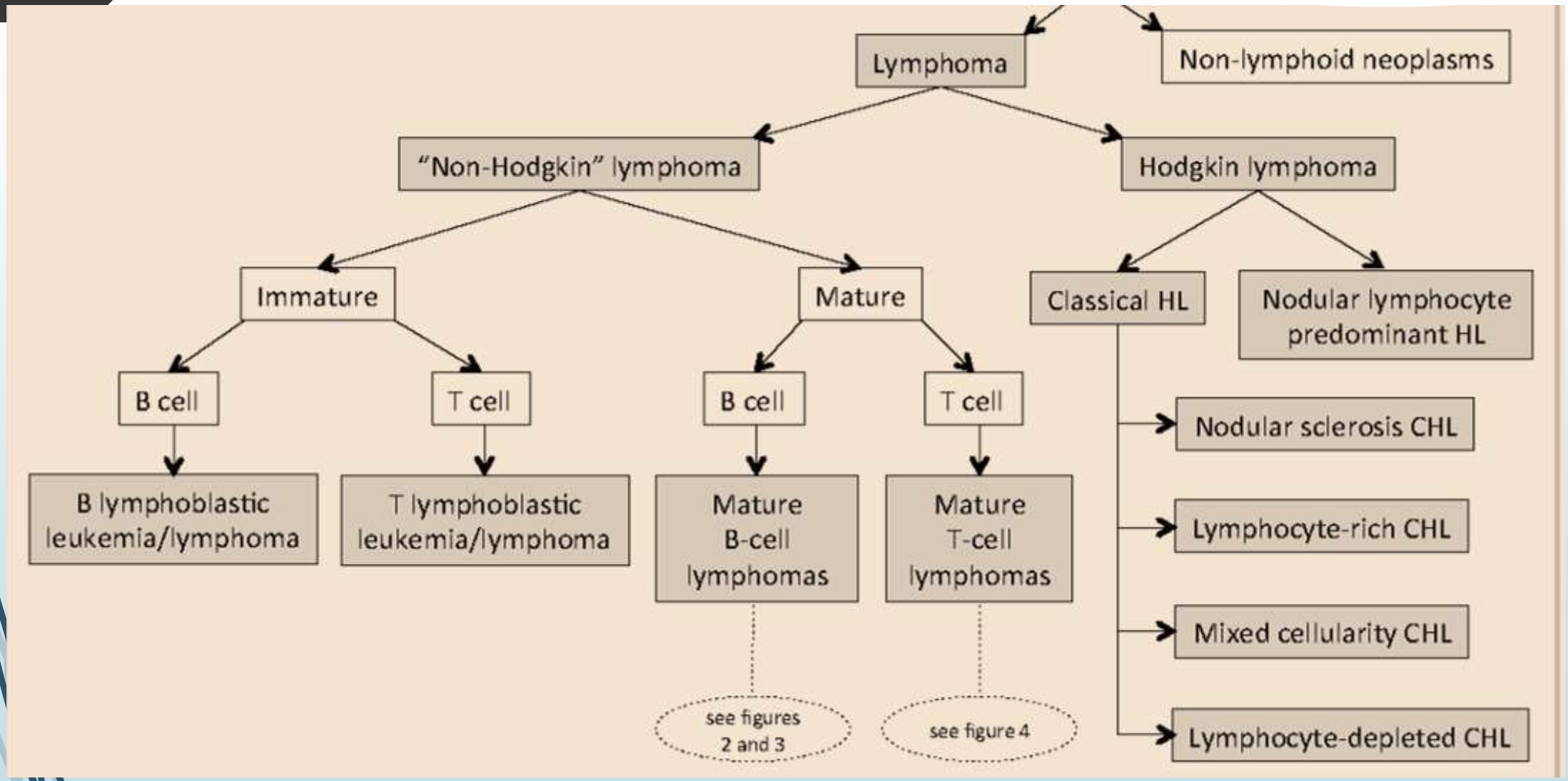
Lymphoma :disturbed architecture

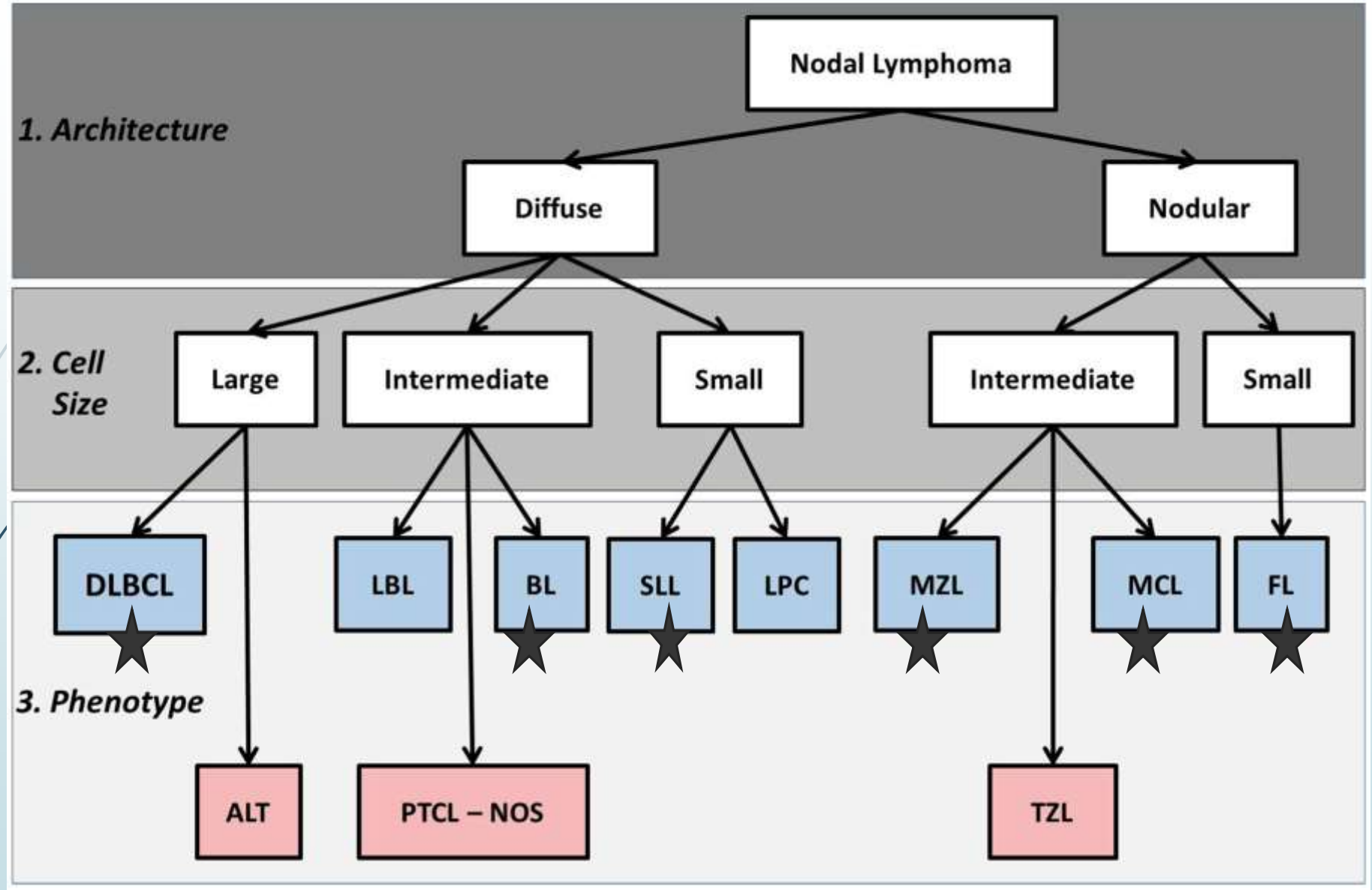


nodular



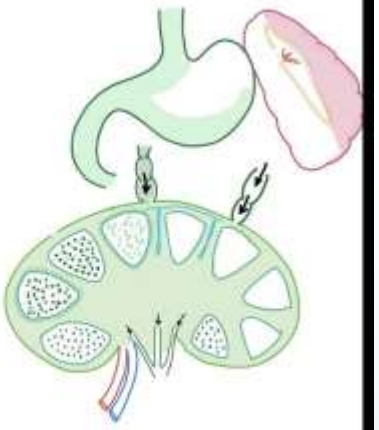
Diffuse


Lymphoma
Non-lymphoid neoplasms
"Non-Hodgkin" lymphoma
Hodgkin lymphoma
Immature
Mature
Classical HL
Nodular lymphocyte predominant HL
B cell
T cell
B cell
T cell
Nodular sclerosis CHL
B lymphoblastic leukemia/lymphoma
T lymphoblastic leukemia/lymphoma
Mature B-cell lymphomas
Mature T-cell lymphomas
Lymphocyte-rich CHL
Mixed cellularity CHL
see figures 2 and 3
see figure 4
Lymphocyte-depleted CHL

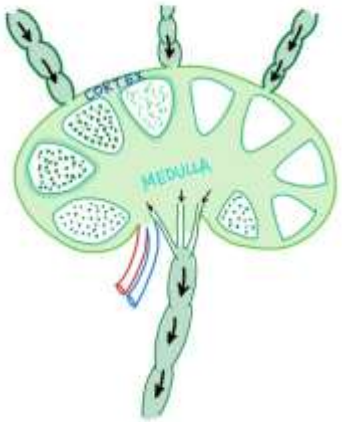

Nodal Lymphoma
1. Architecture
Diffuse
Nodular
2. Cell Size
Large
Intermediate
Small
Intermediate
Small
DLBCL
LBL
BL
SLL
LPC
MZL
MCL
FL
3. Phenotype
ALT
PTCL – NOS
TZL

Follicular Lymphoma

Marginal Zone B-Cell Lymphoma

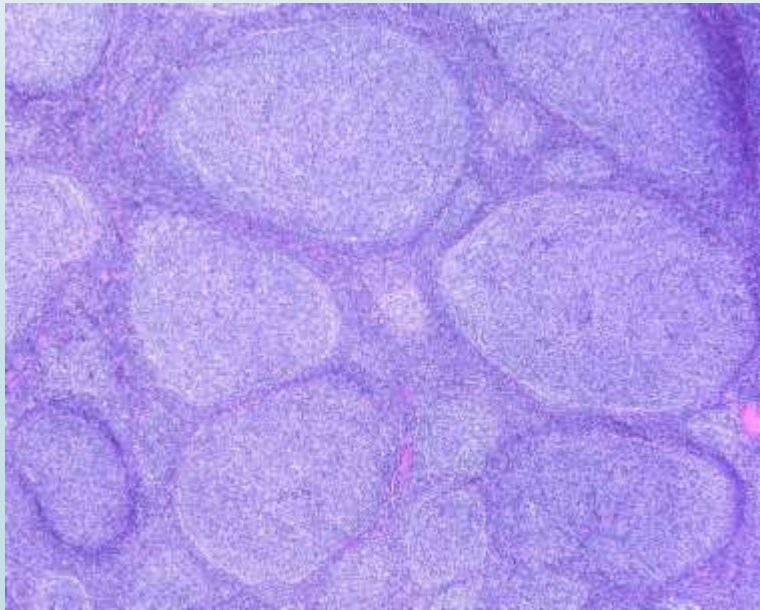


Mantle cell Lymphoma



I. Follicular lymphoma

- A 66-year-old man has noted an increasing number and size of lumps over his body in the past 5 months. On examination, there is firm, nontender inguinal, axillary, and cervical lymphadenopathy. A biopsy specimen of a cervical node shows the following appearance. A bone marrow biopsy specimen shows lymphoid aggregates of similar cells with surface immunoglobulins that are CD10+, but CD5−. Karyotyping of these lymphoid cells indicates the presence of t(14;18). What is the most likely diagnosis?
- A Acute lymphadenitis
- B Hodgkin lymphoma, nodular sclerosis type
- C Follicular lymphoma
- D Mantle cell lymphoma
- E Toxoplasmosis



Follicular lymphoma.

- Relatively common tumor → 40% of the adult NHLs.
- Pathogenesis:

- inappropriate “overexpression” of BCL2 protein (an inhibitor of apoptosis) → contributes to cell survival.
- Genetic:
- a characteristic (14;18) translocation that fuses the BCL2 gene on chromosome 18 to the IgH locus on chromosome 14.

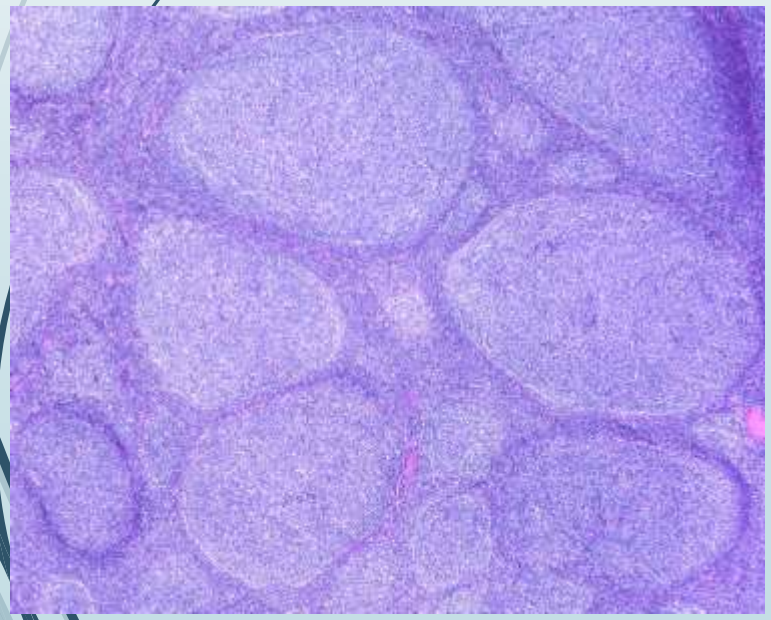
Clinical features

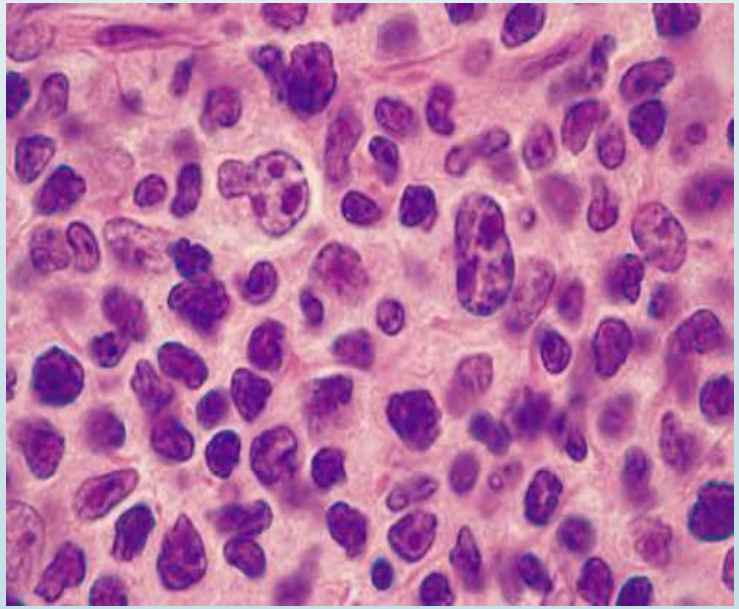
- Older than 50
- Generalized painless lymphadenopathy
- Bone marrow is involved in 80% of cases
- Prolonged survival, not curable disease (indolent)
- 40% transform into DLBCL, **dismal** prognosis

Morphology

- Lymph nodes usually are effaced by a distinctly nodular (follicular) proliferation
- Two types of neoplastic cells,

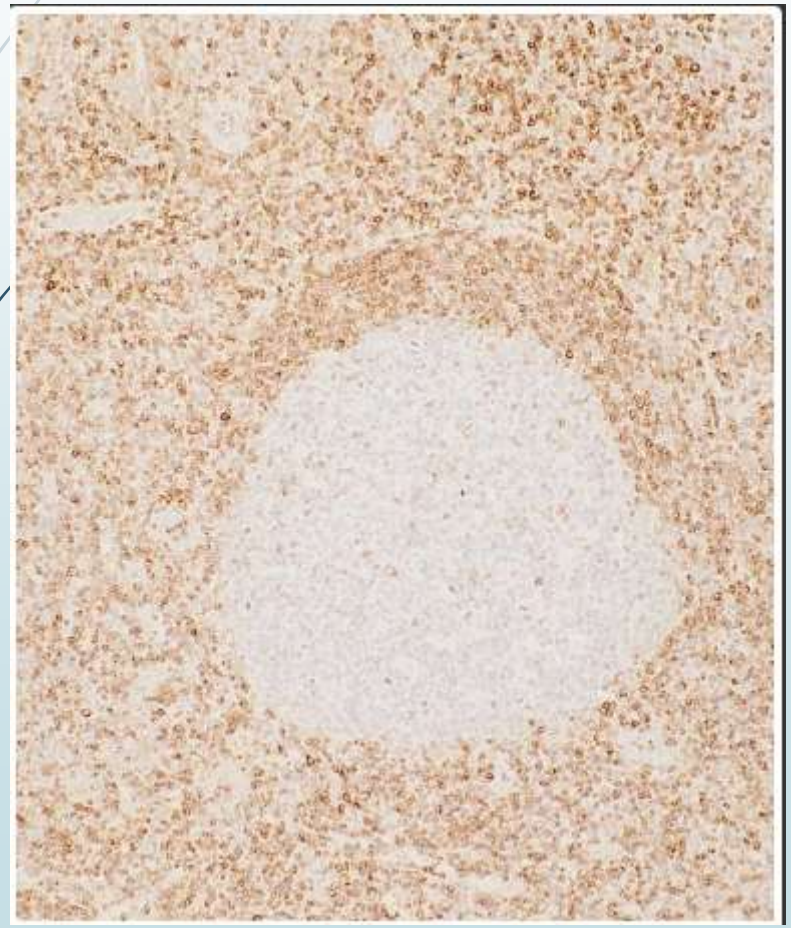
1) the predominant called centrocytes have angular “cleaved” & indistinct nucleoli,
2) the other centroblasts, larger cells with vesicular chromatin, several nucleoli.

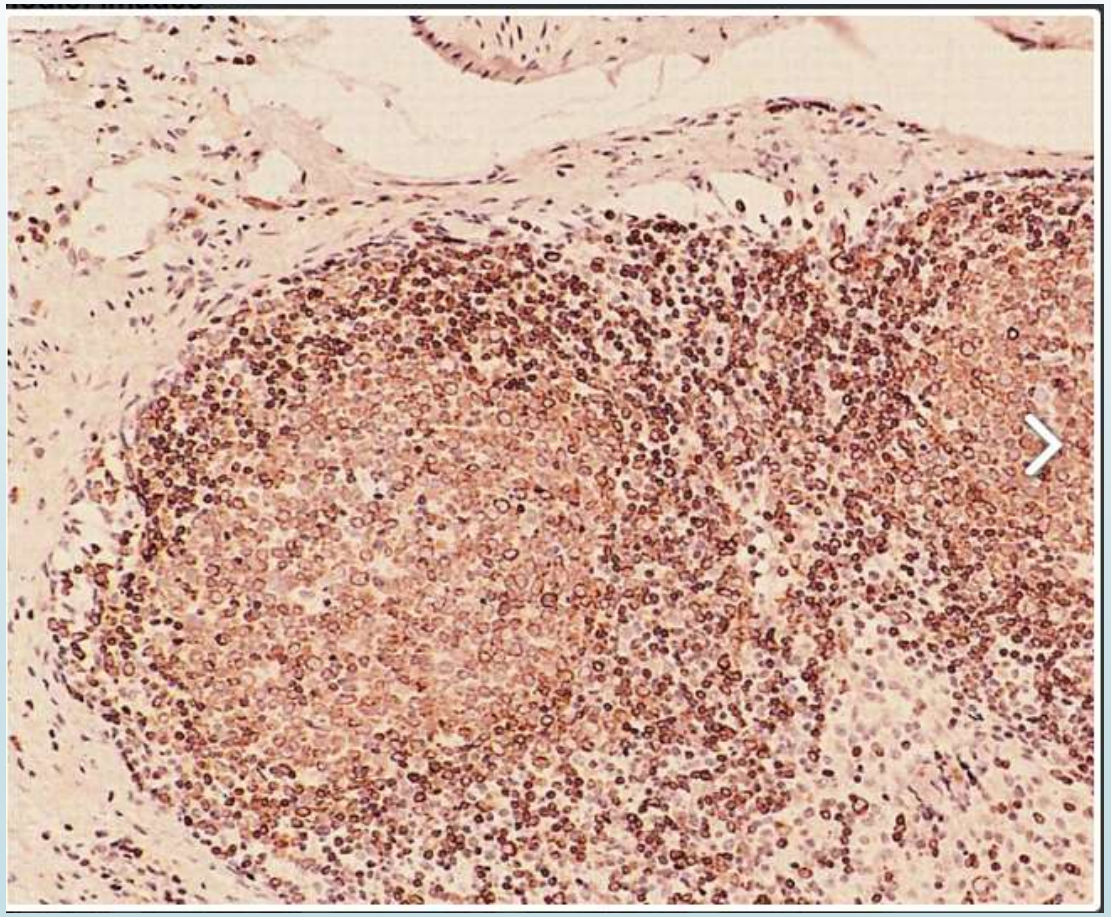




Immunophenotype

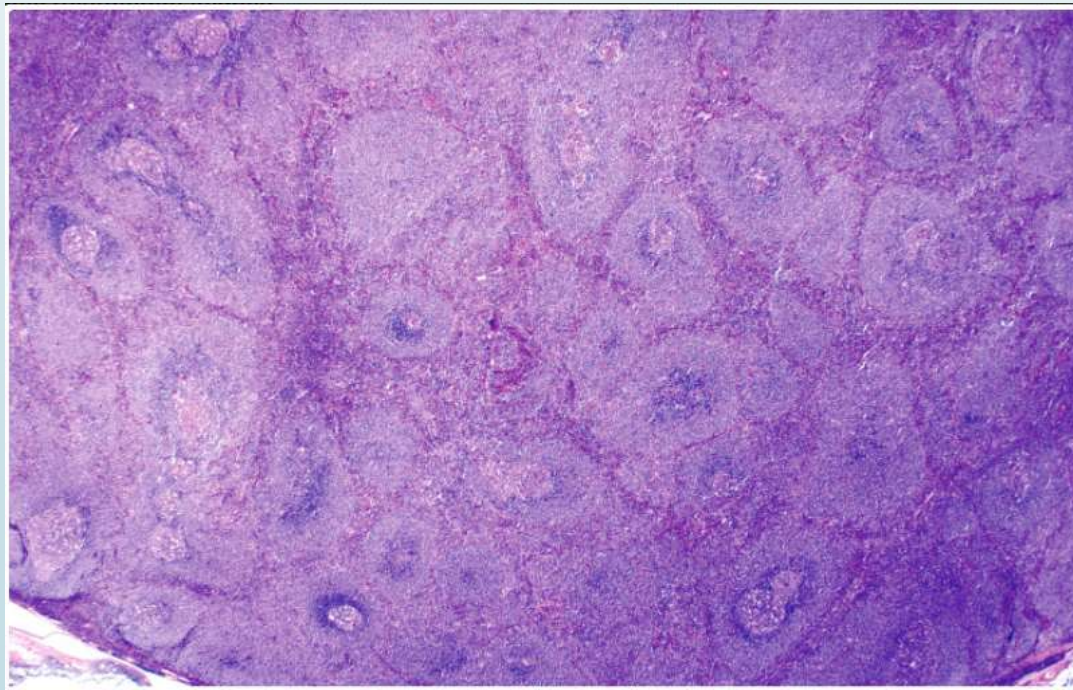
- B-cells markers (mature B cell neoplasm), CD10, BCL2





II. **Mantle Cell Lymphoma**

- A 62-year-old man has had fever and a 4-kg weight loss over the past 6 months. On physical examination, his temperature is 38.6° C. He has generalized nontender lymphadenopathy, and the spleen tip is palpable. A cervical lymph node biopsy specimen illustrated down. Cytogenetic analysis indicates t(11;14) in these cells. What is the most likely diagnosis?
- A Acute lymphoblastic lymphoma
- B Burkitt lymphoma
- C Follicular lymphoma
- D Mantle cell lymphoma
- E Small lymphocytic lymphoma



Mantle Cell Lymphoma

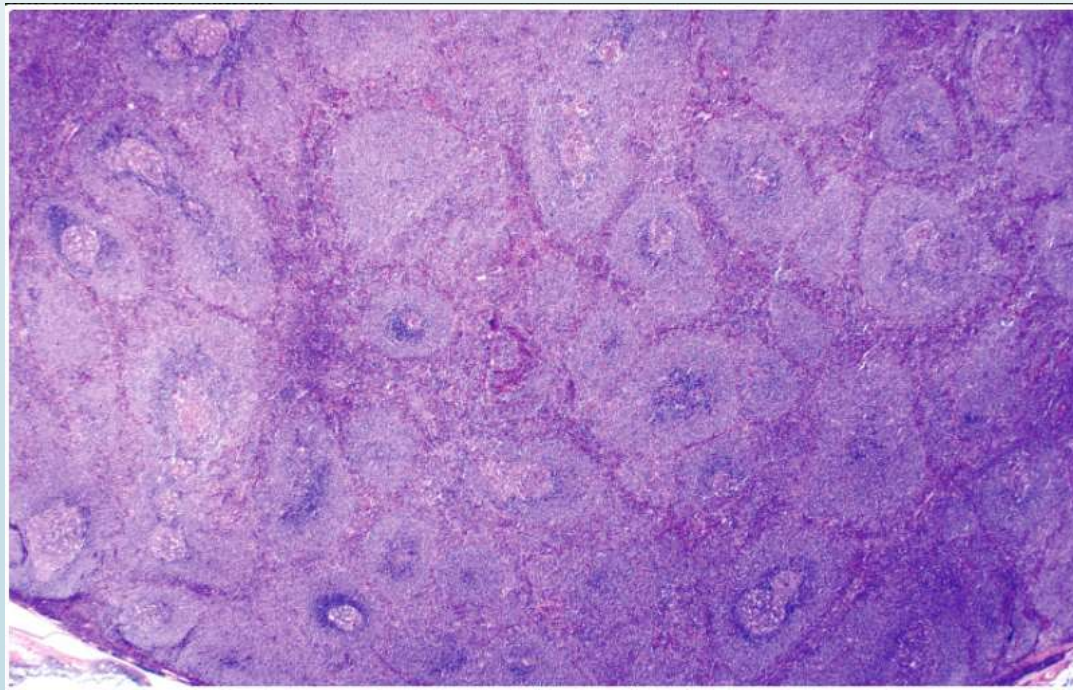
- mainly in men older than 50 years of age.
- All tumors have an (11;14) translocation → fuses the cyclin D1 gene to the IgH locus → overexpression of cyclin D1→ stimulates growth by promoting the progression of cell cycle from G1 to S phases)
- Moderately aggressive & incurable.
- The median survival is 4-6 years.

Clinical features

- Patients Present with fatigue & lymphadenopathy.
- generalized disease involving the bone marrow, spleen, liver, and (often) GIT.

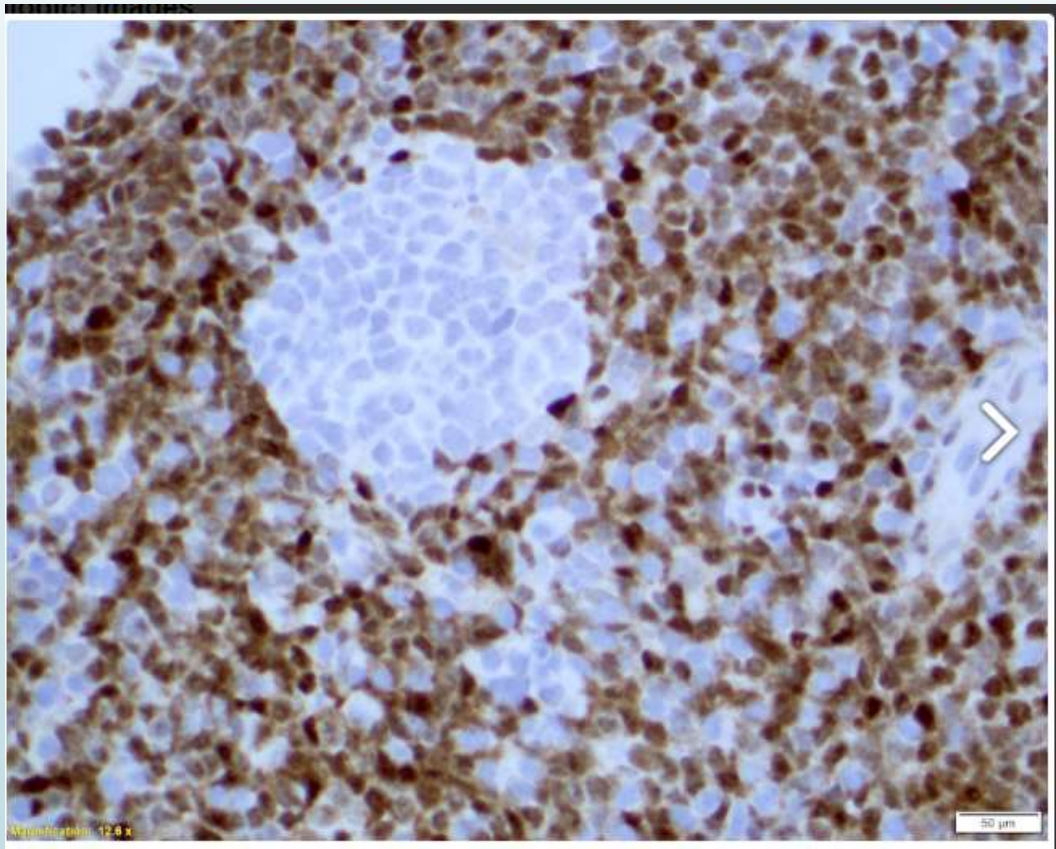
Morphology

- A diffuse or nodular involvement of the lymph node.
- The tumor cells are slightly larger than normal lymphocytes with irregular nucleus, inconspicuous (not clear) nucleoli.
- Bone marrow is involved in most cases.
- sometimes arises in the GIT as multifocal polyps (lymphomatoid polyposis).



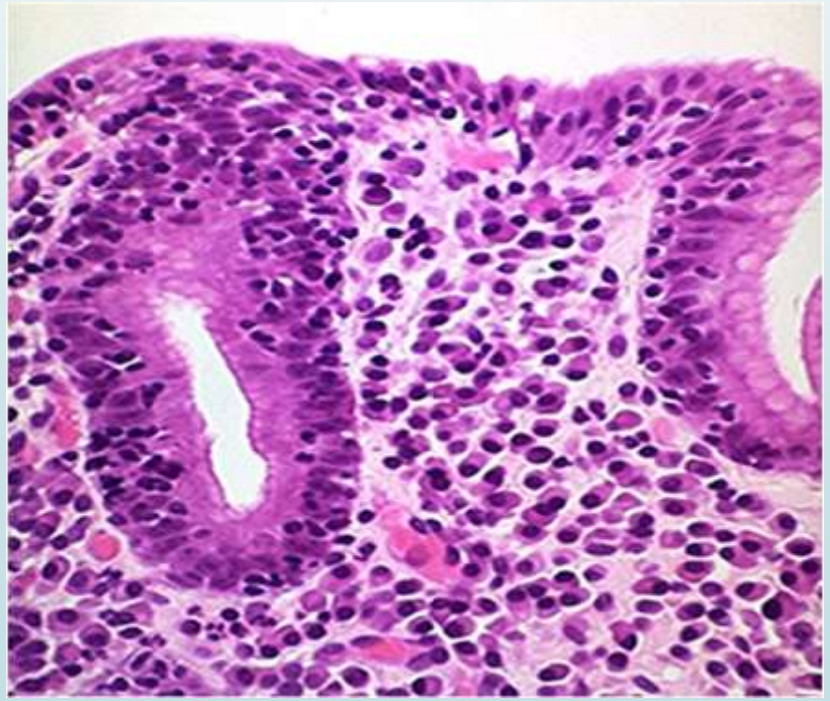
Immunophenotype

- B cell markers.
- CD5.
- Cyclin D1.



III. Extranodal Marginal Zone Lymphoma

- A 54-year-old woman has experienced nausea with vomiting and early satiety for the past 7 months. On physical examination, she is afebrile and has no lymphadenopathy or hepatosplenomegaly. CBC shows hemoglobin, 12.9 g/dL; hematocrit, 41.9%; platelet count, 263,000/mm3; and WBC count, 8430/mm3.Gastric biopsy is shown here. What is the most likely diagnosis?
- A Acute lymphoblastic leukemia
- B Chronic lymphocytic leukemia
- C Diffuse large B-cell lymphoma
- D Follicular lymphoma
- E Hodgkin lymphoma, mixed cellularity type
- F MALT (marginal zone) lymphoma



Extranodal Marginal Zone Lymphoma

- An indolent B cell tumor arises most commonly in epithelial tissues (e.g. GIT, salivary glands, lungs, orbit, & breast)
- an example of a cancer arises within & is sustained by chronic inflammation:

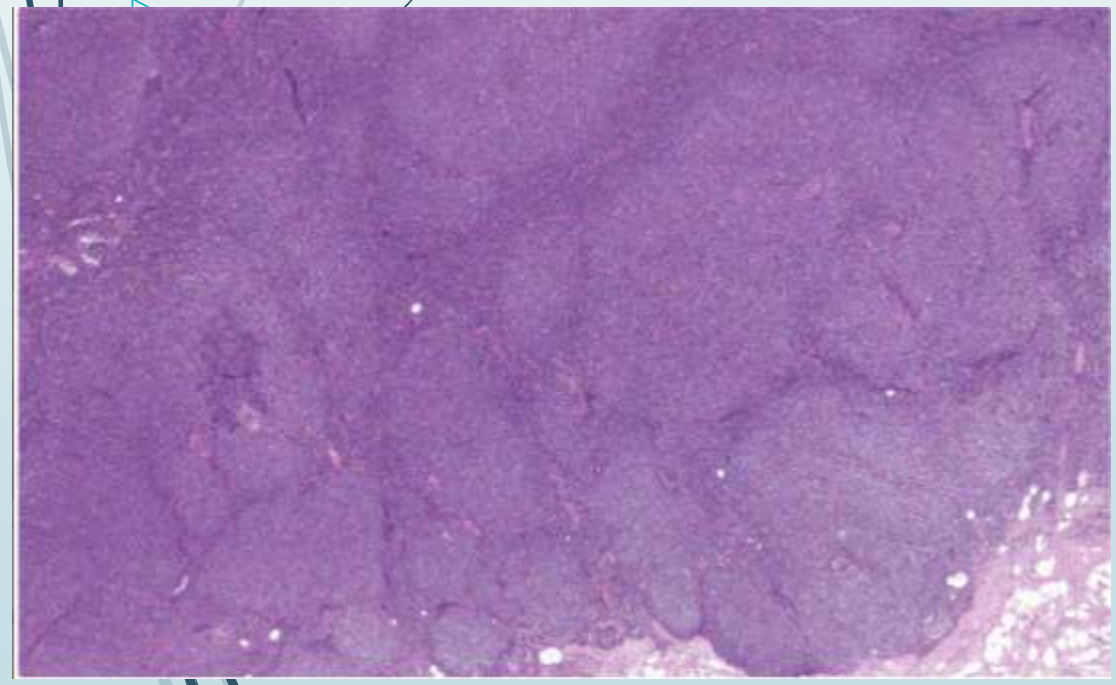
1) autoimmune disorders (salivary gland in Sjögren syndrome & thyroid gland in Hashimoto thyroiditis)
2) Chronic infection (such as H.pylori gastritis).

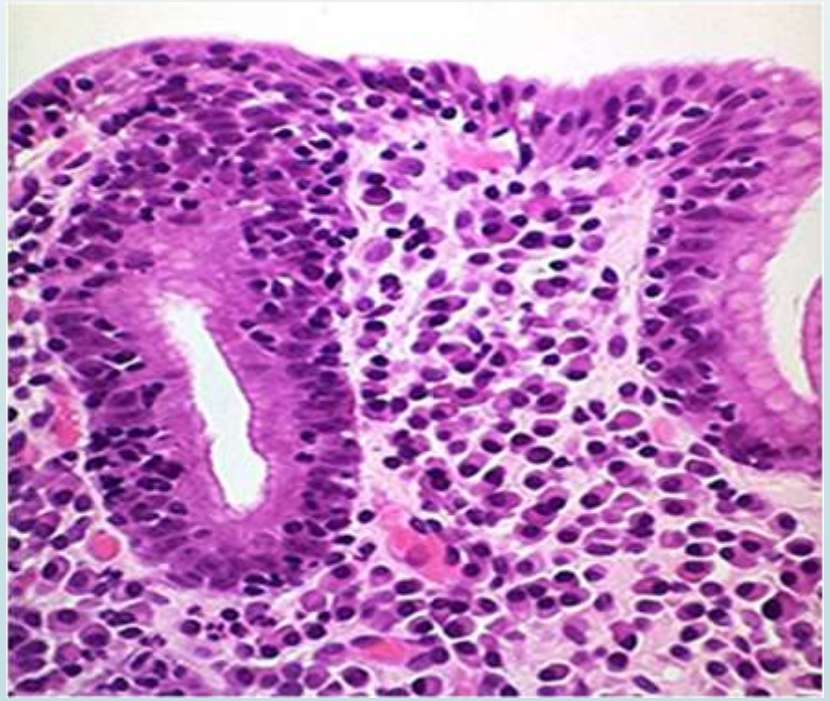
Clinical features

- Present as swelling of the salivary gland, thyroid or orbit or are discovered incidentally in the setting of H. pylori–induced gastritis.
- When localized, they are often cured by simple excision followed by radiotherapy.

Morphology and Immunophenotype

- Nodular, perifollicular and interfollicular lymphoid infiltrate that surrounds variably preserved germinal centers
- Gastric MZL (MALT lymphoma) showing intraepithelial atypical lymphocytes (lymphoepithelial lesion) and plasma cell differentiation in the lamina propria.
- Immunophenotype: B-cell markers.





IV. Chronic Lymphocytic Leukemia/Small Lymaphocytic Lymphoma (CLL/SLL)

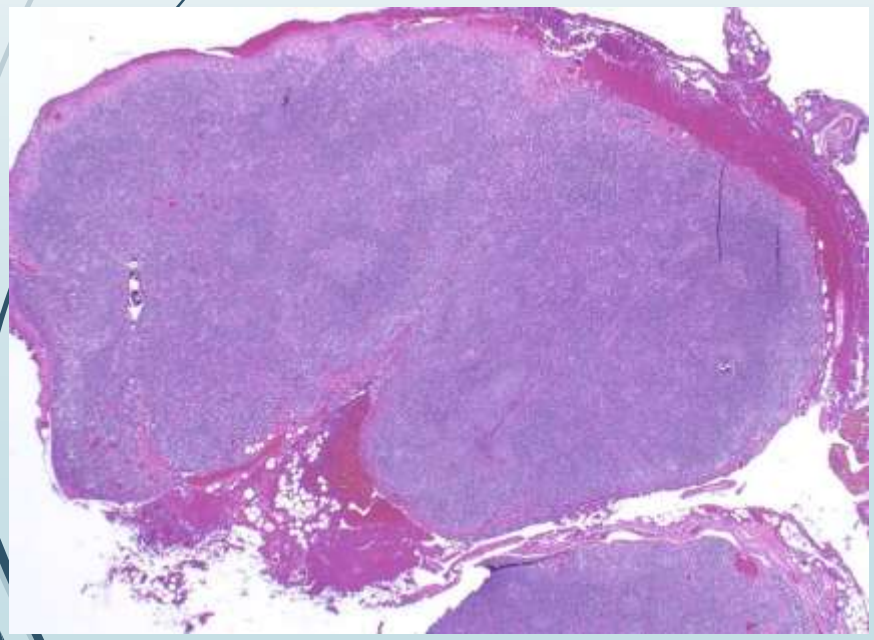
- A 70-year-old man has experienced increasing fatigue for the past 6 months. On physical examination, he has nontender axillary and cervical lymphadenopathy, but there is no hepatosplenomegaly. The CBC shows hemoglobin, 9.5 g/dL; hematocrit, 28%; MCV, 90 µm3; platelet count, 120,000/mm3; and WBC count, 42,000/mm3. His peripheral blood smear shows a monotonous population of small, round, mature looking lymphocytes. Flow cytometry shows these cells to be CD19+, CD5+, and deoxynucleotidyl transferase negative (TdT−), Cytogenetic and molecular analysis of the abnormal cells in his blood are most likely to reveal which of the following alterations?
- A Clonal rearrangement of immunoglobulin genes.
- B Clonal rearrangement of T-cell receptor genes.
- C t(8;14) leading to c-MYC overexpression.
- D t(9;22) leading to BCR-ABL rearrangement .
- E t(14;18) leading to BCL2 overexpression

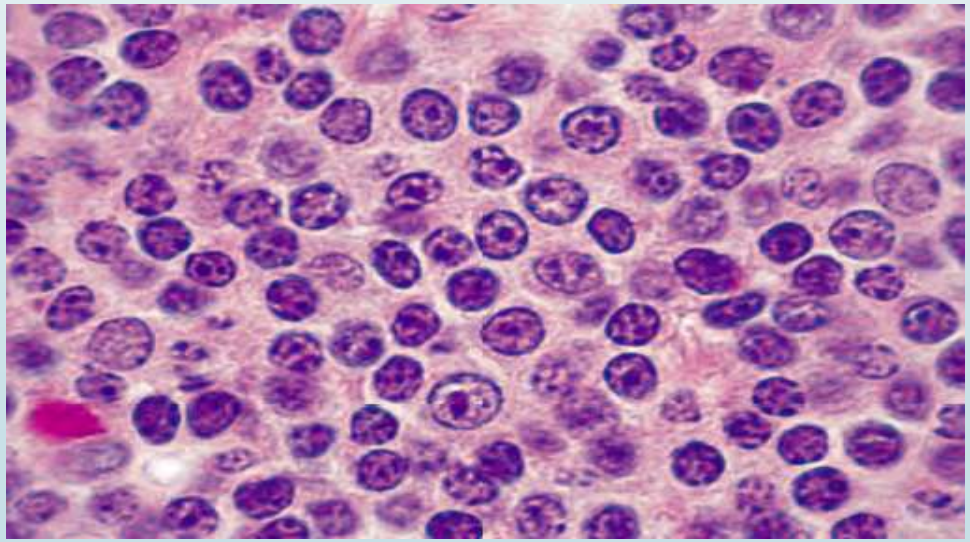
Clinical features

- An indolent, slowly growing tumor, affecting old age
- Either :
- asymptomatic.
- Symptomatic: easy fatigability, weight loss, anorexia, generalized lymphadenopathy & hepatosplenomegaly.
- Lab: Peripheral lymphocytosis (>5000)
- Complications:
- autoimmune hemolytic anemia.
- thrombocytopenia.
  - CLL & SLL are essentially identical.
  - CLL → If PB involvement count exceeds 5000 cells/μL

Morphology

- Involved lymph nodes are effaced by:
- Sheets of small lymphocytes with dark, round nuclei, clumped chromatin & scanty cytoplasm.
- Small percentage of large lymphocytes with prominent centrally located nucleoli (prolymphocytes).

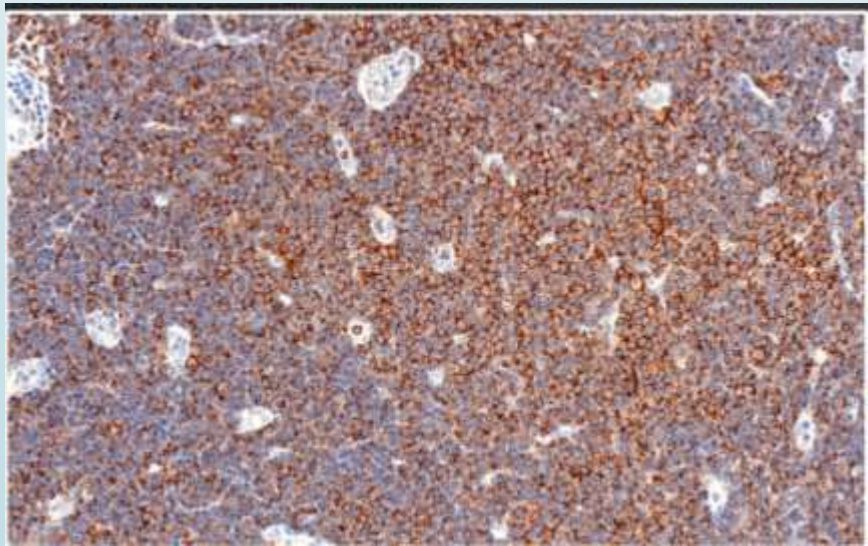




Immunophenotype

- A neoplasm of mature B cells → expressing the CD20, CD5, PAX-5.
- Genetic:
- Clonal rearrangement of immunoglobulin genes.

- Treatment:
- hematopoietic stem cell transplantation (HSCT)



THANK YOU.