2.
Neoplastic Proliferations of White Cells

~ Lymphoid Neoplasms II

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Extranodal Marginal Zone Lymphoma

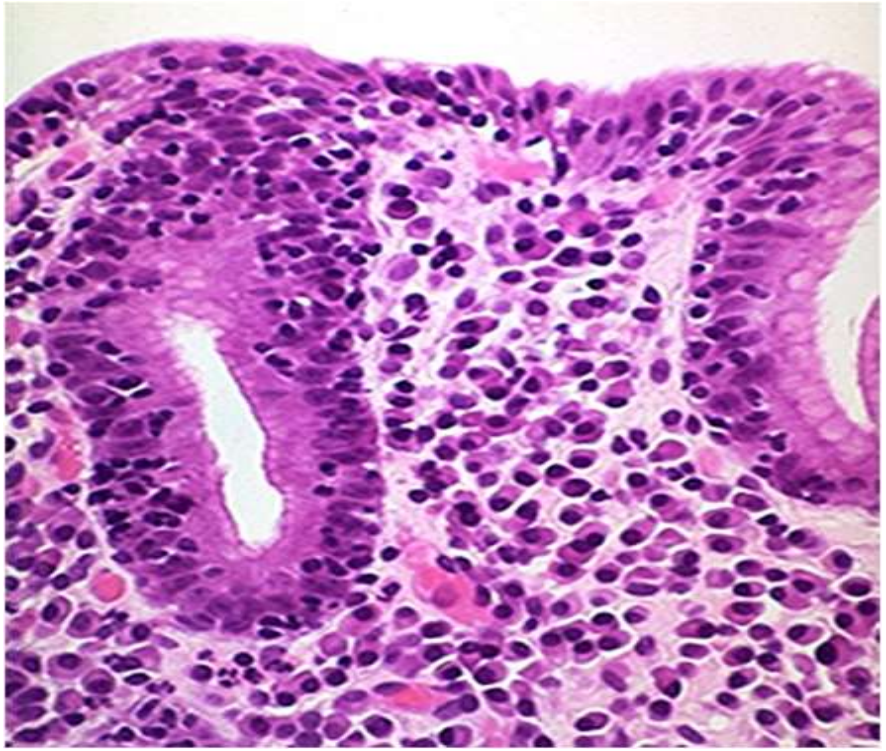
- An indolent B cell tumor arises most commonly in epithelial tissues (e.g. GIT, salivary glands, lungs, orbit, & breast)
- an example of a cancer arises within & is sustained by chronic inflammation:

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

Extranodal Marginal Zone Lymphoma – morphology

- B-cells characteristically infiltrate the epithelium of involved tissues (in small aggregates) → called lymphoepithelial lesions.
- Characteristic features: tumor cells accumulate abundant pale cytoplasm or exhibit plasma cell differentiation.
- Immunophenotype: B-cell markers.

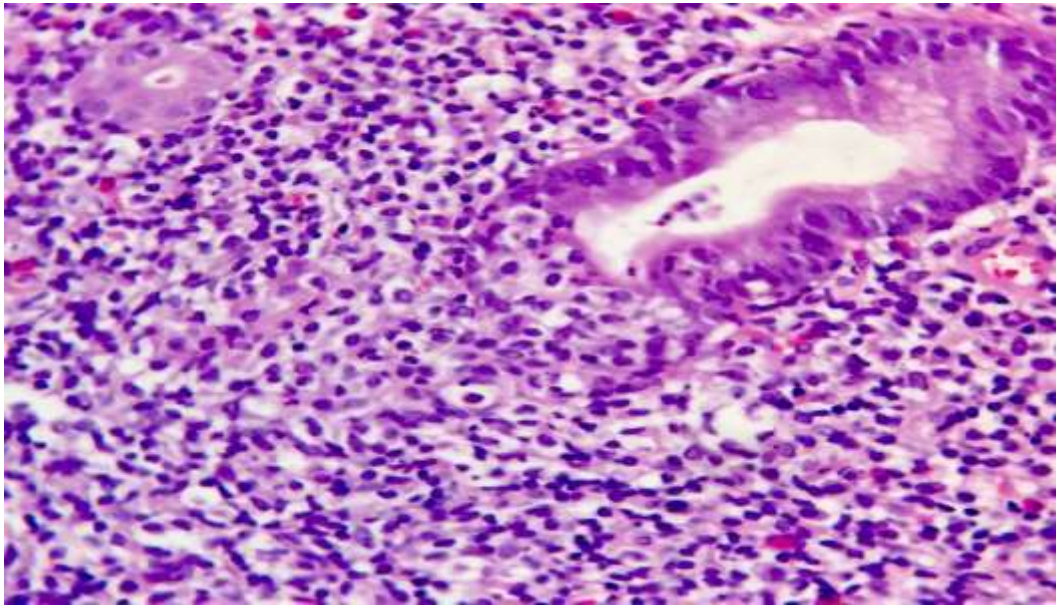
Extranodal Marginal Zone Lymphoma – morphology



Gastric MZL (MALT lymphoma) showing intraepithelial atypical lymphocytes (lymphoepithelial lesion) and plasma cell differentiation in the lamina propria.

Extranodal Marginal Zone Lymphoma – morphology

Another MALT lymphoma where tumor cells accumulate abundant pale cytoplasm (lymphoepithelial lesion)



Extranodal Marginal Zone Lymphoma – Clinical features

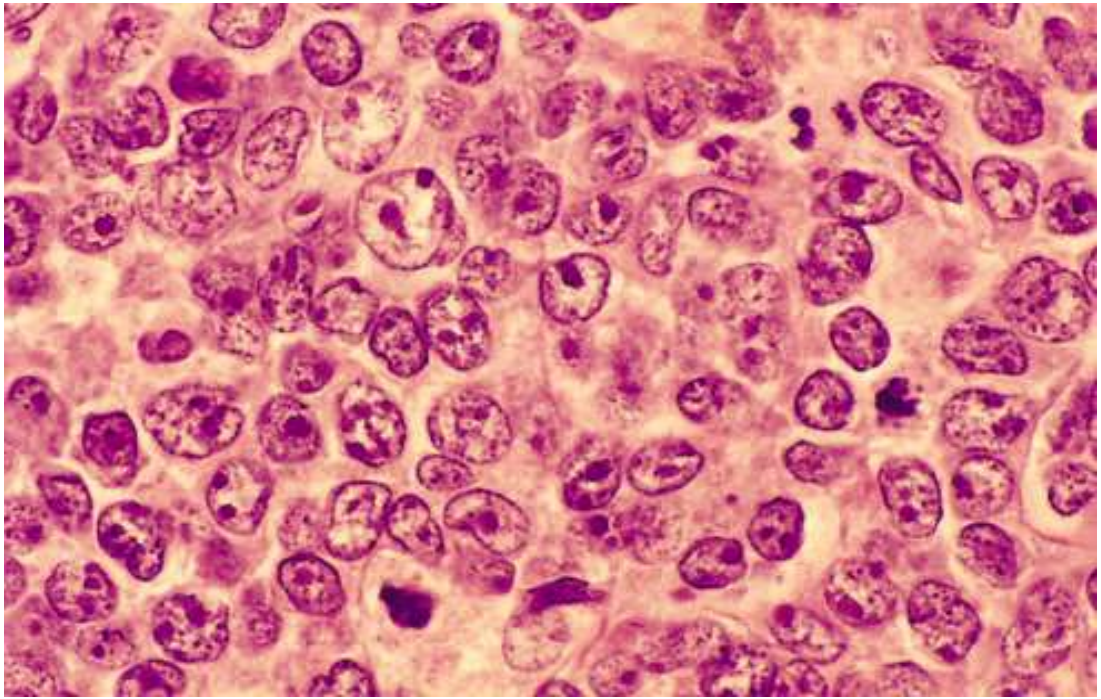
- Present as swelling of the salivary gland, thyroid or orbit or are discovered incidentally in the setting of H. pylori–induced gastritis.
- When localized, they are often cured by simple excision followed by radiotherapy.

Diffuse Large B Cell Lymphoma

- Most common adult lymphoma
- Either de novo or transformation from other low grade tumors (follicular lymphoma).
- **Pathogenesis**: Most of them → Mutations & rearrangements of the BCL6 gene → increased levels of BCL6 protein, an important transcriptional regulator of gene expression in GC B-cells.
- Immunophenotype: B-cell markers, CD10 in some tumors

Diffuse Large B Cell Lymphoma – Morphology

Diffuse infiltration by large neoplastic B cells (three to four times the size of resting lymphocytes) & vary in appearance.



Diffuse Large B Cell Lymphoma – Clinical features

- Median > 60 years of age (but Can occur at any age)
- Generalized lymphadenopathy
- Can occur in extranodal sites (GIT)
- An aggressive and rapidly fatal lymphoma if not treated
- 50% cure with treatment.

Burkitt Lymphoma

- Highly aggressive tumor which can be:

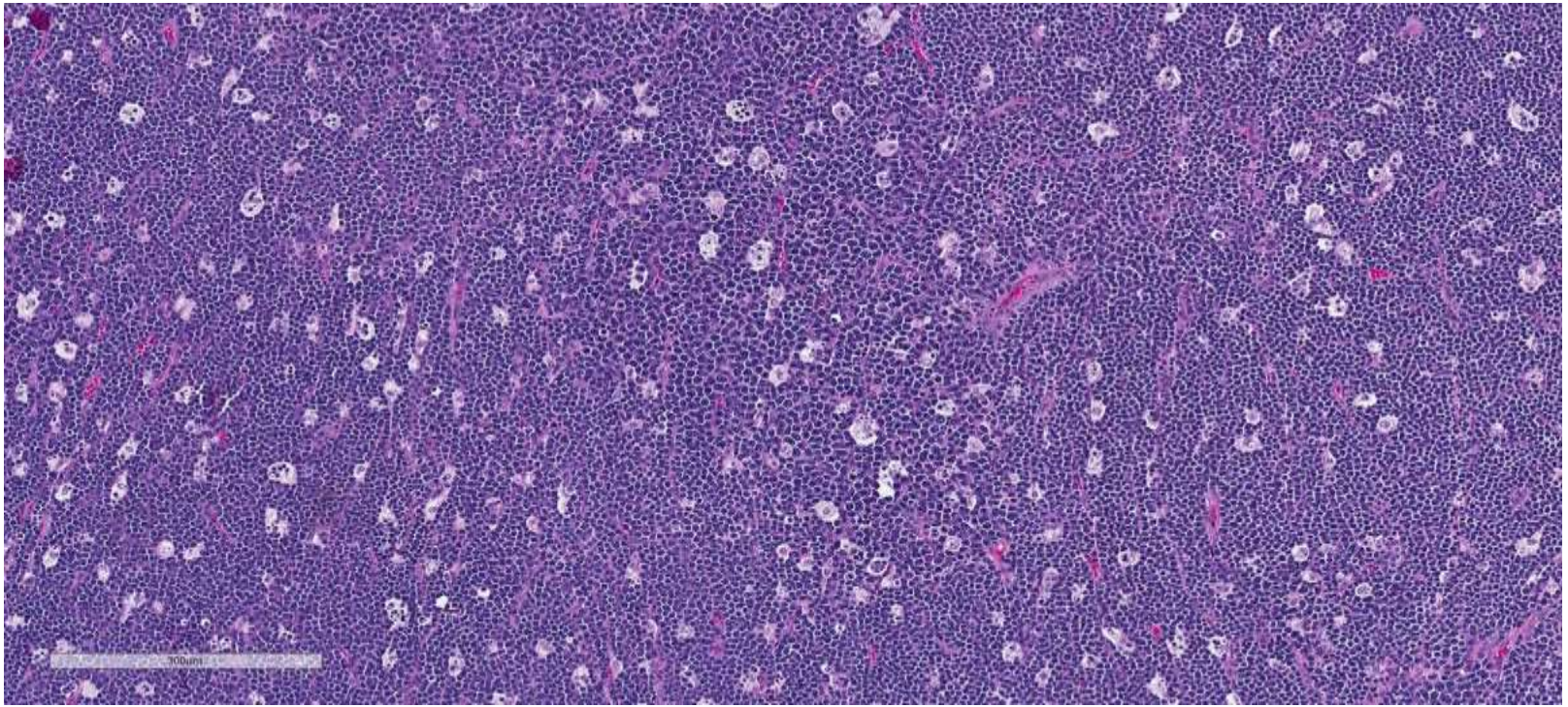
1) Endemic in parts of Africa (ass with EBV)
2) Sporadically in other geographic areas

- Pathogenesis: translocations involving MYC gene on chr. 8 → MYC overexpression (a master regulator of Warburg metabolism (aerobic glycolysis), a cancer hallmark that is associated with rapid cell growth).
- The fastest growing human tumor!!

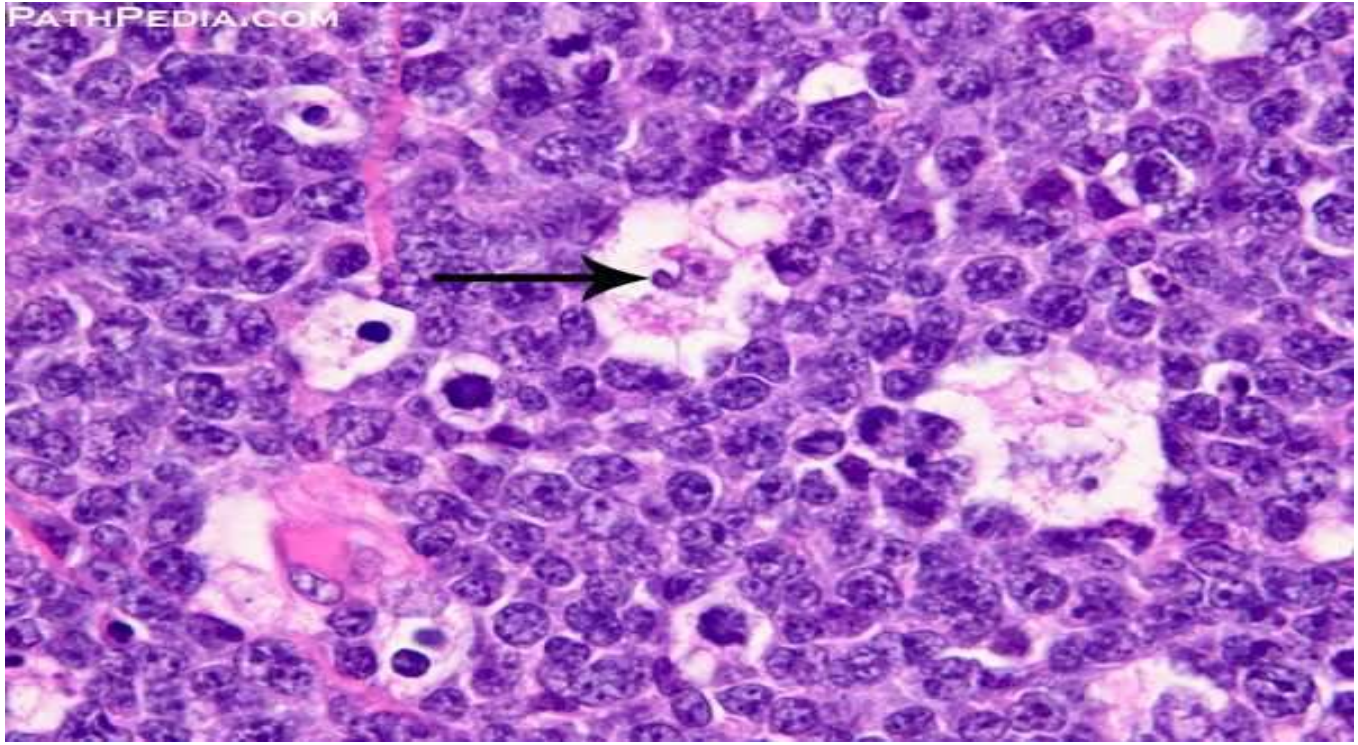
Burkitt Lymphoma – Morphology

- Intermediate size lymphocytes (Variable cytoplasm, several nucleoli).
- Very high rates of proliferation and apoptosis (high turnover) → numerous mitoses & tissue macrophages containing ingested nuclear debris.
- These benign macrophages often are surrounded by a clear space, creating a "starry sky" pattern.
- Immunophenotype: B-cell markers, CD10

Burkitt Lymphoma – Morphology



Burkitt Lymphoma – Morphology



Burkitt Lymphoma – Clinical features

- Both types affect children & young adults.
- Usually arises at extranodal sites:

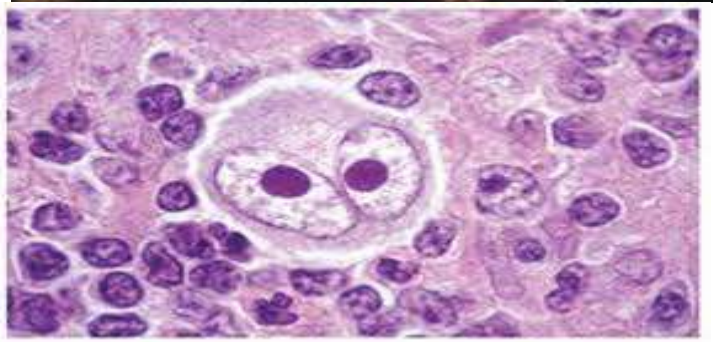
1) Endemic → maxillary or mandibular masses,
2) Sporadic → abdominal tumors (bowel & ovaries)

- Highly aggressive; can be cured with very intensive chemotherapy regimens.

Burkitt Lymphoma – Clinical features

Hodgkin Lymphoma

- A distinctive group of B-cell neoplasms → characterized by the presence of RS cell.
- Unlike most NHLs, they arise in a single lymph node or group & spread in a stepwise fashion to anatomically contiguous nodes.



Hodgkin Lymphoma – major subtypes

- Classic HL
  - Nodular sclerosis
  - Mixed cellularity
  - Lymphocyte-rich
  - Lymphocyte-depleted
- Nodular lymphocyte predominant HL (NLP HL)

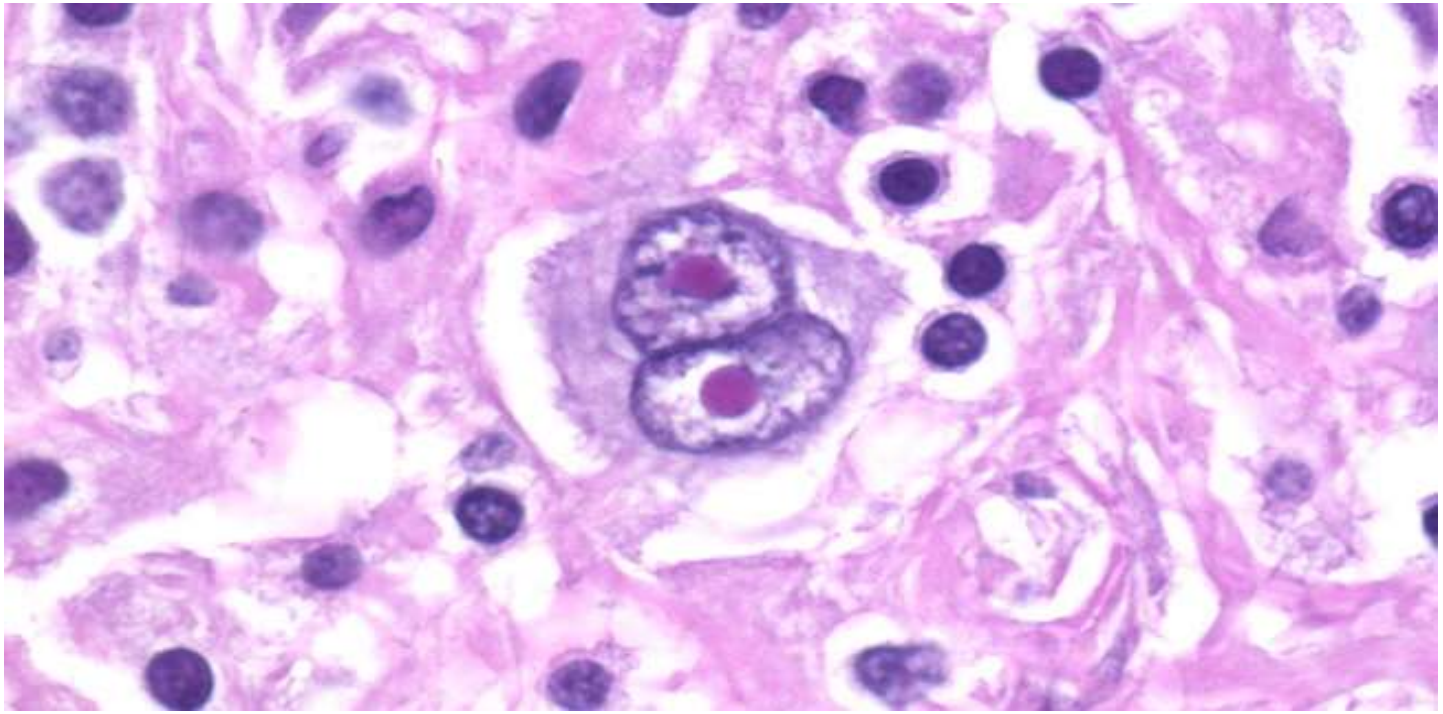
} **The two most common forms**

Hodgkin Lymphoma – morphology

- **Reed-Sternberg (RS) cell:** a very large cell with an enormous multilobate nucleus, exceptionally prominent nucleoli (inclusion-like) & abundant cytoplasm.
- RS cells are surrounded by a heterogeneous inflammatory infiltrate containing small lymphocytes, eosinophils, plasma cells, and macrophages.
- These characteristic nonneoplastic, inflammatory cells are generated by cytokines secreted by RS cells (IL-5,TGF-β, & IL-13).

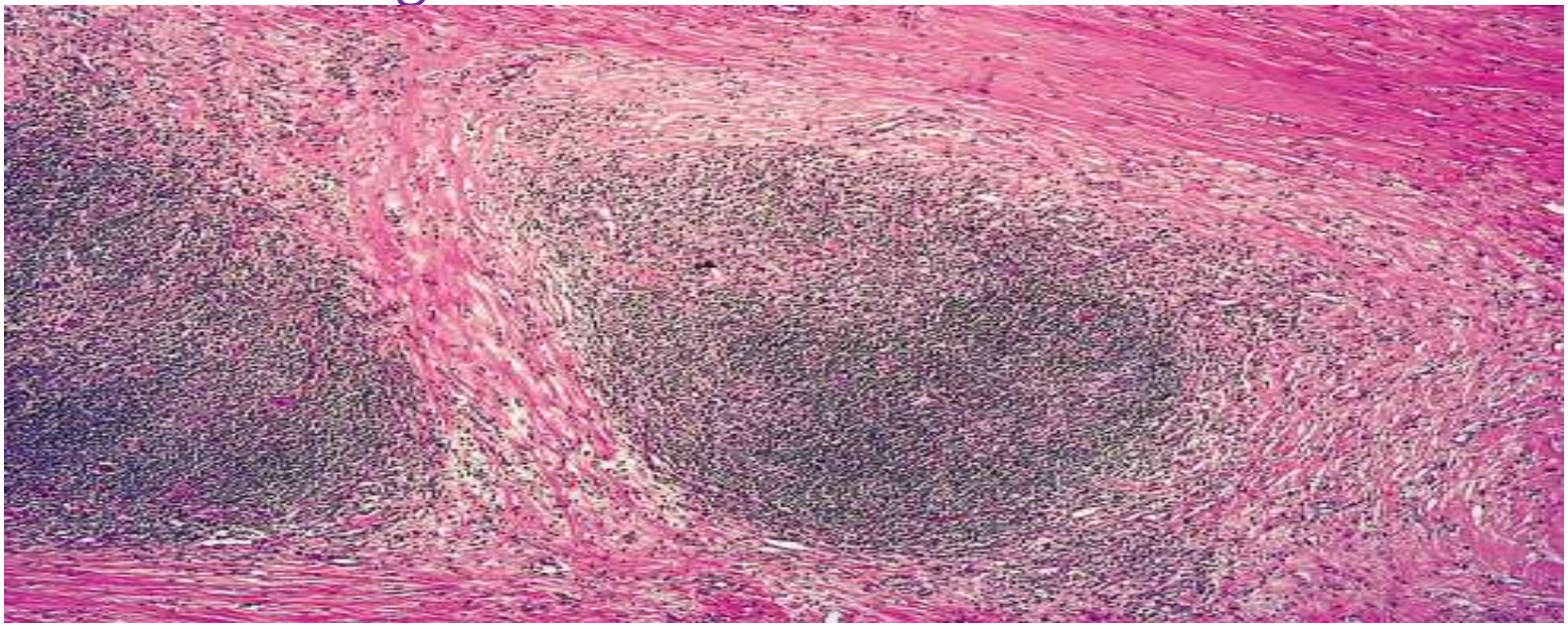
Hodgkin Lymphoma – morphology

owl-eye appearance of RS cells



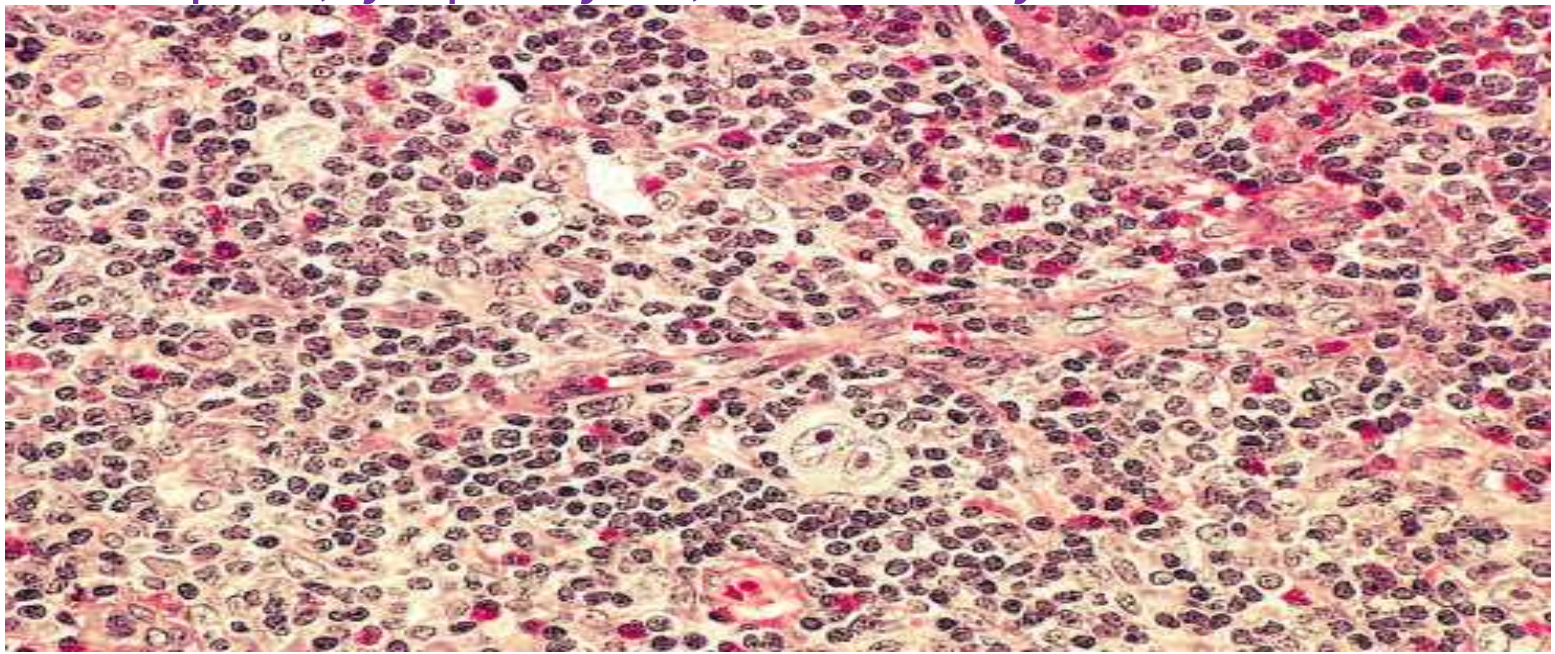
Hodgkin Lymphoma – morphology

HL- nodular sclerosis type: well-defined bands of pink, acellular collagen that divide the tumor cells in nodules..



Hodgkin Lymphoma – morphology

HL- mixed-cellularity type: RS cell surrounded by eosinophils, lymphocytes, and histiocytes.



Hodgkin Lymphoma – Immunophenotype

- In Classic: Typical RS cells express CD15 and CD30 and fail to express B-cell & T-cell markers.
- In NLP HL: RS variant cells, express B cell markers (e.g., CD20) and fail to express CD15 and CD30.
- HL is a cardinal example of a tumor that escapes from the host immune response by expressing proteins that inhibit T cell function → RS cells express high levels of PD ligands → factors that antagonize T cell responses.

Hodgkin Lymphoma – Clinical features

- Usually Young age
  - But can affect any age
- Single lymph node or region of lymph nodes
  - Cervical and mediastinal
  - Rarely tonsils, Waldeyer ring or extranodal sites.
- Manifests as painless lymphadenopathy, patients in advanced disease (stages III & IV) are more likely to exhibit B symptoms (fever, weight loss, night sweats) as well as pruritus & anemia.

Hodgkin Lymphoma – Clinical features

- Spreads in a contiguous manner.
- Treated with chemotherapy, sometimes together with involved field radiotherapy.
- The outlook, even in advanced disease, is very good, the 5-year survival rate for patients with stage 1-2 disease is more than 90%.

Hodgkin Lymphoma – Clinical features

Hodgkin Lymphoma	Non-Hodgkin Lymphoma
More often localized to a single axial group of nodes (cervical, mediastinal, paraaortic)	More frequent involvement of multiple peripheral nodes
Orderly spread by contiguity	Noncontiguous spread
Mesenteric nodes and Waldeyer ring rarely involved	Mesenteric nodes and Waldeyer ring commonly involved
Extranodal involvement uncommon	Extranodal involvement common

Mycosis Fungoides and Sézary Syndrome

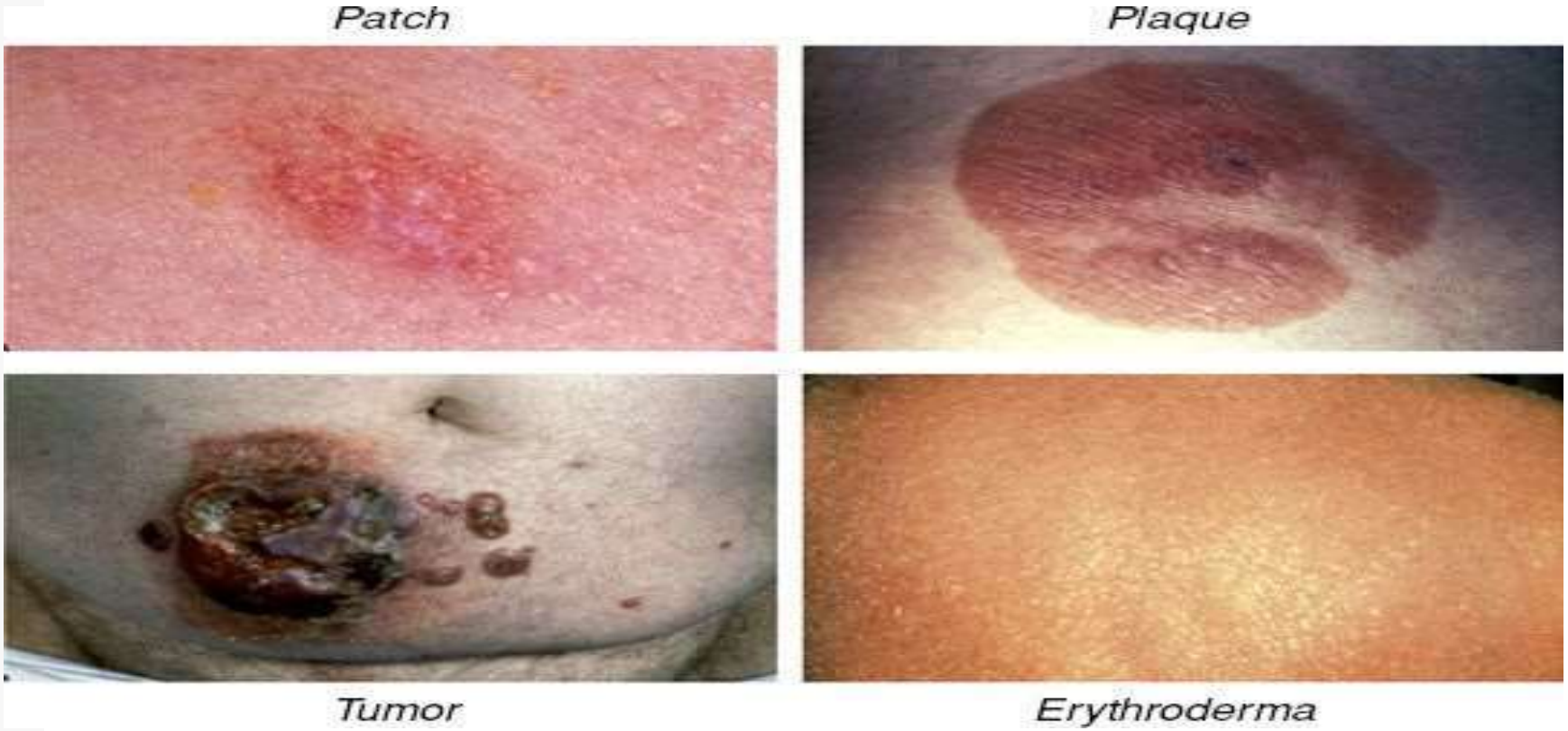
- In MF, a neoplastic CD4+ T cells home to the skin.
- So it is a form of **cutaneous T cell lymphoma**.
- Usually manifests in three stages:

1) A nonspecific erythrodermic rash (patches)
2) Progresses in time to a plaque phase.
3) A tumor phase.

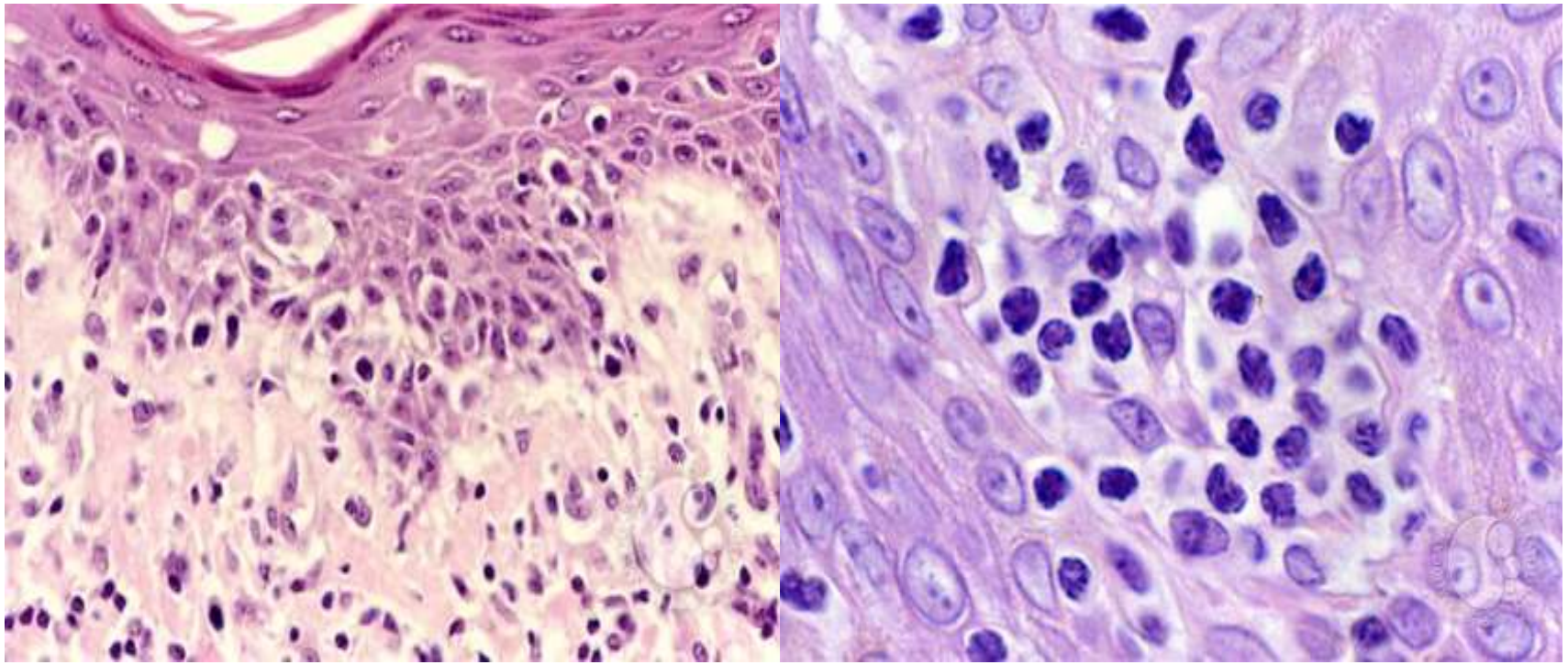
Mycosis Fungoides and Sézary Syndrome –morphology

- **Histologically**, infiltration of epidermis & upper dermis by neoplastic T cells with marked infolding of the nuclear membranes → a **cerebriform** appearance.
- **Immunophenotype:** Tumor cells are CD4 +, CD8 -

Mycosis Fungoides and Sézary Syndrome –morphology



Mycosis Fungoides and Sézary Syndrome –morphology



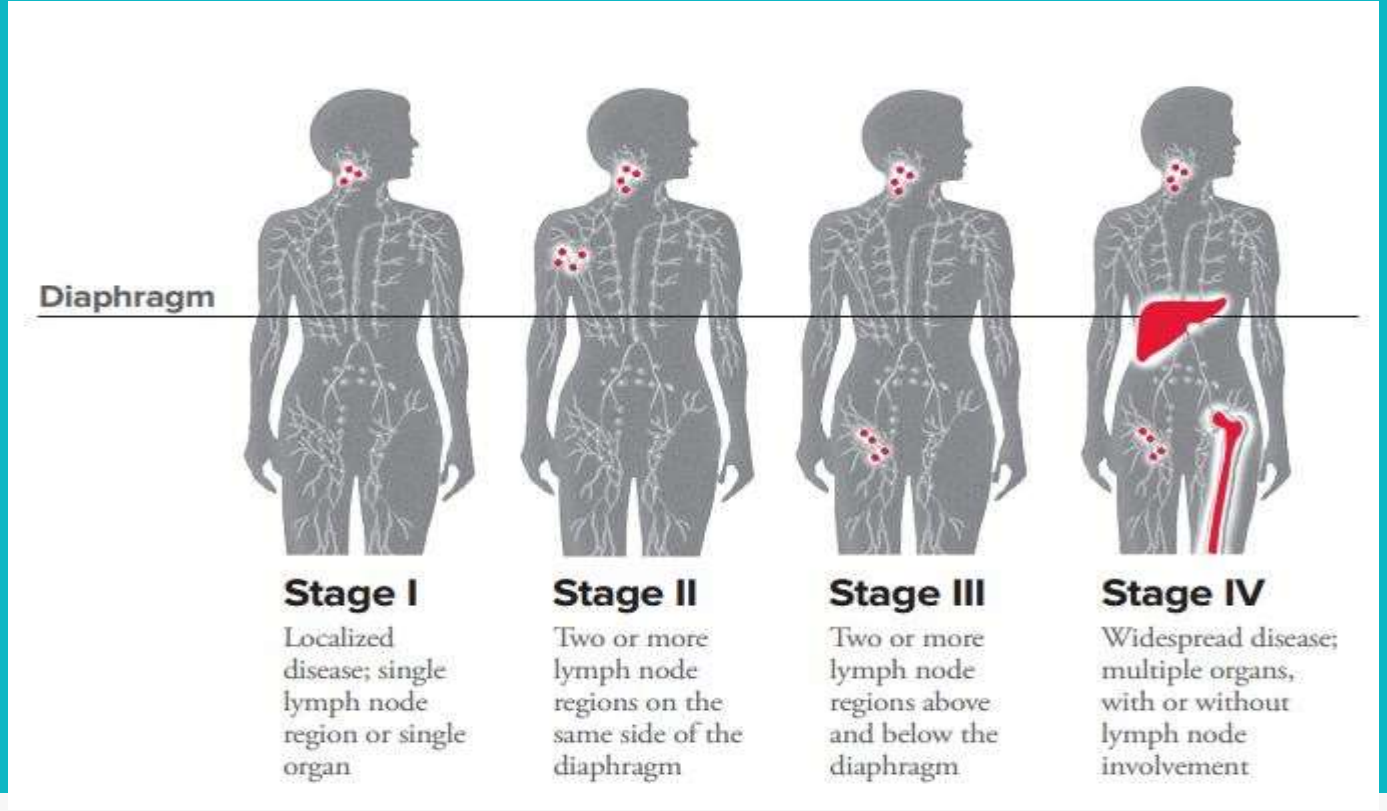
Mycosis Fungoides and Sézary Syndrome – Clinical features

- **Sézary syndrome:** a clinical variant of MF characterized by:

(1) a generalized exfoliative erythroderma

(2) tumor cells (Sézary cells) in the peripheral blood.

- Patients diagnosed with early- stage MF survive for many years.
- Patients with tumor- disease, visceral disease, or Sézary syndrome survive on average for 1-3 years.



Lymphoma staging

THANKS!

Any questions?