

27/3/23

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).

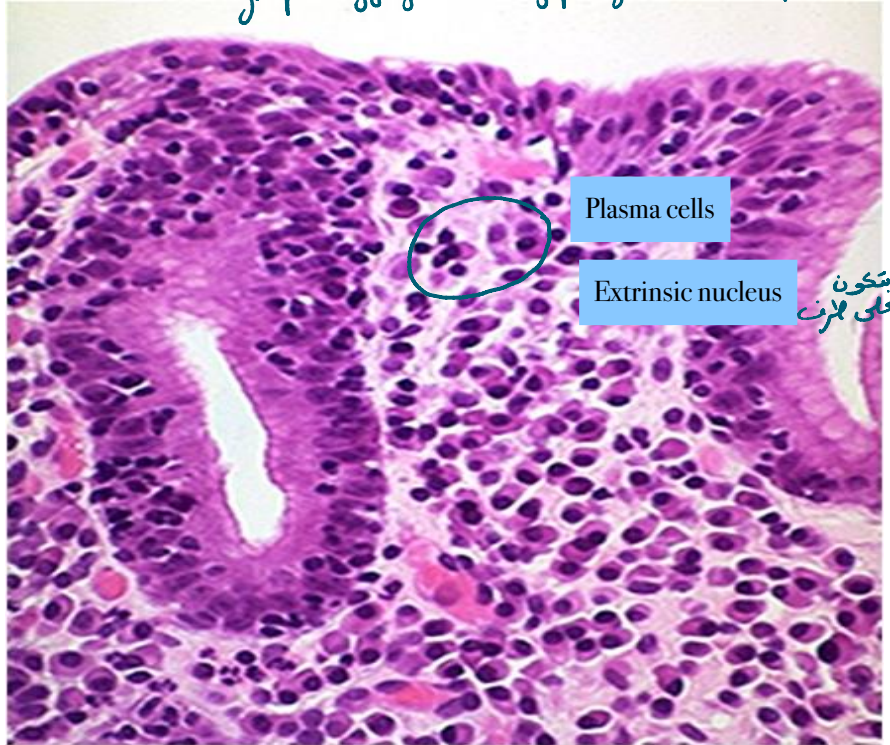
Memory  
is  
Ag-presenting cells.

## 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

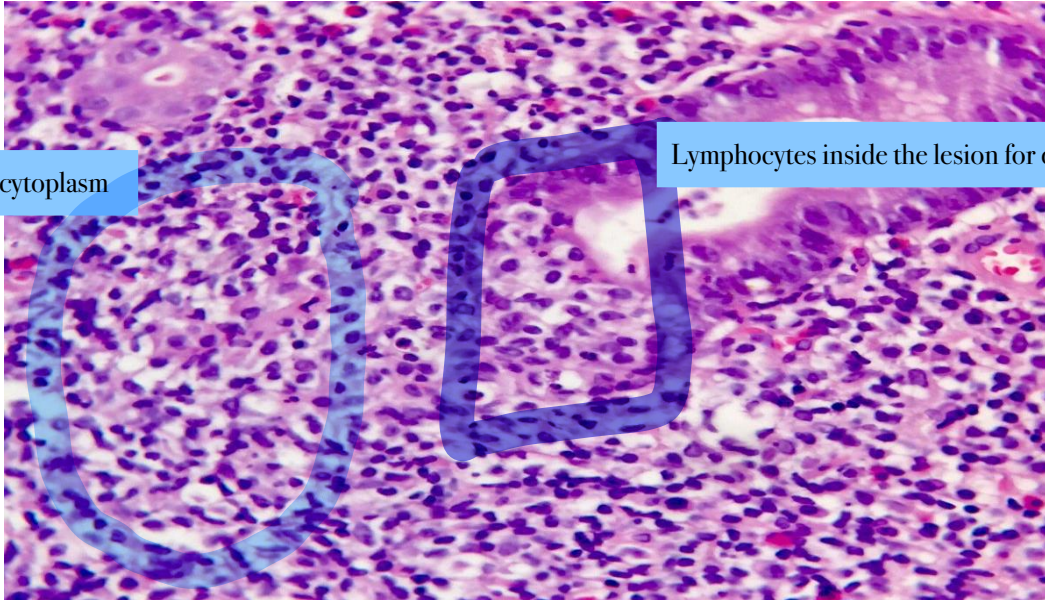
group "aggregates of lymphocyte" inside epithelium.



Gastric MZL (MALT lymphoma) showing intraepithelial atypical lymphocytes  
 (lymphoepithelial lesion) <sup>Stomach</sup>  
 and plasma cell <sup>جاي</sup> <sup>nucleus</sup> <sup>Peripheral</sup>  
 differentiation in the lamina propria.

## Extranodal Marginal Zone Lymphoma - morphology

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



- nucleus smaller.

# Extranodal Marginal Zone Lymphoma – Clinical features

- ▶ Present as <sup>enlargement</sup> 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.

good prognosis 😊

البقيع بدمع  
بالجشاع  
بالجشاع  
بالجشاع  
بالجشاع

# 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

Deletion  
Translocation  
Addition  
Replacment

11

من الأساسي  
من هيك

2

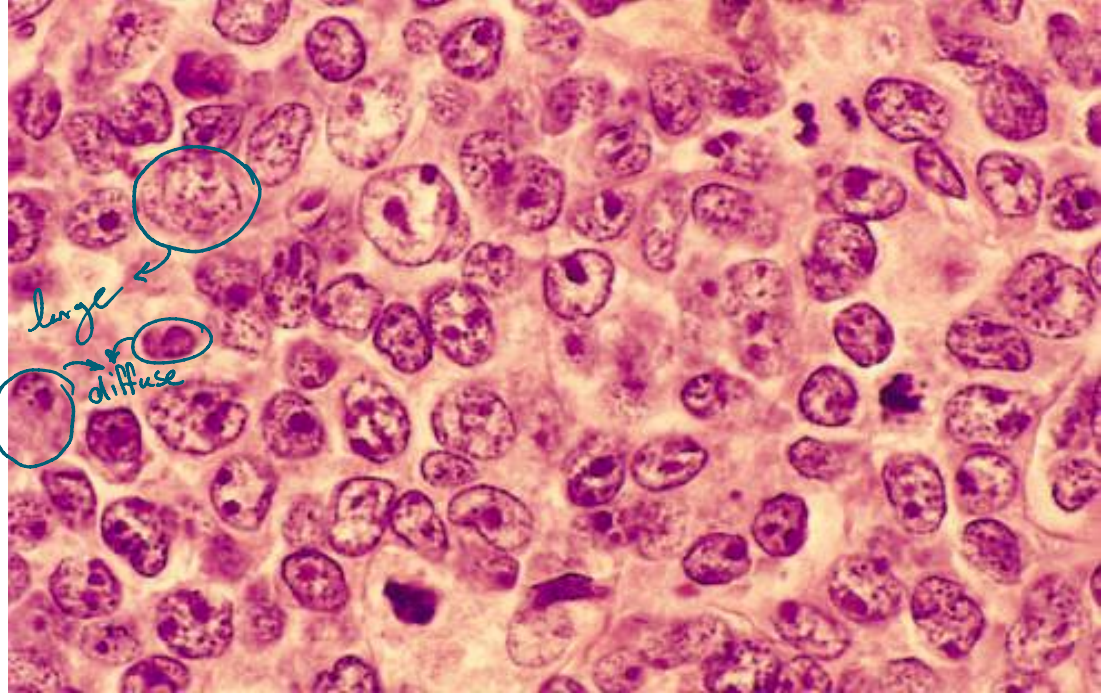
19, 20, 79

# Diffuse Large B Cell Lymphoma - Morphology

- large cells.
- open chromatin.
- A lot of nucleolus. نووي

المخاطبة  
بعض الخلايا  
تحتل  
كل مساحة  
Diffuse infiltration by  
large neoplastic B  
cells (three to four  
times the size of  
resting lymphocytes)  
& vary in appearance.

3-4 larger than lymph node.



## 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 *Higher grade*
- ▶ 50% cure with treatment. *Fatal.*

# 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!!

نوعين

بنتها ر tumor  
لتأثيراتها  
بطريقة أسرع



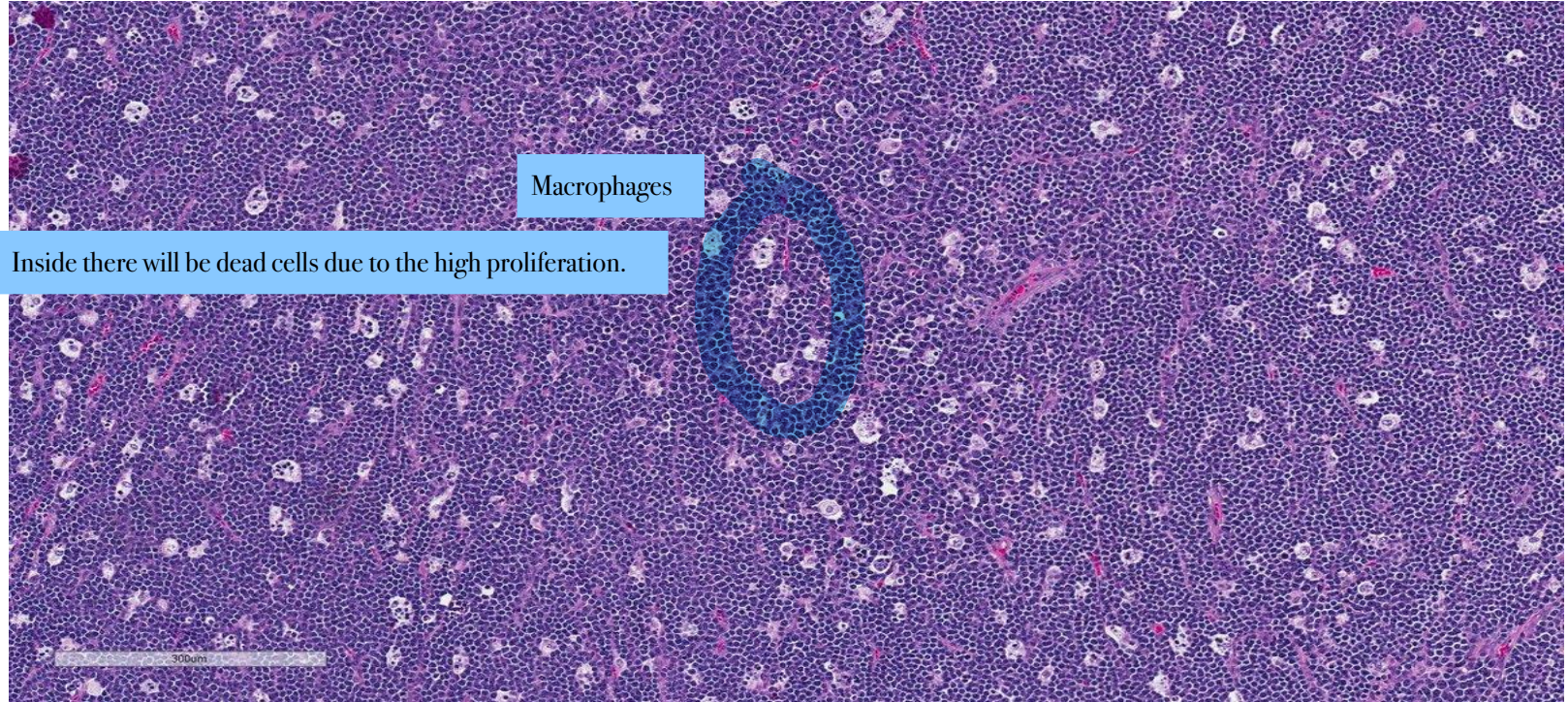
## Burkitt Lymphoma - Morphology

- ▶ 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

خلية بنفوت  
بيجي بدالها.

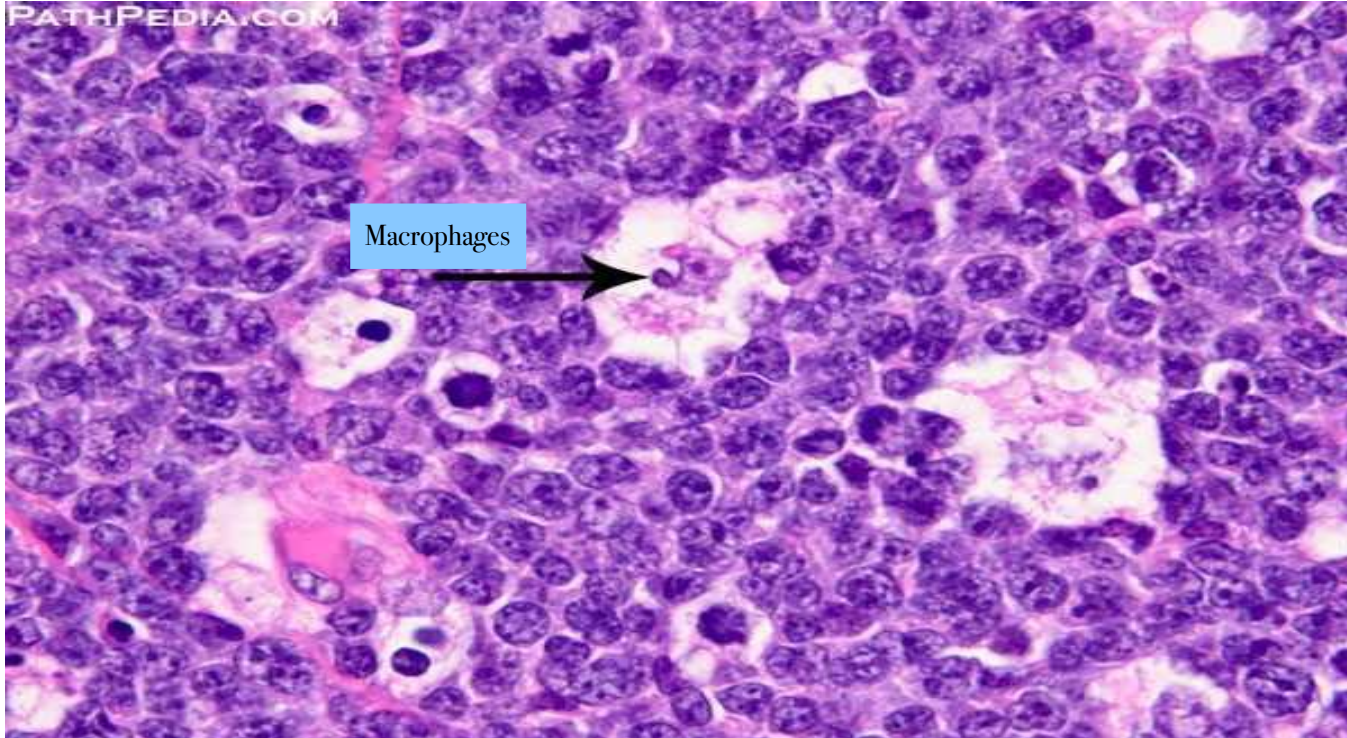
Macrophages ← → Blue cells 'intermediate cells'

# Burkitt Lymphoma - Morphology



# Burkitt Lymphoma - Morphology

*High mitotic activity.*



## 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.

high risk  
high proliferation  
B-cell

chemo-therapy

# Burkitt Lymphoma - Clinical features

Endemic type?

Because its in the  
jaw & mandible.

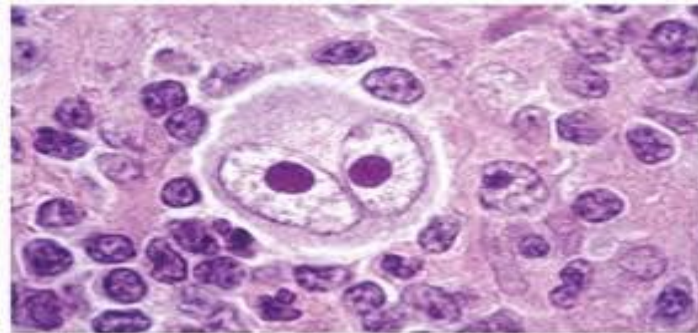
good prognosis specially with  
chemotherapy.



No surgery "resection"  
only for diagnosis.

# Hodgkin Lymphoma

- ▶ A distinctive group of B-cell neoplasms → characterized by the presence of **RS cell**.
- ▶ Unlike most <sup>non hodgkin Lymphoma.</sup> 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**

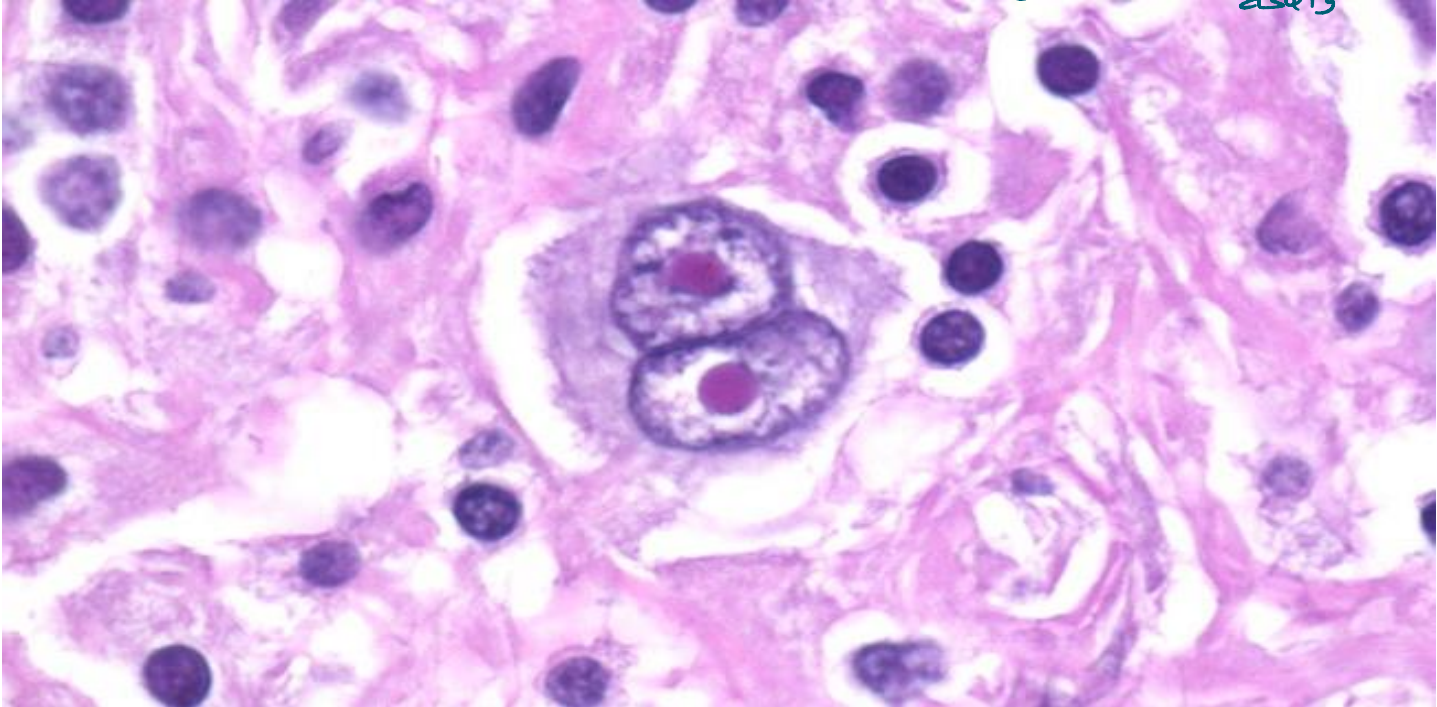
## Hodgkin Lymphoma – morphology

- ▶ **Reed-Sternberg (RS) cell:** <sup>في كان الها حقيقي</sup> a very large cell with an enormous multilobate nucleus, exceptionally prominent nucleoli (inclusion-like) & abundant cytoplasm.
- ▶ <sup>Neoplastic</sup> 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- $\beta$ , & IL-13).

They aren't  
neoplastic cells  
حائهم من  
هرية  
cytokines.

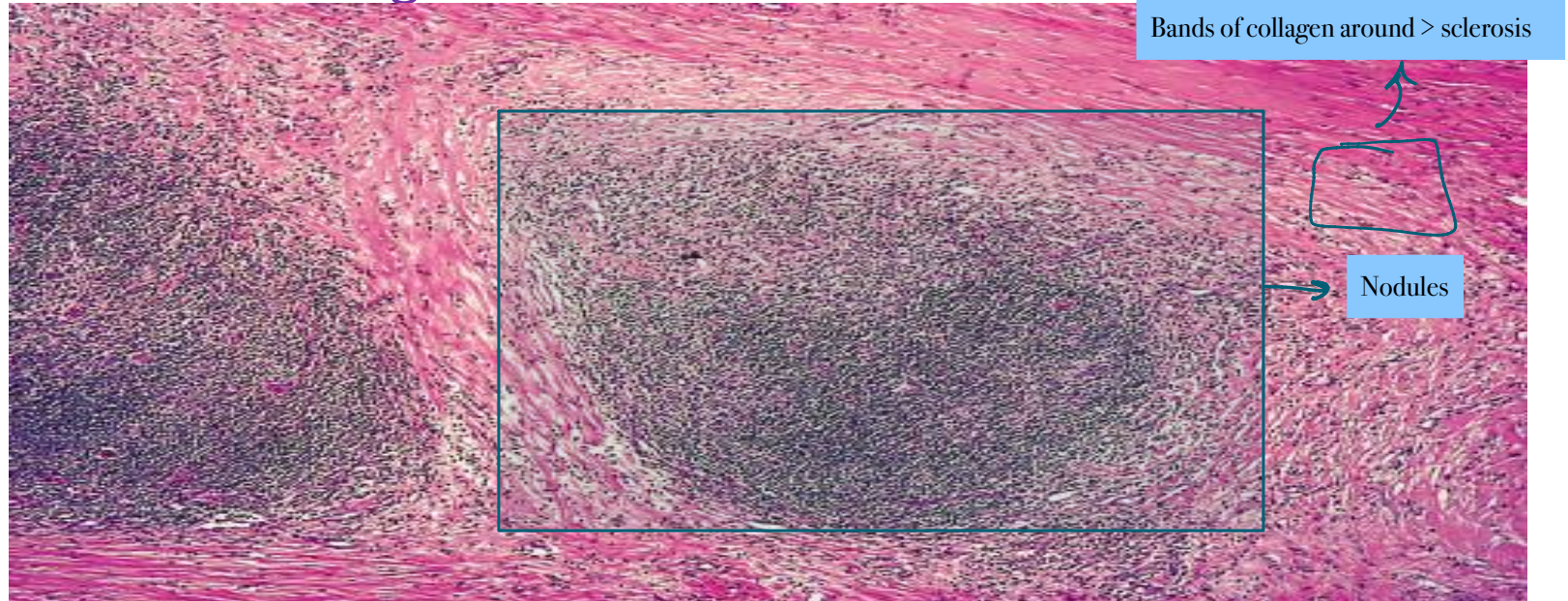
# Hodgkin Lymphoma – morphology

owl-eye appearance of RS cells *Smudge like* ⇒ *سيف بقة  
وانحة*



## Hodgkin Lymphoma – morphology

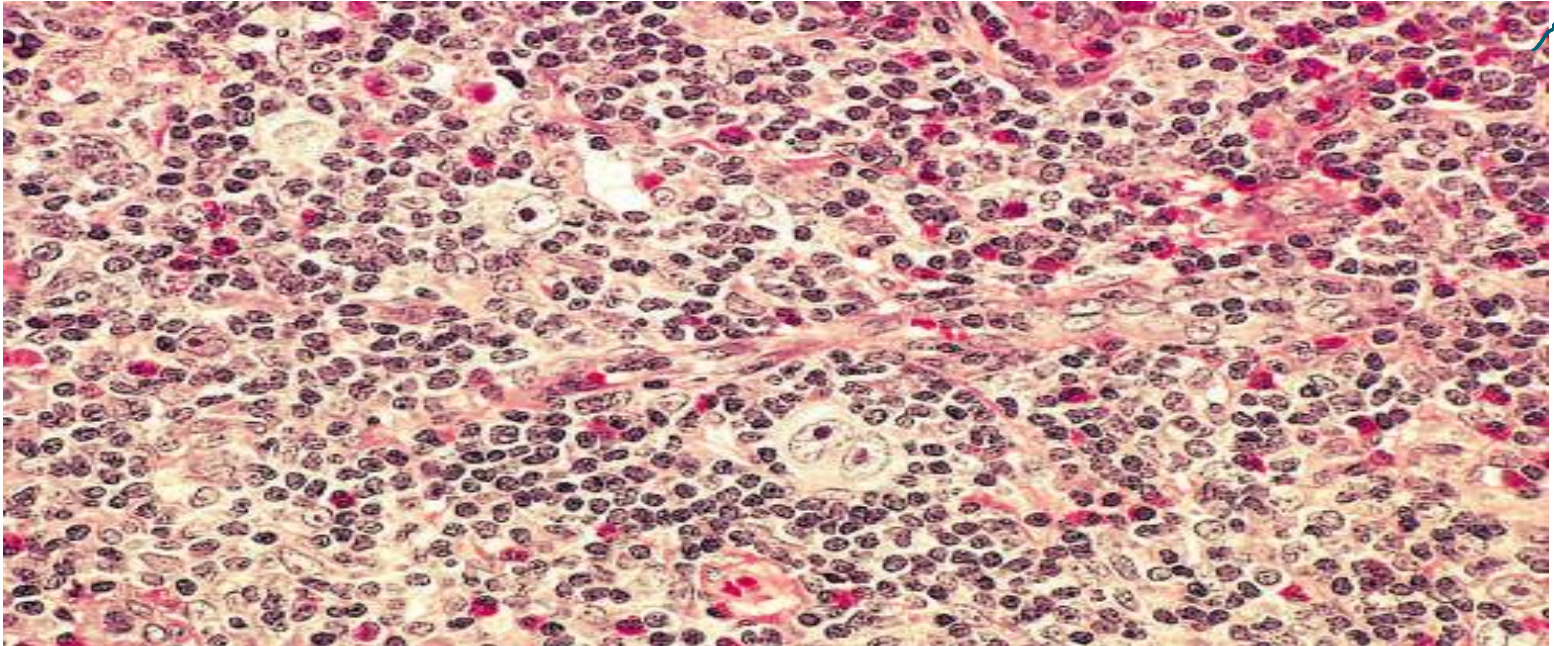
HL- nodular sclerosis type: well-defined bands of pink, acellular collagen that divide the tumor cells in nodules..



# Hodgkin Lymphoma – morphology

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

RS < non  
neoplastic  
عددها أكبر من  
inflammatory  
لونها أحمر  
'eosinophils'



No nodules  
No collagen

# Hodgkin Lymphoma – Immunophenotype

- ▶ In Classic: Typical RS cells **express CD15 and CD30** and **fail** to express B-cell & T-cell markers. *negative.*
- ▶ *not classic.* 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. *“immune therapy”.*

## 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.

البغيم من ال spread

ممكن انتشار  
تدرجياً وإدخال  
تعالج عنيف.

## Hodgkin Lymphoma – Clinical features

- ▶ Spreads in a <sup>جنب بيلان</sup>contiguous manner. Doesn't skip lesion.
- ▶ 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 <u>rarely</u> involved	Mesenteric nodes and Waldeyer ring commonly involved
Extranodal involvement uncommon	Extranodal involvement <u>common</u> like mantle & Diffuse.

~Robin's book.

# Mycosis Fungoides and Sézary Syndrome

فانجوس ار فونجوس  
But not  
Fungal.

- ▶ 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.

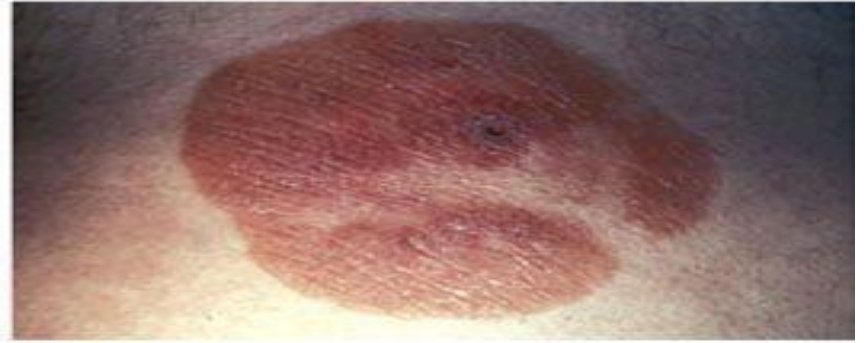
كل ما تقدم  
ال stage  
Prognosis  
أسوأ.

# Mycosis Fungoides and Sézary Syndrome -morphology

Patch



Plaque



Tumor



Sézary Syndrome 'generalised redness'  
WORST

Erythroderma

## Mycosis Fungoides and Sézary Syndrome –morphology

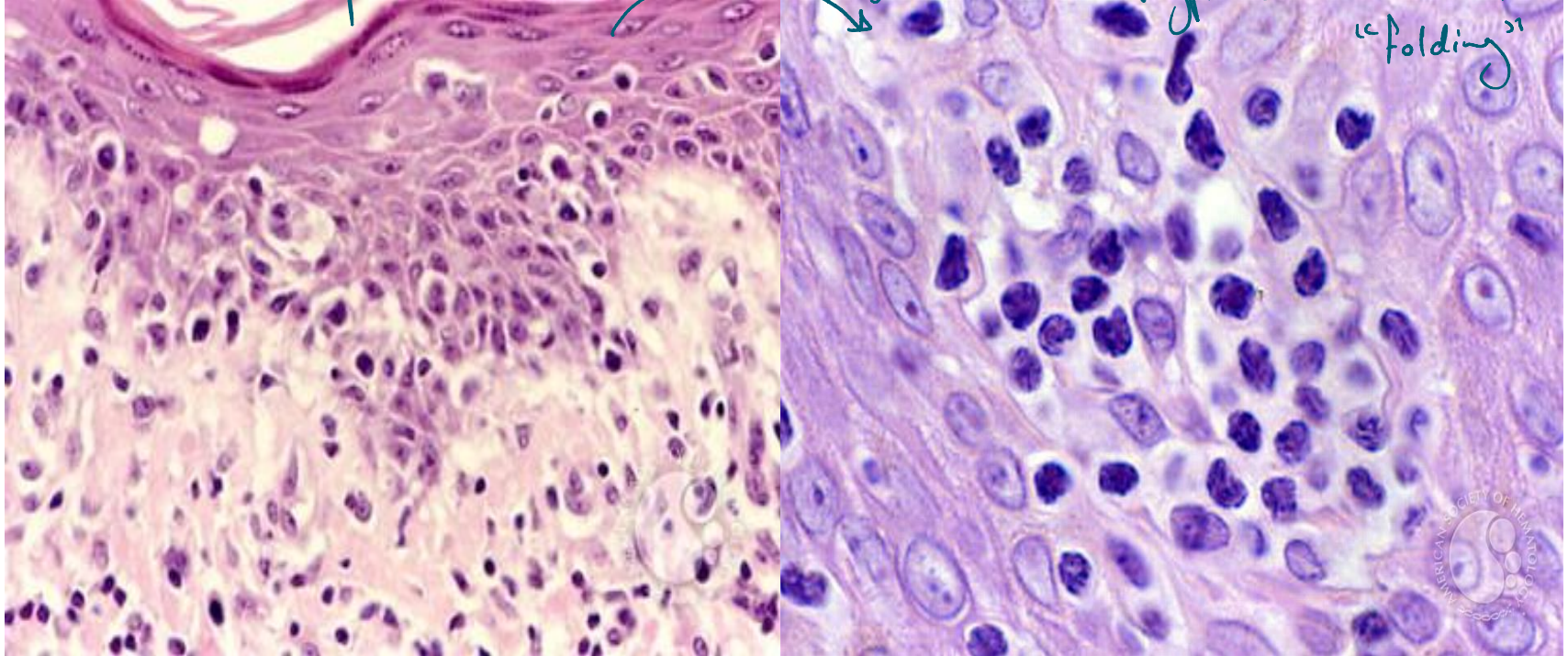
- ▶ **Histologically**, infiltration of epidermis & upper dermis by neoplastic T cells with marked infolding of the nuclear membranes → a cerebriform appearance.
- ▶ **Immunophenotype:** Tumor cells are CD4<sup>+</sup>, CD8 -  
Specific Regulatory

# Mycosis Fungoides and Sézary Syndrome -morphology

epidermis

High power.

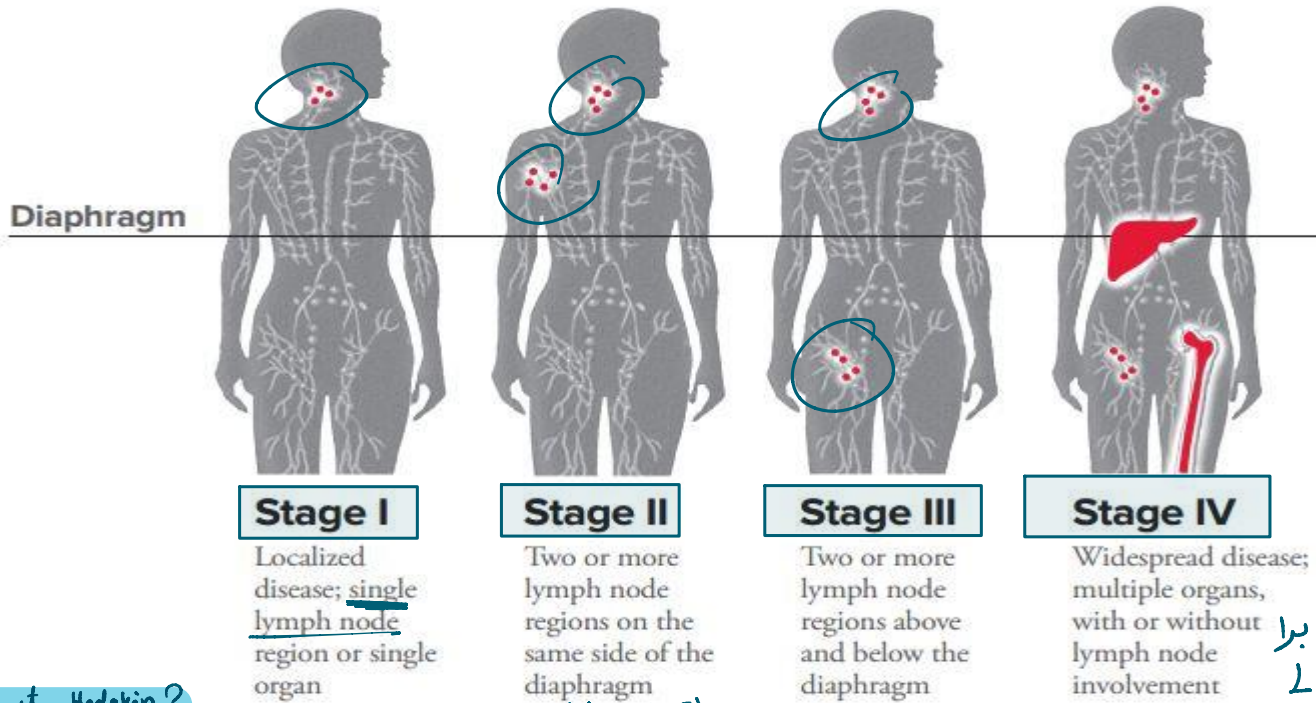
Atypical → cerebriform  
"folding"



## Mycosis Fungoides and Sézary Syndrome – Clinical features

- ▶ **Sézary syndrome**: <sup>→ end stage</sup> 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. *Bad prognosis.*

هون تكمن أهمية staging



Staging is good at Hodgkin?

= Because spread is predictable  
no skip.

التي هي  
التي هي  
diaphragm.

Cross diaphragm

طليبا برا  
Lymph node

# Lymphoma staging