Heme 8

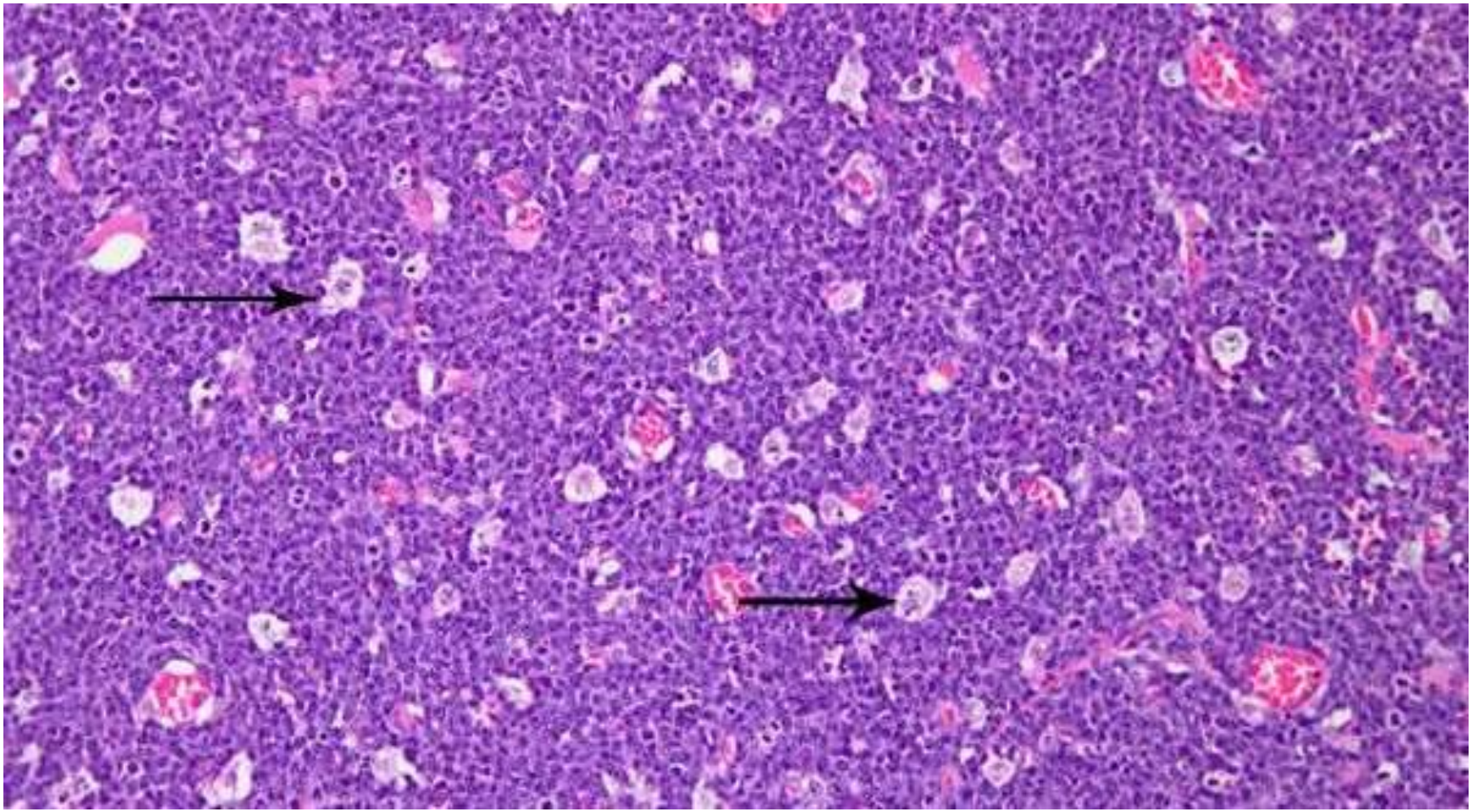
Burkitt lymphoma

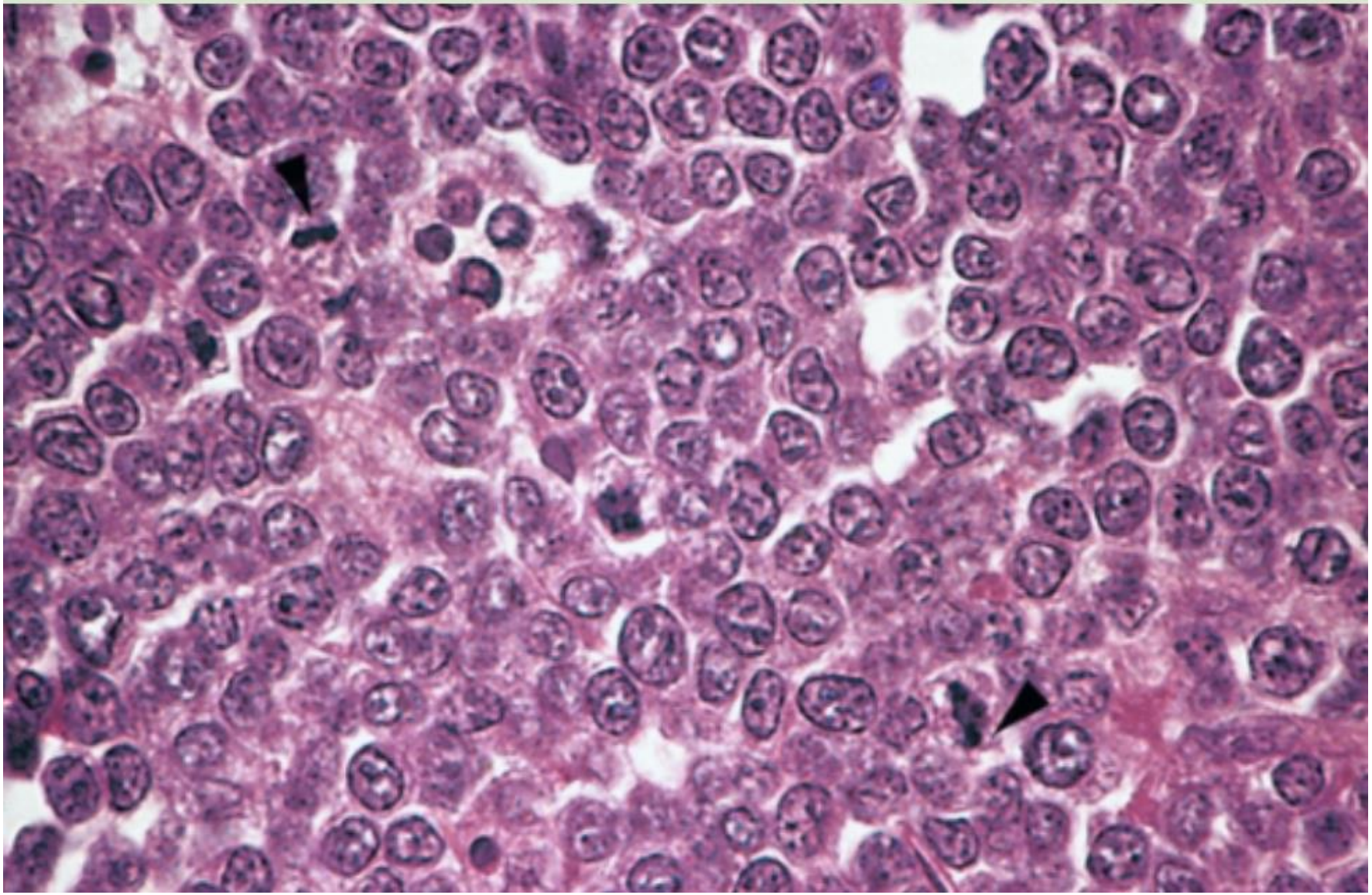
- Sporadic
- Endemic in Africa associated with EBV
- Translocations involving *MYC* gene on chromosome 8
  - Most common is t(8;14)
- Believed to be the fastest growing tumor in humans!!!!


URN

Morphology

- Sheets of medium sized cells
- Starry-sky appearance
- Variable cytoplasm, several nucleoli
- Frequent mitosis





Immunophenotype

- B cell markers
- CD10 positive
- **BCL-2 is NEGATIVE.**

Clinical manifestations

- Tumor of young adults and children
- Endemic: maxillary or mandibular masses
- Sporadic: abdominal masses
- Both are usually extranodal
- Peripheral blood is involved in the majority of cases
  - Must distinguish from ALL
- Aggressive and curable.

- The most specific markers for T cell differentiation
  - CD19
  - CD10
  - CD20
  - CD3
  - CD79

- All the following are good prognostic factors in B-ALL, except:
  - Age 2-10 years
  - Low WBC count
  - T(12;21)
  - Hypodiploidy
  - T(9;22)

  (TWO ANSWERS ARE CORRECT HERE!!!)

- MYC gene translocations are associated with
  - Follicular lymphoma
  - Burkitt lymphoma
  - DLBCL
  - CLL
  - Mantle cell lymphoma

- The most common lymphoma is
  - Follicular lymphoma
  - Burkitt lymphoma
  - DLBCL
  - CLL
  - Mantle cell lymphoma

- What tumor is positive for Cylcin D1
  - Follicular lymphoma
  - Burkitt lymphoma
  - DLBCL
  - CLL
  - Mantle cell lymphoma

New questions!!!

- RS cells in classic HL are of
  - T cell origin
  - B cell origin

- M proteins and Bence jones proteins are composed of
  - Abnormal albumin
  - Clonal Immunoglobulins
  - Abnormal ferritin
  - Abnormal glycoproteins
  - Abnormal ceruloplasmin

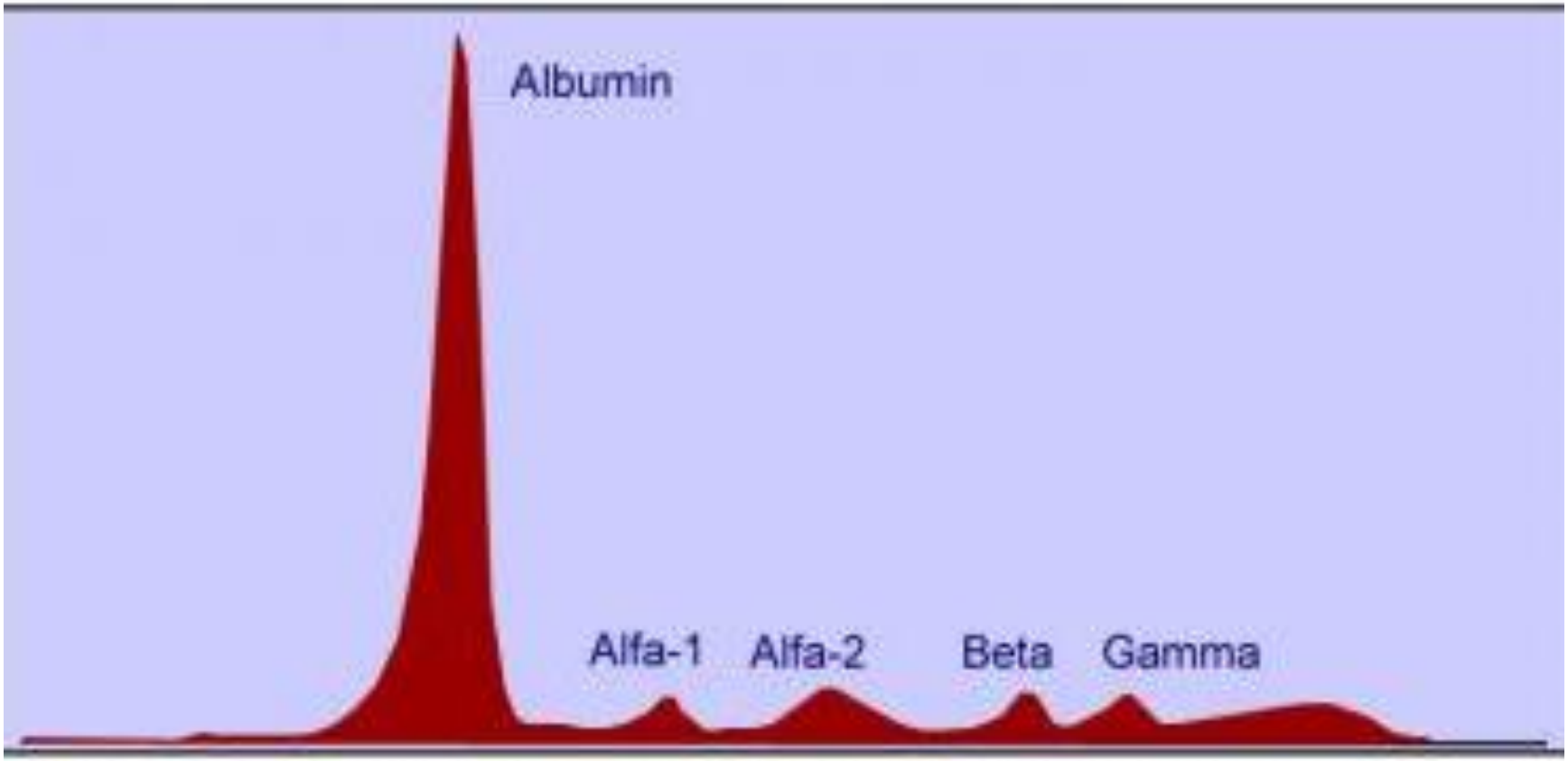
- The most specific marker for langerhans cell differentiation is
  - CD68
  - CD163
  - Langerin
  - CD1a
  - CD20

- One of the following tumors is a T cell neoplasm
  - Mantle cell lymphoma
  - Langerhans cell histiocytosis
  - Sezary syndrome
  - DLBCL
  - Burkitt lymphoma

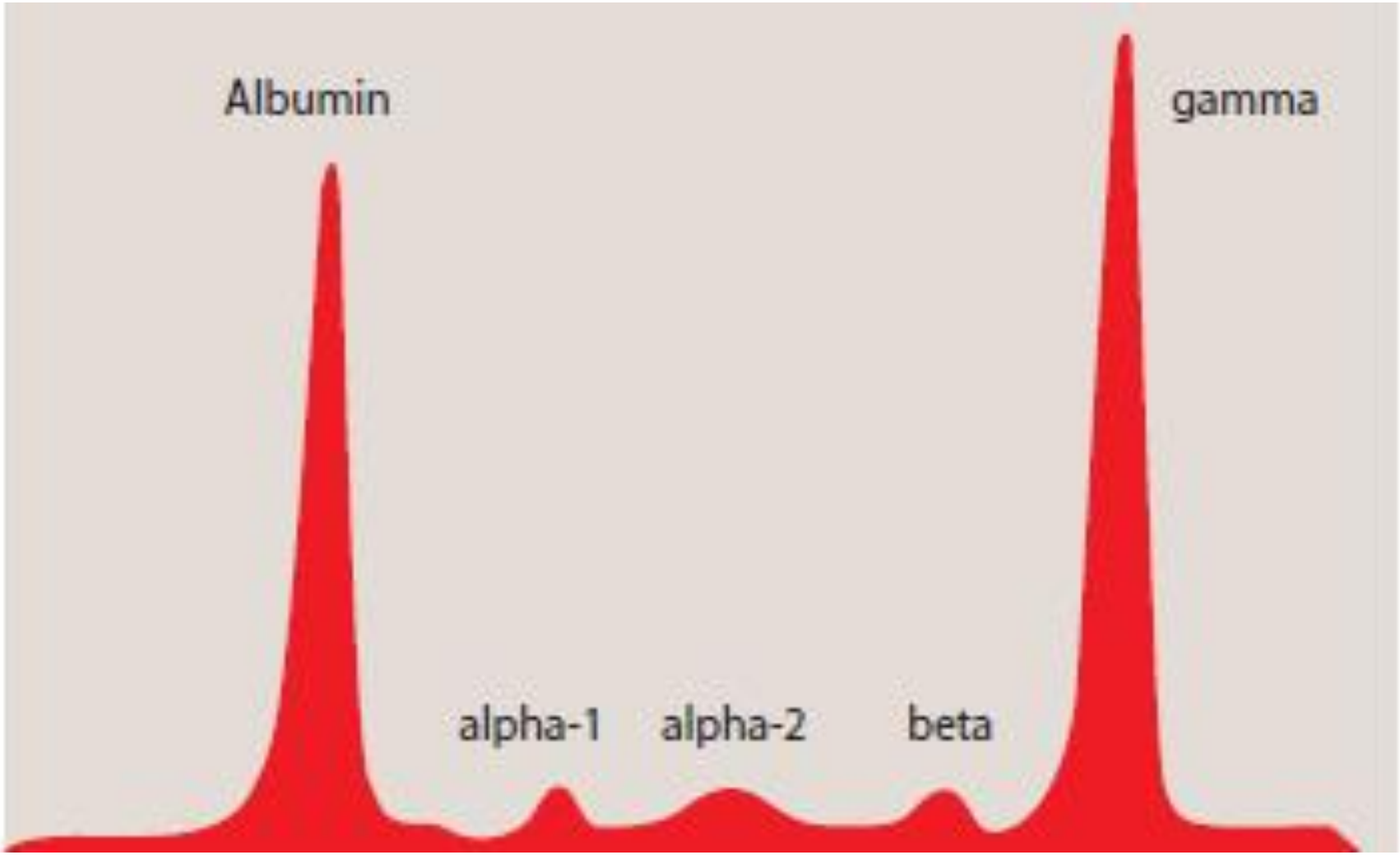
- Neoplastic cells in all the following are positive for CD30, except:
  - Nodular cellularity classic HL
  - Mixed cellularity classic HL
  - Lymphocyte-rich classic HL
  - Lymphocyte-depleted classic HL
  - Nodular lymphocyte predominant HL

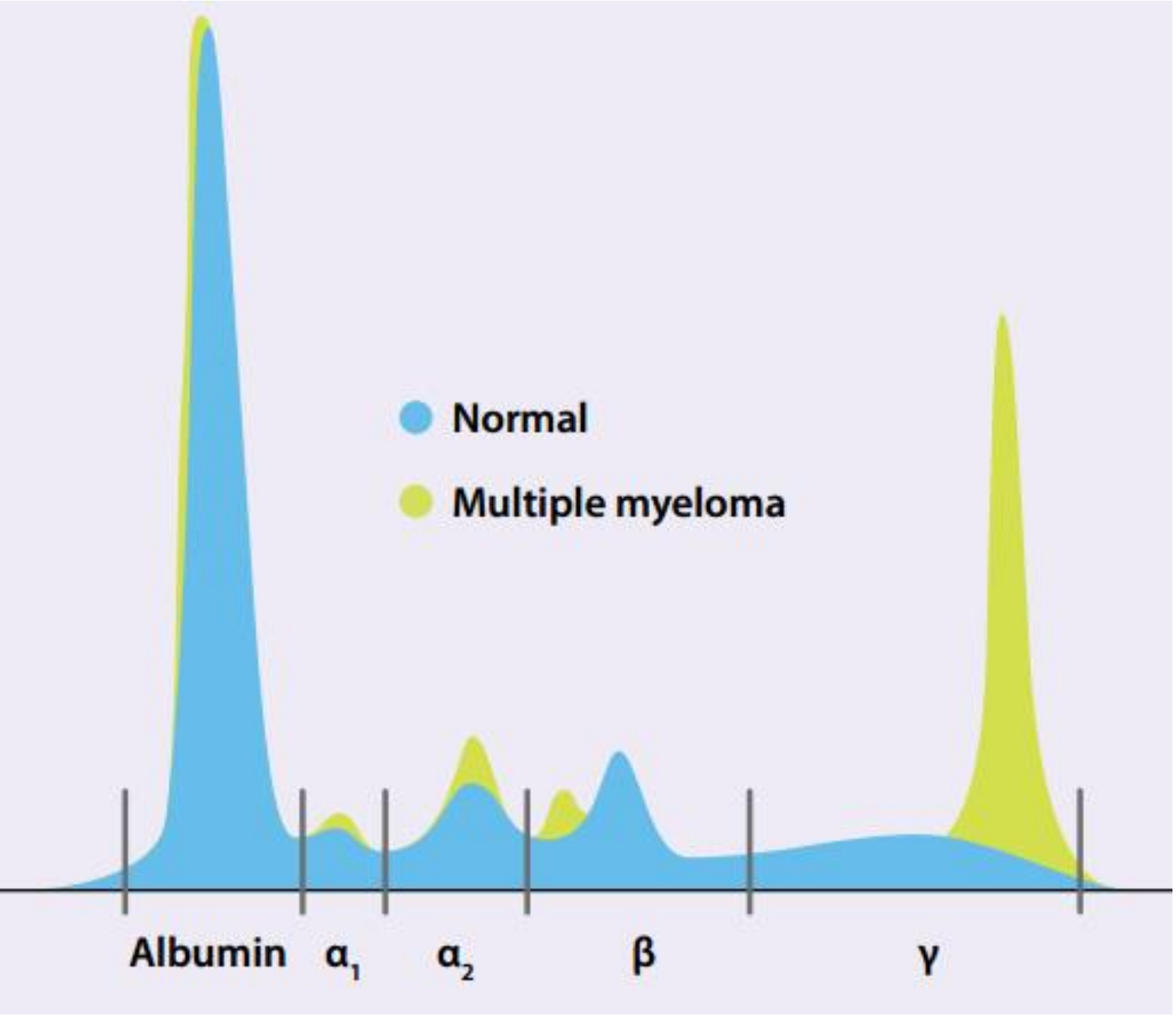
Plasma cell myeloma (multiple myeloma)

- Common lymphoid neoplasm
- Mean age 70
- It is usually confined to bone and bone marrow and does not involve the peripheral blood. However, we can detect clonality by simple serum test (ELECTROPHORESIS)!!!
  - Associated with an M protein
- Associated with lytic bone lesions



Normal serum protein electrophoresis diagram with legend of different zones


Albumin
gamma
alpha-1
alpha-2
beta


Normal
Multiple myeloma
Albumin
α1
α2
β
γ

- The most common M proteins are IgG, IgA and light chains
  - Rarely others
  - Light chains are secreted in urine as well
    - Bence Jones proteins

Pathogenesis

- B cell neoplasm of terminally differentiated B lymphocyte (plasma cell)
  - Several translocation involving IgH, cyclin D1 and D3 as well as Myc.

It affects….

- Bone
- Immune system
- Kidneys

Bone

- Releases factors such as RANKL that increase osteoclast activity
- Other factors that decrease osteoblastic activity
- Net result is
  - Lytic lesions
  - Pathologic fractures
  - Hypercalcemia

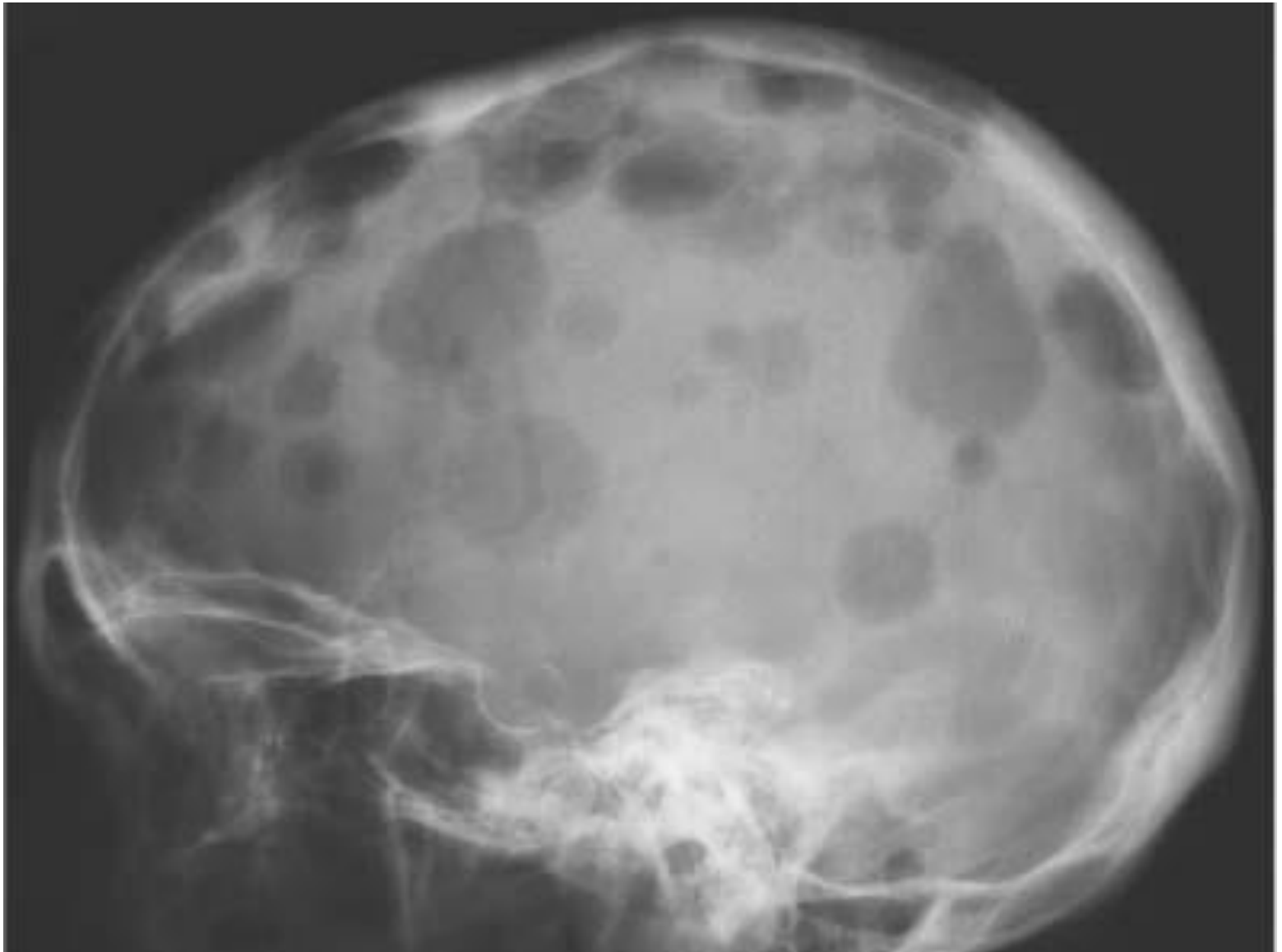
Humoral immunity

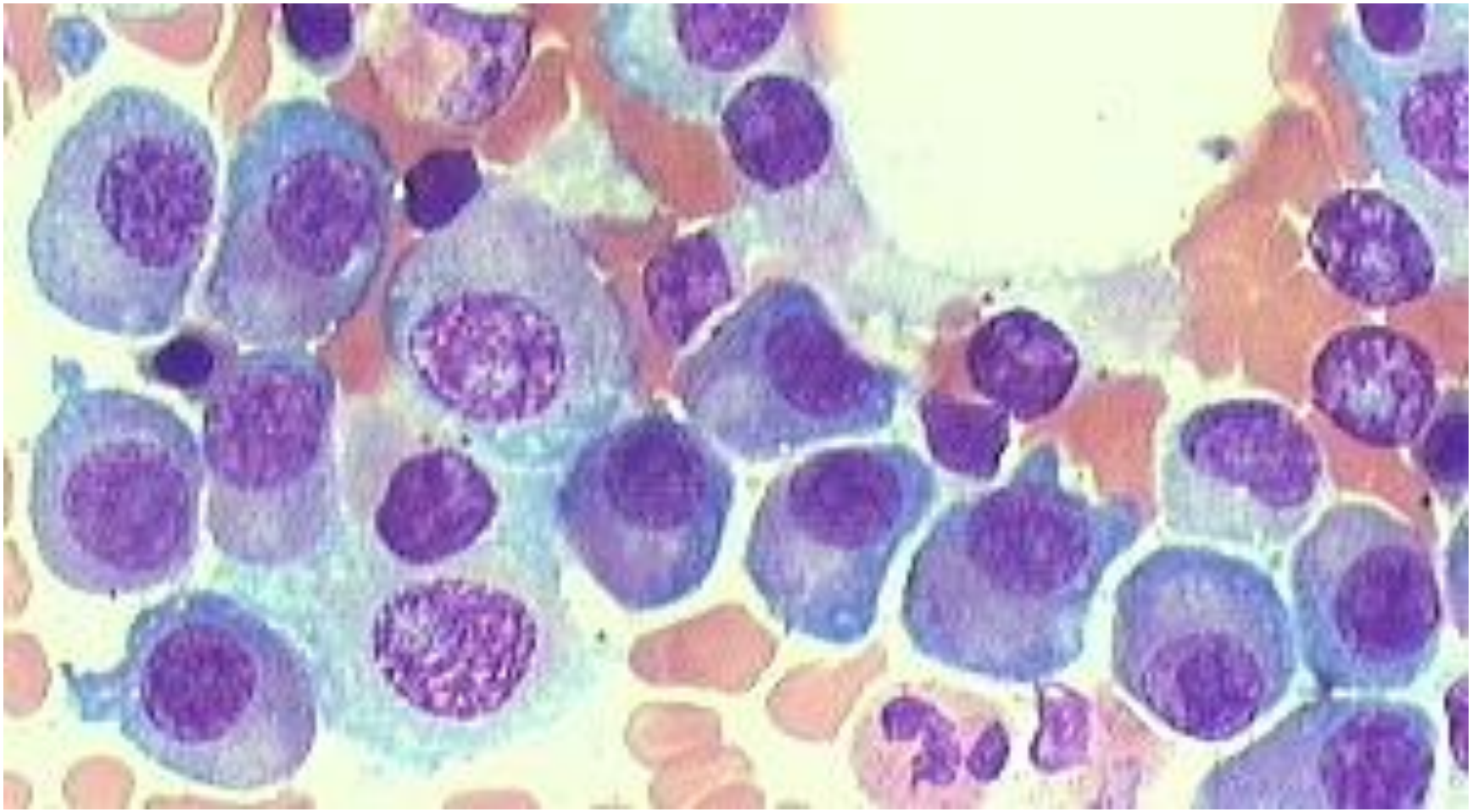
- Functional antibodies are markedly decreased
  - Increase risk of bacterial infections

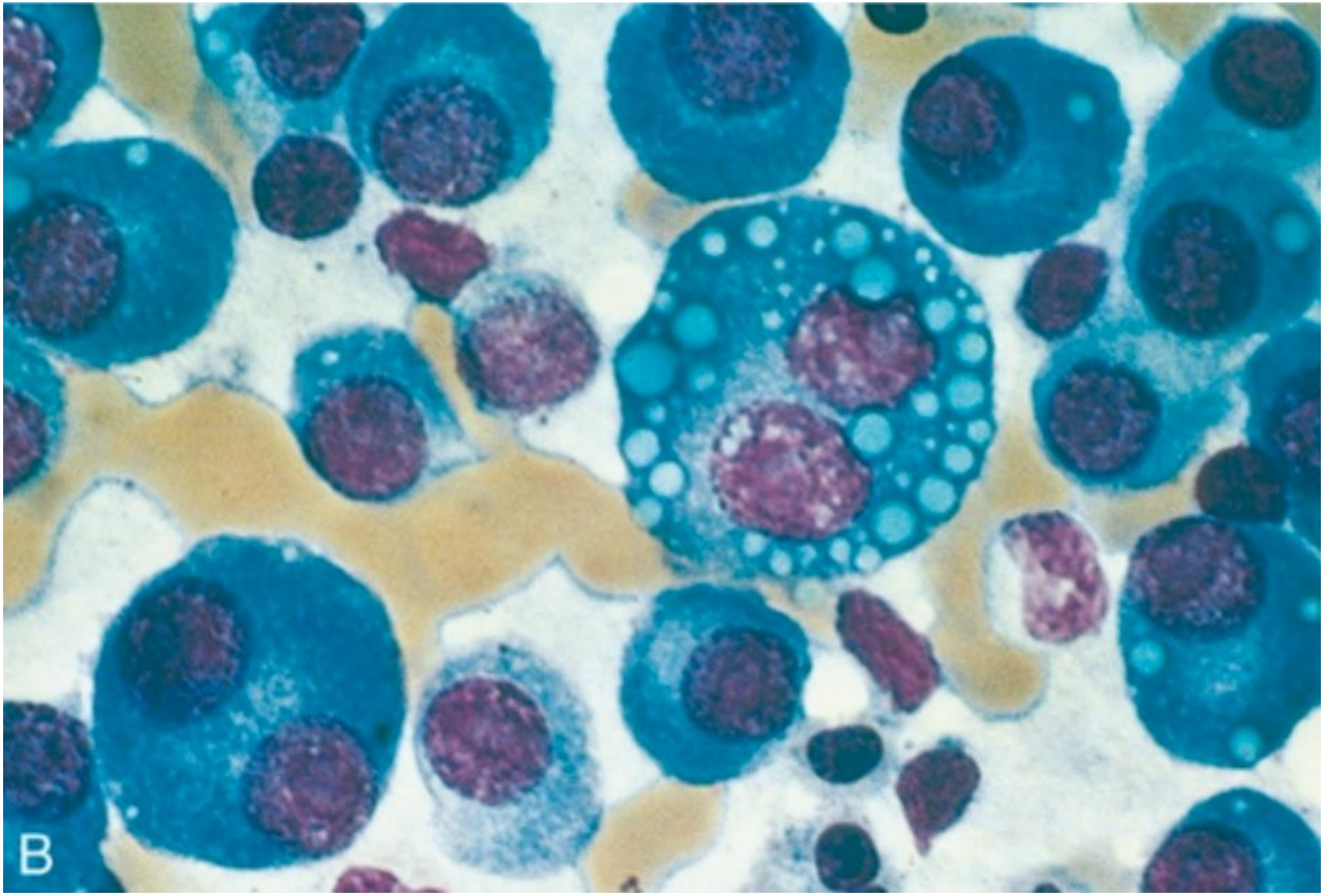
Kidney damage

- Obstructive casts composed of Bence jones proteins in the distal tubules
- Deposition of light chain in the glomeruli
  - Light chain disease
  - Amyloidosis
- Hypercalcemia resulting in renal stones
- Bacterial pyelonephritis

Morphology






B

Clinical manifestations

- Bone pain and pathologic fractures
- Hypercalcemia: neurological manifestations
  - Confusion, lethargy and weakness
- Recurrent bacterial infections
  - The most common of death
- Renal dysfunction
  - Second most common cause of death

Lab findings

- M protein
  - 1% are nonsecretors
- Elevated creatinine or urea
- Elevated calcium levels
- Anemia, thrombocytopenia and leukopenia

- Median survival is 4-7 years
- No cure!!!

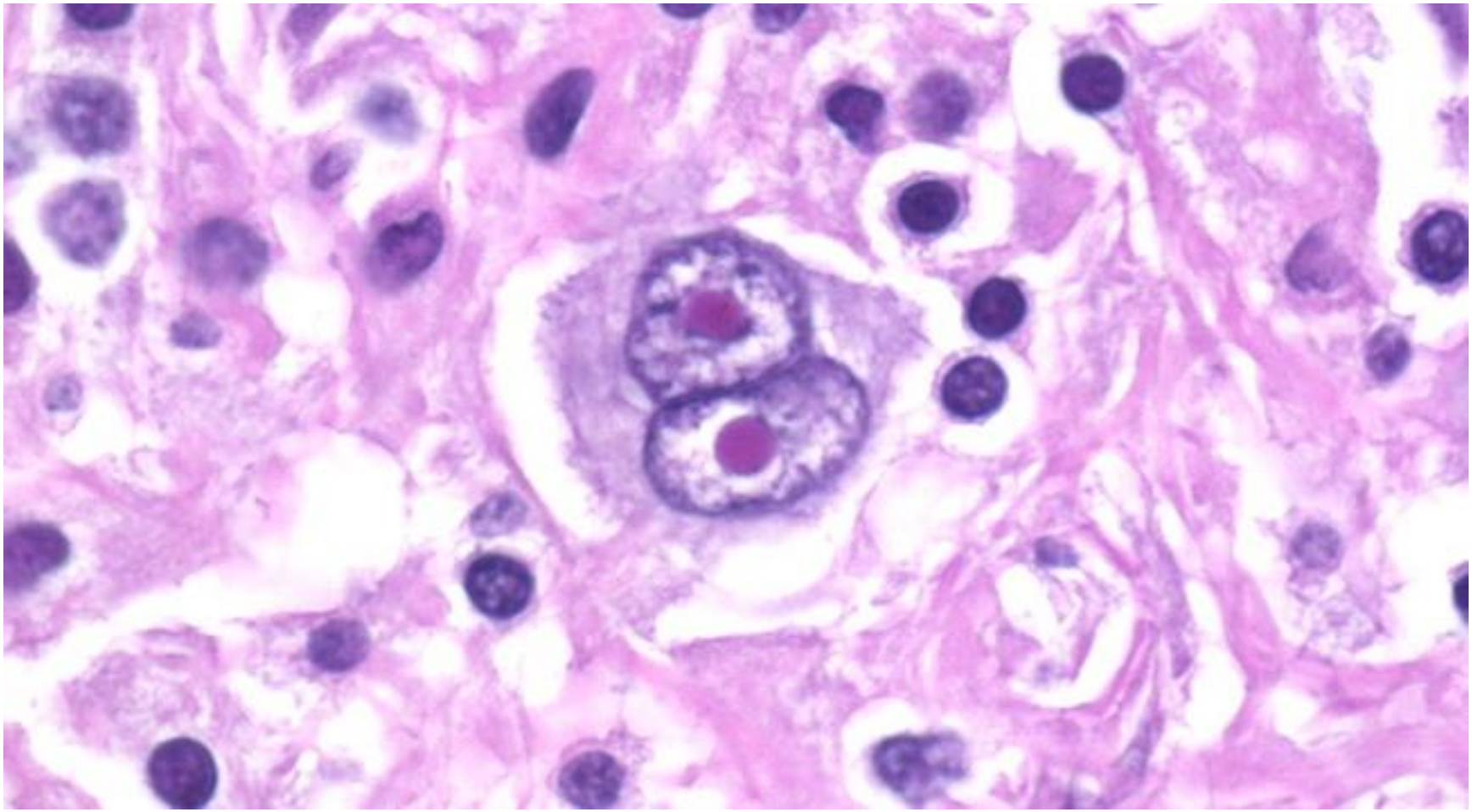
Hodgkin lymphoma

- Different from other B cell lymphoma
  - RS cells
  - Single lymph node or a group of contiguous lymph nodes
- B cell origin

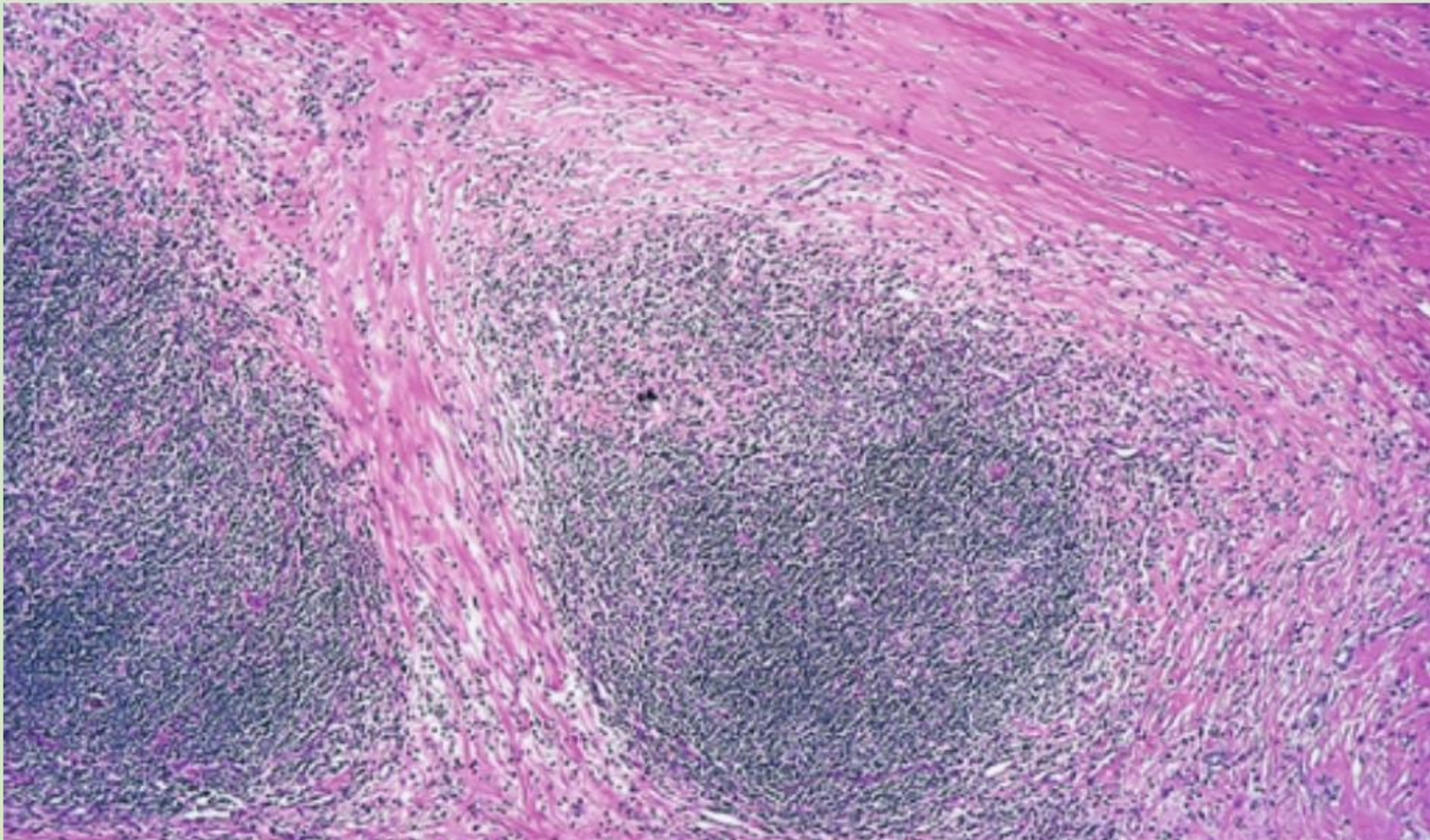
Two major subtypes

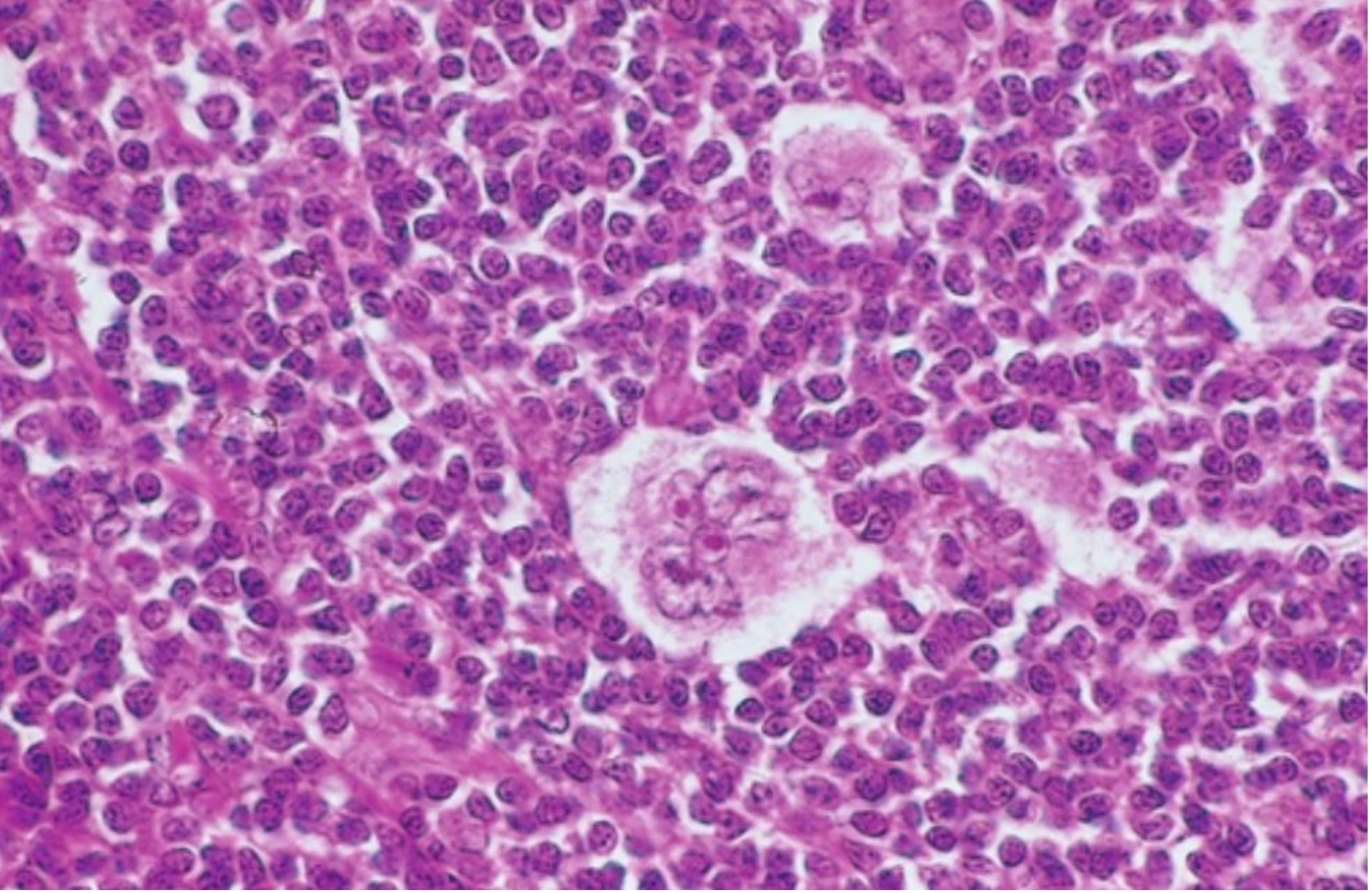
- Classic HL
  - Nodular sclerosis
  - Mixed cellularity
  - Lymphocyte-rich
  - Lymphocyte-depleted
- Nodular lymphocyte predominant HL

Morphology
RS cells

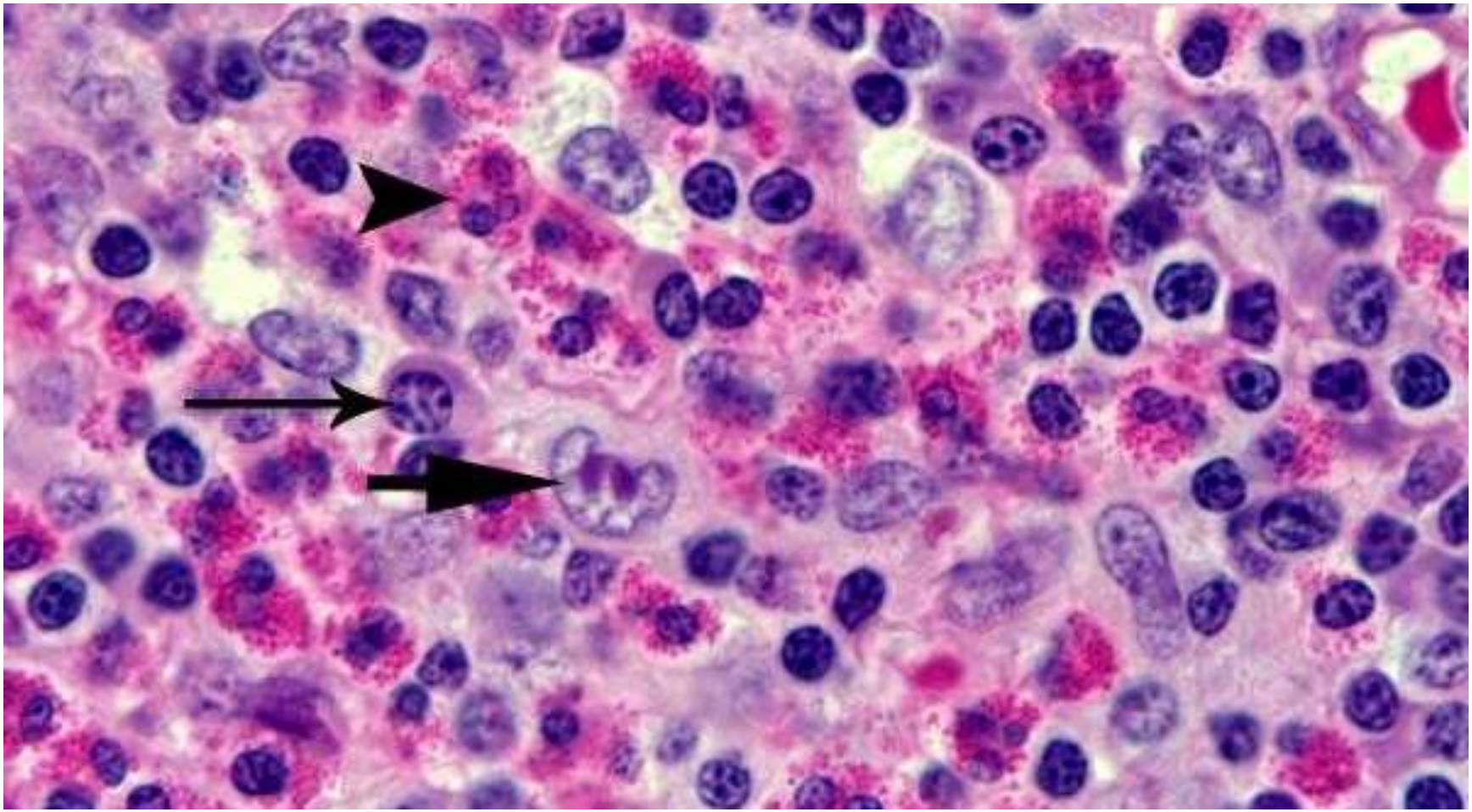


Nodular sclerosis

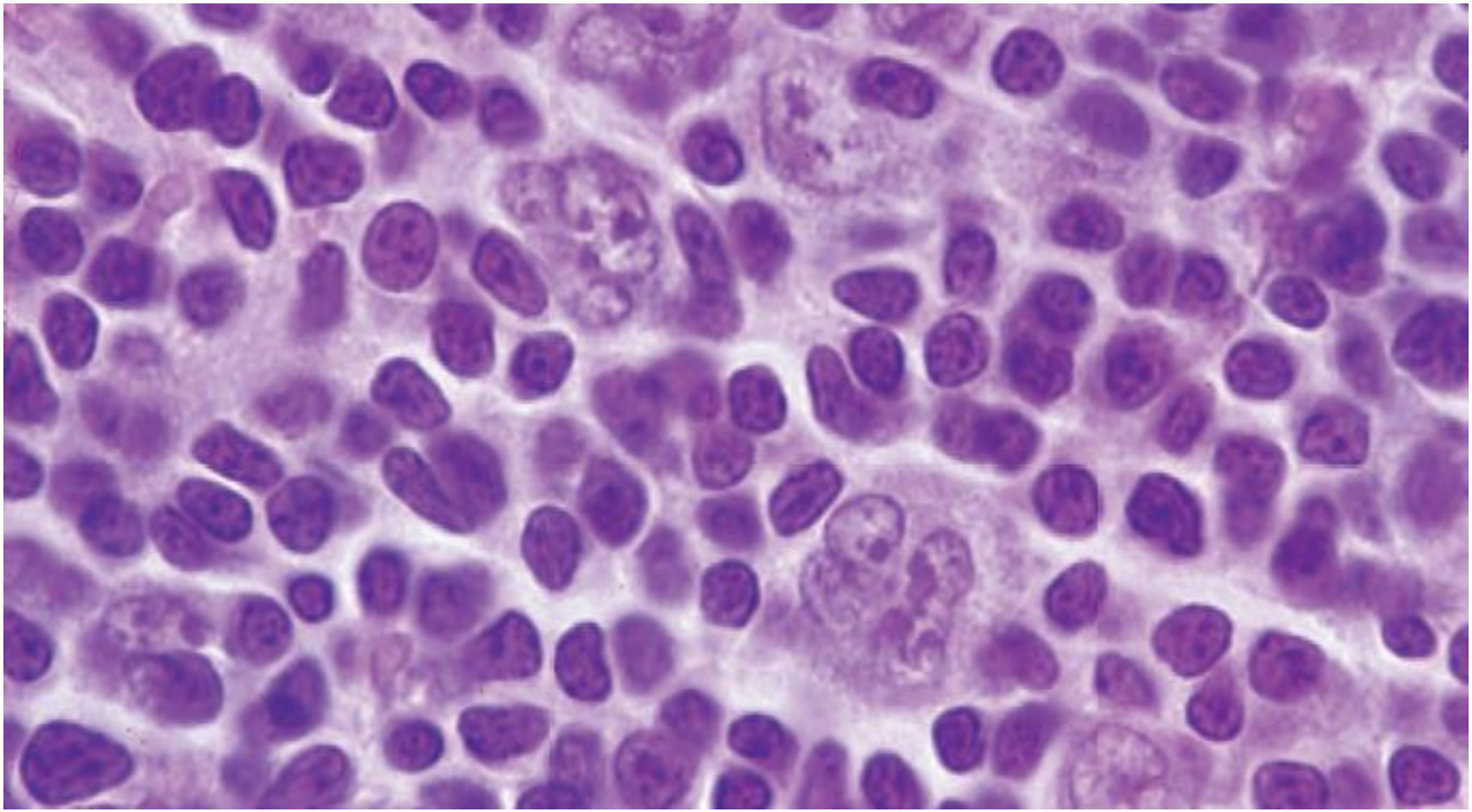




Mixed cellularity



NLP HL
(popcorn cells)



Immunophenotype

- Classic HL
  - CD30+, CD15+, pax5 weakly positive, negative for other B cell markers, negative for T cell markers, negative fro CD34
- NLP HL
  - Positive for B cell markers, negative for CD30, negative for CD15, negative for T cell markers, negative for CD34

Please remember…

- The vast majority of cells in a lymph node with HL are benign
- RS cells secrete
  - IL5 recruiting eosinophils
  - IL13 to promote their own growth
  - TGF-B resulting in fibrosis
  - PDL1 and PDL2 to inhibit T cell function
- They are neoplastic B cells!!!

Clinical manifestations

- Young age
  - Could affect any age
- Single lymph node or region of lymph nodes
  - Cervical and mediastinal
- Rarely involves tonsils, Waldeyer ring or extranodal sites
- Spreads in a contiguous manner

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

Staging system

Stage	Distribution of Disease
I	Involvement of a single lymph node region (I) or involvement of a single extralymphatic organ or tissue (I_E)
II	Involvement of two or more lymph node regions on the same side of the diaphragm alone (II) or with involvement of limited contiguous extralymphatic organs or tissue (II_E)
III	Involvement of lymph node regions on both sides of the diaphragm (III), which may include the spleen (III_S), limited contiguous extralymphatic organ or site (III_E), or both (III_{ES})
IV	Multiple or disseminated foci of involvement of one or more extralymphatic organs or tissues with or without lymphatic involvement

- Prognosis
  - Stage 1-2: 5-year survival more than 90%
  - Stage 3-4: 5-year survival 50%

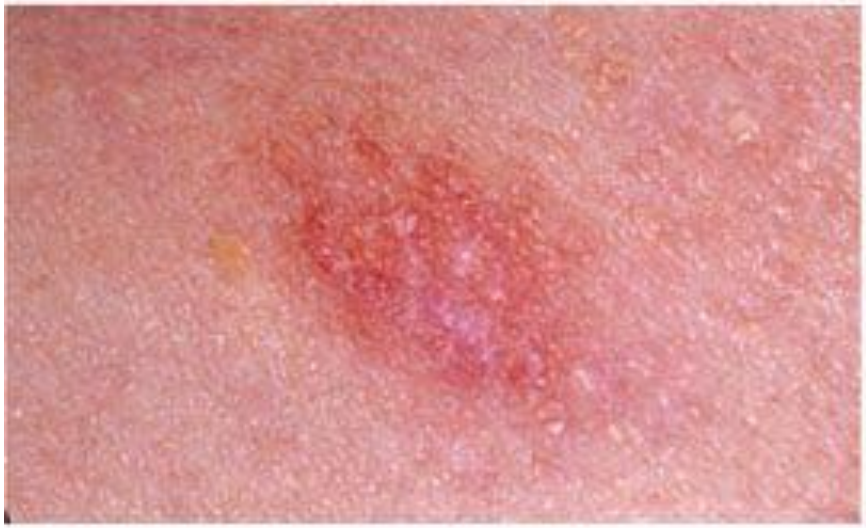
Mycosis fungoides and Sezary syndrome

- MF: a form of cutaneous T cell lymphoma
  - CD4+, CD8-
- Sezary syndrome:
  - Generalized exfoliative erythroderma and circulating tumor cells in the blood

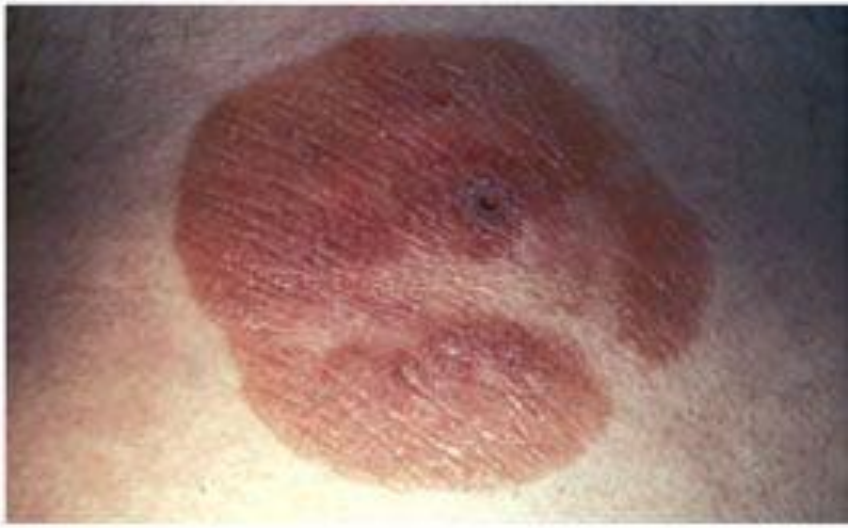
MF has three stages

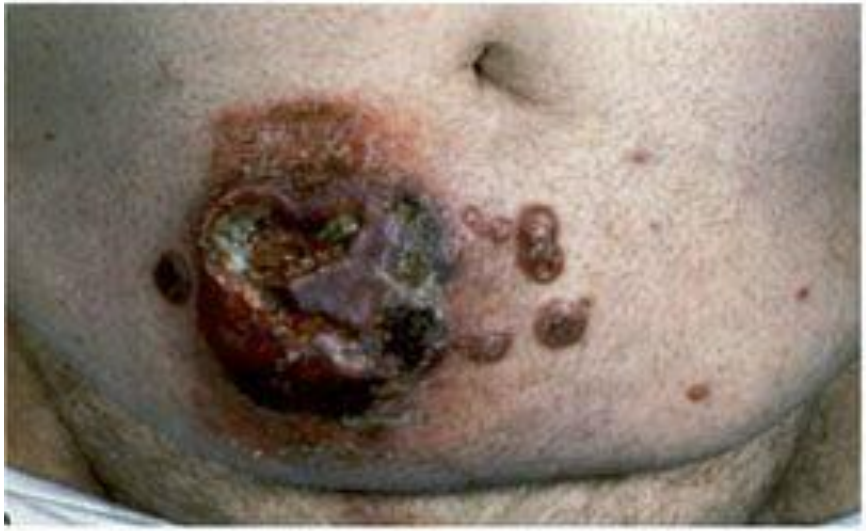
- 1-erythrodermic rash
- 2-plaque phase
- 3- Tumor phase

Patch



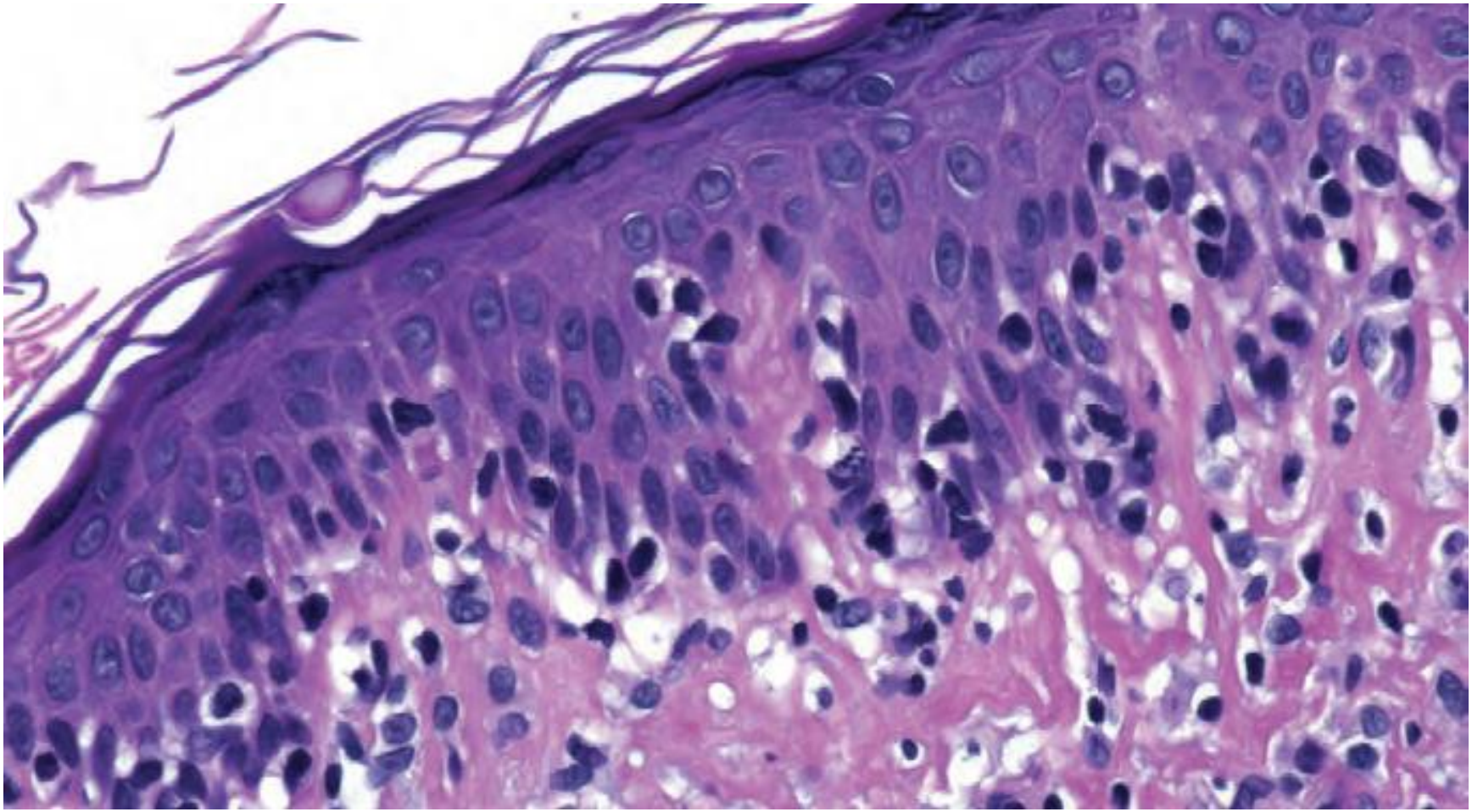
Plaque





Tumor

Erythroderma



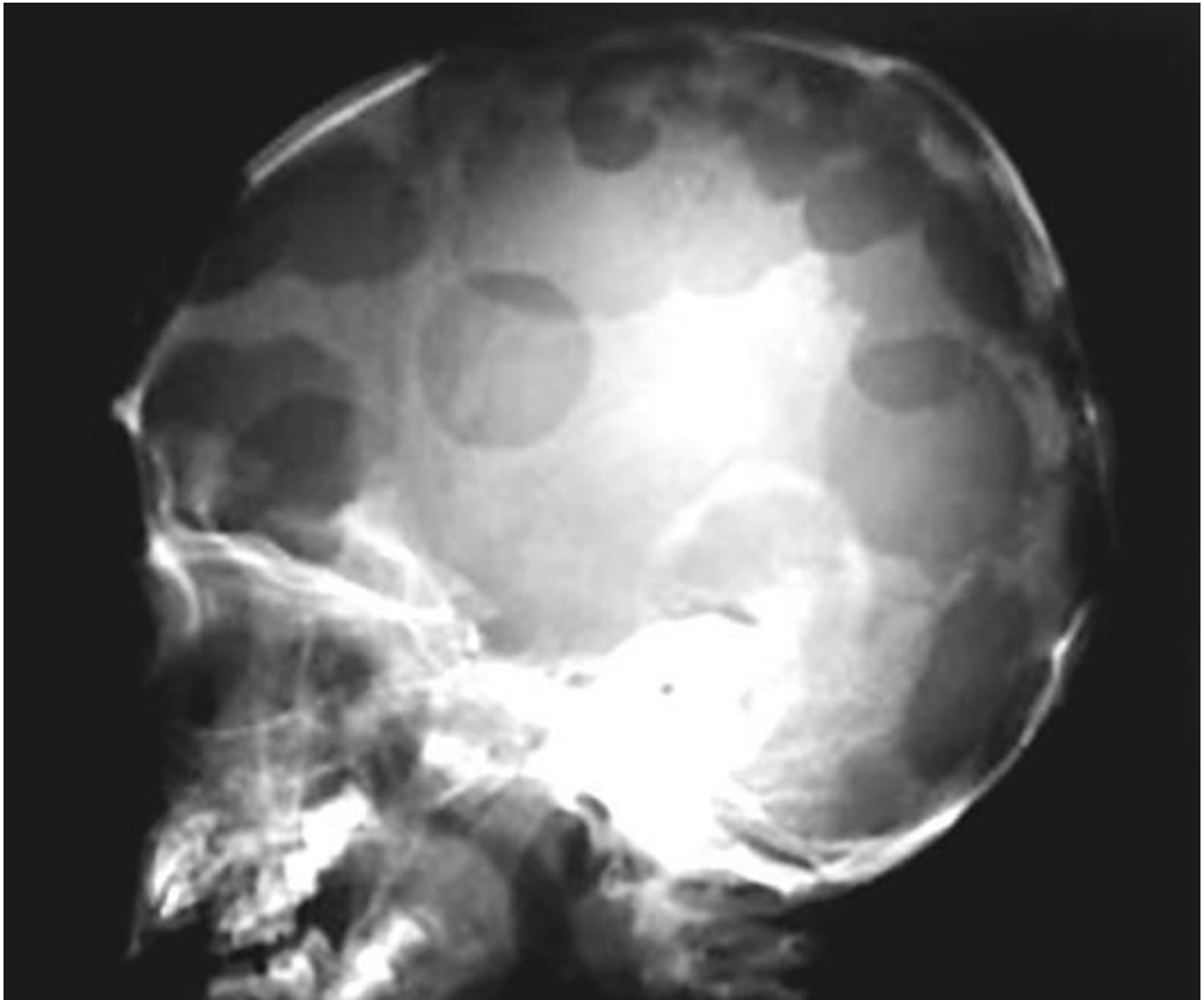
- Prolonged survival if early stage
- Tumor stage, visceral involvement or Sezary syndrome 1-3 years

Histiocytic neoplasms

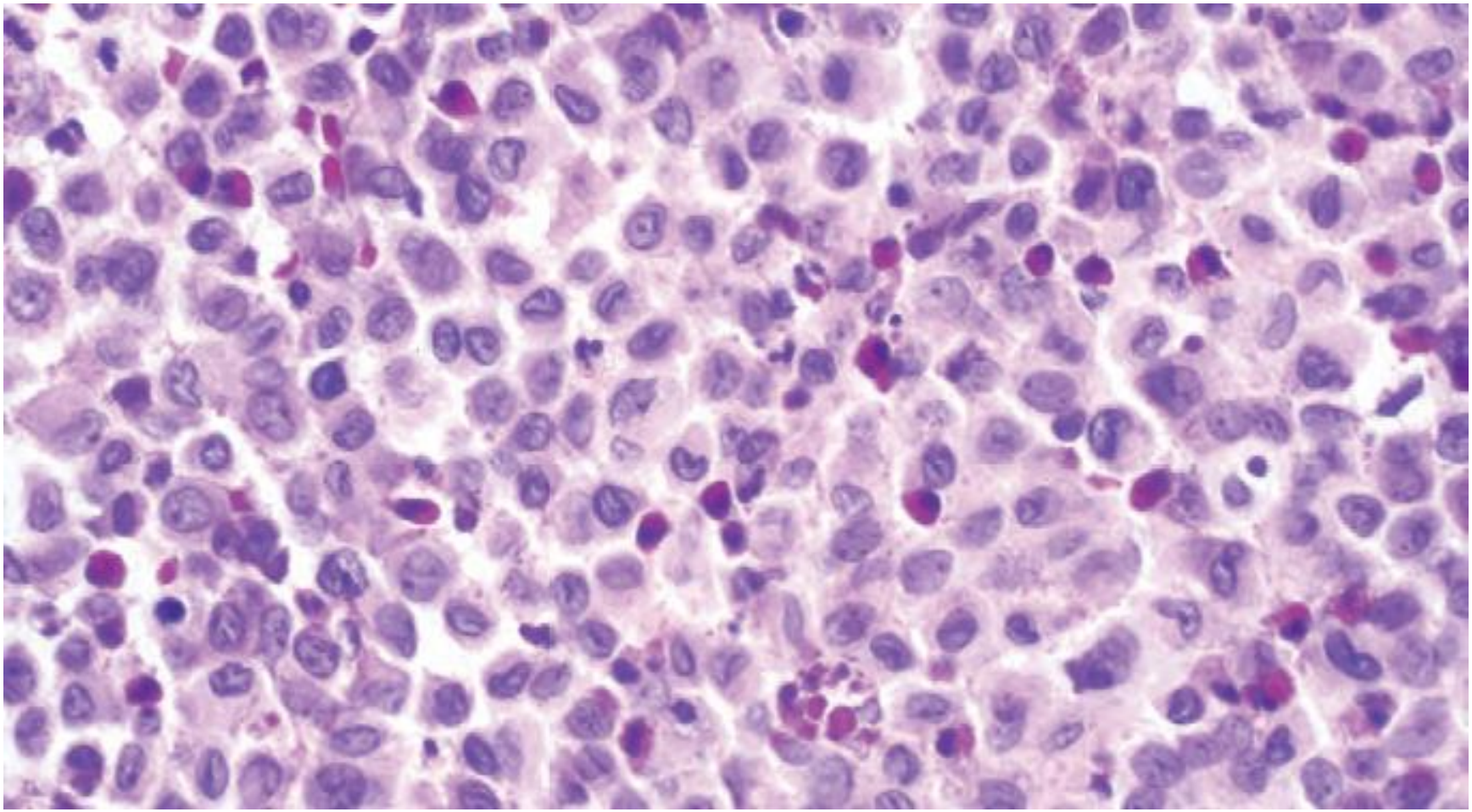
- The most important one is Langerhans cell histiocytosis (previously known as histiocytosis X)
- Langerhans cells: immature dendritic cells in the skin and other organs, present antigens to T cells

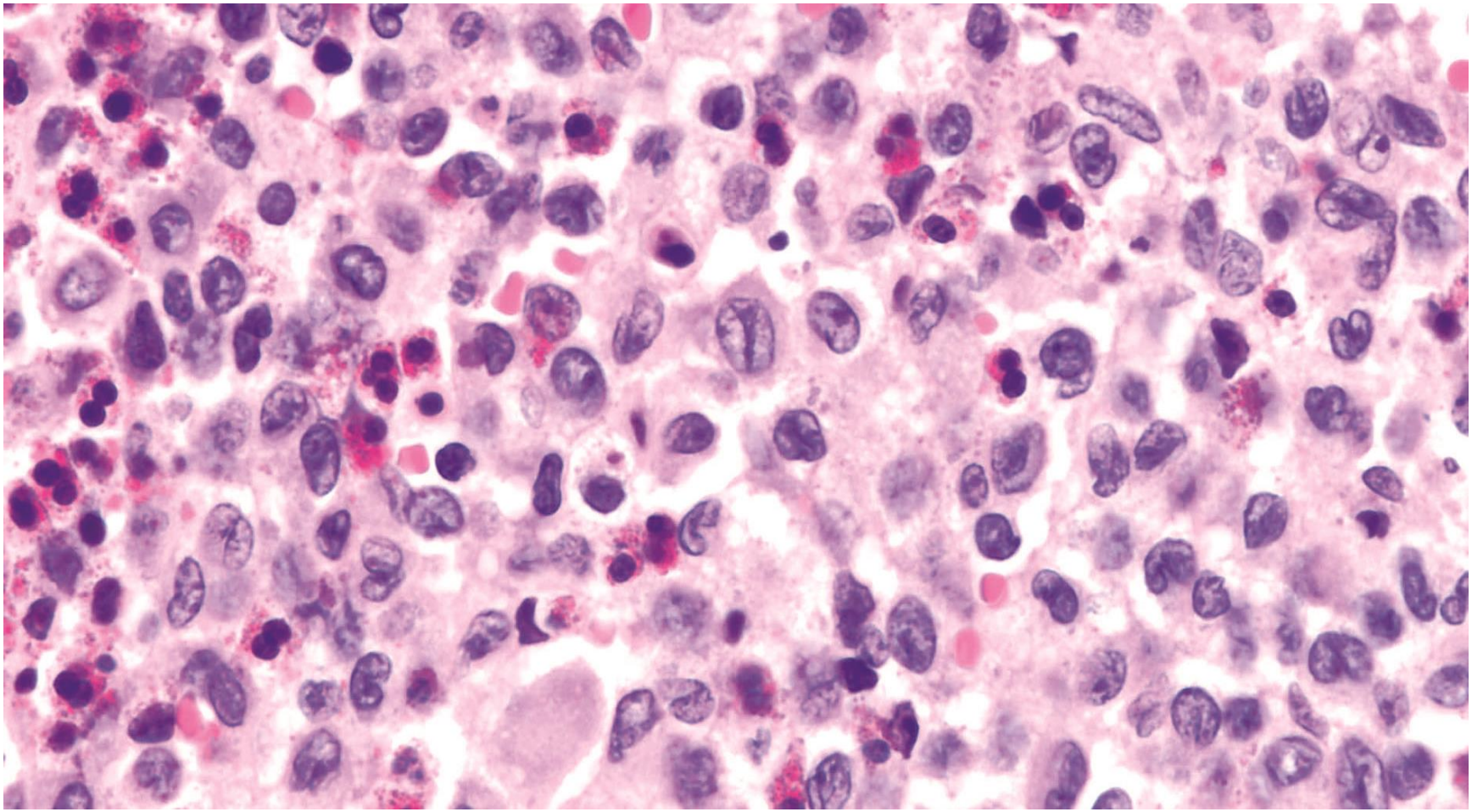
- Affects children less than 2 years of age
- Involves skin, bone, lungs, spleen, or bone marrow.
- Could be unifocal or multifocal
- Associated with BRAF mutation

Morphology



Morphology continued





Immunophenotype

- CD68, CD163, langerin and **CD1a**
  - **CD1a is the most important one and most specific for Langerhans cell differentiation**

New questions!!!

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