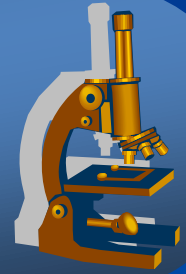


General pathology



General pathology V.
Neoplasms II (hematooncology).
Pathology of lymph nodes.

Summary

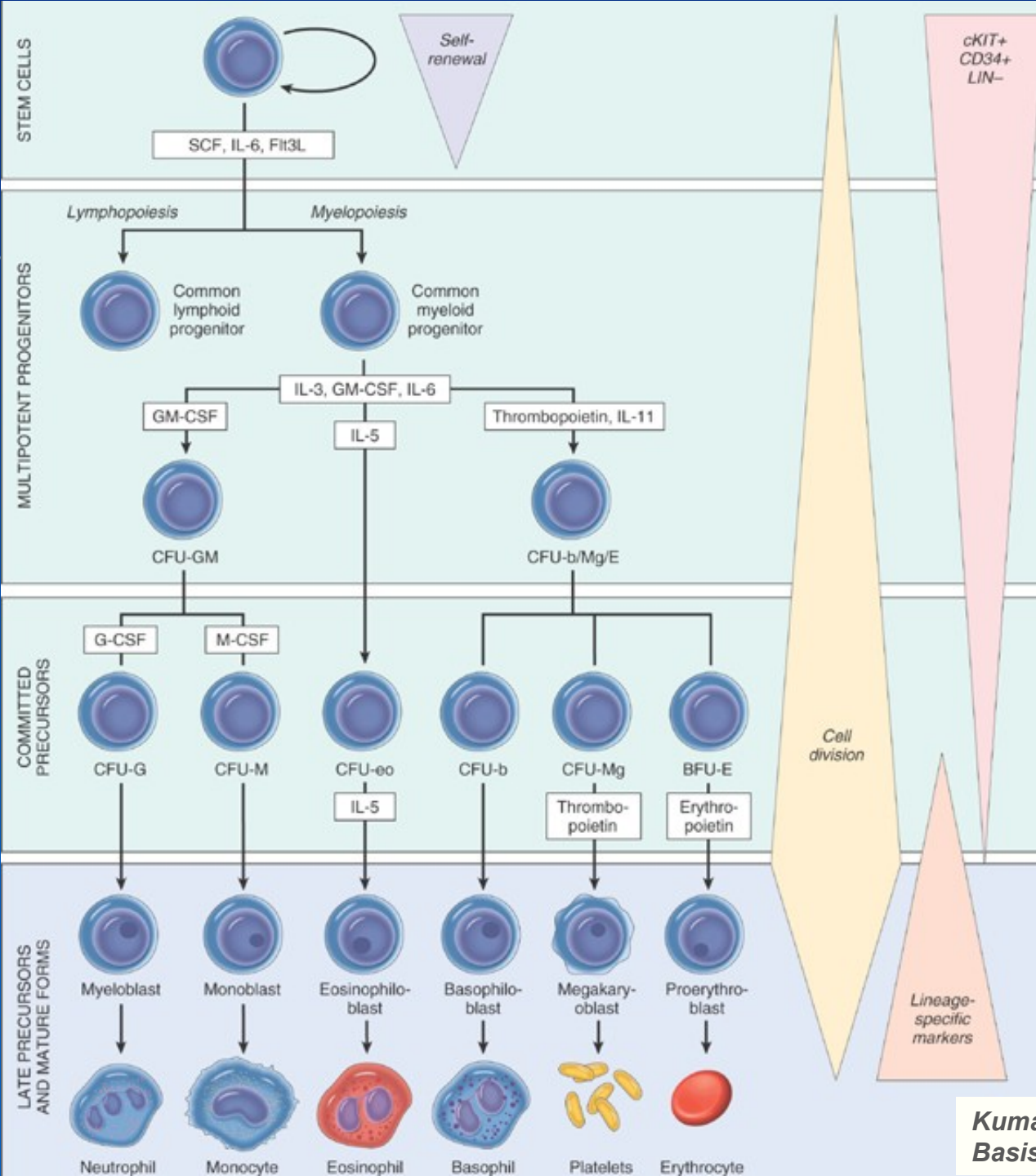


- **Hematopoiesis**
- **Myeloid neoplasms**
- **Lymphoid neoplasms**
 - Non-Hodgkin lymphomas*
 - Hodgkin lymphomas*
- **Reactive lymphadenopathy**

Hematopoiesis

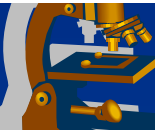


- from **hematopoietic stem cell**
- **HSCs (Hematopoietic Stem Cells): pluripotent, ability of self-renewal (replication)**
 - ⇒ *due to asymmetric cell division variable progenitor cells arise :*
 - **phenotypically identical cells – HSCs**
 - **phenotypically different cells – multipotent cells (progenitors of myeloid cell line or progenitors of lymphoid cell line)**
 - *Regulation of hematopoiesis through specific growth factors*
 - *GF receptors expressed during the development/differentiation on blood cells*



Hematopoietic stem cells

- in BM (<0,1% of cells)



Multipotent progenitors

Multipotent progenitors

Committed precursors

Late precursors and mature forms

- morphologically differentiated

Hematooncology



- **Leukemia (hemoblastosis)**

- *Diffuse replacement of normal BM by leukemic cells with their subsequent variable accumulation in peripheral blood (=leukemization)*
- *Infiltration of peripheral organs (liver, spleen, lymph nodes, meninges, gonads,...)*

- **Lymphoma (hemoblastoma)**

- *Neoplastic/lymphoma cells form tumor/neoplastic mass (nodal and/or extranodal)*

! Lymphomas may also present by leukemic infiltrates and leukemias also form solid neoplastic masses

Hematooncology



- Mutations that inhibit normal differentiation and maturation of progenitor cells, or mutations disrupting the regulation of progenitor and precursor cells by growth factors

⇒ **Unregulated clonal expansion of immature hematopoietic cells → inhibition of normal hemopoiesis → release of immature blast into circulation, infiltration of peripheral organs**

Hematooncological diseases



× Myeloid neoplasms

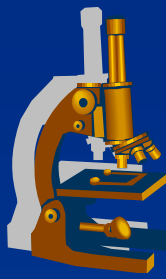
- from stem cells that normally give rise to the formed blood elements (granulocytes, red cells, platelets)
- 3 categories
 - acute myelogenous leukemias
 - myeloproliferative disorders
 - myelodysplastic syndromes

× Lymphoid neoplasms

- non-Hodgkin lymphomas
(incl. lymphocytic leukemias and plasma cell dyskrasias)
- Hodgkin lymphomas

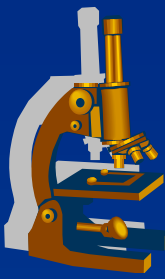
× Histiocytic neoplasms

Etiopathogenesis of hematological diseases



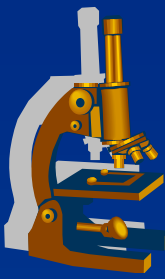
- ???
- **hereditary syndromes**
 - *Inherited genetic instability (Bloom's sy, ataxia teleangiectasia...), Down's sy, NF type I...*
- **oncogenic viruses**
 - *HTLV-1, EBV, HSV-8*
- **chronic stimulation of immune system**
 - *Helicobacter pylori, gluten-sensitive enteropathy (celiac sprue)*
- **iatrogenicity**
 - *radiotherapy, chemotherapy*
- **smoking**

TUMORS of HAEMATOPOETIC and LYMPHATIC TISSUES



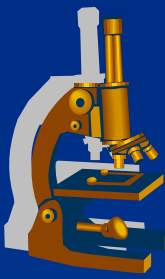
- × **Myelodysplastic syndromes**: clonal stem cell disorders, ineffective haematopoiesis → cytopenias; dysplastic maturation. De novo or after radio/chemotherapy. Progressive marrow failure. May → AML.
- × **Myelodysplastic/myeloproliferative diseases** overlapping features, variably effective haematopoiesis, dysplasia

TUMORS of HAEMATOPOETIC and LYMPHATIC TISSUES



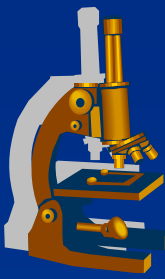
- × acute myeloid leukaemia + related precursor neoplasms** - clonal expansion of myeloid blasts in bone marrow, blood or other tissues (myeloid sarcoma).
- × Class. acc. genetic abnormalities** (in young, good response to therapy and behaviour), multilineage dysplasia (i. e. following MDS, older, drug resistance), therapy-related; other – acc. morphology (modified FAB)

TUMORS of HAEMATOPOETIC and LYMPHATIC TISSUES



- x Histiocytic and dendritic cell neoplasms**
- x from mononuclear phagocytes**
(macrophages, dendritic antigen-presenting cells) – common bone marrow precursor
- x follicular dendritic cells non-myeloid, from mesenchymal stem cell**
- x true histiocytic neoplasm uncommon**
(Langerhans cell histiocytosis, benign disseminated juvenile xanthogranuloma)

LYMPHOID NEOPLASMS



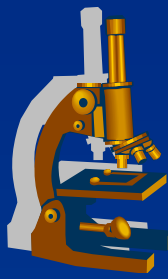
Both lymphoid leukaemias and lymphomas included

- × **Hodgkin lymphoma**

- × **Non-Hodgkin lymphomas** (B cell neoplasms, T and NK cell n.);

- × In B, T+NK – 2 main subcategories:
precursor n. (earliest stages of differentiation; acute lymphoblastic leukaemia/lymphoma)

 - mature** (peripheral) n . (B~normal stages of differentiation, 85%; T~post-thymic; rare NK)



MYELOID NEOPLASMS

Origin from hematopoietic stem cells that typically give rise to monoclonal proliferation replacing normal bone marrow cells.

× Hematopoiesis

• **Myeloid neoplasms**

• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

Myeloid neoplasms



1. Myelodysplastic syndrome (MDS)
2. Acute myeloid leukemia (AML)
3. Chronic myeloproliferative disorders

× Hematopoiesis

• Myeloid neoplasms

• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

MDS



- **Disordered and ineffective maturation of myeloid progenitors**
- ***Bone marrow: hypercellular or normo-cellular***
- ***Peripheral blood: cytopenia of one or more cell lines***
- ***Risk of transformation into AML***
(abnormal stem cell clone genetically unstable → additional mutations → AML)
- **Mostly in older individuals**
 - *Infections, anemia, hemorrhages*
 - *incidence 1-2/100 000 (in older individuals 40/100 000!)*

× Hematopoiesis

• **Myeloid neoplasms**

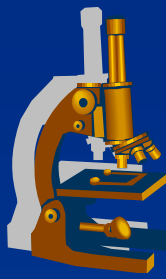
• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

AML



- **Inhibition of normal myeloid differentiation of HSC or myeloid progenitor**

- Replacement of normal BM elements by leukemic blasts
- Hiatus leukemicus
- Immature blasts released into peripheral blood
- Leukemic infiltrates in bone marrow, liver, spleen, lymph nodes....
- Rarely AML presents as a solid mass (granulocytic sarcoma)
- Generally very poor prognosis

⇒ ***clinical signs of marrow failure***

- *anemia* (fatigue, palor)
- *trombocytopenia* (abnormal bleeding)
- *leukopenia* (infections - fever)

- primarily in older adults (median age 50)

× Hematopoiesis

- **Myeloid neoplasms**

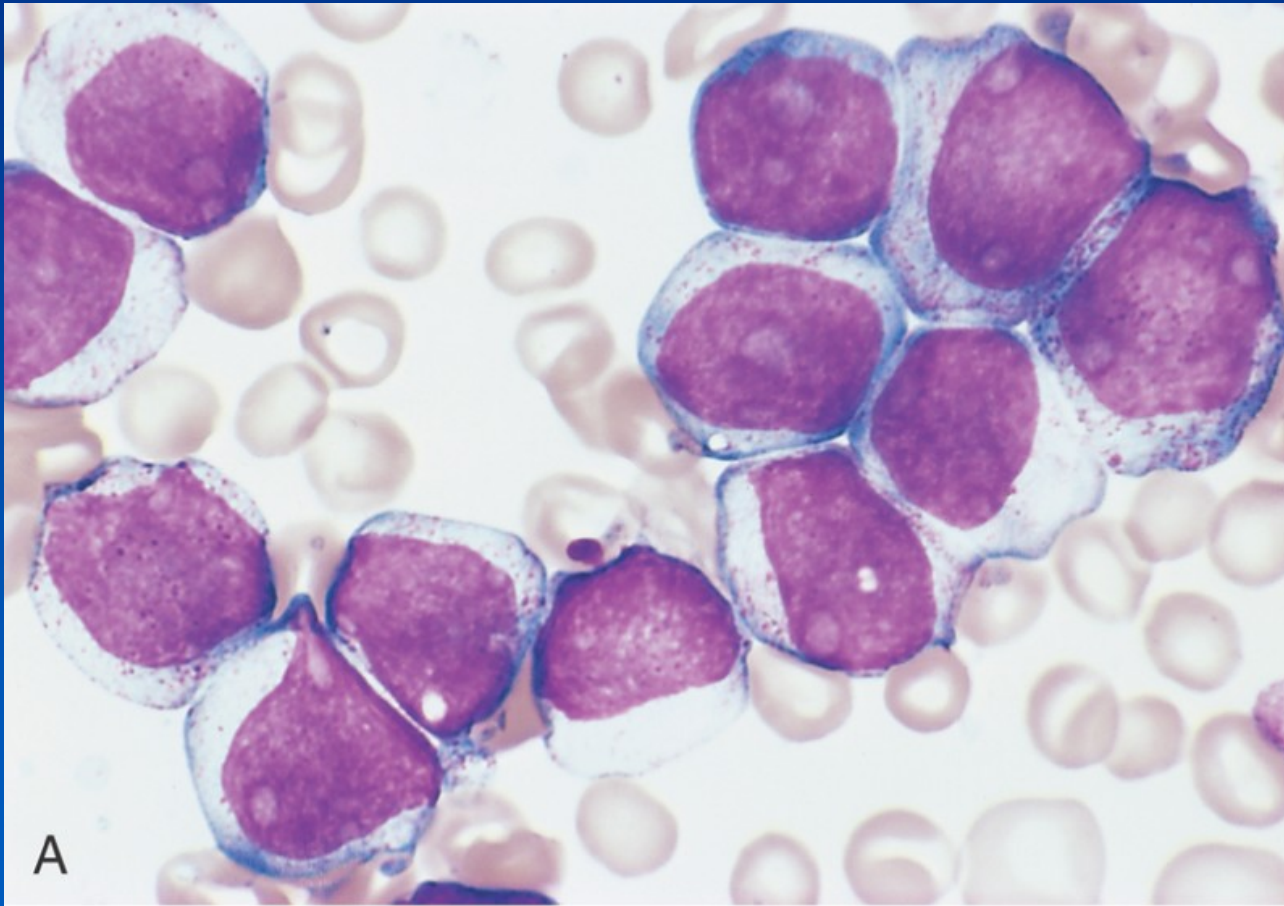
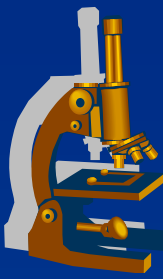
- Lymphoid neoplasms

⇒ *NHL*

⇒ *HL*

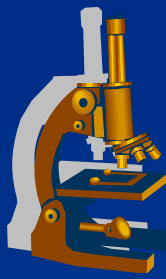
- Reactive lymphadenopathy

AML



Kumar et al: Robbins & Cotran Pathologic Basis of Disease, 8th Edition.
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AML



- WHO classification *(only informative)*
- **I. AML WITH GENETIC ABERRATIONS**
 - ⇒ AML with t(8;21)(q22;q22); prognosis - M2 subtype; morphology: Full range of myelocytic maturation; Auer rods easily found; abnormal cytoplasmic granules
 - ⇒ AML with inv(16)(p13;q22); - M4eo; Myelocytic and monocytic differentiation; abnormal eosinophilic precursors with abnormal basophilic granules
 - ⇒ AML with t(15;17)(q22;11-12); +/-; M3; Numerous Auer rods, often in bundles within individual progranulocytes; primary granules usually very prominent; high incidence of DIC
 - ⇒ AML with t(11q23;q); ☹; M4, M5; Usually some degree of monocytic differentiation
 - ⇒ AML with normal cytogenetics ; ☺; FAB subtype variable Detected by immunohistochemical staining for NPM
- **II. AML WITH MDS-LIKE FEATURES**
 - ⇒ With prior MDS; ☹; Variable Diagnosis based on clinical history
 - ⇒ AML with multilineage dysplasia; ☹; Variable Maturing cells with dysplastic features typical of MDS
 - ⇒ AML with MDS-like cytogenetic aberrations; ☹; Variable Associated with 5q-, 7q-, 20q-aberrations

✗ Hematopoiesis

• Myeloid neoplasms

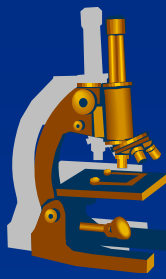
• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

AML



- **III. AML, THERAPY-RELATED; prognosis @@; FAB subtype** Variable
If following alkylator therapy or radiation therapy, 2- to 8-year latency period, MDS-like cytogenetic aberrations (e.g., 5q-, 7q-); if following topoisomerase II inhibitor (e.g., etoposide) therapy, 1- to 3-year latency, translocations involving *MLL* (11q23)
- **IV. AML, NOT OTHERWISE SPECIFIED**
 - ⇒ *AML, minimally differentiated; +/-; M0 subtyp; Negative for myeloperoxidase; myeloid antigens detected on blasts by flow cytometry*
 - ⇒ *AML without maturation; +/-; M1; >3% of blasts positive for myeloperoxidase*
 - ⇒ *AML with myelocytic maturation; +/-; M2; Full range of myelocytic maturation*
 - ⇒ *AML with myelomonocytic maturation; +/-; M4; Myelocytic and monocytic differentiation*
 - ⇒ *AML with monocytic maturation; +/-; M5; nonspecific esterase-positive monoblasts and pro-monocytes predominate in marrow and blood; in M5b subtype, mature monocytes predominate in the blood*
 - ⇒ *AML with erythroid maturation; +/-, M6; defined by >50% dysplastic maturing erythroid precursors and >20% myeloblasts; pure erythroid subtype (M6b) defined by >80% erythroid precursors without myeloblasts*
 - ⇒ *AML with megakaryocytic maturation; +/-; M7; Blasts of megakaryocytic lineage predominate; detected with antibodies against megakaryocyte-specific markers (GPIIb/IIIa or vWF); often associated with marrow fibrosis; most common AML in Down syndrome*

× Hematopoiesis

• **Myeloid neoplasms**

• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

Chronic myeloproliferative disorders



- Neoplastic myeloid progenitors retain the capacity to undergo terminal differentiation but exhibit increased or dysregulated growth
- **Peripheral blood:** increase in one or more lines of the formed elements (red cell, platelets, and/or granulocytes)
- **Neoplastic progenitors homing to secondary hematopoietic organs** (spleen, liver, lymph nodes,...)
→hepatosplenomegaly, lymphadenopathy, extramedullar hematopoiesis
- chronic diseases of adults
- due to genetic alterations ass. with **increased tyrosine kinases activity**(=acquired genetic disorder)→therapy by tyrosine kinase inhibitors

×Hematopoiesis

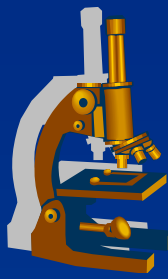
•**Myeloid neoplasms**

•Lymphoid neoplasms

⇒*NHL*

⇒*HL*

•Reactive lymphadenopathy



Chronic myeloproliferative disorders

1. Chronic myeloid leukemia (CML)
2. Essential thrombocythemia
3. Polycythemia vera
4. Primary myelofibrosis

× Hematopoiesis

• **Myeloid neoplasms**

• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

CML



- **Acquired genetic abnormality:** BCR-ABL fusion gene (t(9;22)), derivative chromosome 22 on 9 – Philadelphia chromosome, chimeric protein: BCR-ABL tyrosine kinase
- CML originates from a pluripotent stem cell
- **Clinical course:** slow progression (fatigability, weakness, weight loss) – accelerated phase – blast crisis (~ AML like)
- **Therapy:**
 - ⇒ imatinib mesylate (inhibitor of the BCR-ABL tyrosine kinase)
 - ⇒ bone marrow transplantation

× Hematopoiesis

• **Myeloid neoplasms**

• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

CML



- **Adults** (25-60 years, peak in 4th-5th decade)
- **Elevated leukocyte count** (>100,000 cells μ /l)
- **Hypercellular bone marrow**
(hyperplasia of granulocytic and megakaryocytic precursors)
- **Circulating cells:** predominantly neutrophils, metamyelocytes and myelocytes, myeloblasts <5 %
- Extreme **hepatosplenomegaly**, spleen up to 20 kg
- **Extramedullary hematopoiesis**

✗ Hematopoiesis

• **Myeloid neoplasms**

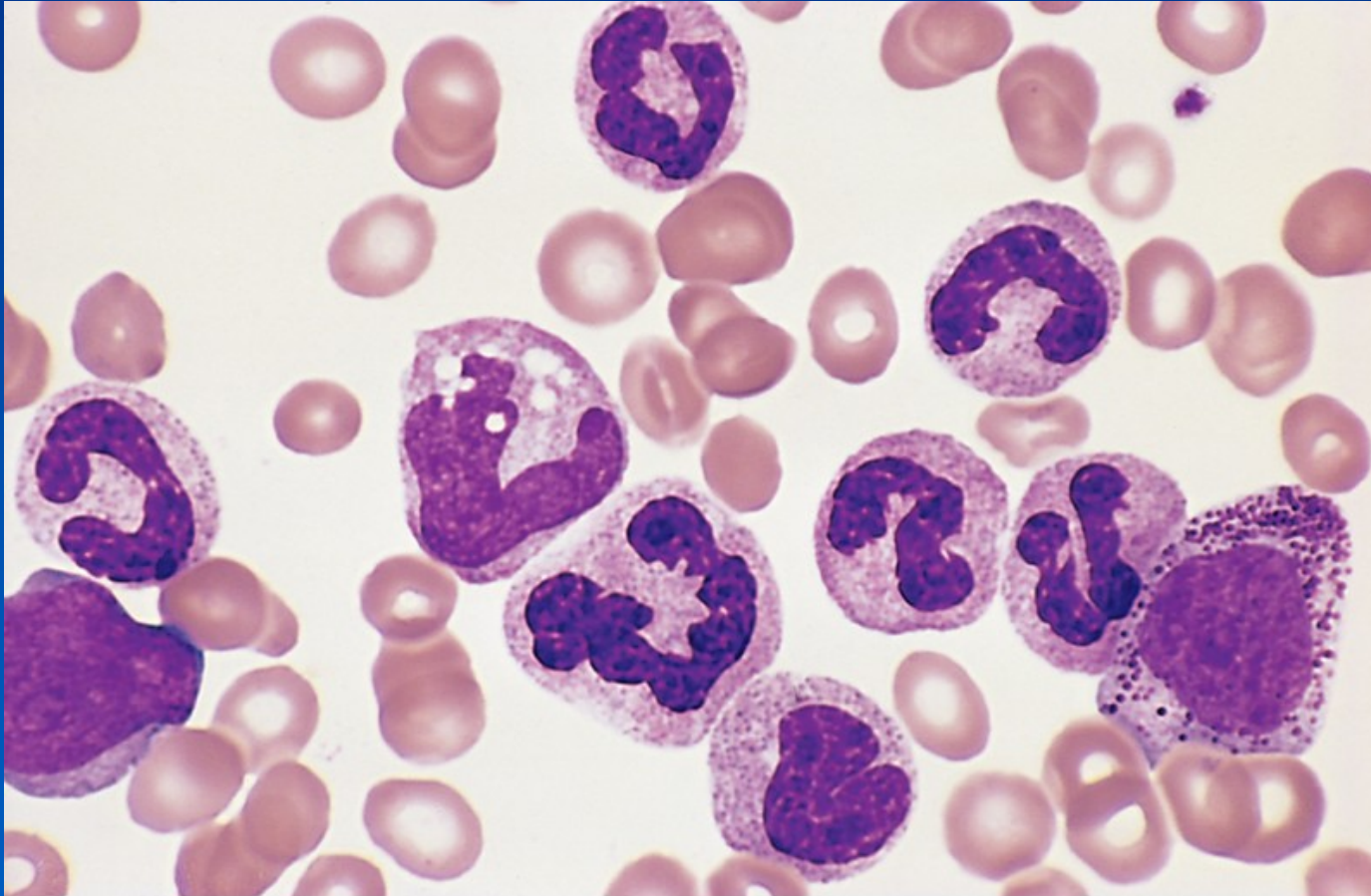
• Lymphoid neoplasms

⇒ NHL

⇒ HL

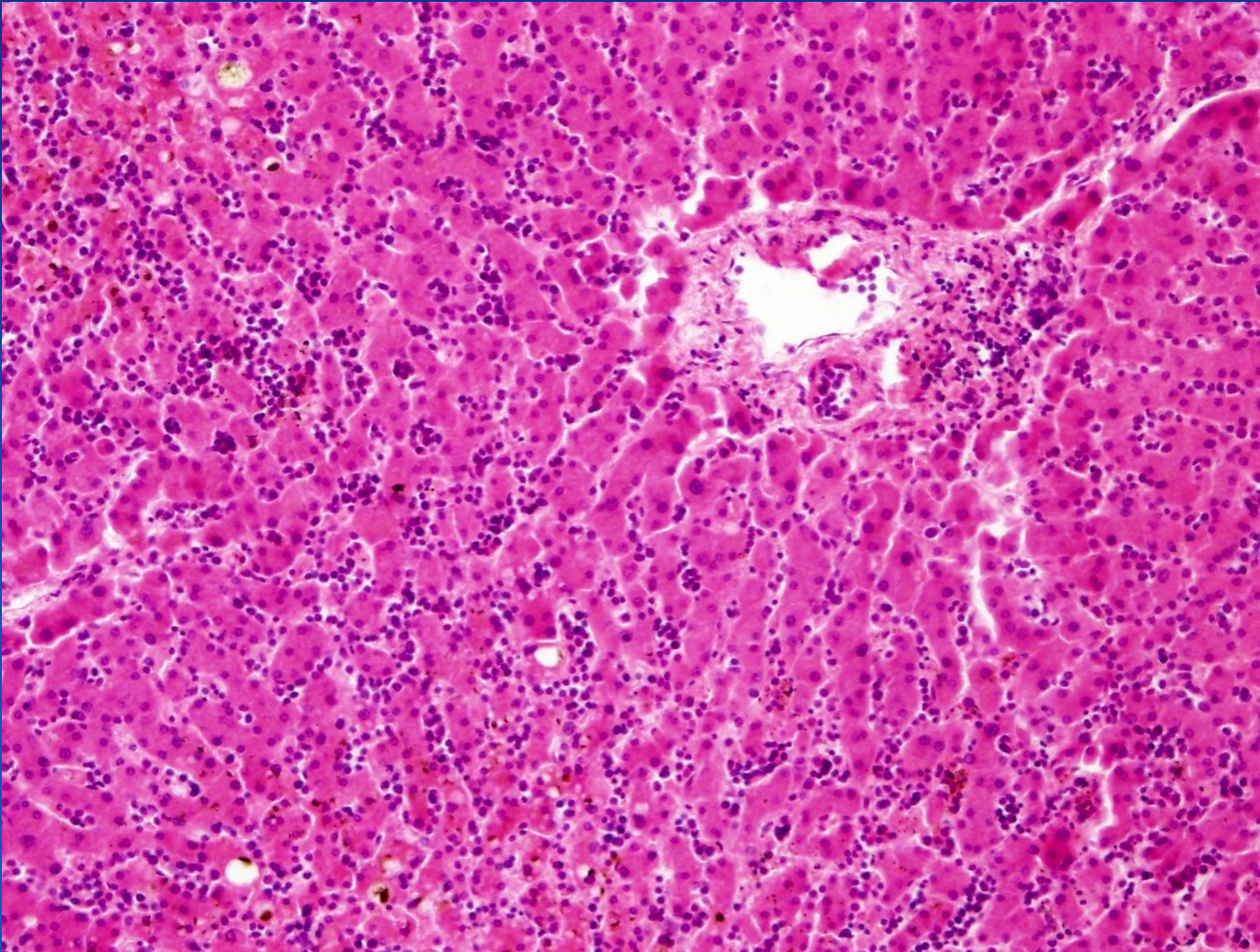
• Reactive lymphadenopathy

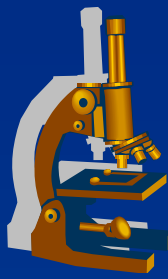
CML



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CML – leukemic cells in liver sinusoids





LYMPHOID NEOPLASMS /LYMPHOMAS

Classification:

→ **non-Hodgkin lymphomas**

(incl. lymphocytic leukemias and plasma cell dyskrasias)

→ **Hodgkin lymphomas**

× Hematopoiesis

× Myeloid
neoplasm

• **Lymphoid
neoplasms**

⇒ NHL

⇒ HL

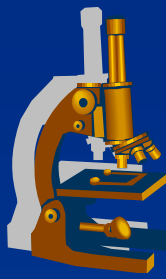
• Reactive
lymphadenopathy

Non-Hodgkin lymphomas / WHO classification



B-Cell Neoplasms	T-Cell Neoplasms
Precursor B-Cell Neoplasms - precursor B-cell leukemia/lymphoma (B-cell acute lymphoblastic leukemia)	Precursor T-Cell Neoplasms - precursor T-cell leukemia/lymphoma (T-cell acute lymphoblastic leukemia)
Peripheral B-Cell Neoplasms	Peripheral T-/NK-Cell Neoplasms

Non-Hodgkin lymphomas / WHO classification



I. Precursor B-Cell Neoplasms

- B-cell acute lymphoblastic leukemia/lymphoma (B-ALL)

II. Peripheral B-Cell Neoplasms

- B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
- B- prolymphocytic leukemia
- Lymphoplasmacytic lymphoma
- **Follicular lymphoma (FL)**
- **Extranodal marginal zone lymphoma (MALT lymphoma)**
- **Mantle cell lymphoma (MCL)**
- Splenic and nodal marginal zone lymphoma
- Hairy cell leukemia
- **Plasmacytoma/plasma cell myeloma**
- **Diffuse large B-cell lymphoma (DLBCL)**
- **Burkitt lymphoma**

× Hematopoiesis

× Myeloid neoplasms

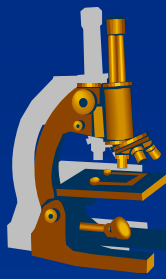
• **Lymphoid neoplasms**

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

Non-Hodgkin lymphomas / WHO classification



III. Precursor T-Cell neoplasms.

- T-cell acute lymphoblastic leukemia/lymphoma (T-ALL)

IV. Peripheral T-/NK-Cell Neoplasms

- T-cell prolymphocytic leukemia
- Mycosis fungoides/Sézary syndrome
- Peripheral T-cell lymphoma, NOS
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large-cell lymphoma
- Enteropathy-type T-cell lymphoma
 - Panniculitis-like T-cell lymphoma
 - Hepatosplenic $\gamma\delta$ T-cell lymphoma
 - NK/T-cell lymphoma, nasal type
 - NK-cell leukemia
- Adult T-cell leukemia/lymphoma (HTLV1)

× Hematopoiesis

× Myeloid neoplasms

• Lymphoid neoplasms

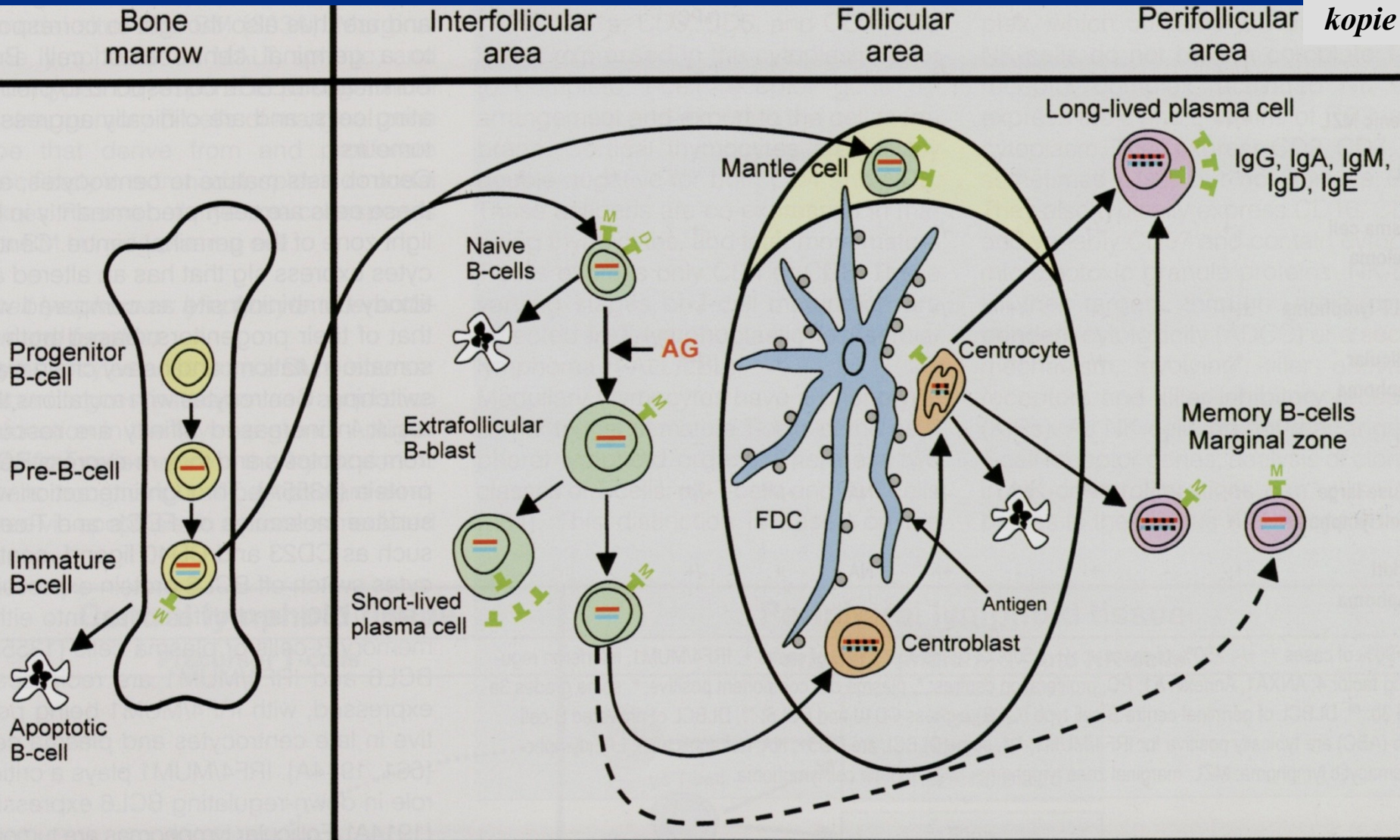
⇒ NHL

⇒ HL

• Reactive lymphadenopathy

LYMPHOID NEOPLASMS (B-cell) – cells of origin

kopie



Precursor B-cell neoplasms
B lymphoblastic leukaemia/lymphoma

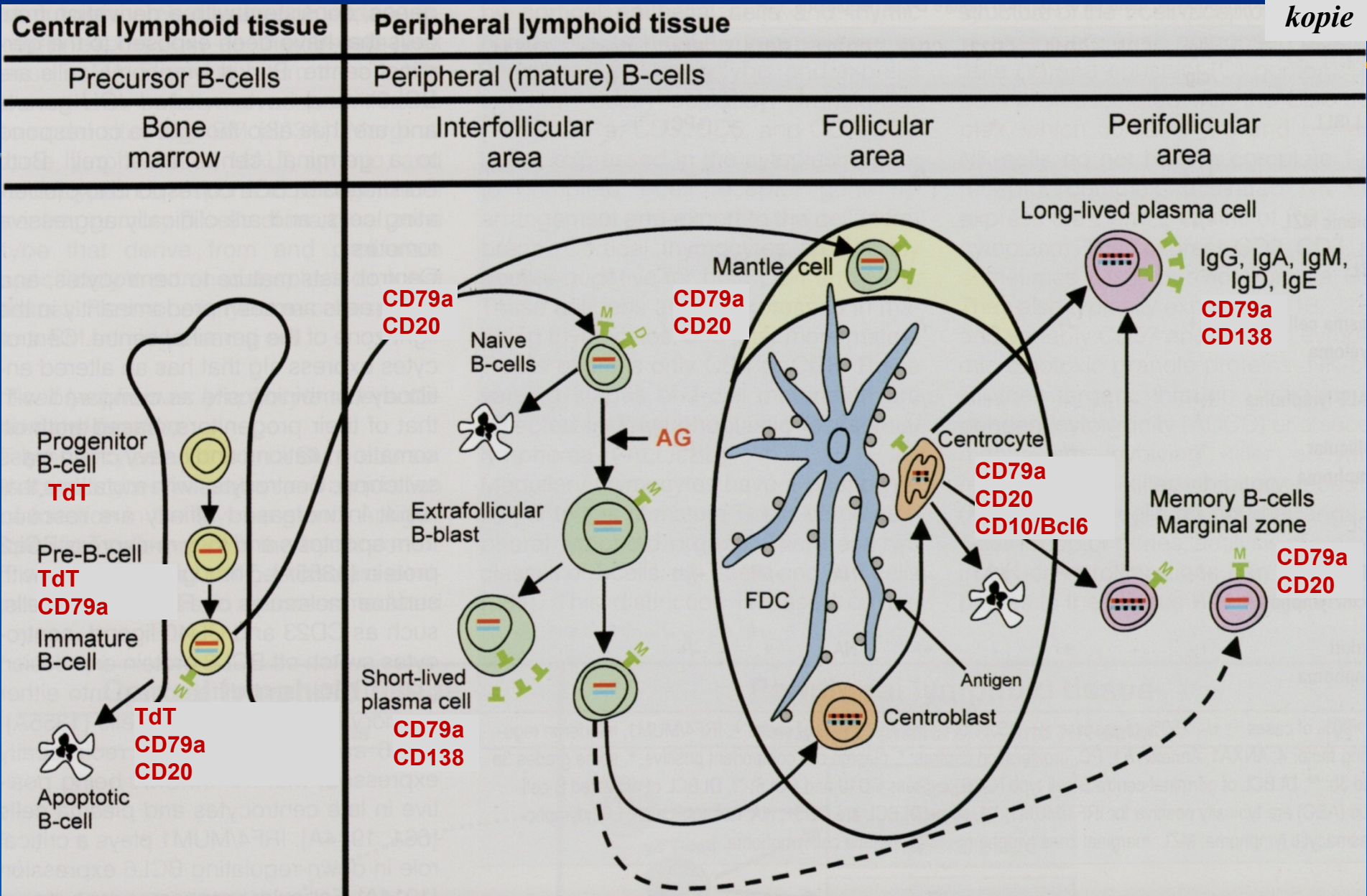
Pre-GC neoplasm
Mantle cell lymphoma

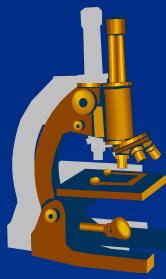
GC neoplasms
Follicular lymphoma
Burkitt lymphoma
DLBCL (some)
Hodgkin lymphoma

Post-GC neoplasms
Marginal zone & MALT lymphoma
Lymphoplasmacytic lymphoma
CLL/SLL, DLBCL (some)
Plasma cell myeloma

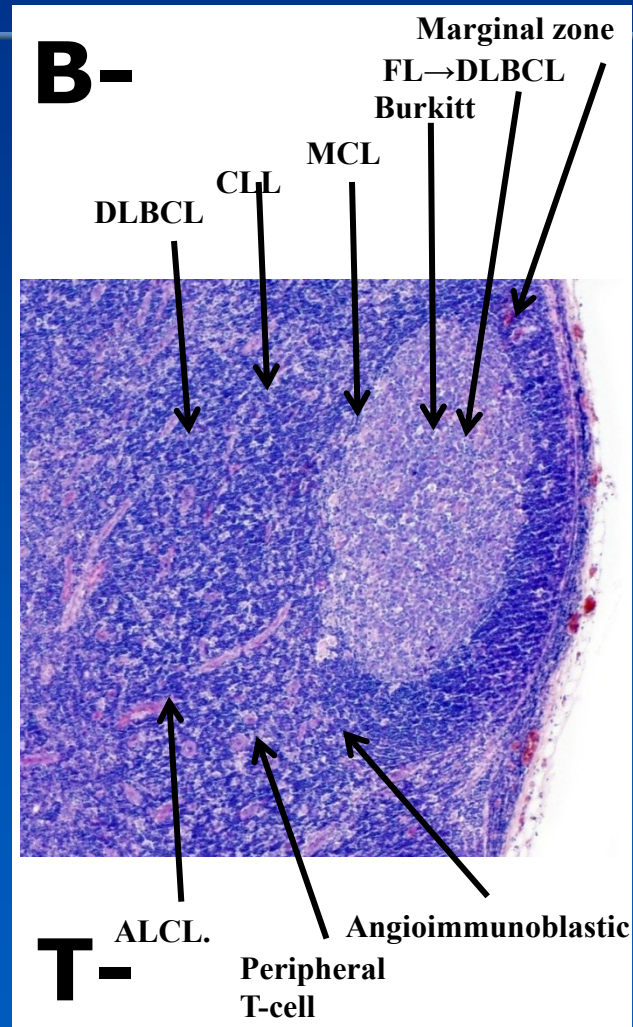
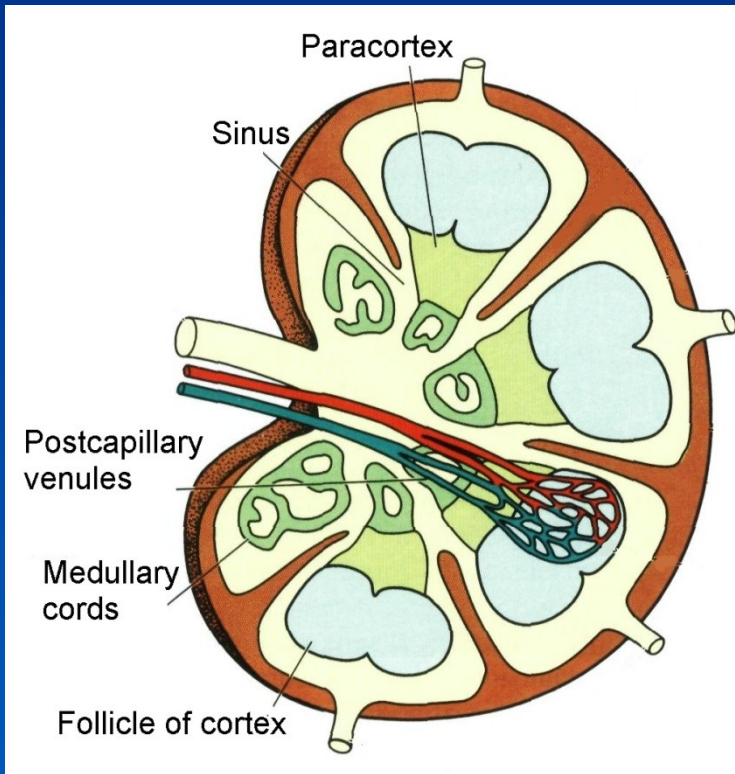
LYMPHOID NEOPLASMS (B-cell) — immunophenotype of cells of origin

kopie





Nodal lymphomas



✗ Hematopoiesis

✗ Myeloid neoplasms

• Lymphoid neoplasms

⇒ NHL

⇒ HL

• Reactive lymphadenopathy

B-cell acute lymphoblastic leukemia/lymphoma (B-ALL)



- **most frequent malignancy in children (peak at age 4)**
- Infiltration of bone marrow, lymph nodes, liver, spleen...
- Neoplastic blasts antiTdT positive (terminal deoxynucleotidyl transferase)
- **Highly aggressive**, but chemosensitive
(⇒ children 2 to 10 years – best prognosis)

× Hematopoiesis

× Myeloid neoplasms

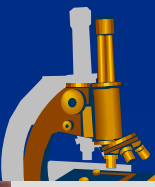
• **Lymphoid neoplasms**

⇒ NHL

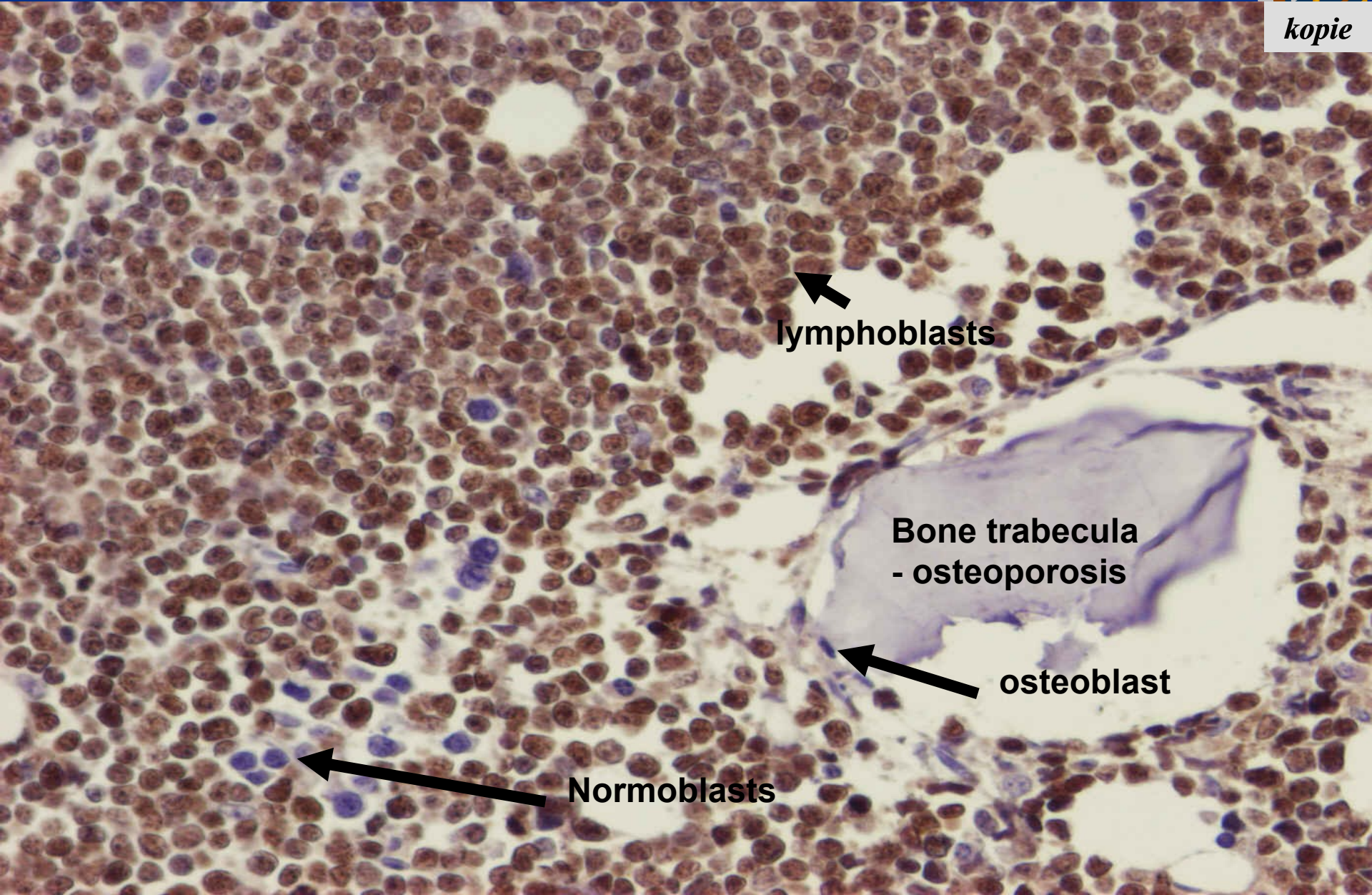
⇒ HL

• Reactive lymphadenopathy

B-ALL, immunohistochemistry: antiTdT



kopie



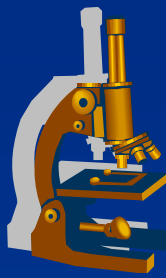
lymphoblasts

Bone trabecula
- osteoporosis

osteoblast

Normoblasts

CLL/SLL



- most frequent leukemia in adults
- generalized lymphadenopathy, hepatosplenomegaly, BM infiltration...
- neoplastic small lymphocytes-like cells, prolymphocytes in proliferative centres
- transformation into high grade lymphoma (into DLBCL = Richter's syndrome)
- usually slowly progressive (10 years and more)

× Hematopoiesis

× Myeloid neoplasms

• **Lymphoid neoplasms**

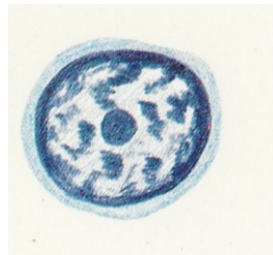
⇒ NHL

⇒ HL

• Reactive lymphadenopathy



lymphocyte

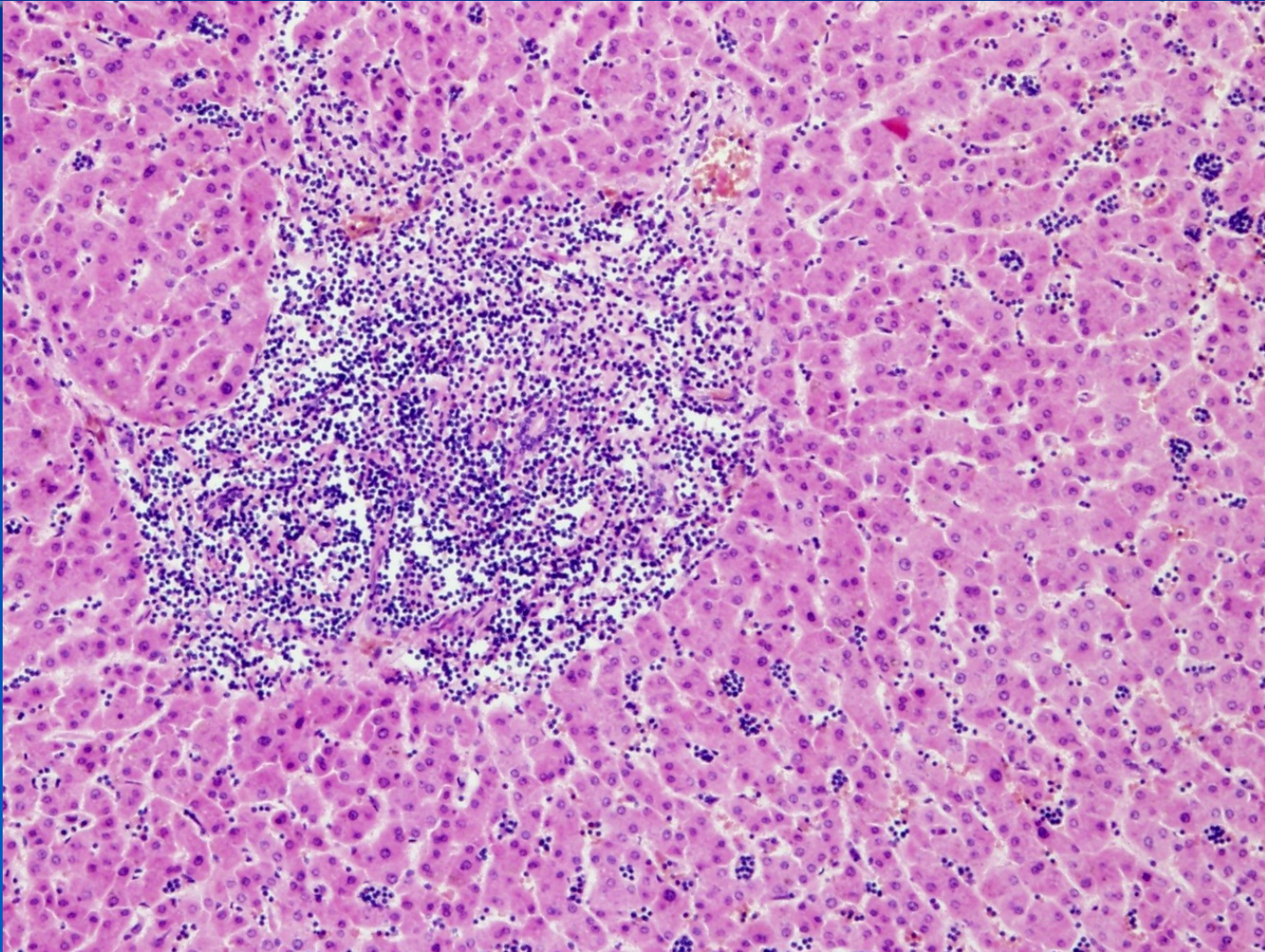


prolymphocyt

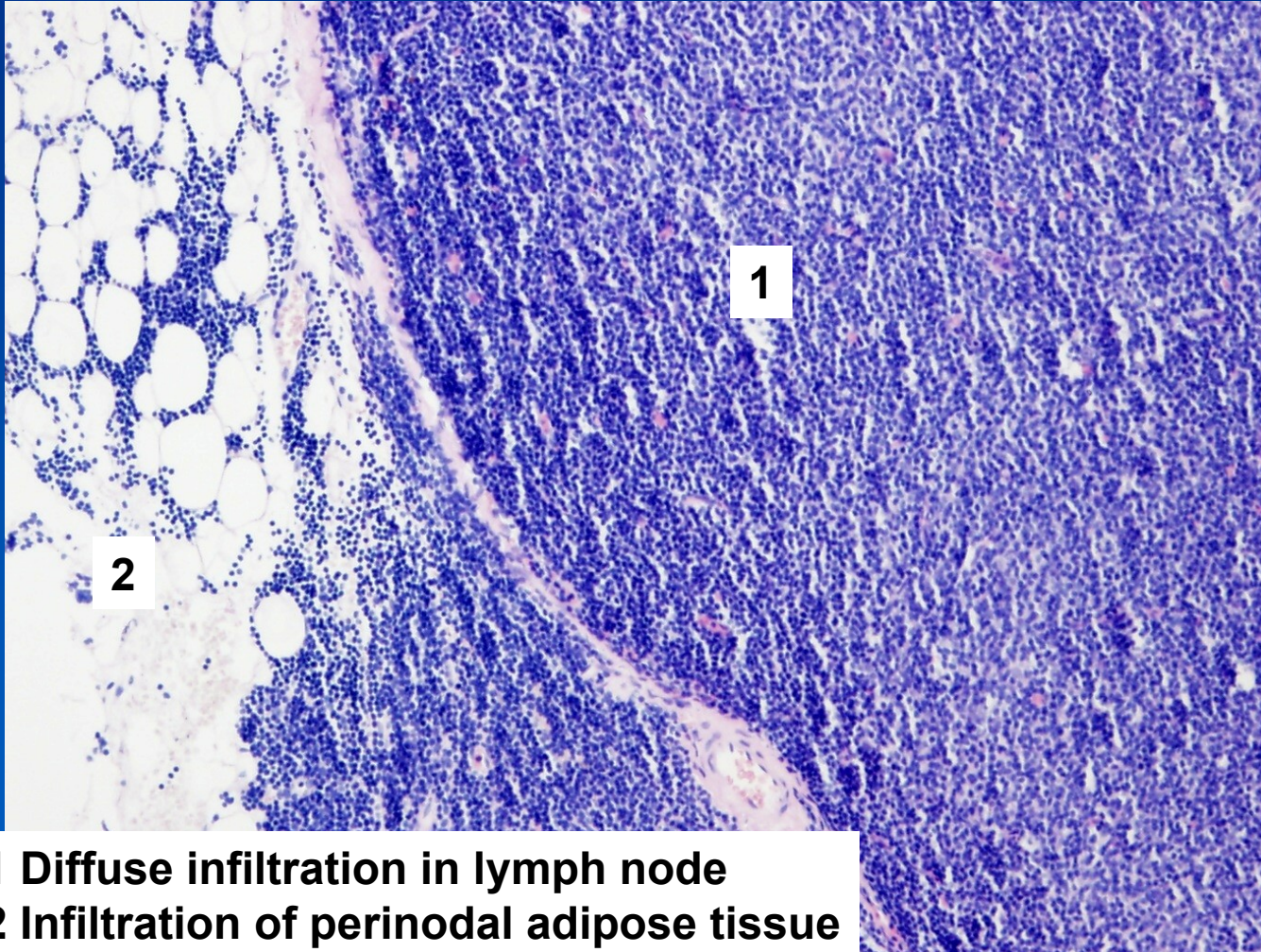


paraimunoblast

B-CLL/SLL: liver - portal infiltration

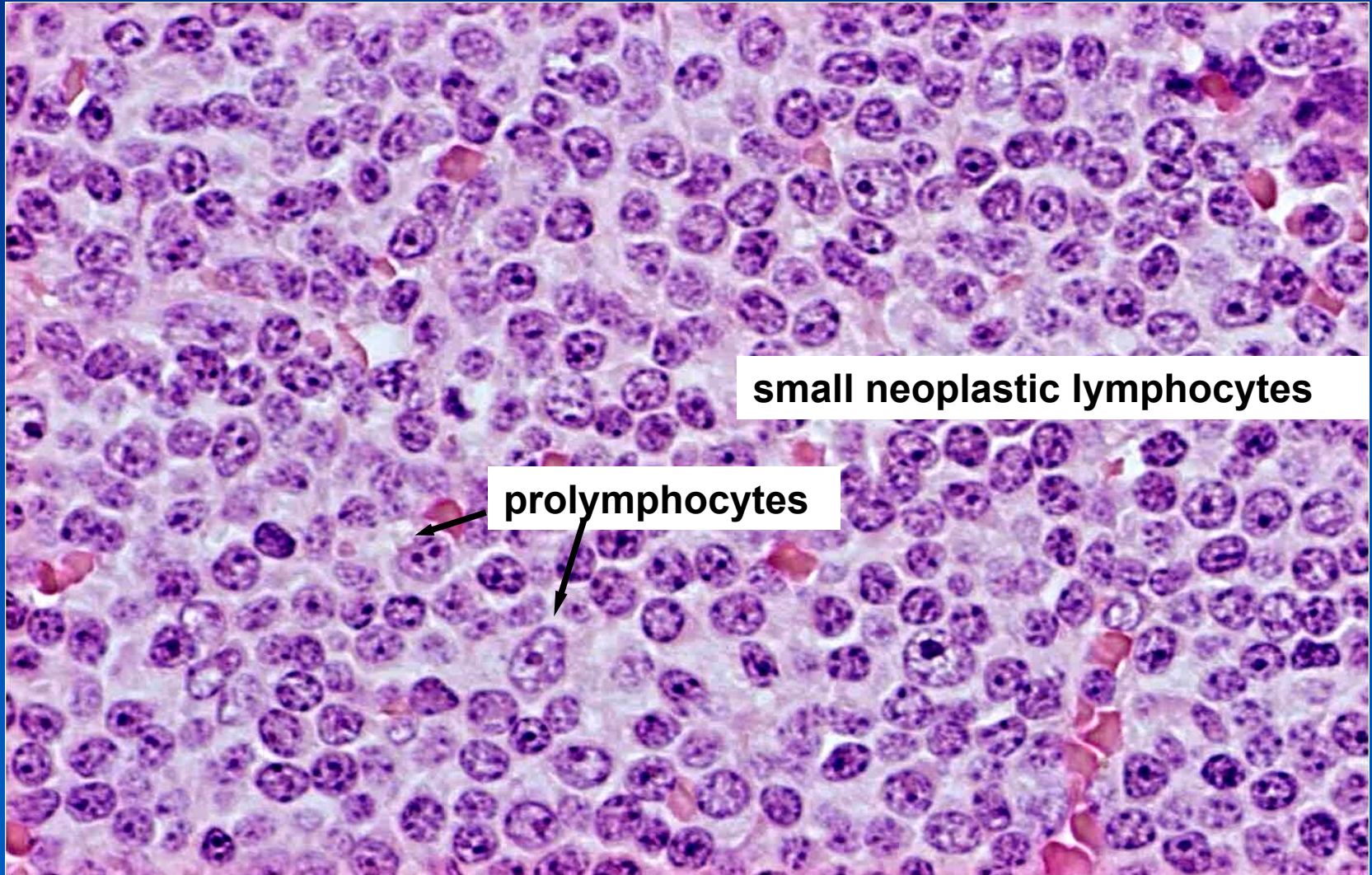


B-CLL/SLL: infiltration in lymph node

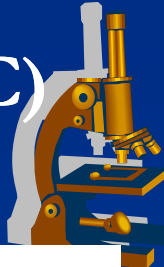


- 1 Diffuse infiltration in lymph node
- 2 Infiltration of perinodal adipose tissue

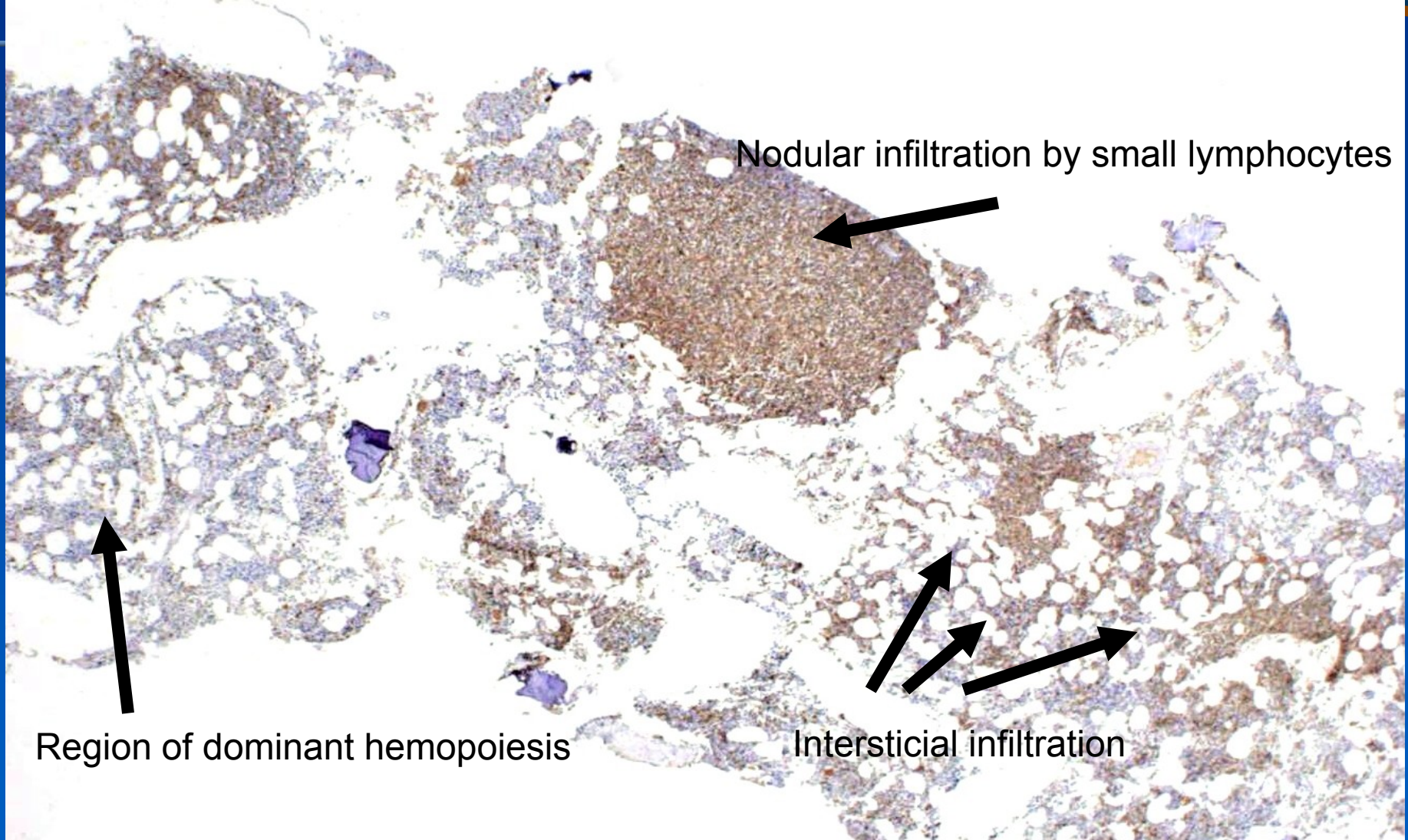
B-CLL/SLL: lymph node infiltration



B-CLL/SLL: bone marrow infiltration (anti CD 20 IHC)



B-cells stained brown

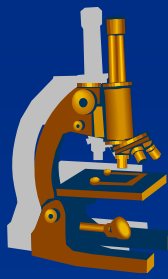


Nodular infiltration by small lymphocytes

Region of dominant hemopoiesis

Interstitial infiltration

Mantle cell lymphoma



- **intermediate grade/aggressive NHL**, middle aged patients/older adults
- progressive despite treatment
- in LN mantle type of growth
 - small cell lymphoma/small lymphocytic cells + epitheloid histiocytes + hyalinized vessels
- also BM, spleen, GIT... involved
- **t(11;14)**

× Hematopoiesis

× Myeloid neoplasms

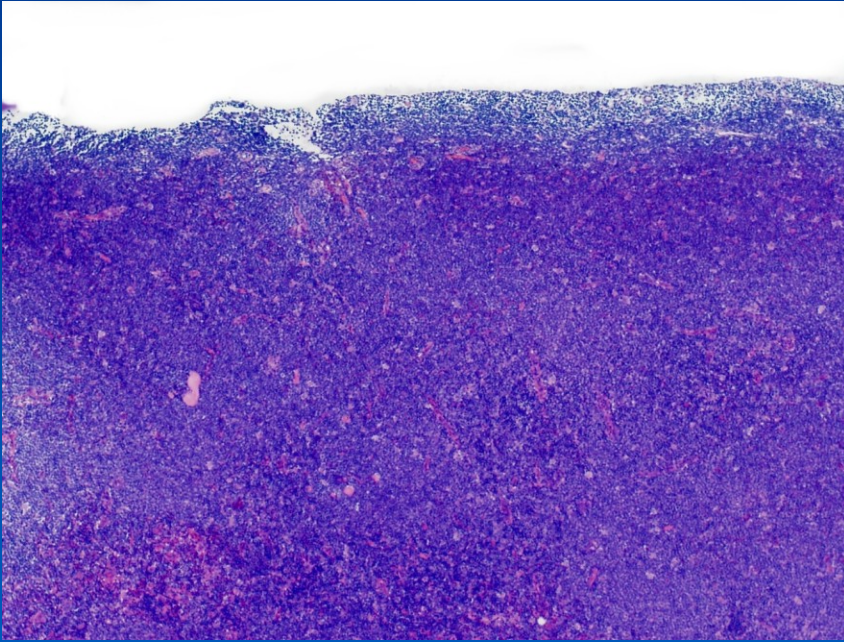
• **Lymphoid neoplasms**

⇒ *NHL*

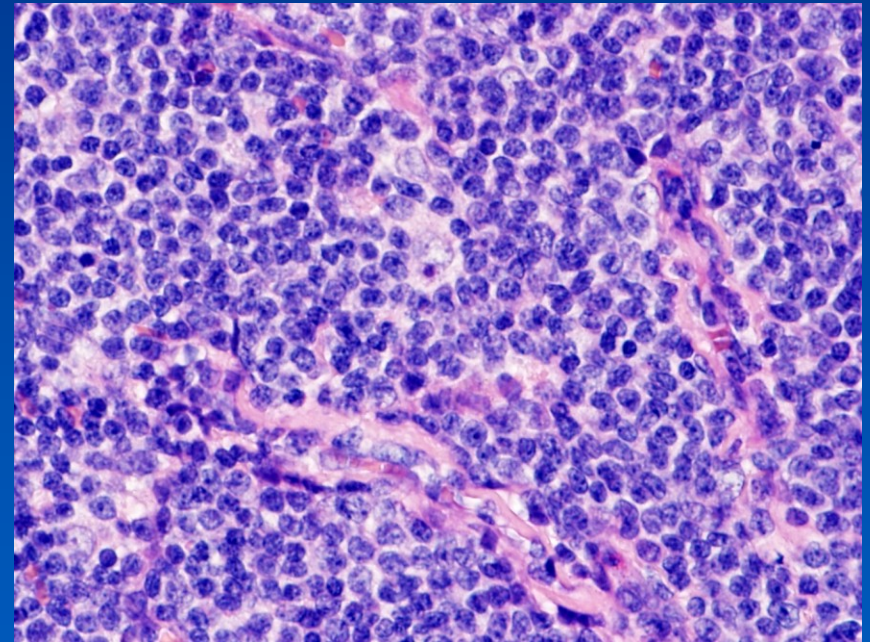
⇒ *HL*

• Reactive lymphadenopathy

MCL

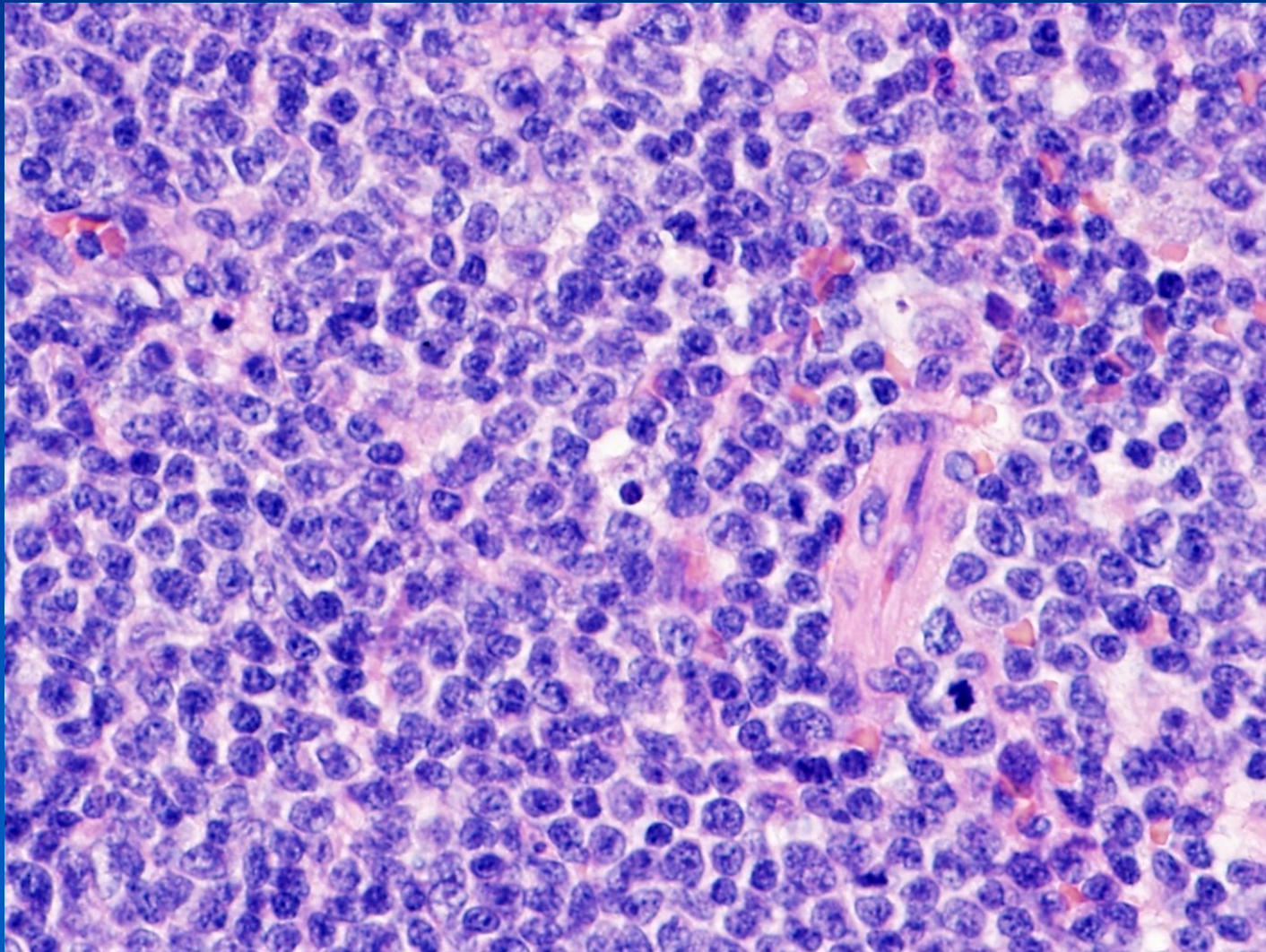
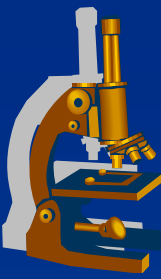


Structure of lymph node replaced by monomorphous lymphoid infiltration.

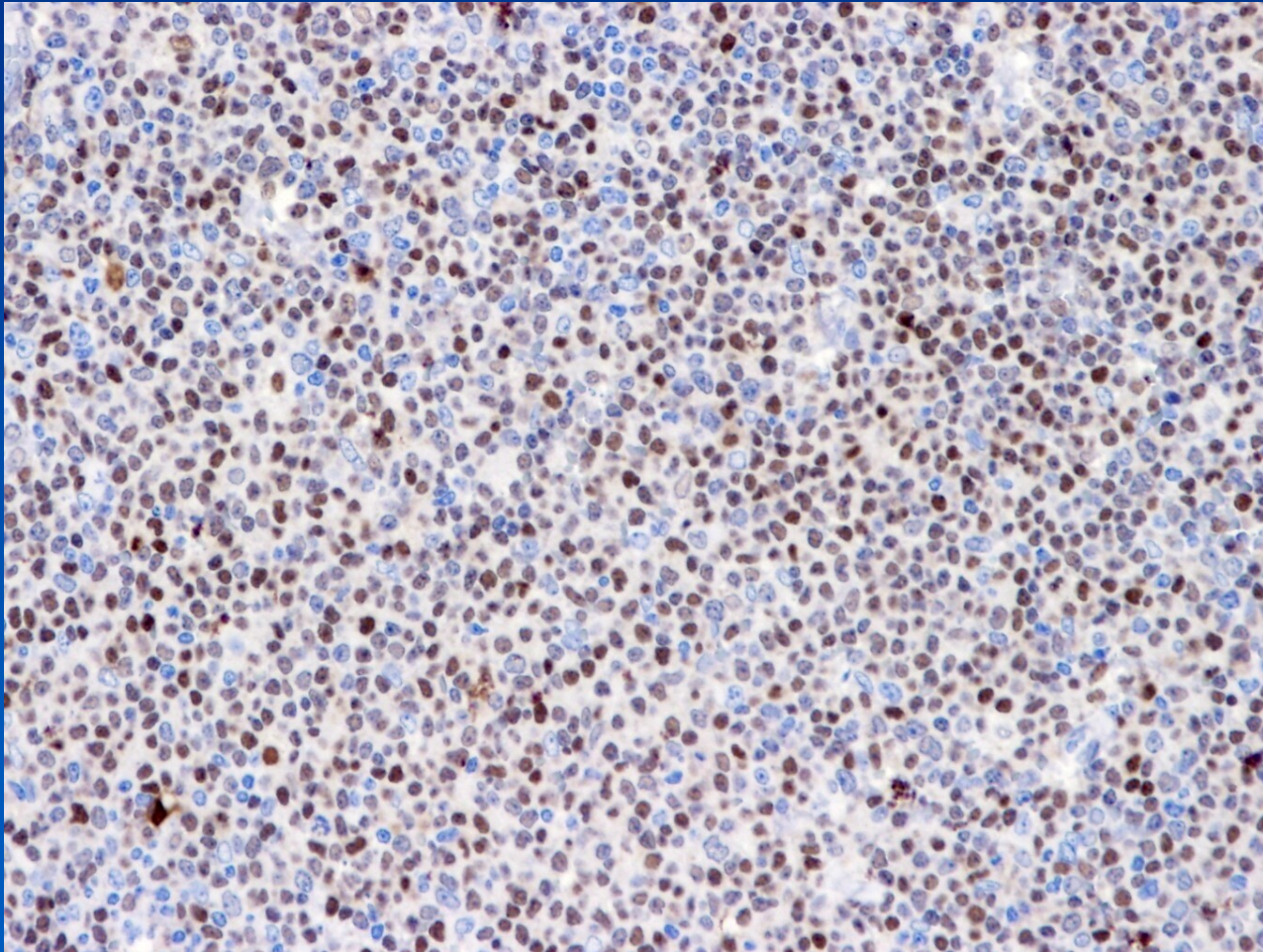


Neoplastic cells bigger than lymphocytes.
Hyalinized vessels.

MCL



MCL – cyclinD1



Follicular lymphoma



- app. **40 %** NHL, older adults
- slowly to moderately progressive (5-10 years)
- Transformation into high grade NHL (DLBCL)
- **generalized lymphadenopathy:**
 - ⇒ *in LN nodular/(diffuse) growth*
 - Resemble normal follicular center B cell (centrocytes and centroblasts)
 - Neoplastic nodules of the same shape and size
 - Loss of germinal center polarization

× Hematopoiesis

× Myeloid neoplasms

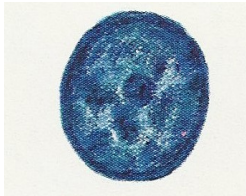
• **Lymphoid neoplasms**

⇒ NHL

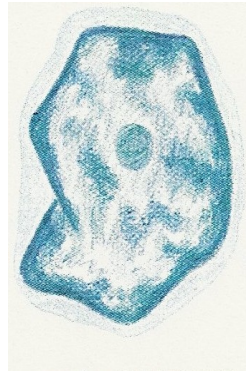
⇒ HL

• Reactive lymphadenopathy

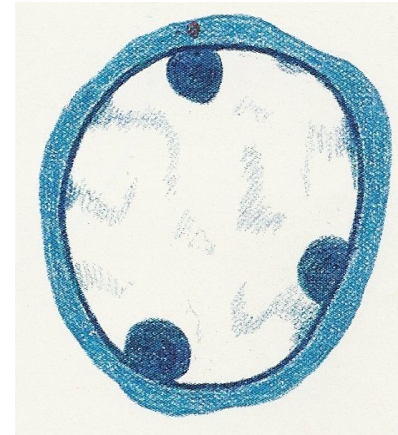
Follicular lymphoma



lymphocyte



centrocyte



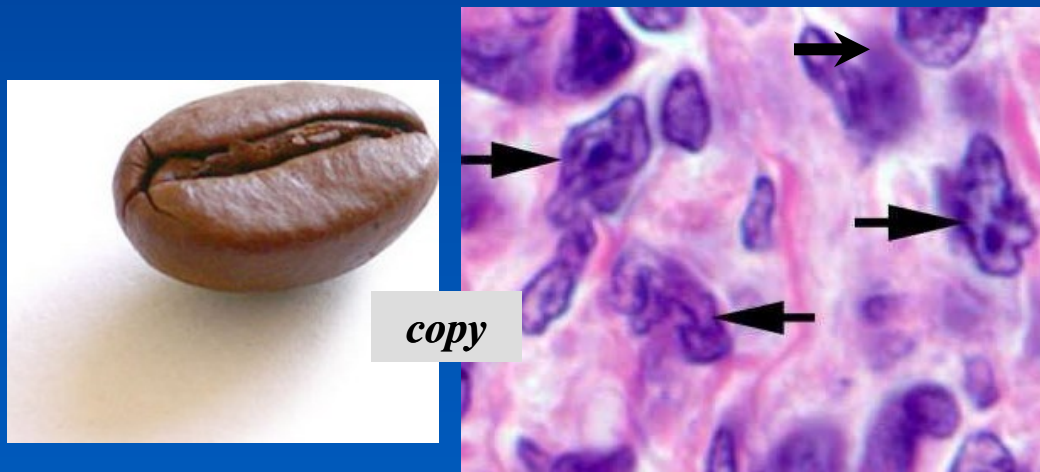
centroblast

Follicular lymphoma



CENTROCYTE

- Small cell with cleaved nuclear outlines



× Hematopoiesis

× Myeloid neoplasms

• Lymphoid neoplasms

⇒ NHL

⇒ HL

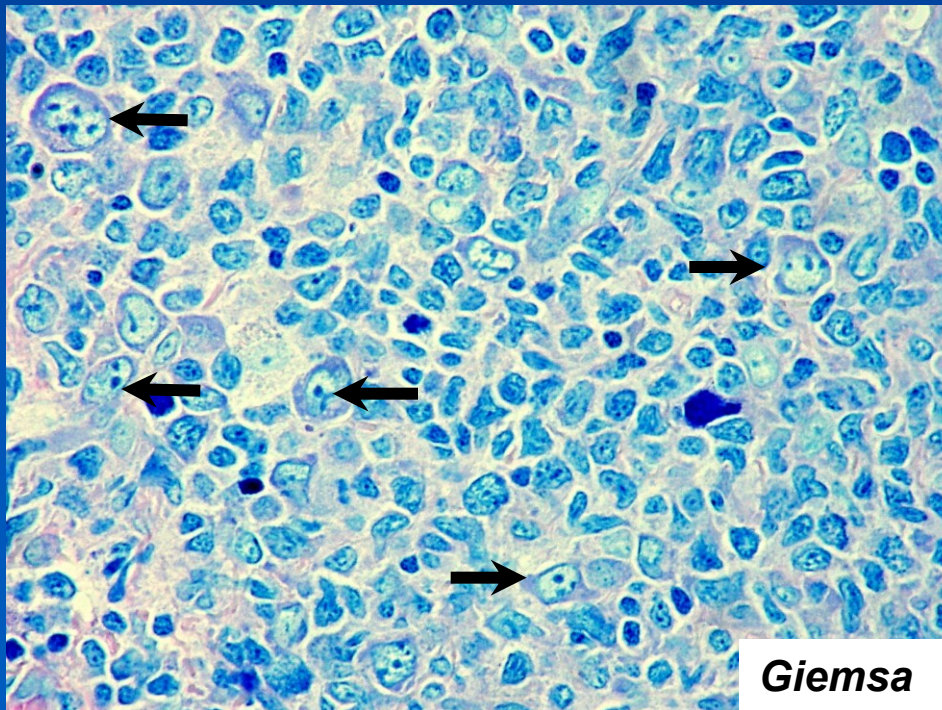
• Reactive lymphadenopathy

Follicular lymphoma



CENTROBLAST

- Larger cell with nucleoli at nuclear membrane



× Hematopoiesis

× Myeloid neoplasms

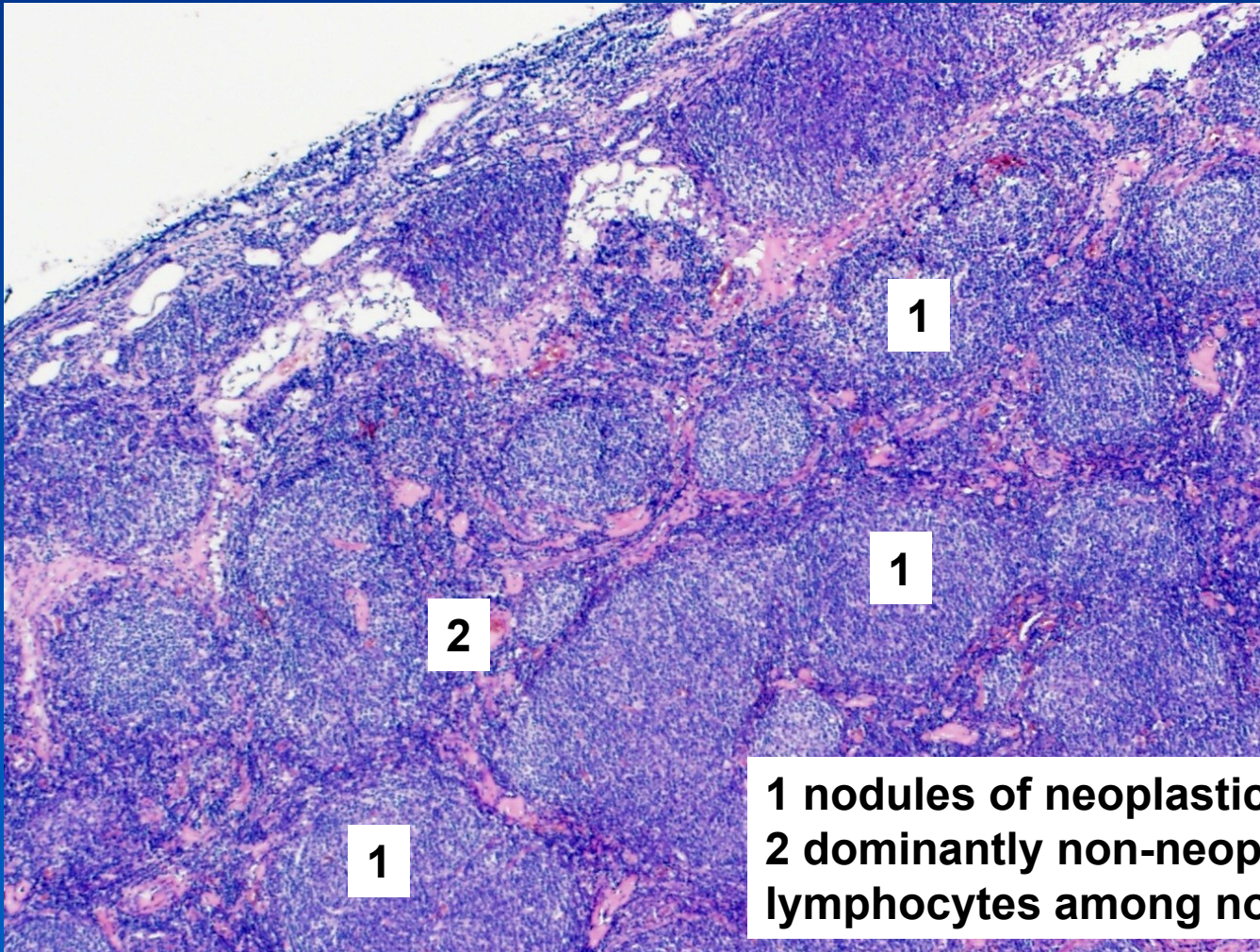
• Lymphoid neoplasms

⇒ NHL

⇒ HL

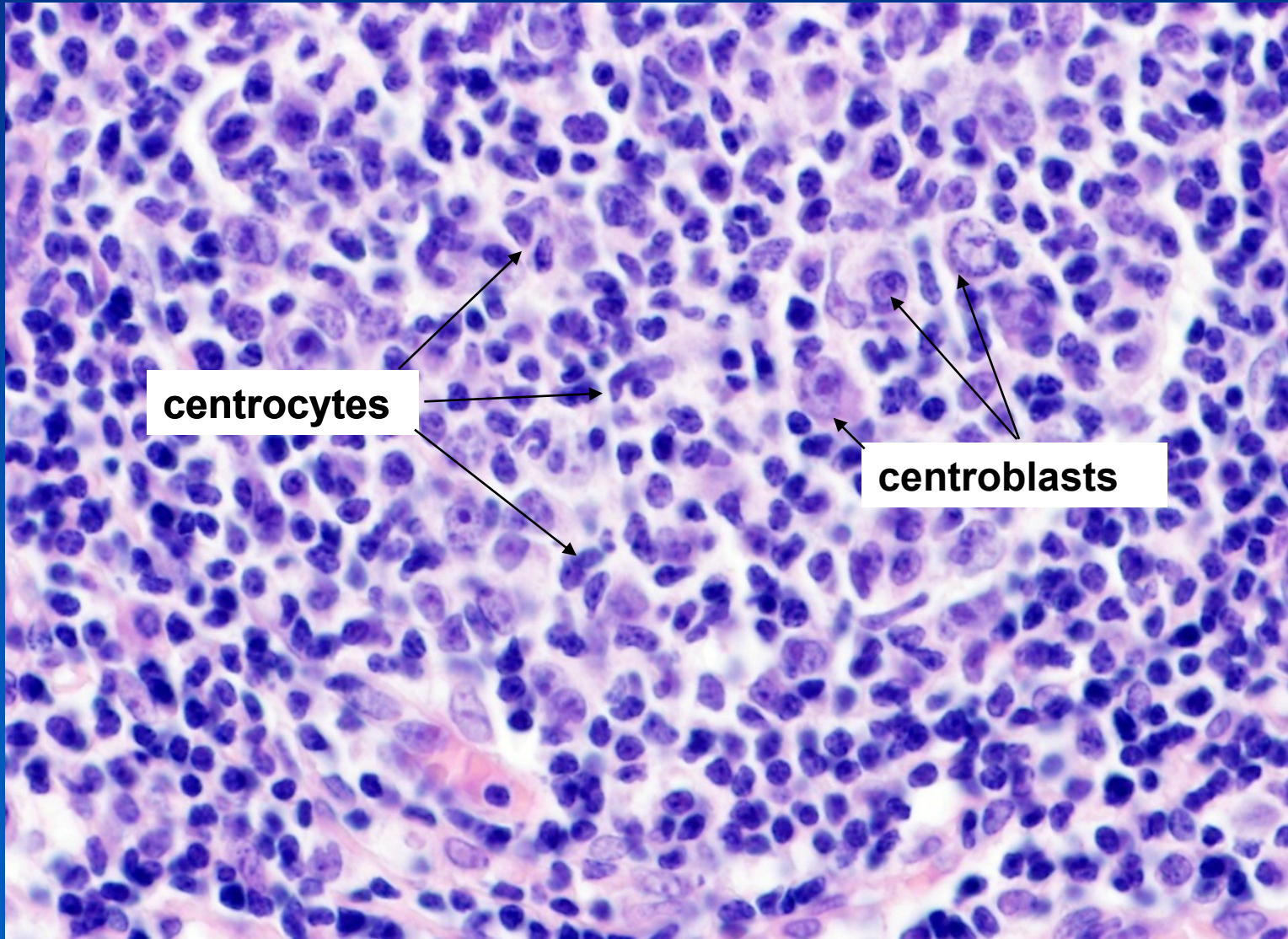
• Reactive lymphadenopathy

Follicular lymphoma

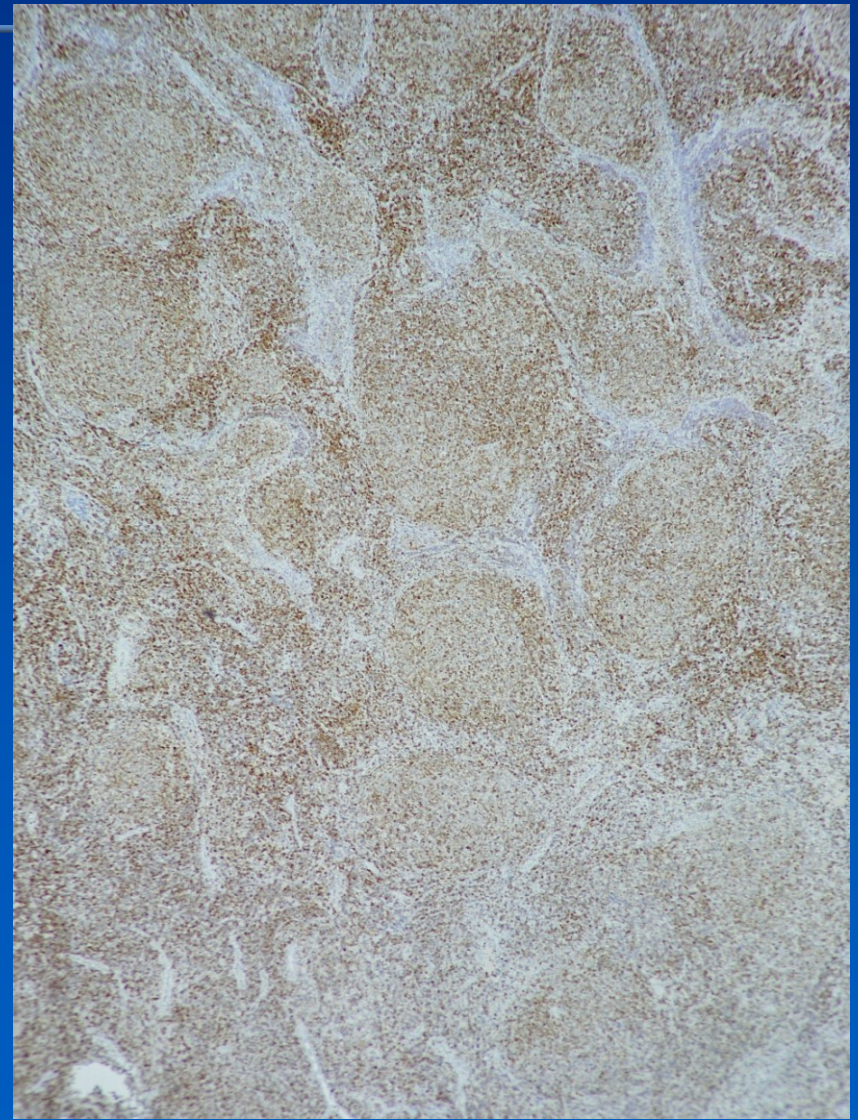
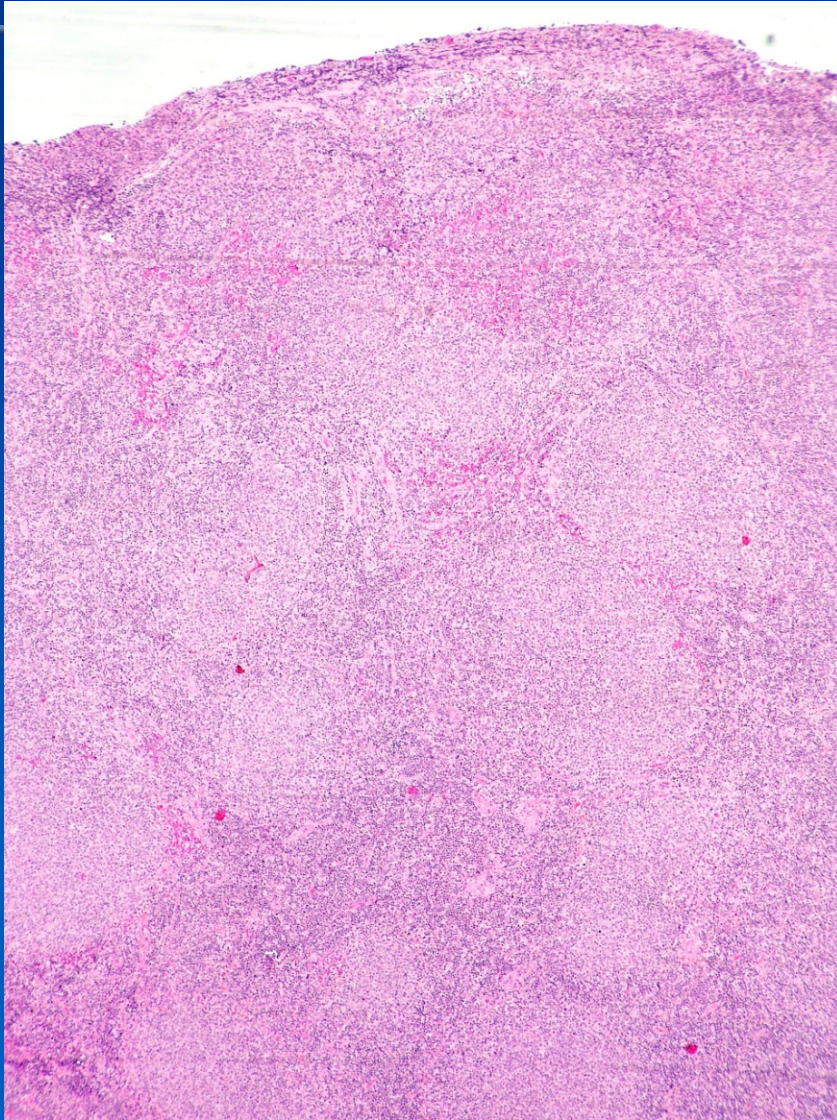
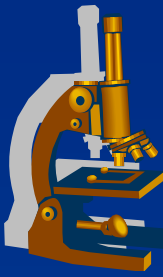


1 nodules of neoplastic cells
2 dominantly non-neoplastic lymphocytes among nodules

Follicular lymphoma

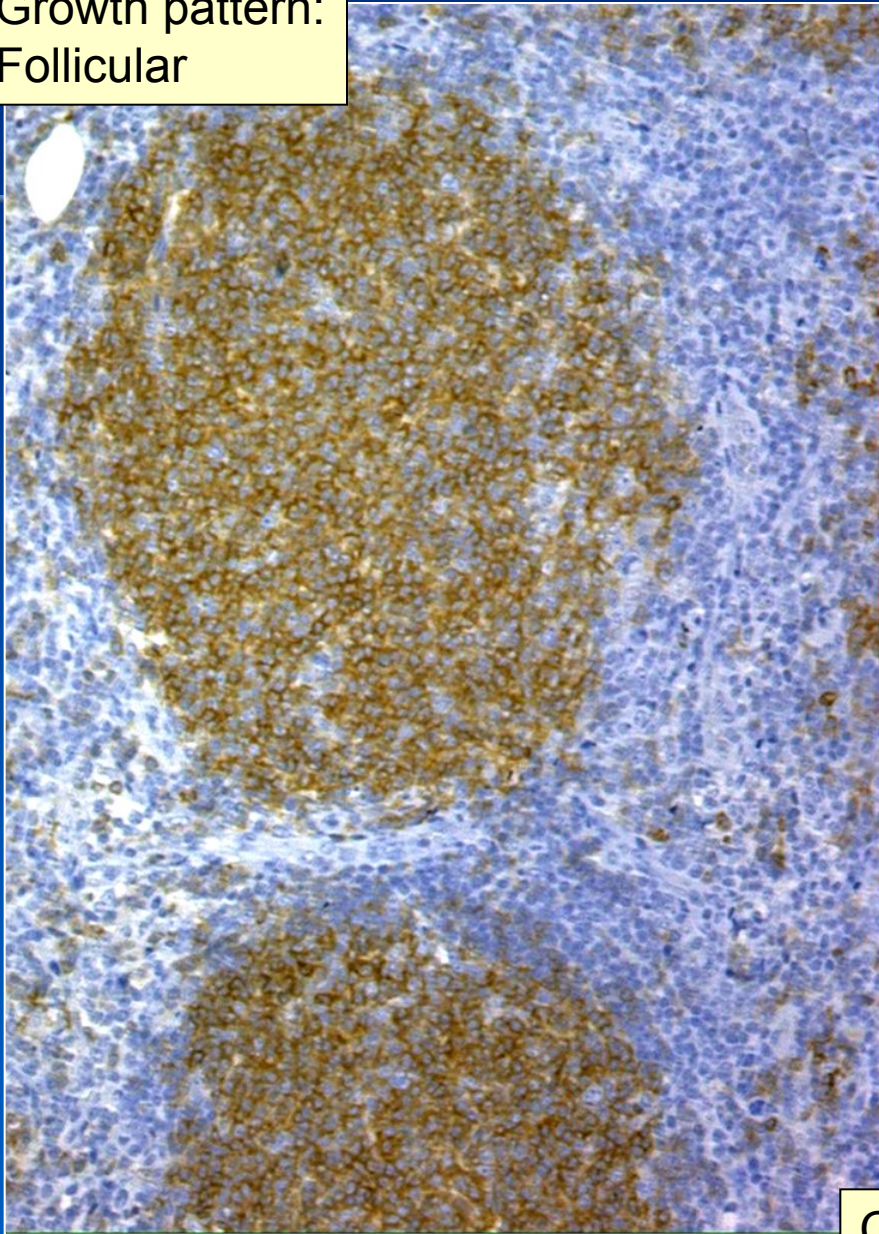


Follicular lymphoma, Bcl-2

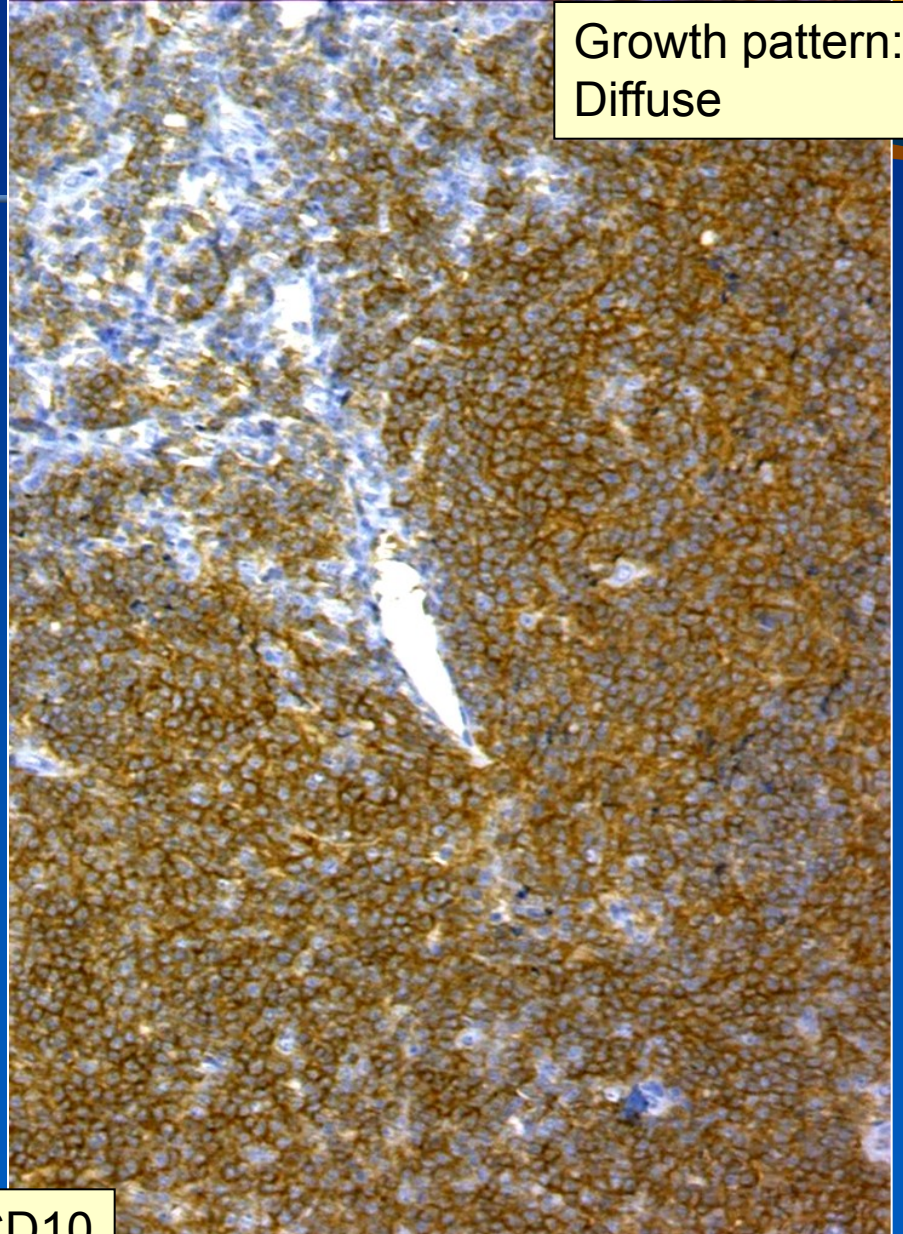


FOLLICULAR LYMPHOMA

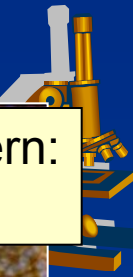
Growth pattern:
Follicular



Growth pattern:
Diffuse



CD10



Marginal zone lymphomas



- Splenic marginal zone lymphoma
- Nodal marginal zone lymphoma
- **Extranodal marginal zone lymphoma (MALT lymphoma)**

Extranodal marginal zone lymphoma (MALT lymphoma)



- **derived from MALT, BALT**
- **chronic stimulation of immune system**
 - e.g.: chronic gastritis assoc. with *Helicobacter pylori* (HP) infection
- low grade/aggressive lymphoma
- some cases treated through eradication of HP

× Hematopoiesis

× Myeloid neoplasms

• **Lymphoid neoplasms**

⇒ *NHL*

⇒ *HL*

• Reactive lymphadenopathy

Diffuse large B-cell lymphoma (DLBCL)



- **older adults**, most frequent lymphoma
- **highly aggressive**
- *de novo* or high grade transformation of low grade lymphoma (CLL, FL, MALToma...)
- nodal or **extranodal** (tonsil, adenoid lymphatic tissue, GIT, skin, bones, thyroid, ...)
 - neoplastic immunoblasts and centroblasts

× Hematopoiesis

× Myeloid neoplasms

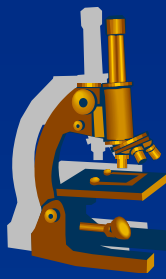
• **Lymphoid neoplasms**

⇒ *NHL*

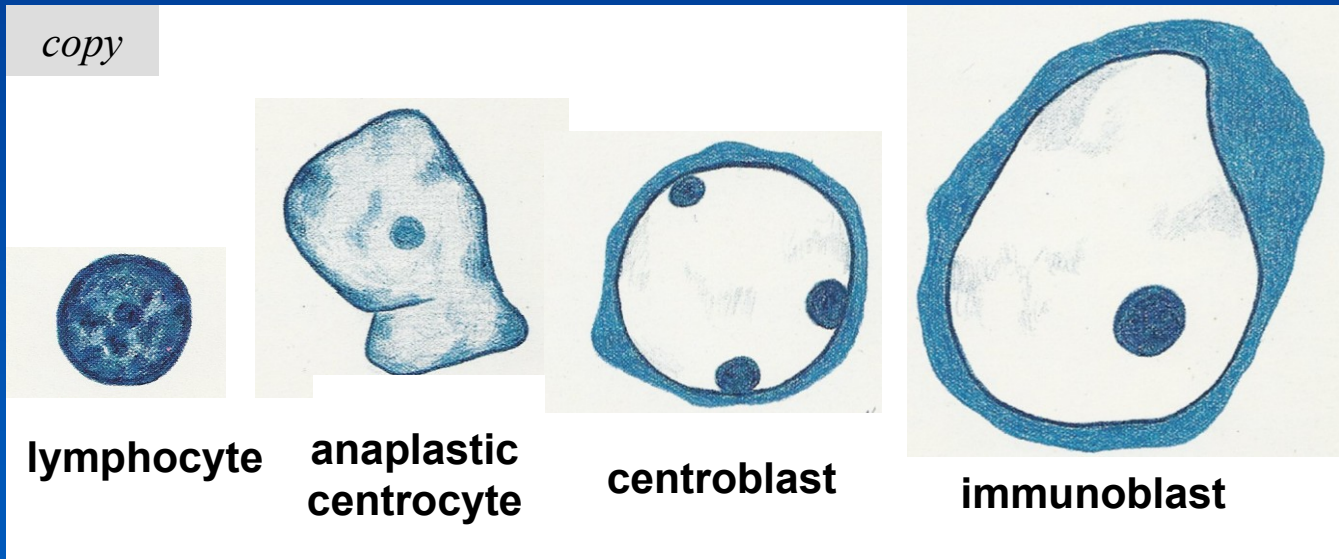
⇒ *HL*

• Reactive lymphadenopathy

Diffuse large B-cell lymphoma (DLBCL)



neoplastic immunoblasts and centroblasts



× Hematopoiesis

× Myeloid
neoplasms

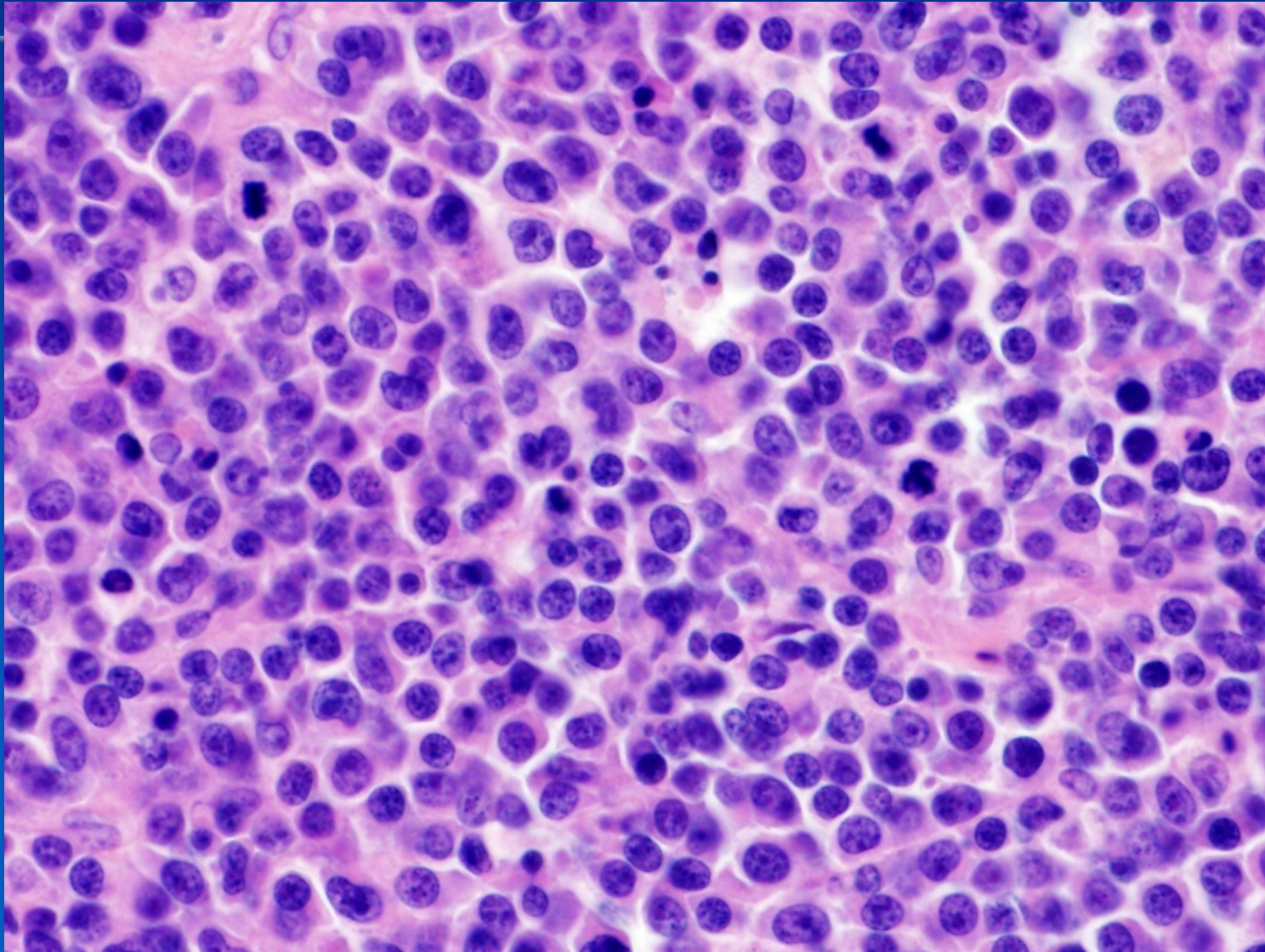
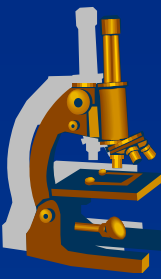
• **Lymphoid
neoplasms**

⇒ *NHL*

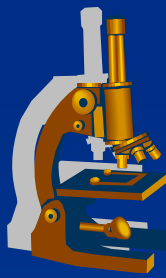
⇒ *HL*

• Reactive
lymphadenopathy

DLBCL - nodal - detail



Burkitt lymphoma



- **extremely highly aggressive NHL**
- **variants:**
 - endemic (in Africa – children, assoc. with EBV)
 - sporadic (in other areas, including Europe, USA,..)
 - Assoc. with immunodeficiency
- **t(8;14) → fusion c-myc/IgH → → → dysregulation, overexpression of c-myc → → → → brisk proliferation**
- **Extranodal bulks:**
 - *head – jaws (endemic variant)*
 - *abdominal tumors (sporadic variant)*

× Hematopoiesis

× Myeloid neoplasms

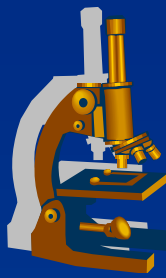
• **Lymphoid neoplasms**

⇒ NHL

⇒ HL



Burkitt lymphoma



- **morphology:**

- Tumor cells uniform, intermediate in size, nuclei round or oval, 2-5 prominent nucleoli, basophilic or amphophilic cytoplasm
- High mitotic rate
- „Starry sky“ pattern

- **therapy:**

- very aggressive chemotherapy regimens, majority of patients cured

× Hematopoiesis

× Myeloid neoplasms

• **Lymphoid neoplasms**

⇒ *NHL*

⇒ *HL*

• Reactive lymphadenopathy

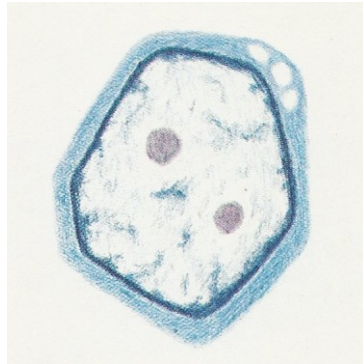
Burkitt lymphoma



copy

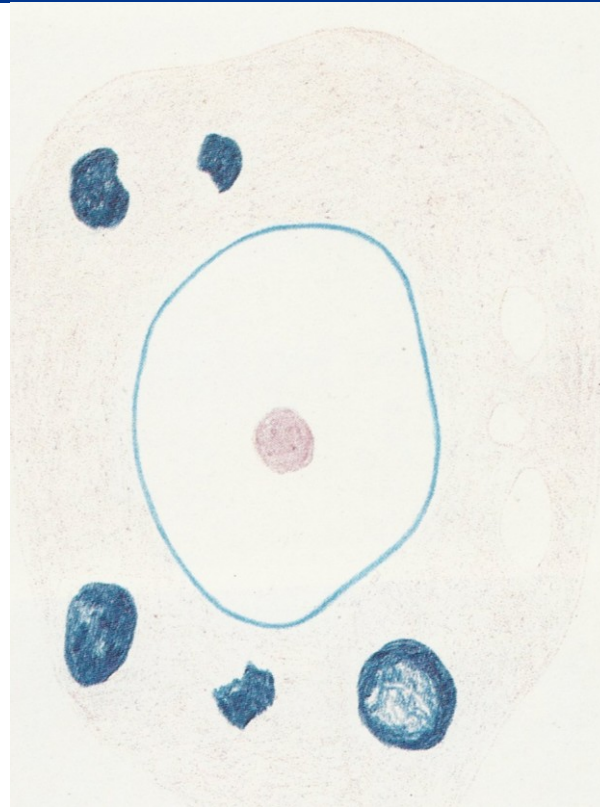


**lymphocyt
e**

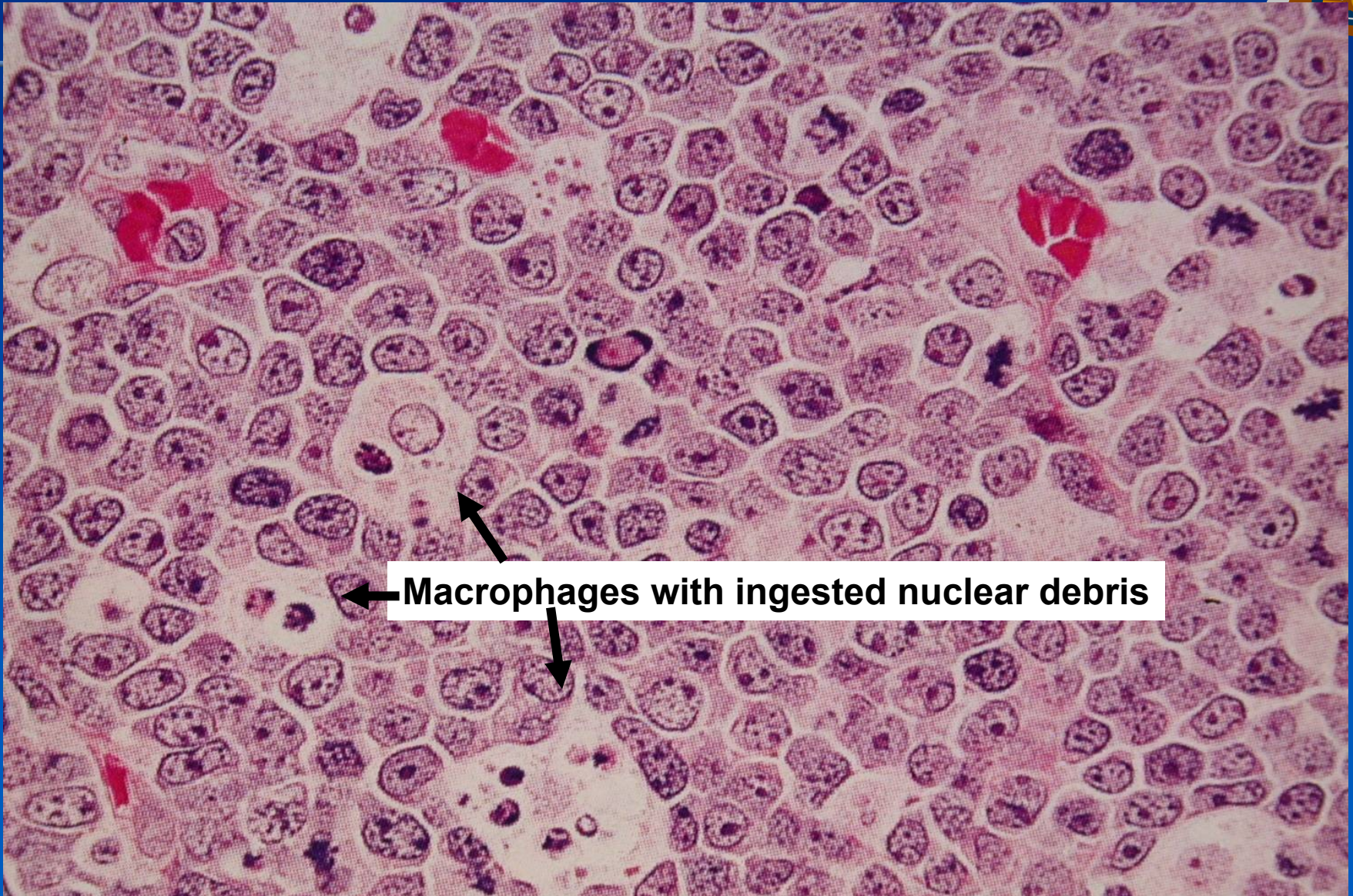
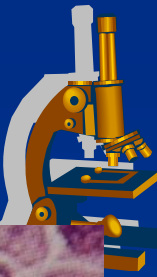


lymphoblast

**macrophage
(starry sky cell)**

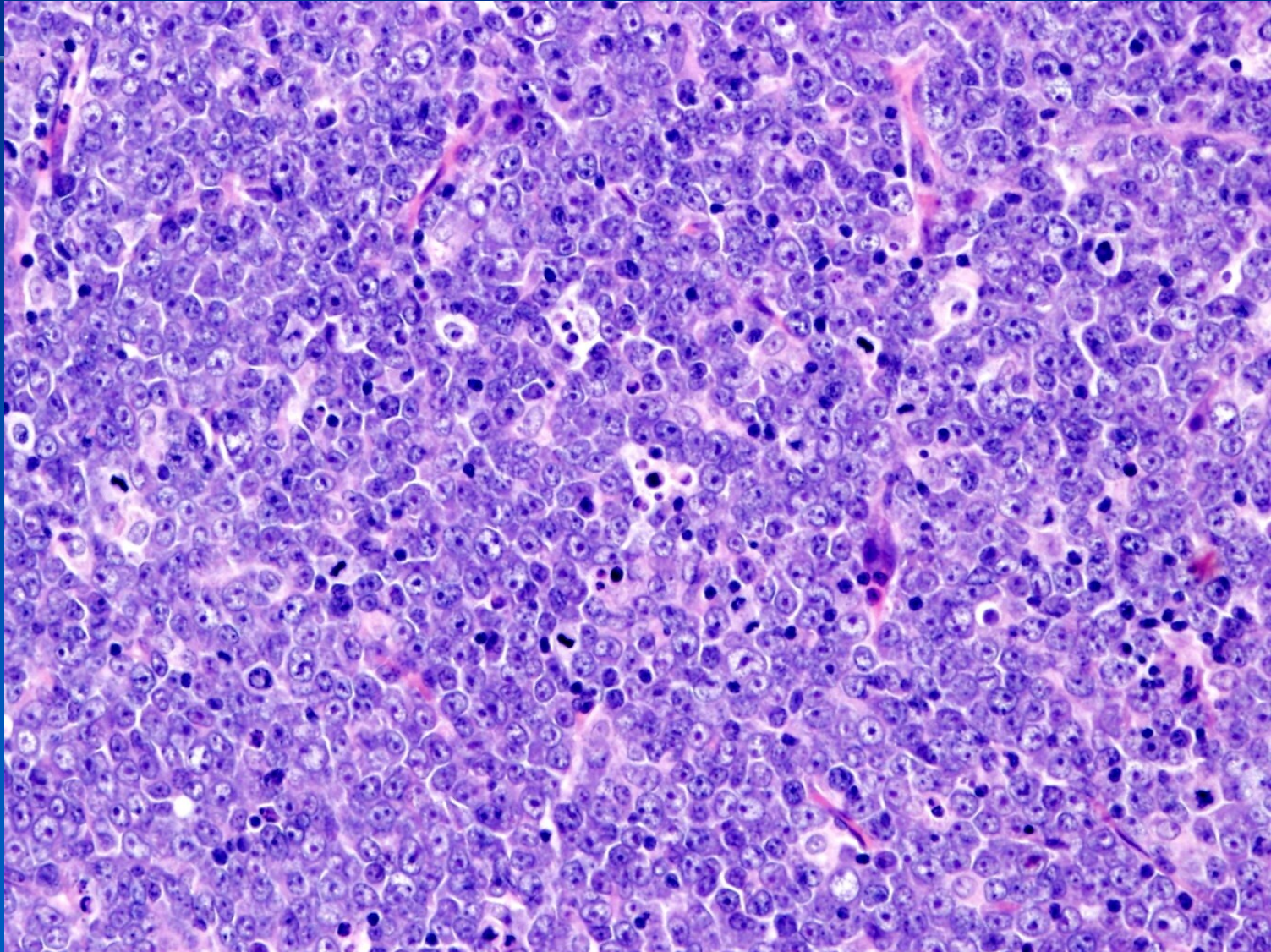
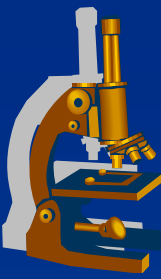


Burkitt lymphoma



Macrophages with ingested nuclear debris

Burkitt lymphoma



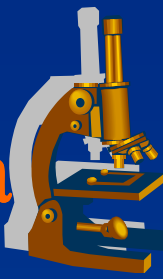
Plasma cell dyskrasias



- ✗ **multiple myeloma**
- ✗ **localizes plasmacytoma (=solitary myeloma)**
- ✗ **heavy chain disease**
- ✗ **primary amyloidosis**
- ✗ **monoclonal gammopathy of unknown significance (MGUS)**

(MGUS patients develop a defined plasma cell dyskrasia at a rate of 1 % per year)

Multiple myeloma, plasmacytoma



- **older adults**
- **1 lesion = plasmacytoma**
- **>1 lesion = multiple myeloma**
 - Lytic lesions throughout the skeletal system → pathological fractures, radiograph of the skull with punch-out bone defects
 - Also BM infiltration → anemia, leucopenia,...
 - Myeloma nephrosis (Bence-Jones proteins)
 - AL amyloidosis

× Hematopoiesis

× Myeloid neoplasms

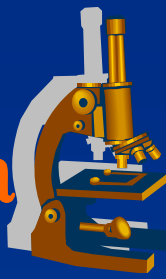
• **Lymphoid neoplasms**

⇒ *NHL*

⇒ *HL*

• **Reactive lymphadenopathy**

Multiple myeloma, plasmacytoma



Micro:

- plasma cells with variable differentiation
- low mitotic activity



× Hematopoiesis

× Myeloid neoplasms

• Lymphoid neoplasms

⇒ NHL

⇒ HL

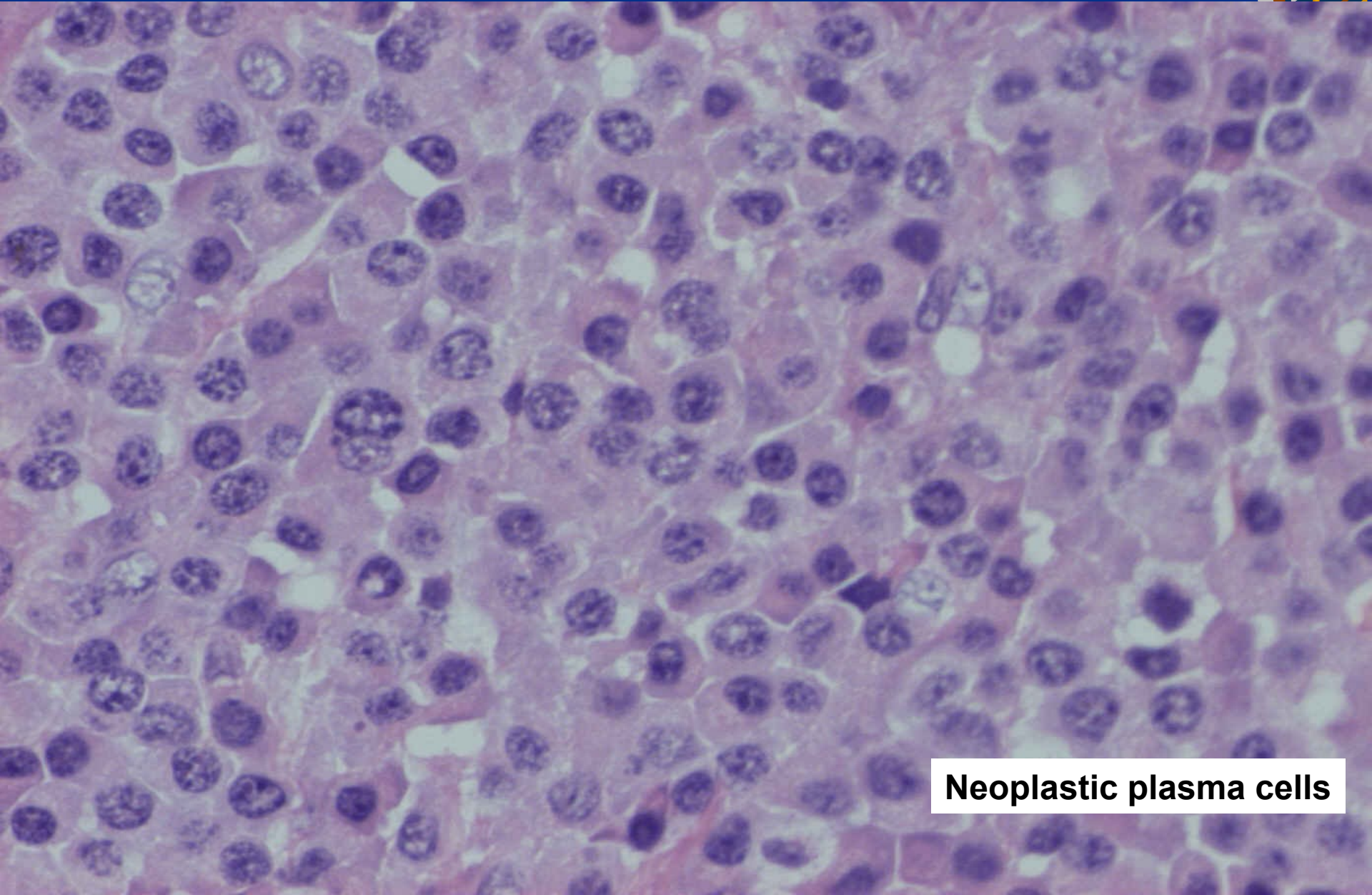
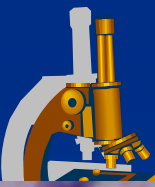
• Reactive lymphadenopathy

Multiple myeloma



Kumar et al: Robbins & Cotran Pathologic Basis of Disease, 8th Edition.
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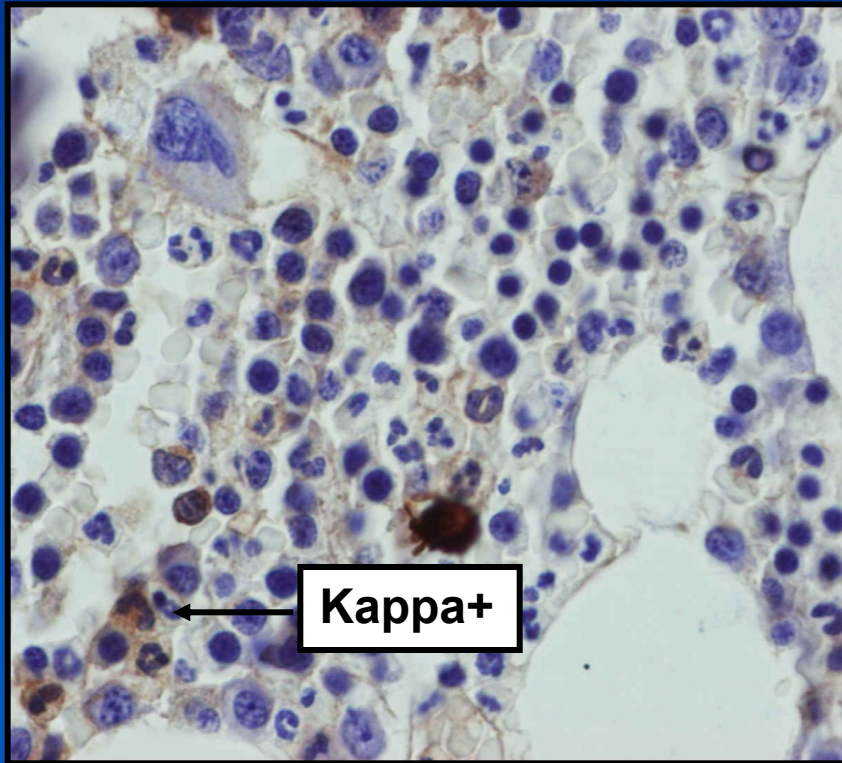
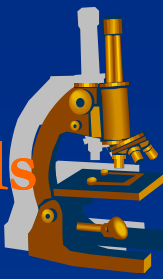
Multiple myeloma – osteolytic lesion



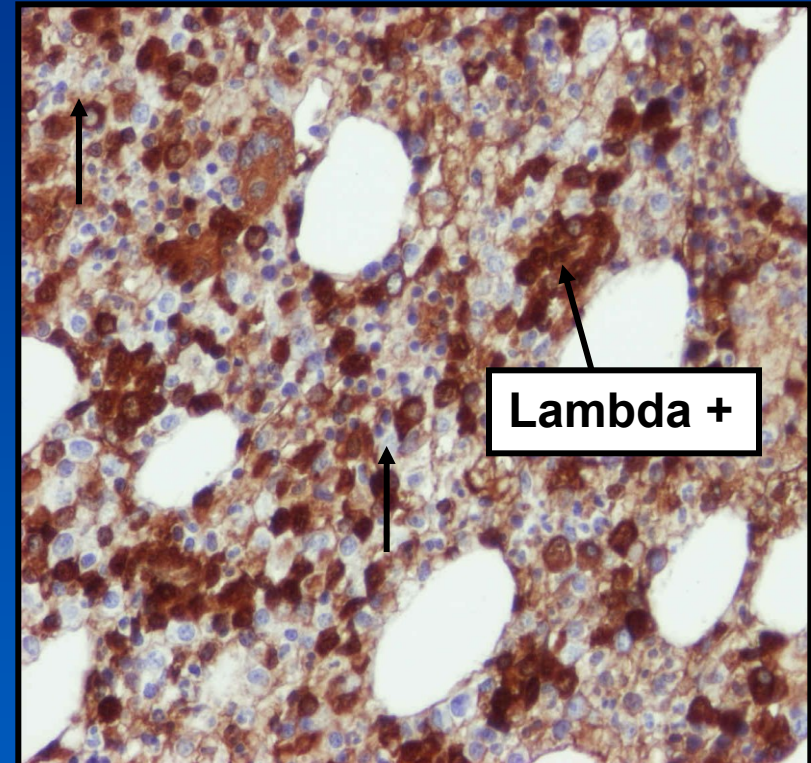
Neoplastic plasma cells

Myeloma:

– IHC proof of monoclonality of neoplastic plasma cells



Kappa light chains Ig



Lambda light chains Ig

T LYMPHOID NEOPLASMS – CELLS OF ORIGIN



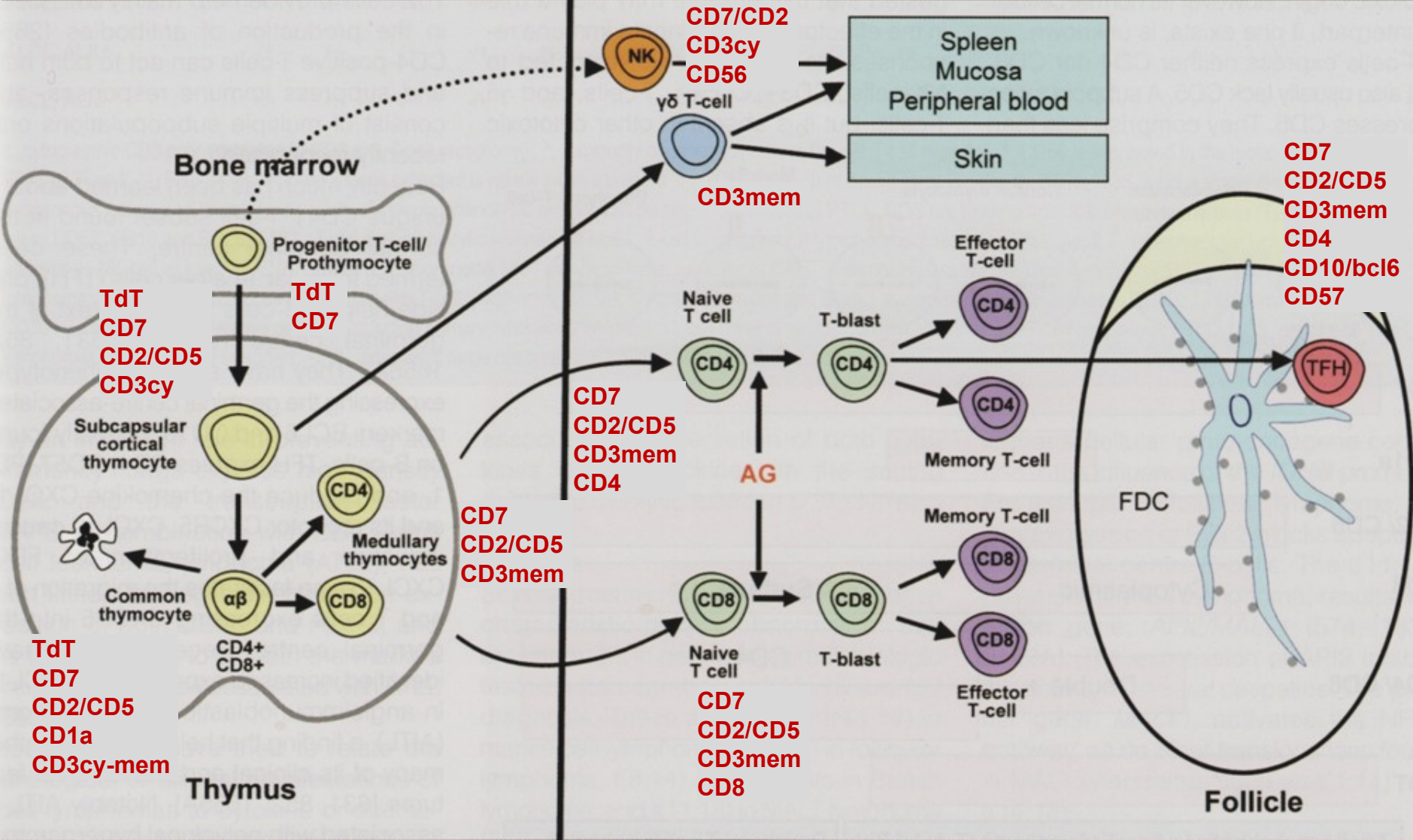
kopie

Central lymphoid tissue

Peripheral lymphoid tissue

Precursor T-cells

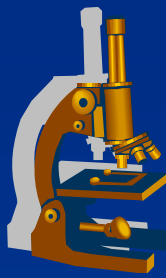
Peripheral (mature) T- and NK-cells



T lymphoblastic lymphoma/leukaemia

Peripheral (mature) T-cell and NK-cell lymphomas/leukaemias

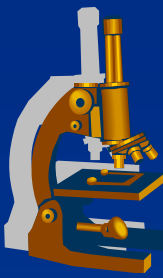
T-cell lymphomas (selected entities)



- **Peripheral T-cell lymphoma, NOS**
- **T-ALL**
 - *B-ALL >>> T-ALL*
- **Mycosis fungoides/Sézary syndrome**
 - *MF: Primary cutaneous lymphoma*
 - *SS: leukemized, erythroderma*
- **Anaplastic Large Cell Lymphoma**
- **Enteropathy-type T-cell lymphoma**
- **Adult T-Cell Leukemia/Lymphoma (HTLV1)**

- × Hematopoiesis
- × Myeloid neoplasms
- **Lymphoid neoplasms**
 - ⇒ *NHL*
 - ⇒ *HL*
- Reactive lymphadenopathy

Differences between HL and NHL



Hodgkin lymphoma	Non-Hodgkin Lymphoma
Usually localized to a single axial group of LN (cervical, mediastinal, para-aortic)	Involvement of multiple peripheral LN
Contiguous spreading	Non-contiguous spreading
Mesenteric LN and Waldeyer ring rarely involved commonly involved
Extranodal rare	Extranodal common
Diagnostic (neoplastic) cells admixed with reactive non-malignant inflammatory cells	Neoplastic/lymphoma cells dominate
B-cell origin	B- or T-cell origin

Hodgkin lymphoma



- one of most common malignancies of **young adults**
- **th.:**
 - *RT, CHT → excellent prognosis, but risk of secondary malignancies (MDS, AML, lung ca)*

Hematopoiesis

Myeloid neoplasms

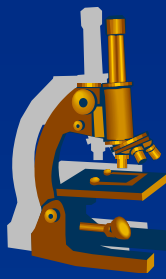
Lymphoid neoplasms

NHL

HL

Reactive
lymphadenopathy

Hodgkin lymphoma - classification



1. Classical HL

⇒ diagnostic cc. **CD15+/ CD30+**, background ly T- >> B-

- **Nodular sclerosis** (lacunar cc., assoc. EBV)
- **Lymphocyte-rich**
- **Mixed cellularity**
- **Lymphocyte depletion**

2. Lymphocyte predominance, nodular

⇒ L&H („popcorn“) cc.: **CD20+/CD15-/ CD30-**, ↓T-ly

× Hematopoiesis

× Myeloid neoplasms

• **Lymphoid neoplasms**

× NHL

⇒ HL

• Reactive lymphadenopathy

Hodgkin lymphoma



diagnostic tumor cells

Reed-Sternberg cells + variants

Chemokines / cytokines production

→ chemotaxis of lymphocytes,
macrophages, granulocytes incl.
eosinophils = reactive non-neoplastic
background

× Hematopoiesis

× Myeloid
neoplasms

• **Lymphoid
neoplasms**

× *NHL*

⇒ *HL*

• Reactive
lymphadenopathy

Diagnostic cells of HL



copy



Sternberg c.



Hodgkin c.



Reed-Sternberg c.

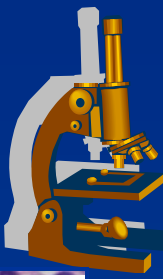


L&H c.

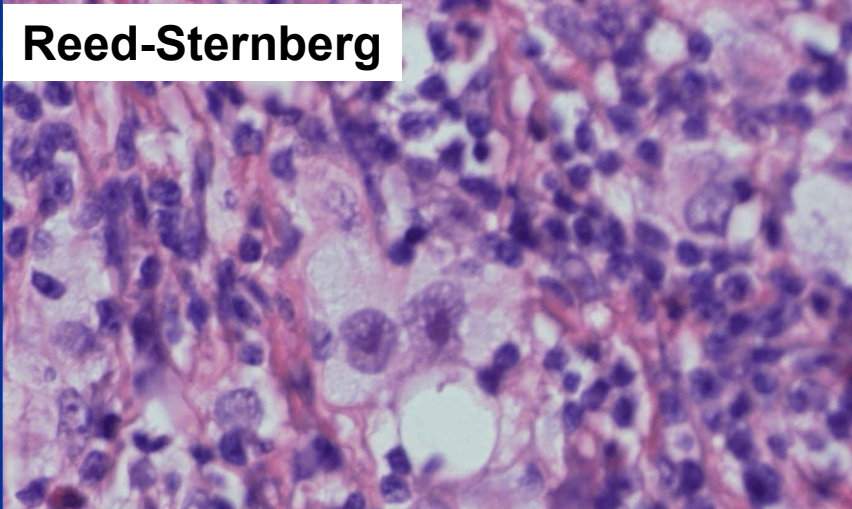


Lacunar c.

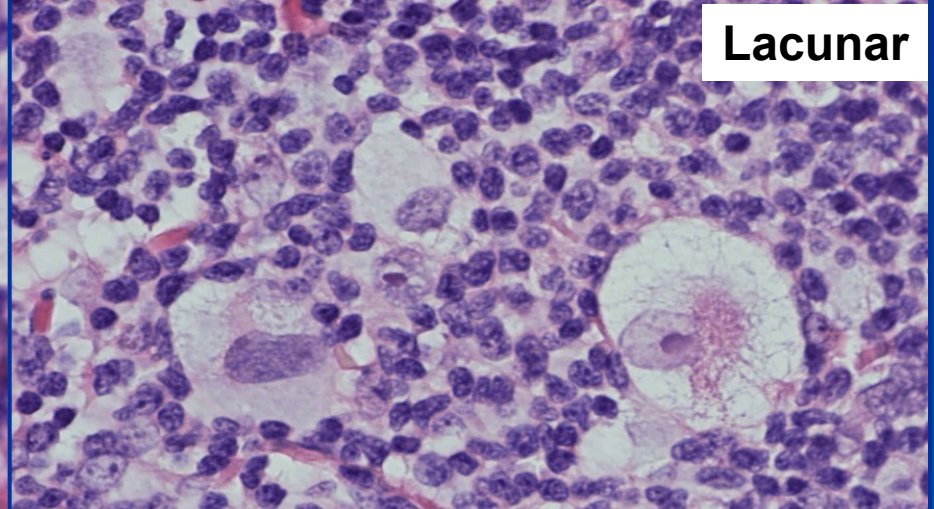
Diagnostic cells - classical HL



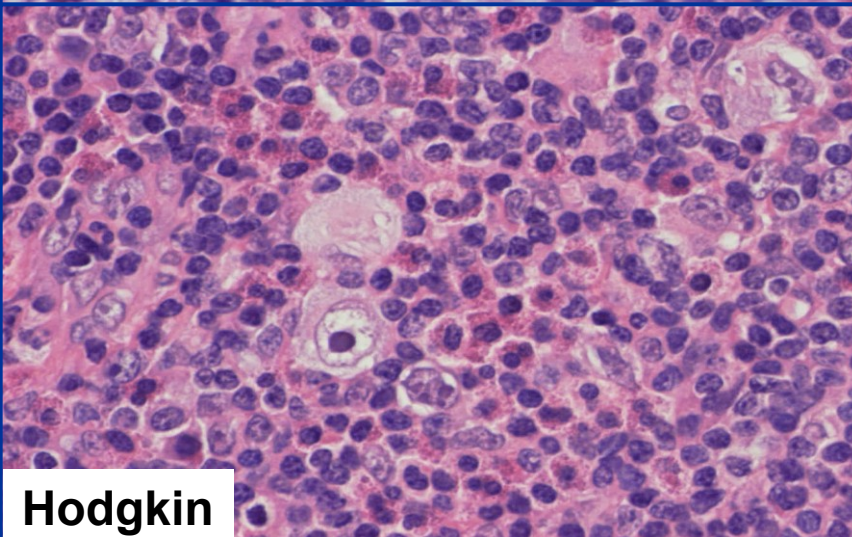
Reed-Sternberg



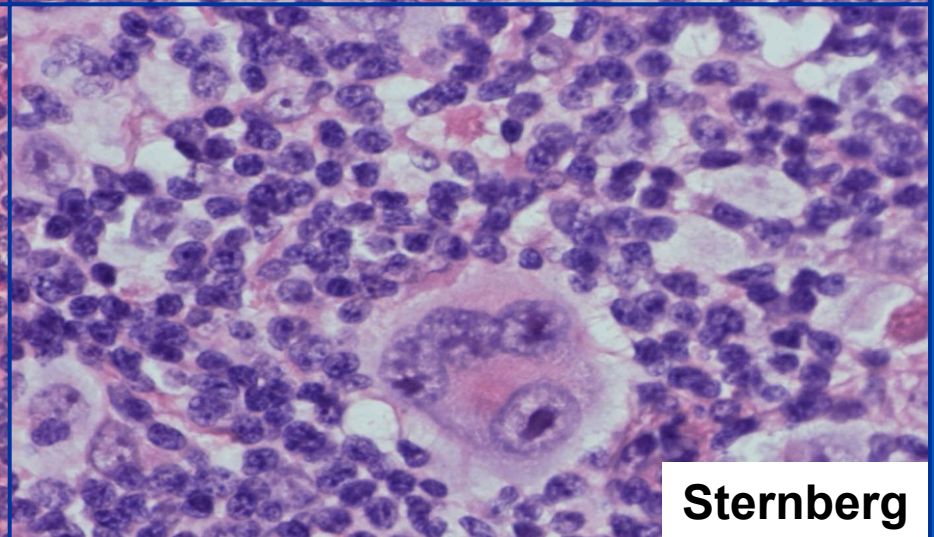
Lacunar



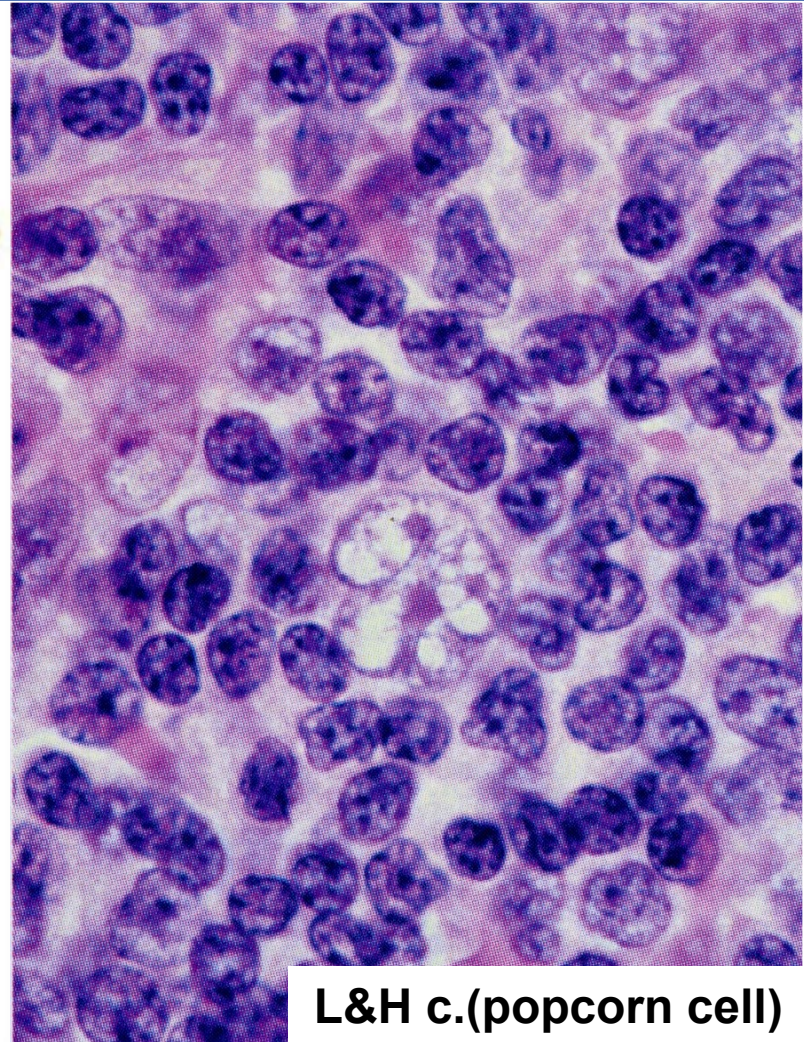
Hodgkin



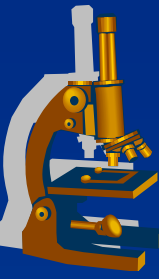
Sternberg



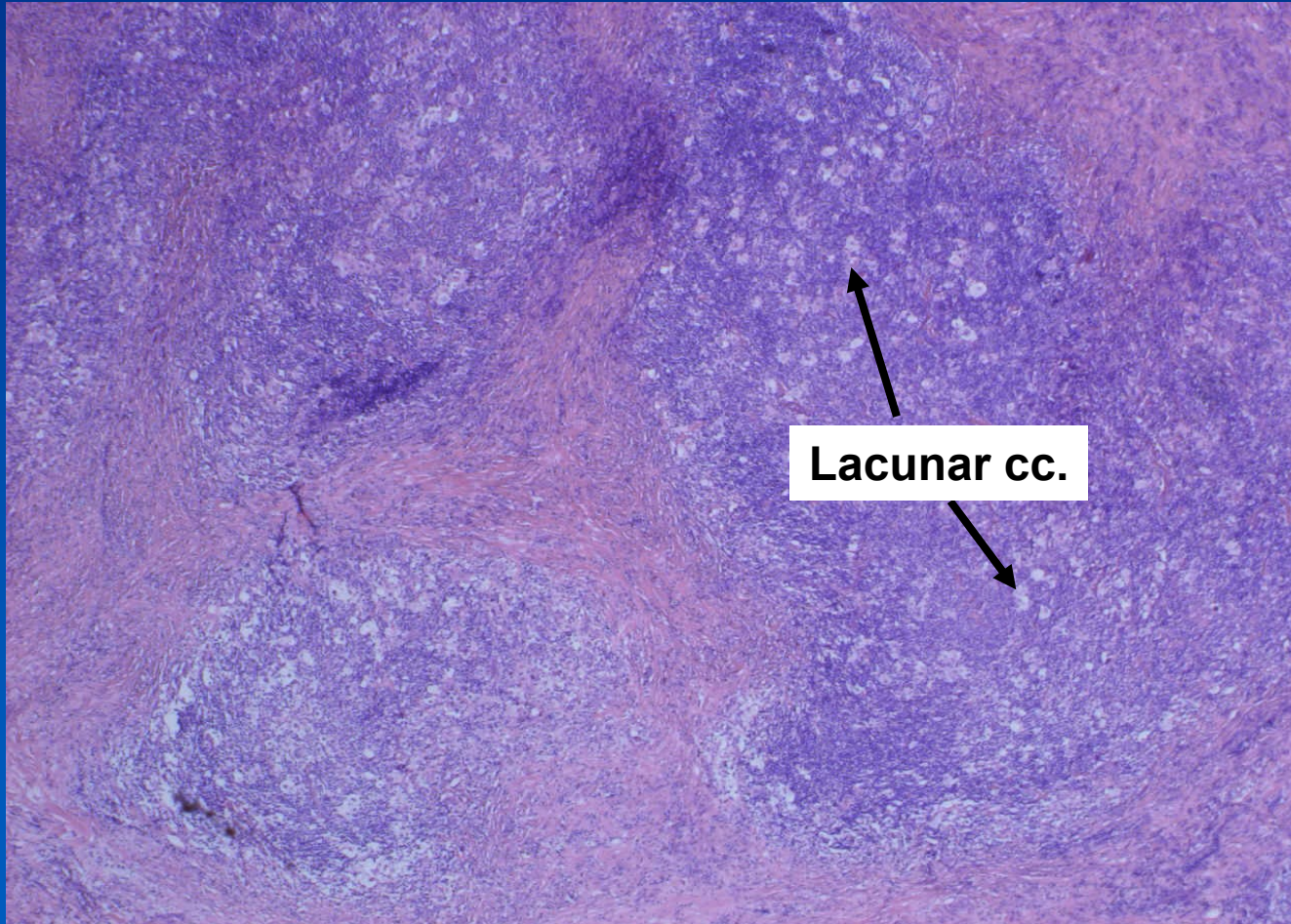
Lymphocyte predominance, nodular: diagnostic cell



L&H c.(popcorn cell)

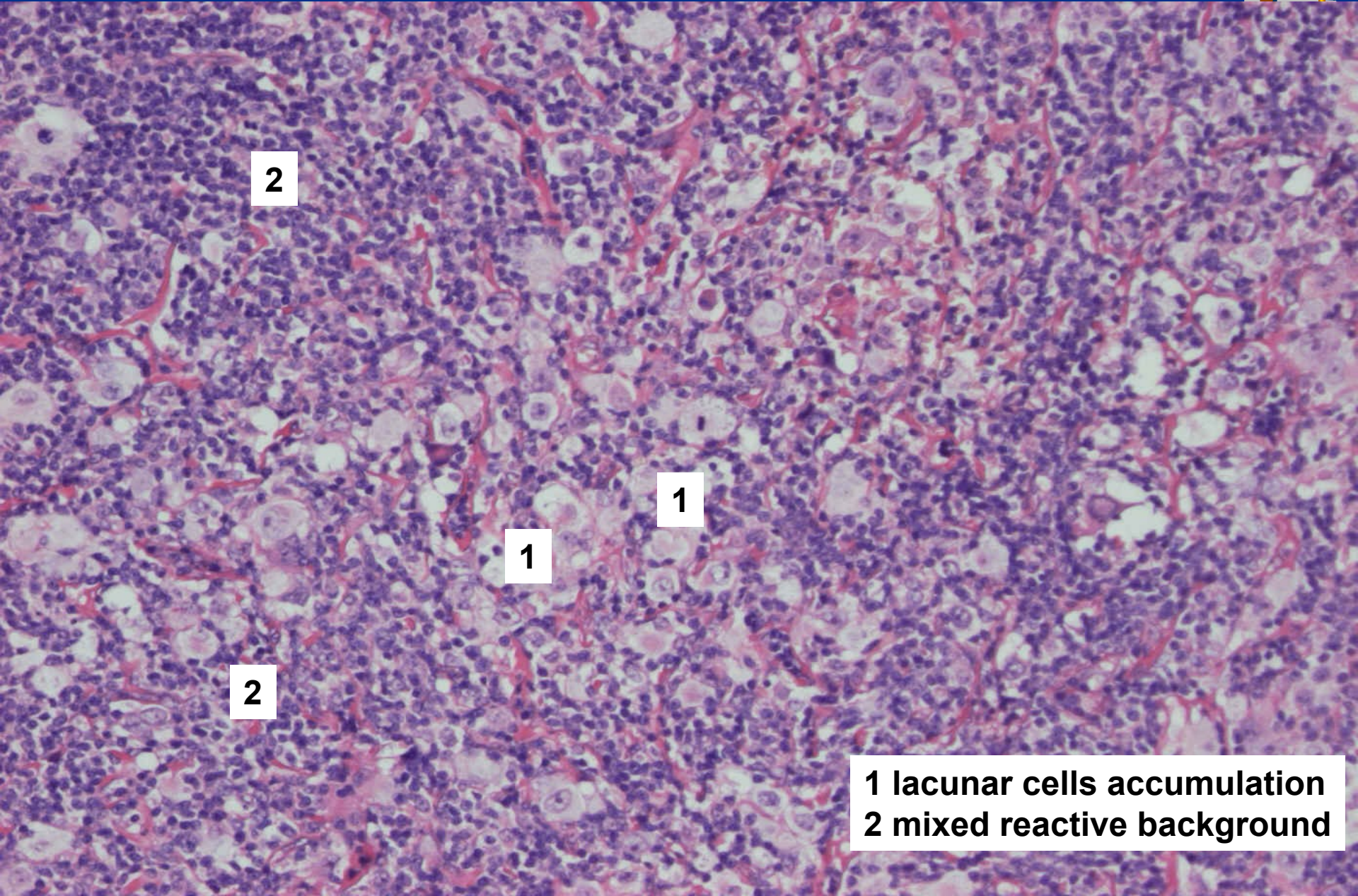
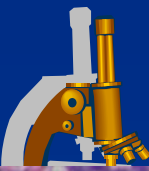


Hodgkin lymphoma, classical, nodular sclerosis



Lacunar cc.

Hodgkin lymphoma, classical, nodular sclerosis



2

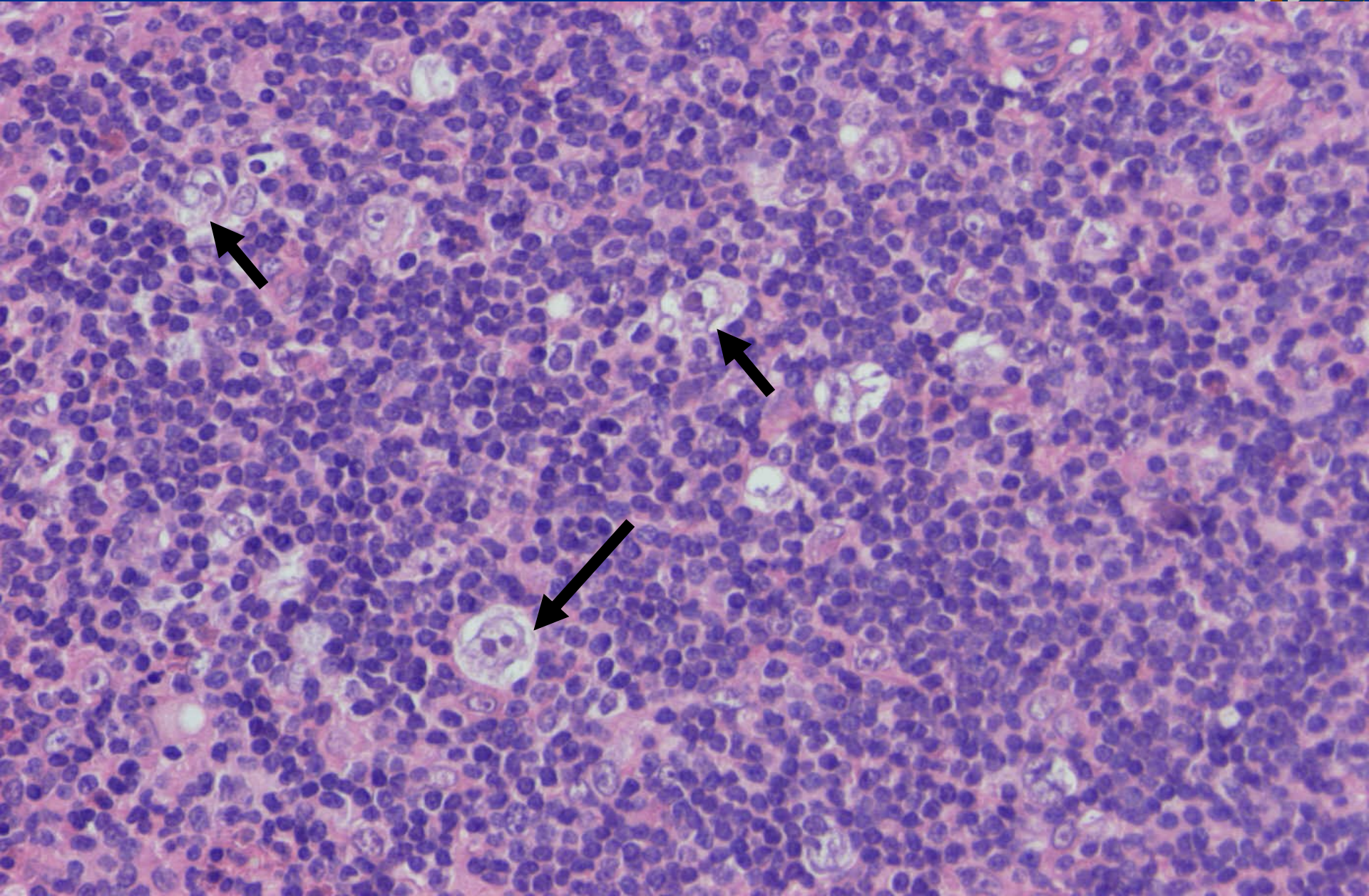
1

1

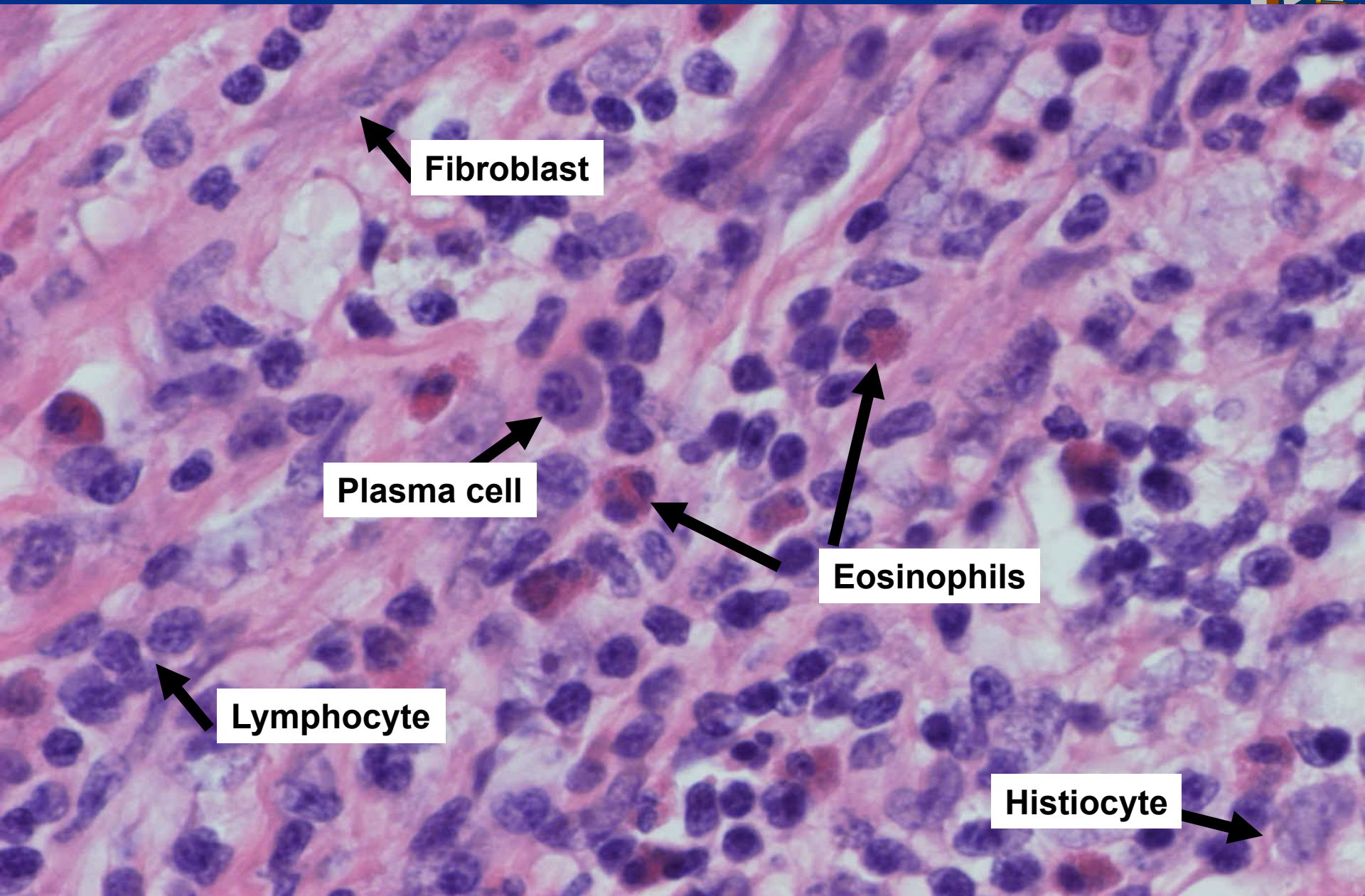
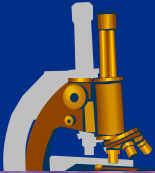
2

1 lacunar cells accumulation
2 mixed reactive background

HL, classical, mixed cellularity – Hodgkin cc., RS cc.



Classical HL – cells of the non-neoplastic background



Fibroblast

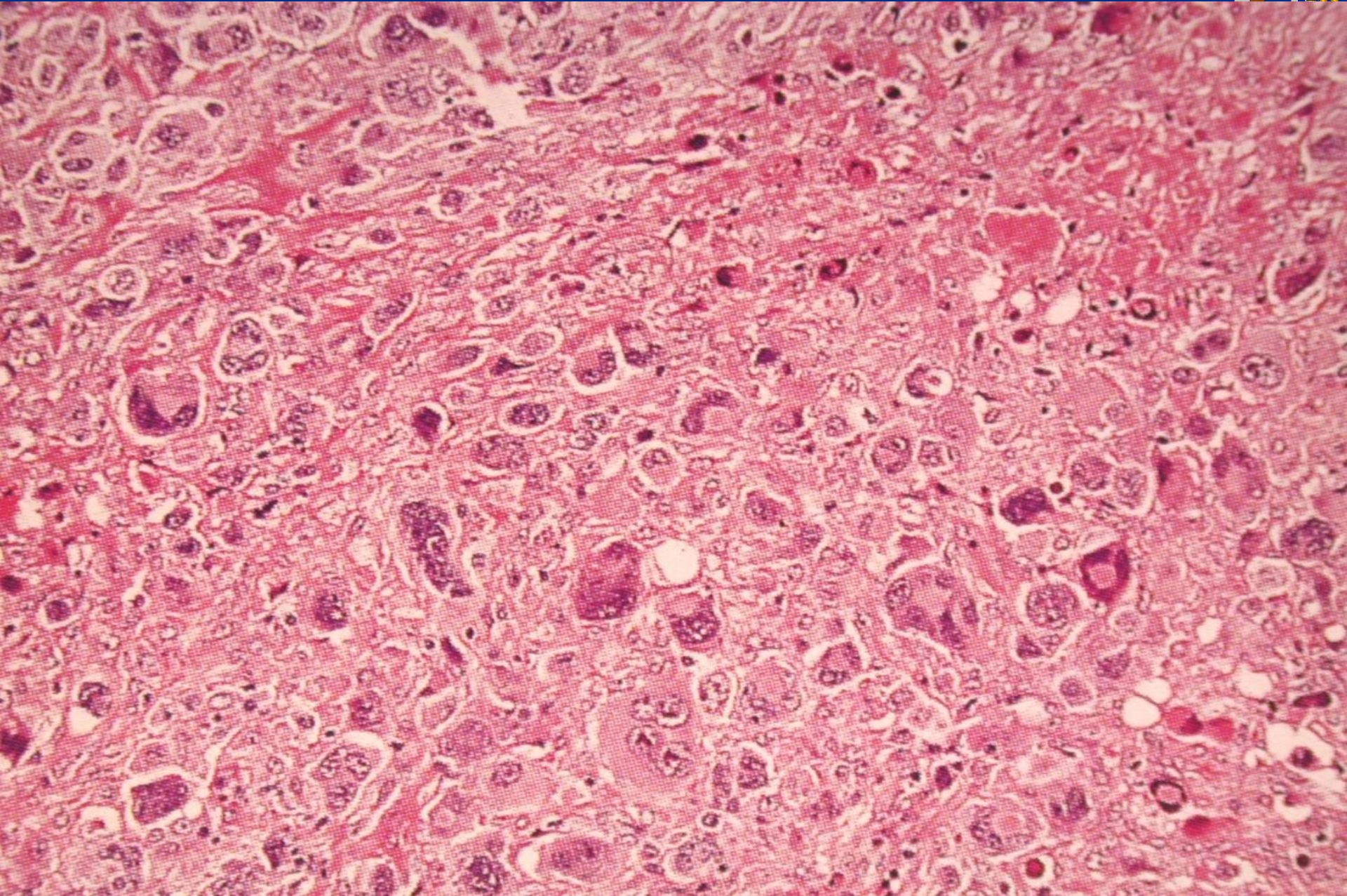
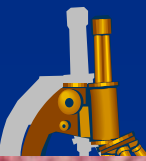
Plasma cell

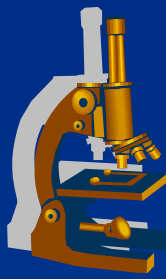
Eosinophils

Lymphocyte

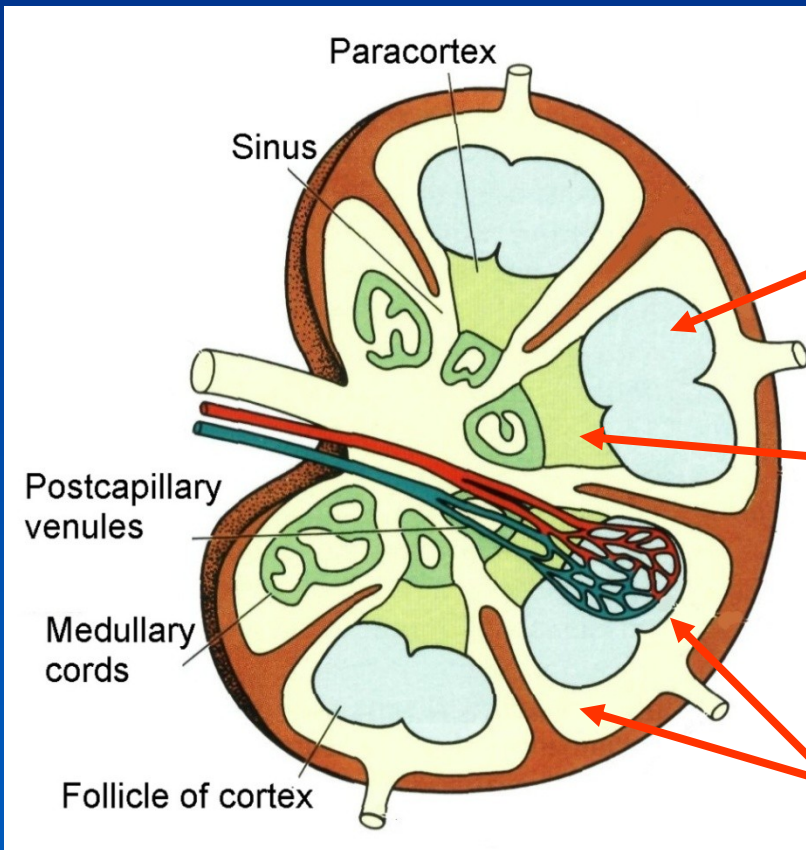
Histiocyte

Classical HL – lymphocyte depletion





Reactive lymphadenopathy



- **Reactive hyperplasia:**
 - Follicular (B)*
(bacteria, sterile inflammation)
 - Paracortical (T)*
(viruses, chronic inflammations)
- **Sinus histiocytosis**

- ✗ Hematopoiesis
- ✗ Myeloid neoplasms
- ✗ Lymphoid neoplasms
 - ✗ NHL
 - ✗ HL
- **Reactive lymphadenopathy**

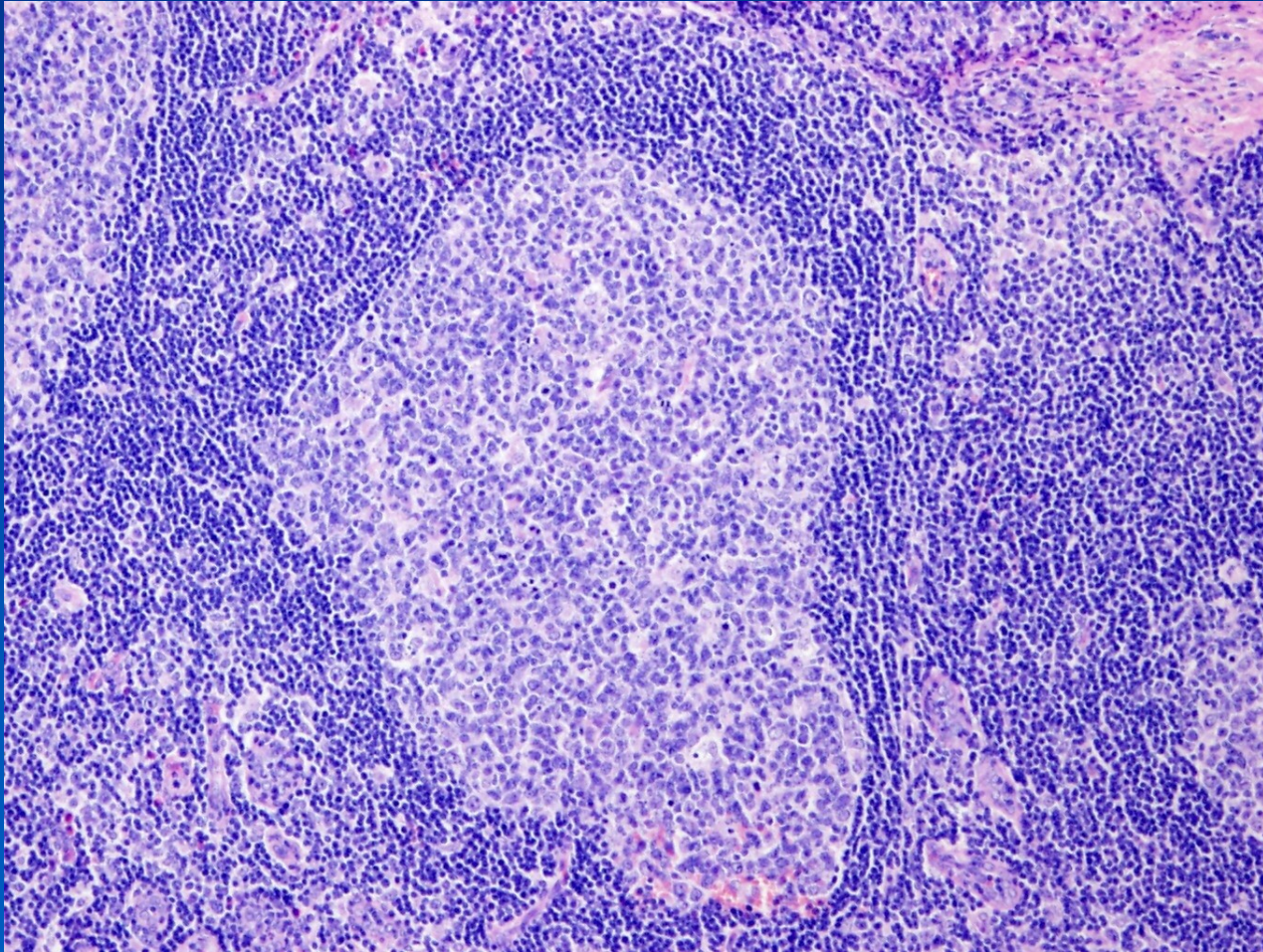
Reactive lymphadenopathy



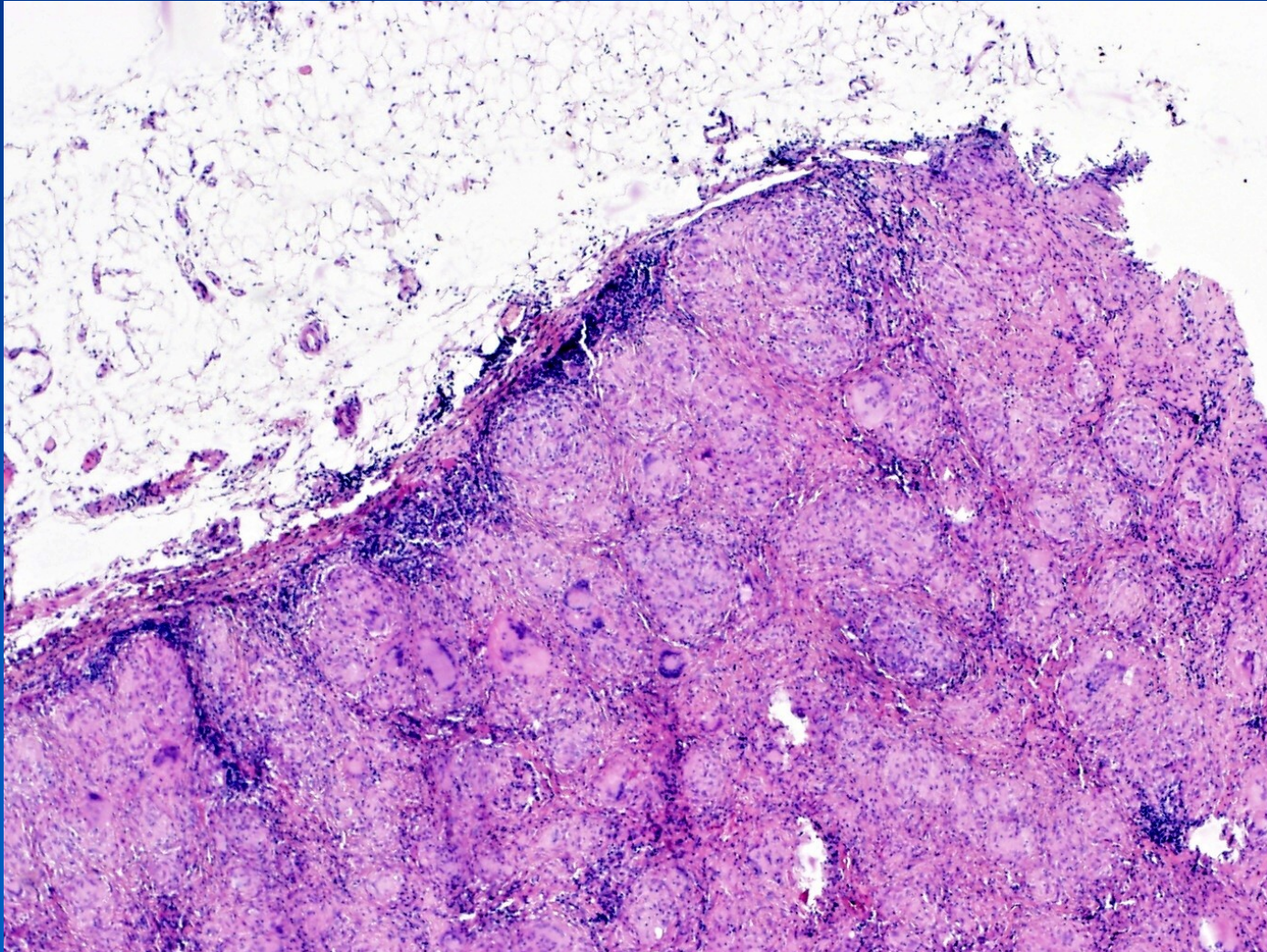
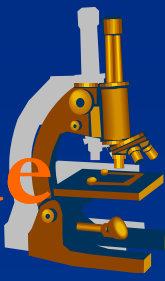
- **follicular hyperplasia**
 - Enlarged, irregular (in shape and size), polarized germinal centers, tingible macrophages, mitotic activity in GC
 - Bacterial infections, RA, toxoplasmosis, ...
- **paracortical hyperplasia**
 - Reactive changes in T-cell regions of LN
 - Parafollicular T-cell transformation into large proliferating blasts
 - Viral infections, vaccinations, drugs (phenytoin)
- **sinus histiocytosis**
 - Distention and prominence of lymphatic sinusoids: hypertrophy of lining endothelial cells and infiltrate of macrophages
 - Usually non-specific reaction, also in LN draining cancers
- **granulomatous inflammation** (see General Pathology III)
 - *necrotizing* (TBC, cat scratch disease)
 - *Non-necrotizing* (sarcoidosis)

- × Hematopoiesis
- × Myeloid neoplasms
- × Lymphoid neoplasms
 - × NHL
 - × HL
- **Reactive lymphadenopathy**

Follicular hyperplasia - reactive



Sarcoidosis - mediastinal lymph node



Sarcoidosis - mediastinal lymph node

