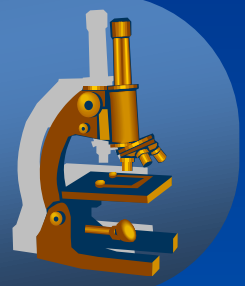
General pathology

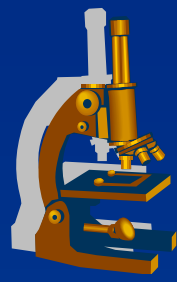


General pathology V.

Neoplasms II (hematooncology).

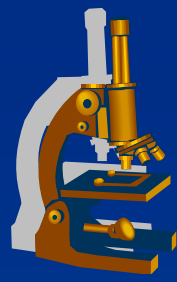
Pathology of lymph nodes.

Summary



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

Hematopoiesis

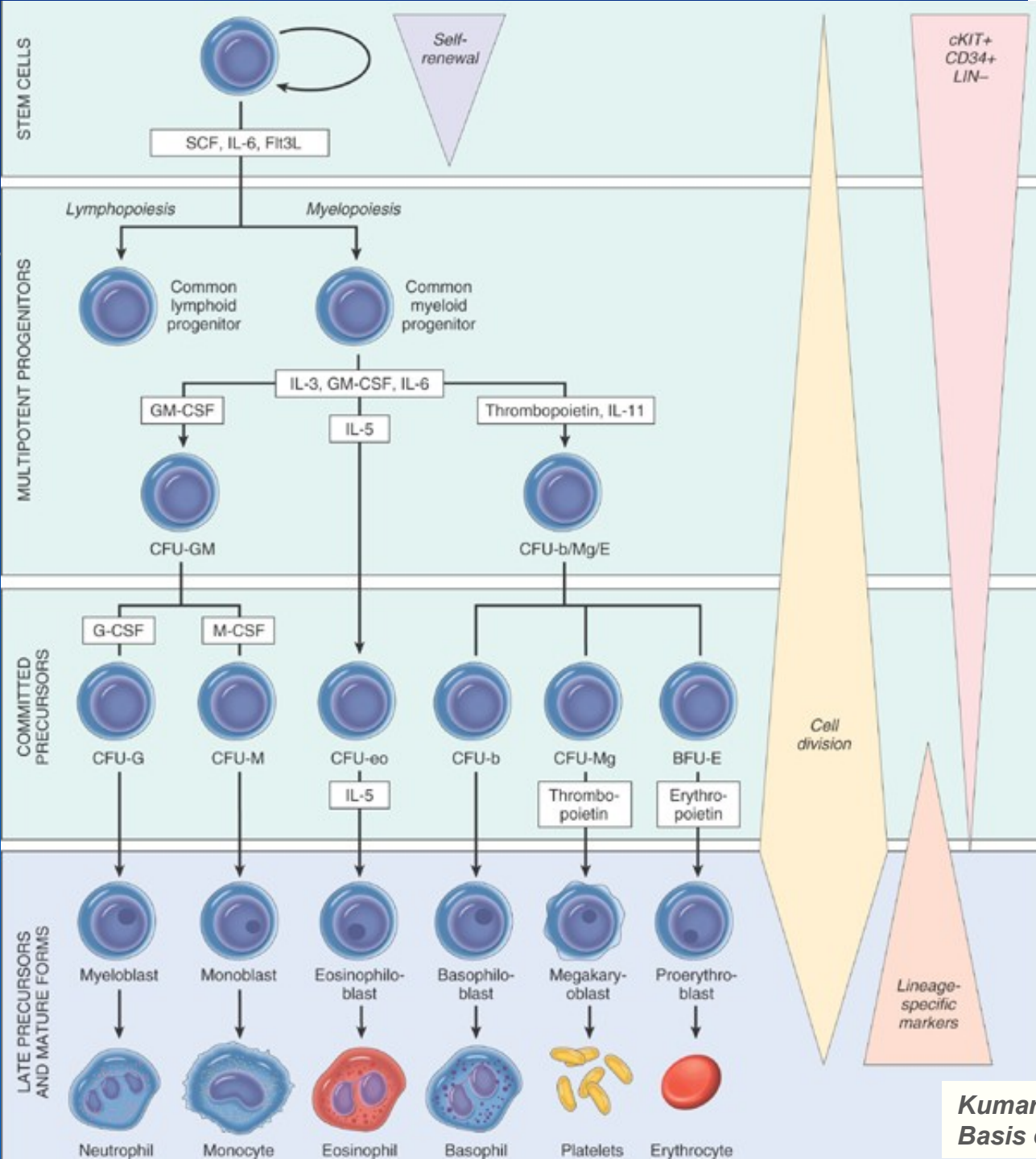


- from **hematopoietic stem cell**

- **HSCs** (***H****ematopoietic* ***S****tem* ***C****ells*): ***pluripotent****, ability of self-renewal (replication)*

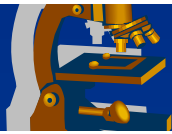
  ⇒ *due to asymetric cell division variable progenitor cells arise :*
  - **fenotypically identical cells –** HSCs
  - **fenotypically different cells –** multipotent cells **(progenitors of myeloid cell line or progenitors of lymhoid cell line)**

  - *Regulation of hematopiesis through specific growth factors*
  - *GF receptors expressed during the development/differentiation on blood cells*



Hematopoetic stem cells

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



Multipotent progenitors

Multipotent progenitors

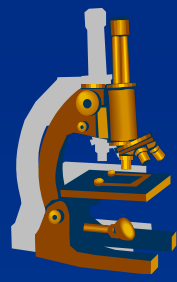
Committed precursors

Late precursors and mature forms

- morphologically differentiated

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

Hematooncology

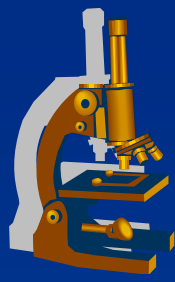


- **Leukemia (hemoblastosis)**
  - ***Diffuse replacement of normal BM by leukemic cells with their subsequent variable accumulation in peripheral blood (=leukemization)***
  - ***Infiltration of peripheral organs (liver, spleen, lymph nodes, meninges, gonads,….)***

- **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 massess

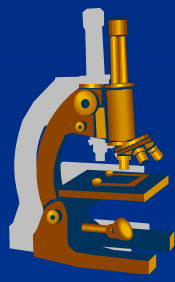
Hematooncology



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

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

Hematooncological diseases



Myeloid neoplasms

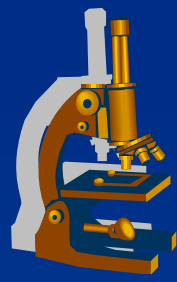
- from stem cells that normally give rise to the formed blood elements (granulocytes, red cells, platelets)
- 3 categories
  → acute myelogenous leukemias
  → myeloproliferative disorders
  → myelodysplastic syndromes

Lymphoid neoplasms

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

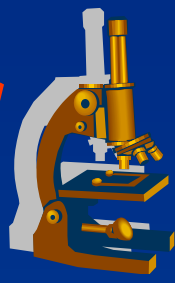
Histiocytic neoplasms

Etiopathogenesis of hematooncological diseases



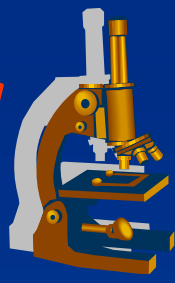
- ???
- **hereditary syndromes**
  - ***Inherited genetic instability*** *(Bloom´s sy, ataxia teleangiectasia…)****, Down´s sy, NF type I…***
- **oncogenic viruses**
  - ***HTLV-1, EBV, HSV-8***
- **chronic stimulation of immune system**
  - ***Helicobacter pylori, gluten-sensitive enteropathy (celiac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

TUMORS of HAEMATOPOETIC and LYMPHATIC TISSUES



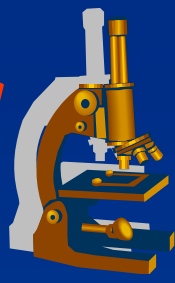
- **Myelodysplastic syndromes:** clonal stem cell disorders, ineffective haematopoesis→ cytopenias; dysplastic maturation. De novo or after radio/chemotherapy. Progressive marrow failure. May → AML.
- **Myelodysplastic/myeloproliferative diseases** overlapping features, variably effective haematopoesis,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

TUMORS of HAEMATOPOETIC and LYMPHATIC TISSUES



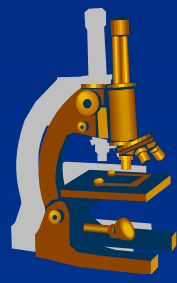
- **acute myeloid leukaemia + related precursor neoplasms** - clonal expansion of myeloid blasts in bone marrow, blood or other tissues (myeloid sarcoma).
- Class. acc. genetic abnormalities (in young, good response to therapy and behaviour), multilineage dysplasia (i. e. following MDS, older, drug resistance),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

TUMORS of HAEMATOPOETIC and LYMPHATIC TISSUES



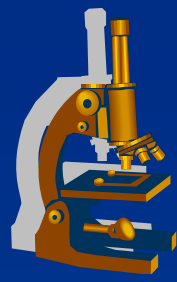
- **Histiocytic and dendritic cell neoplasms**
- from mononuclear phagocytes (macrophages, dendritic antigen-presenting cells) – common bone marrow precursor
- follicular dendritic cells non-myeloid, from mesenchymal stem cell
- true histiocytic neoplasm uncommon (Langerhans cell histiocytosis, benign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

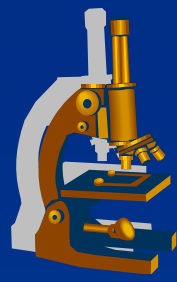


MYELOID NEOPLASMS

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

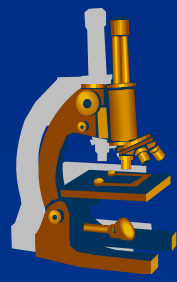
Myeloid neoplasms



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

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

MDS



- **<u>Disordered and ineffective maturation of myeloid progenitors</u>**

- ***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***
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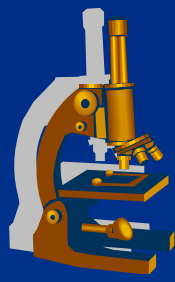
AML



- **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

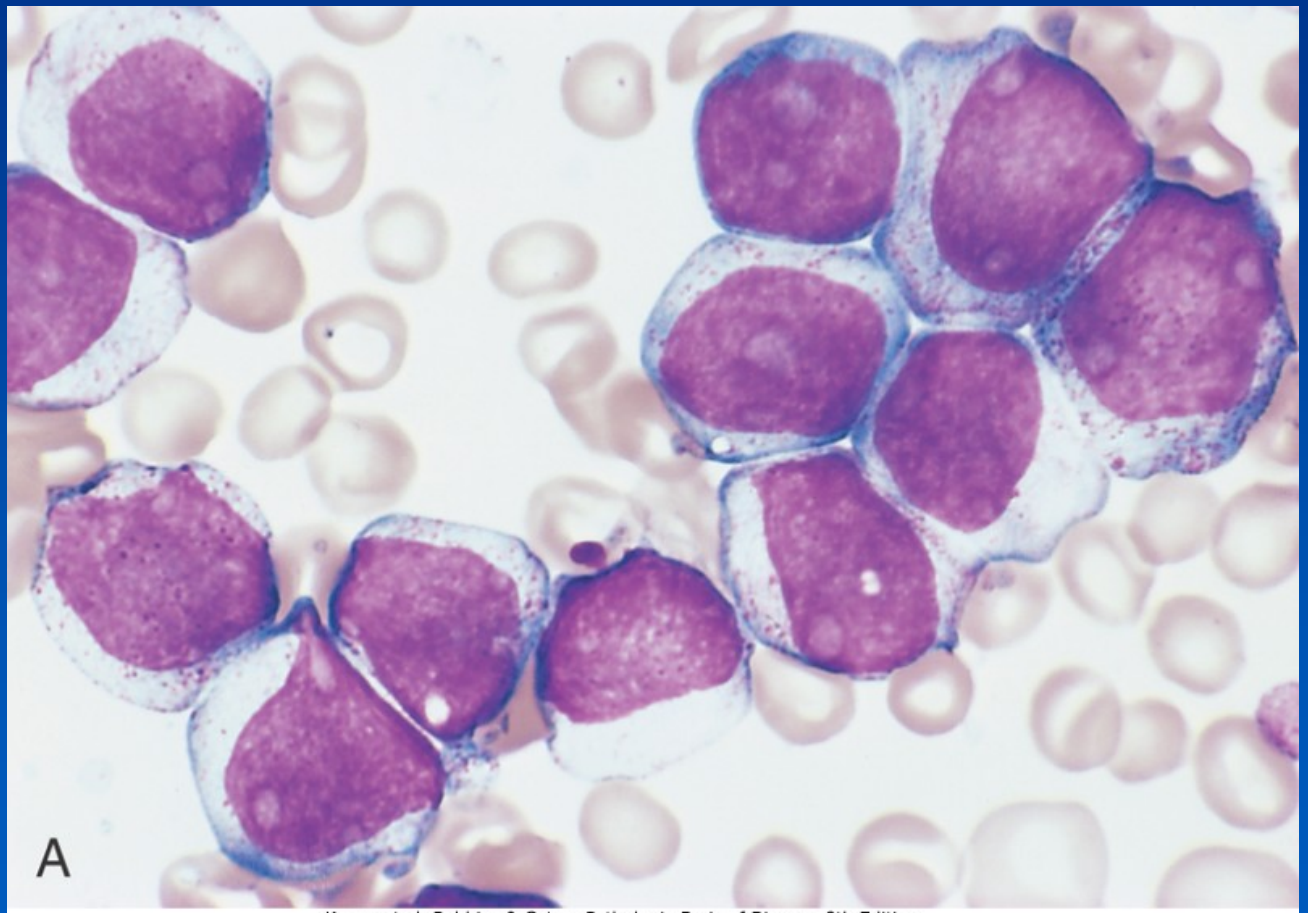
⇒ ***Clinical signs of marrow failure***

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

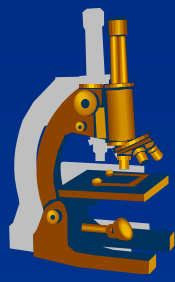
- primarily in older adults (median age 50)

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

AML



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;v); ☹; 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***
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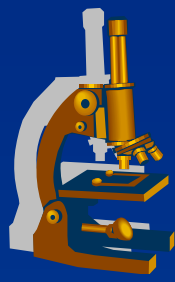
AML

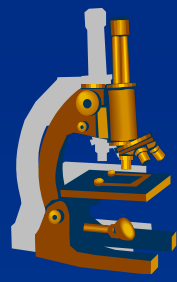


- ***III. AML, THERAPY-RELATED; prognosis ☹☹; FAB subtype*** Variable
  If following alkylator therapy or radiation therapy, 2- to 8-year latency period, MDS-like cytogenetic aberrations (e.g., 5q-, 7q-); if following topoisomerase II inhibitor (e.g., etoposide) therapy, 1- to 3-year latency, translocations 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***
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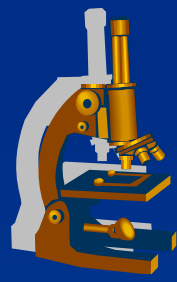
- Reactive lymphadenopathy

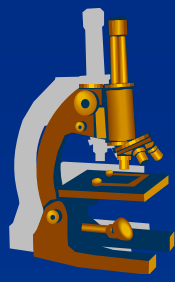
Chronic myeloproliferative disorders



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**
- Lympohid neoplasms
  - ⇨ ***NHL***
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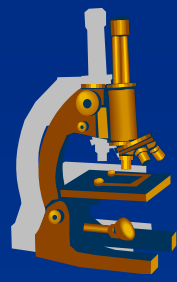
CML



- **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 neutrofils, metamyelocytes and myelocytes, myeloblasts <5 %
- Extreme **hepatosplenomegaly**, spleen up to 20 kg
- Extramedullary hematopoiesis

- Hematopoiesis
- **Myeloid neoplasms**
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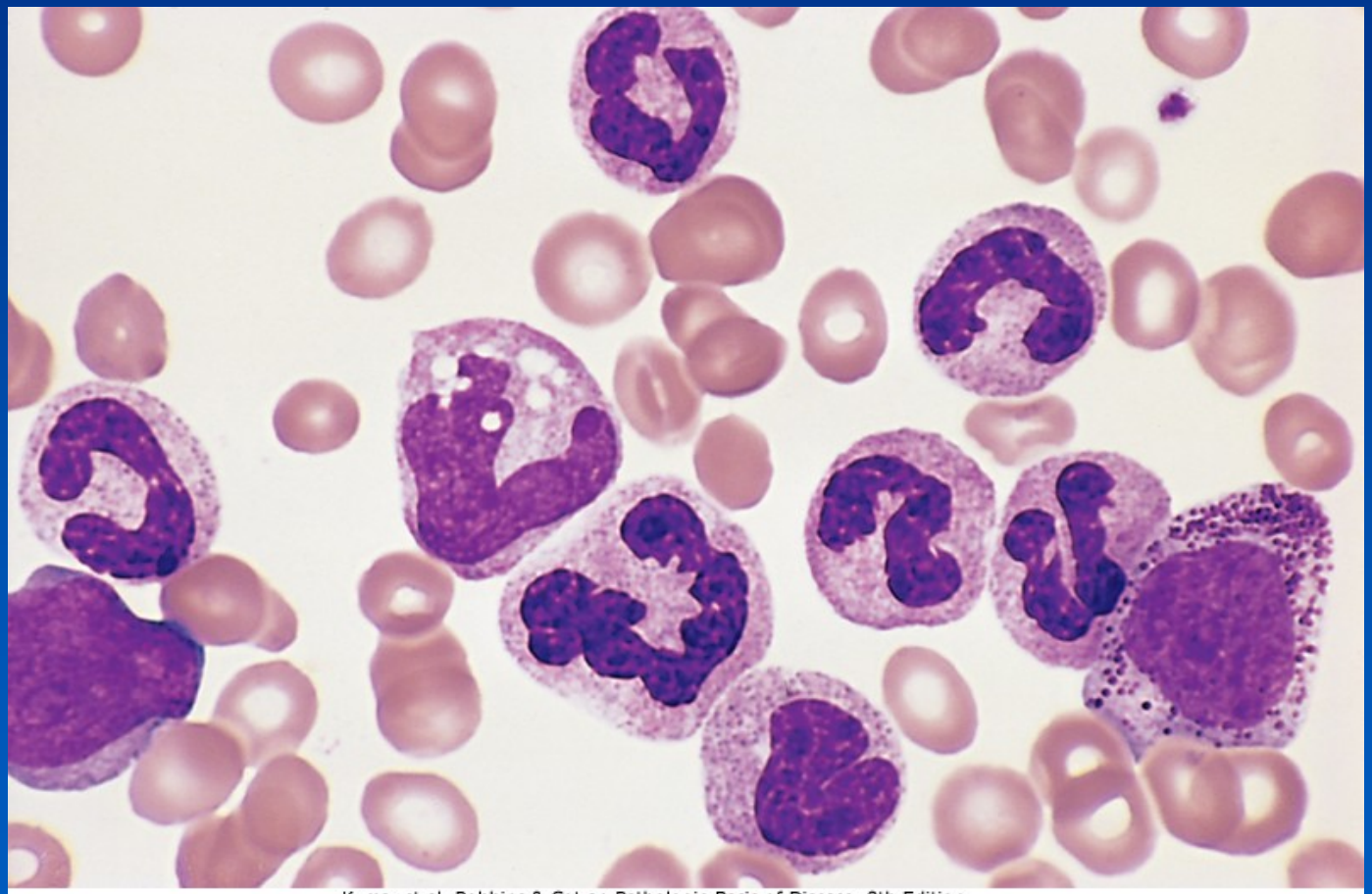
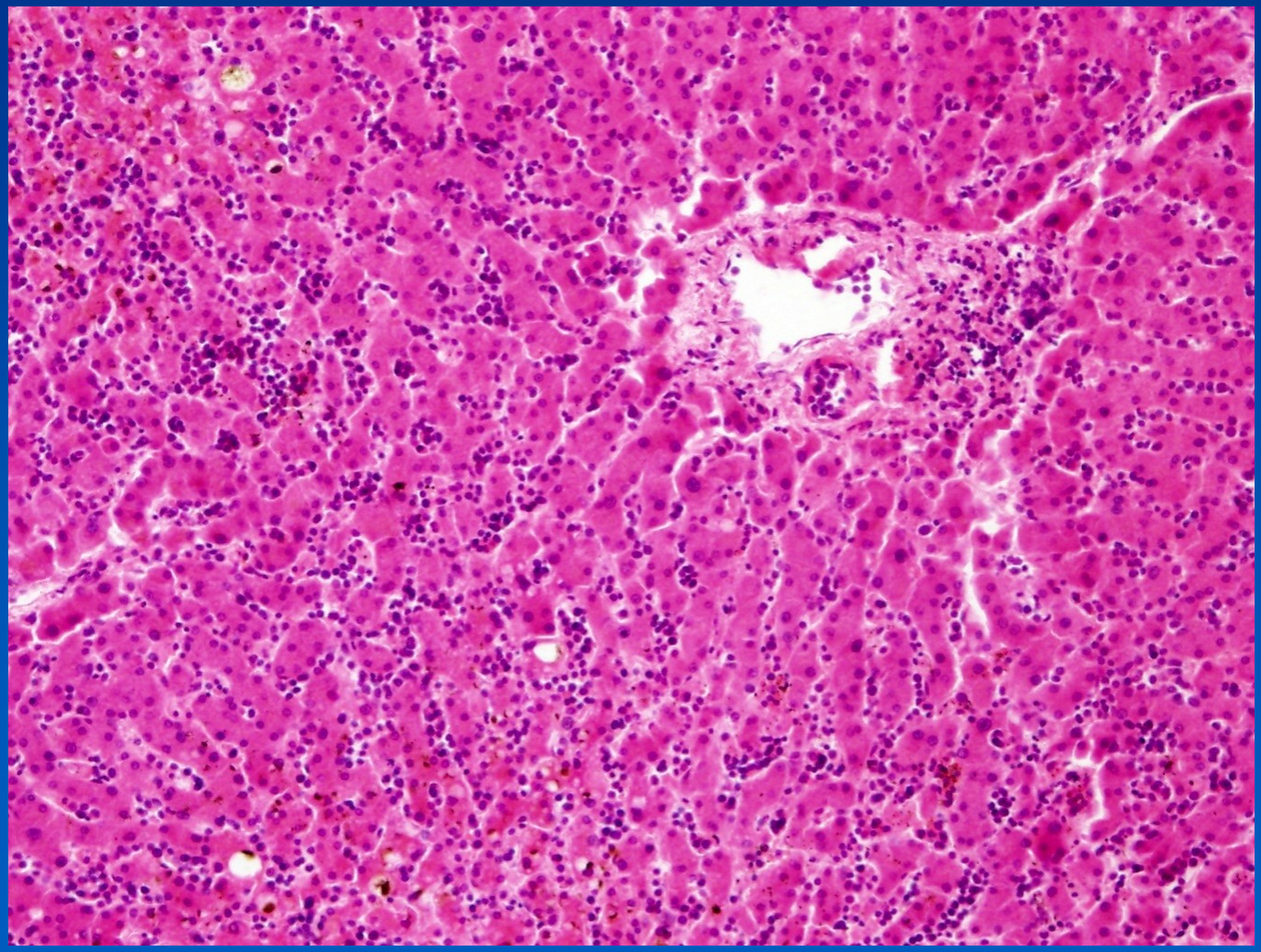
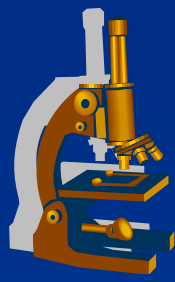
CML



CML – leukemic cells in liver sinusoids





LYMPHOID NEOPLASMS /LYMPHOMAS

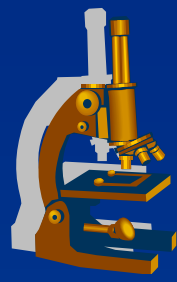
Classification:

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

→ **Hodgkin lymphomas**

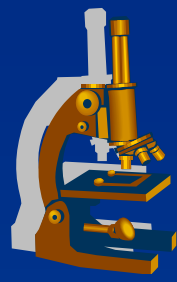
- Hematopoiesis
- Myeloid neoplasm
- **Lymphoid neoplasms**
  - ***NHL***
  - ***HL***
- Reactive lymphadenopathy

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

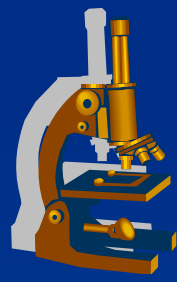
- **B-cell acute lymphoblastic leukemia/lymphoma (B-ALL)**

II. Peripheral B-Cell Neoplasms

- **B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)**
- B- prolymphocytic leukemia
- Lymphoplasmacytic lymphhoma
- **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)**

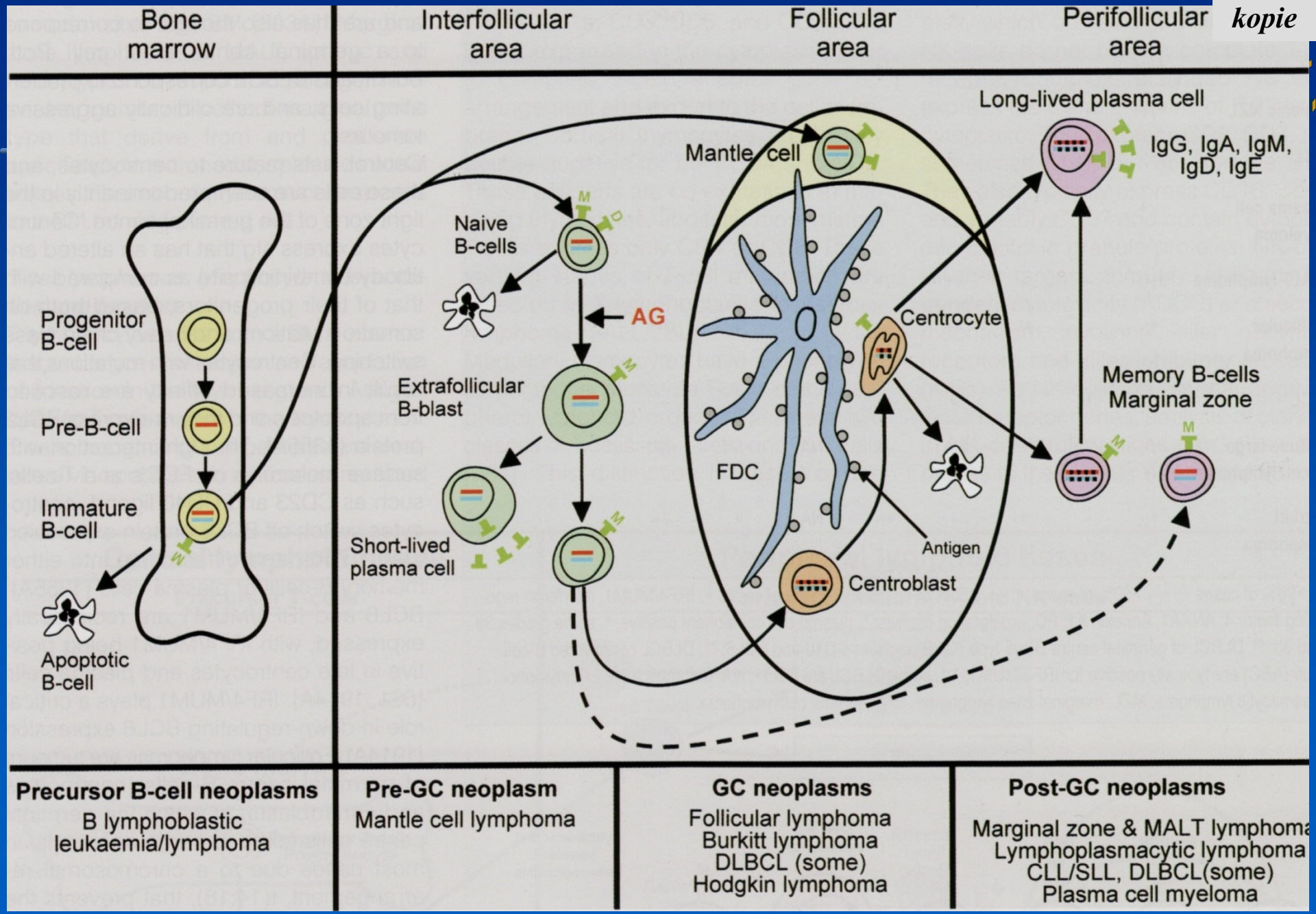
IV. Peripheral T-/NK-Cell Neoplasms

- 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 γδ T-cell lymphoma
- NK/T-cell lymphoma, nasal type
- NK-cell leukemia
- **Adult T-cell leukamia/lymphoma (HTLV1)**

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

LYMPHOID NEOPLASMS (B-cell) – cells of origin

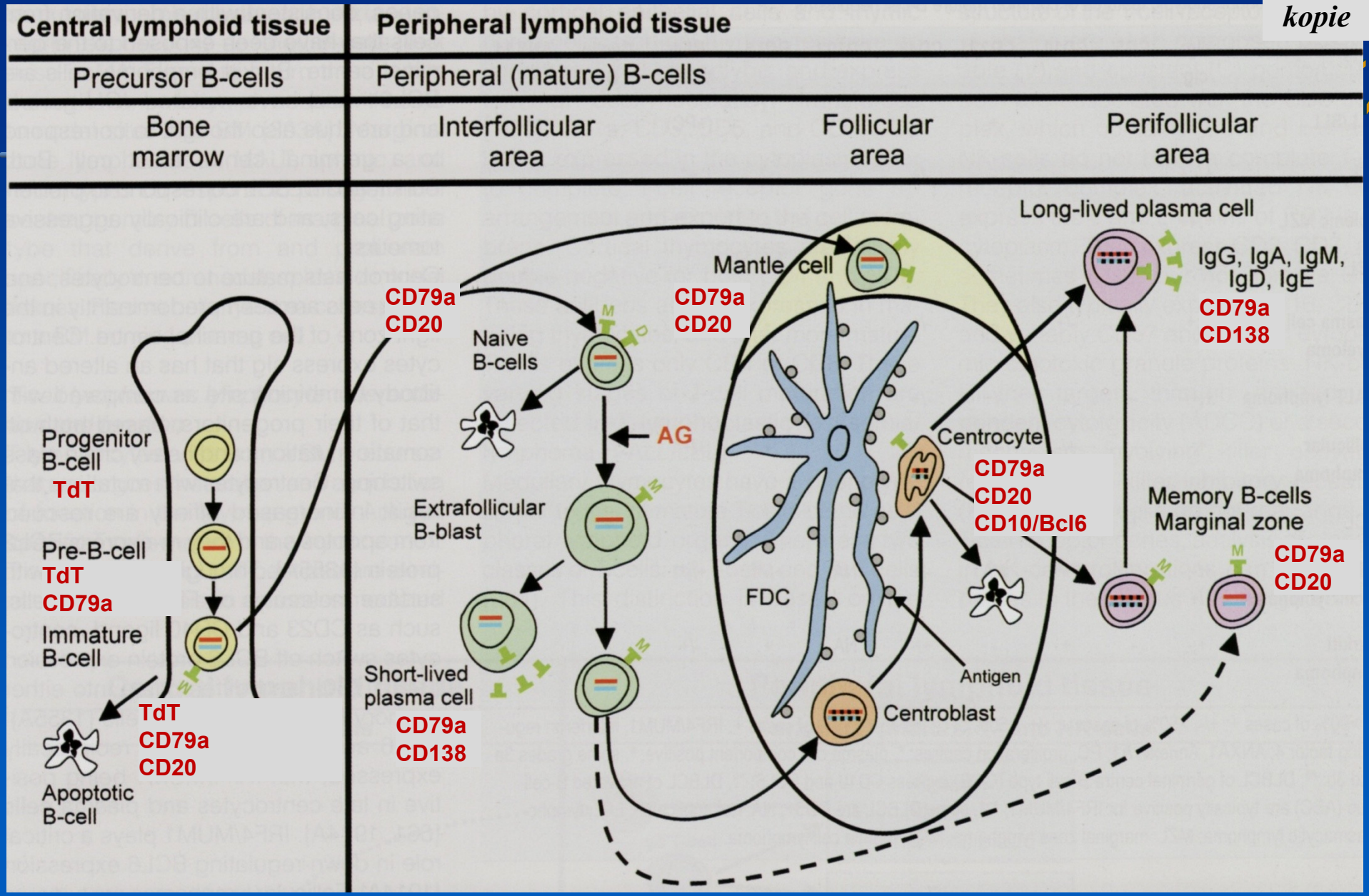
kopie



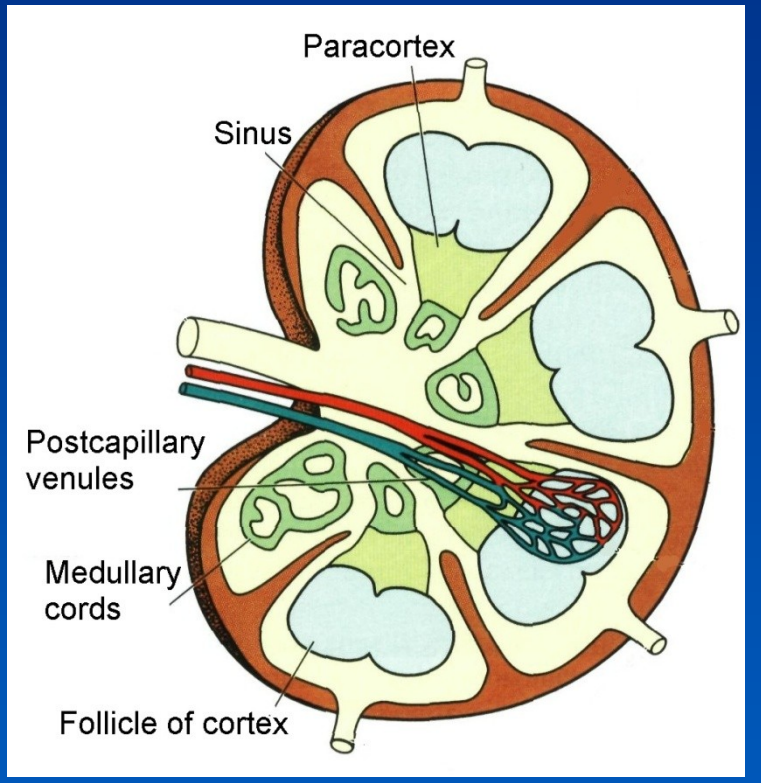
Precursor B-cell neoplasms	Pre-GC neoplasm	GC neoplasms	Post-GC neoplasms
B lymphoblastic leukaemia/lymphoma	Mantle cell lymphoma	Follicular lymphoma Burkitt lymphoma DLBCL (some) Hodgkin lymphoma	Marginal zone & MALT lymphoma Lymphoplasmacytic lymphoma CLL/SLL, DLBCL(some) Plasma cell myeloma

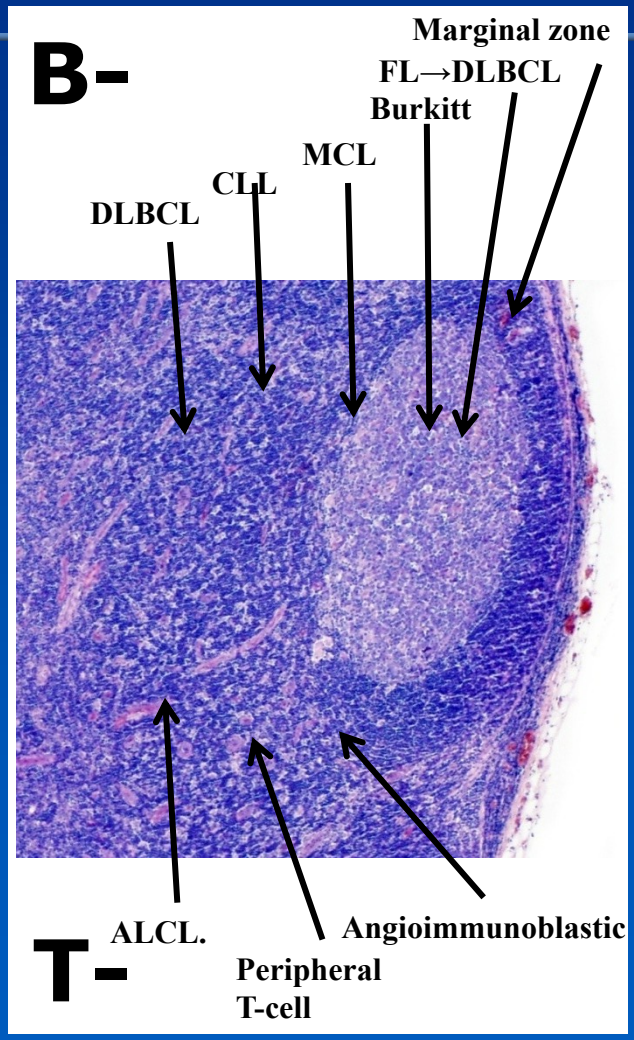
LYMPHOID NEOPLASMS (B-cell) — immunophenotype of cells of origin

kopie



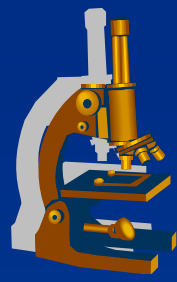
Nodal lymphomas





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

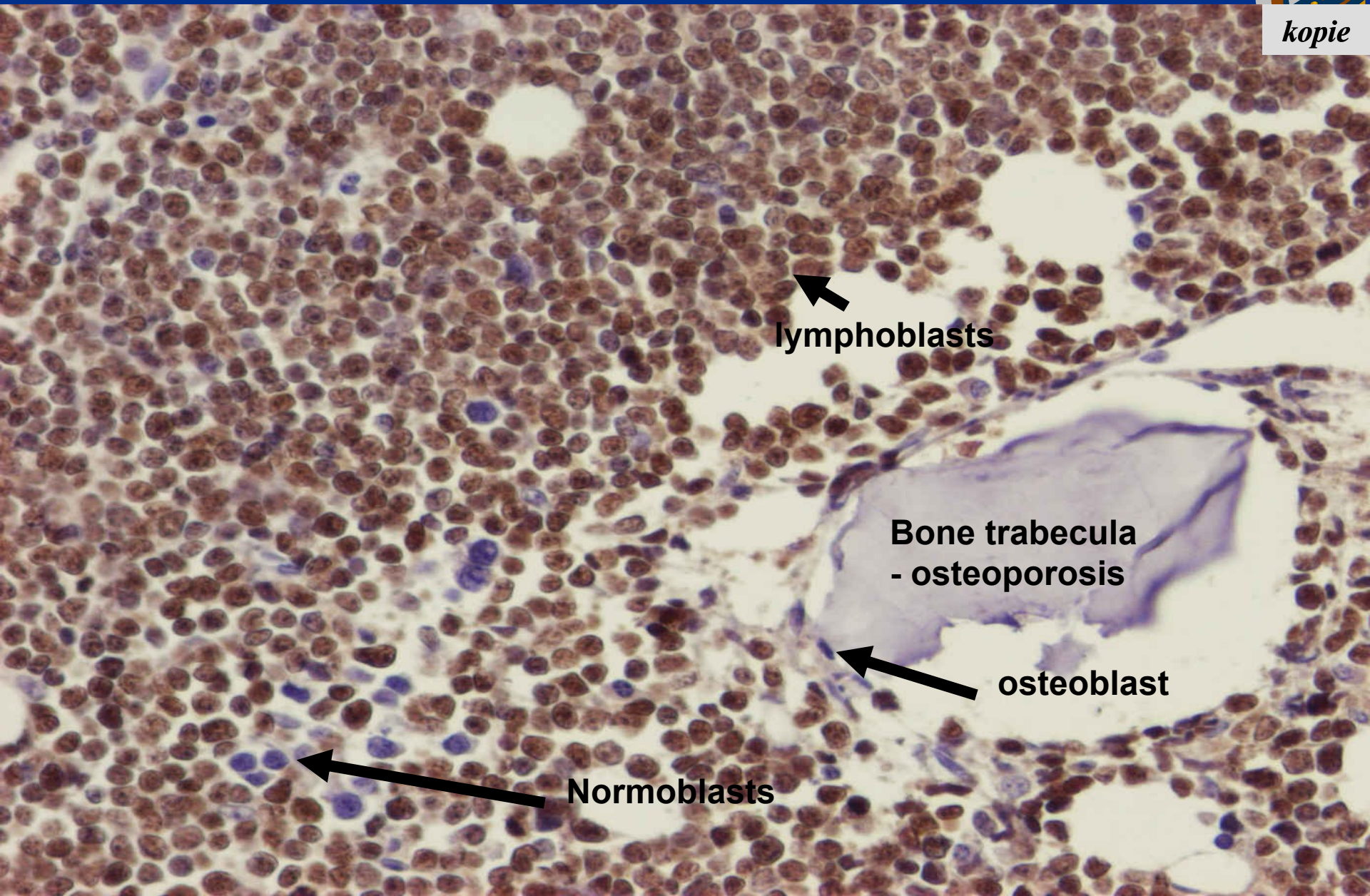
B-cell acute lymphoblastic leukemia/lymphoma (B-ALL)



- **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

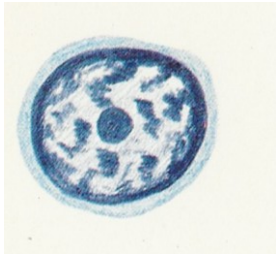


kopie

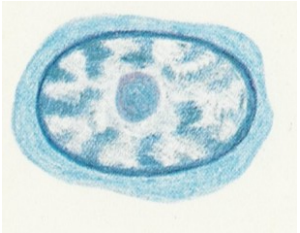
CLL/SLL

- 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)

lymphocyte



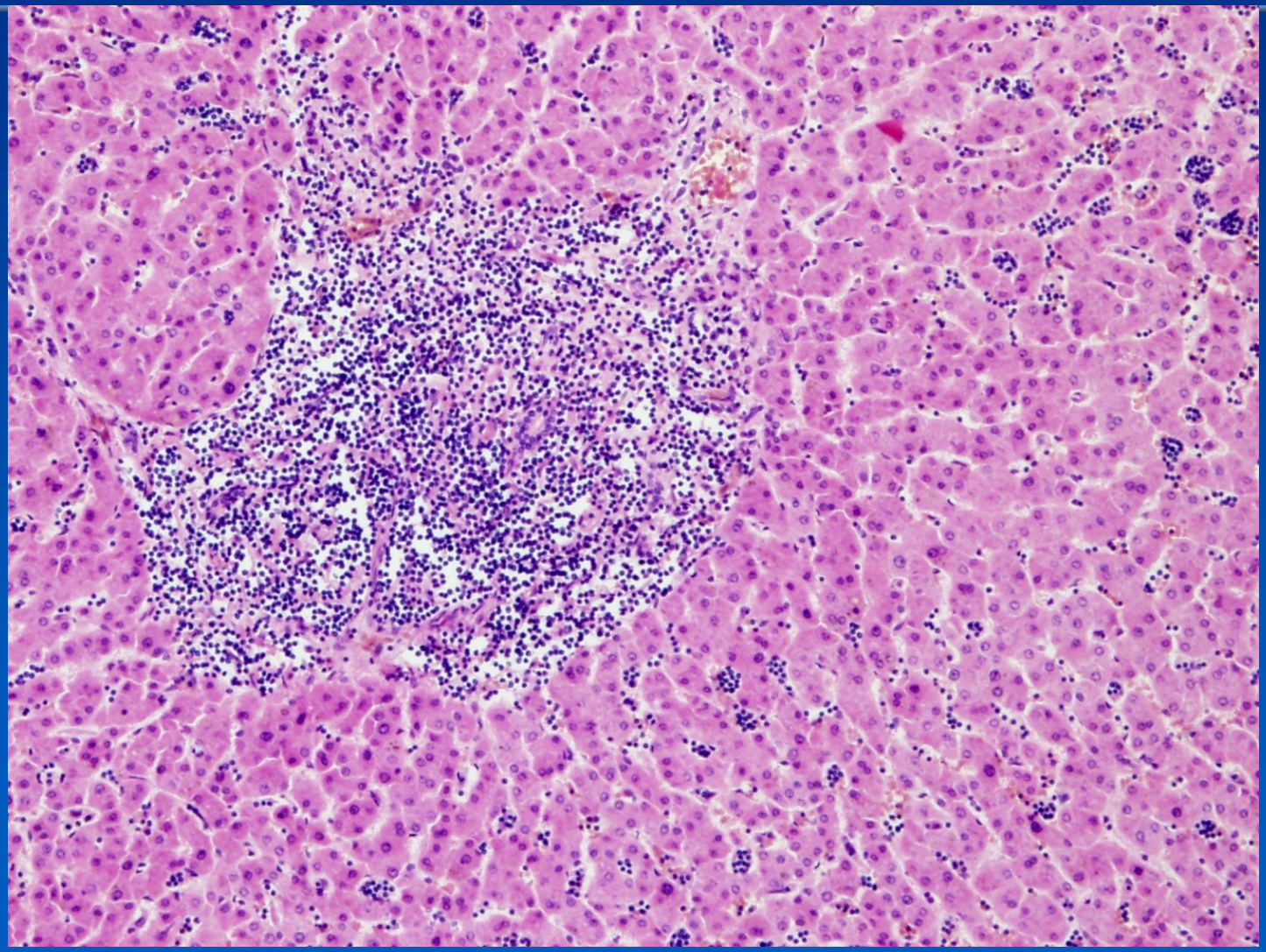
prolymfocyt



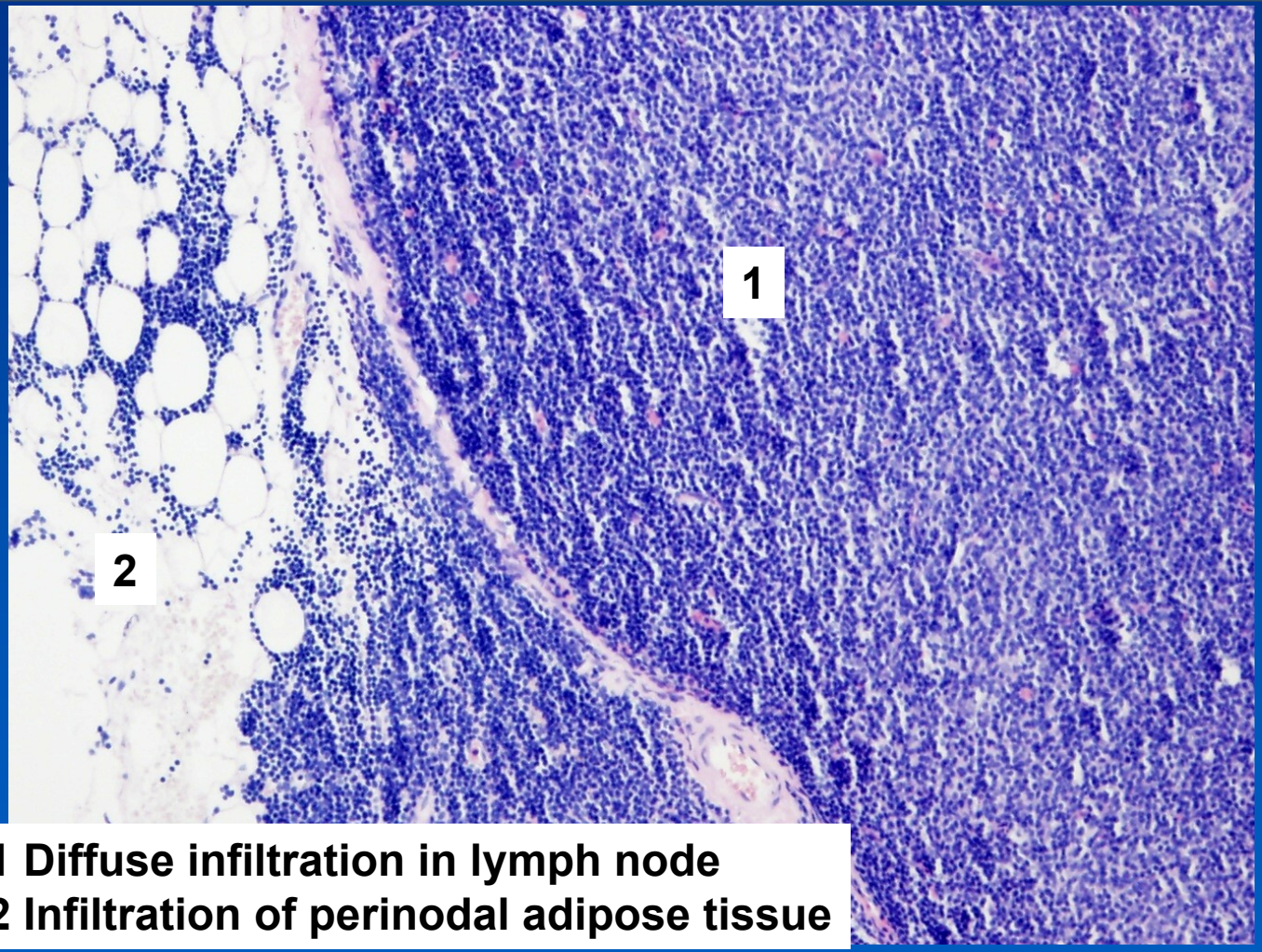
paraimunoblast

- Hematopoiesus
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

B-CLL/SLL: liver - portal infiltration

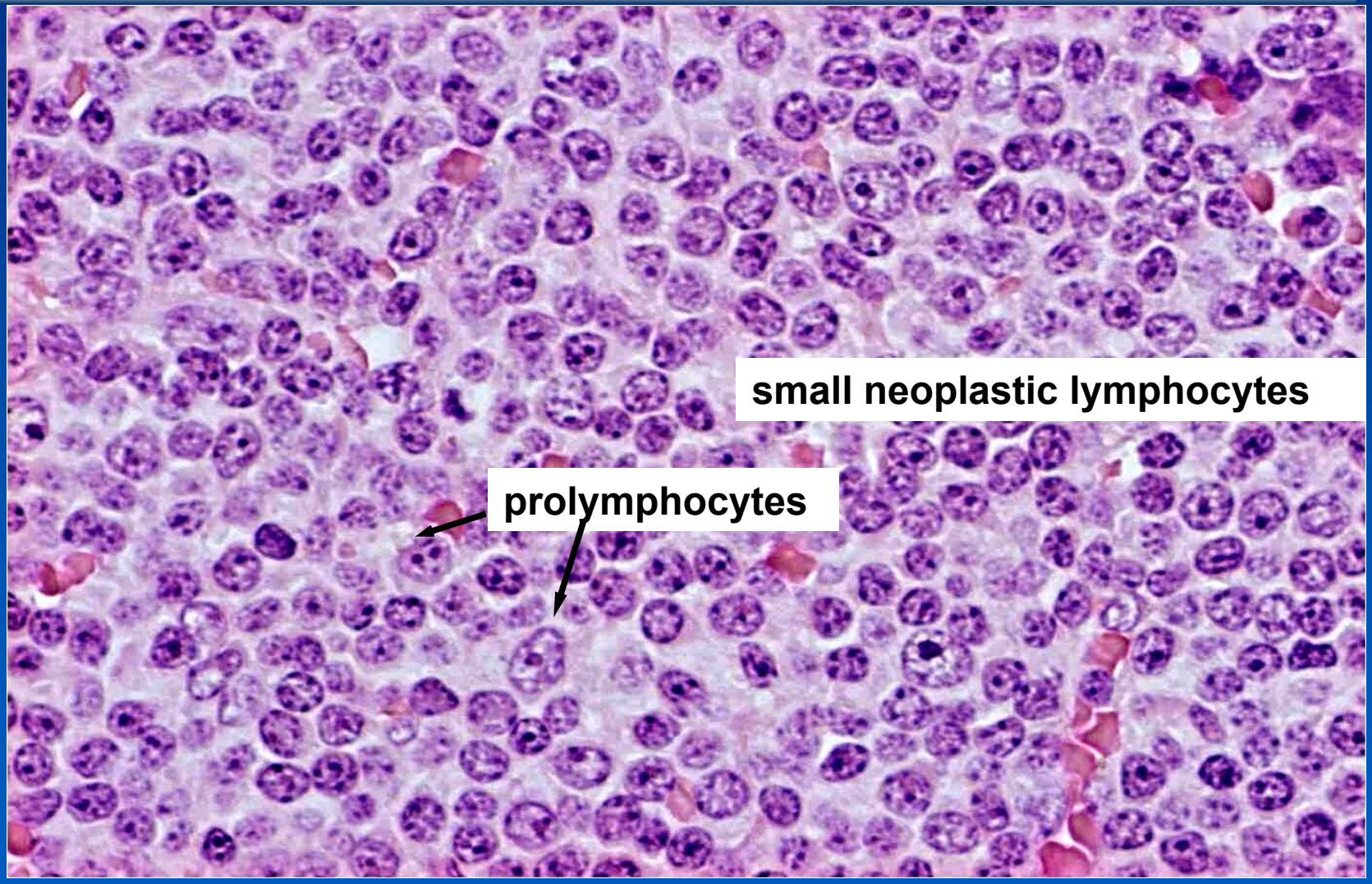


B-CLL/SLL: infiltration in lymph node

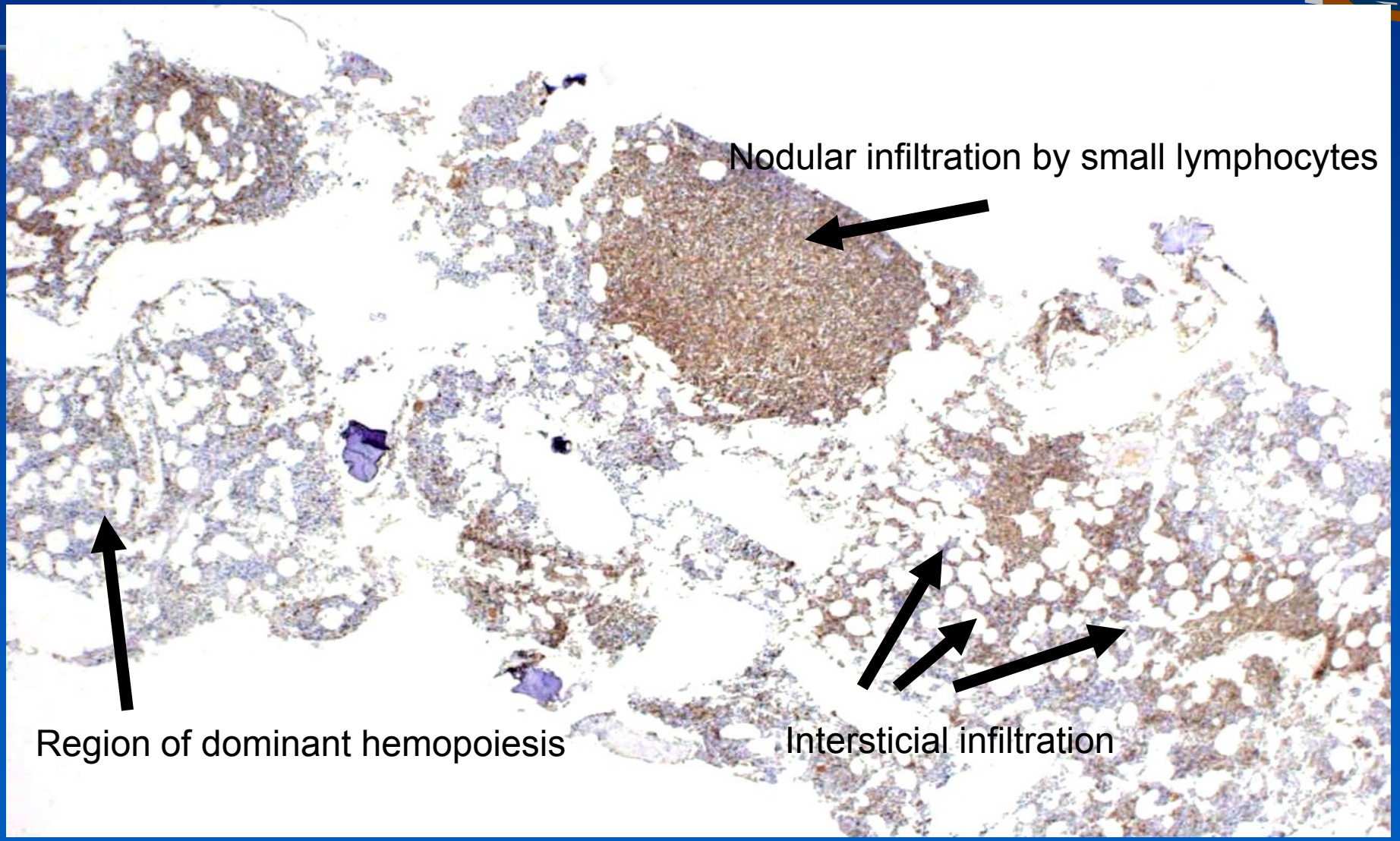


1 Diffuse infiltration in lymph node
2 Infiltration of perinodal adipose tissue

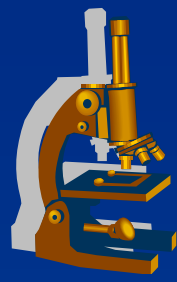
B-CLL/SLL: lymph node infiltration



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



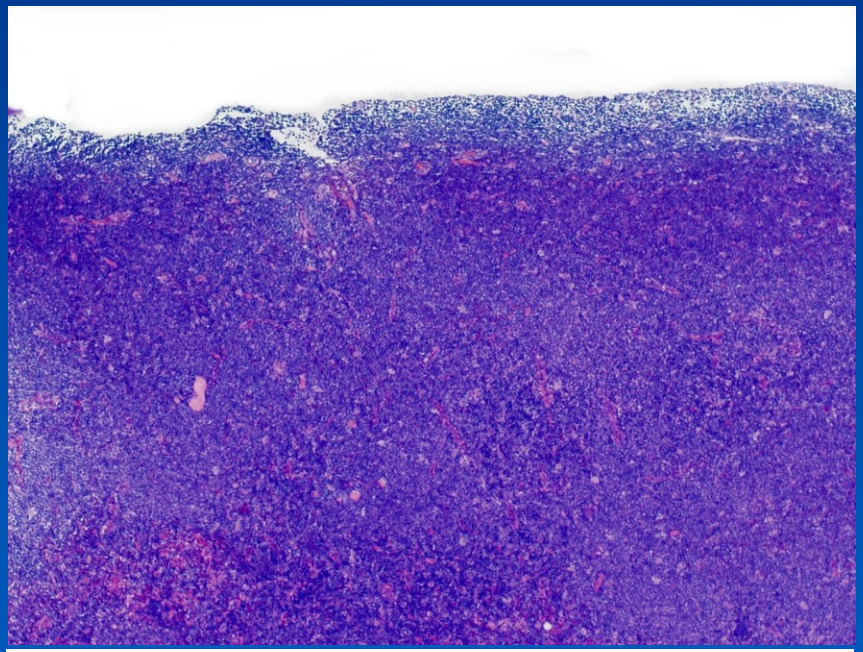
Mantle cell lymphoma



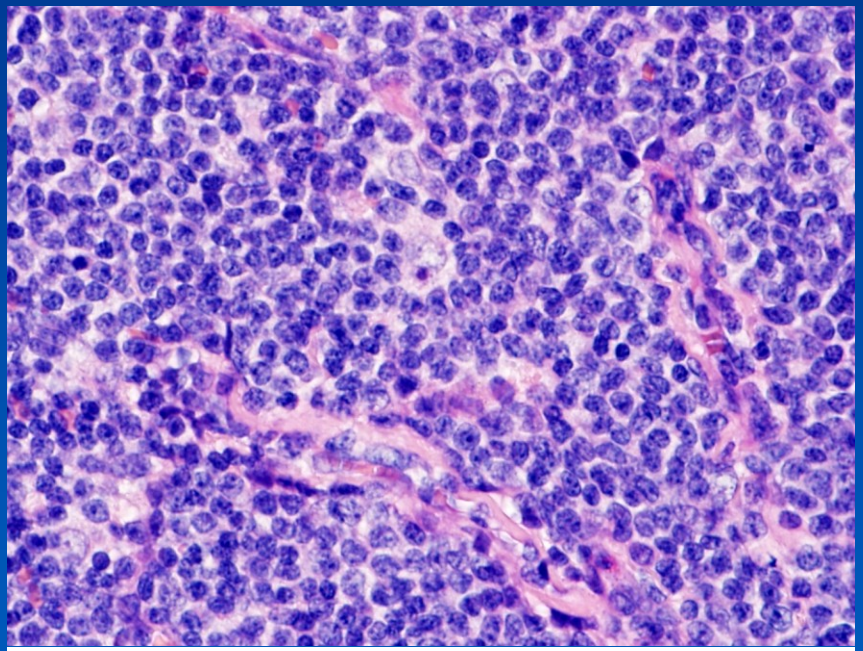
- **intermediate grade/aggressive** NHL, middle aged pacients/older adults
- progressive despite treatment
- in LN mantle type of growth
  - small cell lymphoma/small lymphocytic cells + epiteloid histiocytes + hyalinized vessels
- also BM, spleen, GIT… involved
- **t(11;14)**

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

MCL

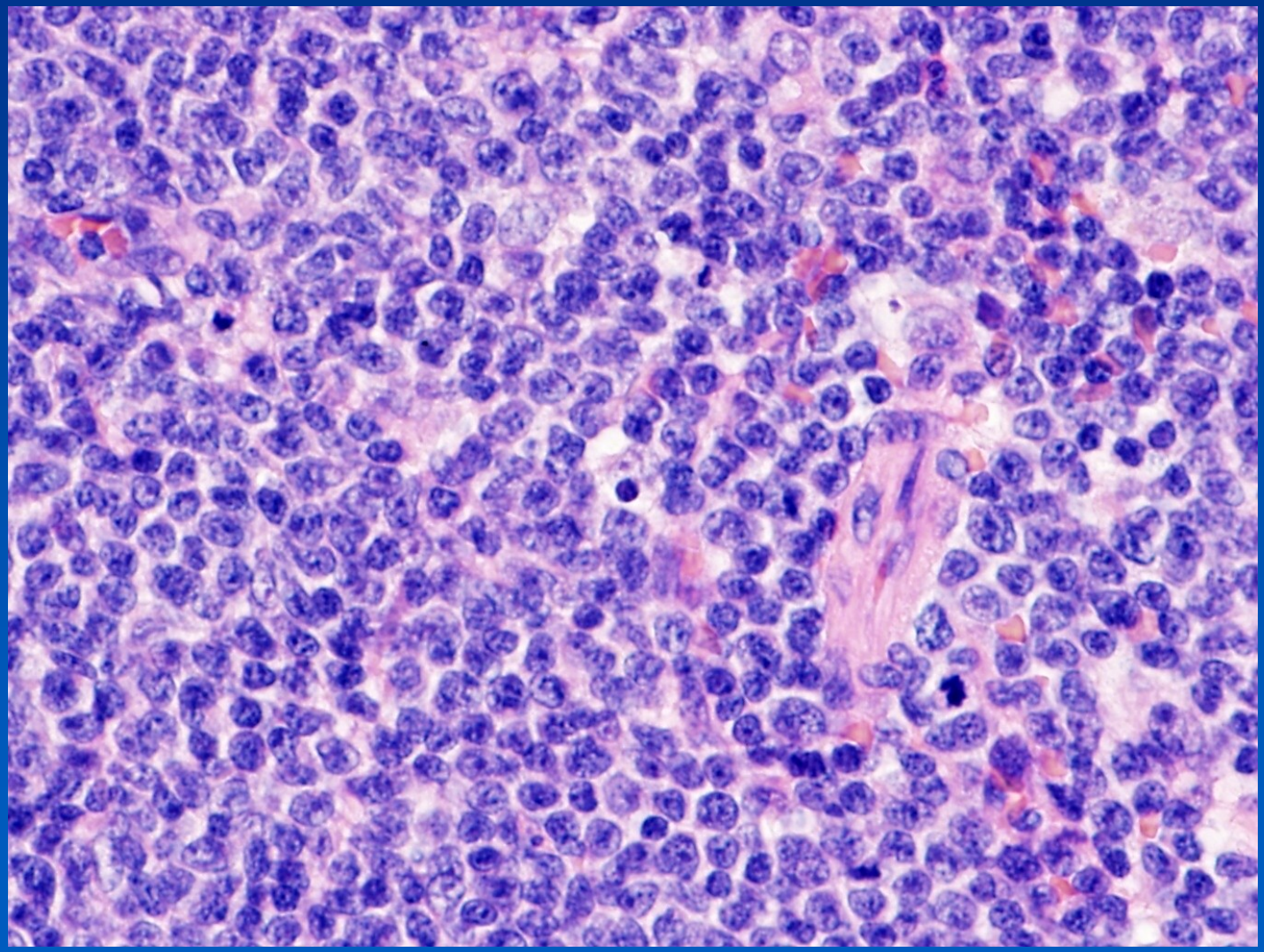


Structure of lymph node replaced by monomorphous lymphoid infiltration.

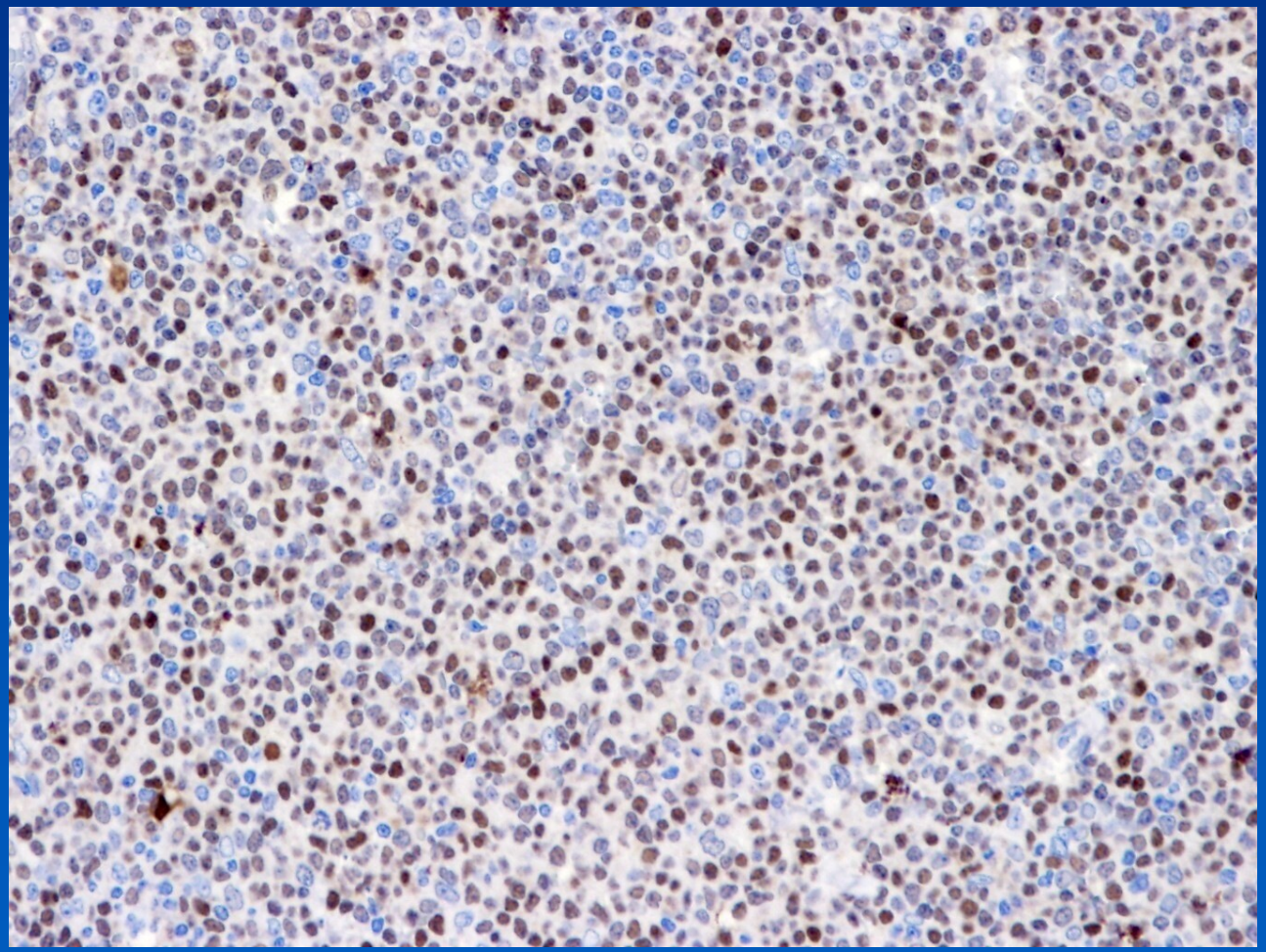


Neoplastic cells bigger than lymphocytes.
Hyalinized vessels.

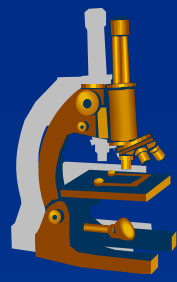
MCL



MCL – cyclinD1



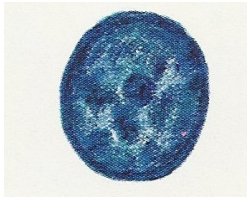
Follicular lymphoma



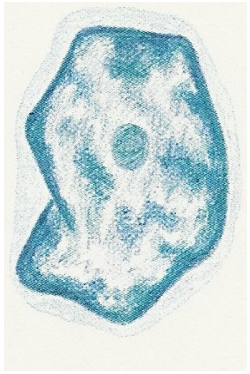
- app. **40 %** NHL, older adults
- slowly to moderately progressive (5-10 years)
- Transformation into high grade NHL (DLBCL)
- **generalized lymphadenopathy:**
  - ⇨ ***in LN nodular/(diffuse) growth***
    - Resemble normal follicular center B cell (centrocytes and centroblasts)
    - Neoplastic nodules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

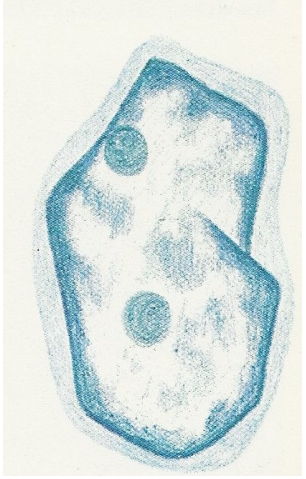
- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

Follicular lymphoma

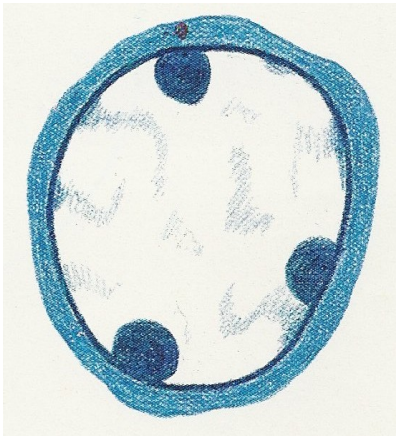


lymphocyte





centrocyte



centroblast

Follicular lymphoma

CENTROCYTE

- **Small cell with cleaved nuclear outlines**

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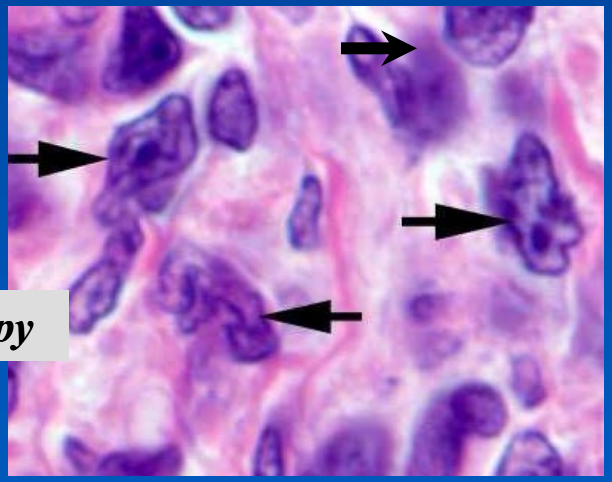
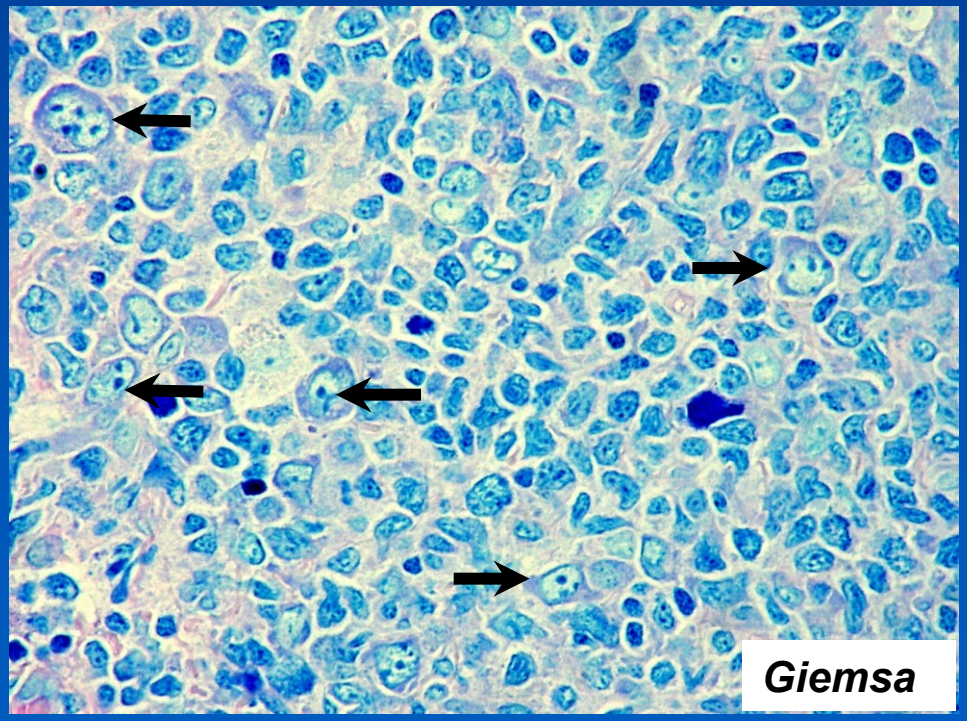


- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

Follicular lymphoma

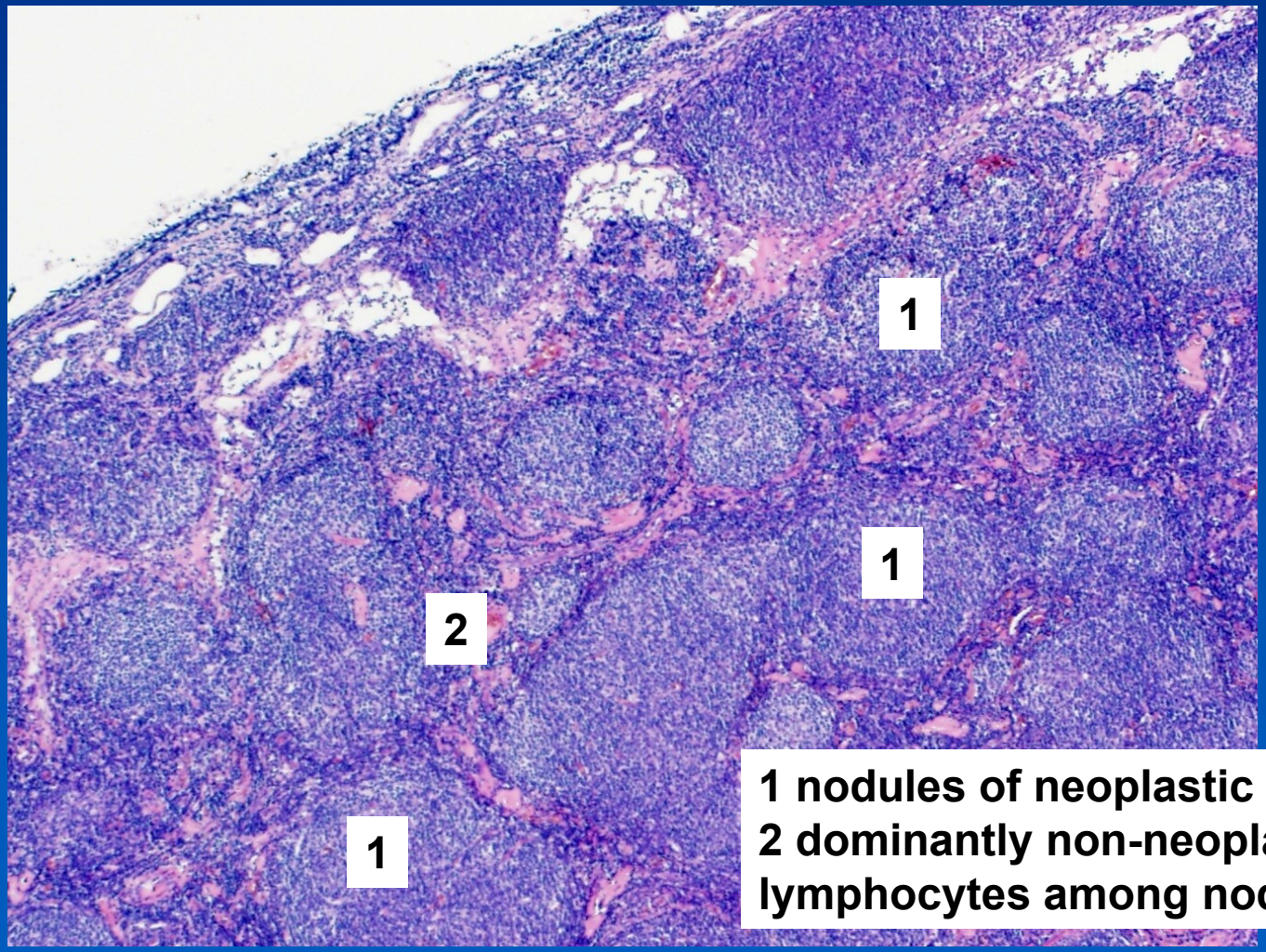
CENTROBLAST

- **Larger cell with nucleoli at nuclear membrane**



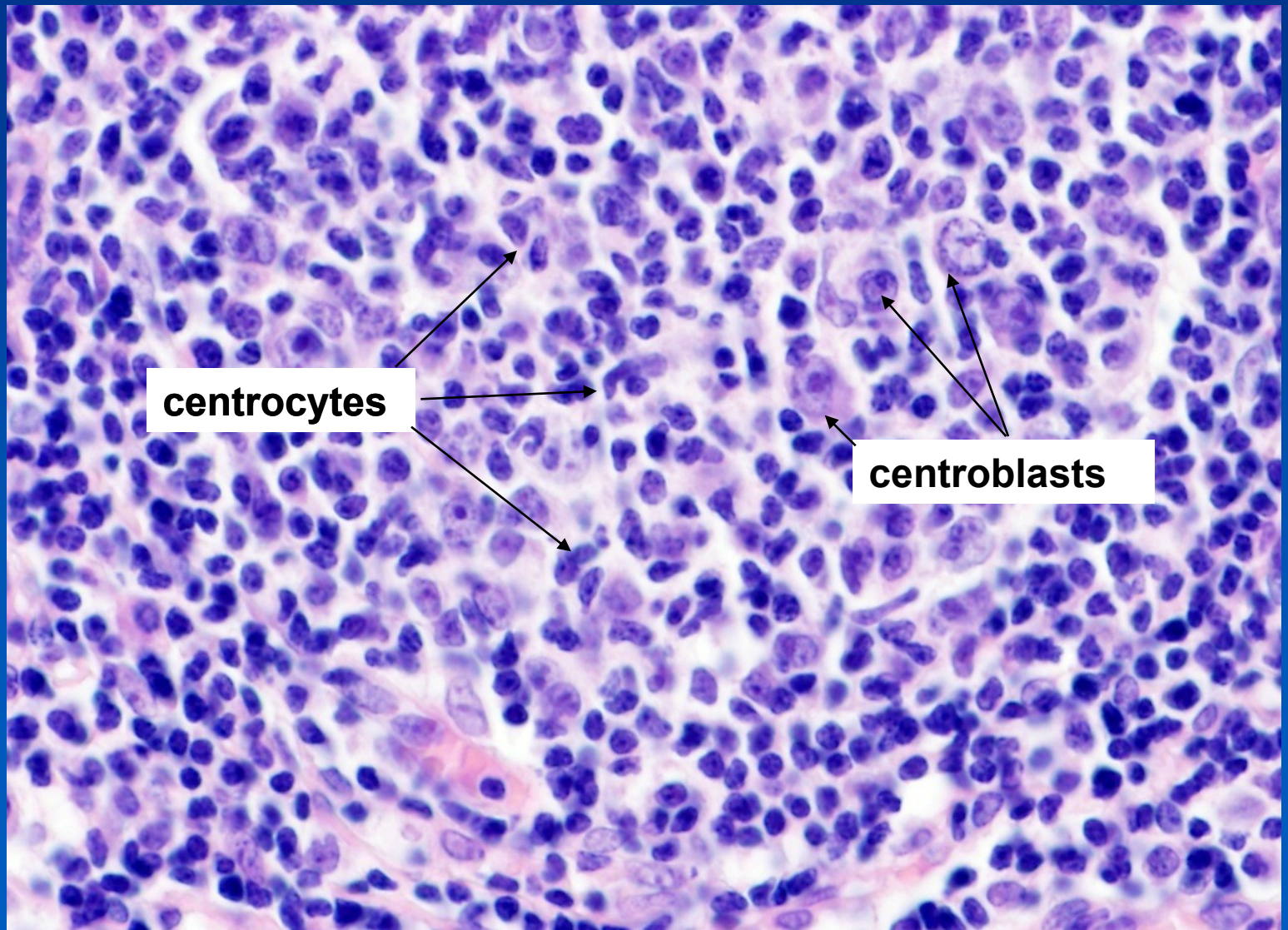
- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

Follicular lymphoma

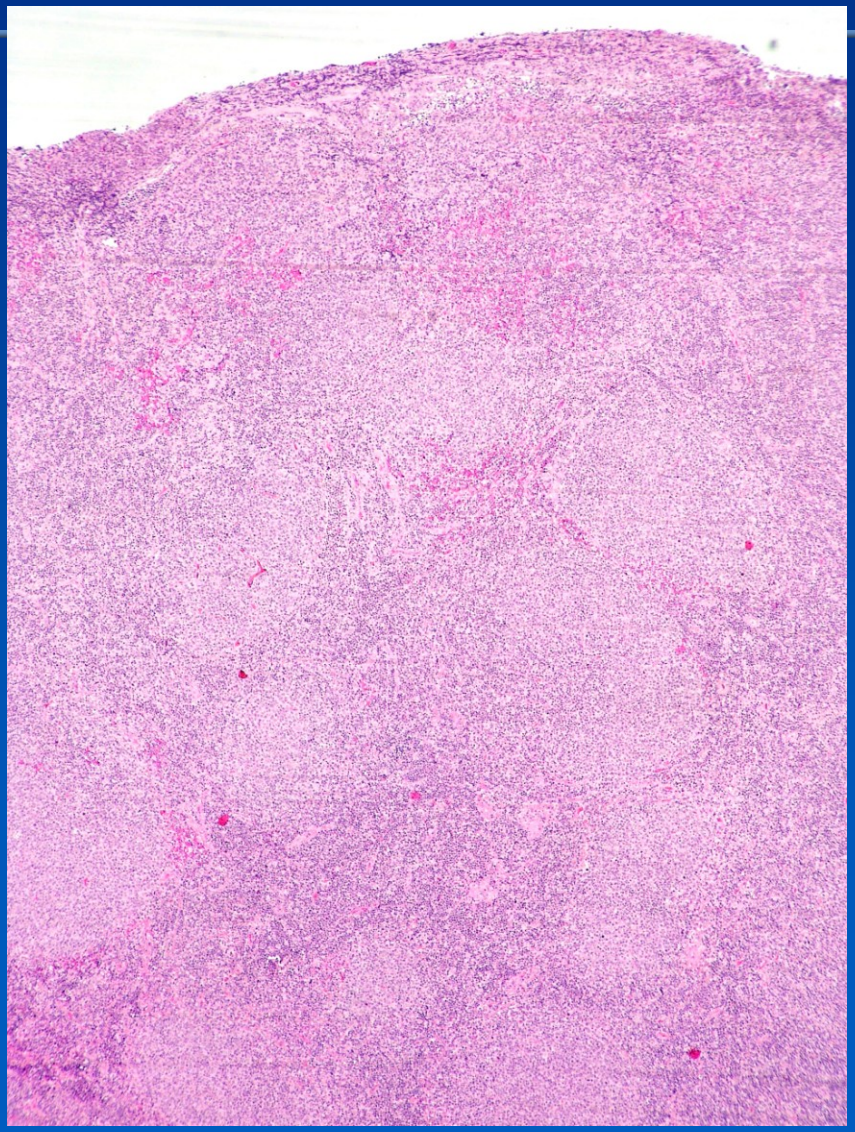


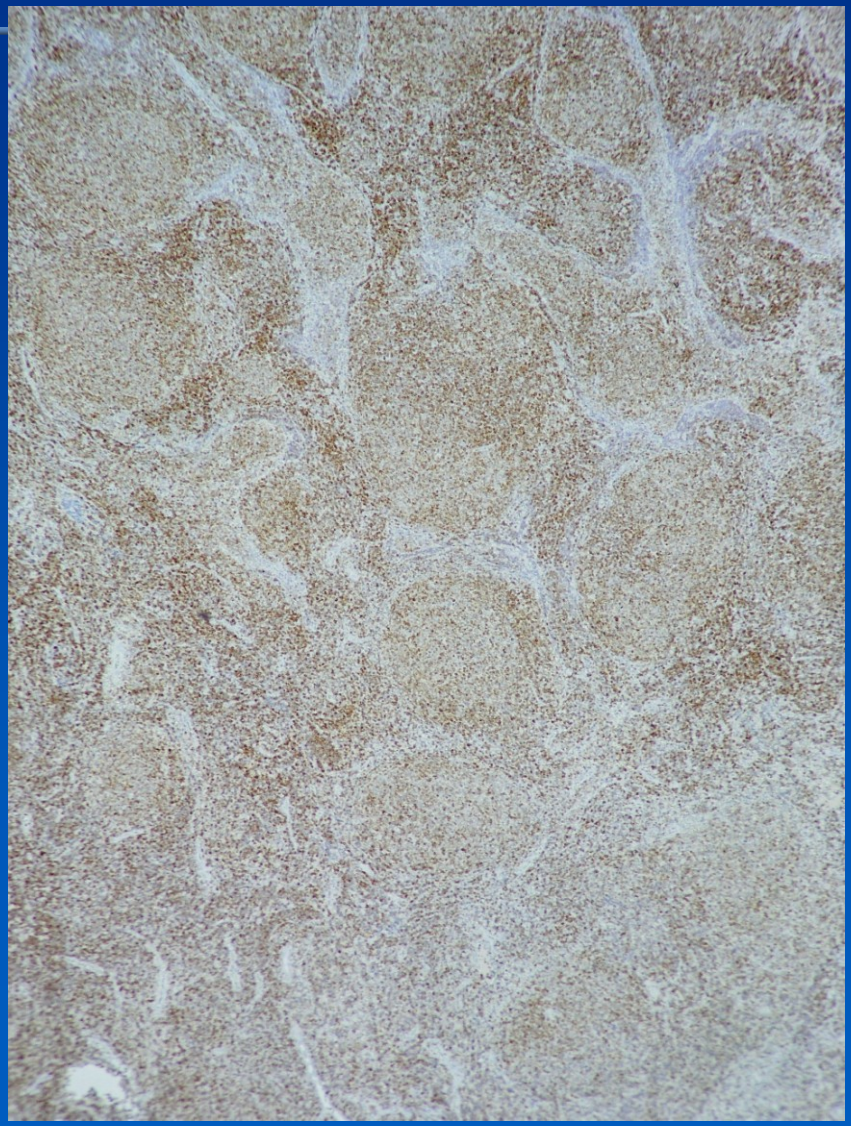
1 nodules of neoplastic cells
2 dominantly non-neoplastic lymphocytes among nodules

Follicular lymphoma



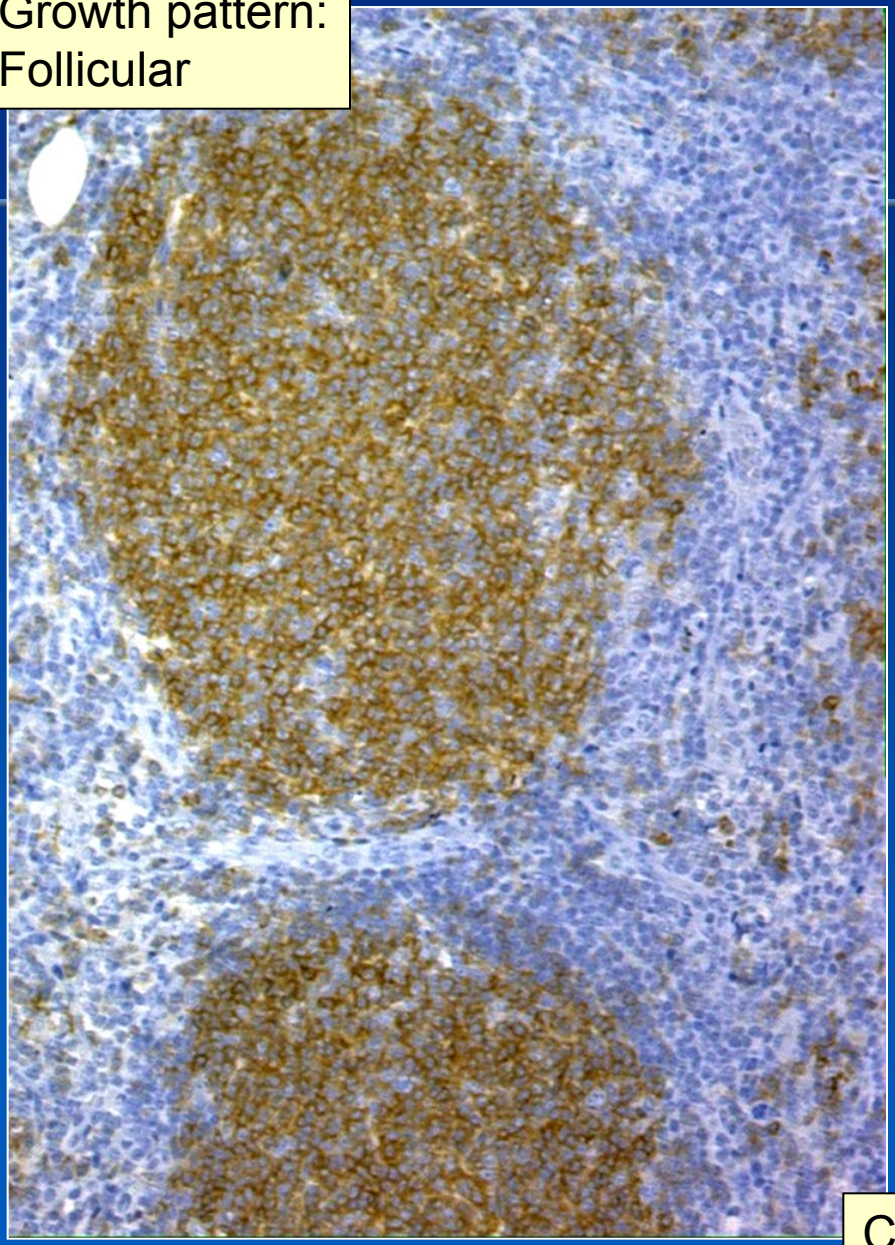
Follicular lymphoma, Bcl-2

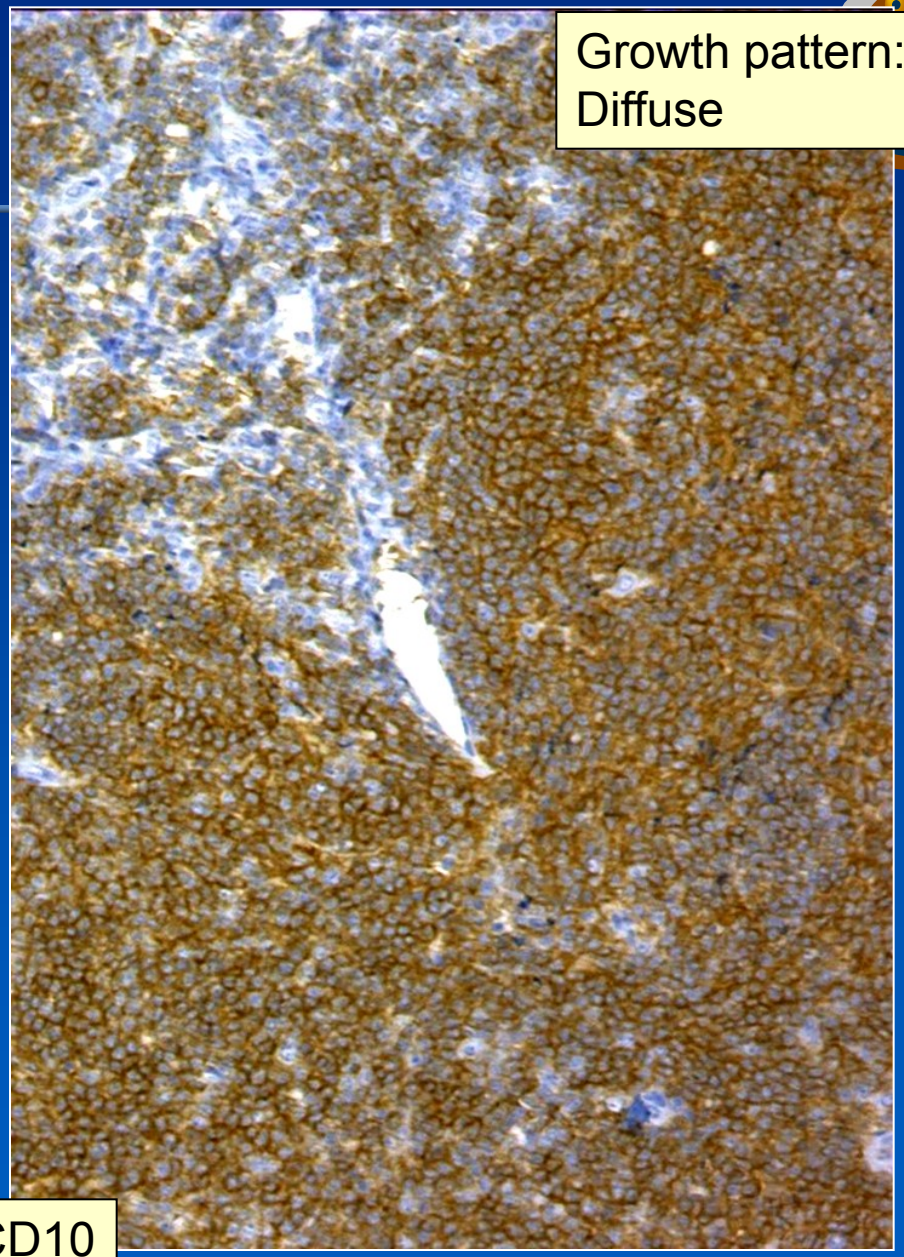




FOLLICULAR LYMPHOMA

Growth pattern:
Follicular

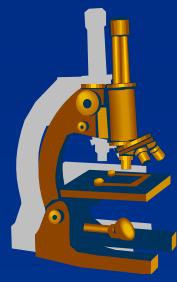




Growth pattern:
Diffuse

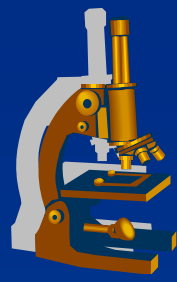
CD10

Marginal zone lymphomas



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

Extranodal marginal zone lymphoma (MALT lymphoma)

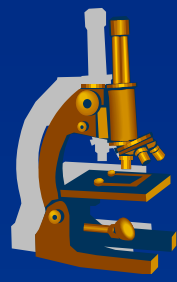


- **derived from MALT, BALT**
- **chronic stimulation of immune system**
  - e.g.: chronic gastritis assoc. with Helicobacter pylori (HP) infection

- 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
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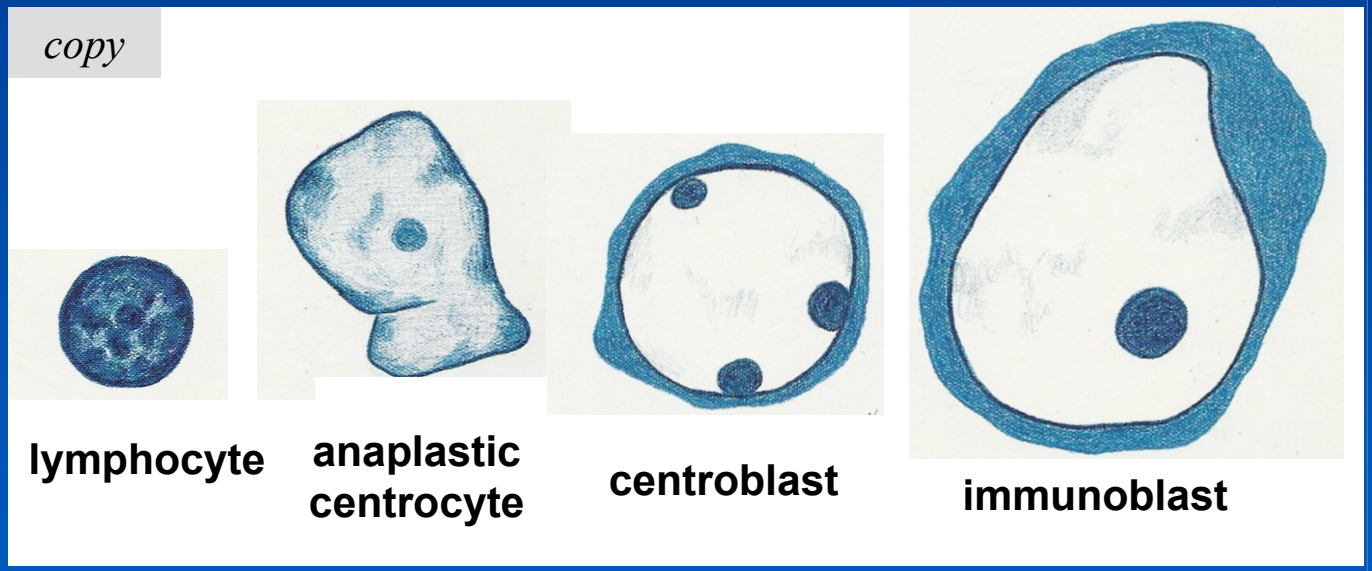
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

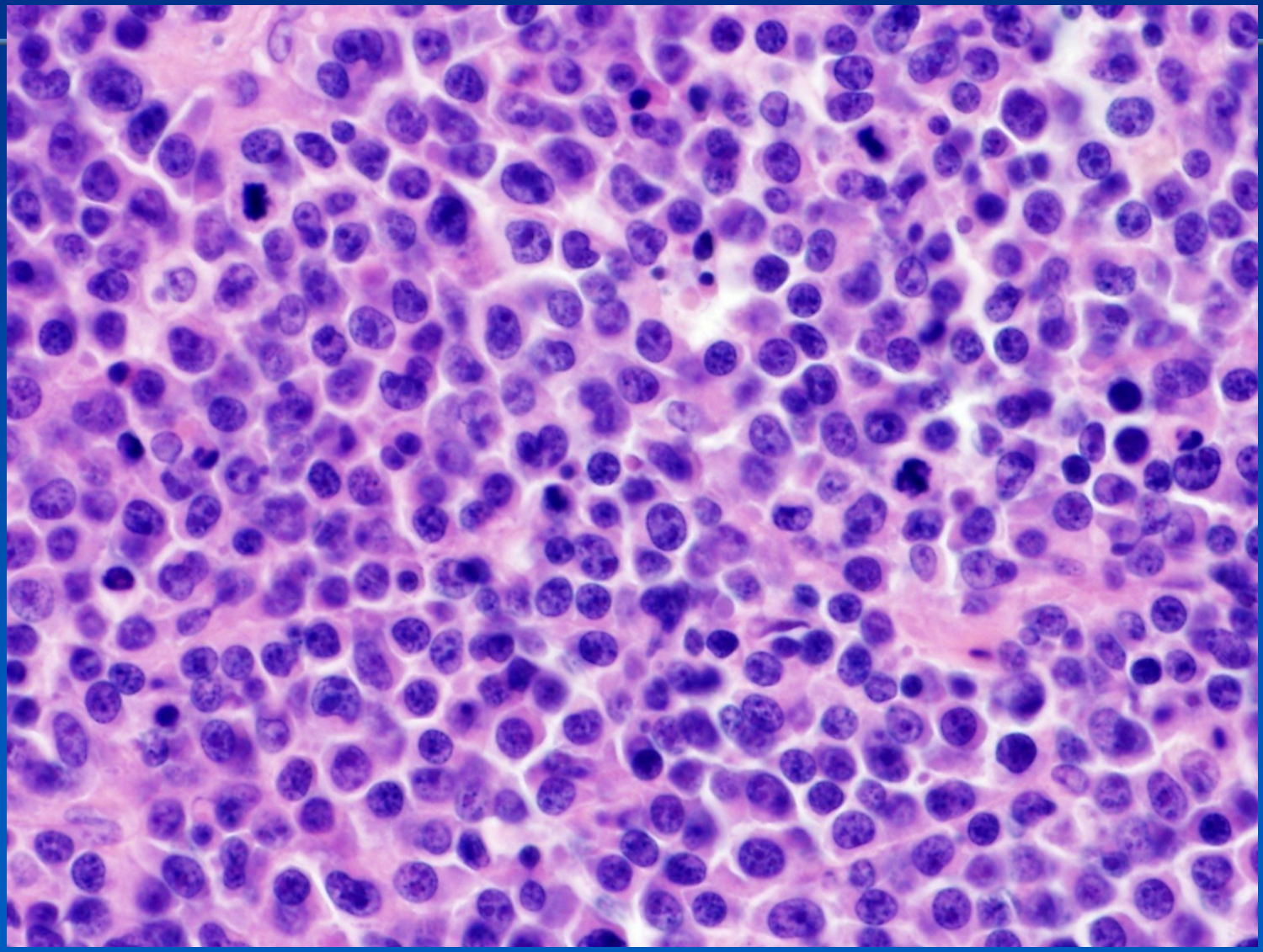
Diffuse large B-cell lymphoma (DLBCL)

neoplastic immunoblasts and centroblasts



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

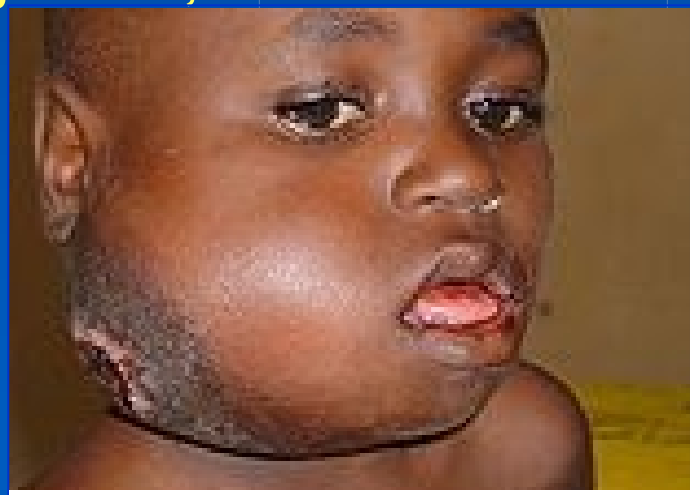
DLBCL - nodal - detail



Burkitt lymphoma

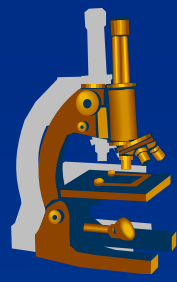
- **extremely highly aggressive NHL**
- **variants:**
  - **endemic (in Africa – children, assoc. with EBV)**
  - **sporadic (in other areas, including Europe, USA,..)**
  - **Assoc. with immunodeficiency**
- **t(8;14) → fusion c-myc/IgH → → → dysregulation, overexpression of c-myc → → → → brisk proliferation**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

- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***



Copy according to Blyth M., 2002

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

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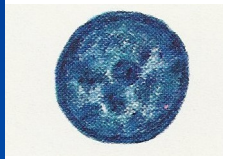
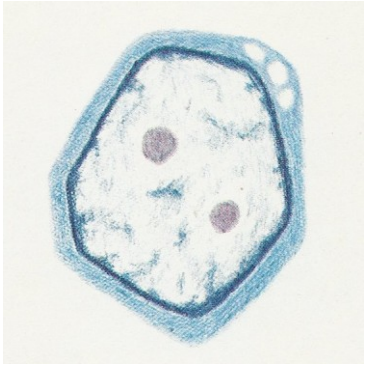
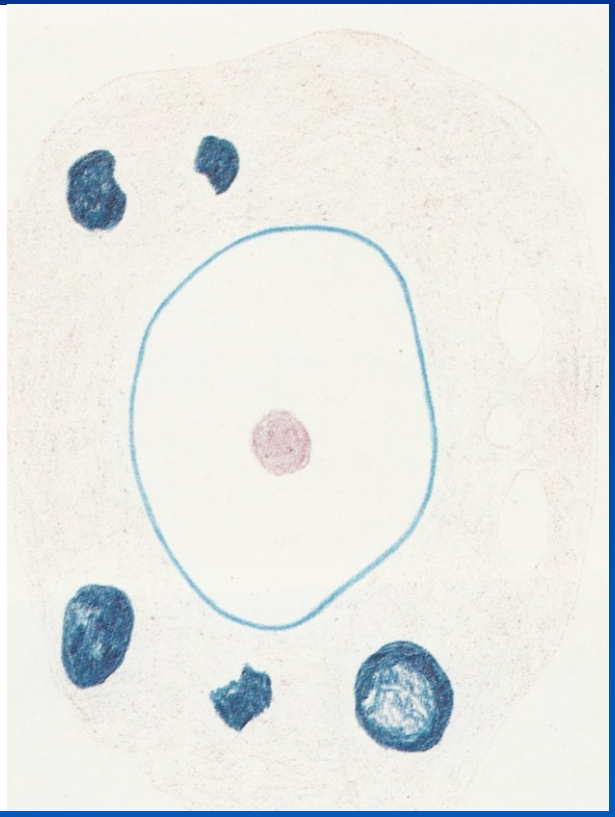


lymphocyte

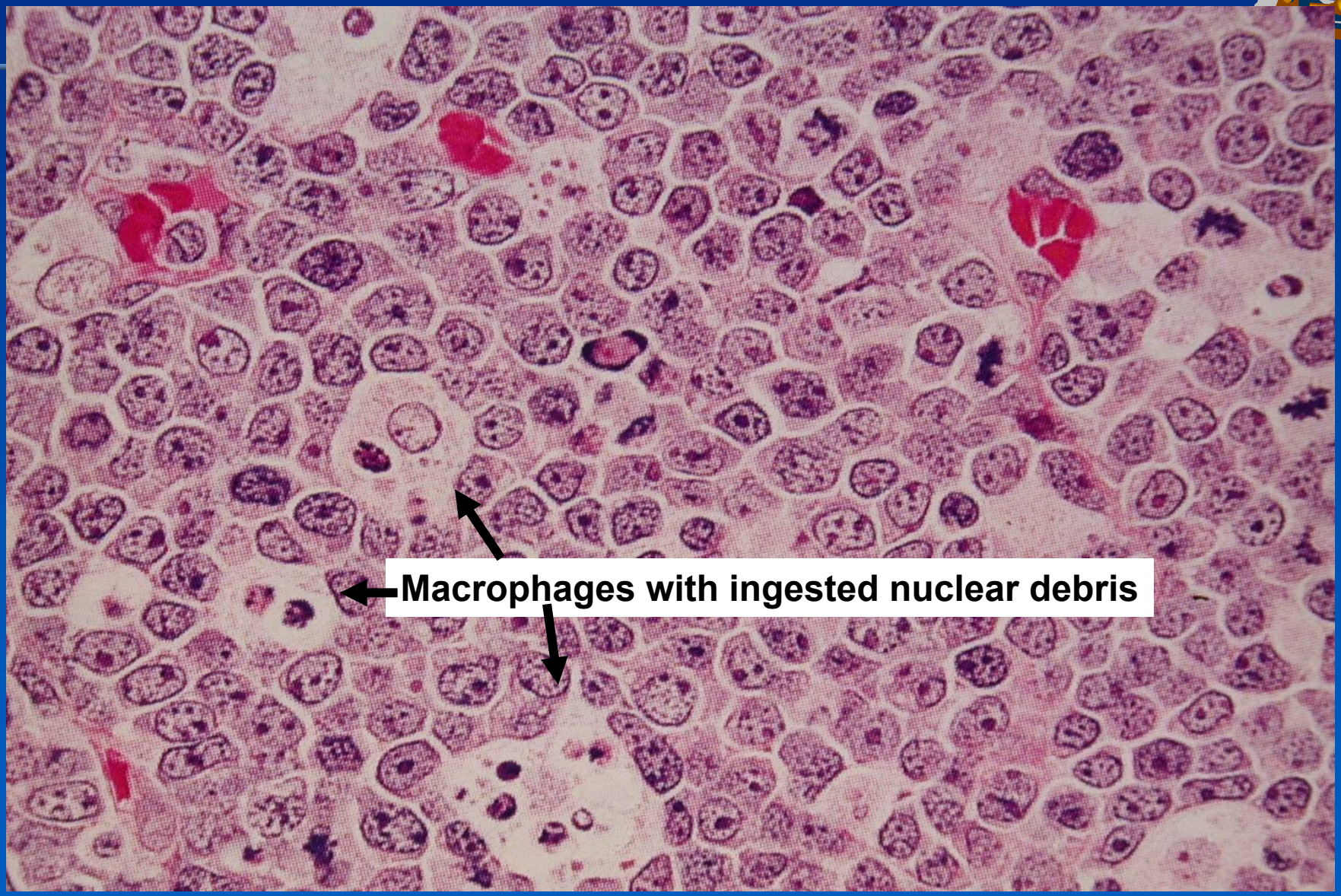


lymphoblast

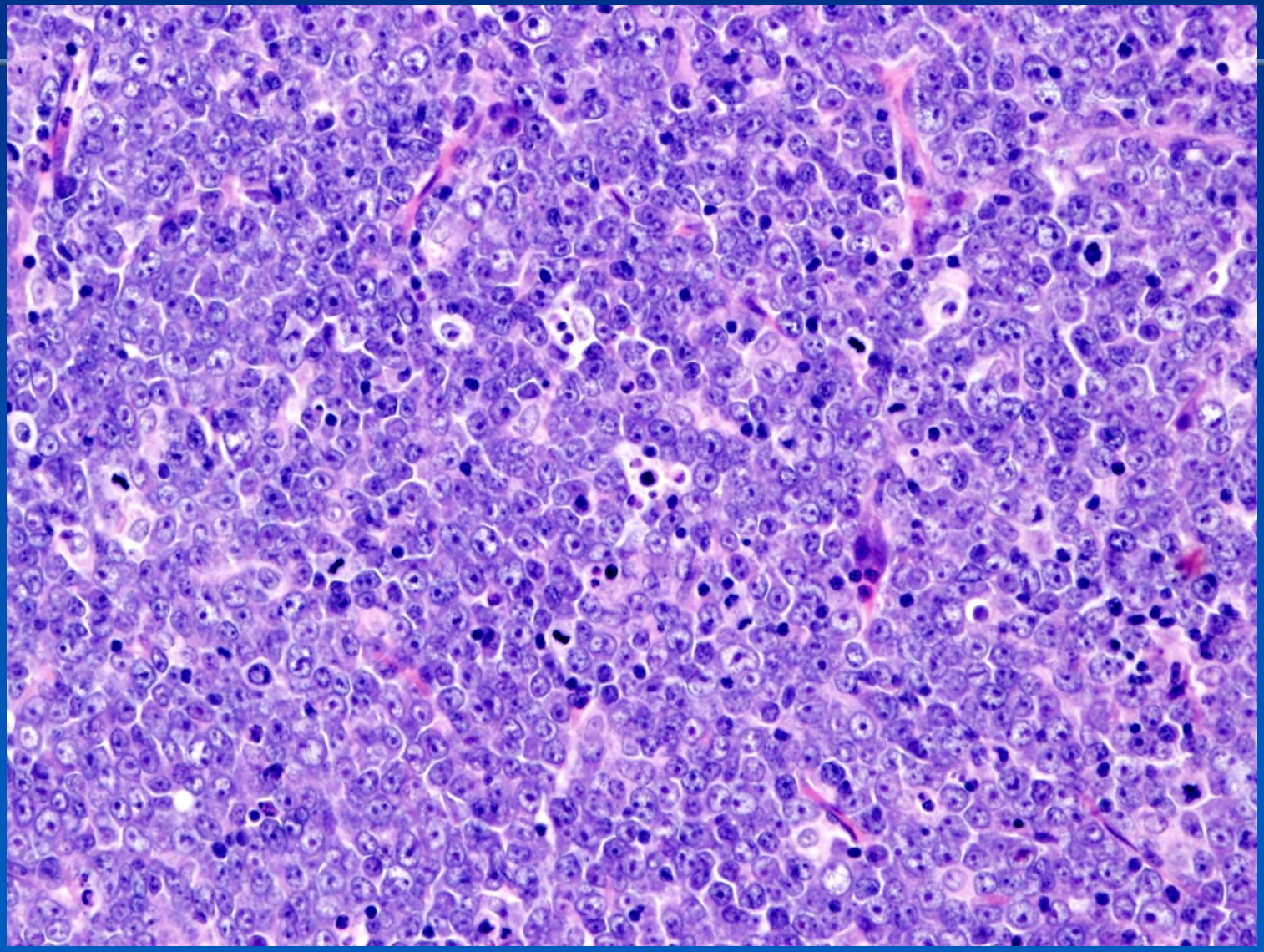


macrophage
(starry sky cell)

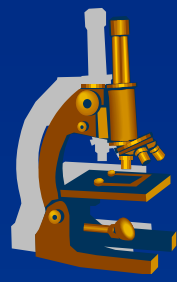
Burkitt lymphoma



Burkitt lymphoma



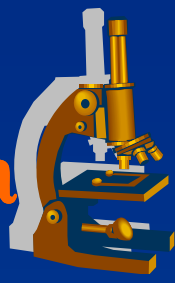
Plasma cell dyskrasias



- **multiple myeloma**
- **localizes plasmacytoma** (=solitary myeloma)
- heavy chain disease
- primary amyloidosis
- monoclonal gammapathy 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

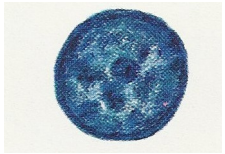
- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

Multiple myeloma, plasmacytoma

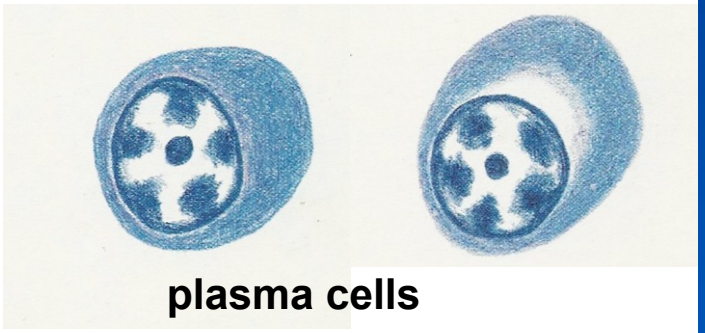
Micro:

- **plasma cells with variable differentiation**
- **low mitotic acitivity**

copy



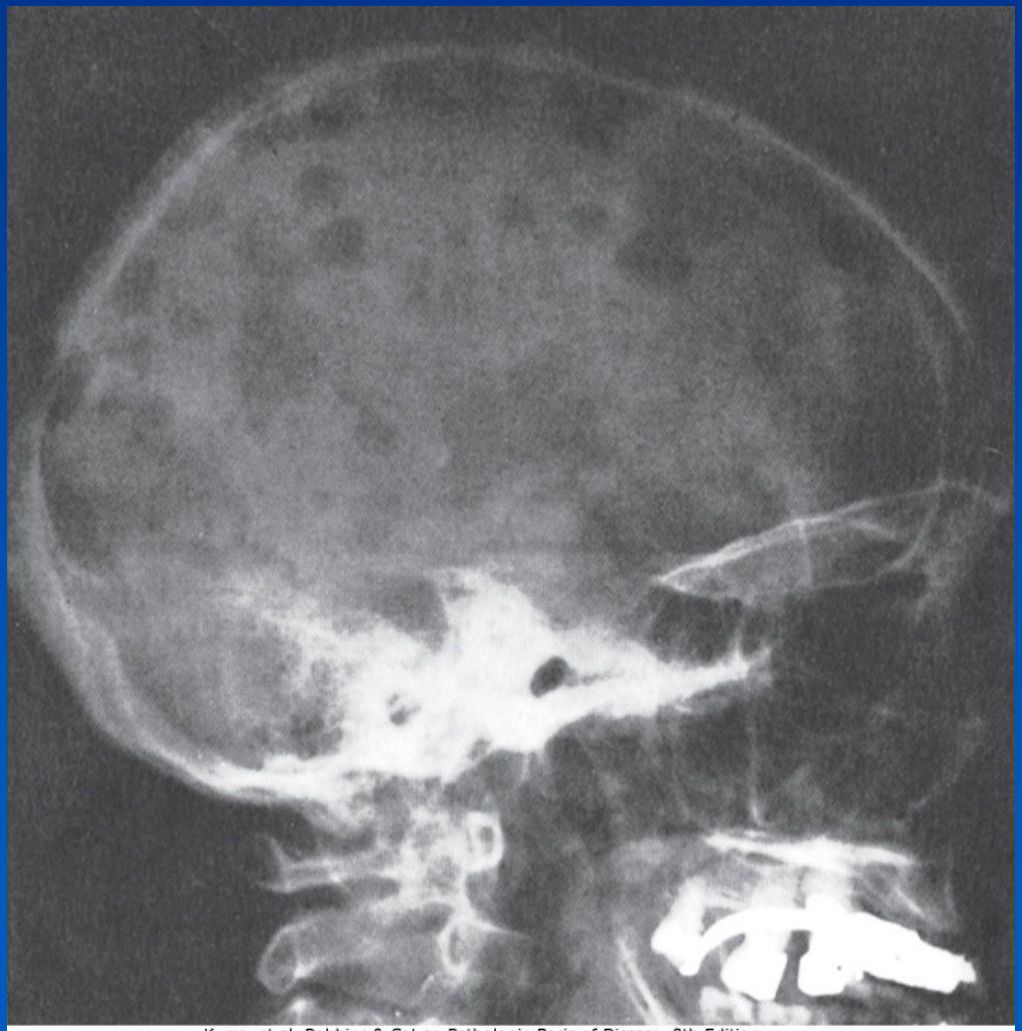
lymphocyte



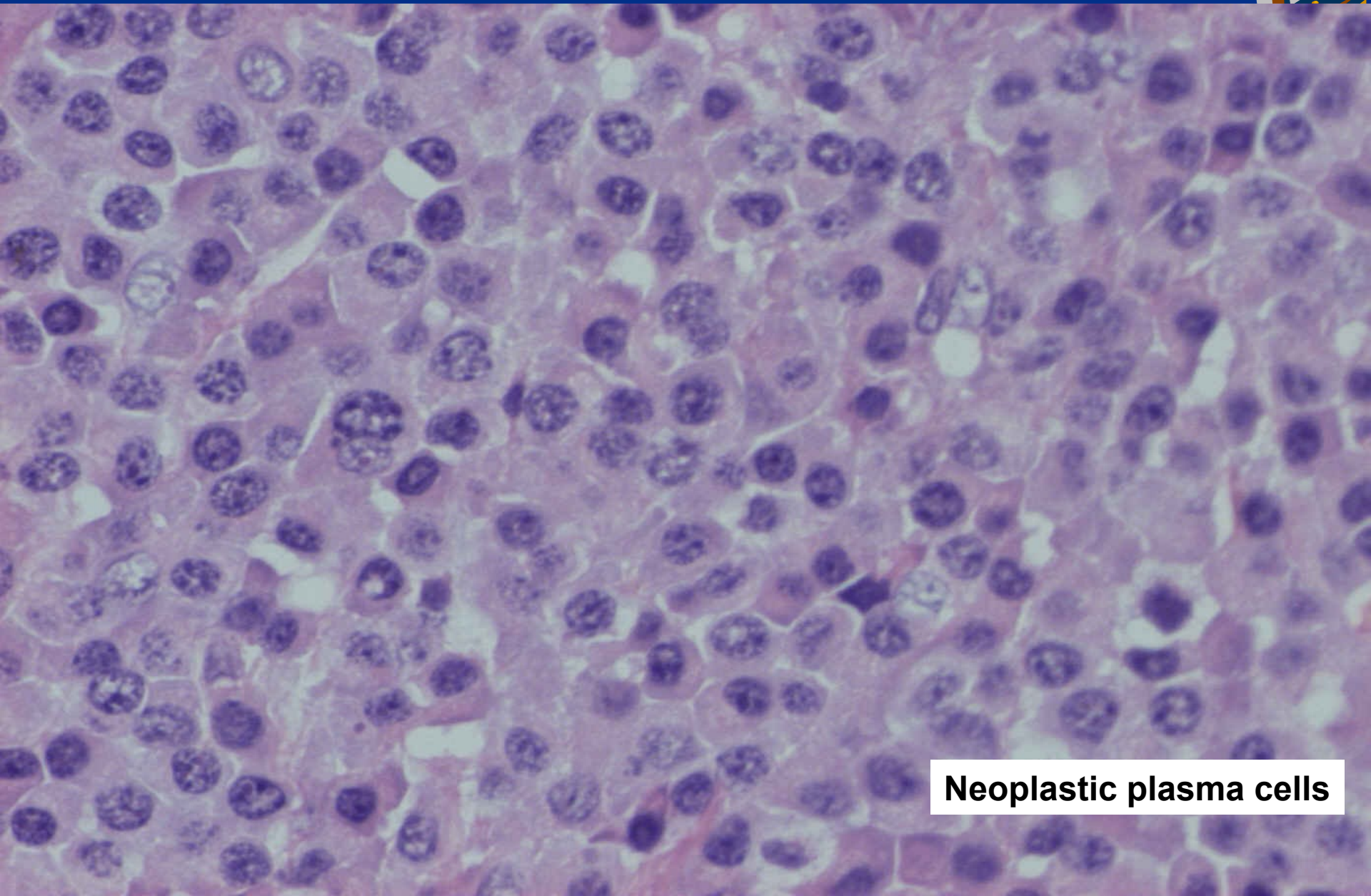
plasma cells

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

Multiple myeloma

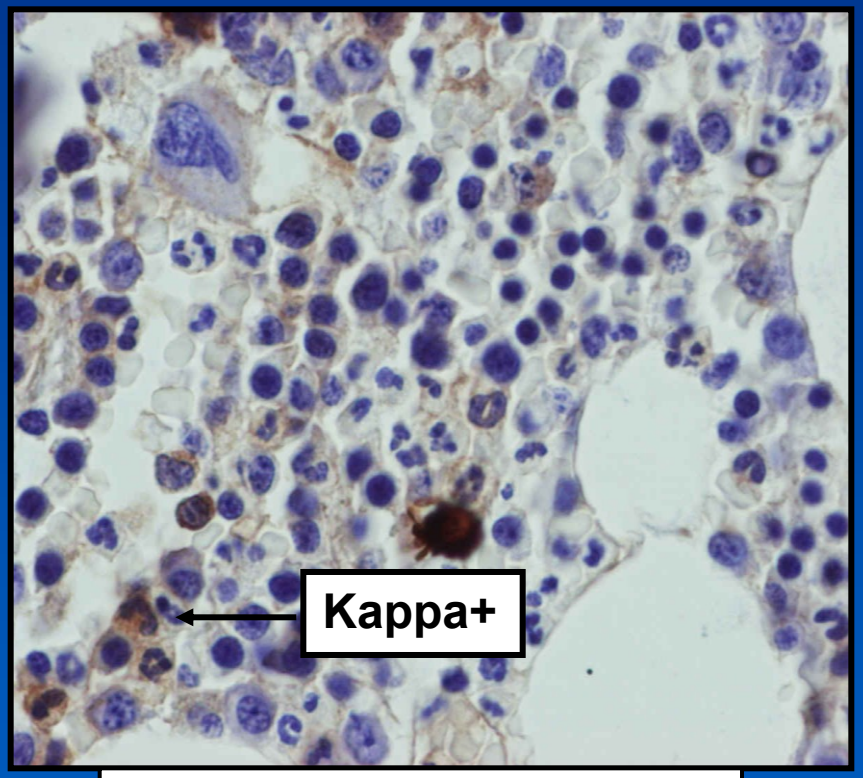


Multiple myeloma – osteolytic lesion

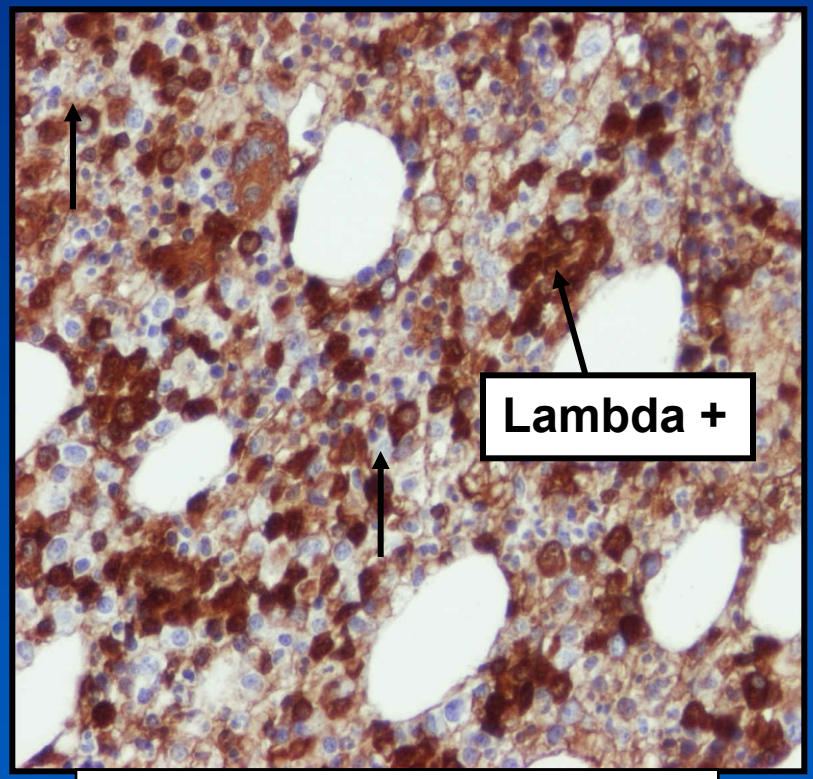


Myeloma:

– IHC proof of monoclonality of neoplastic plasma cells



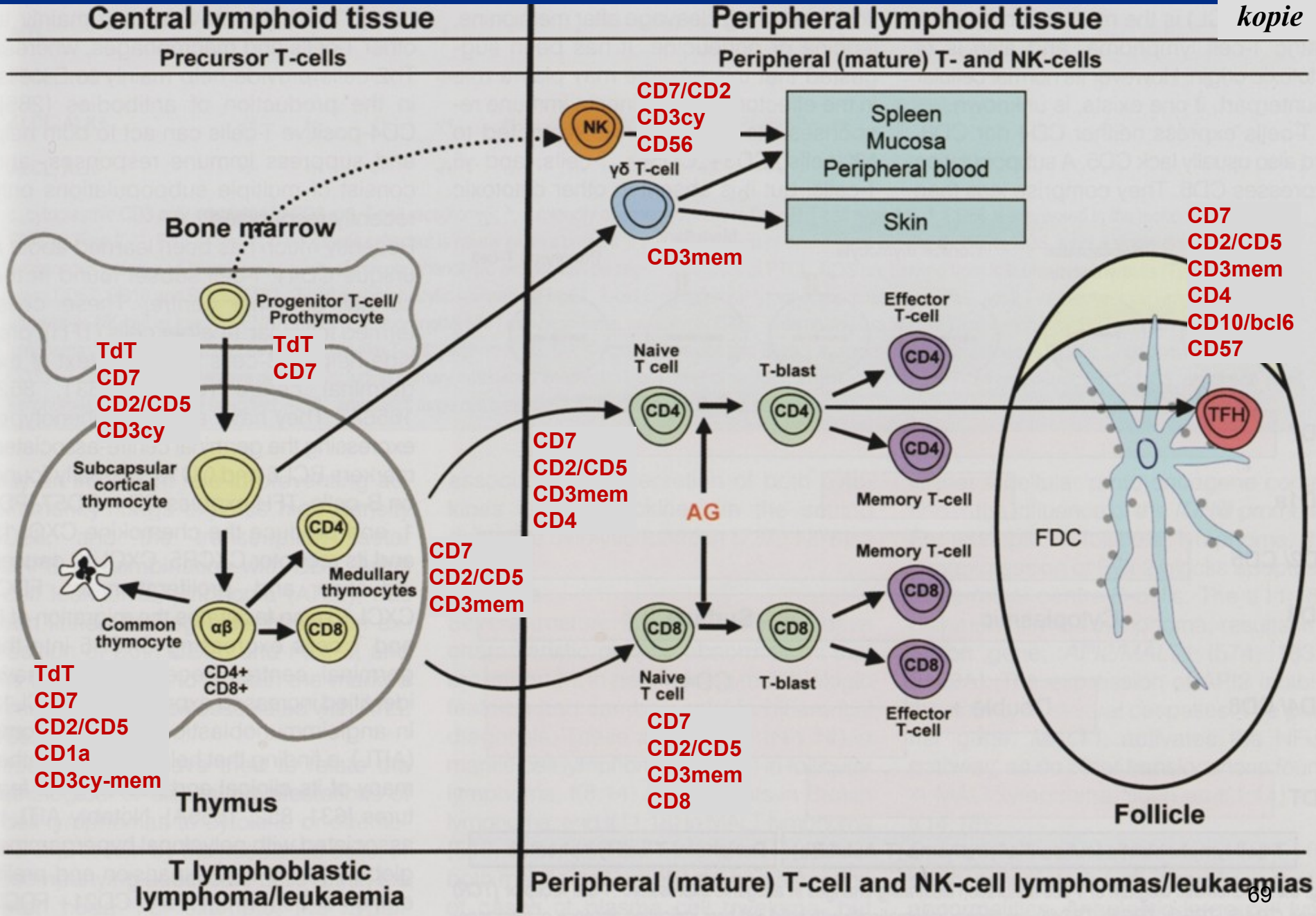
Kappa light chains Ig



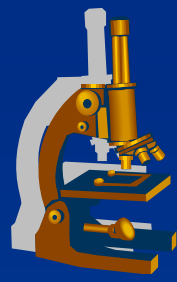
Lambda light chains Ig

T LYMPHOID NEOPLASMS – CELLS OF ORIGIN

kopie



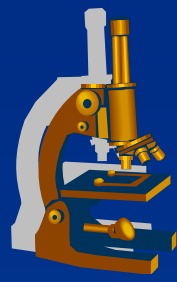
T-cell lymphomas
(selected entities)



- **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)

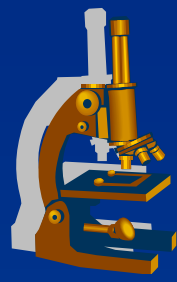
- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - ⇨ ***NHL***
  - ⇨ ***HL***
- Reactive lymphadenopathy

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 **<u>young adults</u>**
- **th.:**
  - *RT, CHT → excellent prognosis,* ***but risk of secondary malignancies (MDS, AML, lung ca)***

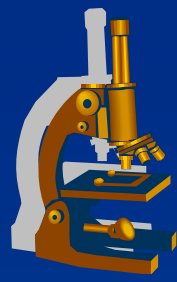
Hematopoiesis

Myeloid neoplasms

Lymphoid neoplasms
NHL
HL

Reactive lymphadenopathy

Hodgkin lymphoma - classification



1. Classical HL

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

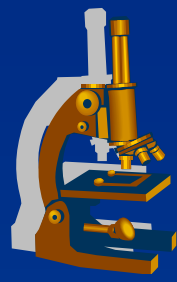
- **Nodular sclerosis** (**lacunar cc**., assoc. **EBV**)
- **Lymphocyte-rich**
- **Mixed cellularity**
- **Lymphocyte depletion**

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

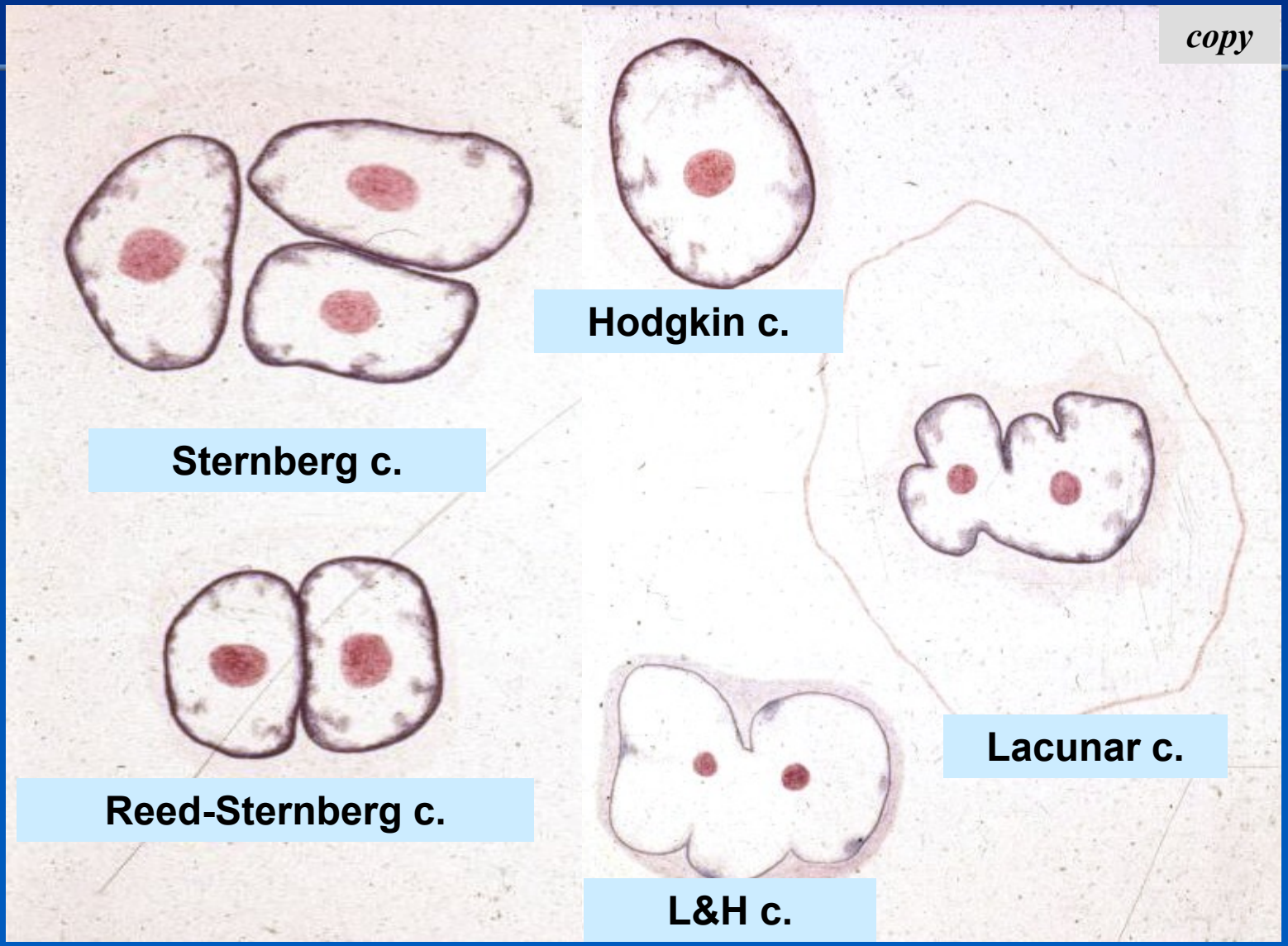
Reed-Sternberg cells + variants

Chemokines / cytokines production

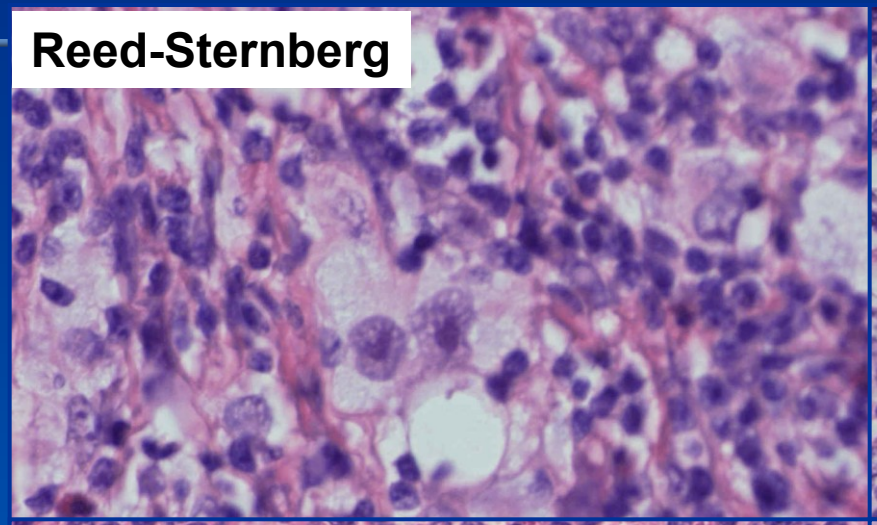
→ chemotaxis of lymphocytes, macrophages, granulocytes incl. eosinophils = reactive non-neoplastic background

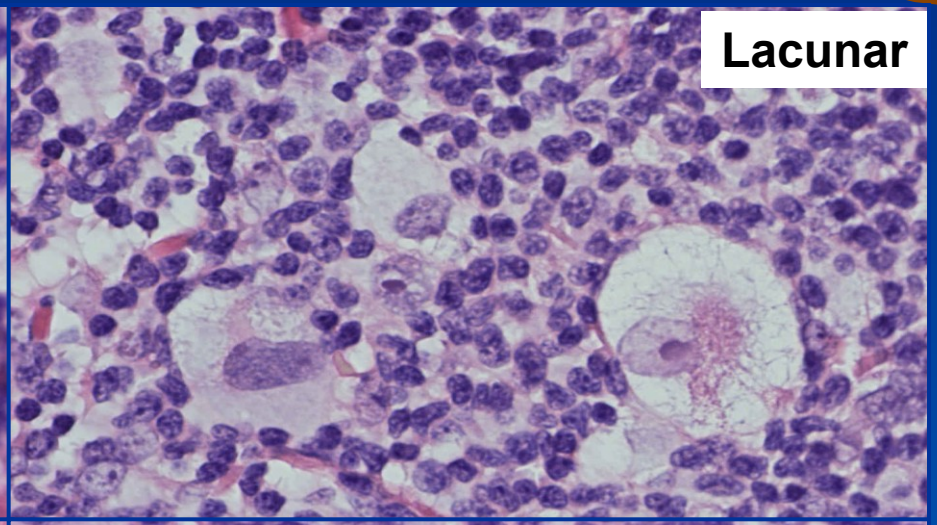
- Hematopoiesis
- Myeloid neoplasms
- **Lymphoid neoplasms**
  - *NHL*
  - ⇨ *HL*
- Reactive lymphadenopathy

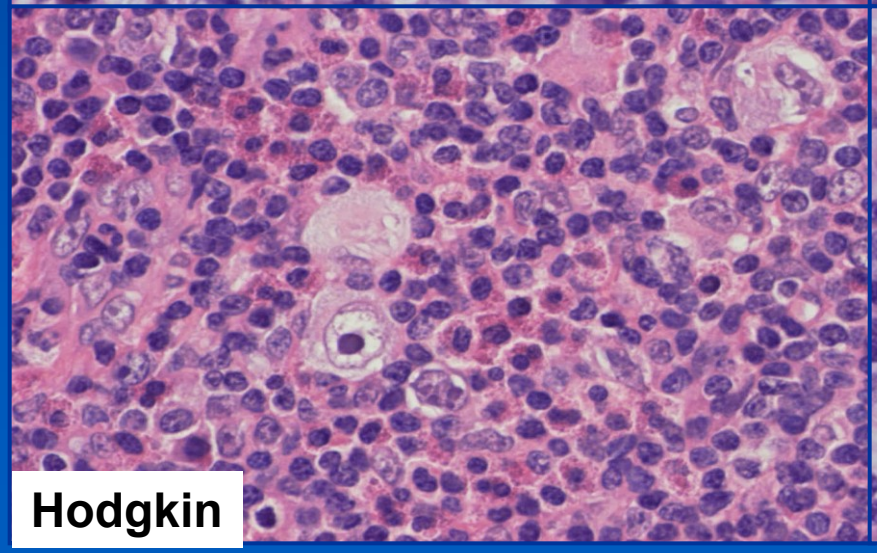
Diagnostic cells of HL

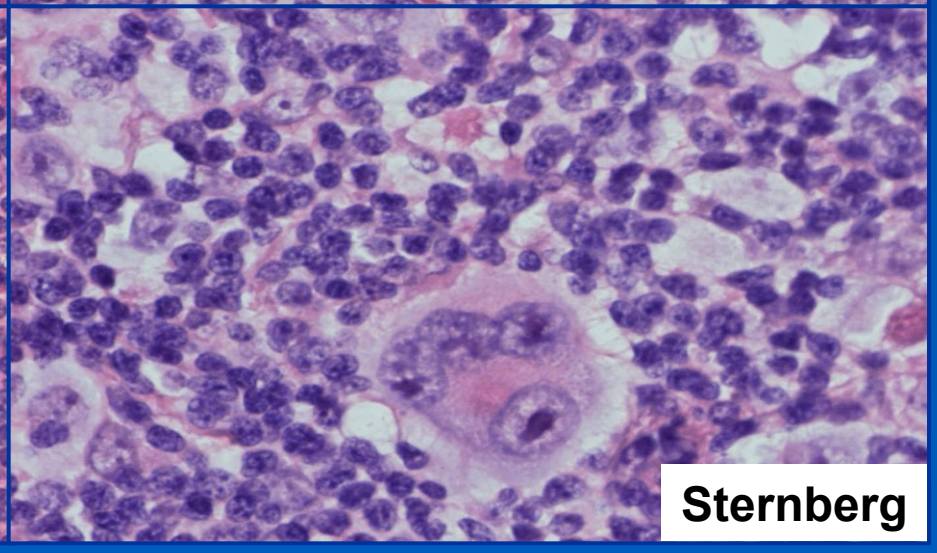


Diagnostic cells - classical HL

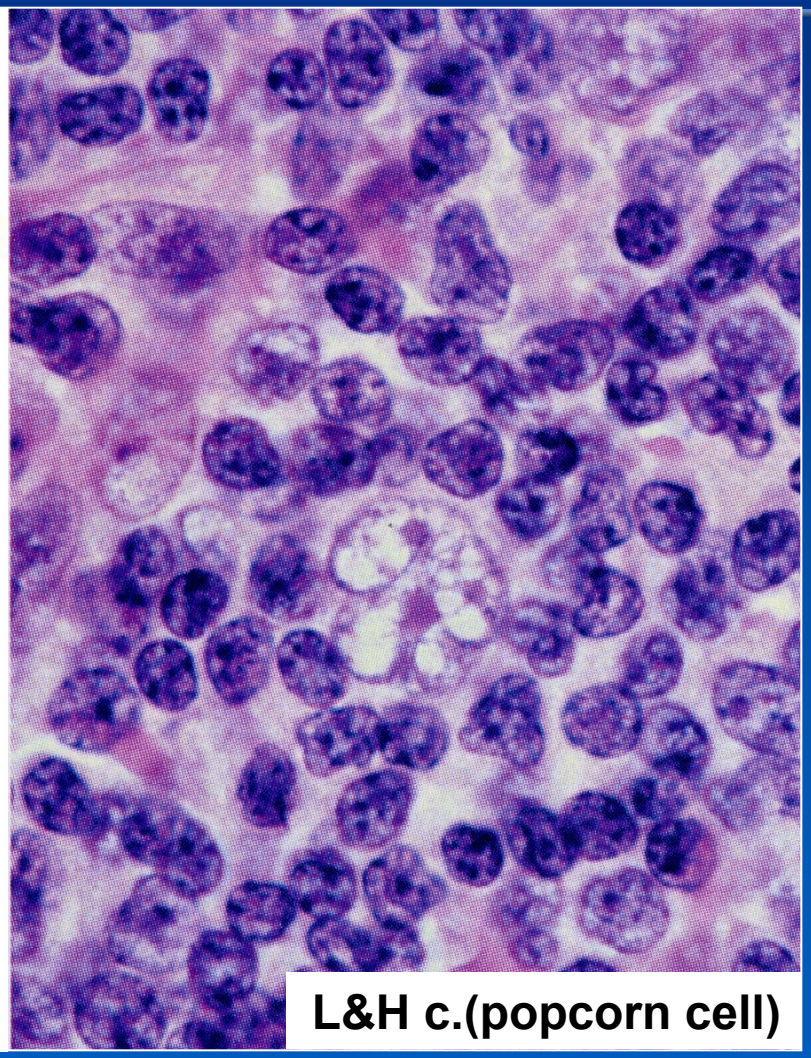






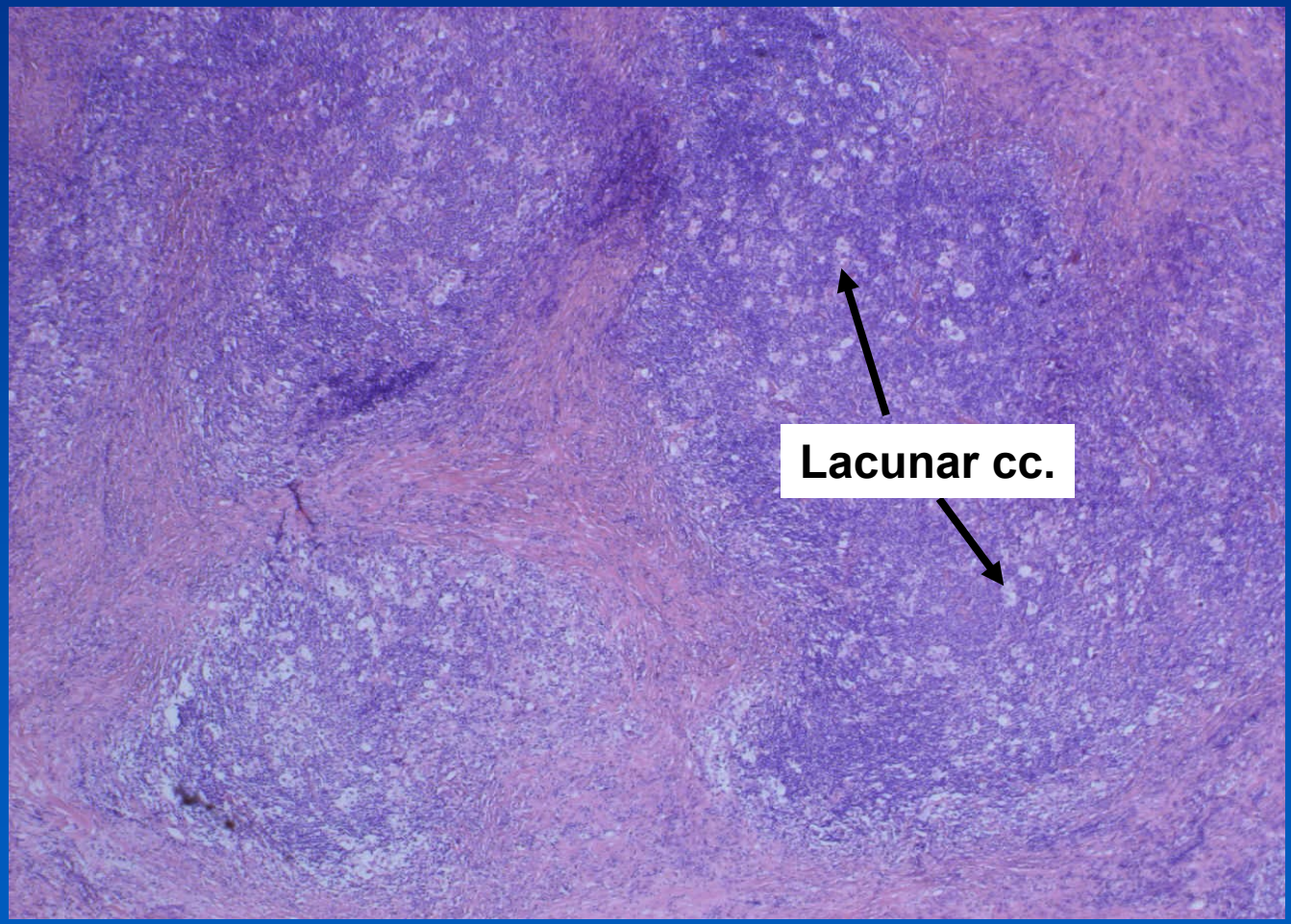


Lymphocyte predominance, nodular: diagnostic cell

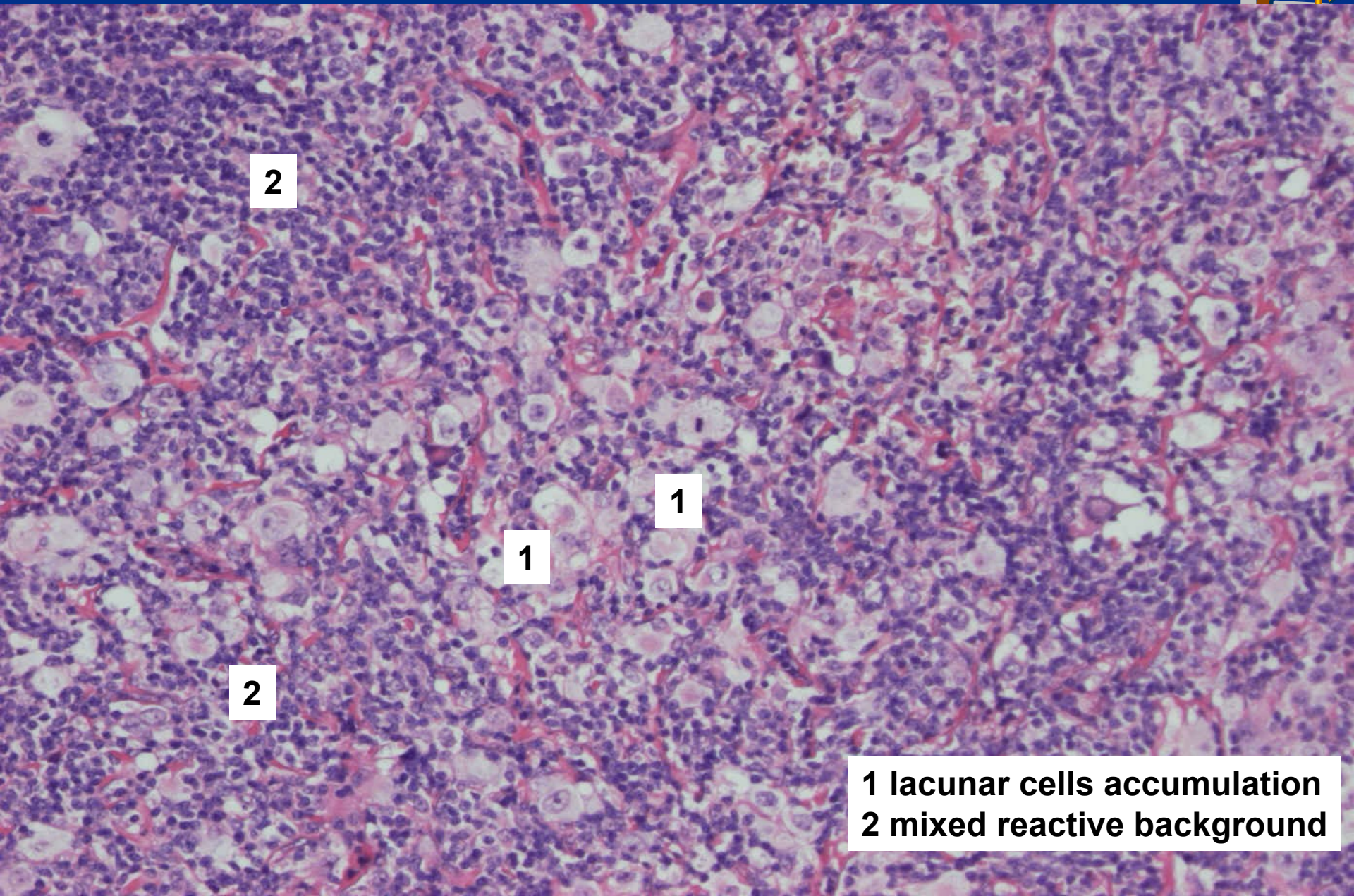


L&H c.(popcorn cell)

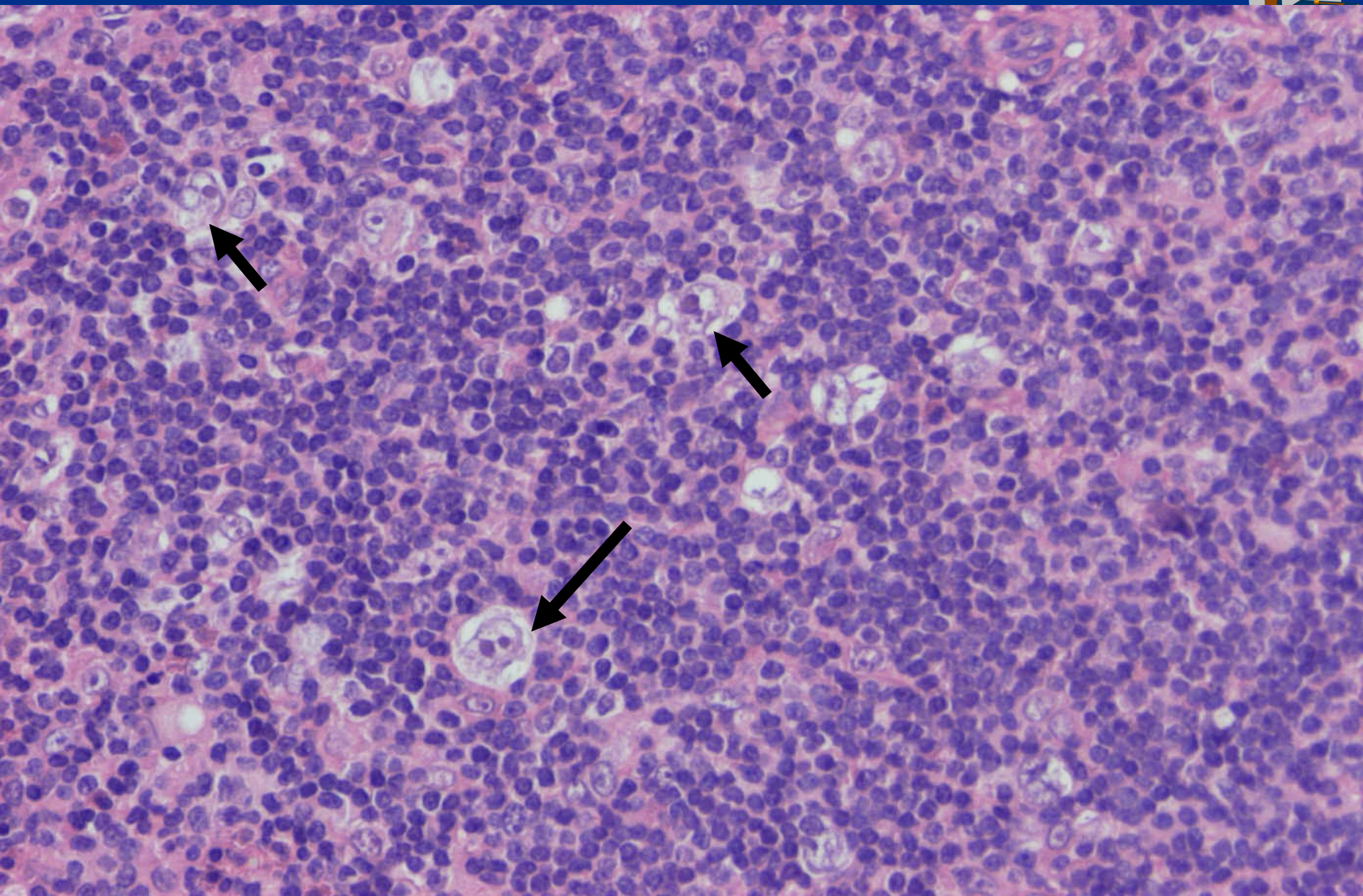
Hodgkin lymphoma, classical, nodular sclerosis



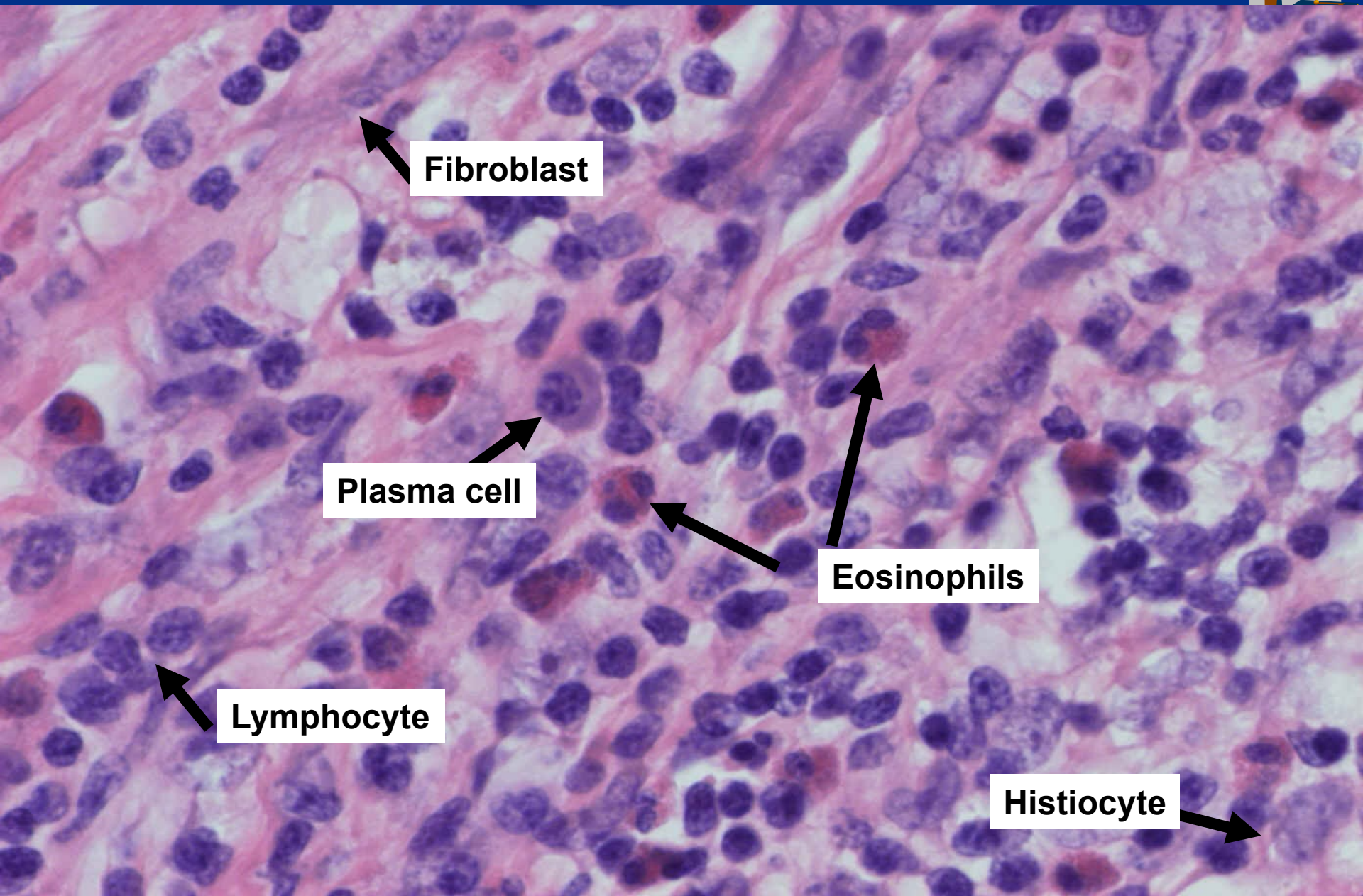
Hodgkin lymphoma, classical, nodular sclerosis



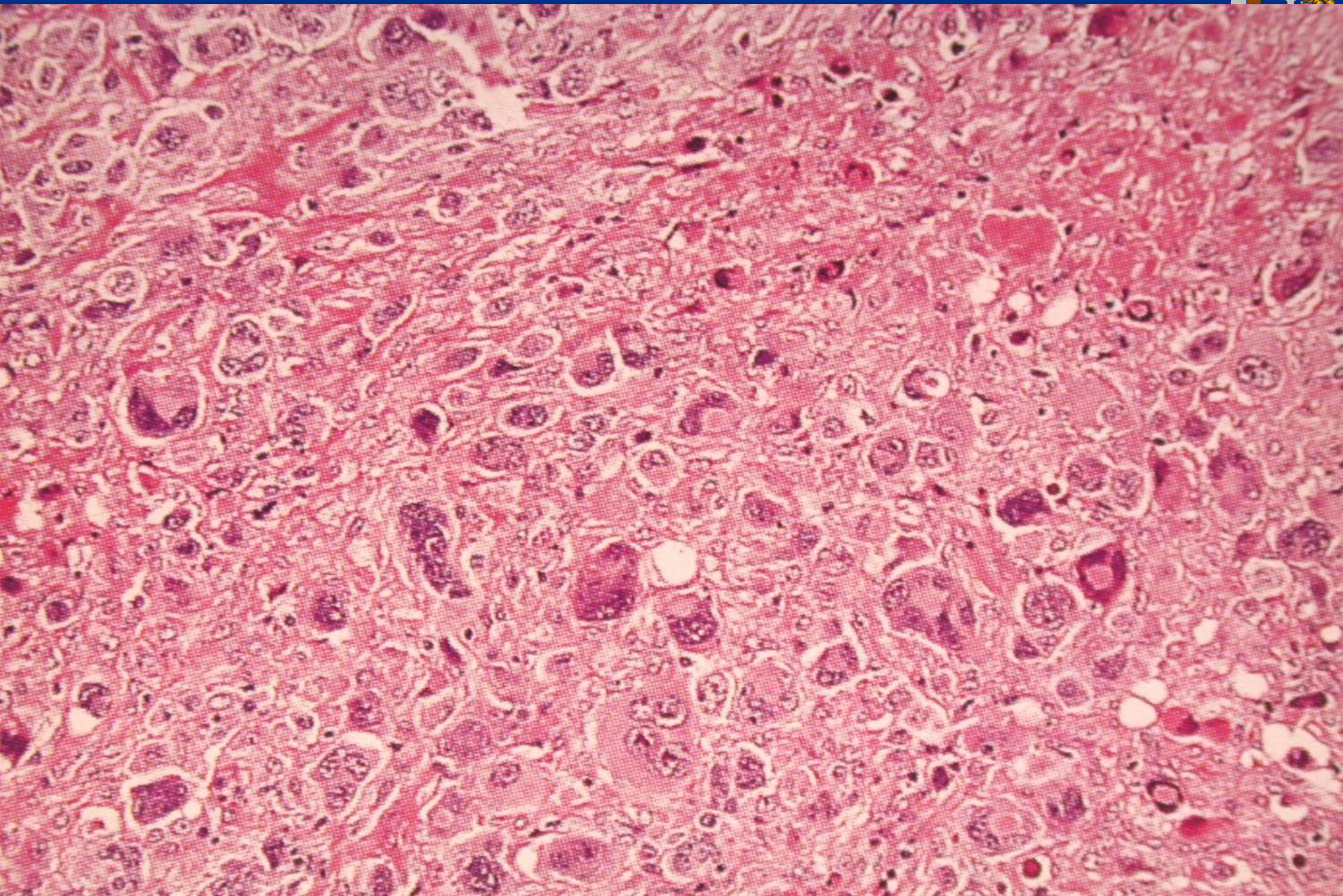
HL, classical, mixed cellularity – Hodgkin cc., RS cc



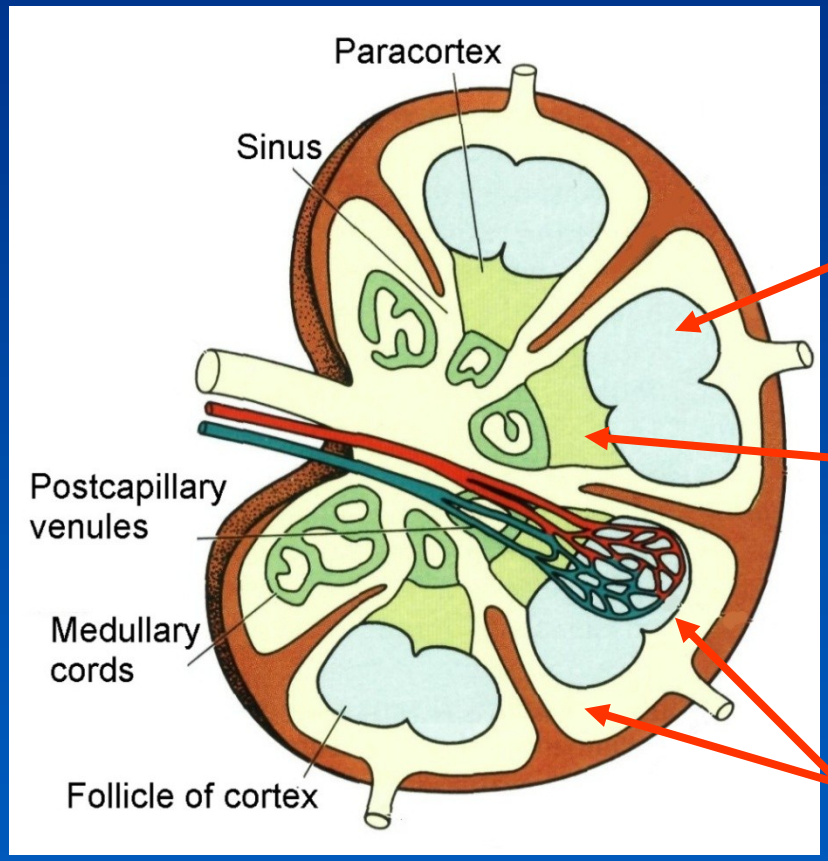
Classical HL – cells of the non-neoplastic background



Classical HL – lymphocyte depletion



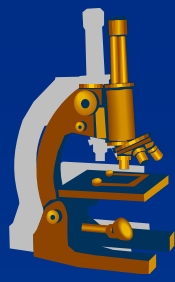
Reactive lymphadenopathy



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

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

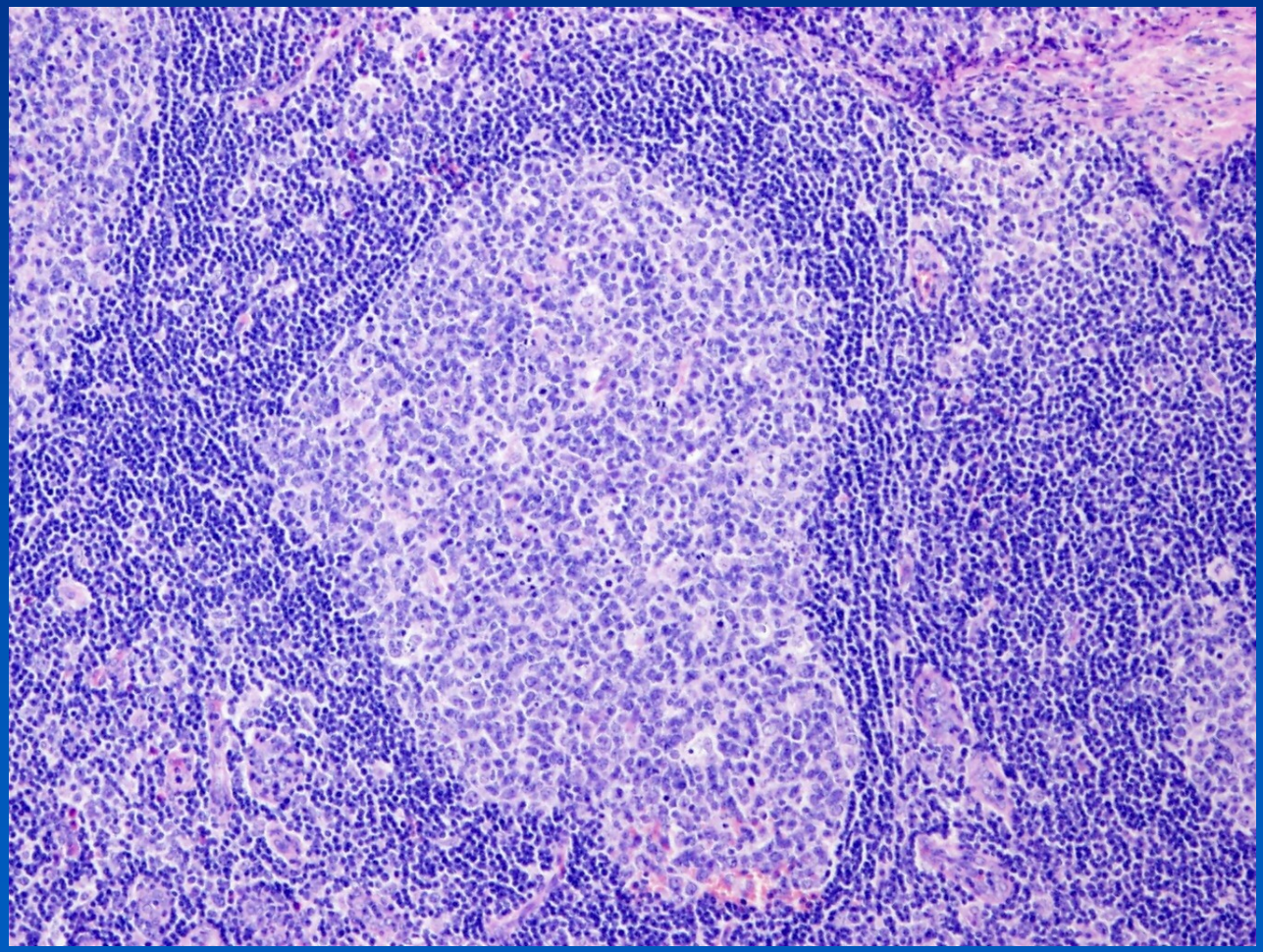
Reactive lymphadenopathy



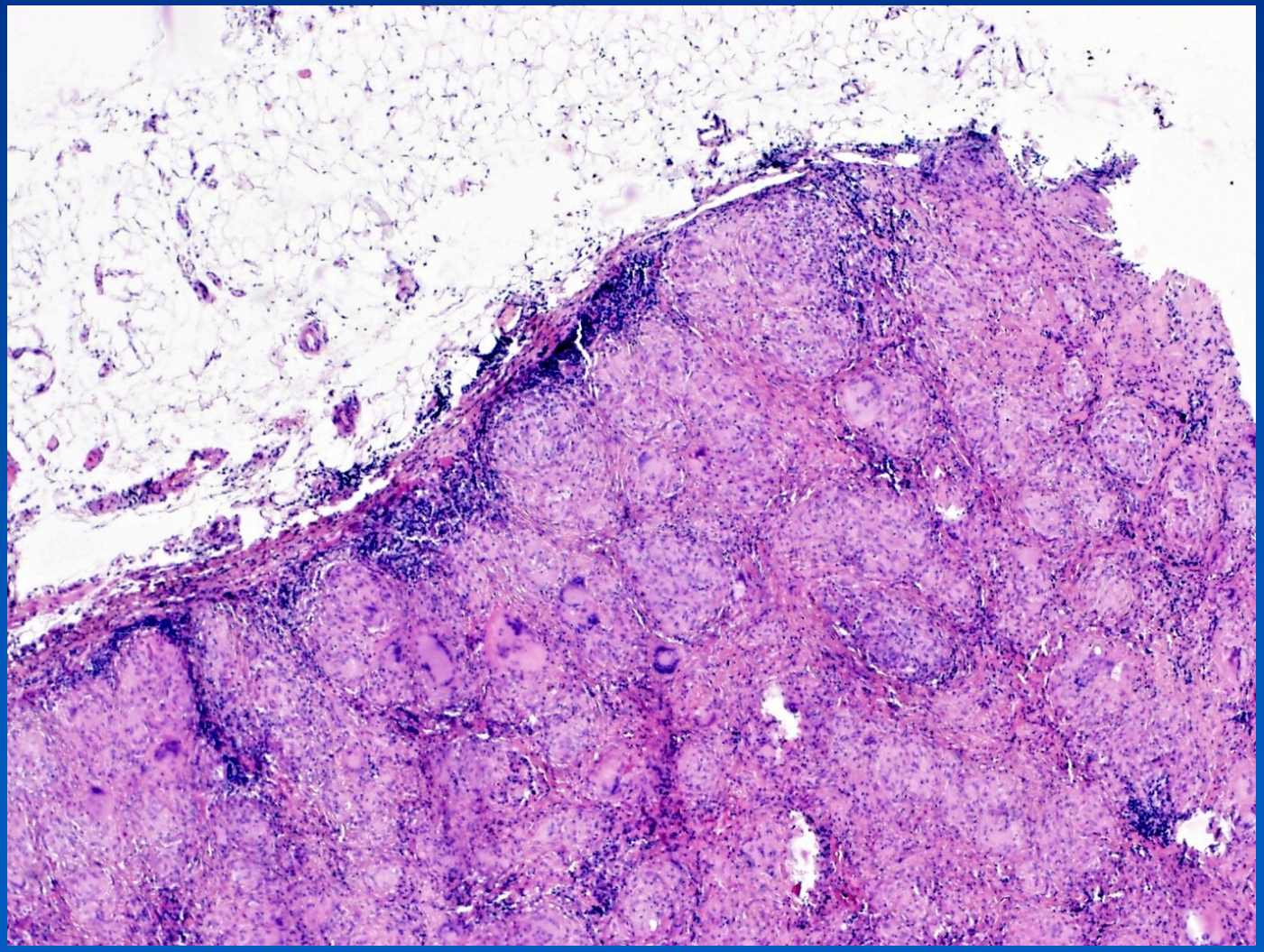
- **follicular hyperplasia**
  - Enlarged, irregular (in shape and size), polarized germinal centers, tingible macrophages, mitotic activity in GC
  - Bacterial infections, RA, toxoplasmosis, …
- **paracortical hyperplasia**
  - Reactive changes in T-cell regions of LN
  - Parafollicular T-cell transformation 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***
- **Reacive lymphadenopathy**

Follicular hyperplasia - reactive



Sarcoidosis - mediastinal lymph node



Sarcoidosis - mediastinal lymph node