

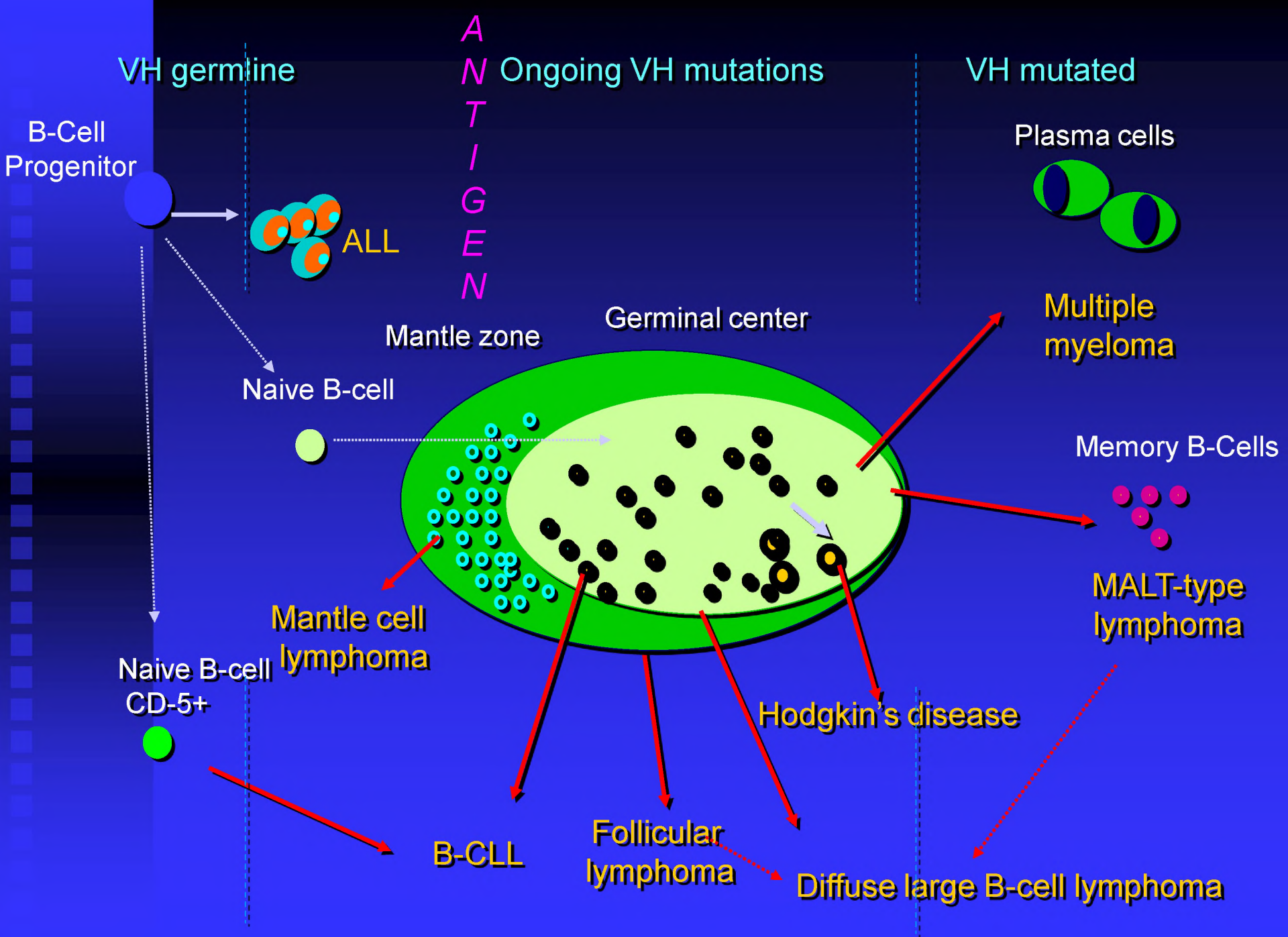
Lymphomas & leukemias

■ Clinical classification

- ◆ Low-grade, indolent lymphomas
- ◆ Intermediate-grade lymphomas
- ◆ High-grade, aggressive lymphomas

■ Histogenetic classification

- ◆ Based on the assumption that lymphomas can be classified in accordance with the resemblance with normal lymphocyte subsets
- ◆ B-cell neoplasms, different subtypes
- ◆ T-cell neoplasms, different subtypes

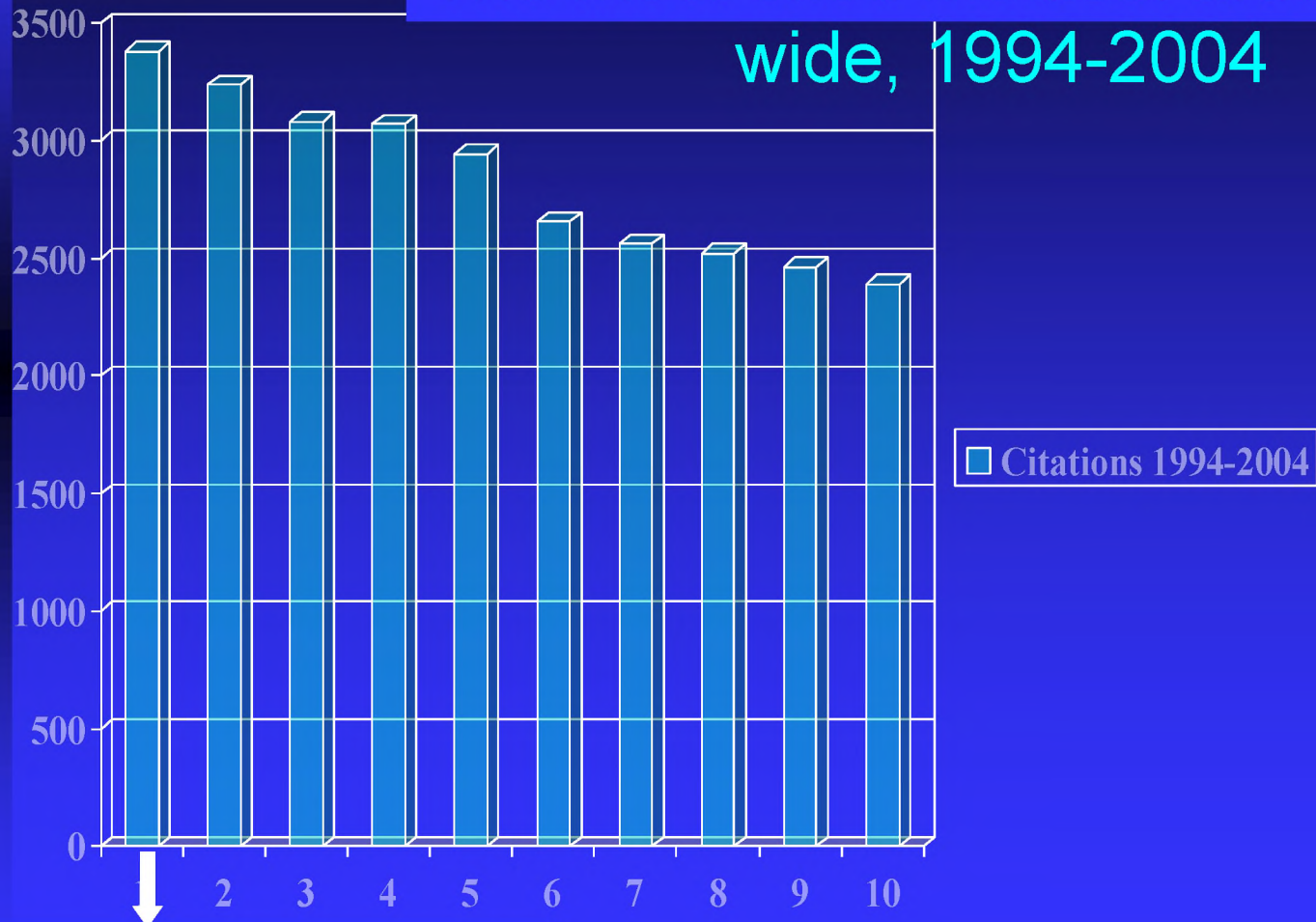


REAL Classification

- Useful to clinicians and histopathologists
- Reproducible, easy to use
- Requires phenotypic and genotypic examinations
- Easy to modify and up-date
- Adopted on an international basis

ISI, Institute for Scientific Information

The most cited medical article world
wide, 1994-2004



REAL classification 1994

REAL Classification

- Hodgkin lymphoma
 - ◆ Different subtypes
- B-cell lymphoma
 - ◆ Different subtypes
- T-cell lymphomas
 - ◆ Different subtypes

WHO (2001)

B-cell neoplasms

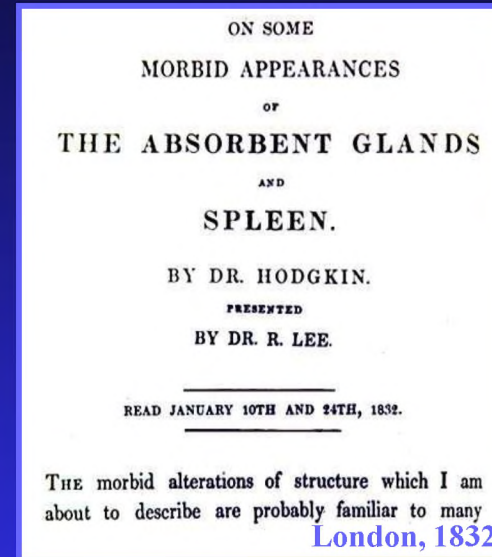
- B-ALL/LB
- B-CLL/SLL
- B-PLL
- Hairy cell leukemia
- Follicular lymphoma, grades I-III
- Mantle cell lymphoma
- Nodal marginal zone lymphoma
- Extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (MALT)
- Splenic marginal zone lymphoma
- Lymphoplasmacytic lymphoma
- Multiple myeloma
- Diffuse large B-cell lymphoma
- Mediastinal (thymic) large B-cell lymphoma
- Burkitt lymphoma
- Intravascular large B-cell lymphoma
- Primary effusion lymphoma
- Lymphomatoid granulomatosis

T-cell neoplasms

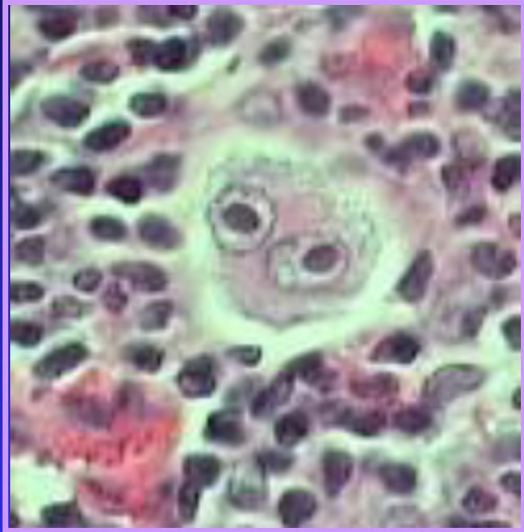
- T-ALL-LB
- T-PLL
- T-cell large granular lymphocytic (LGL) leukemia
- Adult T-cell leukemia/lymphoma
- Mycosis fungoides/Sezary syndrome
- Subcutaneous panniculitis-like T-cell lymphoma
- Primary cutaneous CD30-positive T-cell lymphoproliferative disorder
- Extranodal T/NK cell lymphoma, nasal-type
- Hepatosplenic T-cell lymphoma
- Enteropathy-type T-cell lymphoma
- Peripheral T-cell lymphoma, unspecified
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large cell lymphoma
- Aggressive NK cell leukemia
- Blastic NK-cell lymphoma

Hodgkin lymphoma

Thomas Hodgkin 1798-1866



Hodgkin Lymphoma



1898 Carl Sternberg
1902 Dorothy Reed

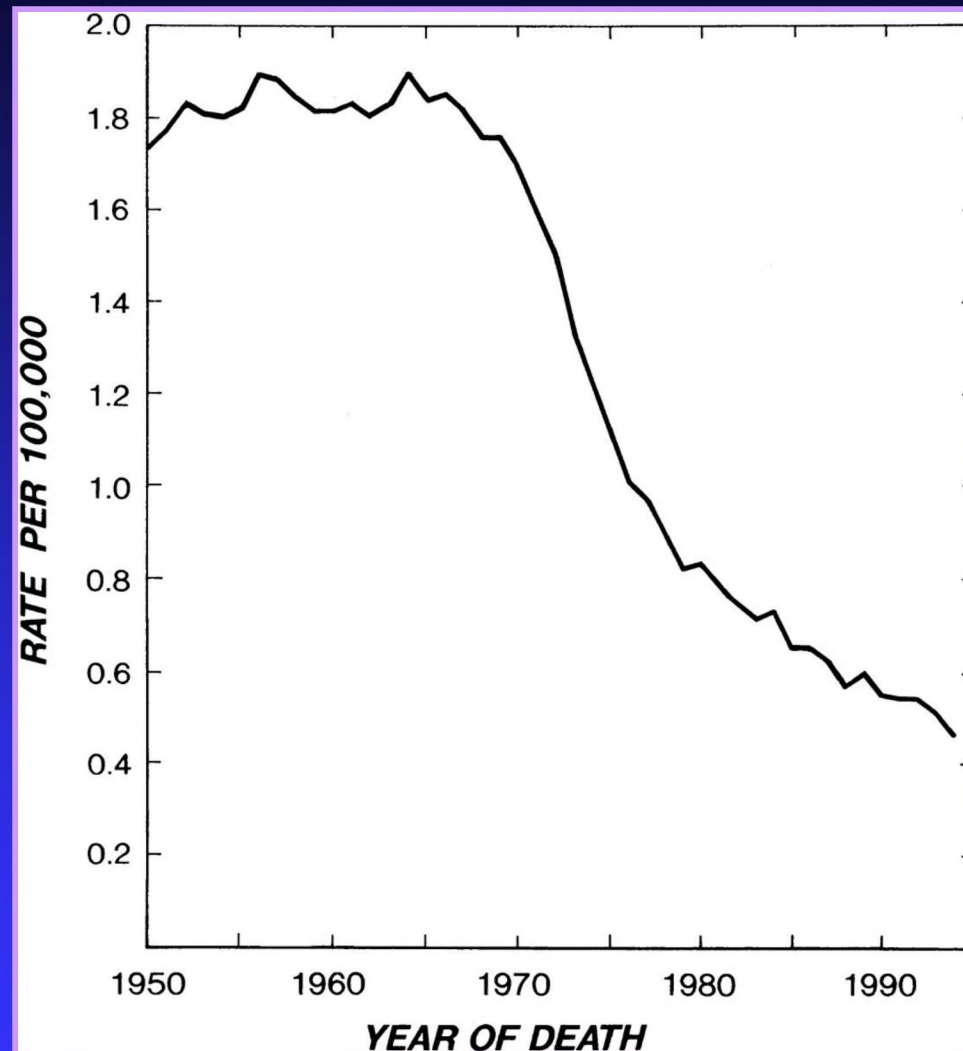
Hodgkin and Reed-Sternberg (HRS) cells
combined with a benign inflammatory
infiltrate.

Hodgkin Lymphoma: Clinical

- bimodal age distribution
- incidence peaks in young adults
- nodal presentation
- painless lymphadenopathy
- contiguous spread
- may have toxic B symptoms
 - fever
 - night sweats
 - weight loss
 - pruritis



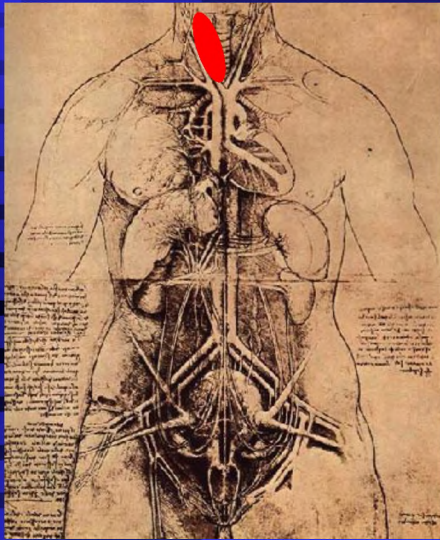
Hodgkin's lymphoma mortality in U. S. white patients, 1950-1994.



Ries et al: SEER Cancer Statistics Review, 1973-1994,
National Cancer Institute. NIH Pub. No. 97-2789, 1997

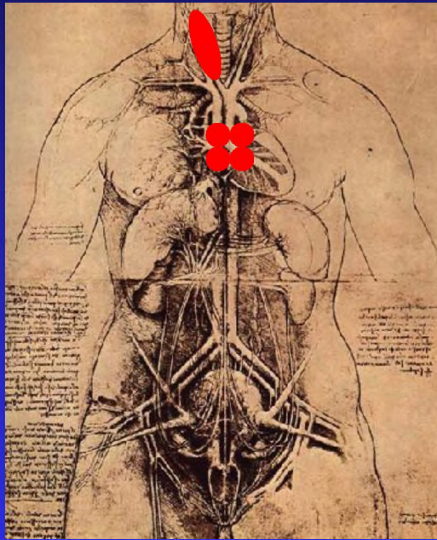
Lymphoma Staging

I



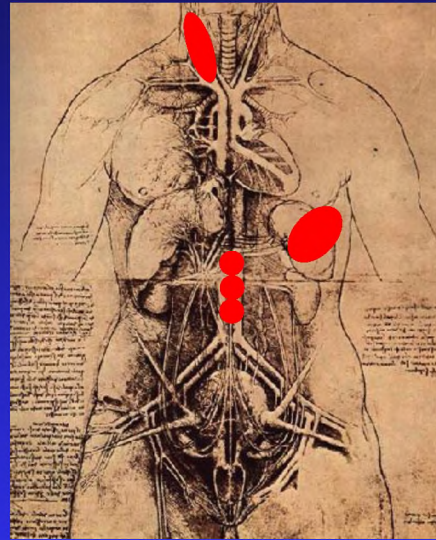
one node site

II



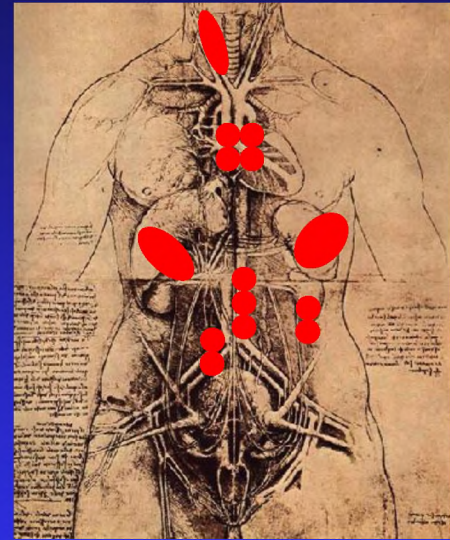
> one site
same side of
diaphragm

III



both sides of
diaphragm

IV



extra nodal
sites

Carbone PP et al. Cancer Res 1971, 31:1860-1

Lister TA et al. J Clin Oncol 1989, 7:1630-6

Gobbi PG et al. Cancer 1985, 56:2874-80

Staging of Hodgkin's Lymphoma

- Stage I. Involvement of a single lymph node region or lymphoid structure (spleen, thymus, Waldeyer's ring), or involvement of a single extralymphatic site (I_E).
- Stage II. Involvement of two or more lymph node regions on the same side of the diaphragm (II) which may be accompanied by localized contiguous involvement of an extralymphatic organ or site (II_E). The number of anatomic sites may be indicated by a numerical subscript.
- Stage III. Involvement of lymph node regions on both sides of the diaphragm (III) which may also be accompanied by involvement of the spleen (III_S) or by localized contiguous involvement of an extralymphatic organ or site (III_E).
- Stage IV. Diffuse or disseminated involvement of one or more extralymphatic organs or tissues, with or without associated lymph node involvement.

Notes: (1) The absence or presence of fever ($>38^{\circ}\text{C}$) and/or unexplained weight loss ($>10\%$ of body weight) in the preceding 6 months are denoted by the suffix letters A and B, respectively. (2) If staging laparotomy/splenectomy has been performed the designation is pathological stage (PS), if not clinical stage (CS). (3) Stage III may be subdivided into III₁ to designate involvement of only the upper abdominal nodes and/or spleen, and III₂ to designate involvement of the paraaortic and/or pelvic nodes. (4) A mediastinal mass $>1/3$ maximum chest diameter or a lymphoid mass >10 cm in diameter may be designated by the subscript "x."

I



III



IV



Carbone PP et al. *Cancer Res* 1971, 31:1860-1

Lister TA et al. *J Clin Oncol* 1989, 7:1630-6

Gobbi PG et al. *Cancer* 1985, 56:2874-80

HL: Two Biological Entities

Lymphocyte predominance (10 %)

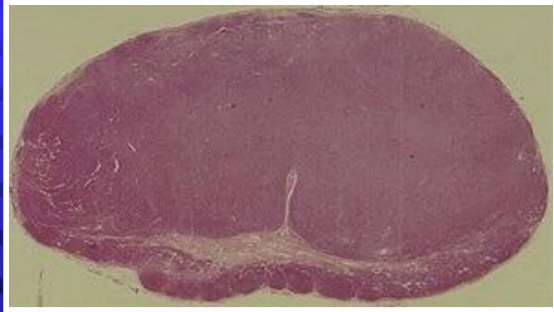
Classical Hodgkin (90%)

- ◆ Clinical features and behaviour
- ◆ Morphology
- ◆ Immunophenotype

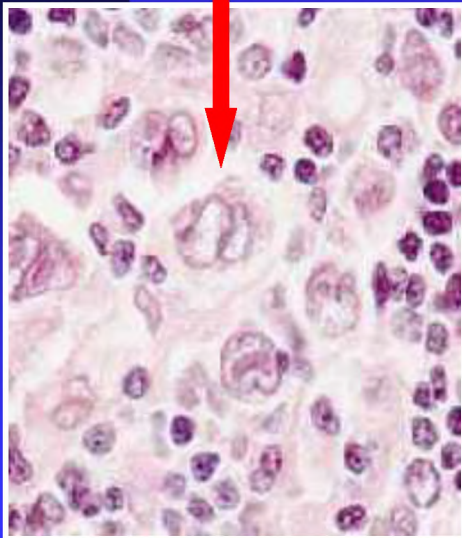
Hodgkin Lymphoma

- Lymphocyte predominance
 - Nodular (10%)
 - Diffuse (rare)
- Classical Hodgkin
 - Nodular sclerosis (60%)
 - Mixed cellularity (30%)
 - Lymphocyte rich classical HL (rare)
 - Lymphocyte depletion (rare)

Nodular Lymphocyte Predominance Hodgkin Lymphoma



Popcorn cell



Morphology

- nodular (& diffuse)
- popcorn L&H cells
- small B-cells

Immunology

- B cell phenotype
- CD20, 79, 45 +/-
- CD30 -
- CD57 T cells +
- EMA +
- EBV -

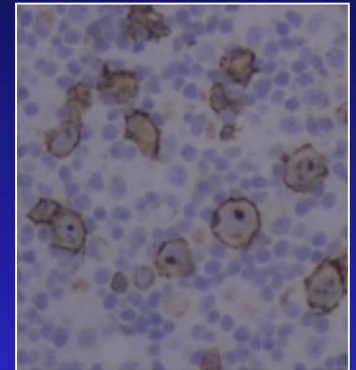
Genetics

- none specific

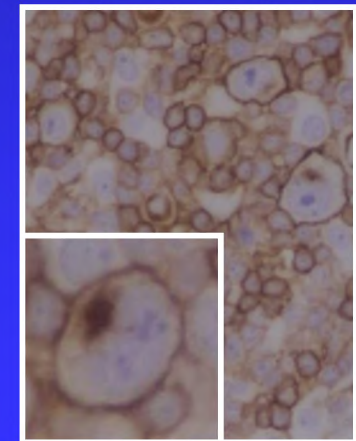
Clinical

- males > females
- indolent

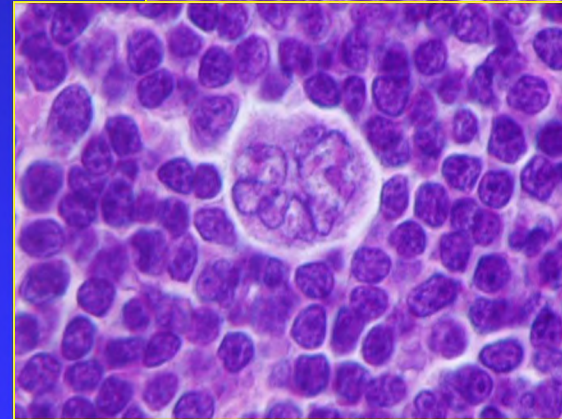
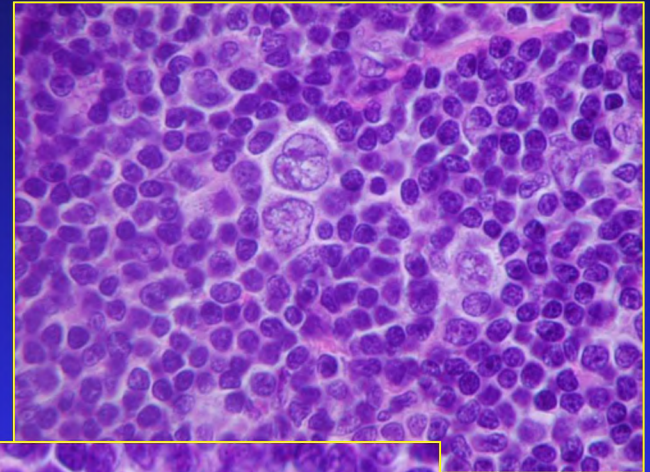
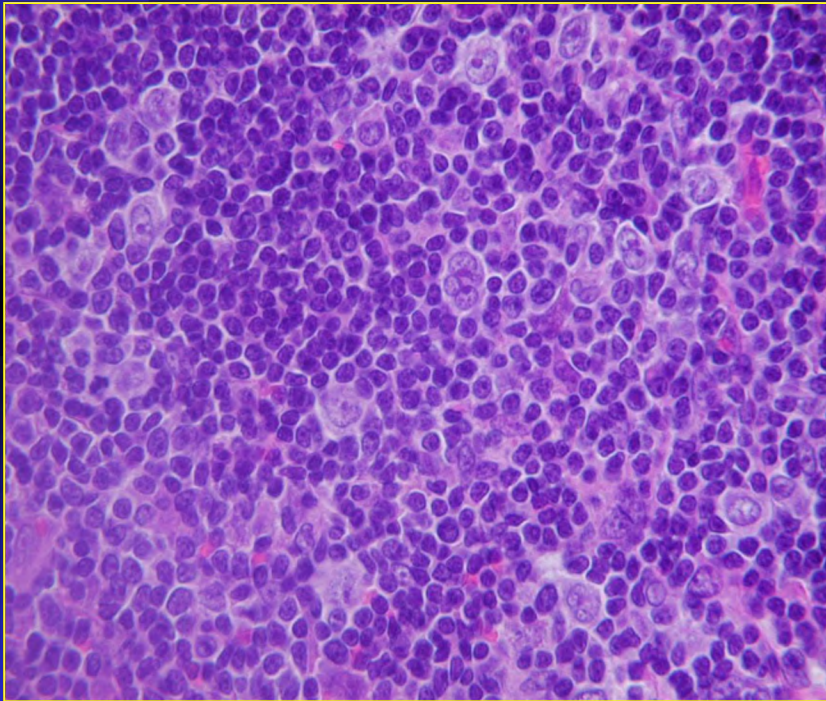
EMA



CD20



HL, lymphocyte predominance

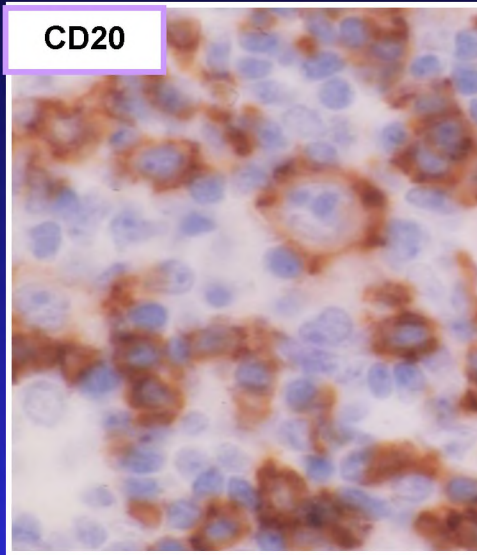


Nodular Lymphocyte Predominance Hodgkin Lymphoma

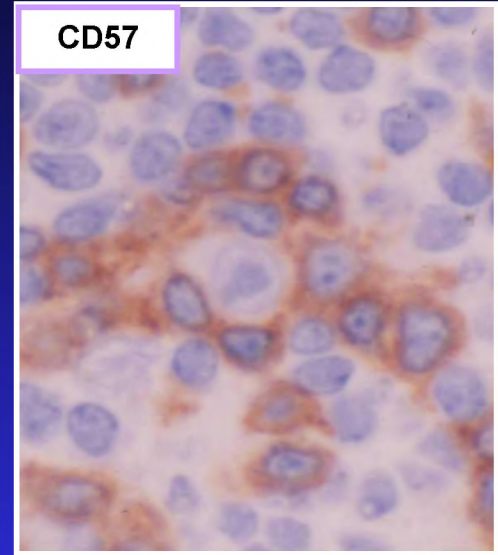
Popcorn cell



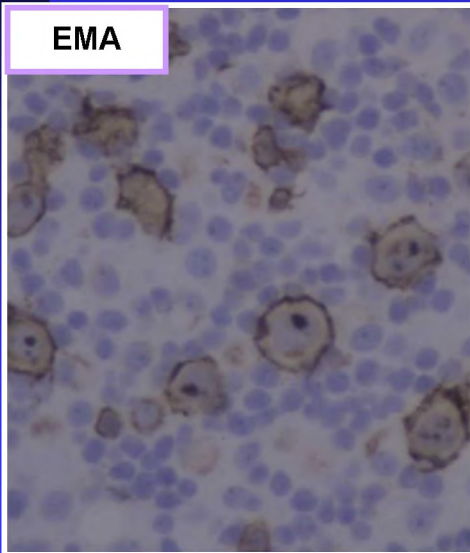
CD20



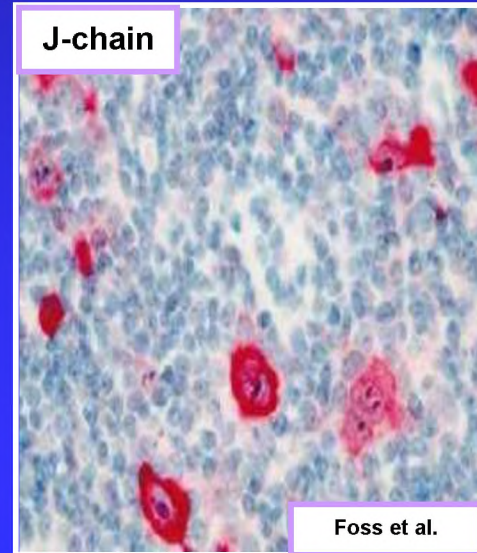
CD57



EMA

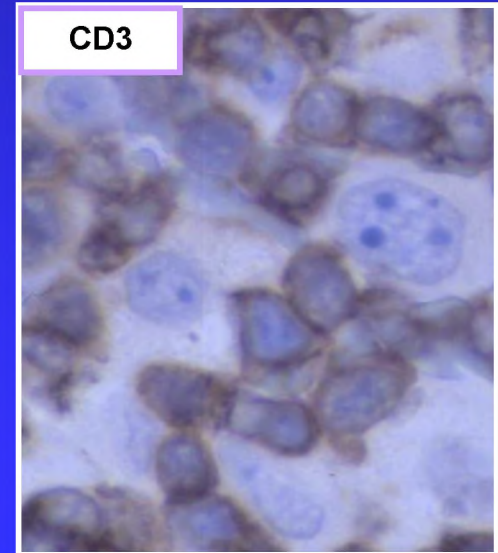


J-chain



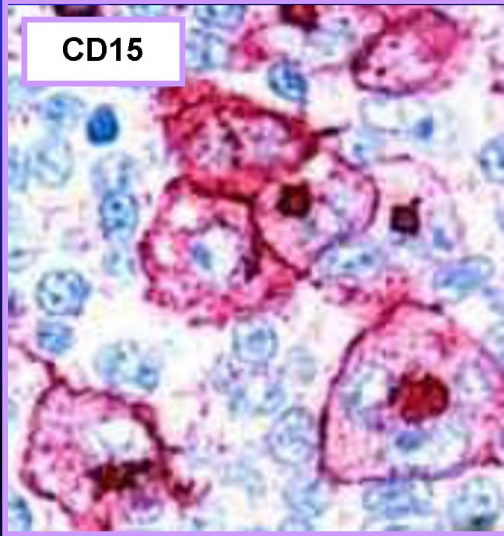
Foss et al.

CD3

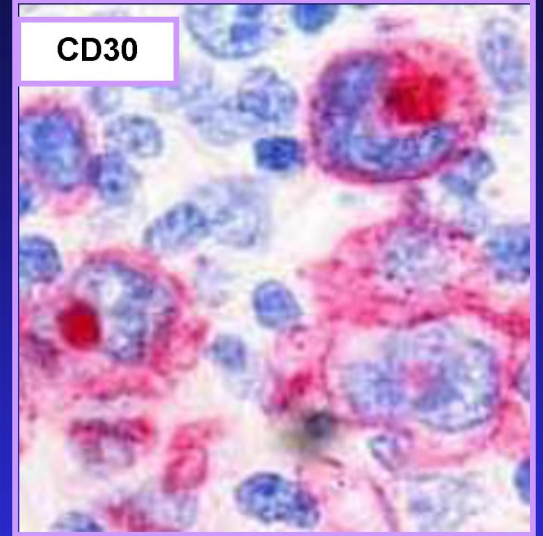


Classical Hodgkin Lymphoma

CD15



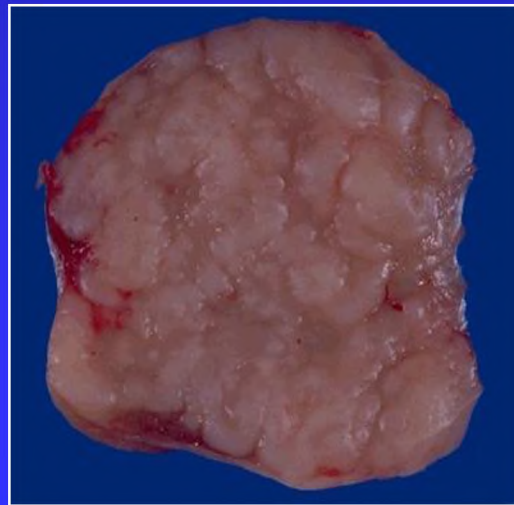
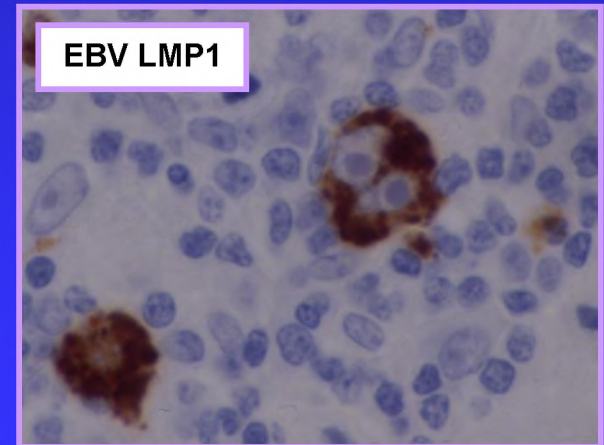
CD30



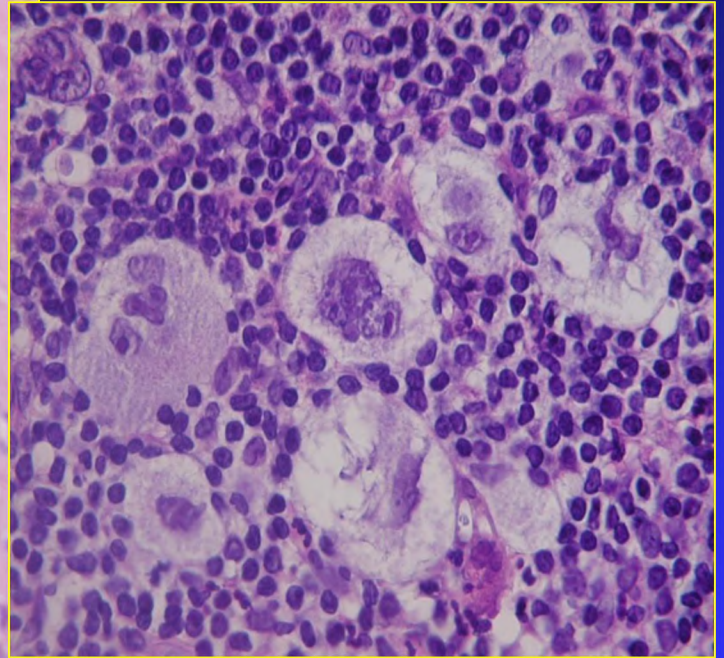
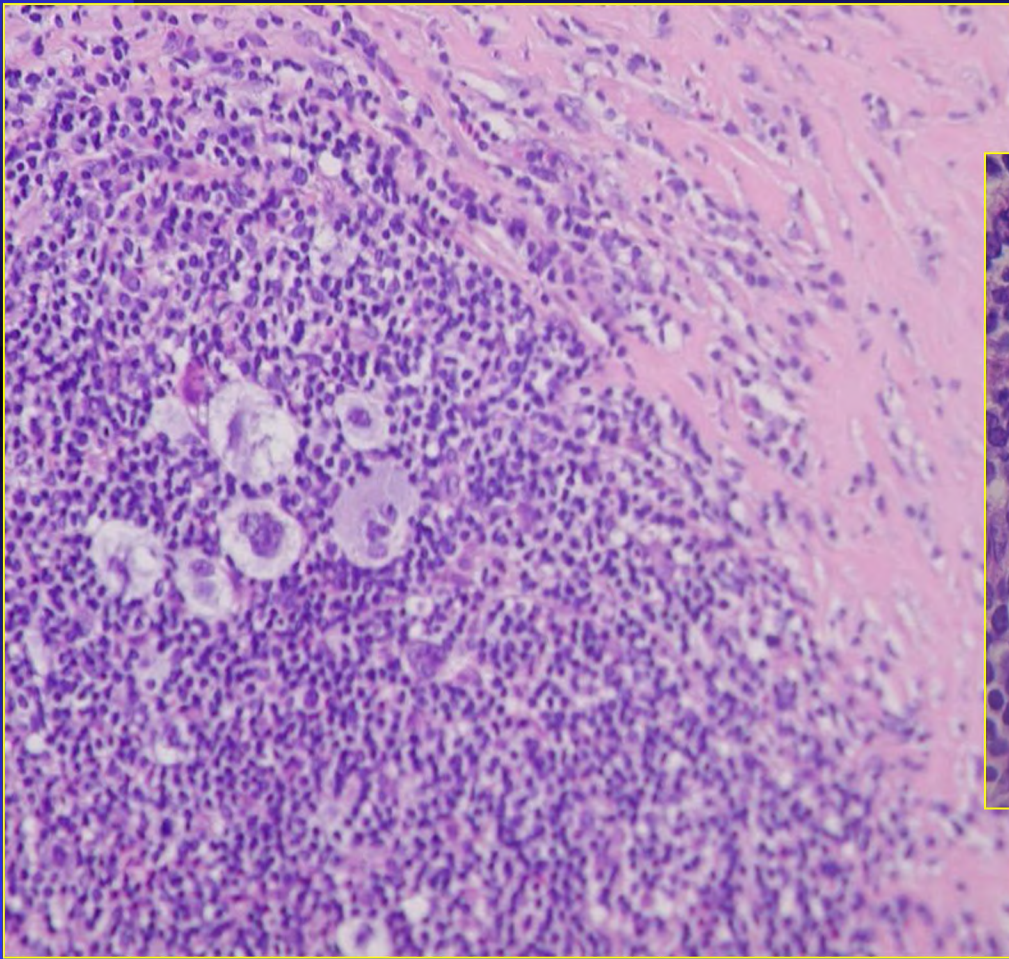
EBER ISH



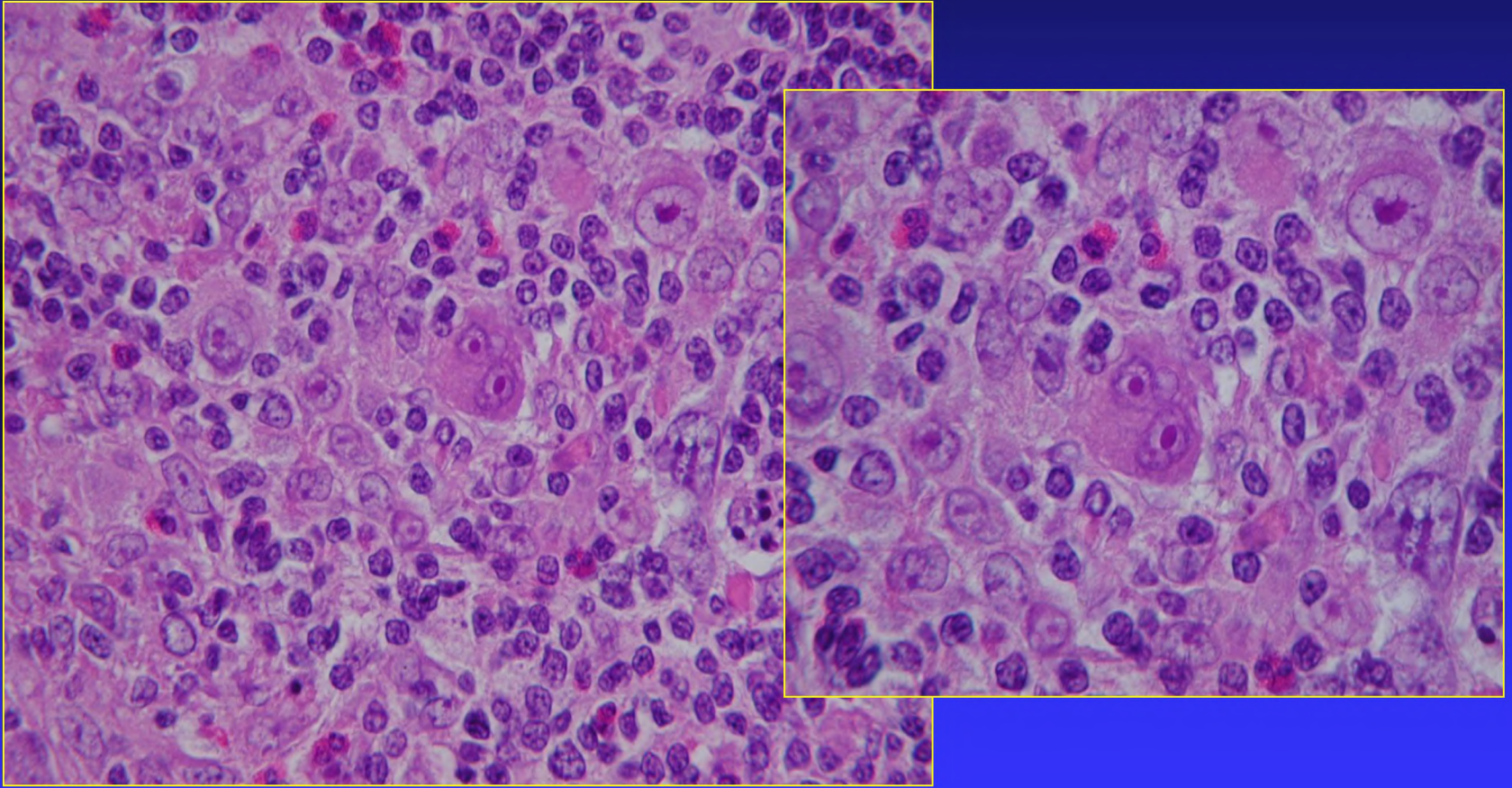
EBV LMP1



HL, nodular sclerosis



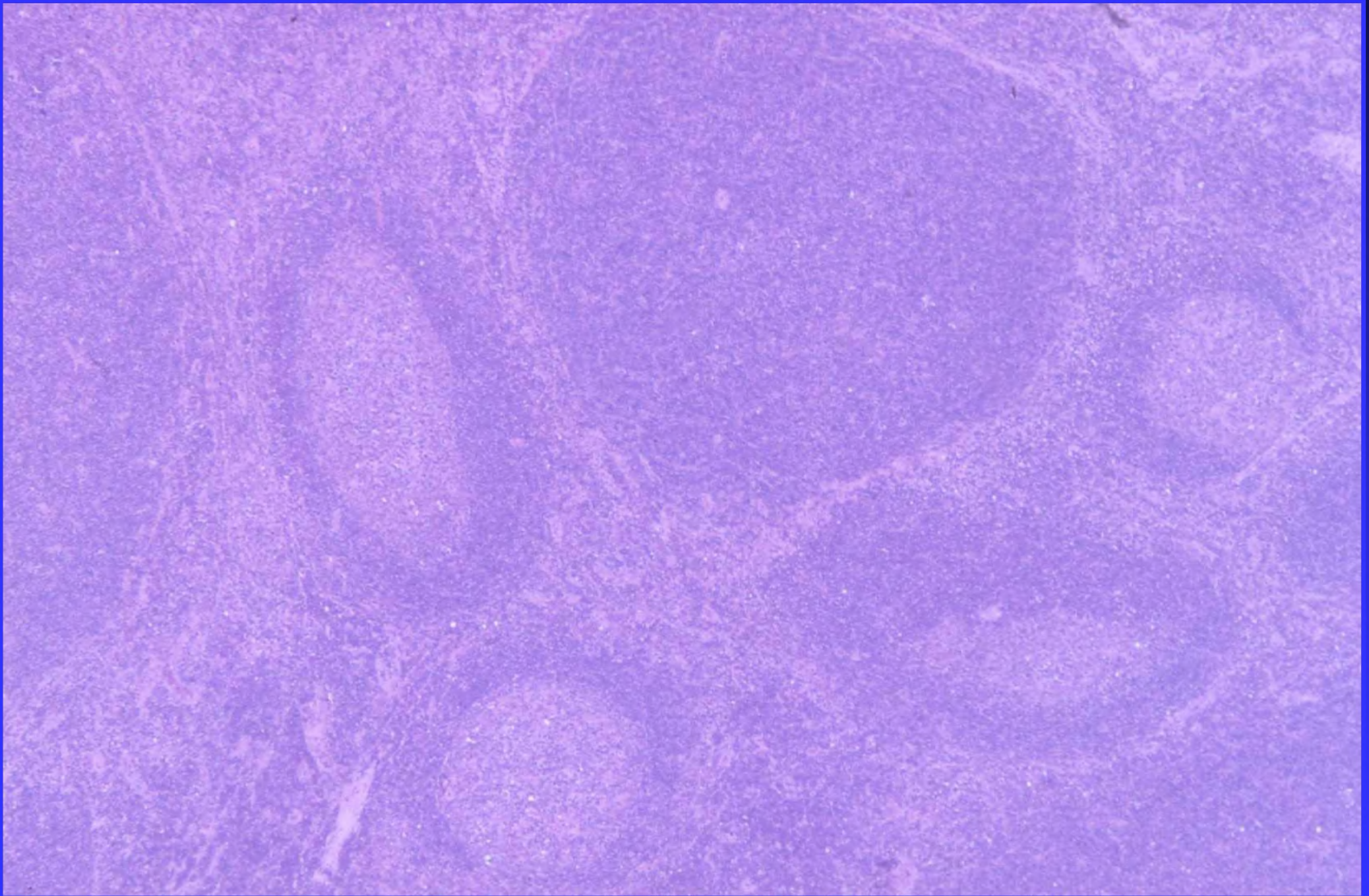
HL, mixed cellularity



Differential Diagnosis of HL

- NLPHL *vs* progressive transformation of germinal centres
- LPHL *vs* T-cell / Histiocyte Rich B-cell Lymphoma
- Classical HL *vs* T-cell lymphoma
- Classical HL *vs* anaplastic large cell lymphoma

Progressive Transformation of Germinal Centres



HL vs Peripheral T-Cell Lymphoma

- Favours PTL
 - ◆ Nuclear atypia in background T-cells
 - ◆ T-cell antigen expression
 - ◆ TCR gene rearrangements
- RS-like cells may be present in both
- EBV may be present in both

B-cell neoplasms

WHO: B-Cell Neoplasms (2001)

- B-ALL/LB
- B-CLL/SLL
- B-PLL
- Hairy cell leukemia
- Follicular lymphoma, grades I-III
- Mantle cell lymphoma
- Nodal marginal zone lymphoma,
- Extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (MALT)
- Splenic marginal zone lymphoma
- Lymphoplasmacytic lymphoma
- Multiple myeloma
- Diffuse large B-cell lymphoma
- Mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- Primary effusion lymphoma
- Burkitt lymphoma
- Lymphomatoid granulomatosis

Small B-cell lymphomas

- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- Follicular lymphoma
- Mantle cell lymphoma
- Marginal zone lymphoma
- Hairy cell leukemia
- Prolymphocytic leukemia

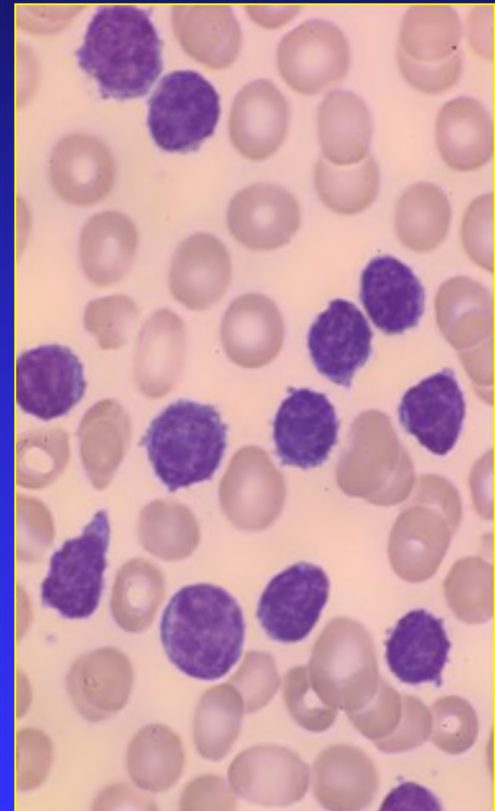
Chronic lymphocytic leukemia

Small lymphocytic lymphoma

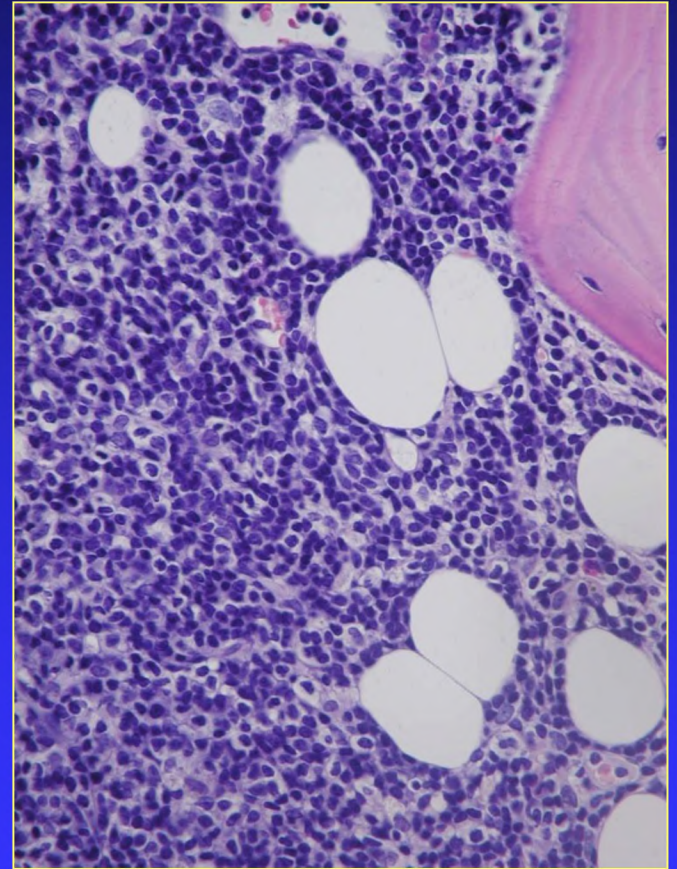
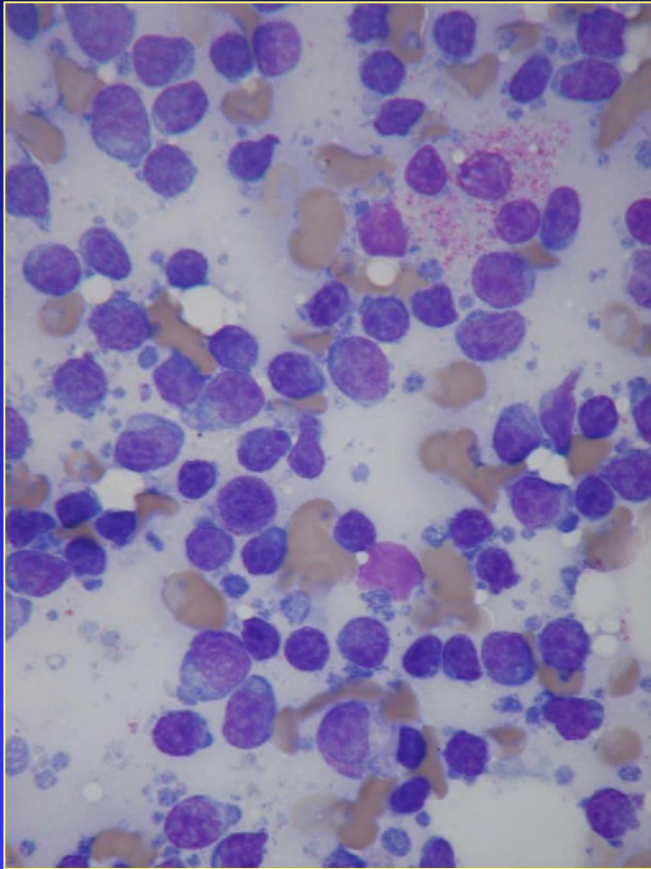
- Frequent, adults, elderly
- Asymptomatic
- Anemia, thrombocytopenia, fatigue, lymphadenopathy, splenomegaly
- Blood and bone marrow lymphocytosis
- Rarely isolated lymph node involvement (small lymphocytic lymphoma)
- Indolent, but variable

Chronic lymphocytic leukemia

- Small lymphocytes
- Round nuclei, sparse cytoplasm
- CD20+, CD5+, CD23+, CD10-
- Trisomy 12 (20%); del 13q14 (50%)
- IgVH genes mutated in some patients



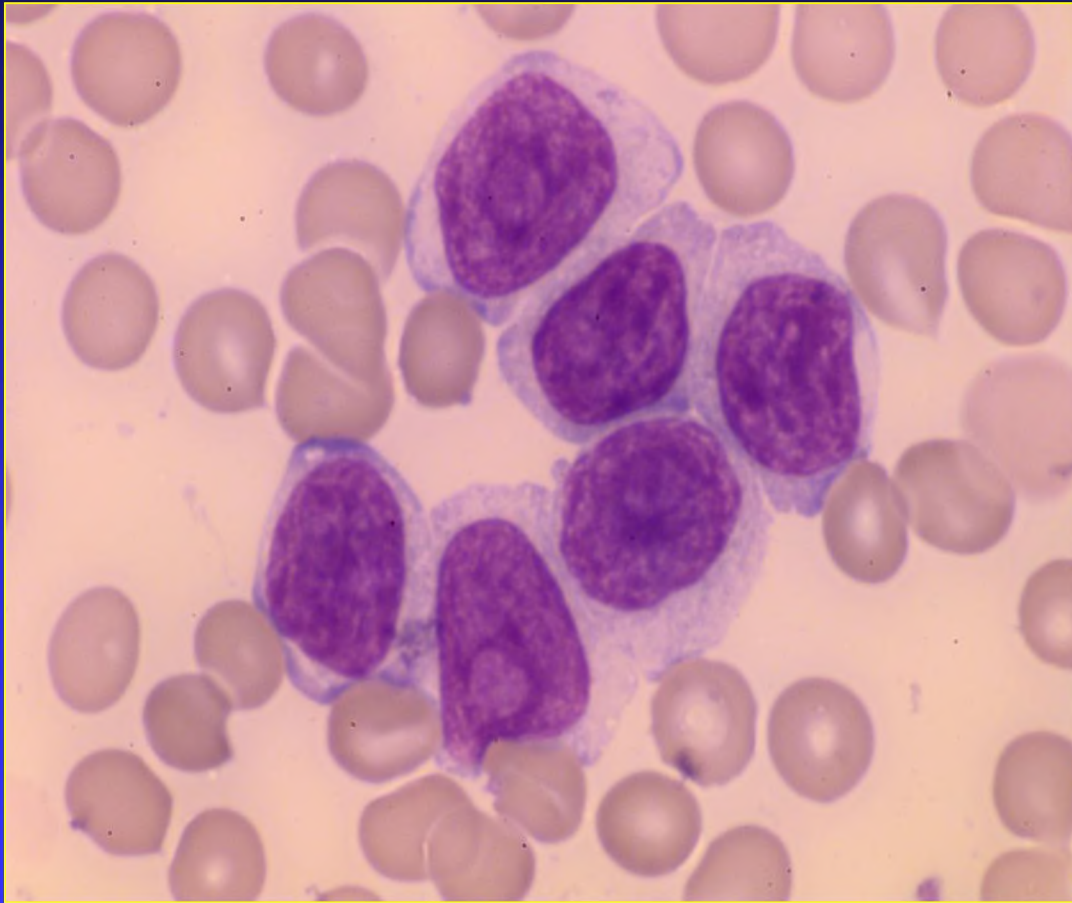
CLL, bone marrow



CLL, prognosis

- Prognosis usually good, but variable
- IgVH gene mutations is a major prognostic indicator

Prolymphocytic leukemia



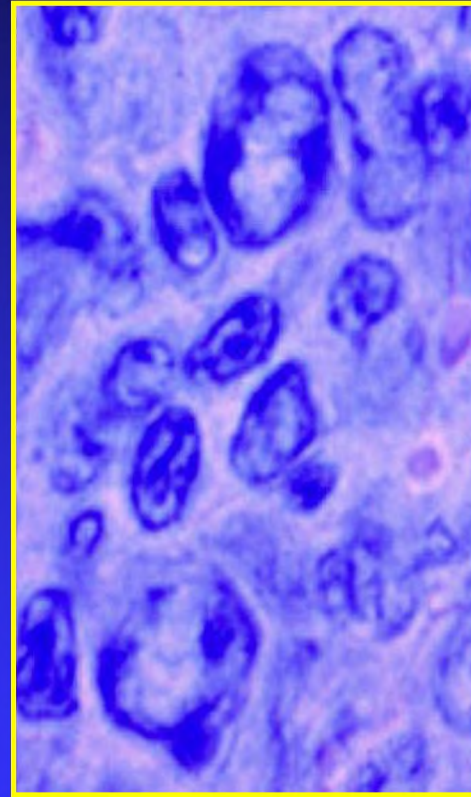
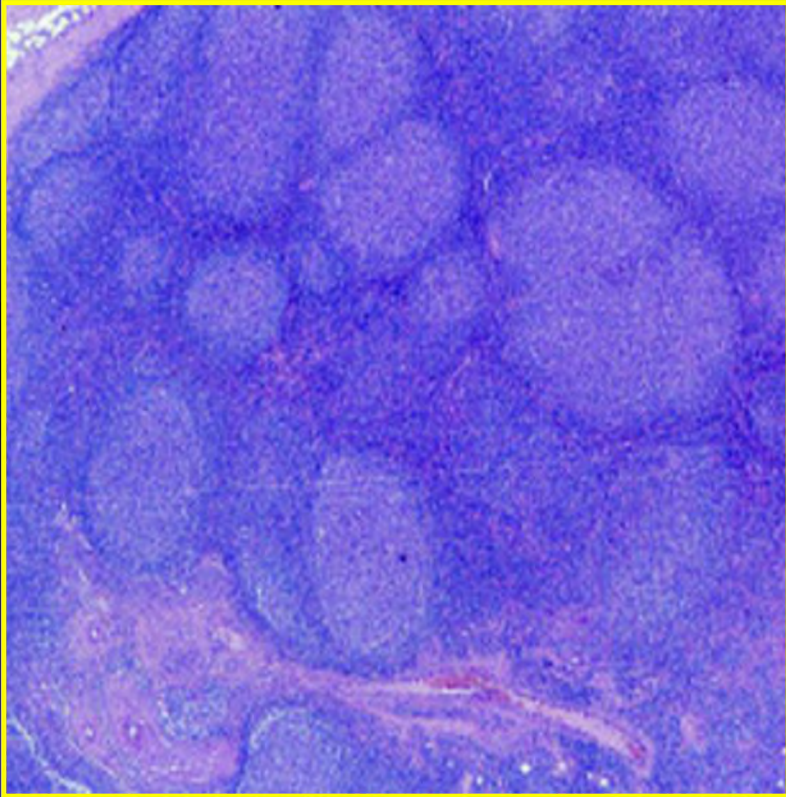
Follicular lymphoma

- Frequent (Western countries), adults, elderly
- Lymphadenopathy, often disseminated
- Constitutional symptoms, anemia, thrombocytopenia
- Indolent, but transformation to DLBCL is frequent (30%)

Follicular lymphoma

- Follicular infiltrates of centrocytes and centroblasts
- Graded according to the number of centroblasts
- Bone marrow: paratrabecular infiltrates
- CD20+, CD10+, Bcl-6+, CD23-, CD5-
- t(14;18), Bcl-2+
- Somatic IgVH mutations

Follicular lymphoma



Follicular Lymphoma

Grading

I < 5 centroblasts/HPF

II 5-15 centroblasts/HPF

III > 15 centroblasts/HPF

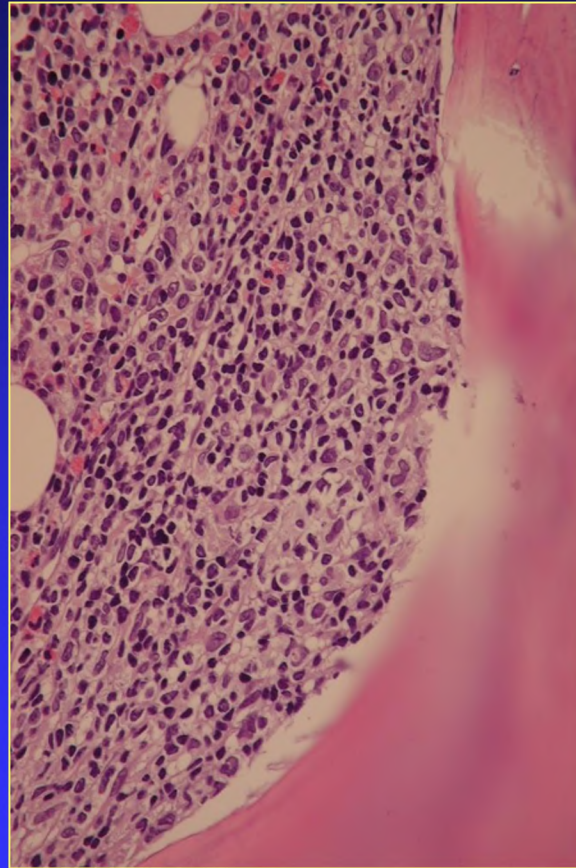
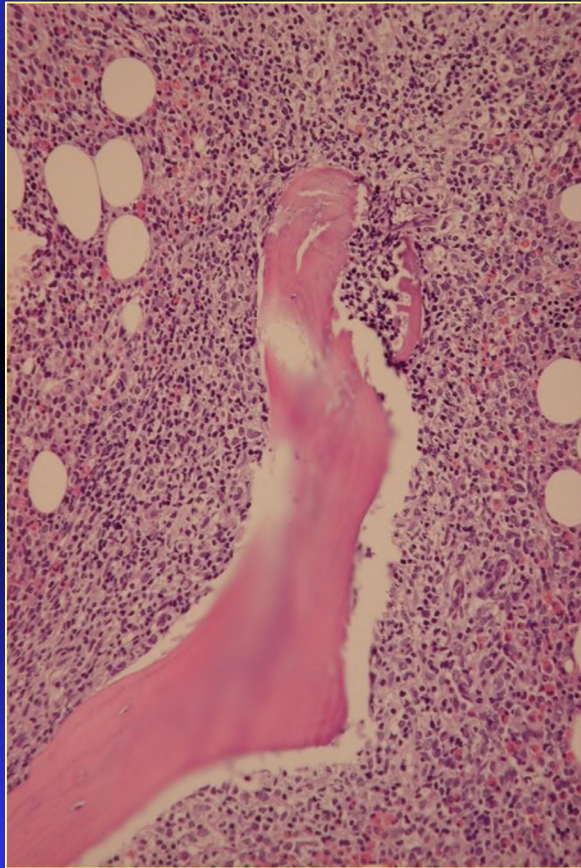
IIIa > 15 centroblasts, but still mixed

IIIb solid sheets of centroblasts

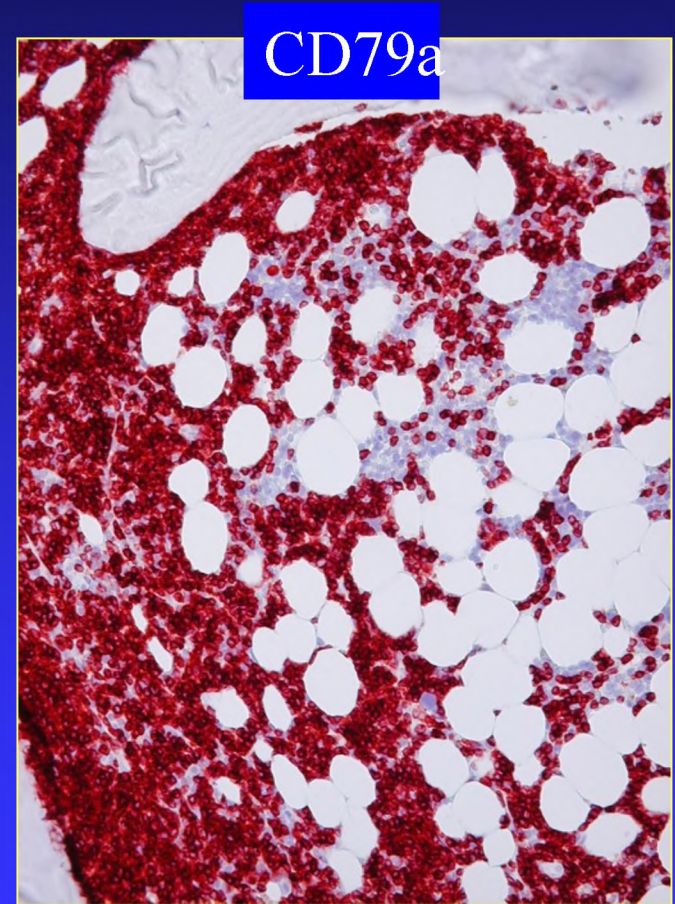
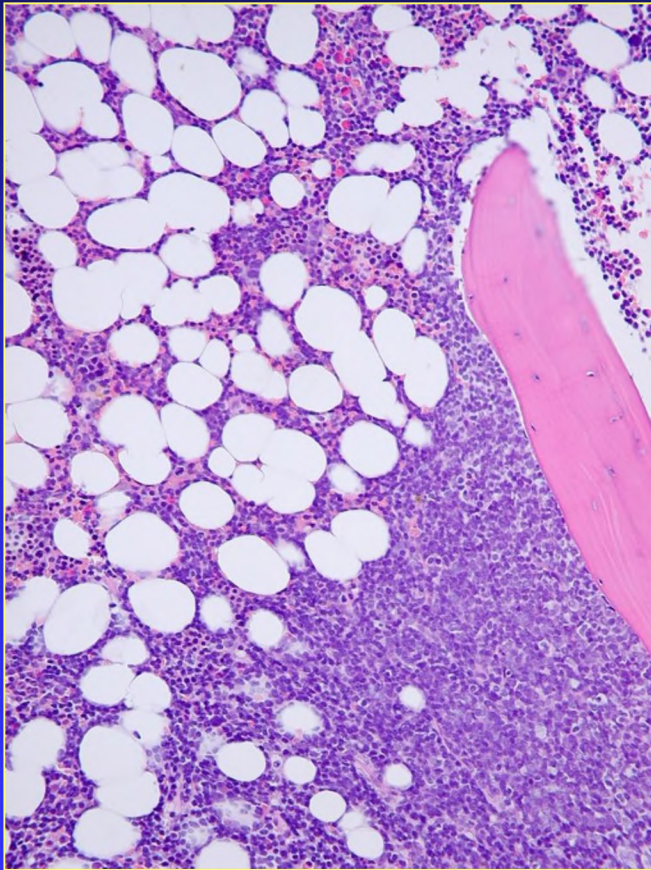
- IIIb may be more closely related to DLBCL than to FCC ?



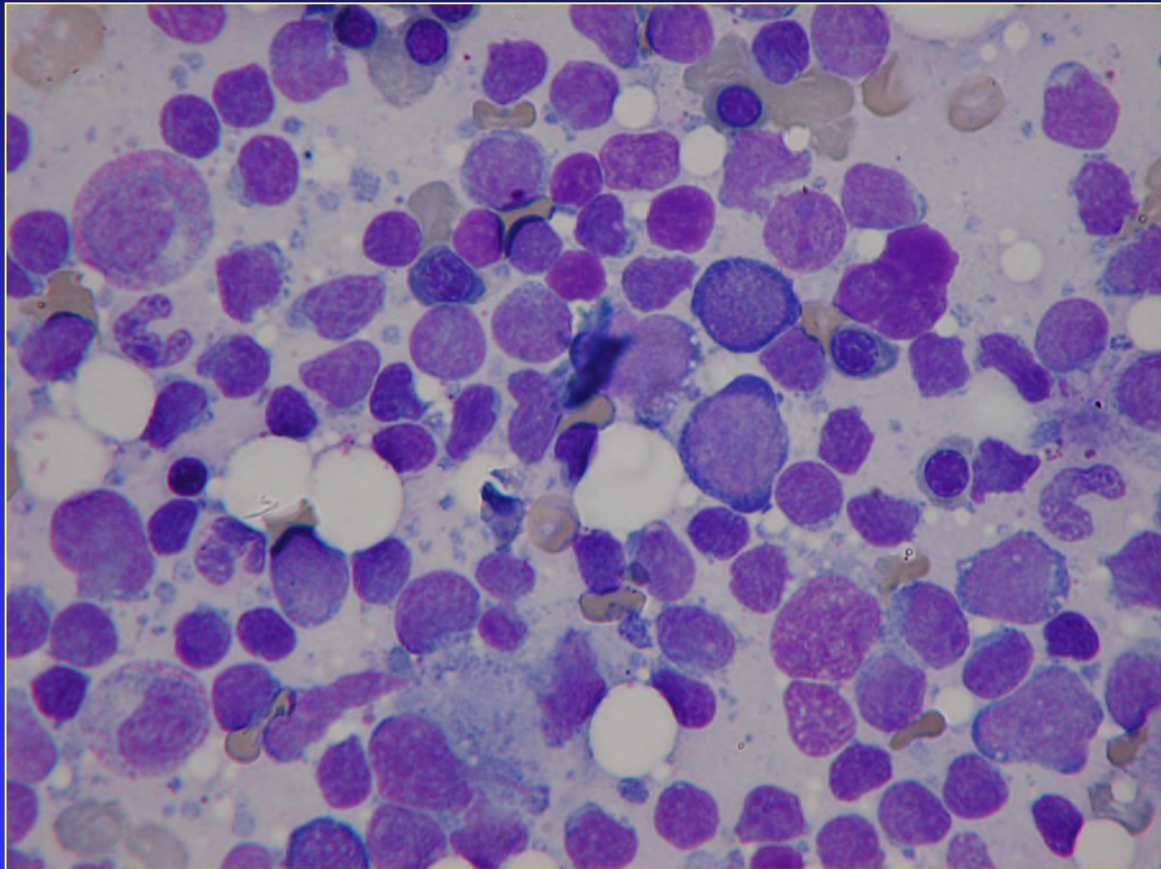
Follicular Lymphoma, bone marrow



Follicular Lymphoma, bone marrow



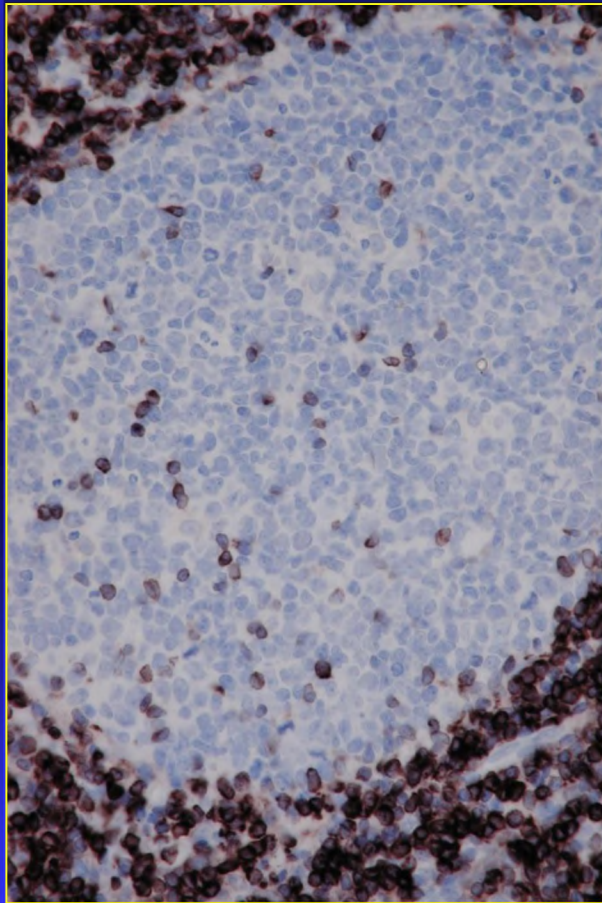
Follicular Lymphoma, bone marrow



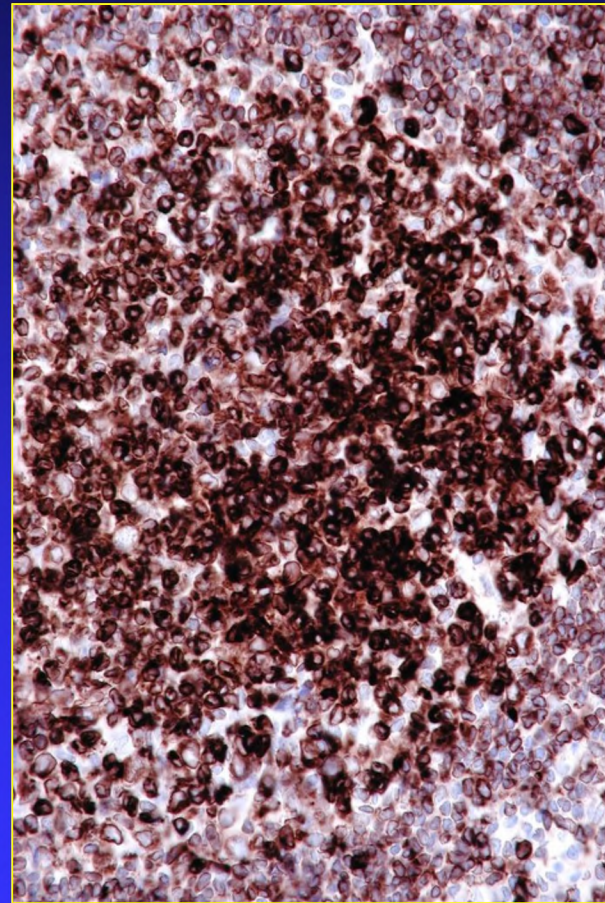
Phenotype

	CD20	CD10	Bcl-6	CD23	CD5
FL	+	+	+	-	-
CLL	+	-	-	+	+

Bcl-2



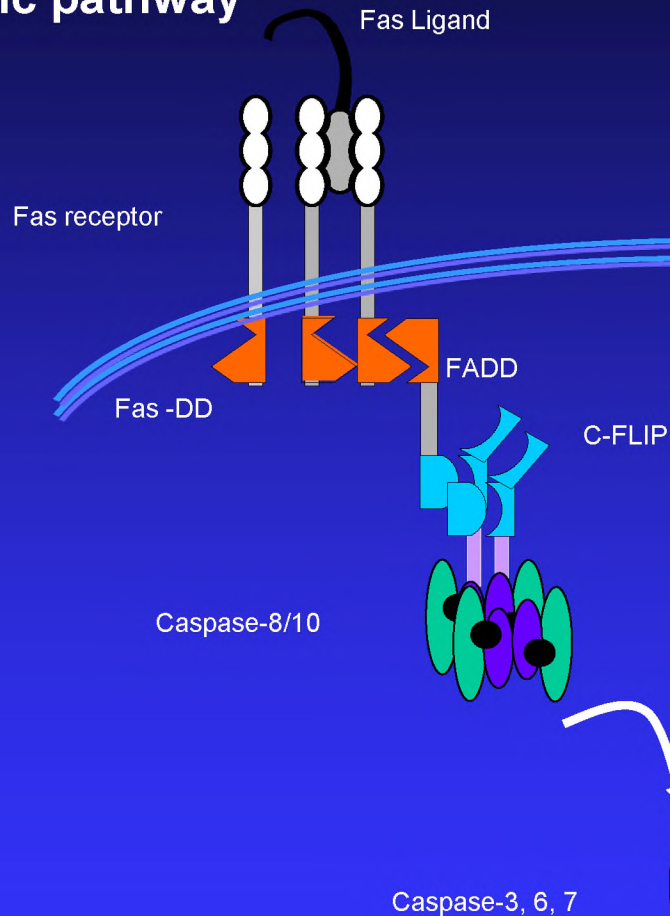
Normal follicle



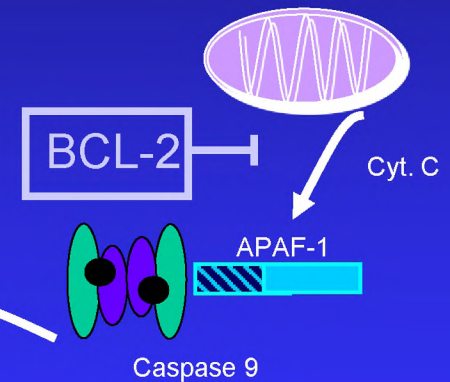
Neoplastic follicle

Pathways to apoptosis

Extrinsic pathway



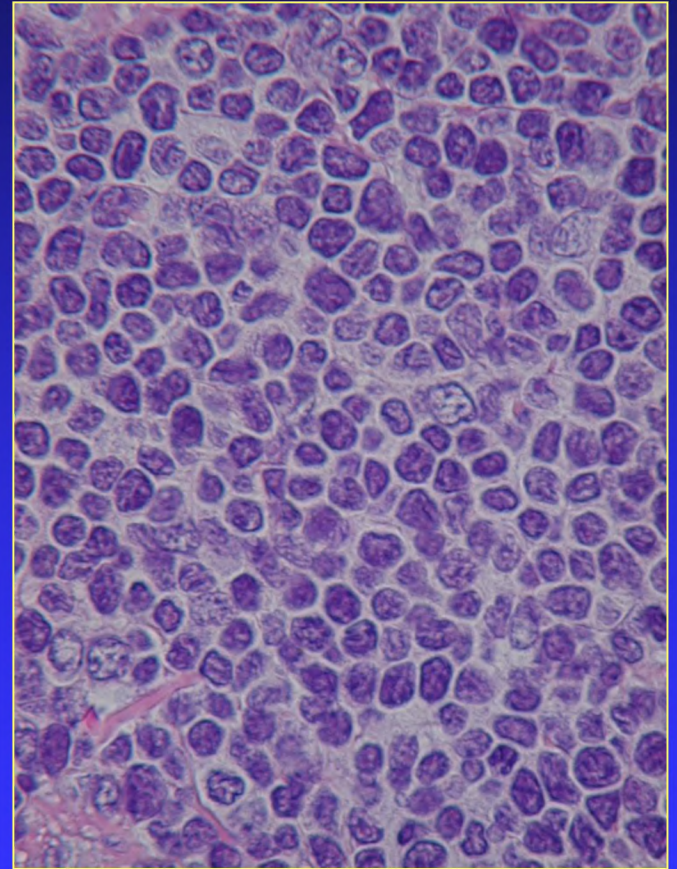
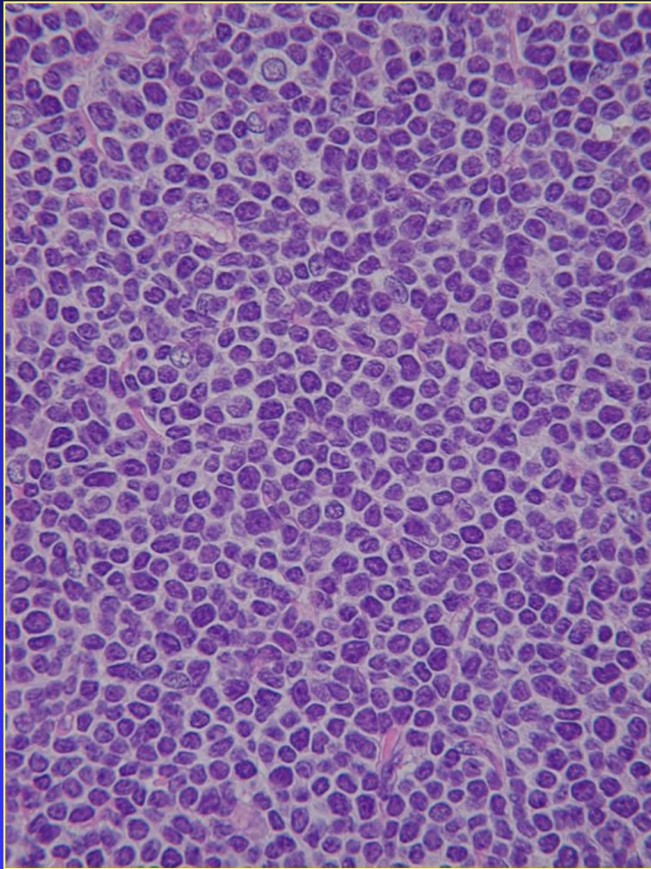
Intrinsic pathway



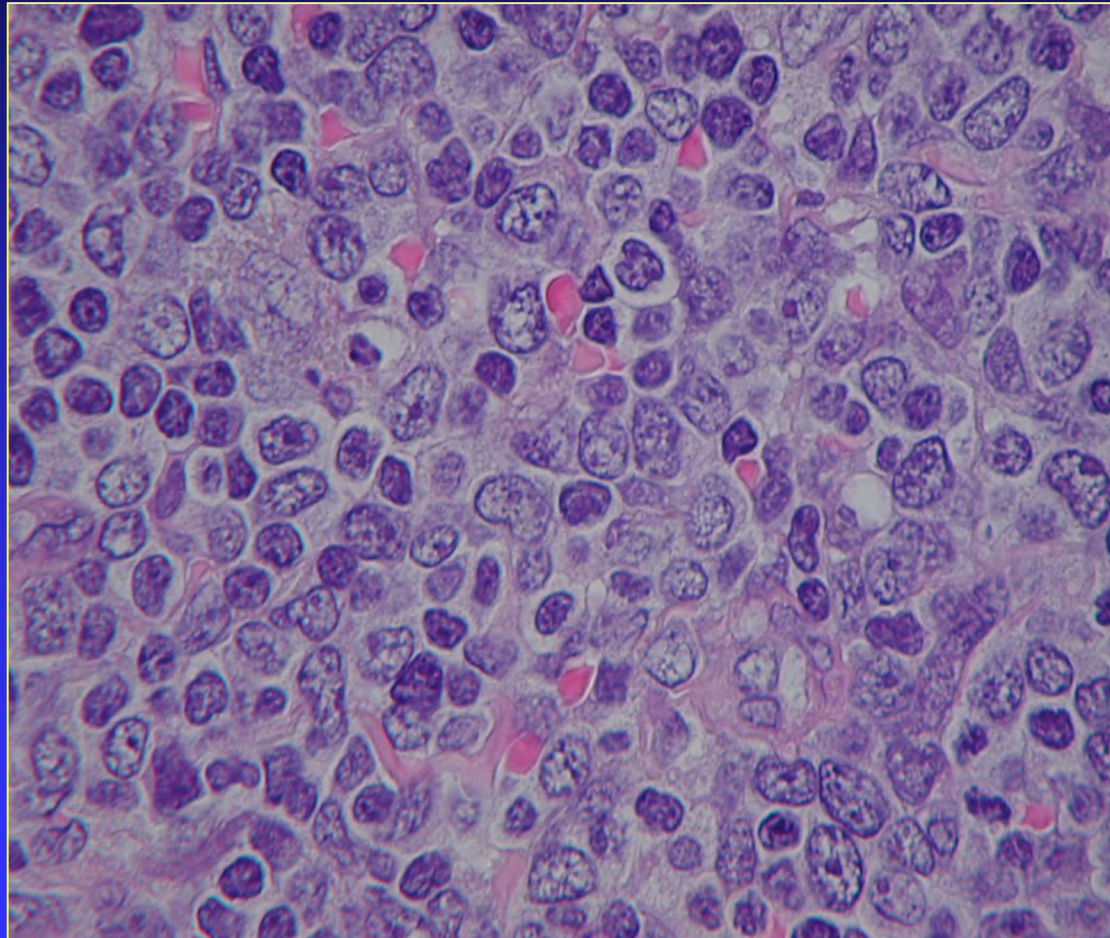
Mantle cell lymphoma

- Rare, elderly, disseminated, aggressive
 - Cleaved cells (centrocytes), small to medium
 - CD20+, CD79a+, CD5+, CD10-, Bcl-6-, CD23-
 - t(11;14), cyclin D1+
-
- Variants: Blastoid; pleomorphic; lymphomatous polyposis

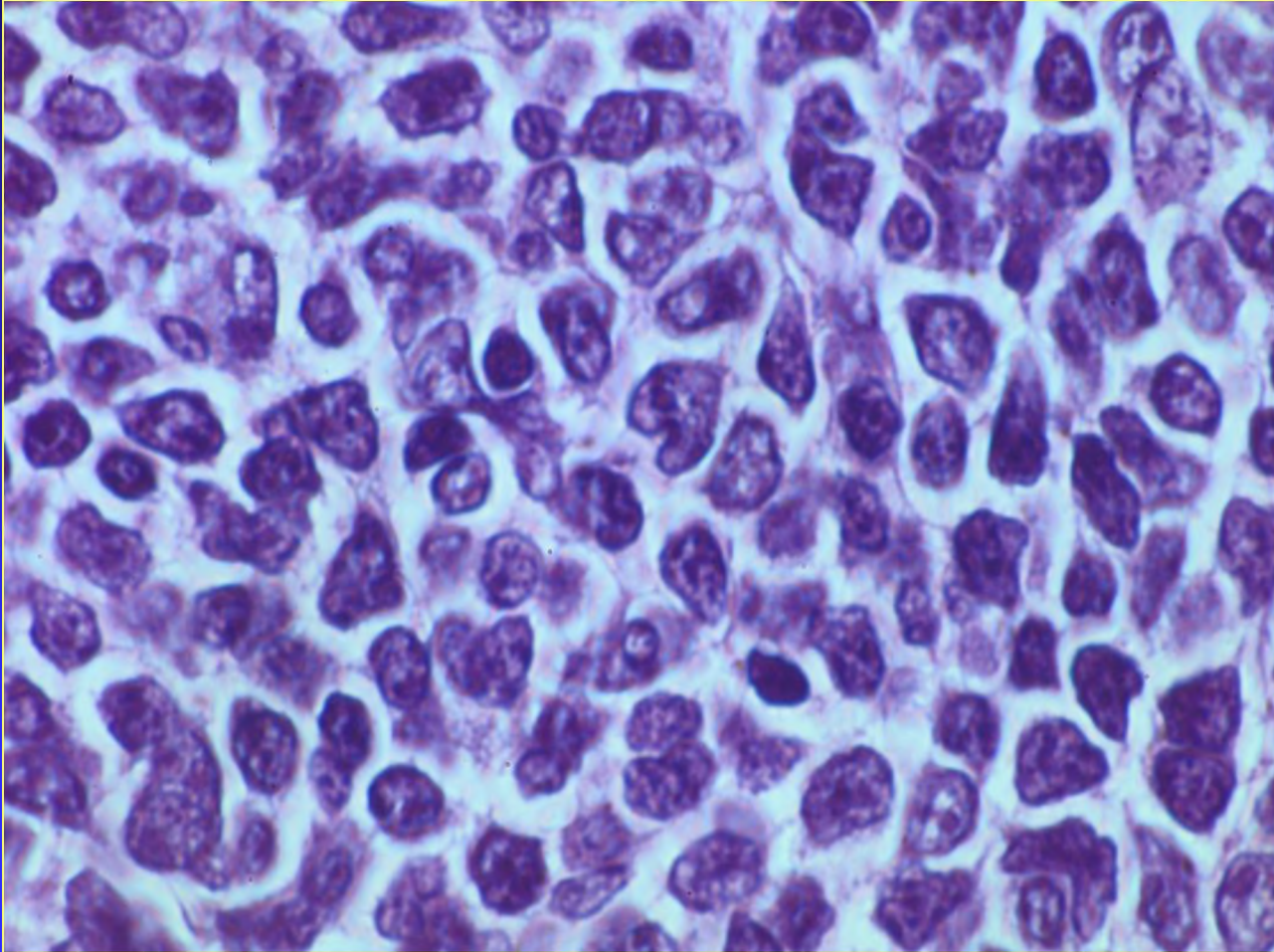
Mantle cell lymphoma



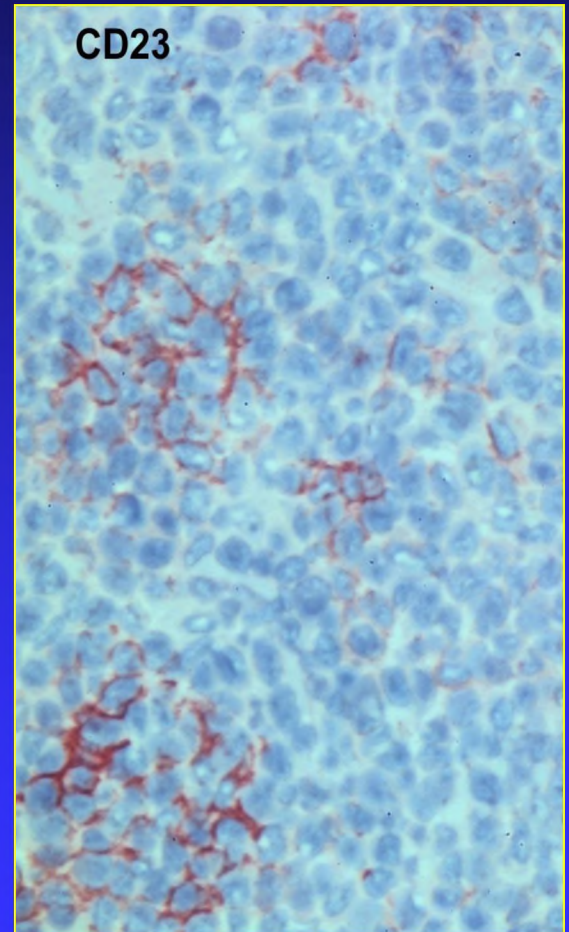
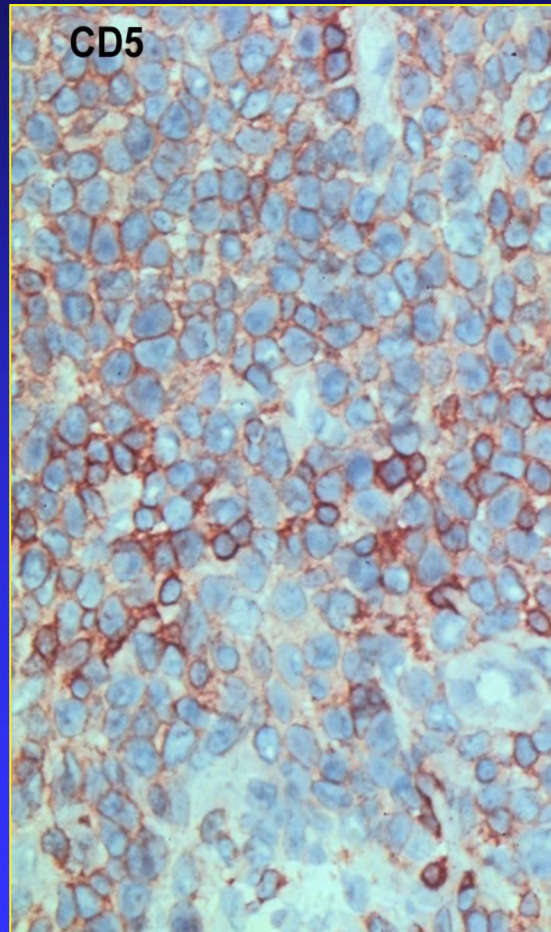
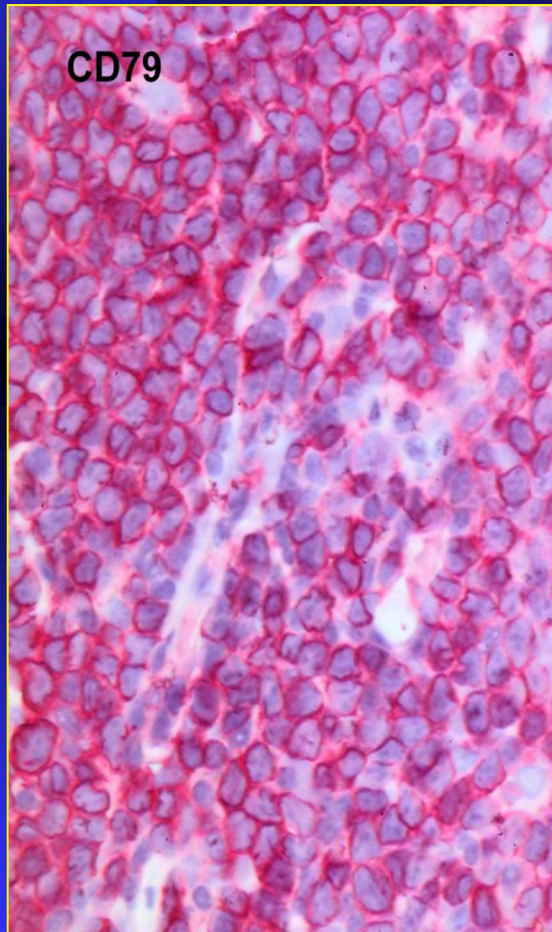
Mantle cell lymphoma



Mantle cell lymphoma



Mantle cell lymphoma



Phenotype

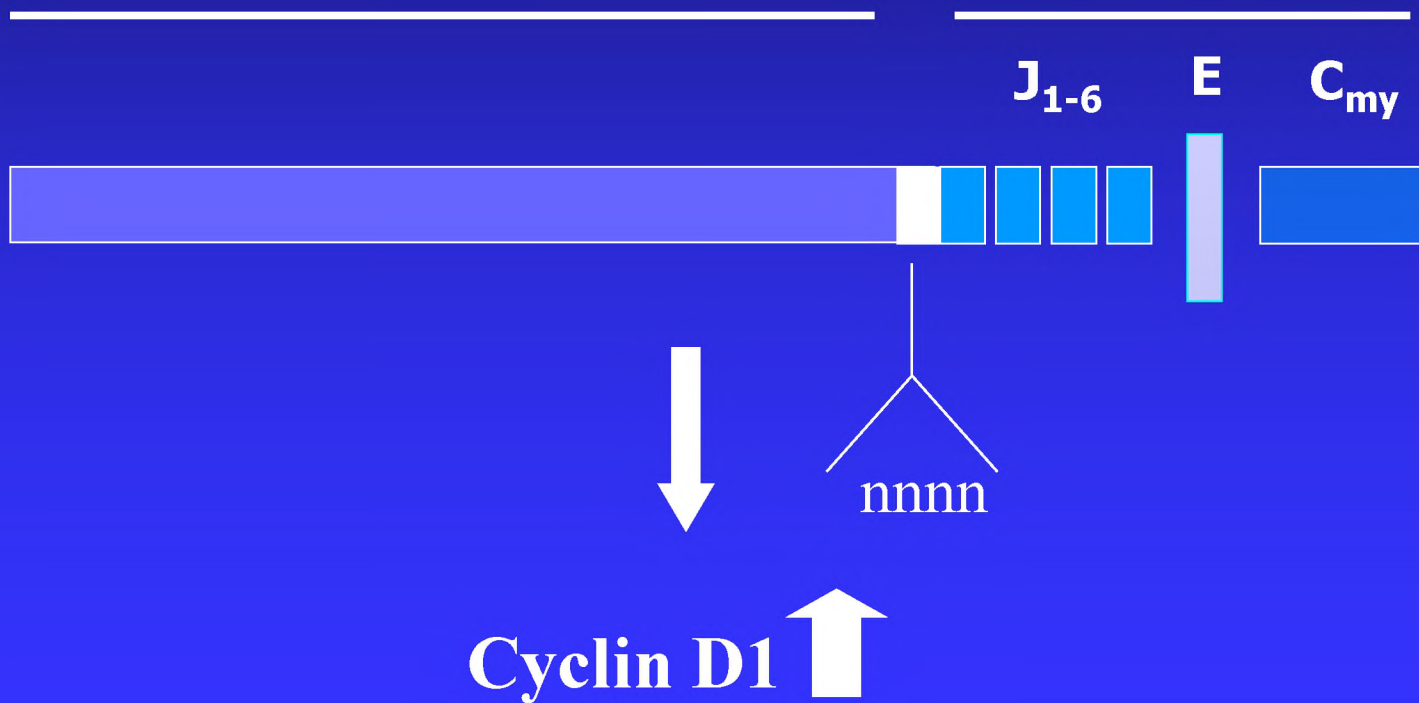
	CD20	CD10	Bcl-6	CD23	CD5
MCL	+	-	-	-	+
FL	+	+	+	-	-
CLL	+	-	-	+	+

t(11;14)

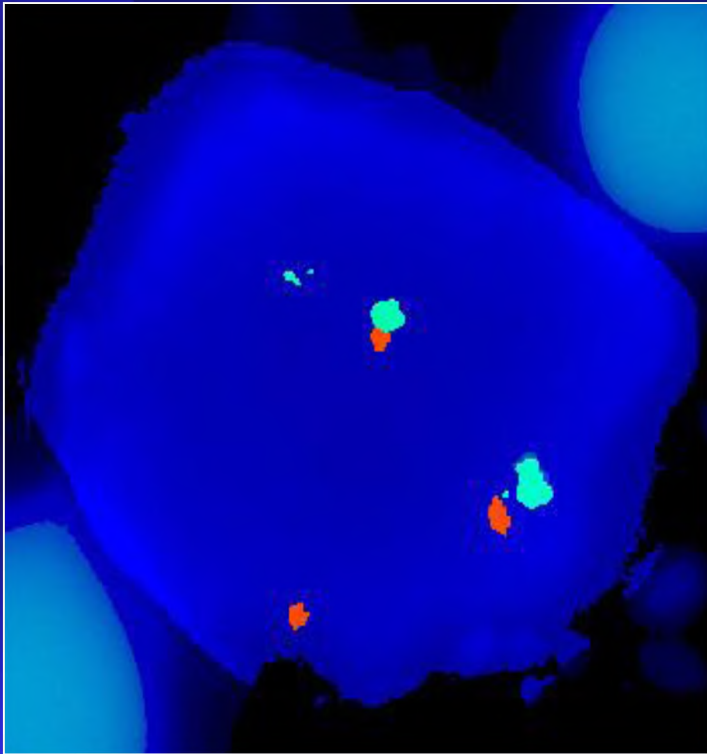
Chromosome 14+

Cyclin D1

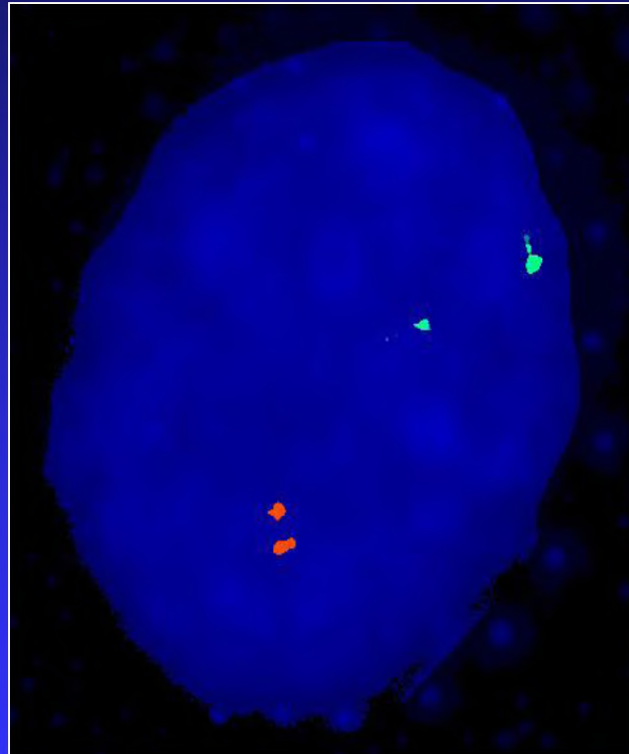
IgH



t(11;14)

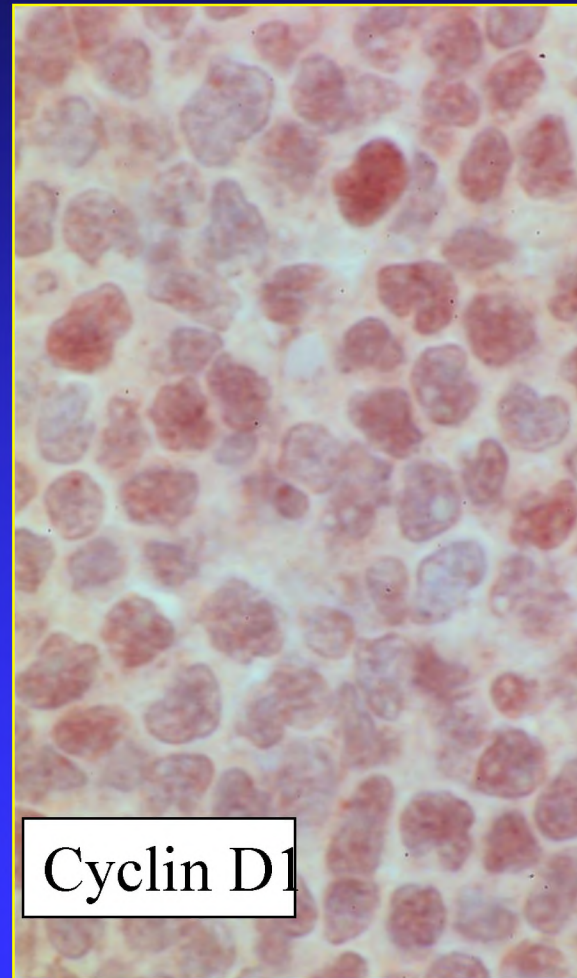
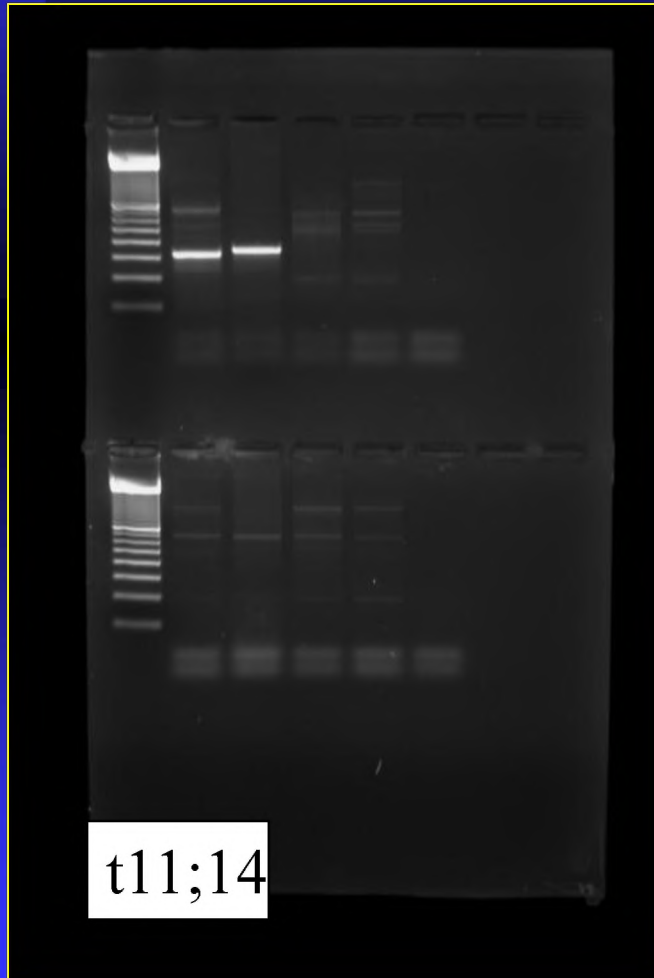


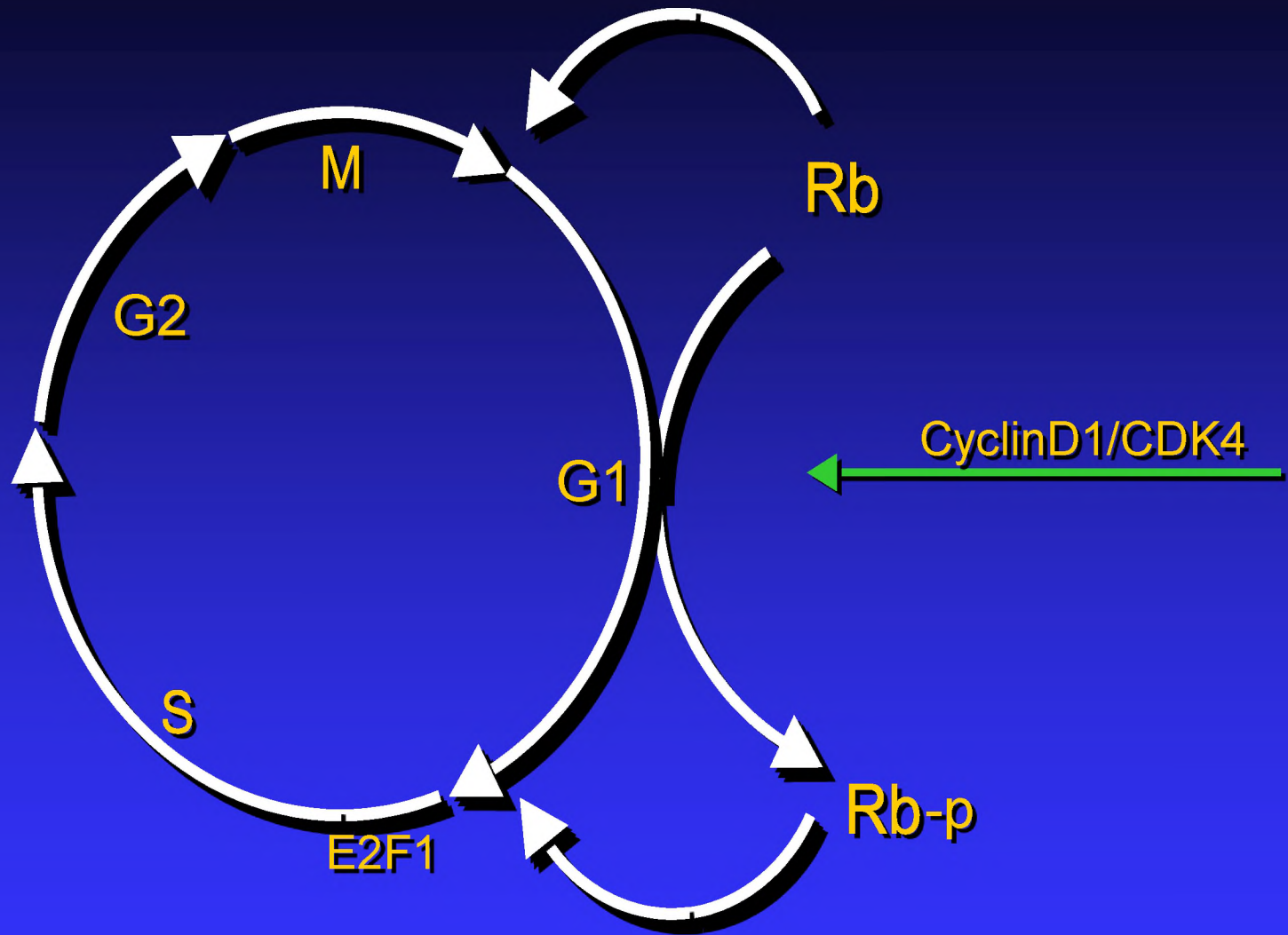
Mantle cell lymphoma



Control

Mantle cell lymphoma





Marginal Zone Lymphomas

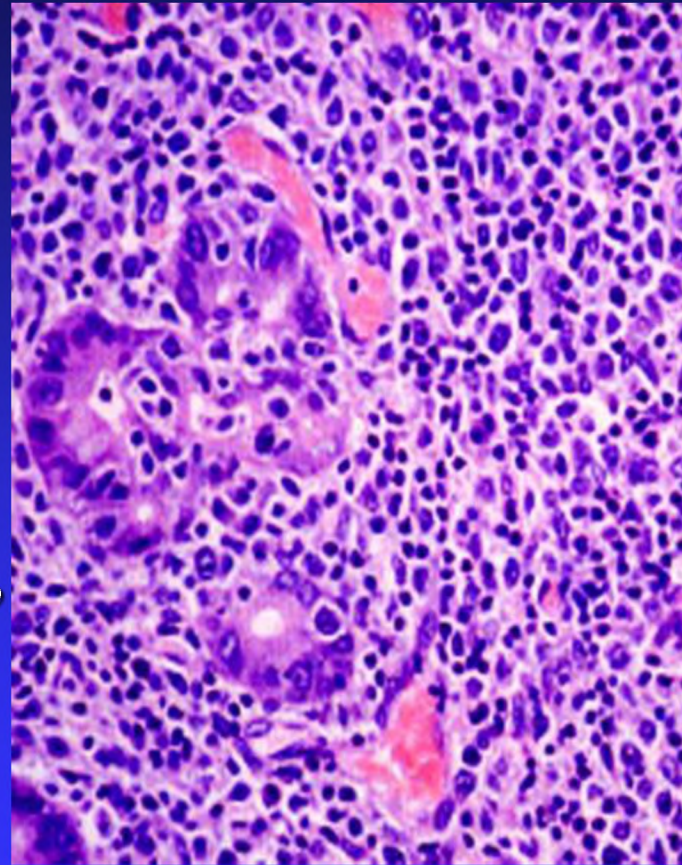
- Extranodal
- Nodal
- Splenic

Extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALT lymphoma)

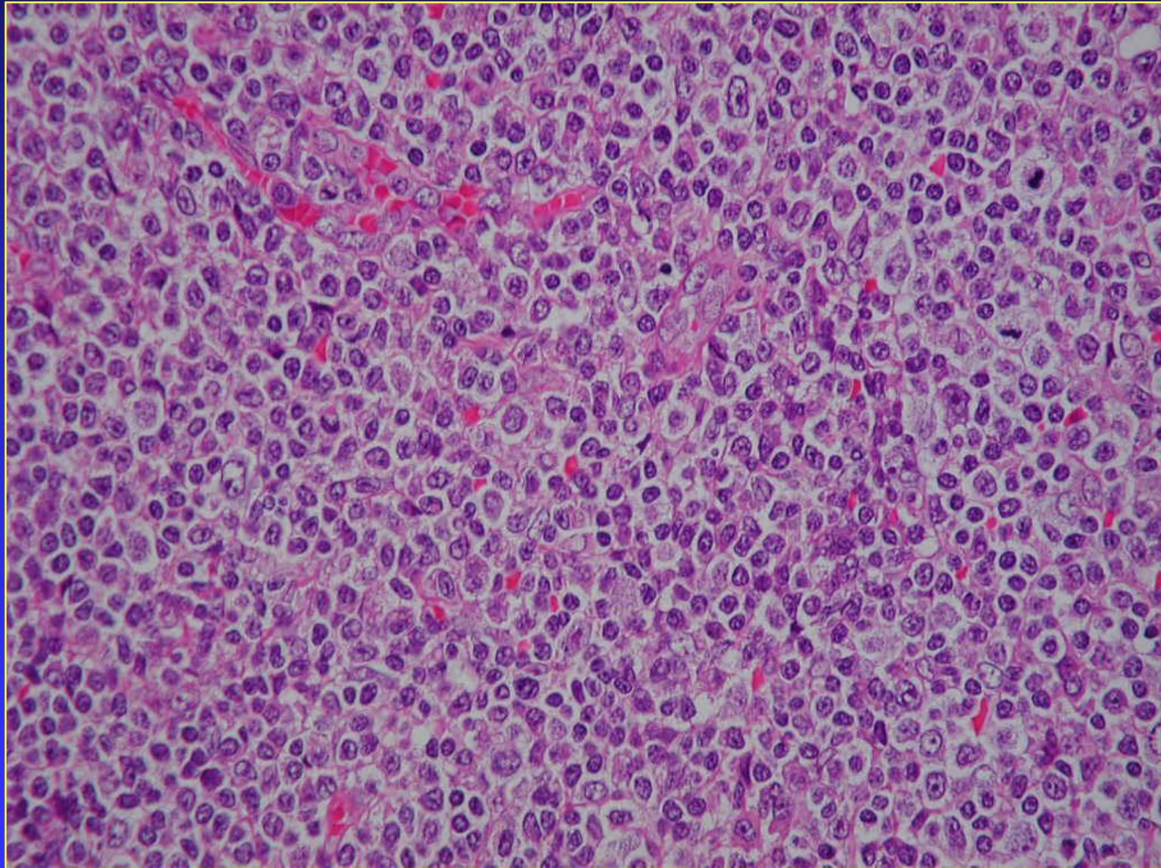
- Relatively frequent, elderly, $F > M$
- Stomach, thyroid, salivary glands, lung, skin, eye, breast
- Often localized, indolent
- Can transform to diffuse large B-cell lymphoma

MALT lymphoma

- Centrocyte-like cells, small lymphocytes, plasma cells
- Lymphoepithelial lesions
- CD20+, CD5-, CD10-, Bcl-6-, CD23-
- Trisomy 3; t(11;18); t(14;18) (Ig;MLT)



MALT lymphoma



Phenotype

	CD20	CD10	Bcl-6	CD23	CD5
MZL	+	-	-	-	-
FL	+	+	+	-	-
CLL	+	-	-	+	+
MCL	+	-	-	-	+

Large B-cell lymphomas

- Diffuse large B-cell lymphoma
- Mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- Primary effusion lymphoma
- Burkitt lymphoma

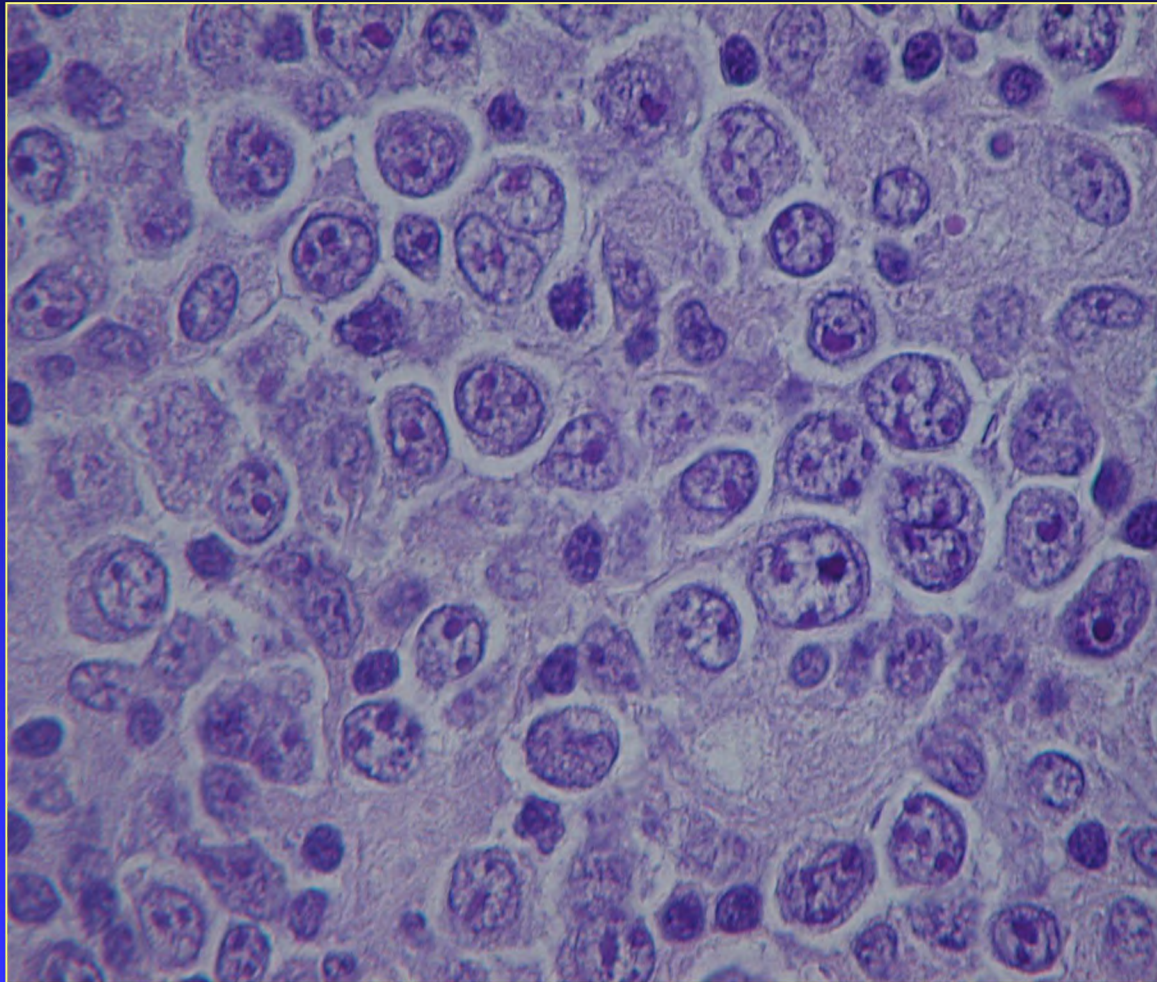
Diffuse large B-cell lymphoma

- Most frequent lymphoma in Western countries; incidence is increasing
- Different morphological variants
- No unique phenotype or genotype
- The overall 5-year survival is poor (50%)
- Behaviour is very different from one patient to another
- Presumably more than one entity

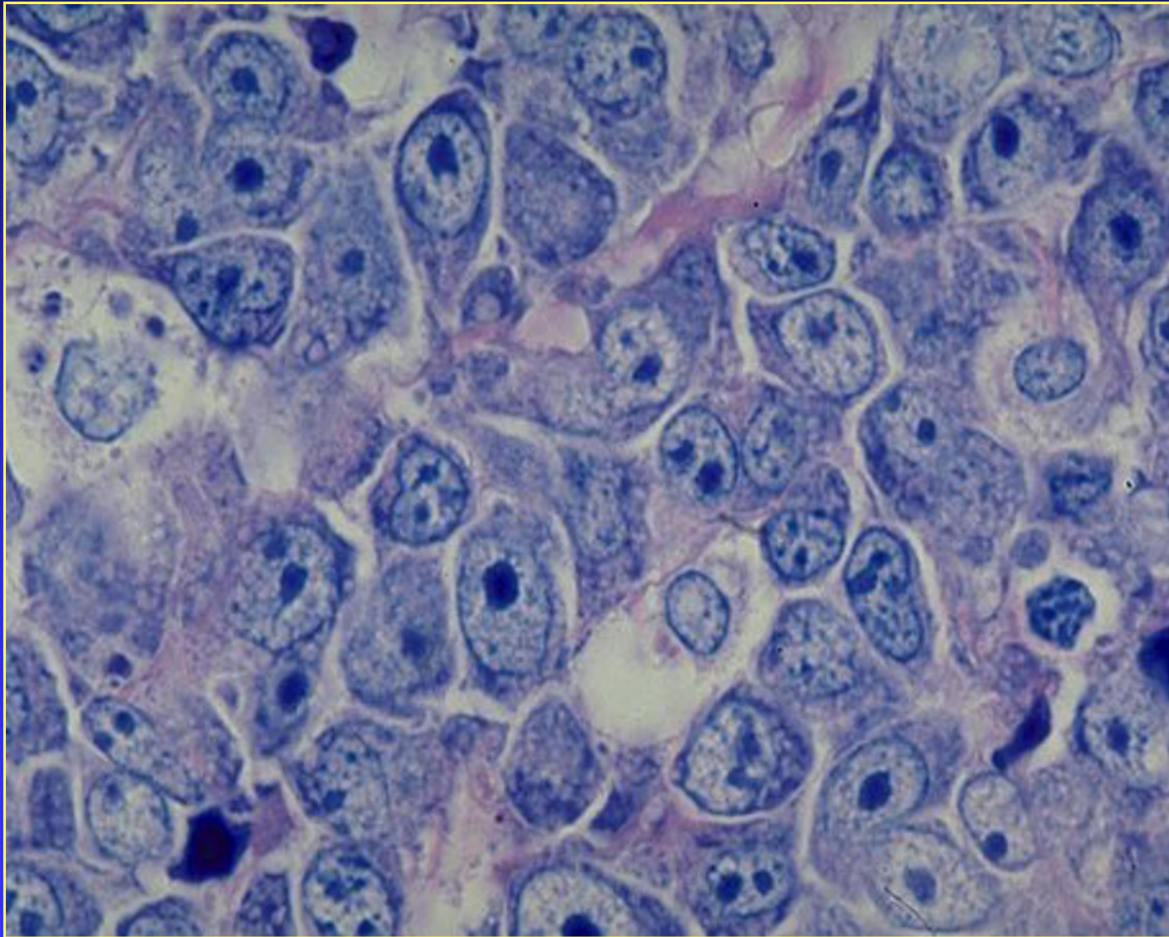
Diffuse large B-cell lymphoma

- Morphological variants
 - ◆ Centroblastic
 - ◆ Immunoblastic
 - ◆ Tcell/histiocyte rich
 - ◆ Anaplastic
 - ◆ Plasmablastic
 - ◆ Diffuse large B-cell lymphoma, ALK-positive

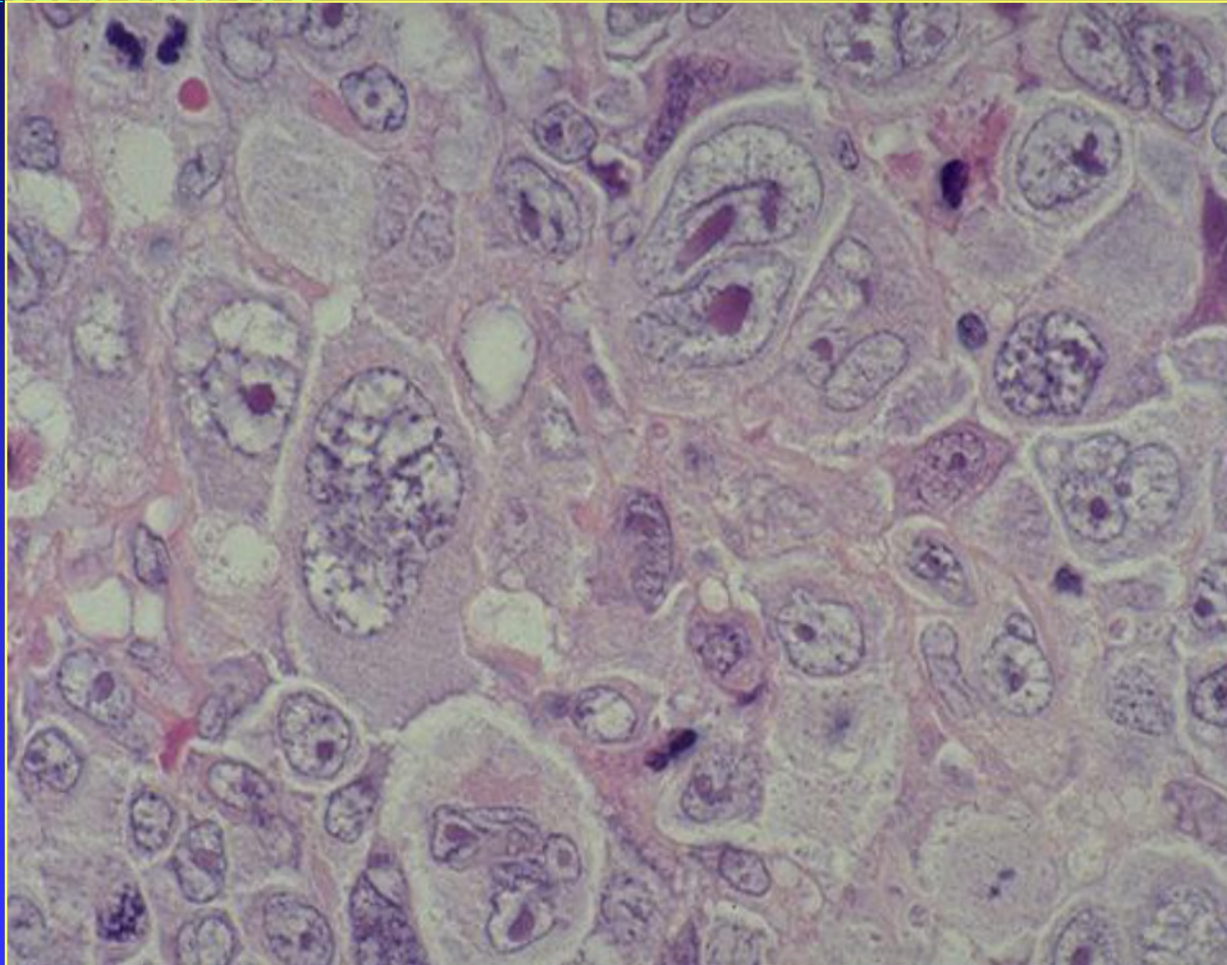
Diffuse large B-cell lymphoma, centroblastic



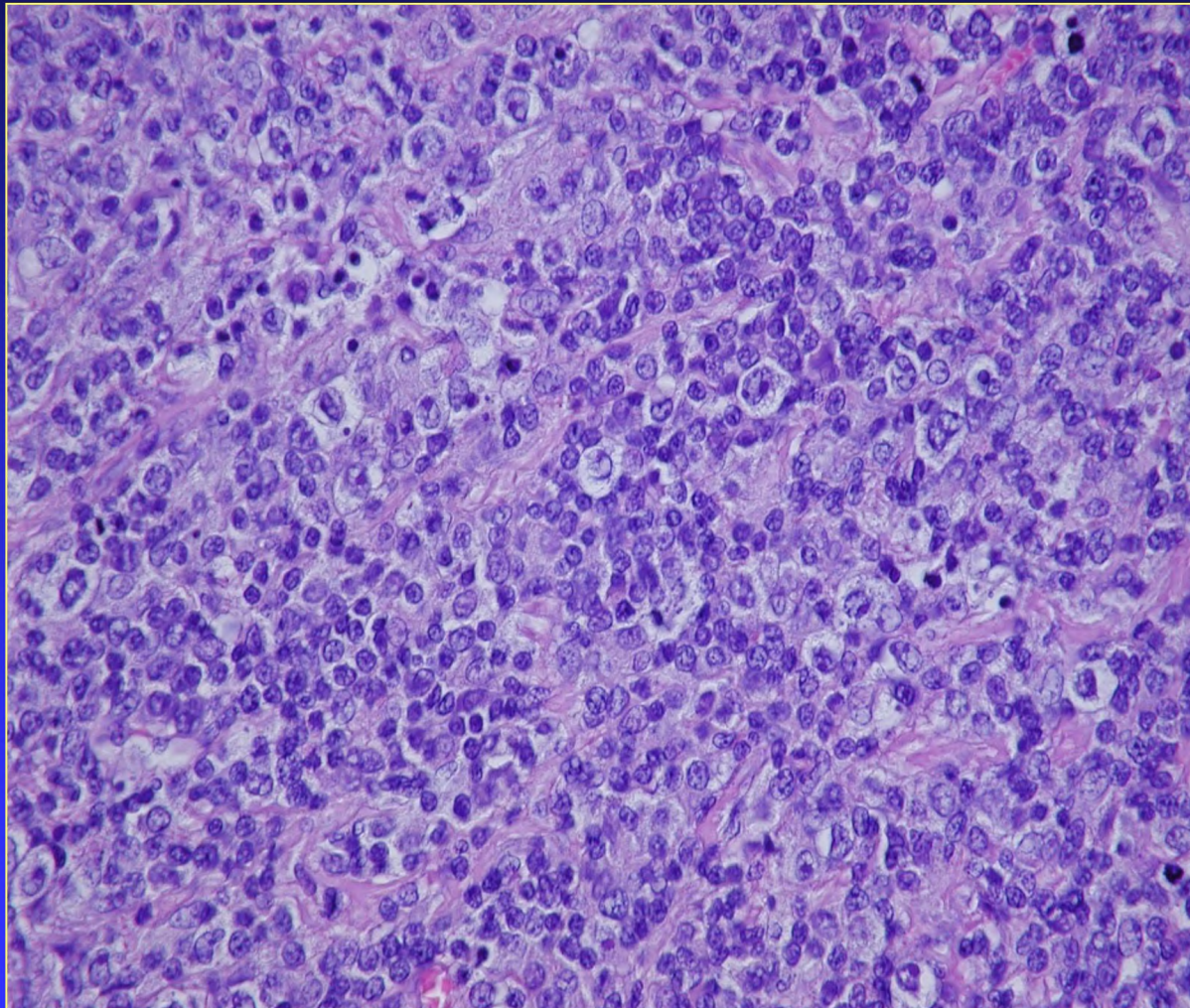
Diffuse large B-cell lymphoma, immunoblastic



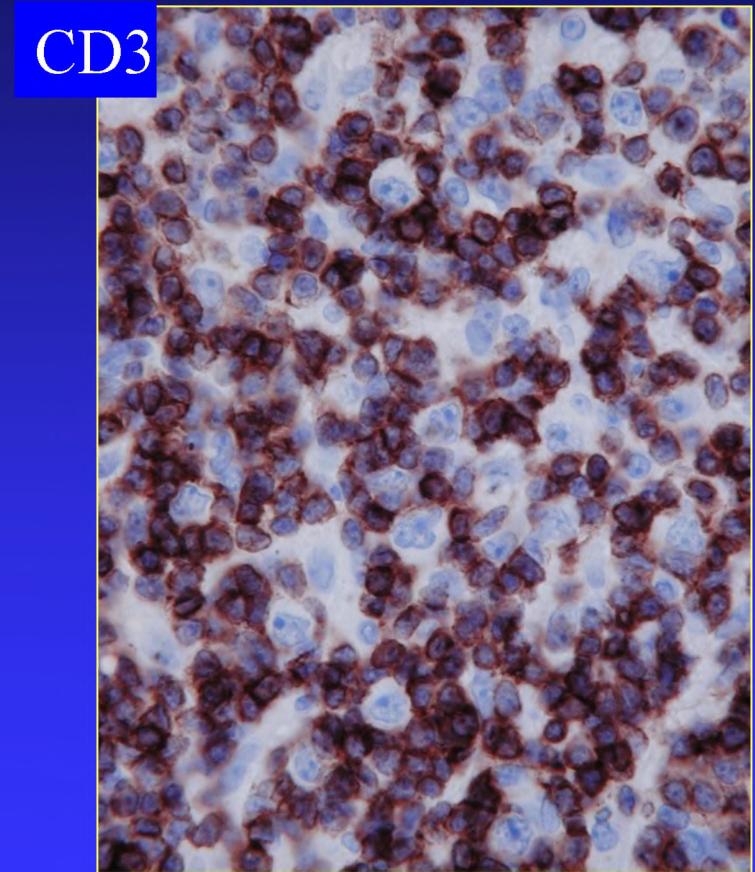
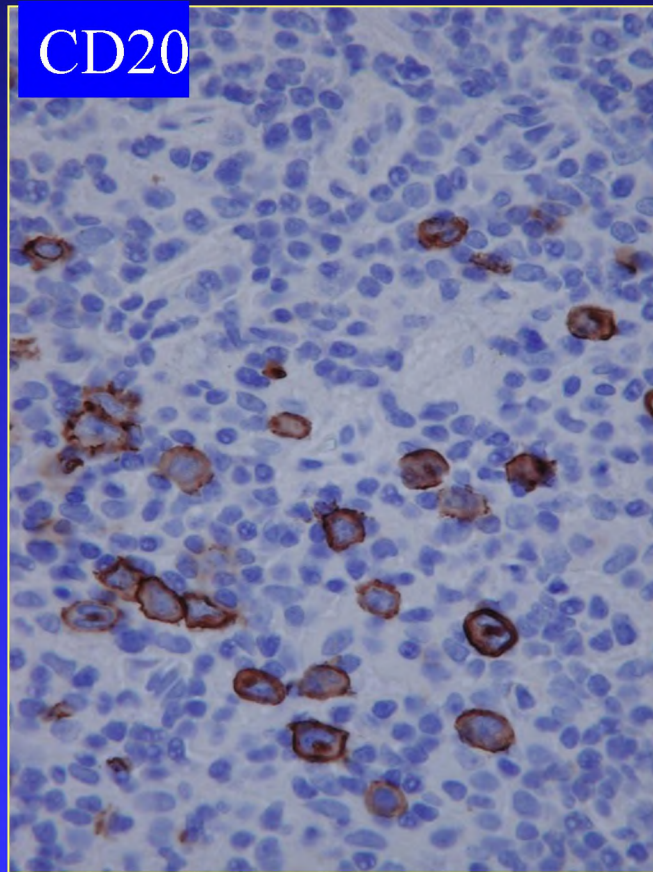
Diffuse large B-cell lymphoma, anaplastic



T-cell rich large B-cell lymphoma



T-cell rich large B-cell lymphoma



Small B-cell lymphomas, diagnostic procedures

Phenotypic

- ◆ Standard: CD20, CD79a, CD3, CD5, CD10, CD23, Bcl-2, Cyclin D1
- ◆ CLL: CD38, Zap 70
- ◆ HCL: DBA44, CD103, CD11c, CD25, TRAP

Genotypic

- ◆ t(14;18) (Ig;Bcl2); t(11;14) (Cyclin D1;Ig), t(14;18) (Ig;MALT)
- ◆ IgH clonal R; IgVH mutations

Large B-cell lymphomas

- Diffuse large B-cell lymphoma
- Mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- Primary effusion lymphoma
- Burkitt lymphoma

Acute Leukemias

- Acute myeloid leukemia
- Acute lymphoblastic leukemia

Acute leukemia

- Acute leukemia is characterized by a rapid increase in the number of immature blood cells. The crowding that results from such cells makes the bone marrow unable to produce healthy blood cells. Immediate treatment is required in acute leukemia because of the rapid progression and accumulation of the malignant cells, which then spill over into the bloodstream and spread to other organs of the body. Acute forms of leukemia are the most common forms of leukemia in children.

Chronic leukemia

- Chronic leukemia is characterized by the excessive buildup of relatively mature, but still abnormal, white blood cells. Typically taking months or years to progress, the cells are produced at a much higher rate than normal, resulting in many abnormal white blood cells. Whereas acute leukemia must be treated immediately, chronic forms are sometimes monitored for some time before treatment to ensure maximum effectiveness of therapy. Chronic leukemia mostly occurs in older people, but can occur in any age group.

Specific types

- Acute lymphoblastic leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)
- Acute myelogenous leukemia (AML)
- Chronic myelogenous leukemia (CML)
- Hairy cell leukemia (HCL)
- T-cell prolymphocytic leukemia (T-PLL)
- Large granular lymphocytic leukemia
- Adult T-cell leukemia
- Clonal eosinophilias

Acute myeloid leukemias

- A clonal expansion of myeloid blasts in bone marrow, blood or other tissue.
- Blast count in marrow 20 % or higher
- Four major categories:
 - a) AML with recurrent genetic abnormalities
 - b) AML with multilineage dysplasia
 - c) AML and MDS, therapy-related
 - d) AML not otherwise categorised

The diagnosis of AML

- Clinical features
- Morphology in blood, bone marrow or infiltrates
- Cytochemistry
- Immunohistochemistry
- Cytogenetics

Acute myeloid leukaemia

- The blast % is lowered from 30% (FAB) to 20% (WHO)
- Median age of onset = 60 yrs
- Incidence 4 –10 / 100,000
- Etiology

Clinical features

- In some cases pancytopenia, in others leucocytosis with many blasts.
- Bleeding disorders, disseminated intravascular dissemination, recurrent infections.
- Myeloid sarcomas at presentation (skin, bone structures and lymph nodes).

Morphology

- Myeloblasts: varying in size but larger than lymphocytes. Several nucleoli. Cytoplasm with no, few or many azurophilic granules, and/or Auer rods.
- Blast count: erythroblasts are counted separately. Myeloblasts, abnormal promyelocytes, monoblasts and promonocytes included in blast count.

Cytochemistry

- **Myeloperoxidase***:** specific for myeloid differentiation (some monoblasts). Peroxidase can be detected in unstained smears for up to 4 weeks.
- **Sudan Black B*:** reactivity for myelo- and monoblasts. Less specific than MPO.
- **Non-specific esterase (ANA)*:** reacts with lympho- and myeloblasts. In monoblasts ANA-positivity can be inhibited with the addition of fluorid, this can also happen in lymphoblasts.

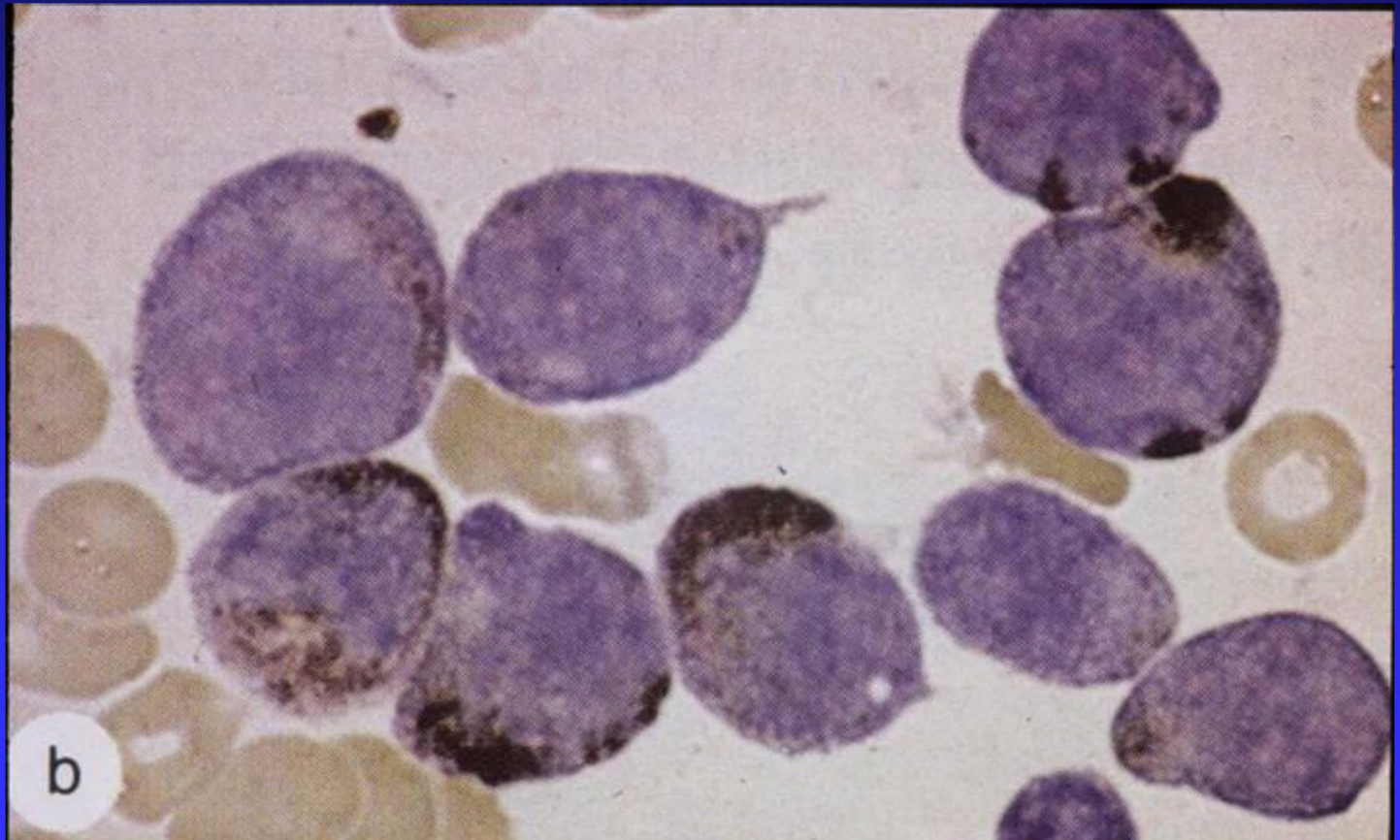
Cytochemistry

CYTOCHEMICAL PROFILES OF ACUTE LEUKEMIAS

	MPO/SBB	CAE	NSE	PAS	Acid Phosphatase
Acute lymphoblastic leukemia	–	–	+/– (focal)	+ (75%)	+/– (focal T-cell ALL)
Acute myeloid leukemia	+	+	+ (monocytic, diffuse)	–/+	+

MPO = Myeloperoxidase, SBB = Sudan black B, CAE=Chloroacetate esterase, NSE = Nonspecific esterase,
PAS = Periodic acid–Schiff.

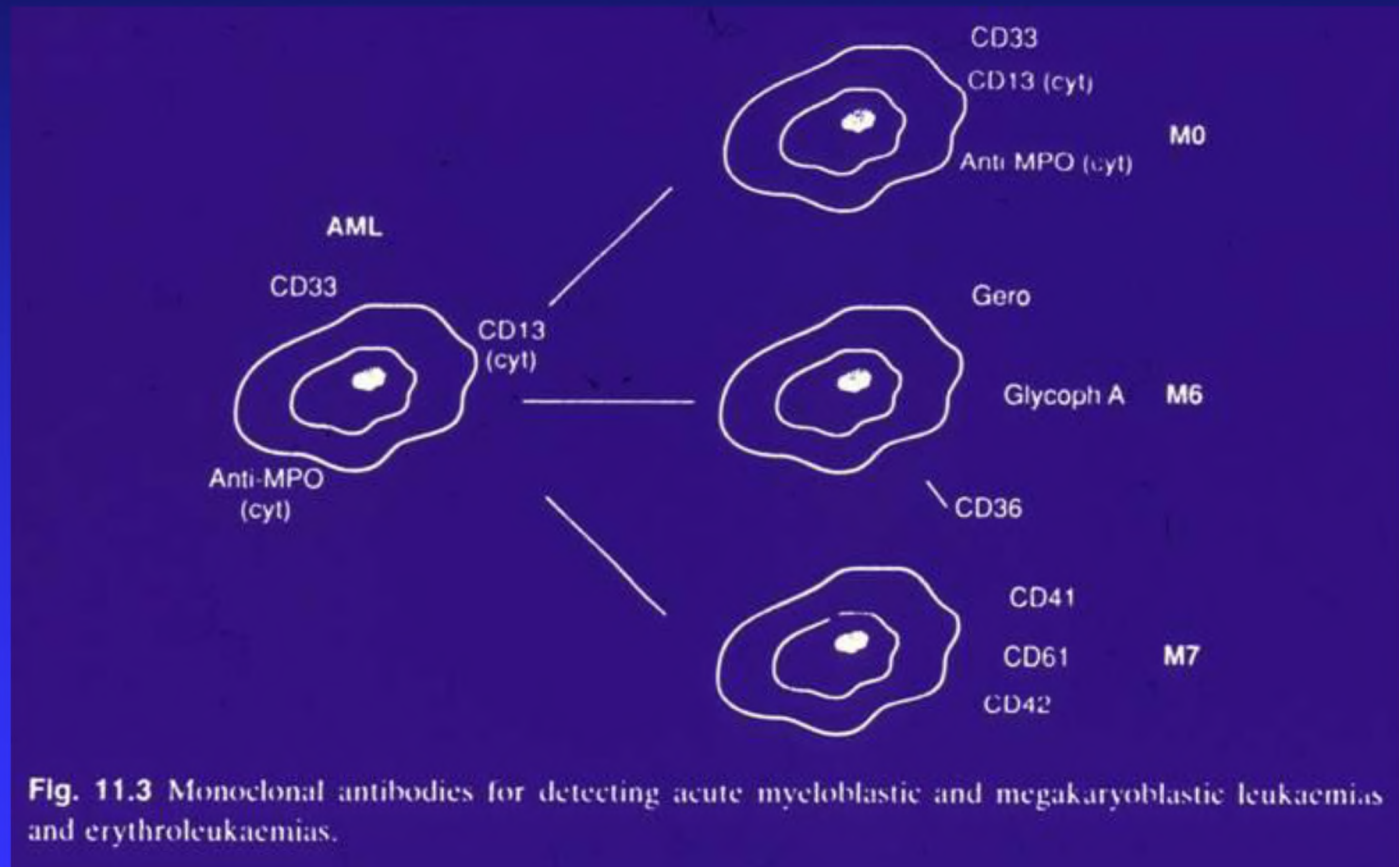
Cytochemistry: MPO



Immunophenotyping

- Important to distinguish between ALL and AML.
- Flow cytometry often superior to IHC.
- Combining IHC and flow cytometry makes accurate lineage ID possible.

Acute myeloid leukaemia: role of immunophenotyping



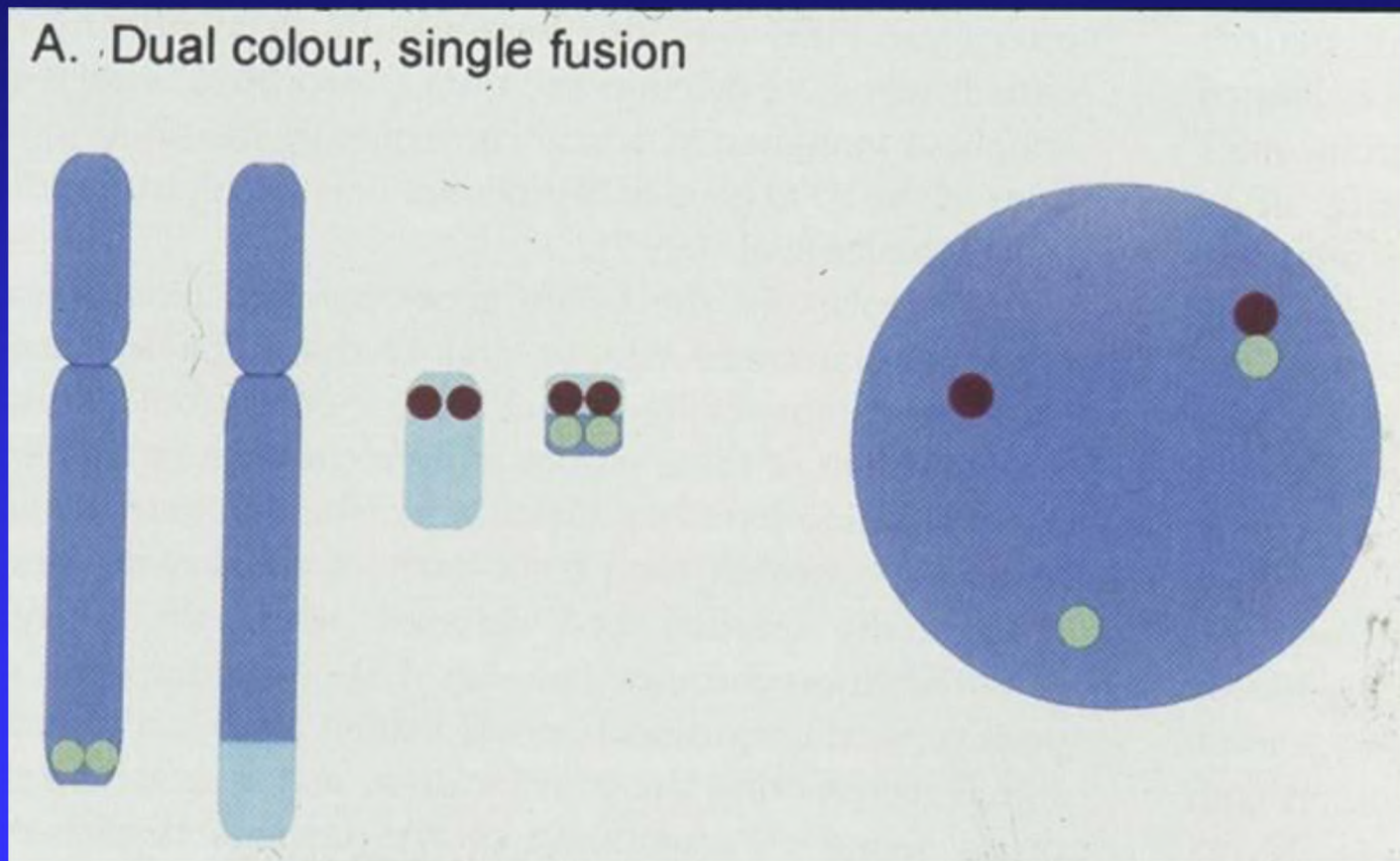
WHO's panel

- Precursors: CD34, CD45, HLA-Dr, Tdt
- B-lineage: CD19, CD20, CD22, CD79a
- T-lineage: CD2, CD3, CD5, CD7
- Myeloid: CD13, CD33, CD15, CD117, MPO
- Megakaryoblastic: CD41, CD61
- Suppl: MDR-1, glycophorin A, CD71.

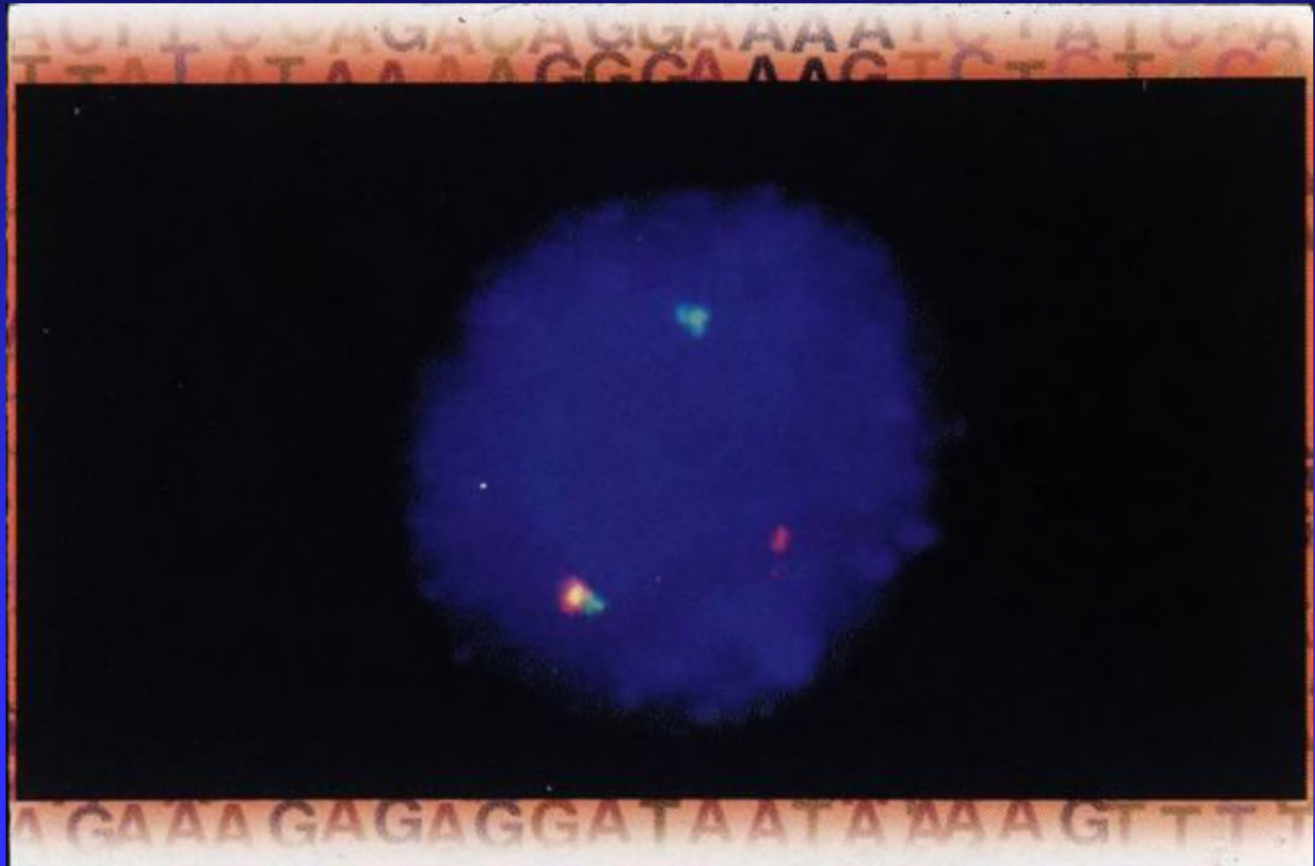
Cytogenetics

- Karyotyping
- Fluorescence in Situ Hybridisation (FISH)
- Polymerase Chain Reaction (PCR)

Detection of fusion genes by FISH



Detection of fusion genes by FISH



AML with recurrent genetic abnormalities

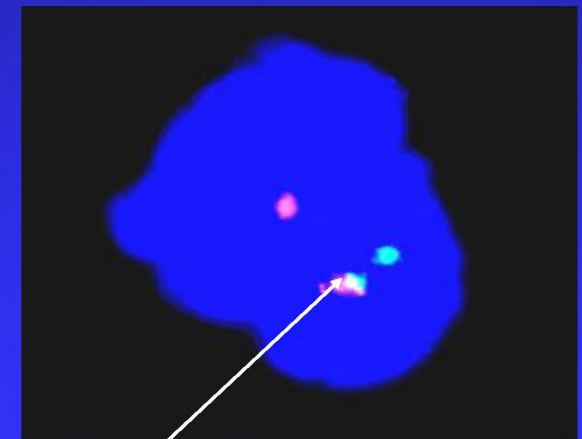
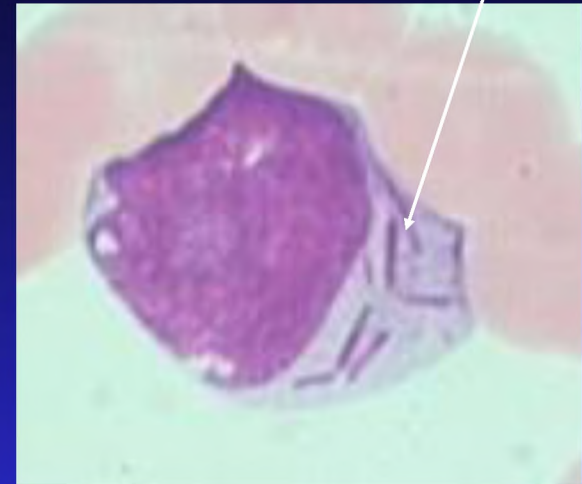
- AML with t(8;21)
- AML with abnormal eosinophils inv (16) or t(16;16)
- AML with rearrangement of 17q12 (acute promyelocytic leukemia)
- AML with 11q23 (MLL) rearrangement

AML with t(8;21)

5-12 % of AML

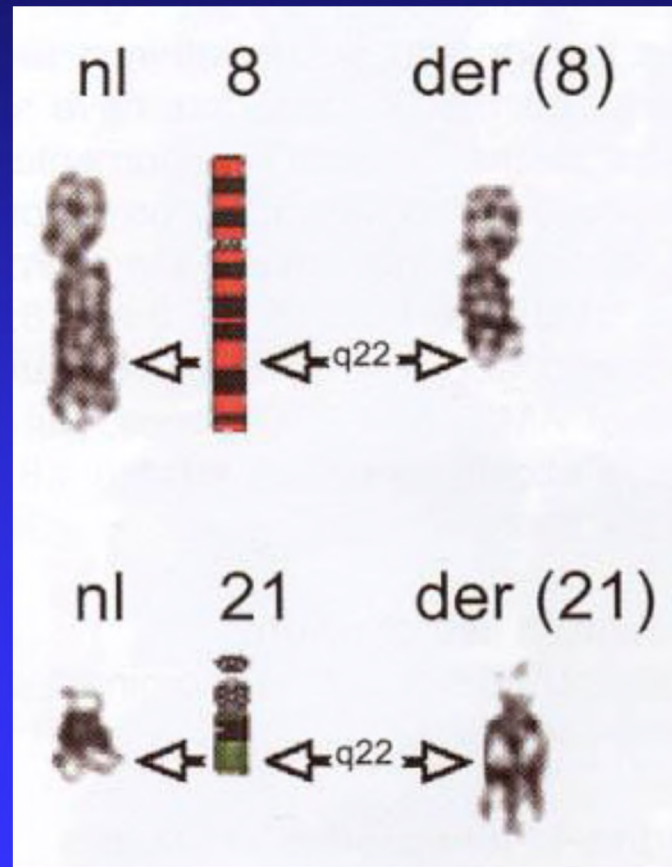
- AML with differentiation in neutrophil lineage
- Myeloid sarcomas may be present
- Younger patients
- T(8;21) is sufficient for AML-diagnosis
- Auer rods frequently found, even in mature neutrophils
- CD34, CD56, CD19 on some cells
- Good response to chemotherapy

Auer rods



T(8;21)

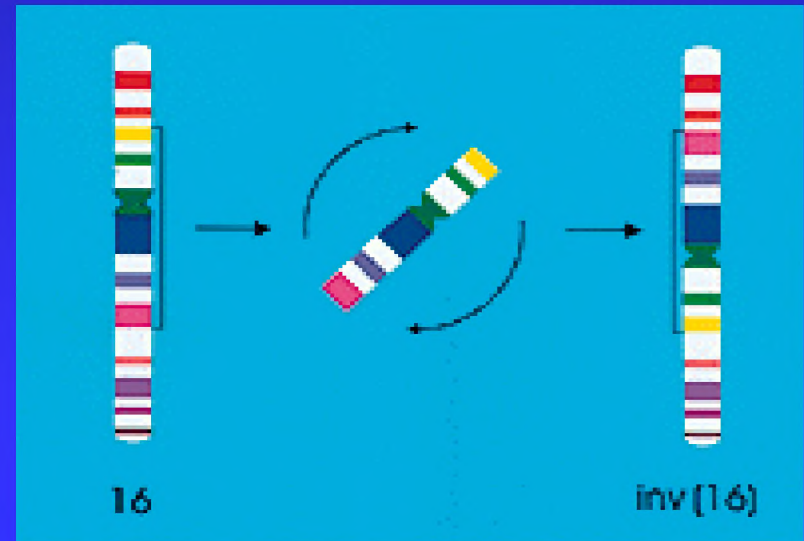
Acute myeloid leukaemia with $t(8;21)(q22;q22)$; *AML1/ETO*



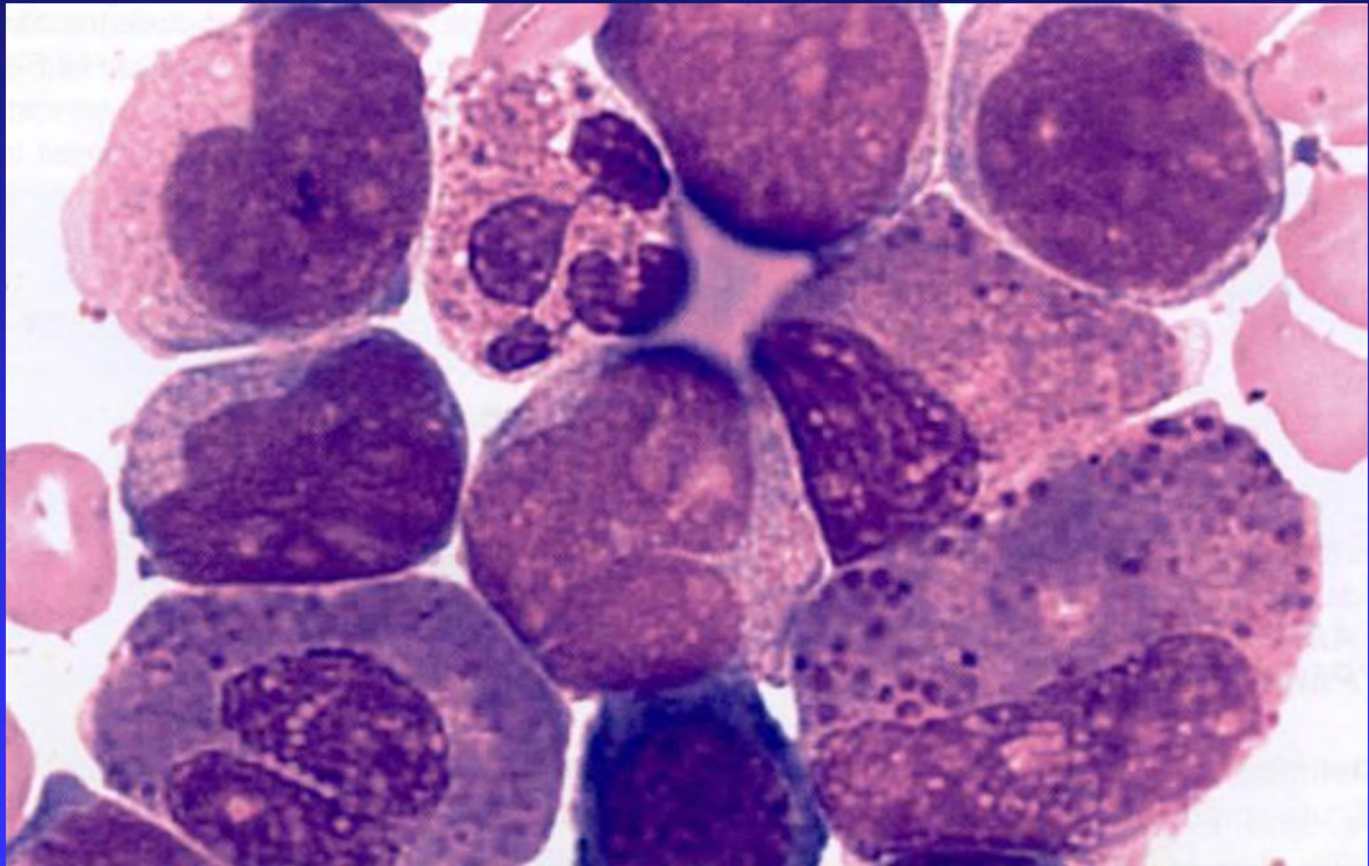
AML with inv(16) or t(16;16)

10-12 % of AML

- Monocytic/granulocytic
- Abnormal eosinophils
- Myeloid sarcoma may be present
- Auer rods can be present
- > 3 % MPO+ blasts
- Monocytic markers
- Favorable prognosis



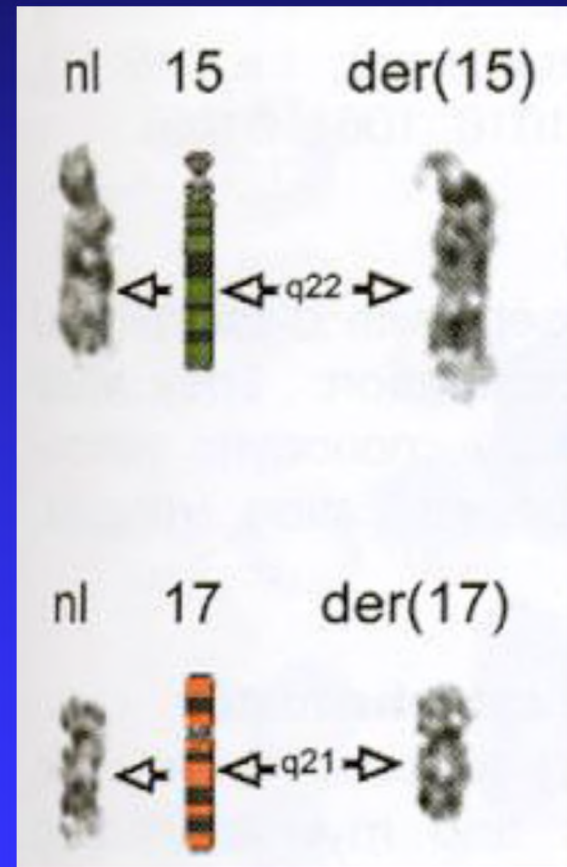
Acute myeloid leukaemia with $\text{inv}(16)(\text{p}13\text{q}22)$ or $\text{t}(16;16)(\text{p}13;\text{q}22)$; $\text{CBF}\beta/\text{MYH11}$



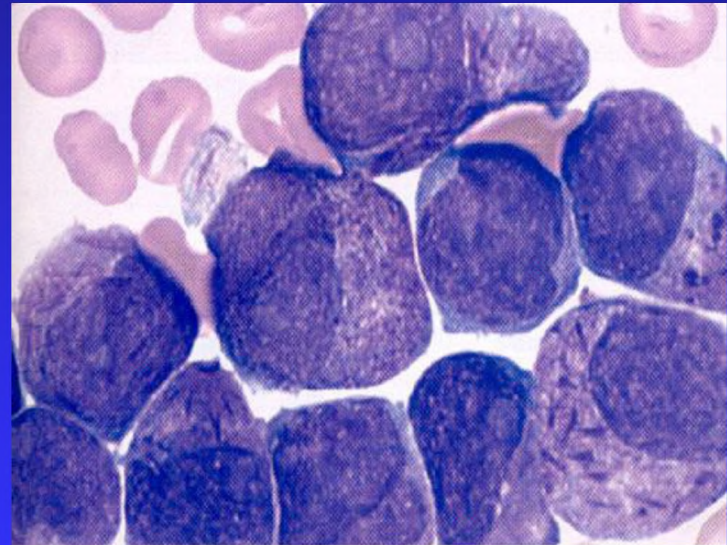
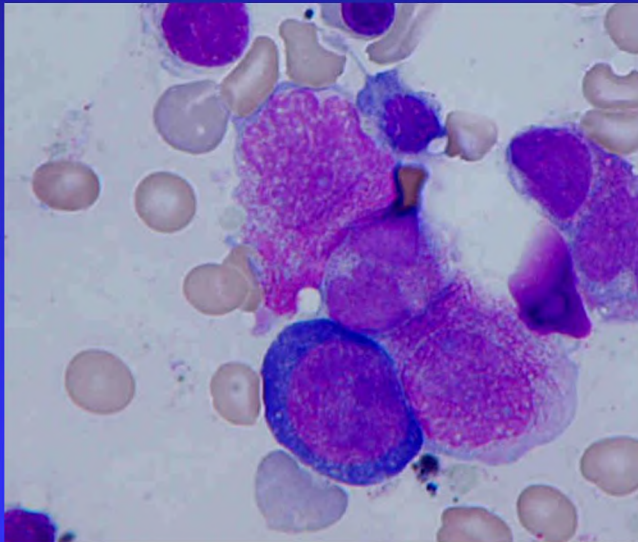
AML with t(15;17)

5-8 % of AML

- Middleaged
- Abnormal promyelocytes
- Hypergranular/microgranular
- Often present with DIC
- Variant translocations
- Treatment with ATRA – differentiation - favorable

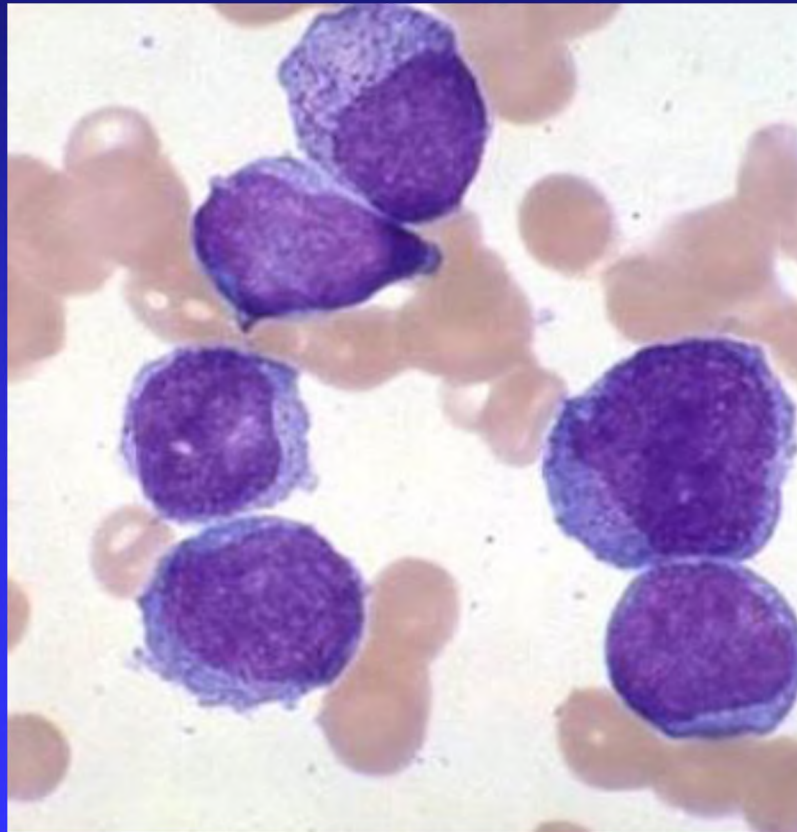


AML with t(15;17) promyelocytic leukaemia



AML with t(15;17)

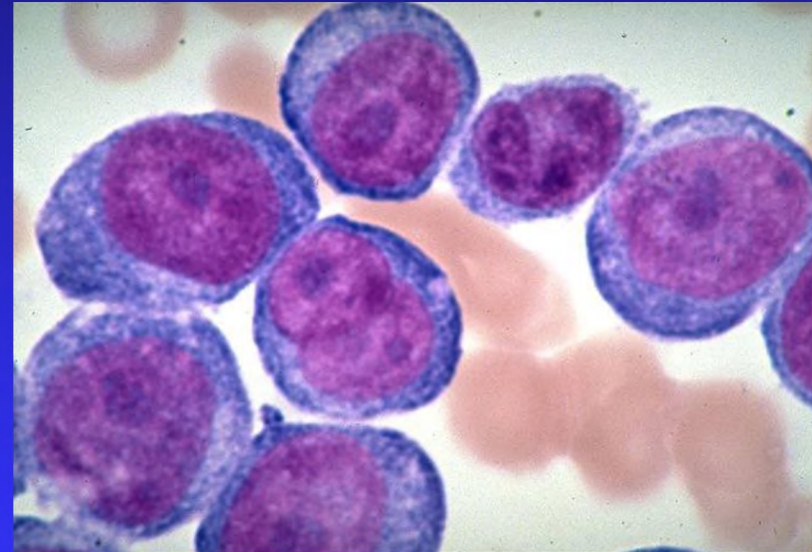
Microgranular variant



AML with 11q23 (MLL) rearrangement

5-6 % of AML

- More common in children (infants)
- Post-therapy AML
- May present with DIC
- Often myelomonocytic features
- MLL gene is involved translocations with up to 20 partner chromosomes
- Intermediate survival

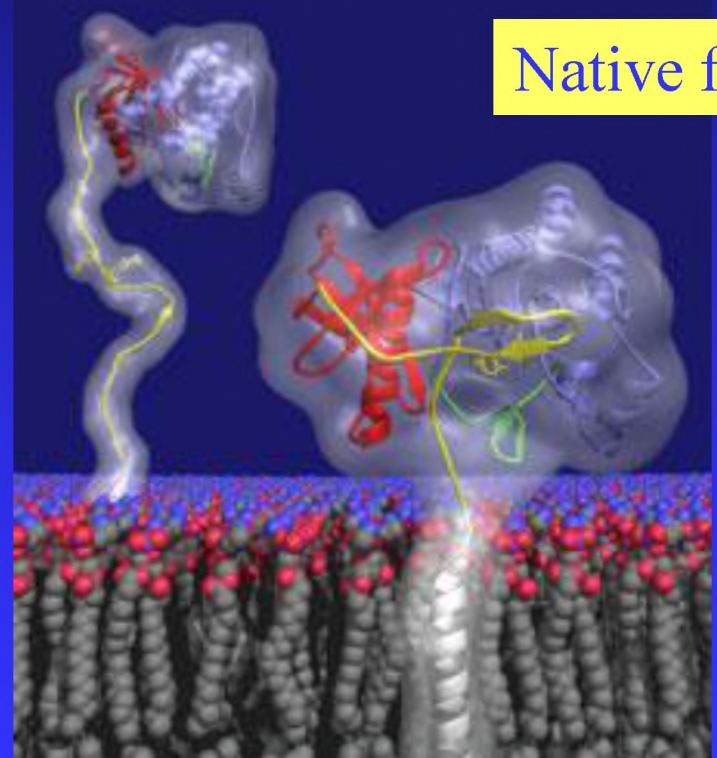


AML with Flt3 abnormalities

- Flt3 is a tyrosin kinase on haematopoietic cells
- Flt3 activating abnormalities on 30 % of AML
- Causes cell proliferation, inhibition of apoptosis and blocking of cell differentiation

Mutated form

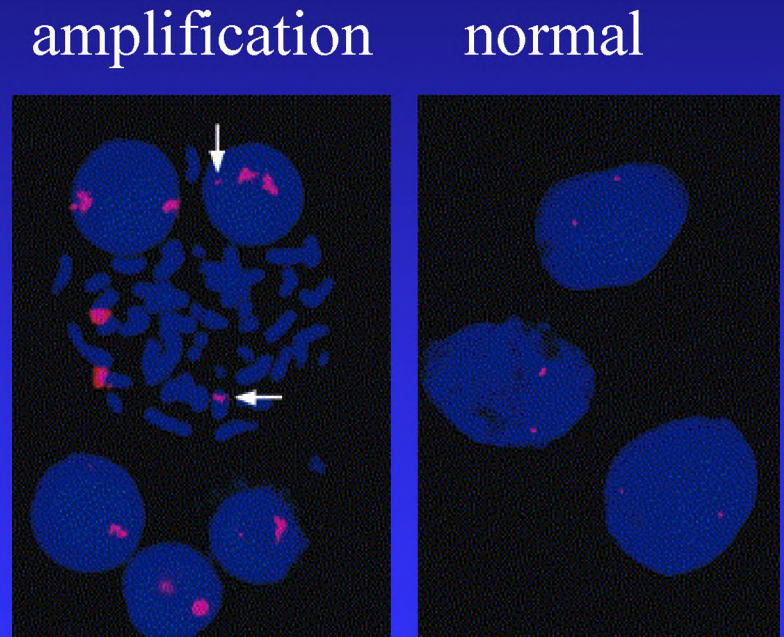
Native form



Flt3 :

a possible target for treatment?

- Flt3 amplified, over-expressed or mutated
- Blocking Flt3 induces tumor death in mice
- Abnormal Flt3 are used as target for designing new drugs
- Anti-Flt3 inhibits MLL-leukemias as well

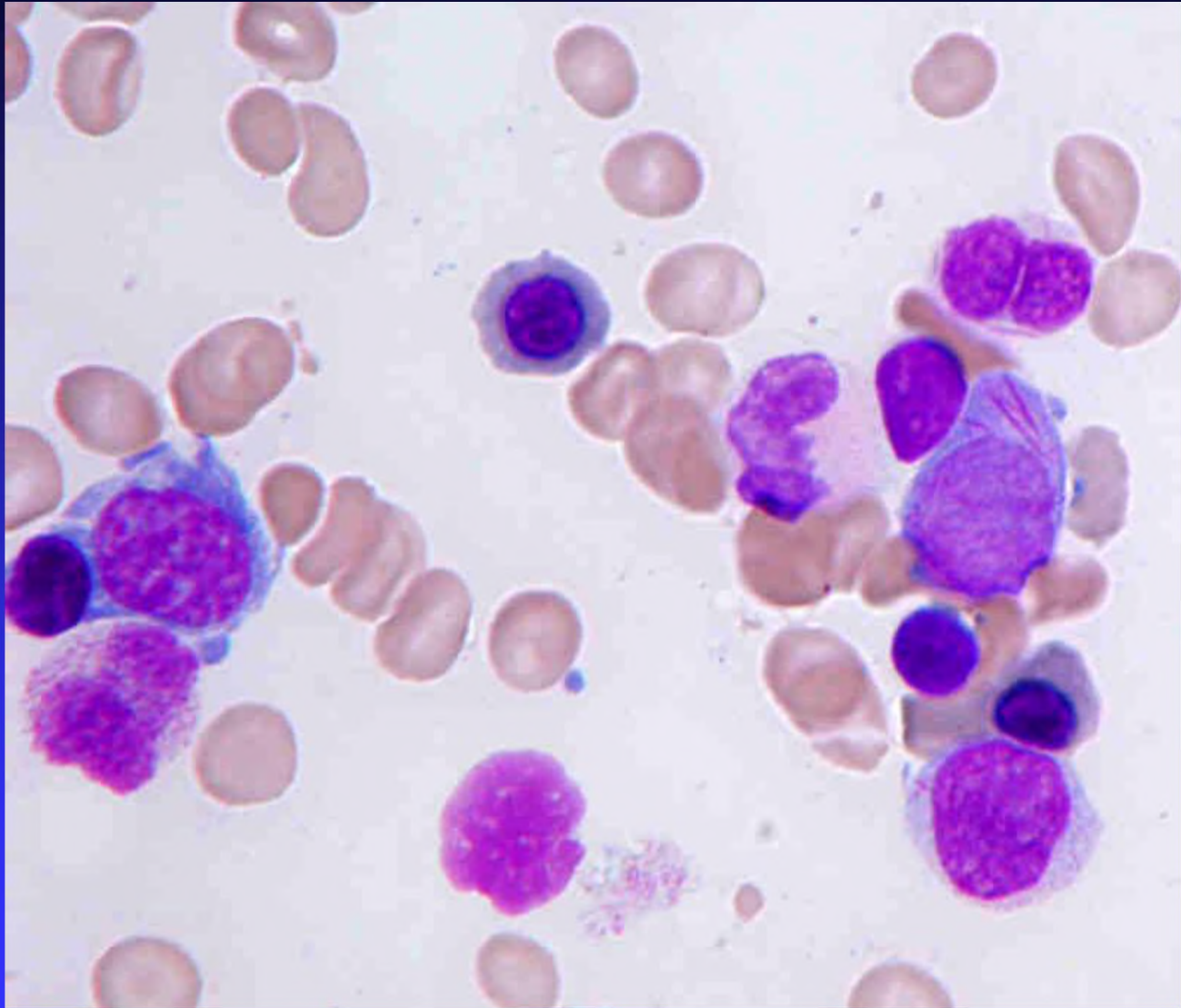


FISH for Flt 3 locus

AML with multilineage dysplasia

- Dysplasia in 2 or more myeloid cell lines
- Dysplasia in $> 50\%$ of at least 2 lines
- Elderly patients
- Presents with pancytopenia
- Immunophenotype reflects heterogeneity
- Often CD56 and/or CD7
- Genetics are similar to MDS
- Poor prognosis

AML with MDS



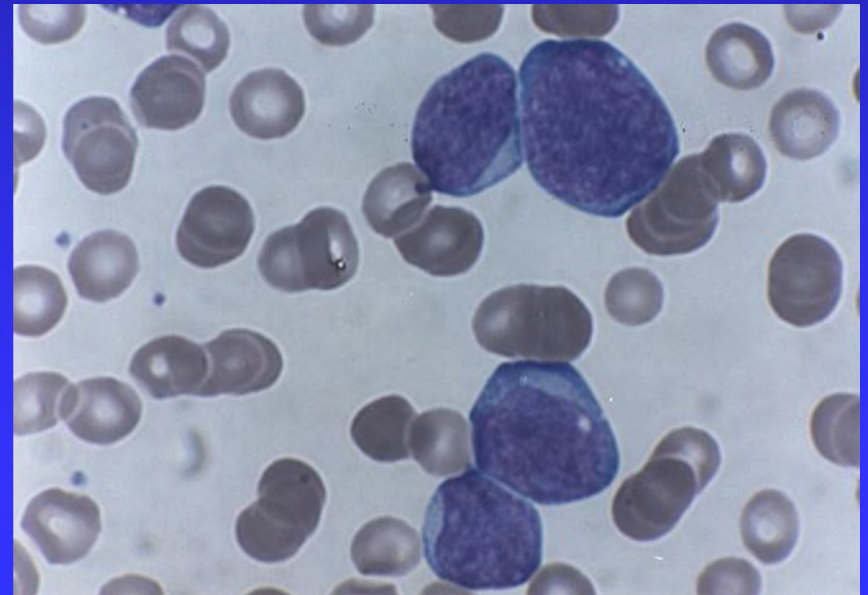
AML and MDS, therapy related

- Prior treatment with chemo- or radiation therapy. Bone marrow transplantation.
- Alkylating agent/radiation: 5-6 years, bone marrow failure, MDS eventually progression to AML. Often associated with 21q22 abnormalities. Short survival.
- Topoisomerase II inhibitor: 2-3 years, often presents with AML M5 (monoblastic/cytic). Often associated with MLL-rearrangement. Survival unknown.

AML, minimally differentiated

5 % of AML

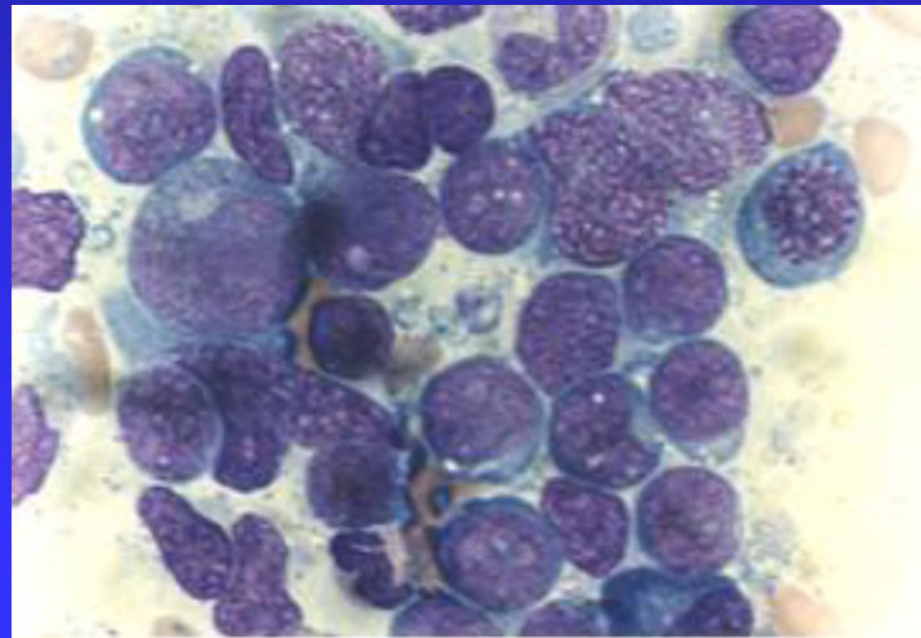
- Presents with marrow failure or leucocytosis.
- Blasts undifferentiated, CD13, 33 or 117, <3% MPO+.
- Exclude ALL by IHC/flow.
- Genetics: complex karyotypes, trisomies or monosomies.
- Poor prognosis



AML without maturation

10 % of AML

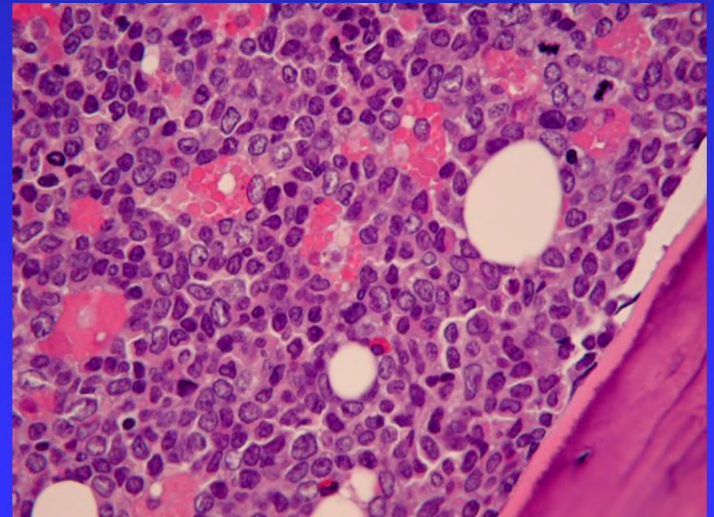
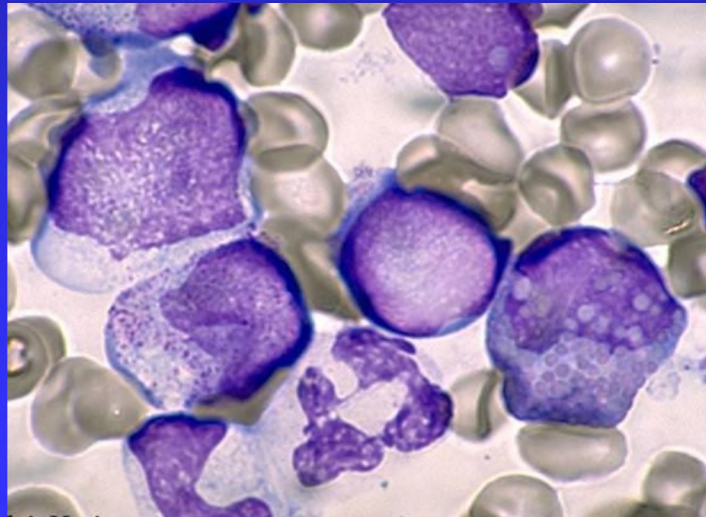
- Primarily adults with marrow failure
- High blast count in bone marrow
- No maturation beyond myeloblast, > 3% MPO
- No specific genetic changes
- Aggressive course



AML with maturation

30-45 % of AML

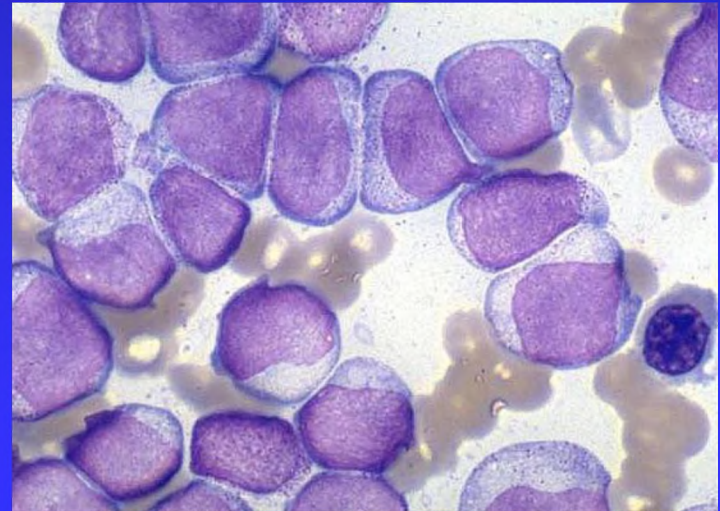
- All ages, symptoms of marrow failure
- Promyelocytes, myelocytes and further < 10 %
- Signs of MDS in neutrophils often present
- No unique, t(8;16) associated with haemophagocytosis



AML, myelomonocytic

15-25 % of AML

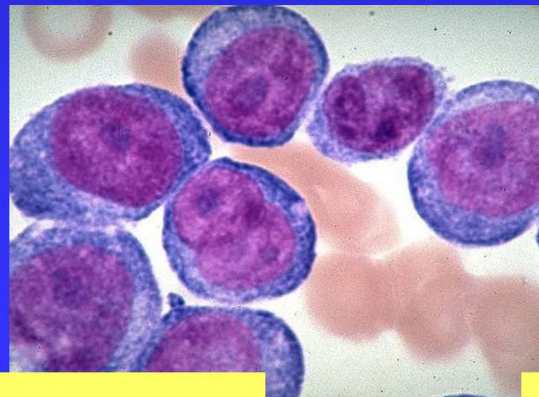
- All age groups, signs of marrow failure
- >20 % monocytes/monoblasts, > 20 % myeloid precursors
- Nonspecific genetic changes, no inv(16) or 11q23
- Responds to therapy, intermediate survival



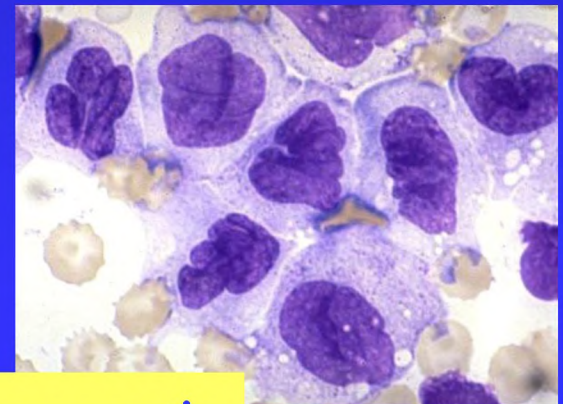
AML monocytic/monoblastic

5-10 % of AML

- All ages, also children and infants
- Monocytic 80 % of cells monocytes (cd68+, lysozyme+)
- Monoblastic 80 % of cells monoblasts (cd4, cd11c, cd13 and cd33)
- Bleeding disorders and extramedullary involvement
- No specific genetic abnormalities, t(8;16) associated with haemophagocytosis



monoblastic

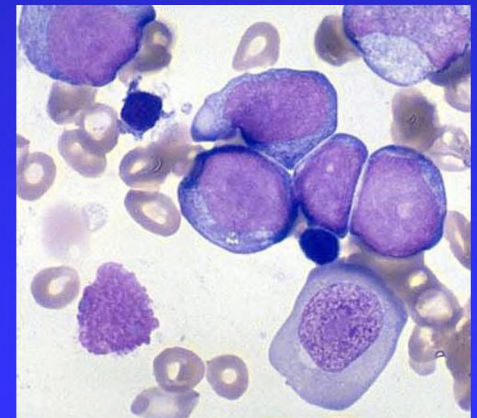
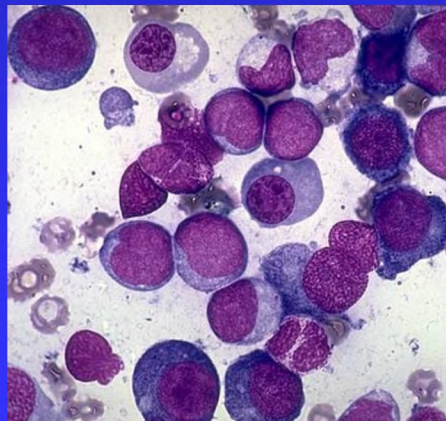


monocytic

AML erythroid

5-6 % of AML

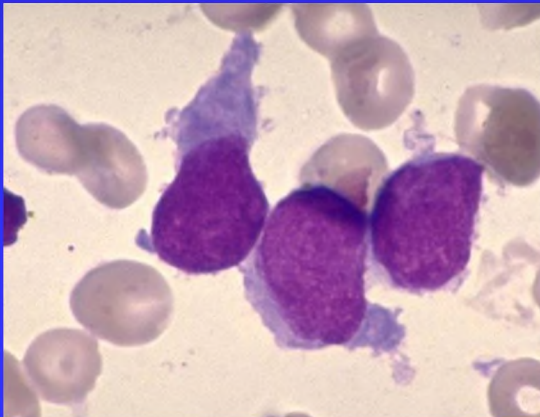
- Mainly adults
- Pure erythroid AML >80 % of marrow cells red
- Erythroid/myeloid AML >50 % red, > of non-erythroid cells myeloblasts.
- May evolve from MDS, often dysplastic erythroblasts
- Aggressive clinical course, poor survival



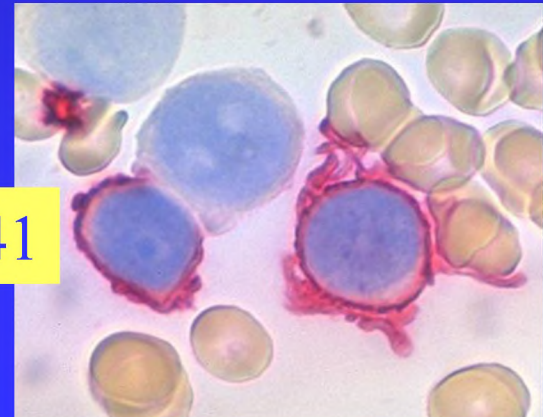
AML megakaryoblastic

3-5 % of AML

- All ages, presents with cytopenias, often with dysplasia. Bone lytic lesions and abdominal tumors in children.
- Megakaryoblasts medium to large with nucleoli and basophilic irregular cytoplasm. Micromegakaryocytes. CD61+, marrow fibrosis.
- No specific genetic abnormality, in children t(1;22).
- Prognosis poor



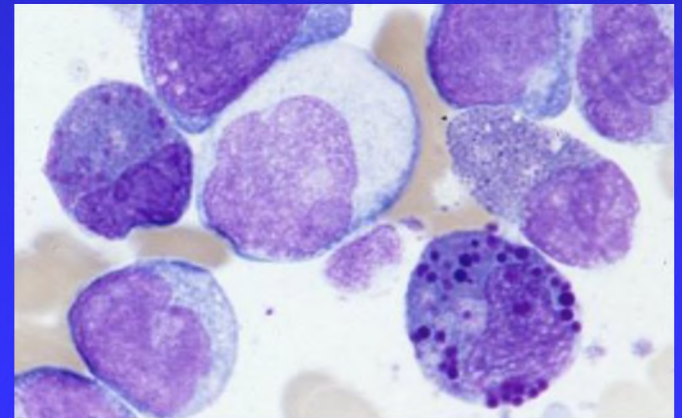
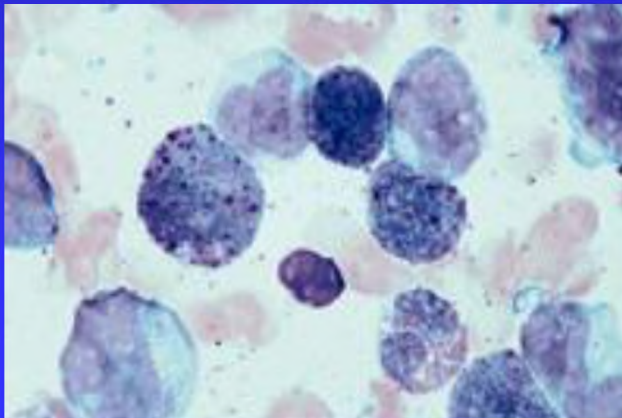
CD41



AML, basophilic

< 1 % of AML

- Rare, symptoms related to bone marrow failure, cutaneous or visceral involvement
- Differentiation to basophils, metachromatic reaction in toluidin blue, CD9, +/- Tdt.
- Poor prognosis



Acute panmyelosis with myelofibrosis

Very rare

- Symptoms due to marrow failure
- Can be secondary
- Multilineage dysplasia, proliferation and fibrosis, marrow hypercellular, splenomegaly in chronical course
- Differential diagnosis CMPD, metastatic disease, other types of AML

Myeloid sarcoma

- An extramedullary tumour mass of myeloid blasts/precur-sors
- May precede leukemia
- Can be blastic, immature or differentiated like other AML's.
- Genetics and immunophenotype reflect subtype
- Clinical course depend on extent of disease

Acute leukaemia of ambiguous lineage

less than 4 % of acute leukaemia

- Undifferentiated leukaemia:
- All ages, bone marrow failure
- No specific markers (CD79a, CD22, CD3 or MPO)
- Bilineal/biphenotypic leukaemia:
- Dual blastpopulation or one blast population coexpressing lineage specific markers (T, B or myeloid, CD79a, CD3, MPO)

Genetics: t(9;22), 11q23 rearrangement, complex karyotypes
Prognosis unfavorable

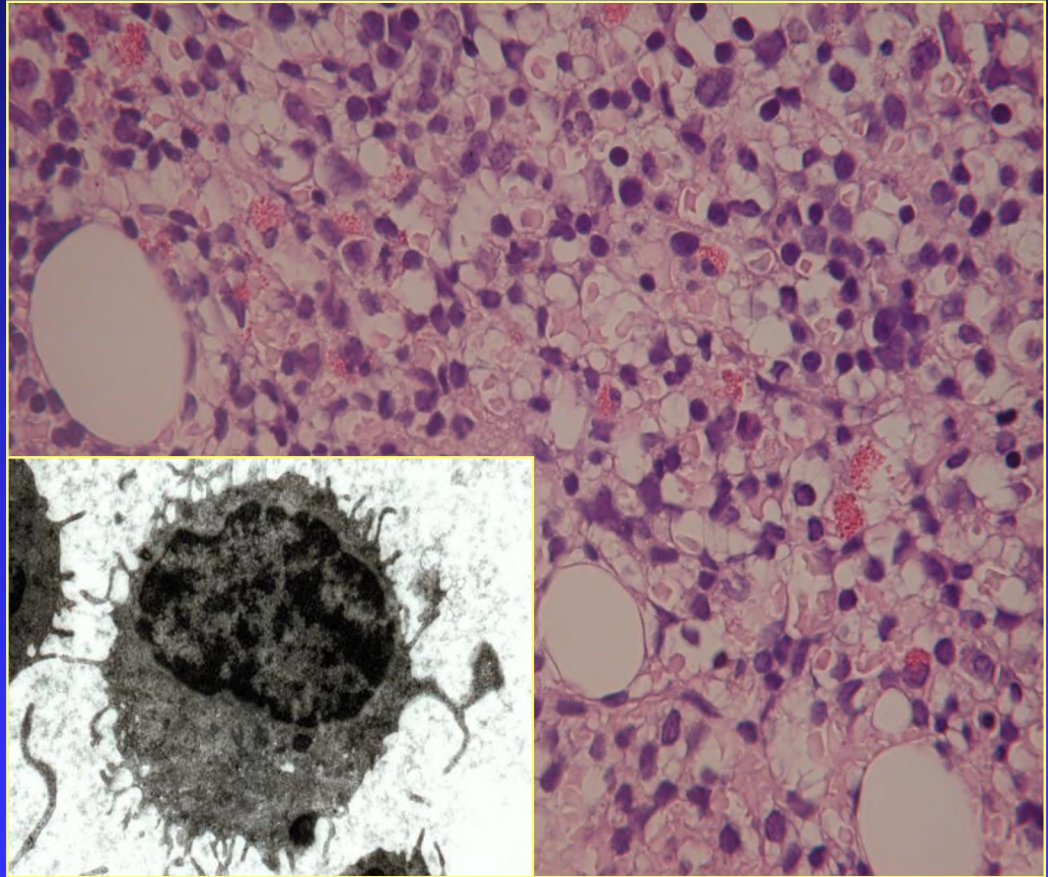
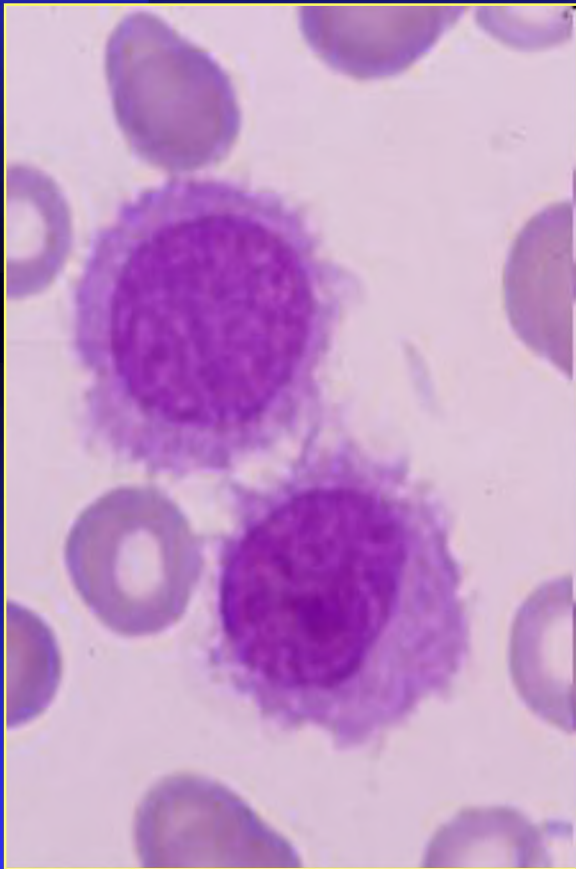
Hairy cell leukemia

- Rare, adults, M>F
- Pancytopenia, splenomegaly
- Indolent
- α -interferon, 2-chlorodeoxyadenosin

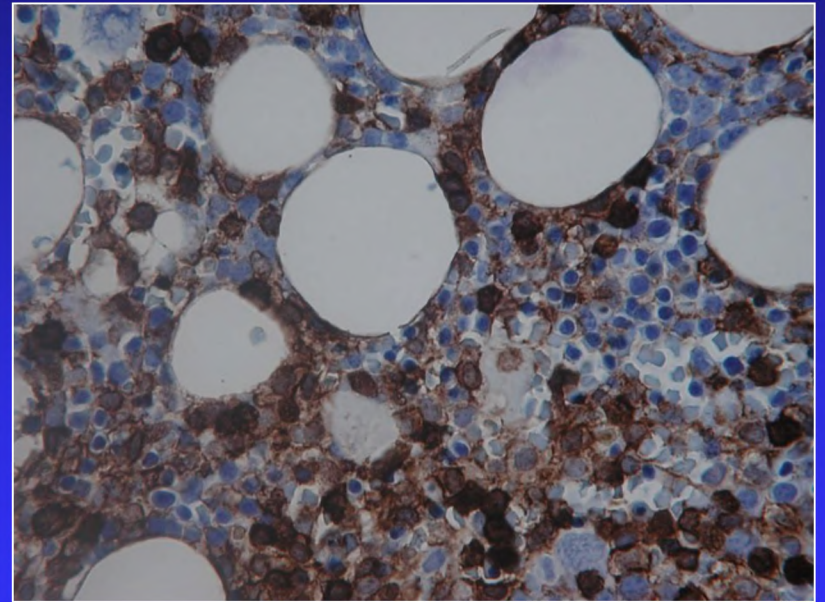
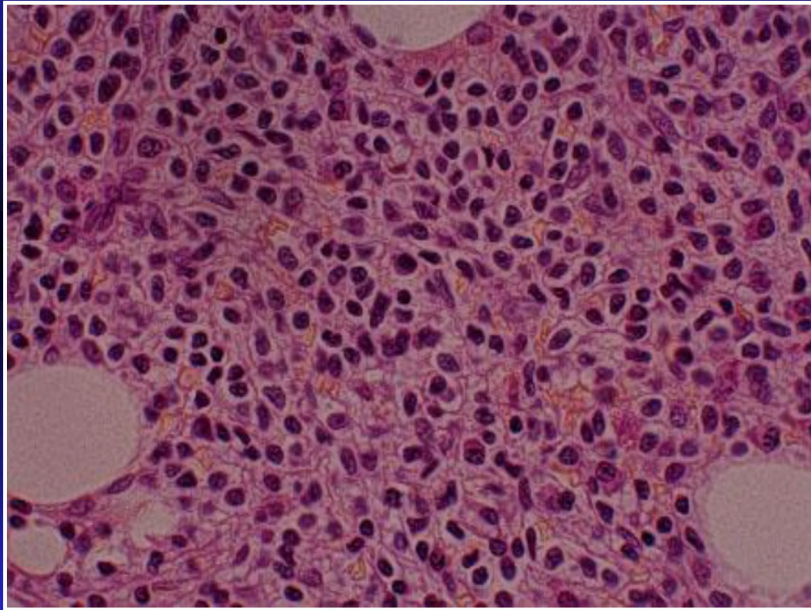
Hairy cell leukemia

- Small to medium, reniform nuclei, abundant pale cytoplasm with hairy projections
- Few neoplastic cells in the blood
- Massive marrow infiltrates, reticular fibrosis (dry tap)
- CD20+, CD79a+, CD25+, CD11c+, CD103+, DBA44+, TRAP+
- CD5-, CD10-, CD23-
- No specific genetic abnormality

Hairy cell leukemia



Hairy cell leukemia



Annexin

Appearances can deceive.....

