Medikamentöse Substanzen,
die als mögliche Ursachen für die Entstehung einer Panzytopathie/ Panmyelopathie bzw. Panmyelophthise in Frage kommen können

Chemische Substanzen

Suchliste wichtiger Medikamente, die möglicherweise eine Panmyelopathie auslösen können. Diejenigen Substanzen, die besonders häufig oder mit besonders hoher Inzidenz angeschuldigt wurden, sind kursiv gedruckt (57, 63a)

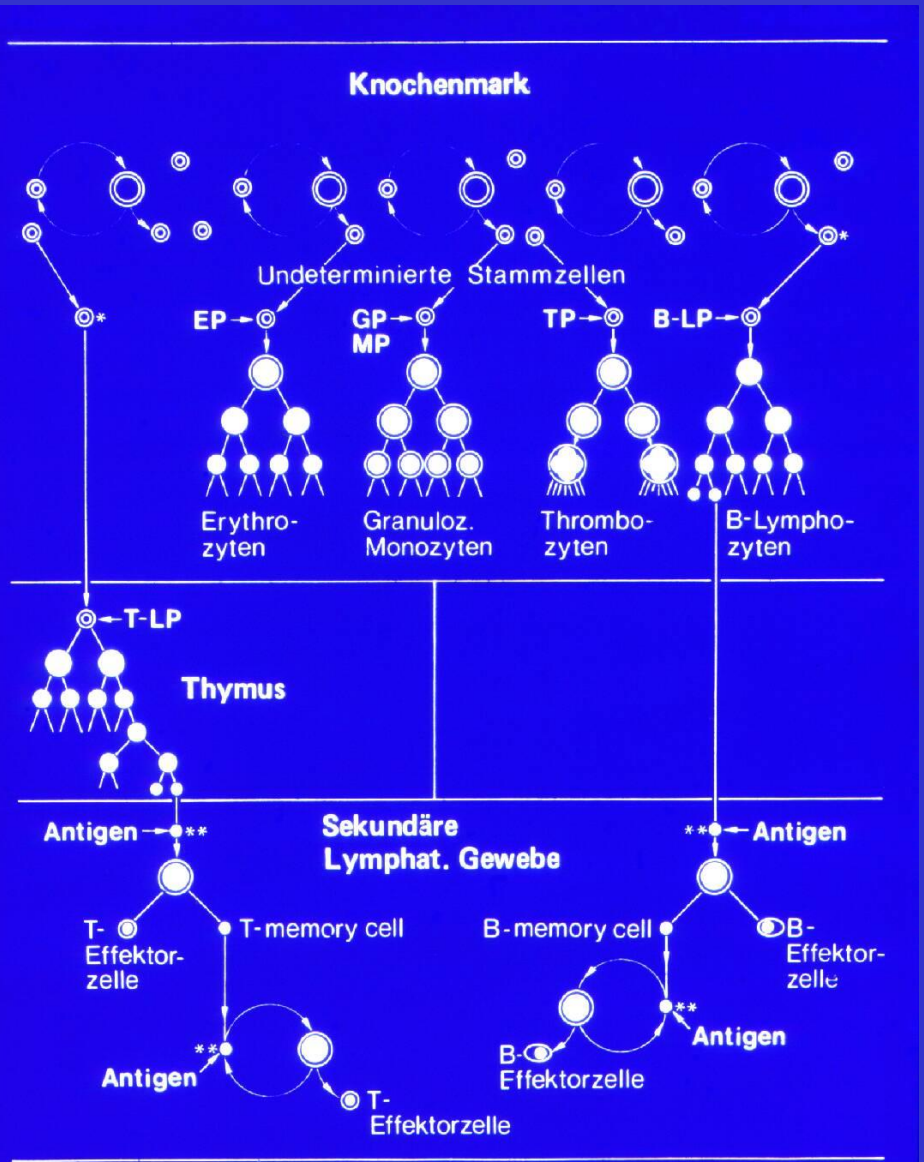
Antibiotika:	*Chloramphenicol*
	Sulfonamide
	Tetracycline
	Penicilline
Antirheumatika, Analgetika:	*Phenylbutazon*
	Oxyphenbutazon
	Gold
	Indomethacin
	Allopurinol
	Colchicin
	Phenacetin
	Penicillamin
	Acetylsalizylsäure
Antikonvulsiva:	*Hydantoine*
	Trimethadion
	Ethosuximid
	Carbamazepin
Anti-Malaria-Mittel:	*Quinacrin* (Atebrin)
	Chloroquin
	Pyrimethamin
Thyreostatika:	*Kaliumperchlorat*
	Carbimazol
	Methimazol
	Thiouracil
Antidiabetika:	*Chlorpropamid*
	Carbutamid
	Tolbutamid
Sedativa und Psychopharmaka:	*Phenothiacine*
	Meprobamat
	Chlordazepoxid
	Lithium
Andere:	*organische Arsenpräparate*
	Antihistaminika
	Thiocyanat
	Chinidinsulfat
	Acetazolamid
	Methyldopa
	Chlorothiazid

Zahlreiche Bilder der folgenden Bildgalerie stammen großenteils aus:

Clinical Hematology Atlas by Jacqueline H. Carr and Bernadette F. Rodak - Saunders Elsevier (2004, Spiral, Revised)

und

Color Atlas of Clinical Hematology
A. Victor Hoffbrand
ISBN 10: 1563755920 / ISBN 13: 9781563755927
Published by Mosby-Year Book, 1994:
Titel: Color Atlas of Clinical Hematology.
Verlag: London etc. ; Mosby Wolfe,
Erscheinungsdatum: 1994
Auflage: 2nd edition



* undeterminierte lymphat. Stammzelle
** determinierte lymphat. Stammzelle (i.c.c.)

Abb. 13.8 Schema der hypothetischen Stammzelldifferenzierung im Knochenmark und lymphatischen Gewebe (nach *Trepel*)

Acute Leukaemia: Morphological Classification*

Myeloid (AML)
M_1: myeloblastic without maturation
M_2: myeloblastic with maturation
M_3: hypergranular promyelocytic
M_4: myelomonocytic
M_5: monocytic
M_6: erythroleukaemia
M_7: megakaryoblastic
Lymphoblastic
L_1: small, monomorphic
L_2: large, heterogeneous
L_3: Burkitt cell-type

*French-American-British (FAB) classification

M1	Blasts ≥ 90% of the BM NEC ≥3% of blasts MPO positive
M2	Blasts ≥30% and ≤90% of NEC in the BM BM monocytic component <20% NEC
M3	Predominance of 'M3' (promyelocytic) blasts
M4	Blasts ≥30% of NEC in the BM BM monocytic component ≥20% NEC and/or PB monocytic cells >5 x 10^9/l
M5	BM monocytic cells (monoblasts and/or promonocytes) >80% NEC
M6	Erythroblasts ≥50% of BM nucleated cells BM blasts ≥30% of NEC
M7	BM megakaryoblasts >30%
M0	MPO negative blasts on light microscopy Lymphoid markers – negative; myeloid markers – positive

AML: FAB Classification

Type	Incidence	Morphology	Cytogenetics
M0	5%	Myeloblasts >90% of the nonerythroid BM cells, no Auer rods, <3% MPO^+	−5, 5q-, −7, 7q-
M1	10–20%	Myeloblasts >90% of the non-erythroid BM cells, rare **Auer** rods, >3% MPO^+	t(9;22)
M2	30%	Myeloblasts <90% of the nonerythroid BM cells, frequent **Auer rods**	t(8;21), t(6;9)
M3	5–10%	30% or more promyelocytes	t(15;17)
M4	30%	20–80% immature monocytes	t(6;9), 5q-, 7q-
		Subtype: with atypical eosinophils (M4Eo)	inv(16), del (16)
M5	10%	80% or more immature monocytes	t(8;16), t(9;11), 11q-
M6	5%	50% or more erythroid precursors	5q-, 7q-, +8
		30% or more myeloblasts in the nonerythroid BM cells	
M7	5%	30% or more megakaryoblasts	+21, t(21)

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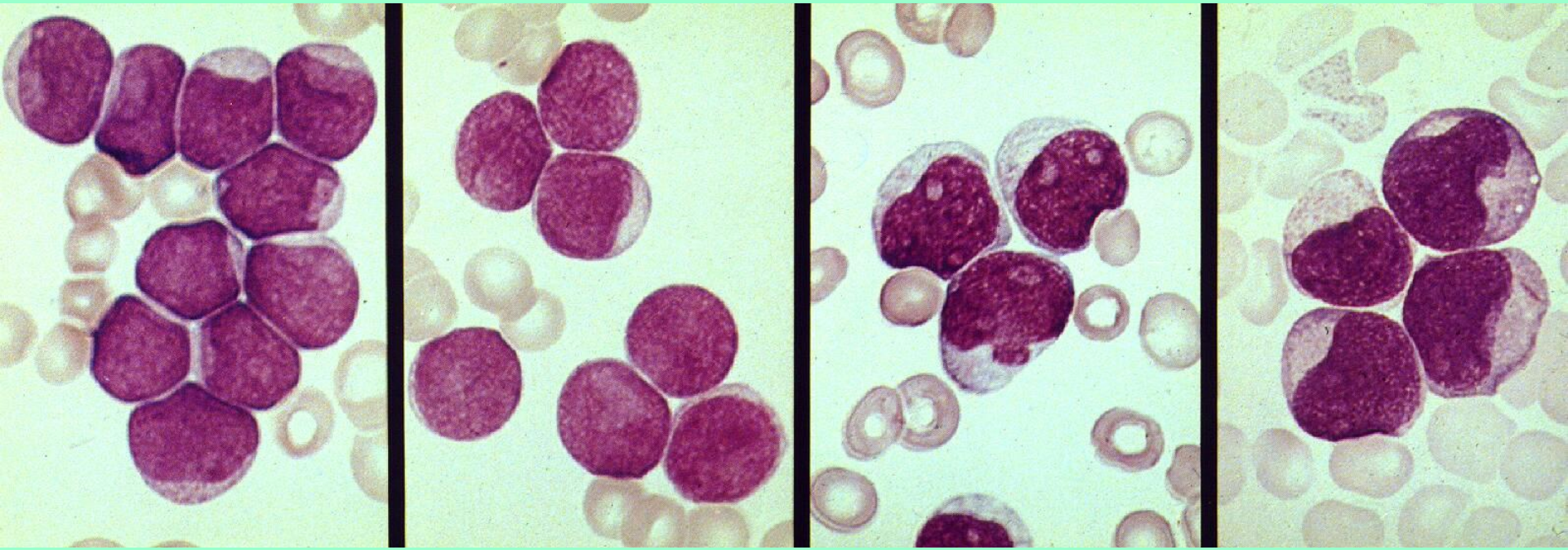
Lymphoblastic

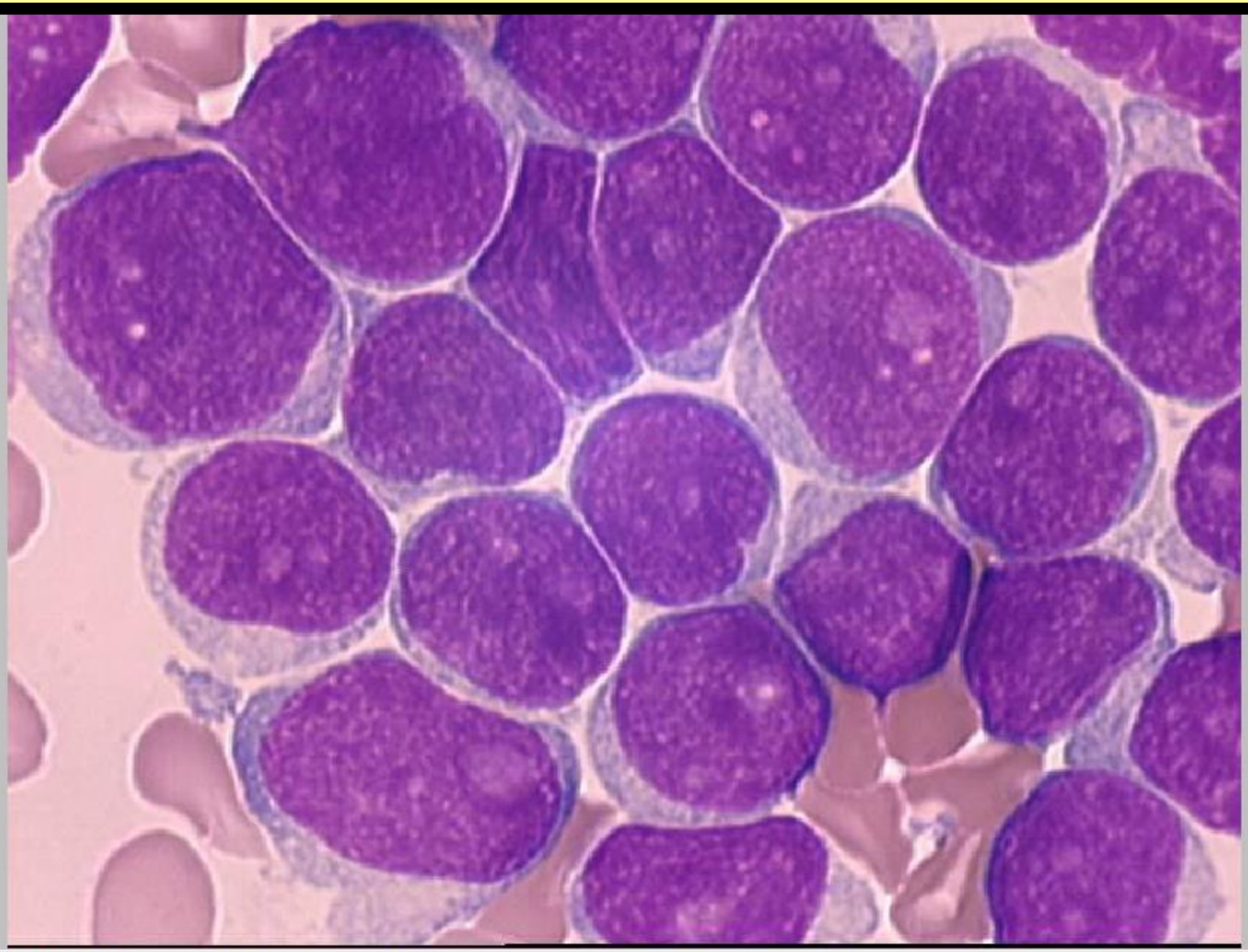
- L_1: small, monomorphic
- L_2: large, heterogeneous
- L_3: Burkitt cell-type

*French-American-British (FAB) classification

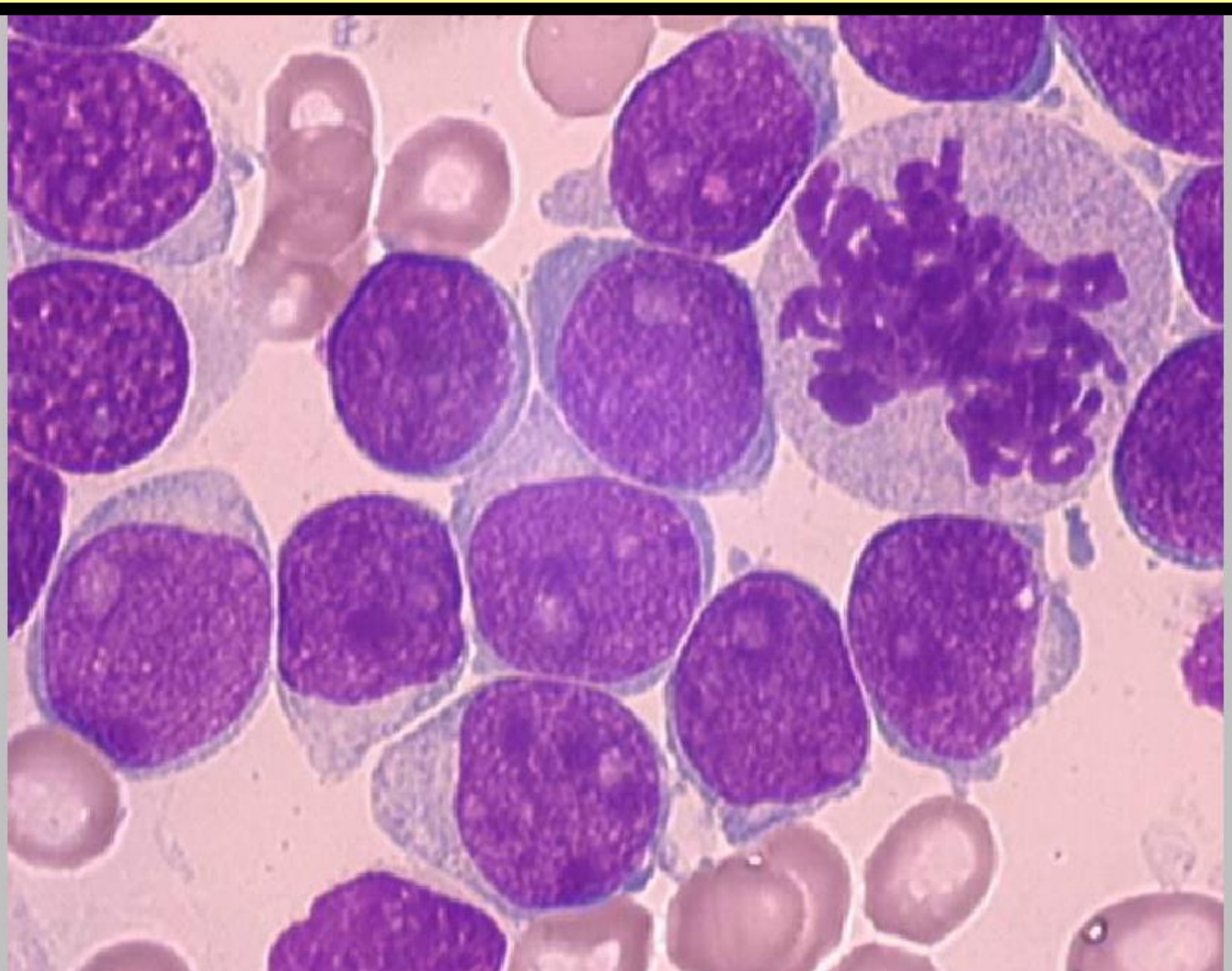
M1- Leukämie :
myeloblastisch ohne Reifung



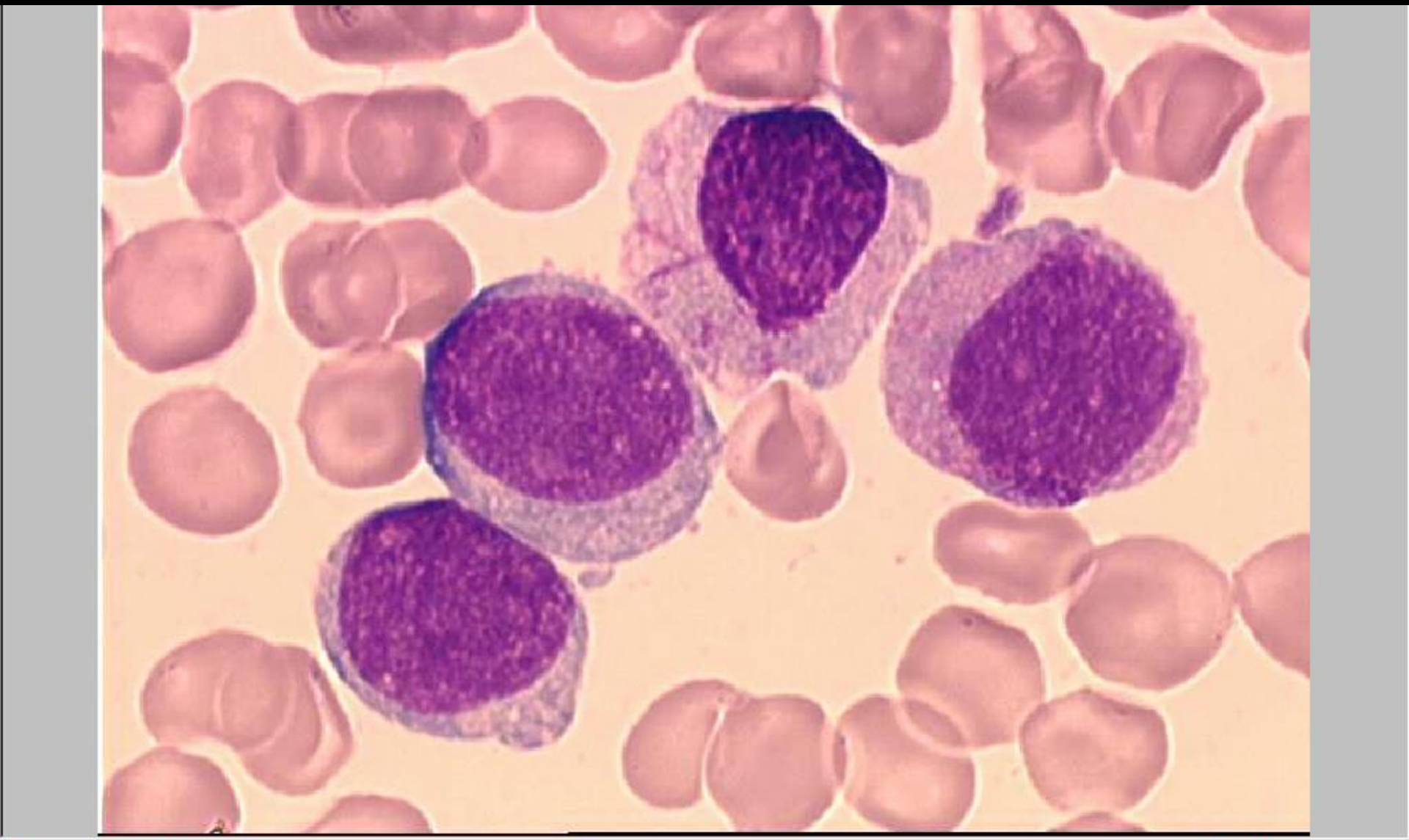
Akute myeloische Leukämie M1:
myeloblastisch ohne Reifung



Akute myeloische Leukämie M1:
myeloblastisch ohne Reifung



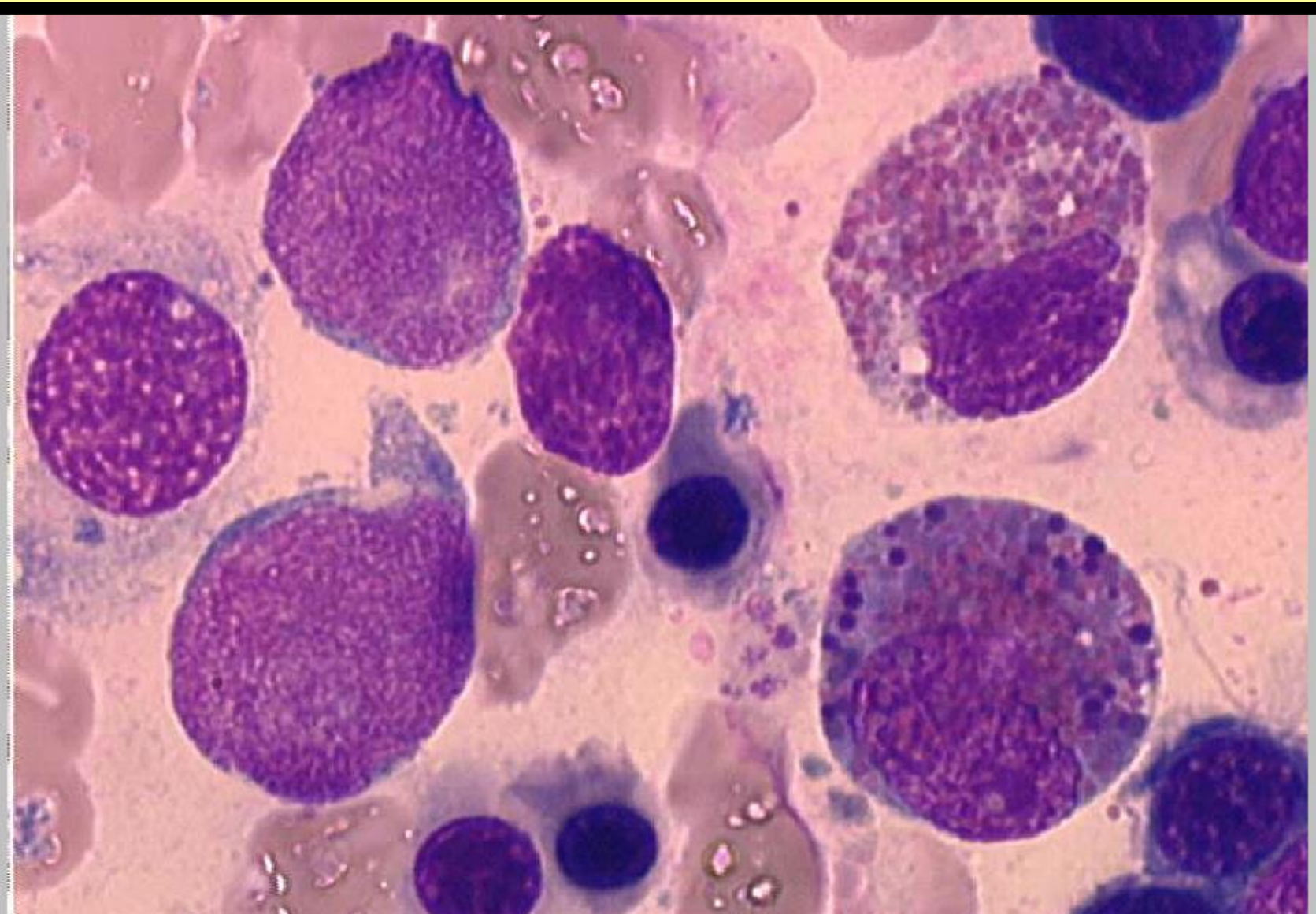
M1 - Leukämie der FAB-Klassifikation.
Atypische Blasten ohne Reifung.



Akute myeloische Leukämie M1:

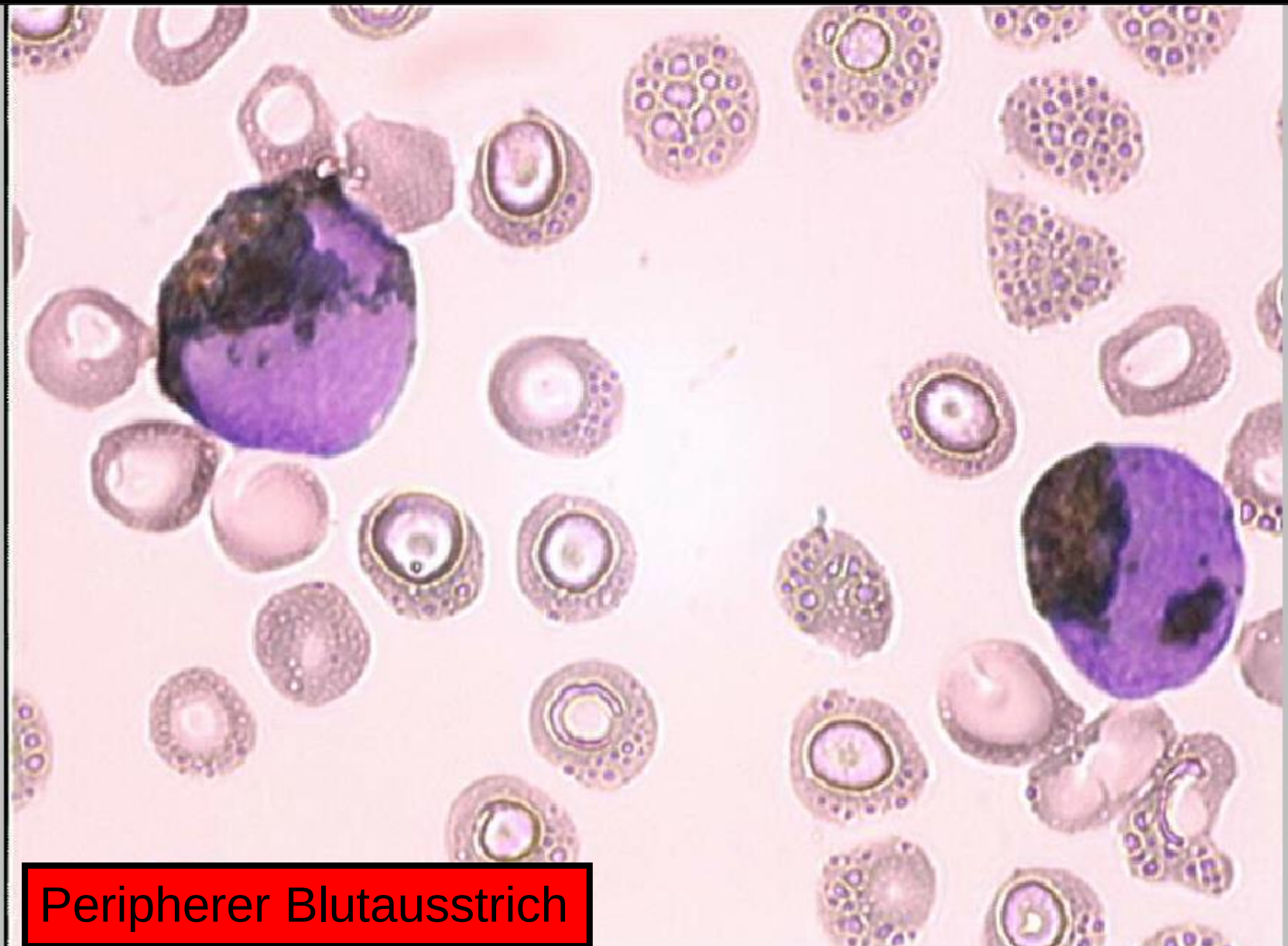
myeloblastisch ohne Reifung mit Eosinophilie

6 Jahre altes Mädchen



Akute myeloische Leukämie M1:

myeloblastisch ohne Reifung - POX+



Peripherer Blutausstrich

Acute Leukaemia: Morphological Classification*

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M_7: megakaryoblastic

Lymphoblastic

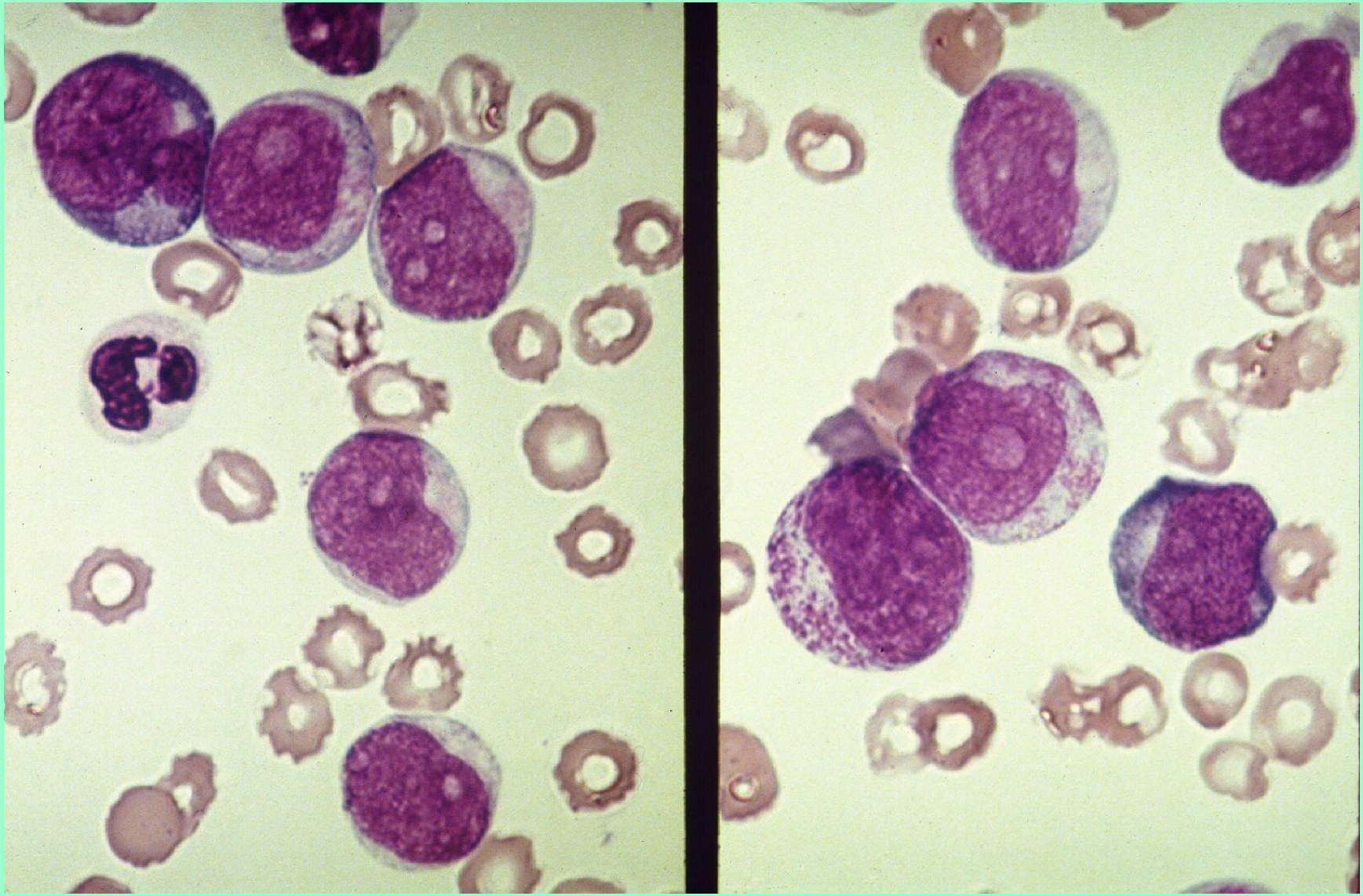
L_1: small, monomorphic

L_2: large, heterogeneous

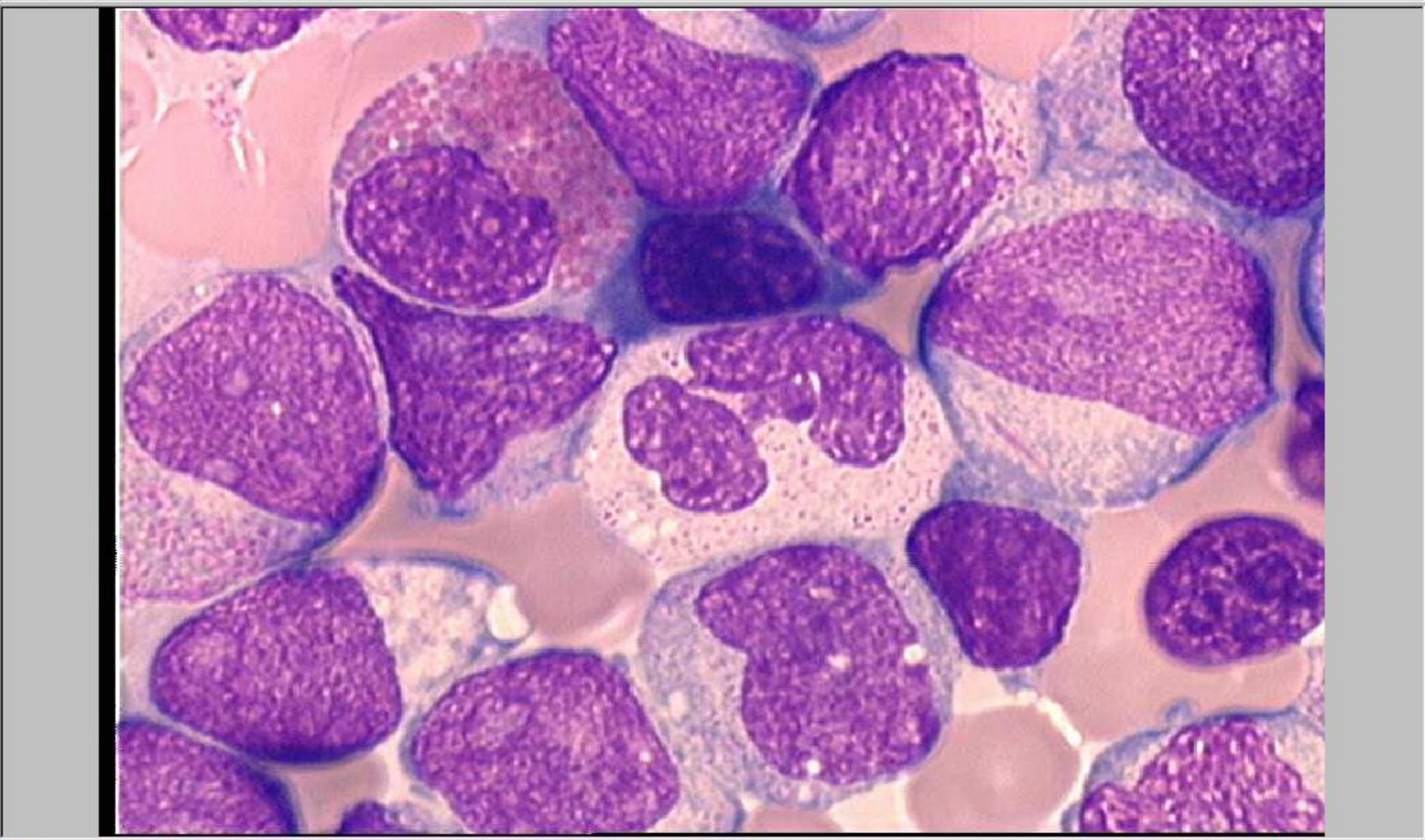
L_3: Burkitt cell-type

*French-American-British (FAB) classification

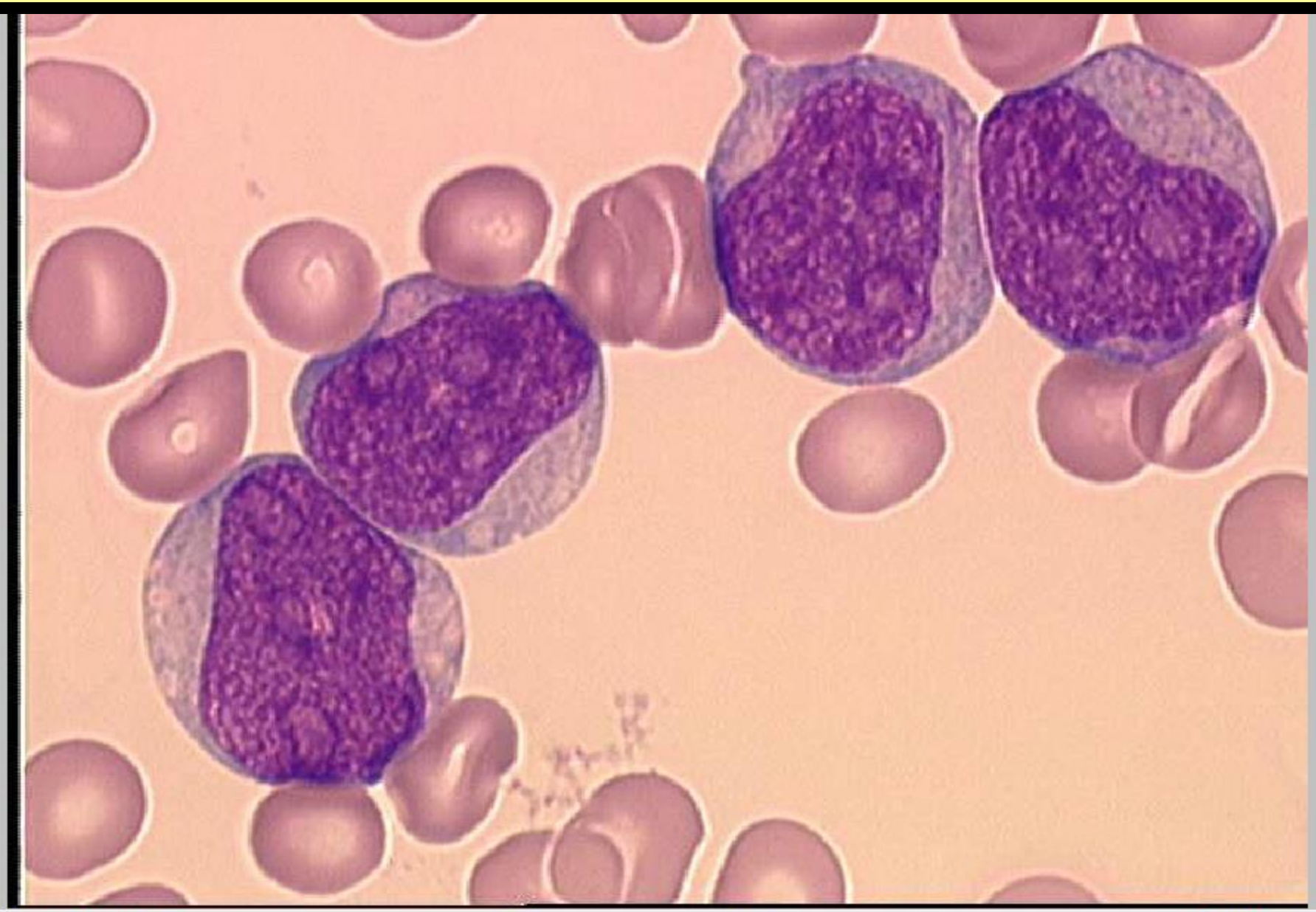
M2- Leukämie :
myeloblastisch mit Reifung



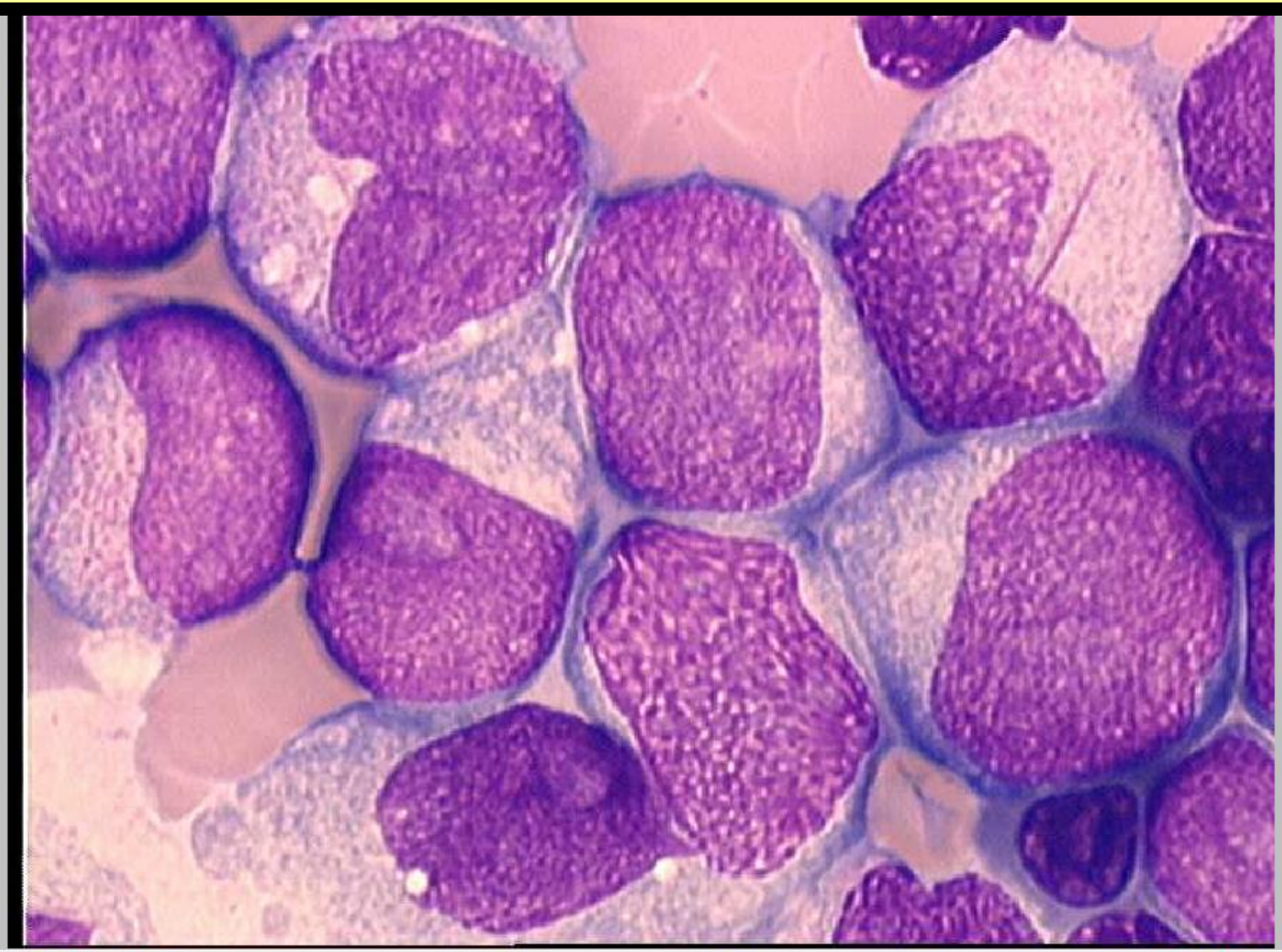
M2 - Leukämie : unterschiedlich große atypische Blasten z. T. mit Auerstäbchen. Vorbestehend REAB(t)



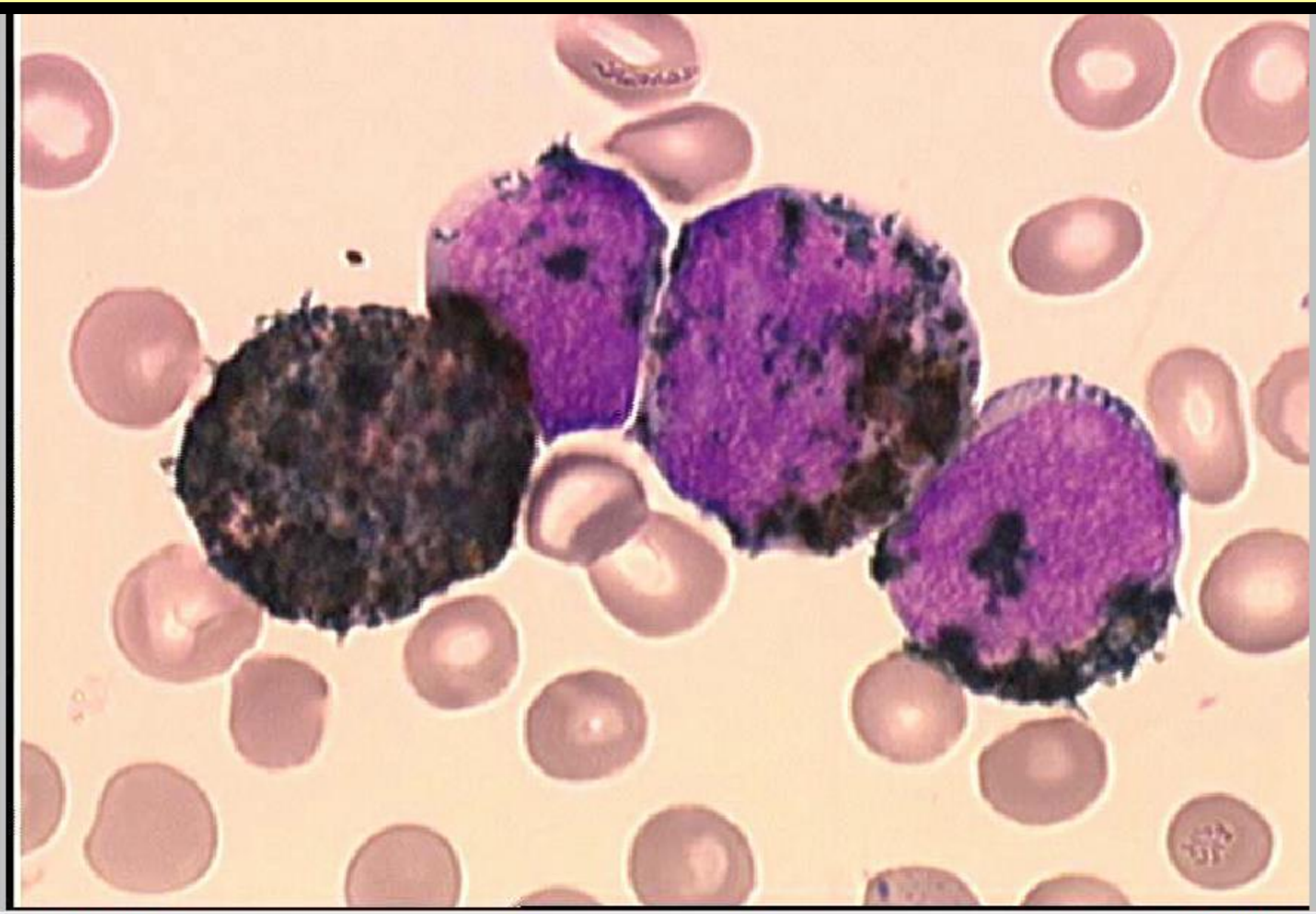
M2 - Leukämie der FAB-Klassifikation.
Atypische Blasten .



M2 - Leukämie der FAB-Klassifikation.
Atypische Blasten .



M2 - Leukämie der FAB-Klassifikation.
Atypische Blasten . 100% MPO-positiv.



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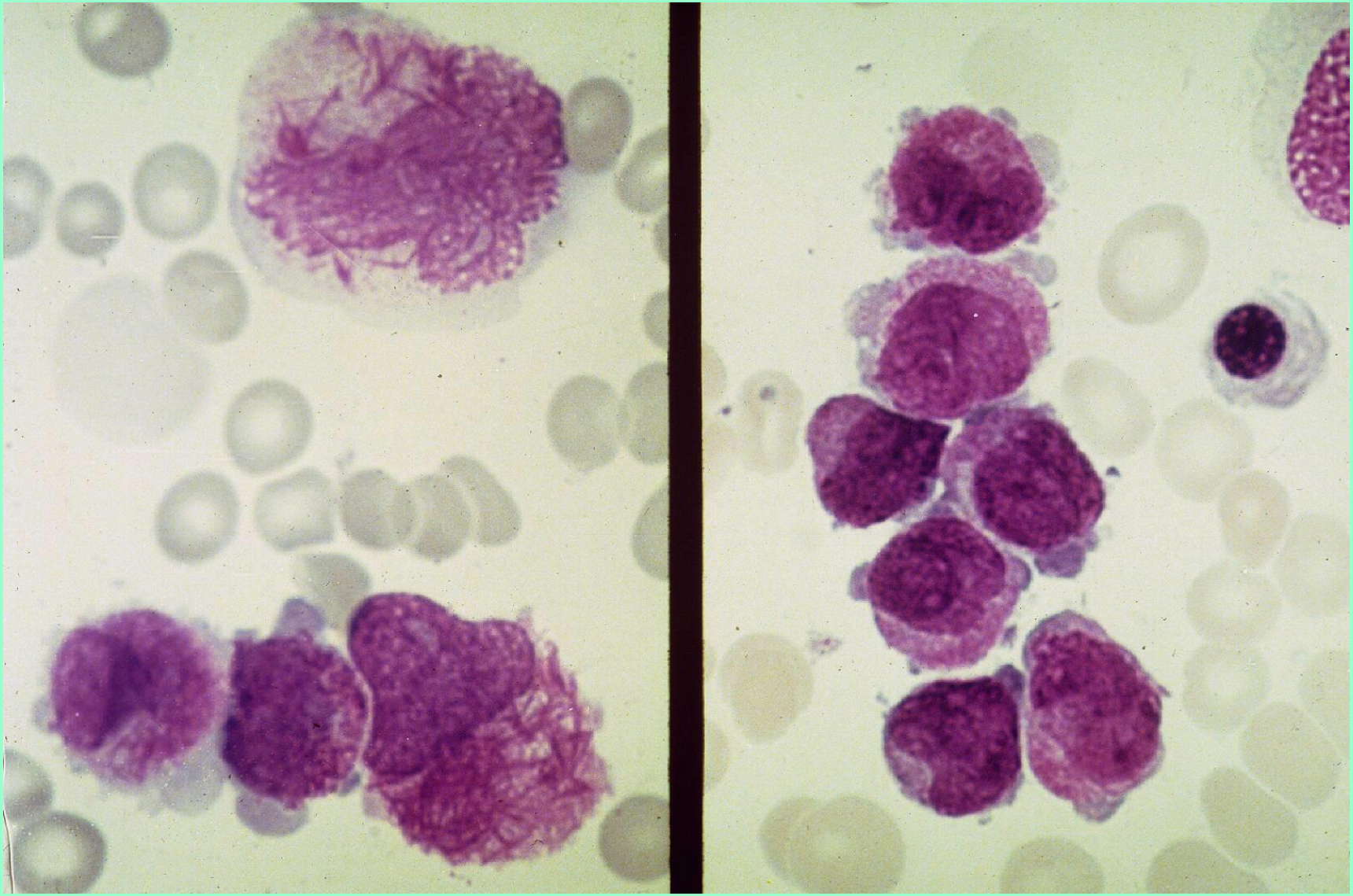
- M_5: monocytic
- M_6: erythroleukaemia
- M_7: megakaryoblastic

Lymphoblastic

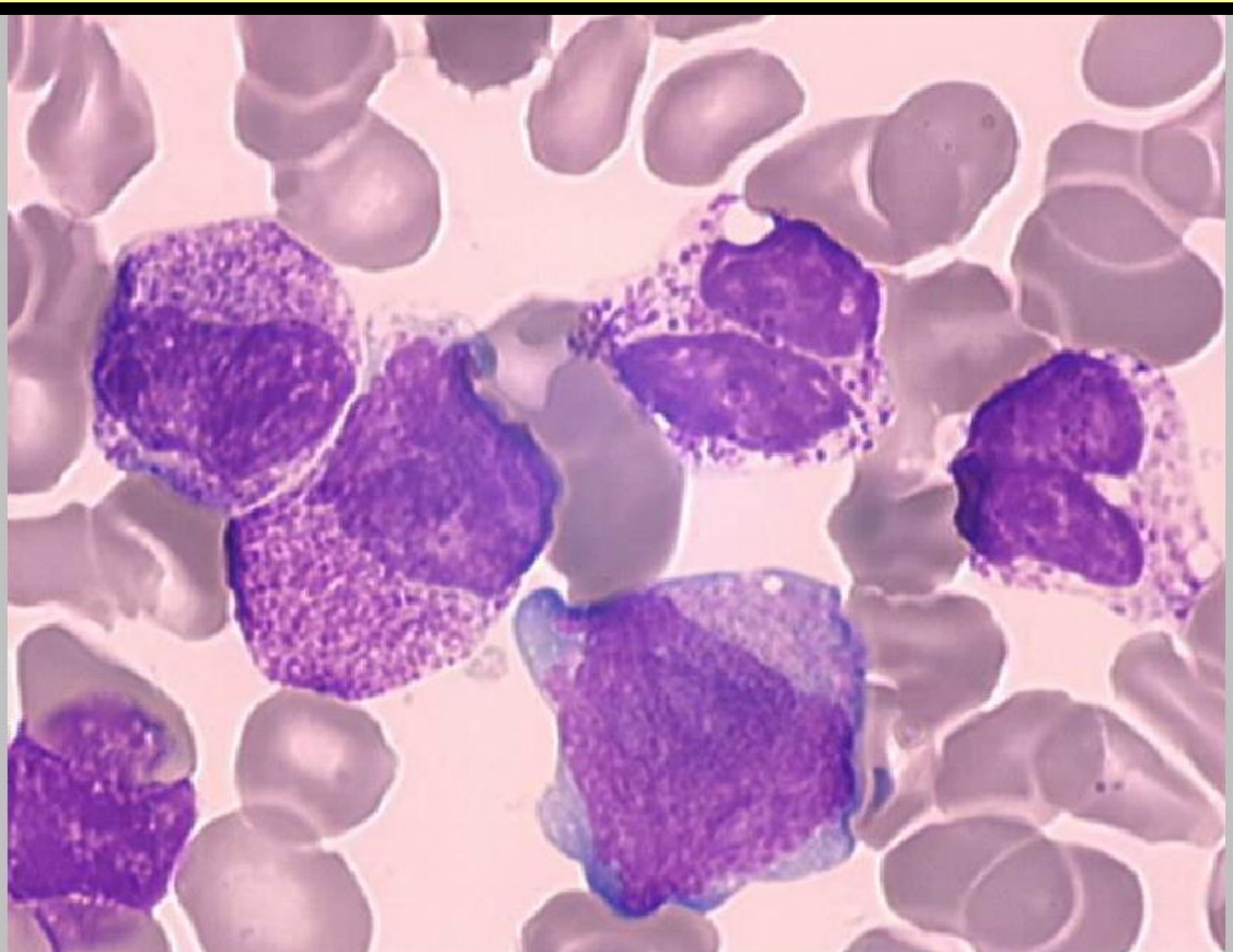
- L_1: small, monomorphic
- L_2: large, heterogeneous
- L_3: Burkitt cell-type

*French-American-British (FAB) classification

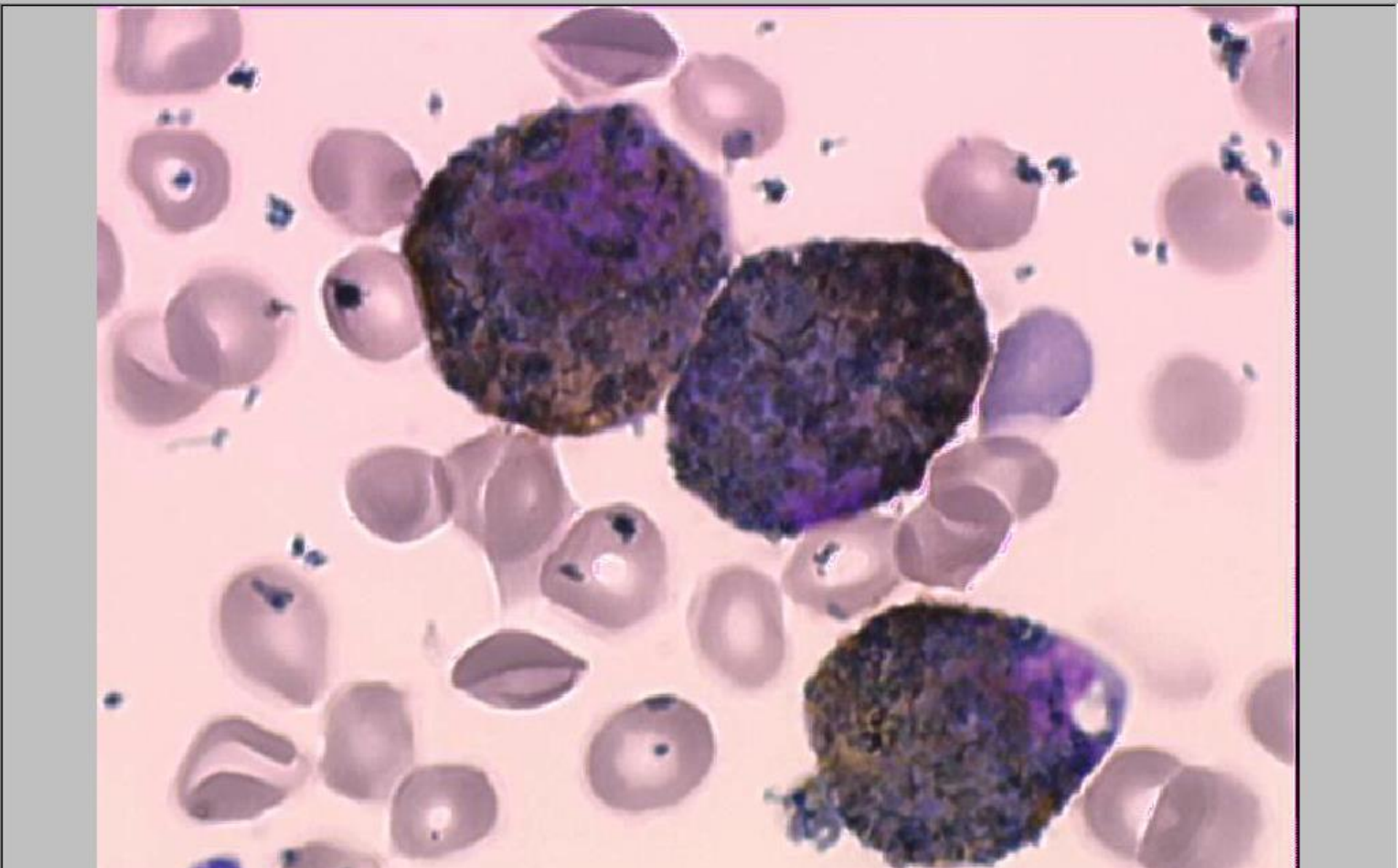
M3- Leukämie : hypergranulär-promyelozytisch



M3- Leukämie : hypergranulär-promyelozytisch



M3- Leukämie : hypergranulär-promyelozytisch



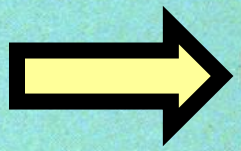
Acute Leukaemia: Morphological Classification*

Myeloid (AML)

M_1: myeloblastic without maturation

M_2: myeloblastic with maturation

M_3: hypergranular promyelocytic



M_4: myelomonocytic

M_5: monocytic

M_6: erythroleukaemia

M_7: megakaryoblastic

Lymphoblastic

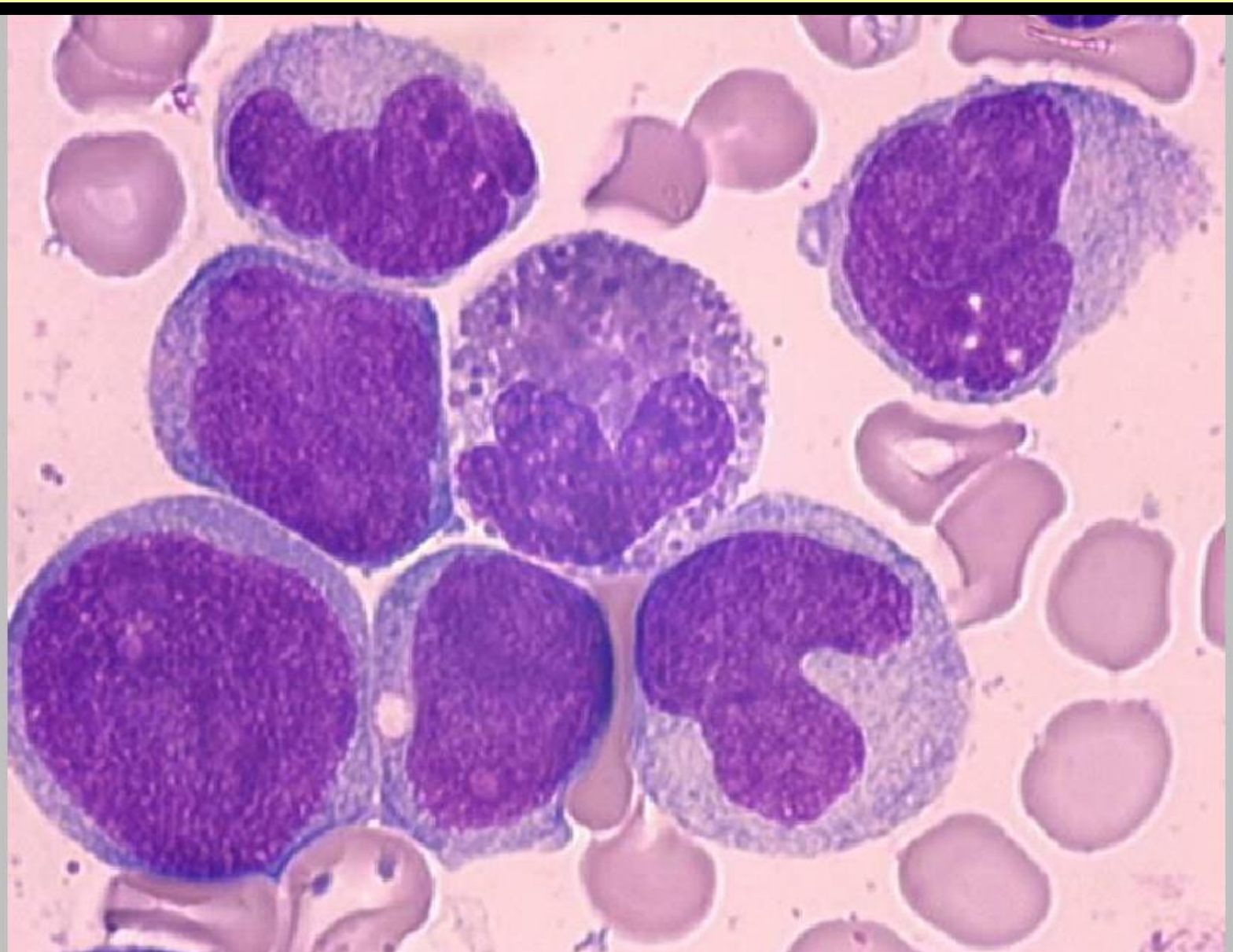
L_1: small, monomorphic

L_2: large, heterogeneous

L_3: Burkitt cell-type

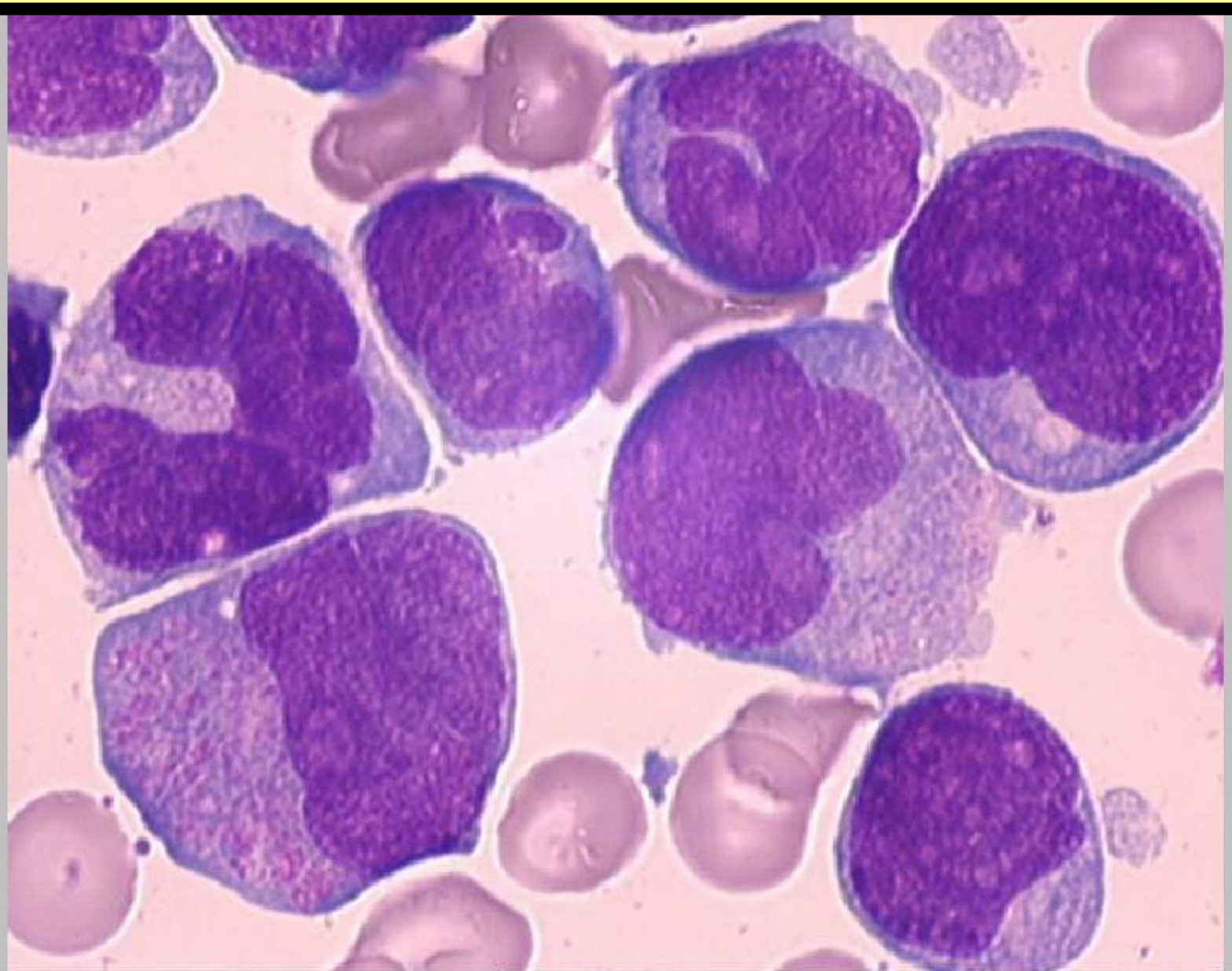
*French-American-British (FAB) classification

Akute myeloische Leukämie: myelo-monozytisch (M4)

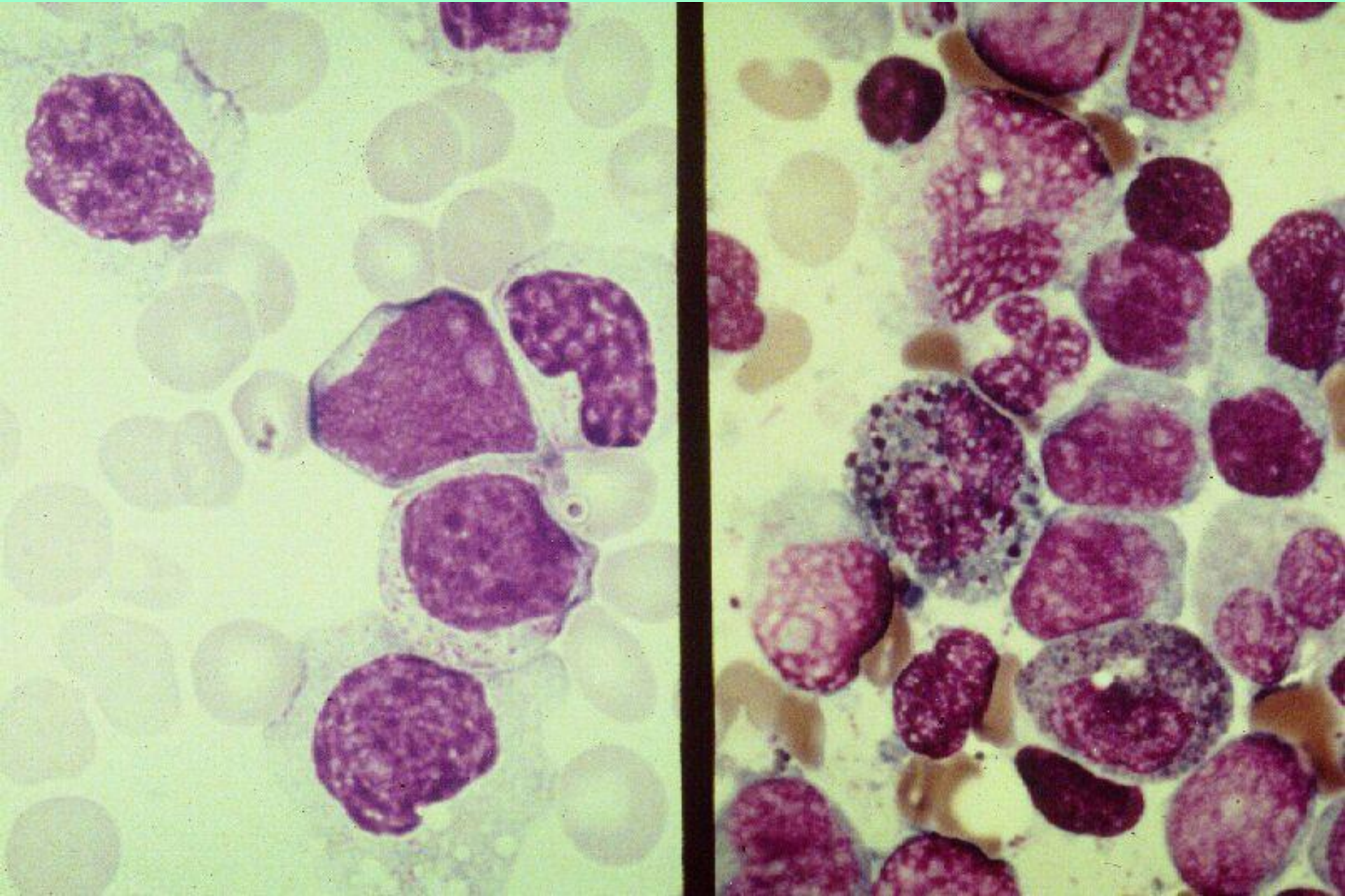


Akute myeloische Leukämie (AML M4 FAB)

21 Jahre alter Mann - Knochenmark



Akute myeloische Leukämie: myelo-monozytisch (M4)



Acute Leukaemia: Morphological Classification*

Myeloid (AML)

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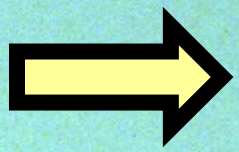
M_2: myeloblastic with maturation

M_3: hypergranular promyelocytic

M_4: myelomonocytic



M_5: monocytic

M_6: erythroleukaemia

M_7: megakaryoblastic

Lymphoblastic

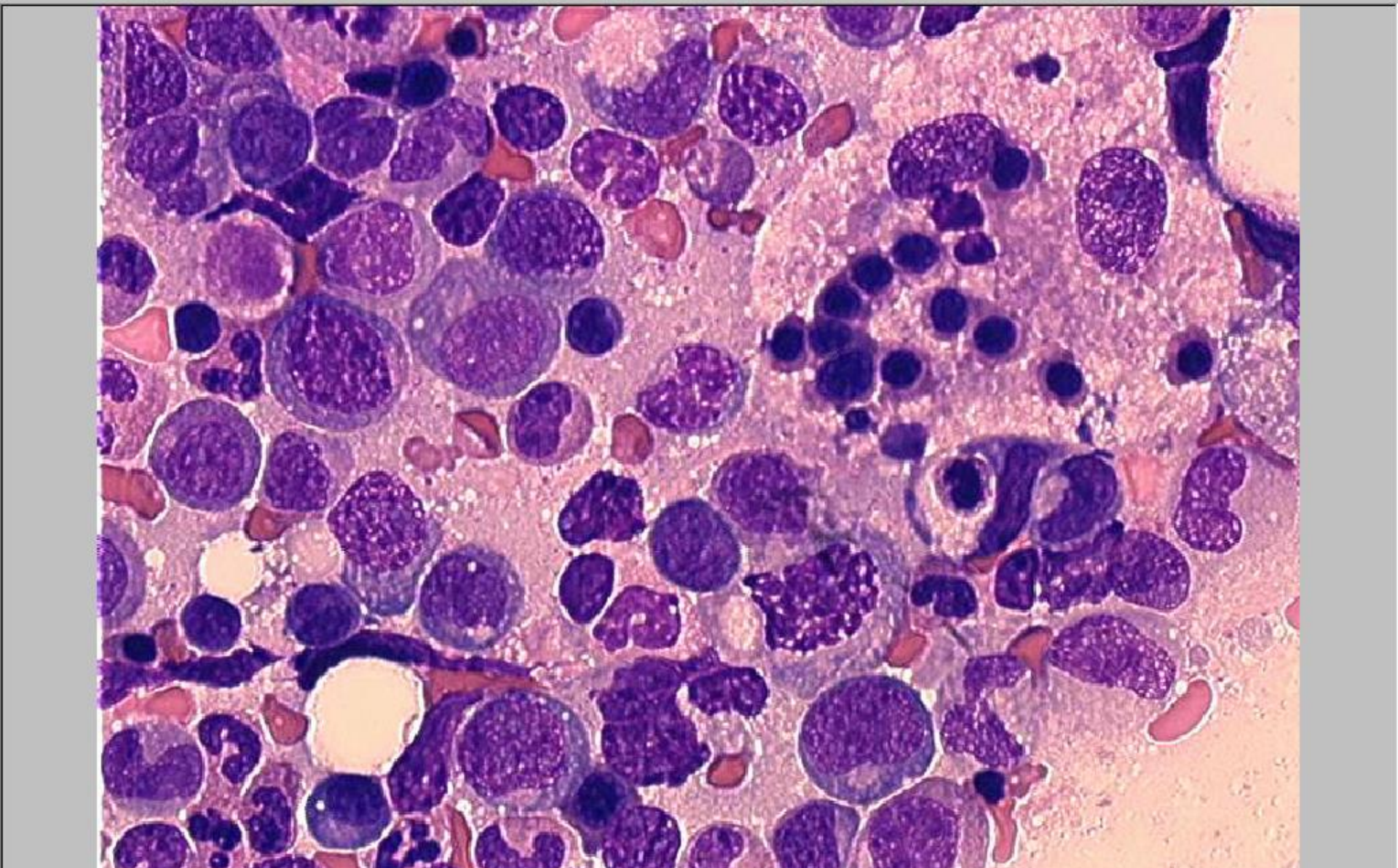
L_1: small, monomorphic

L_2: large, heterogeneous

L_3: Burkitt cell-type

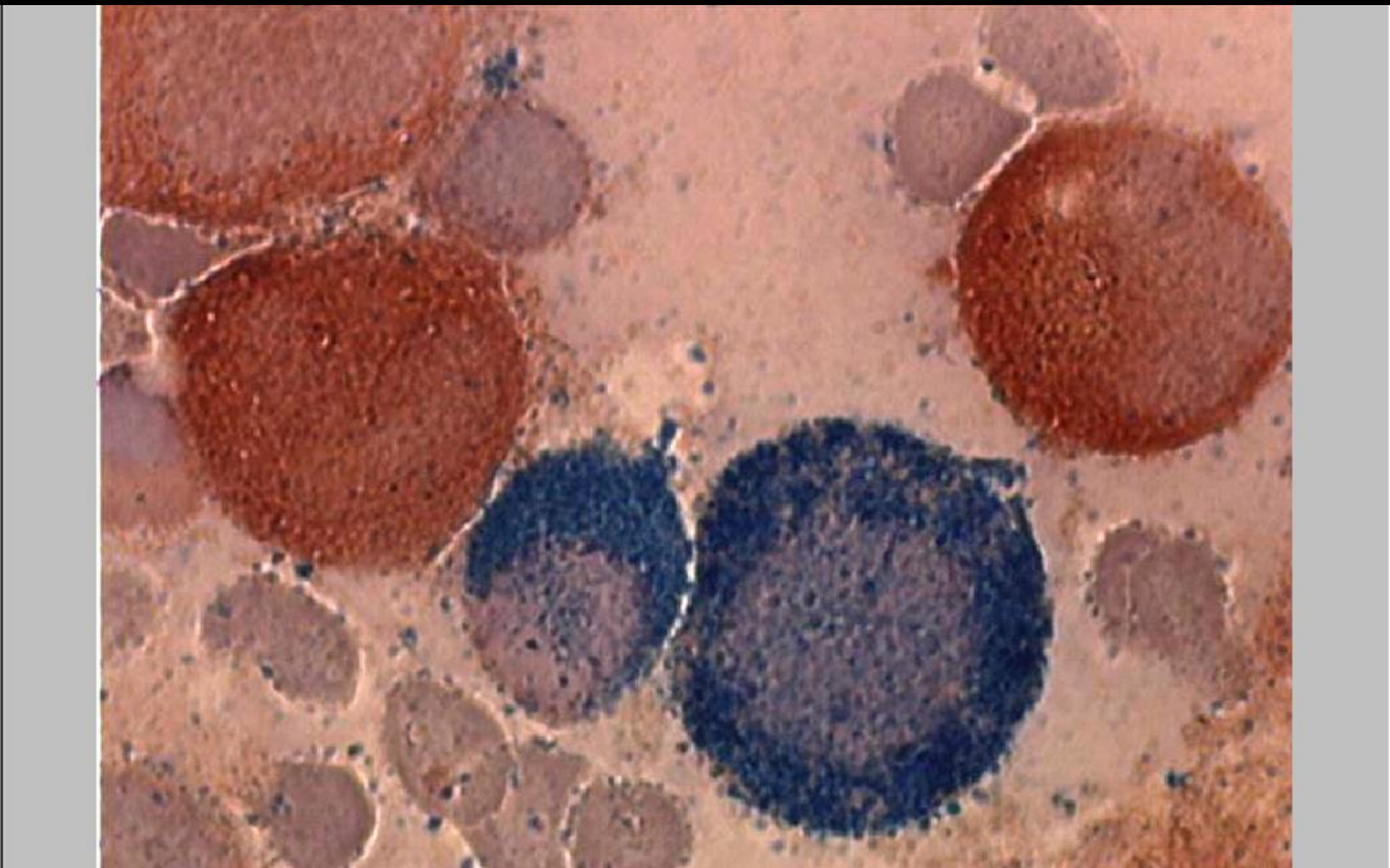
*French-American-British (FAB) classification

Akute myeloische Leukämie: monozytisch (M5)

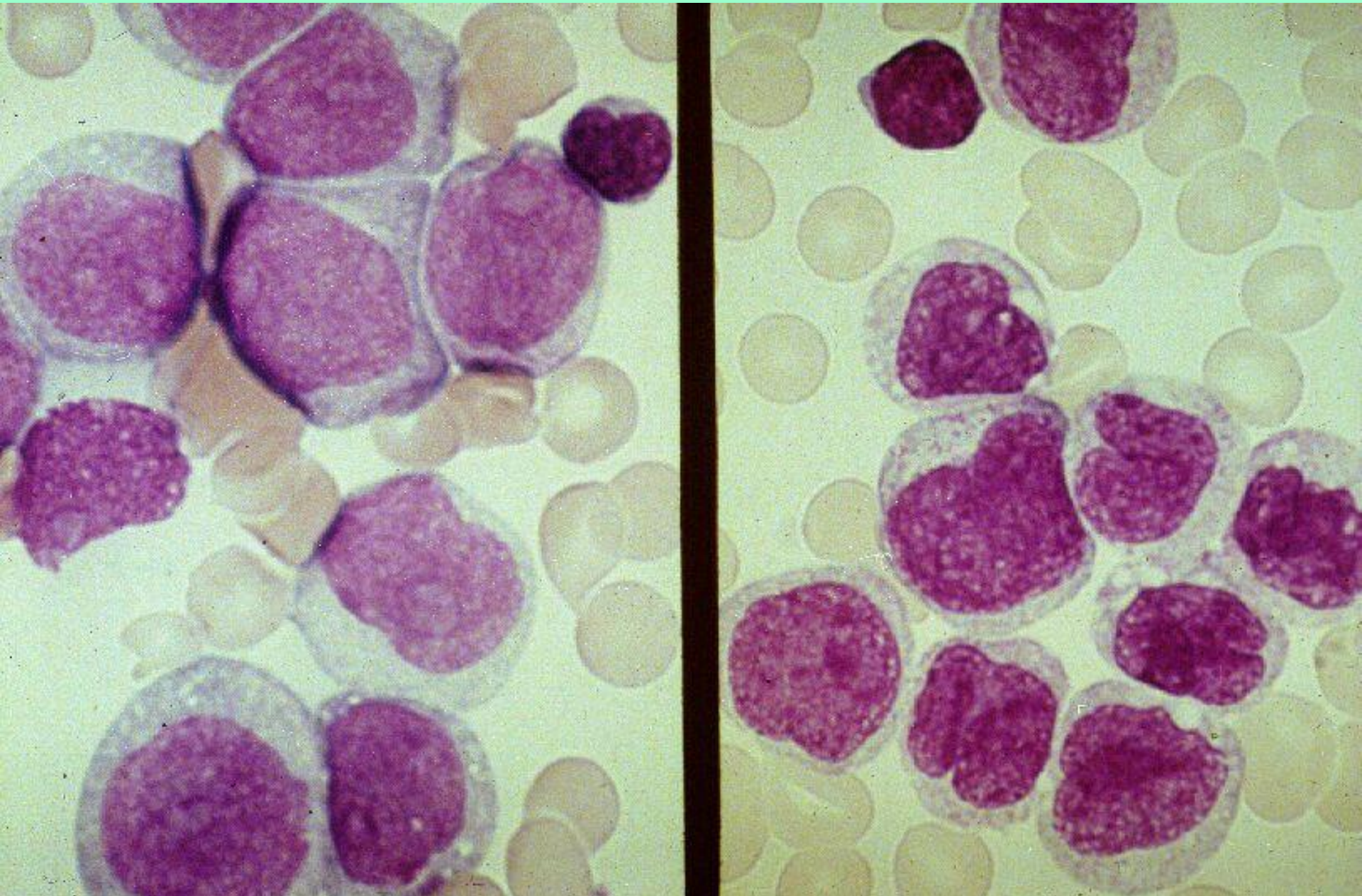


Akute myeloische Leukämie: monozytisch (M5)

Histochemisch : positive Monozytenperoxidase



Akute myeloische Leukämie: monozytisch (M5)



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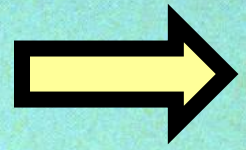
M_4: myelomonocytic

M_5: monocytic



M_6: erythroleukaemia

M_7: megakaryoblastic

Lymphoblastic

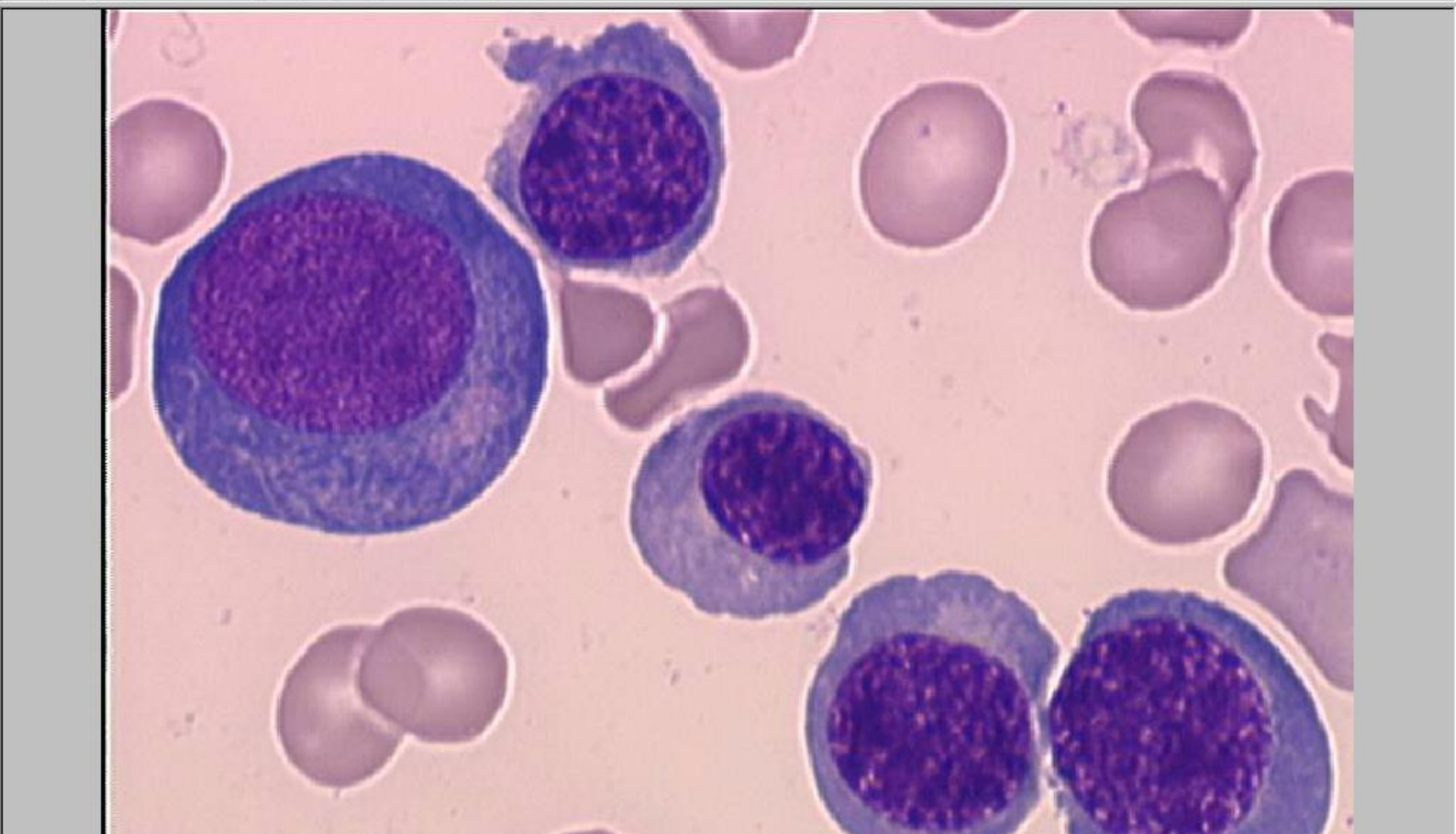
L_1: small, monomorphic

L_2: large, heterogeneous

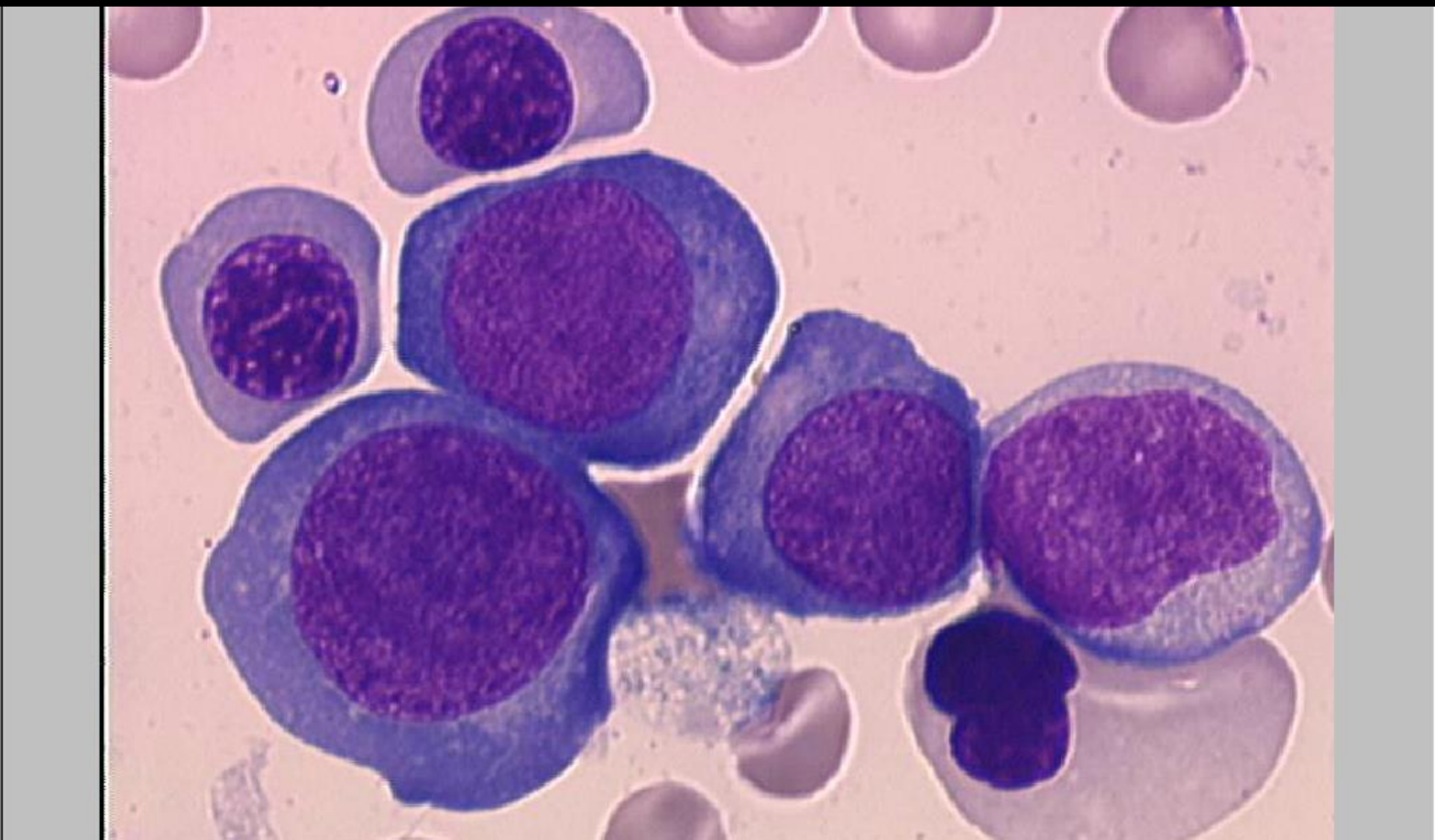
L_3: Burkitt cell-type

*French-American-British (FAB) classification

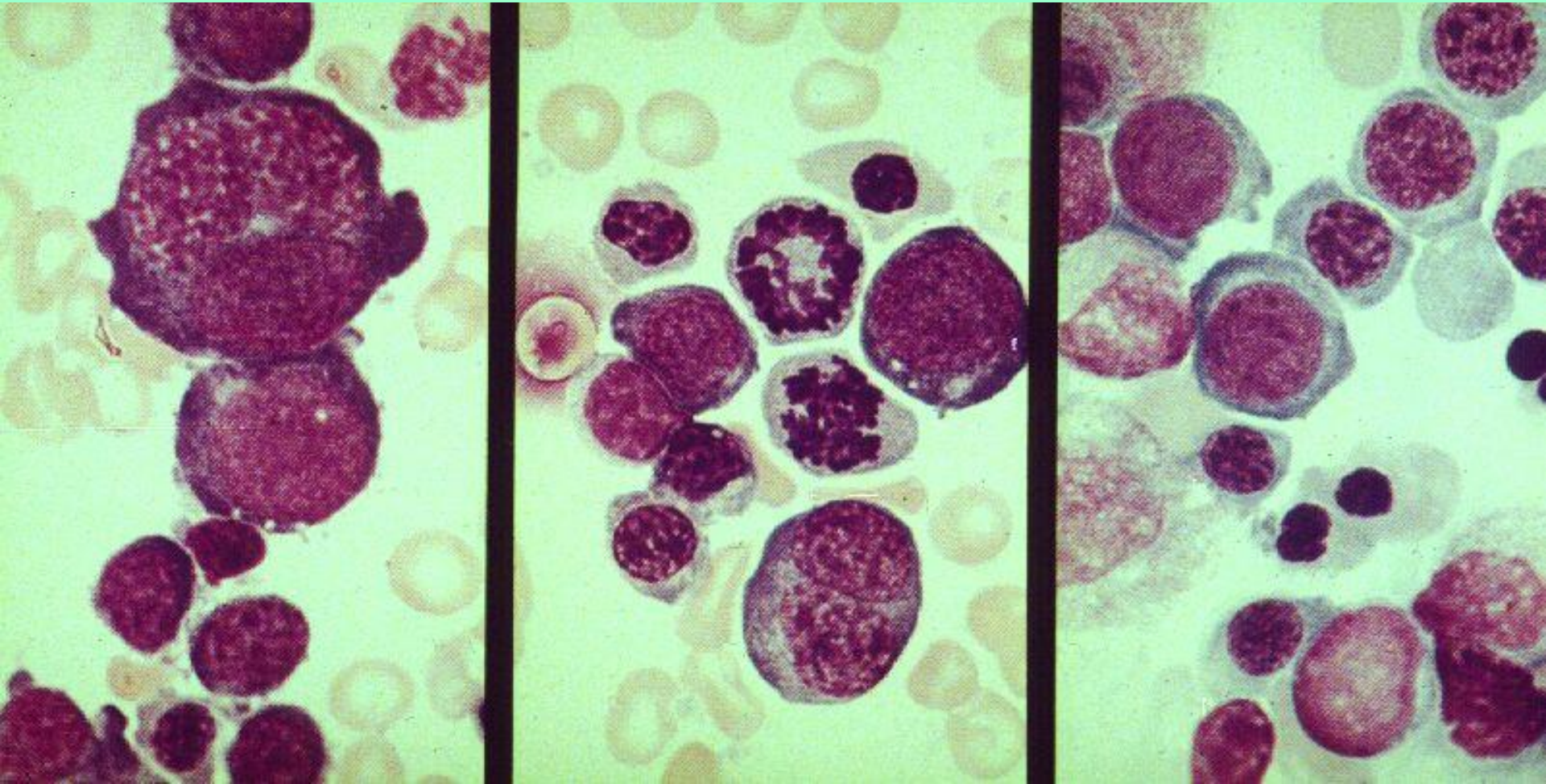
Akute myeloische Leukämie: erythroleukämisch (M6)



Akute myeloische Leukämie: erythroleukämisch (M6)



Akute myeloische Leukämie: erythroleukämisch (M6)



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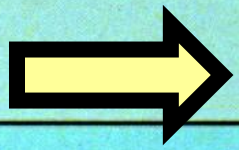
M_6: erythroleukaemia



M_7: megakaryoblastic

Lymphoblastic

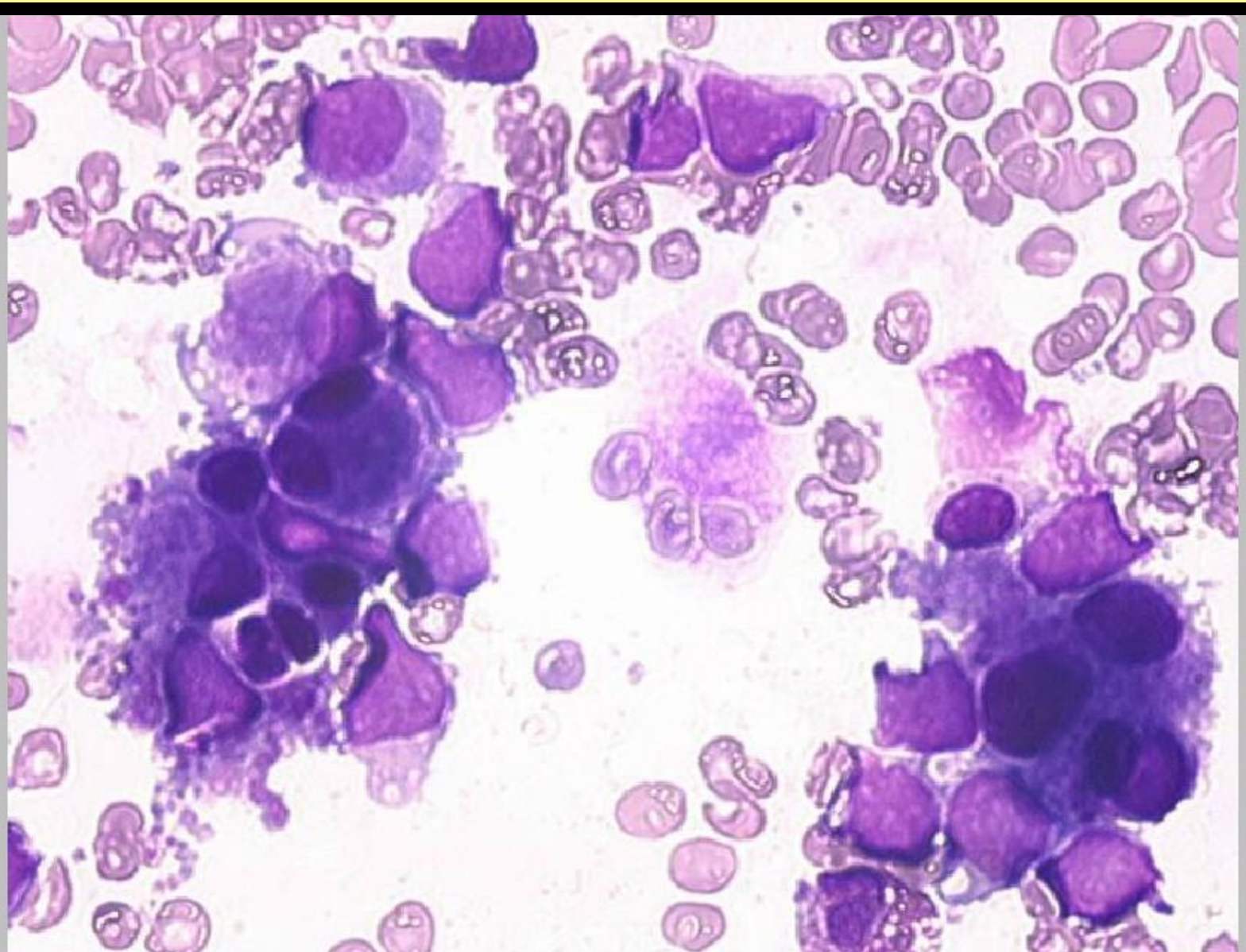
L_1: small, monomorphic

L_2: large, heterogeneous

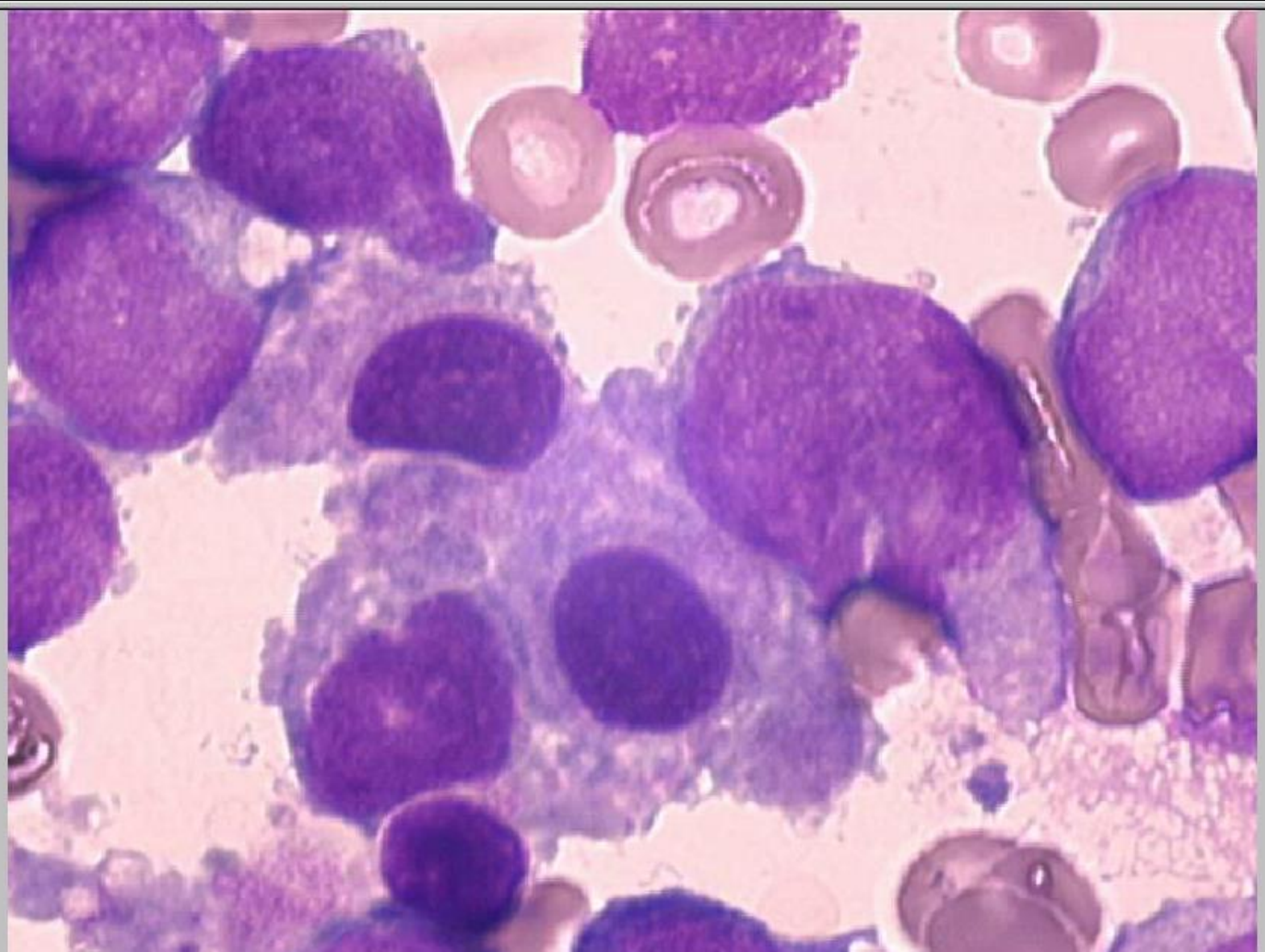
L_3: Burkitt cell-type

*French-American-British (FAB) classification

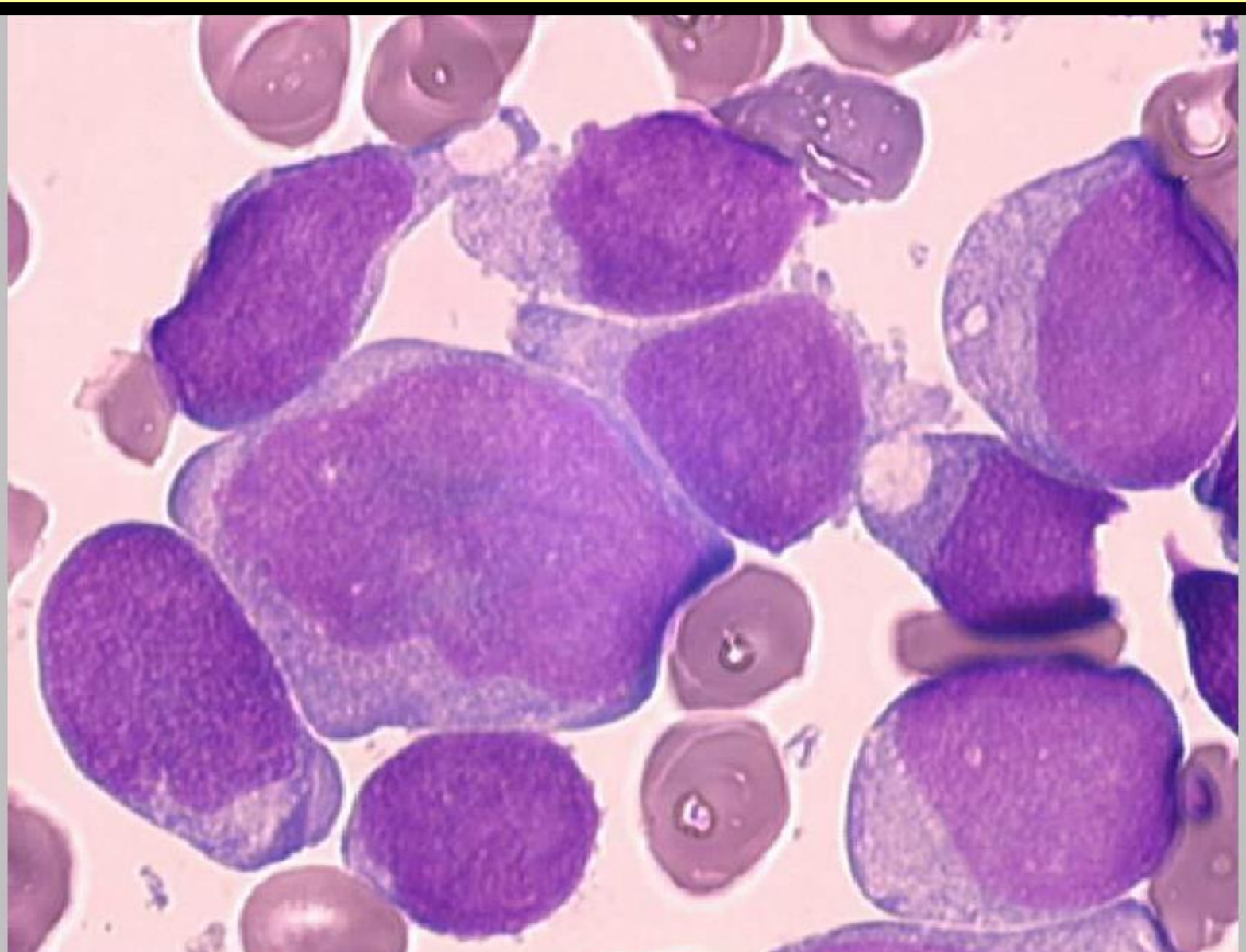
Akute myeloische Leukämie: megakaryozytisch(M7 der FAB-Klassifikation)



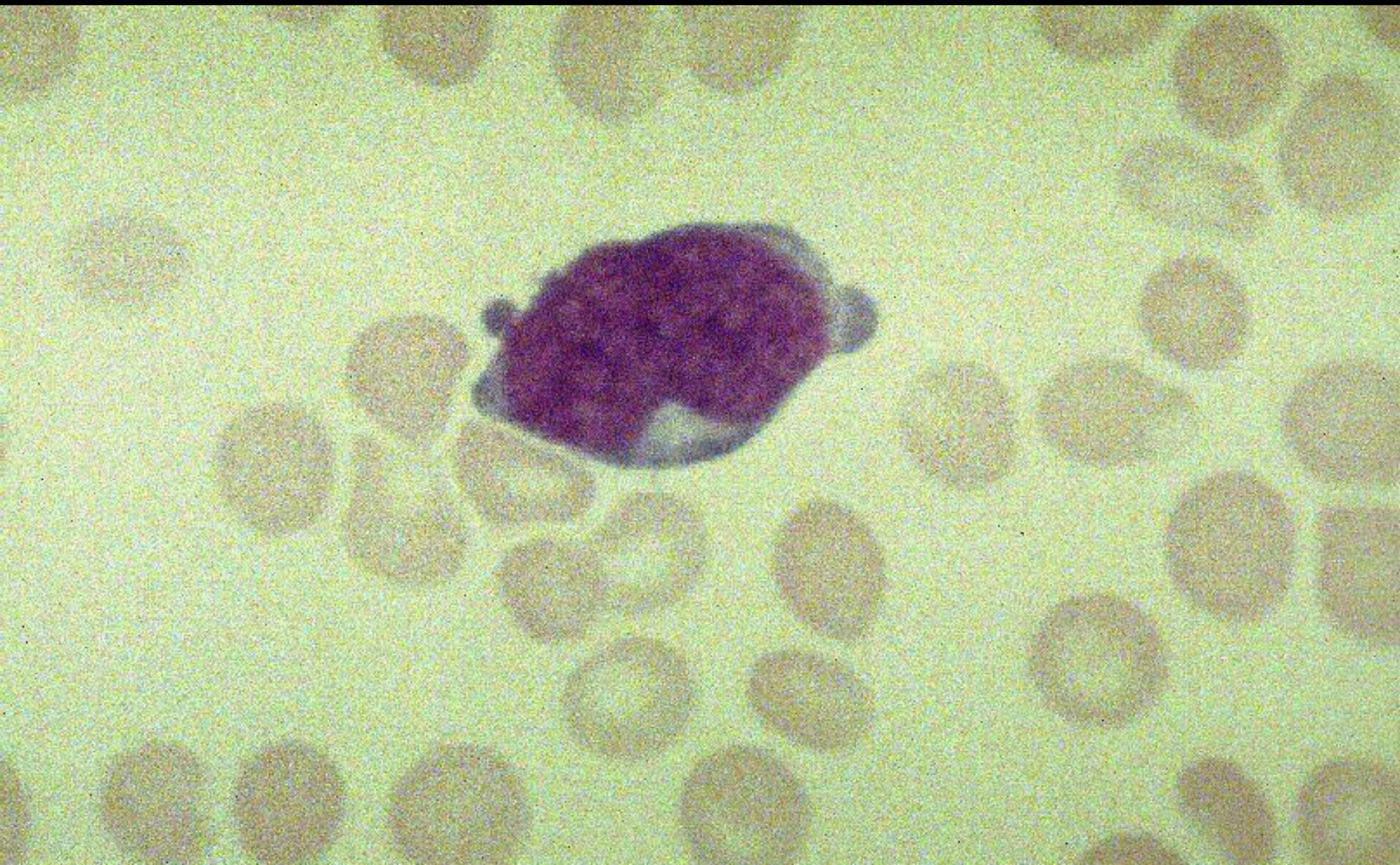
Akute myeloische Leukämie: megakaryozytisch(M7 der FAB-Klassifikation)



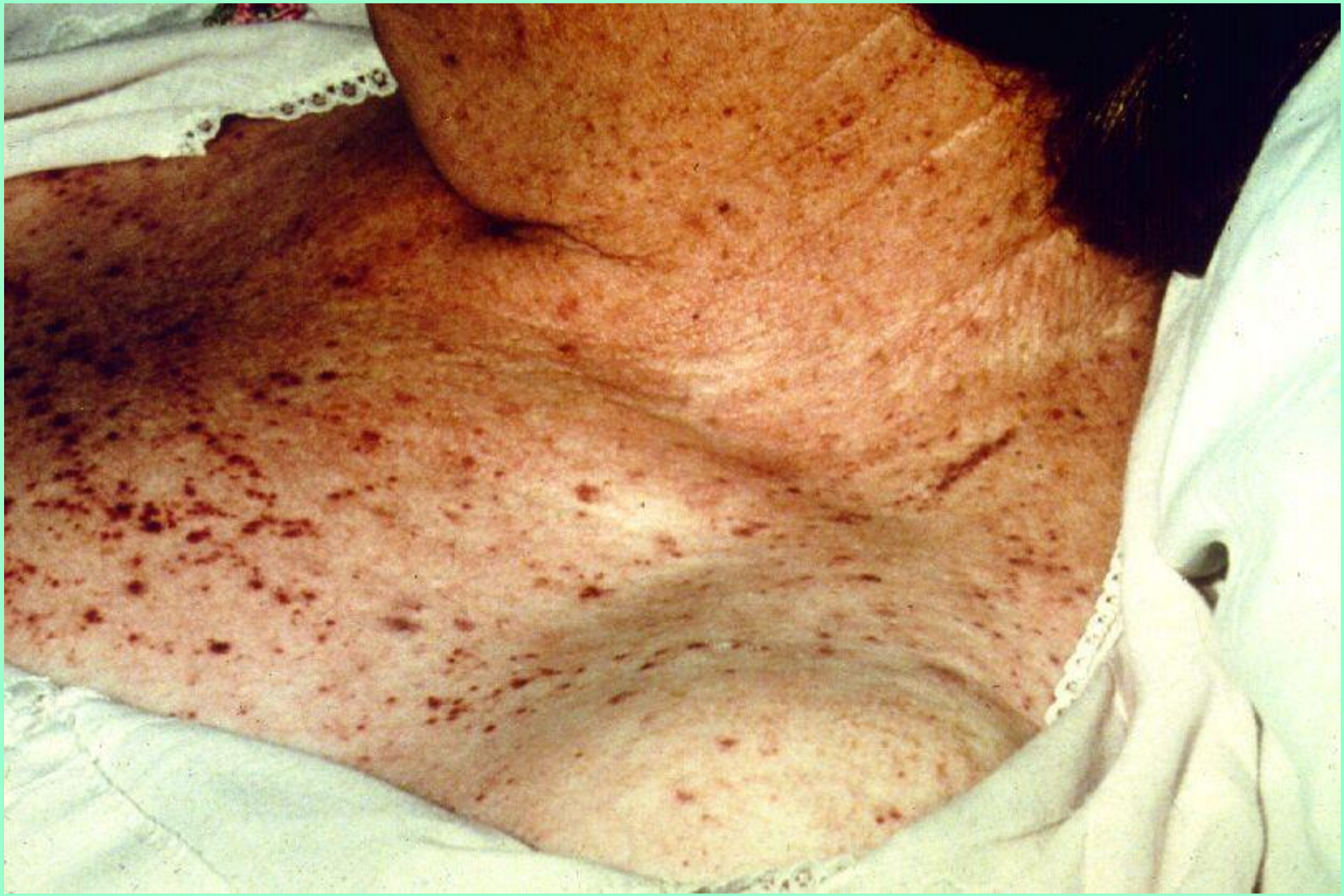
Akute myeloische Leukämie: megakaryozytisch(M7 der FAB-Klassifikation)



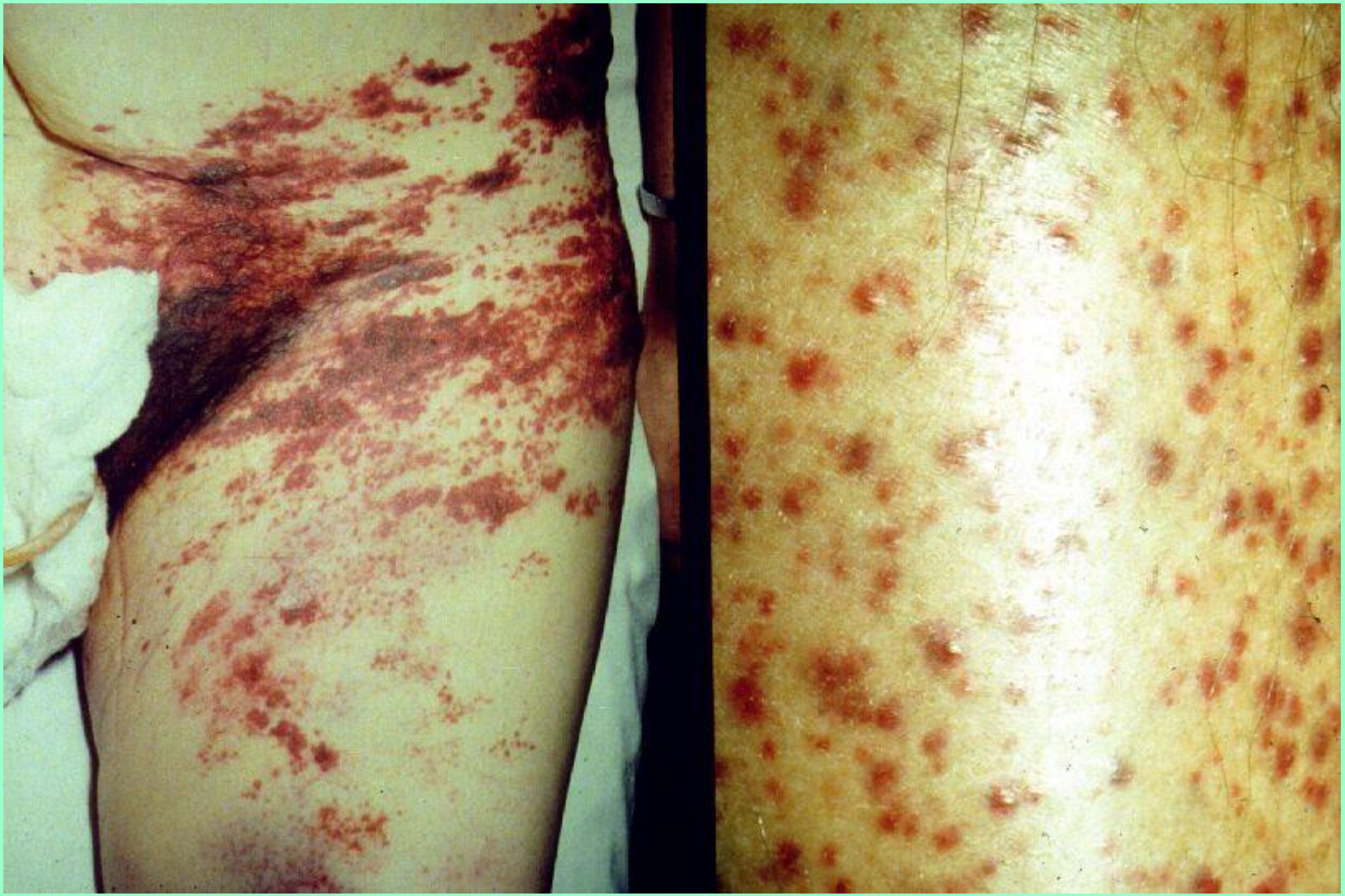
Akute myeloische Leukämie: megakaryozytisch(M7 der FAB-Klassifikation)



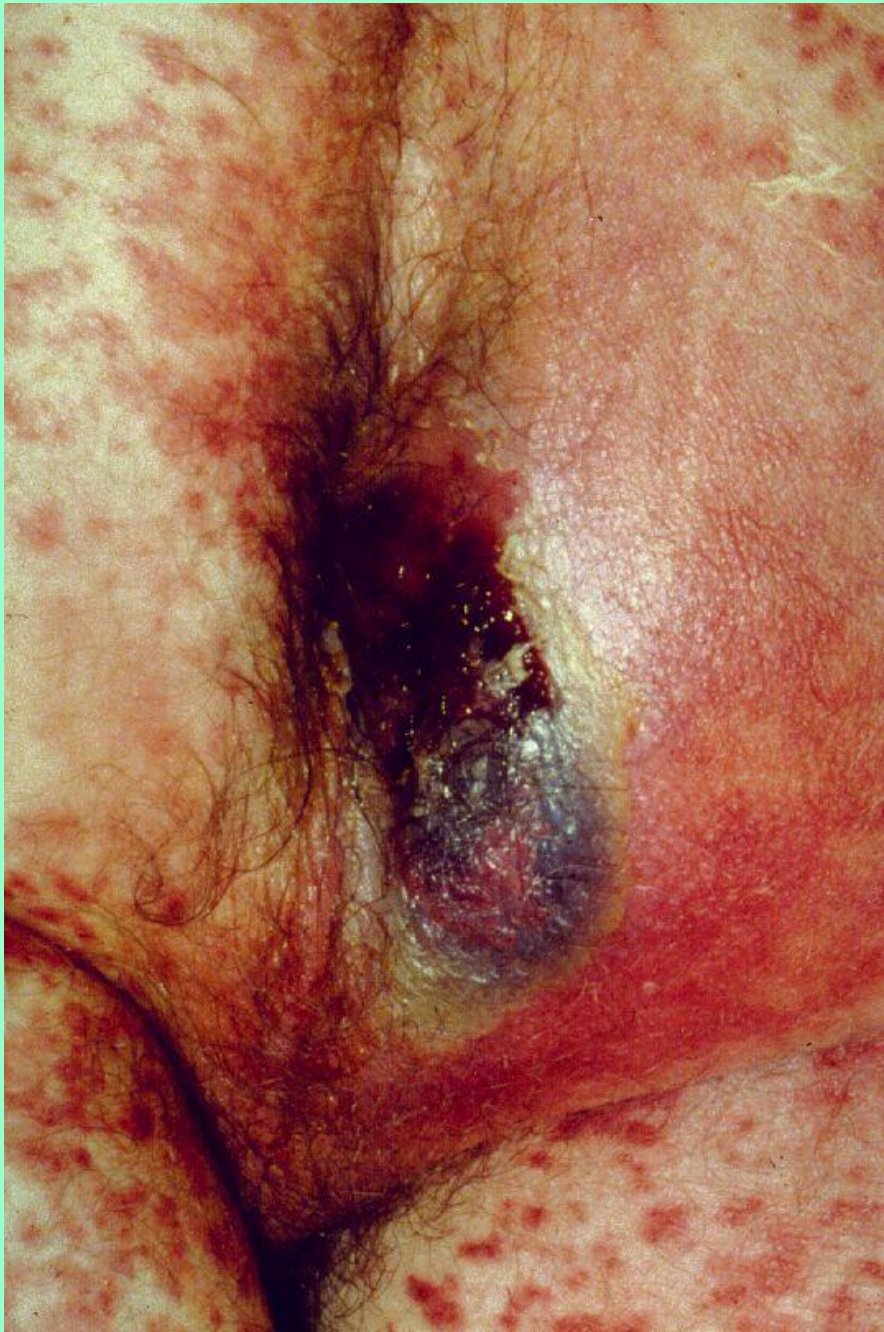
Hautinfiltrate und Hämorrhagien bei AML



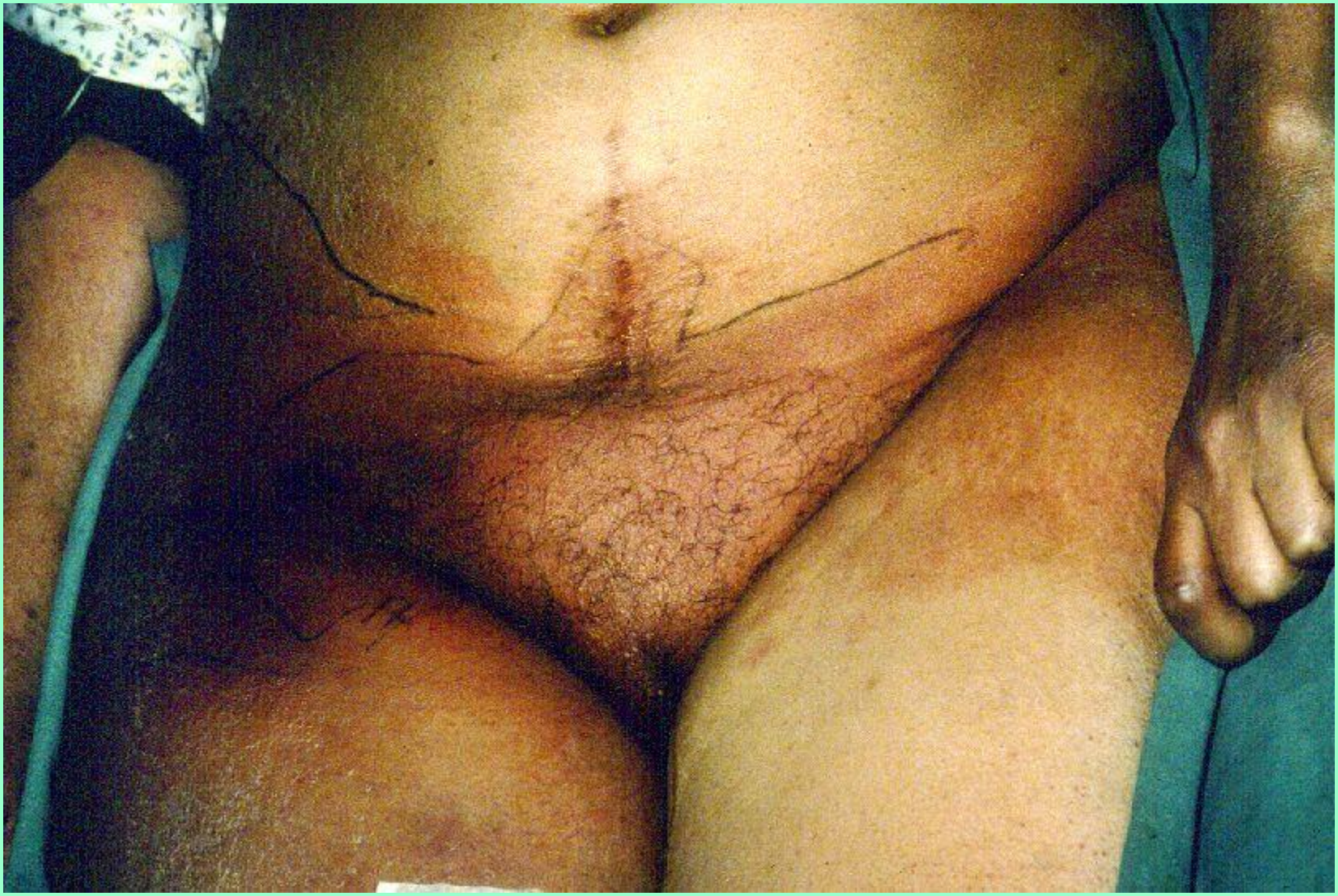
Hautinfiltrate und Hämorrhagien bei AML

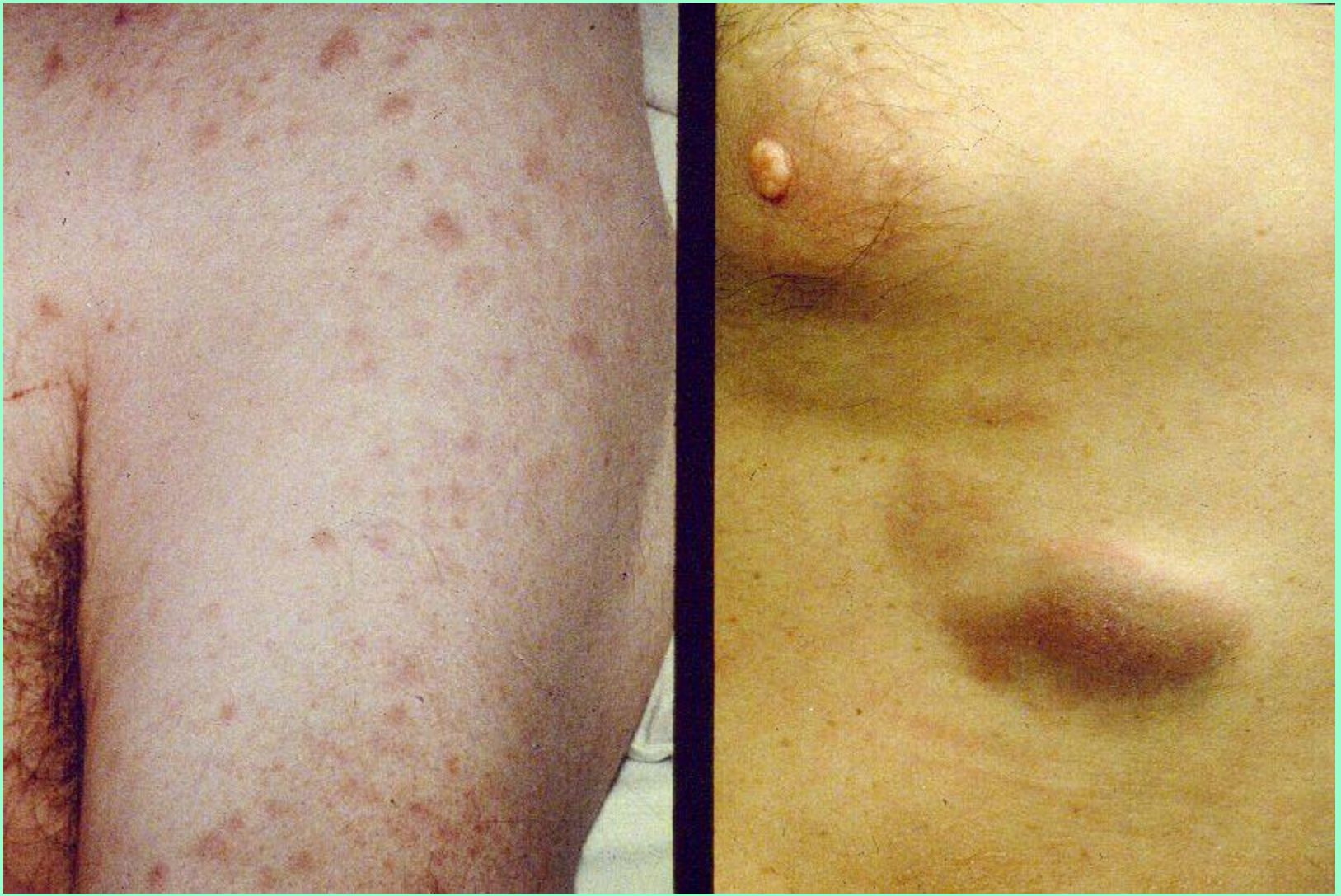


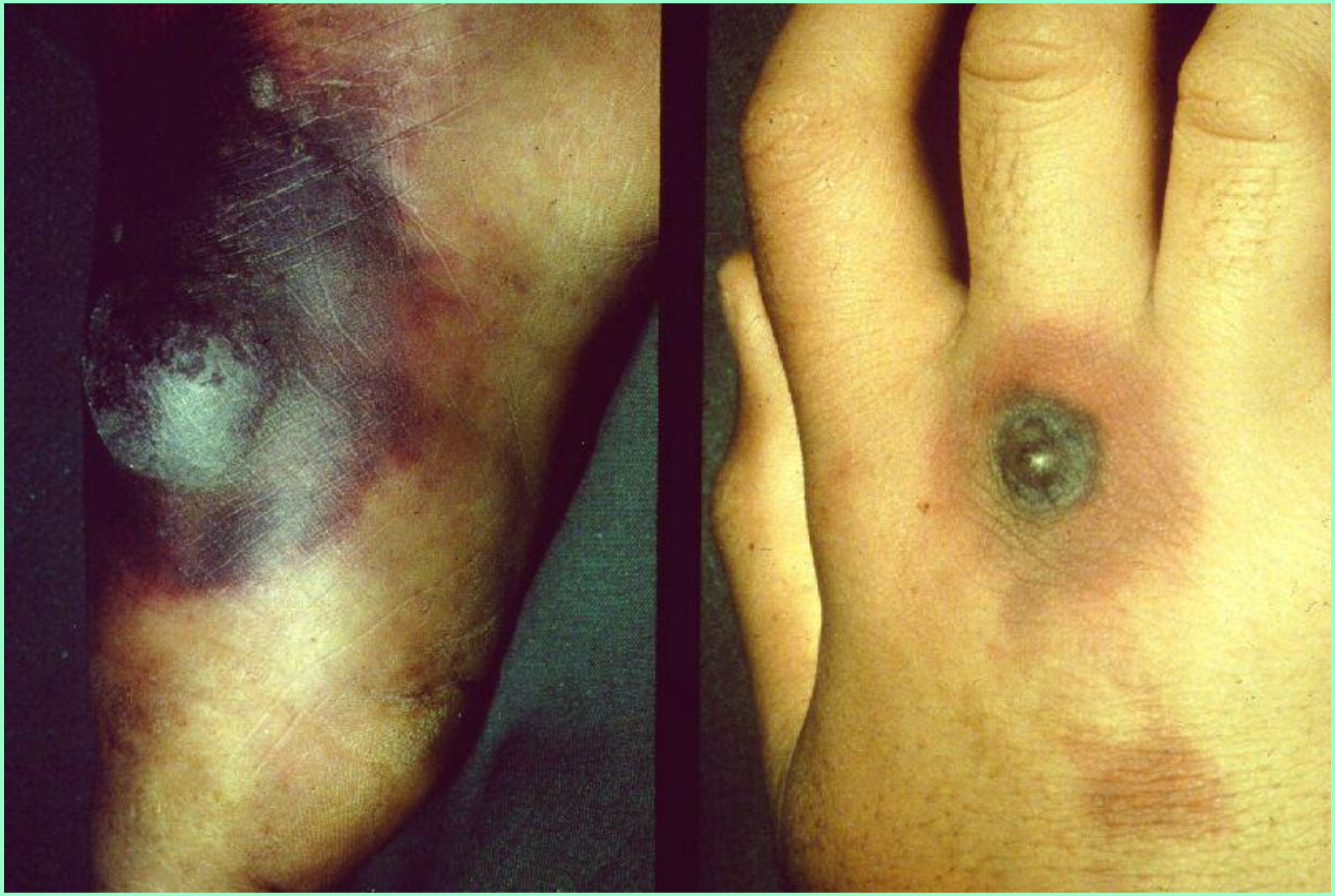
Infektion durch opportunistische Keime und myeloische Hautinfiltrate bei AML



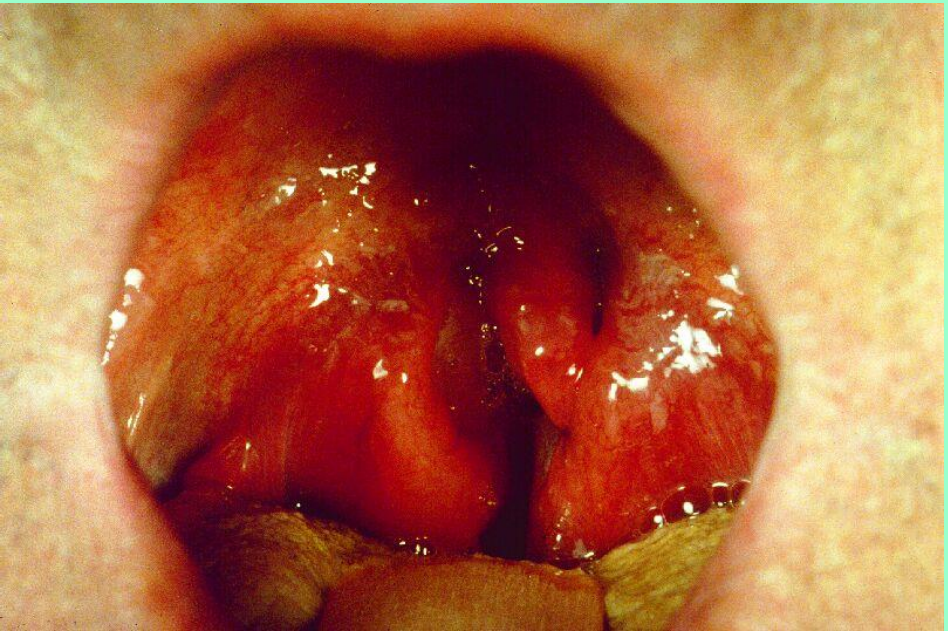
Infektion durch opportunistische Keime und myeloische Hautinfiltrate bei AML

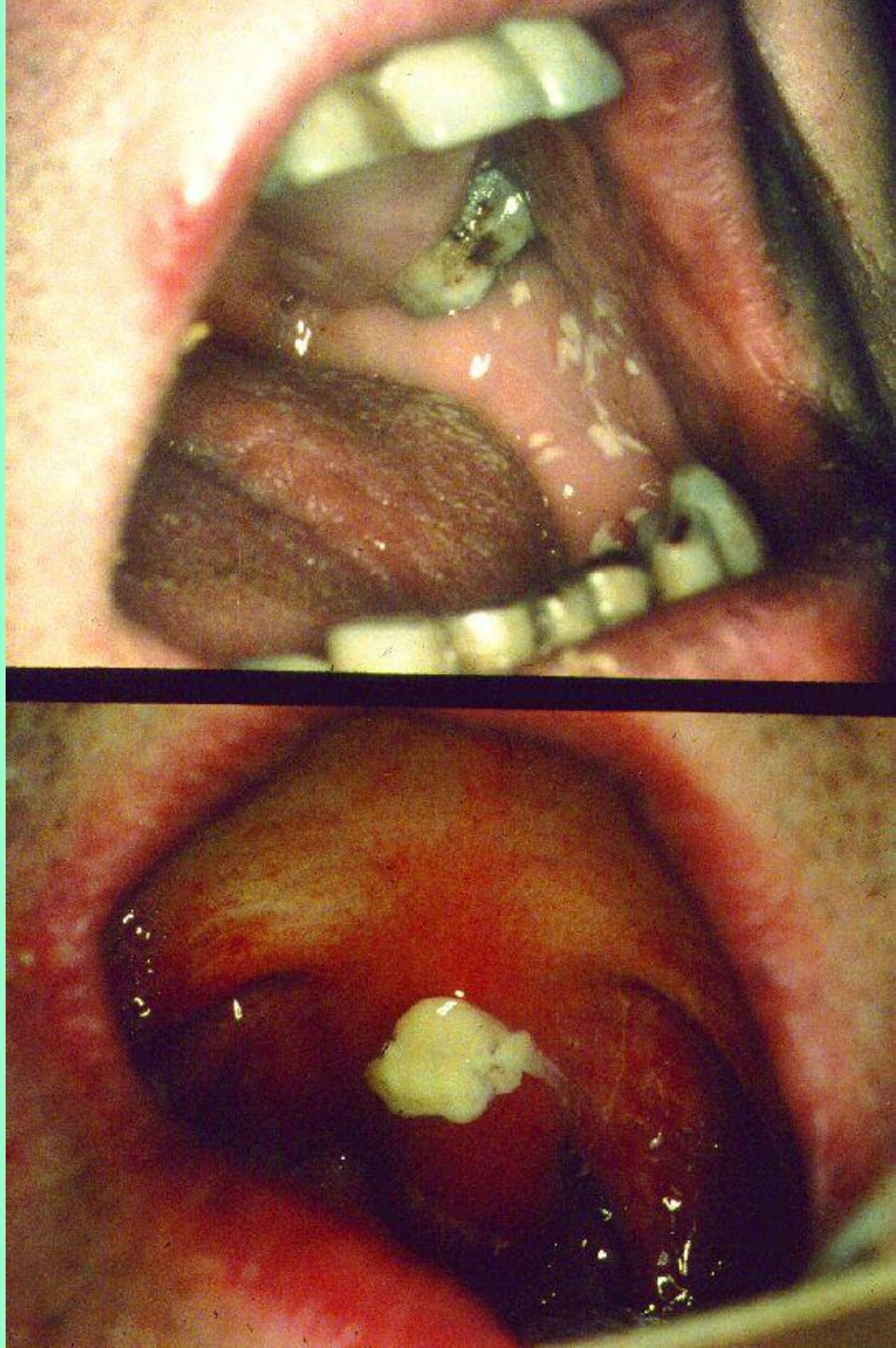


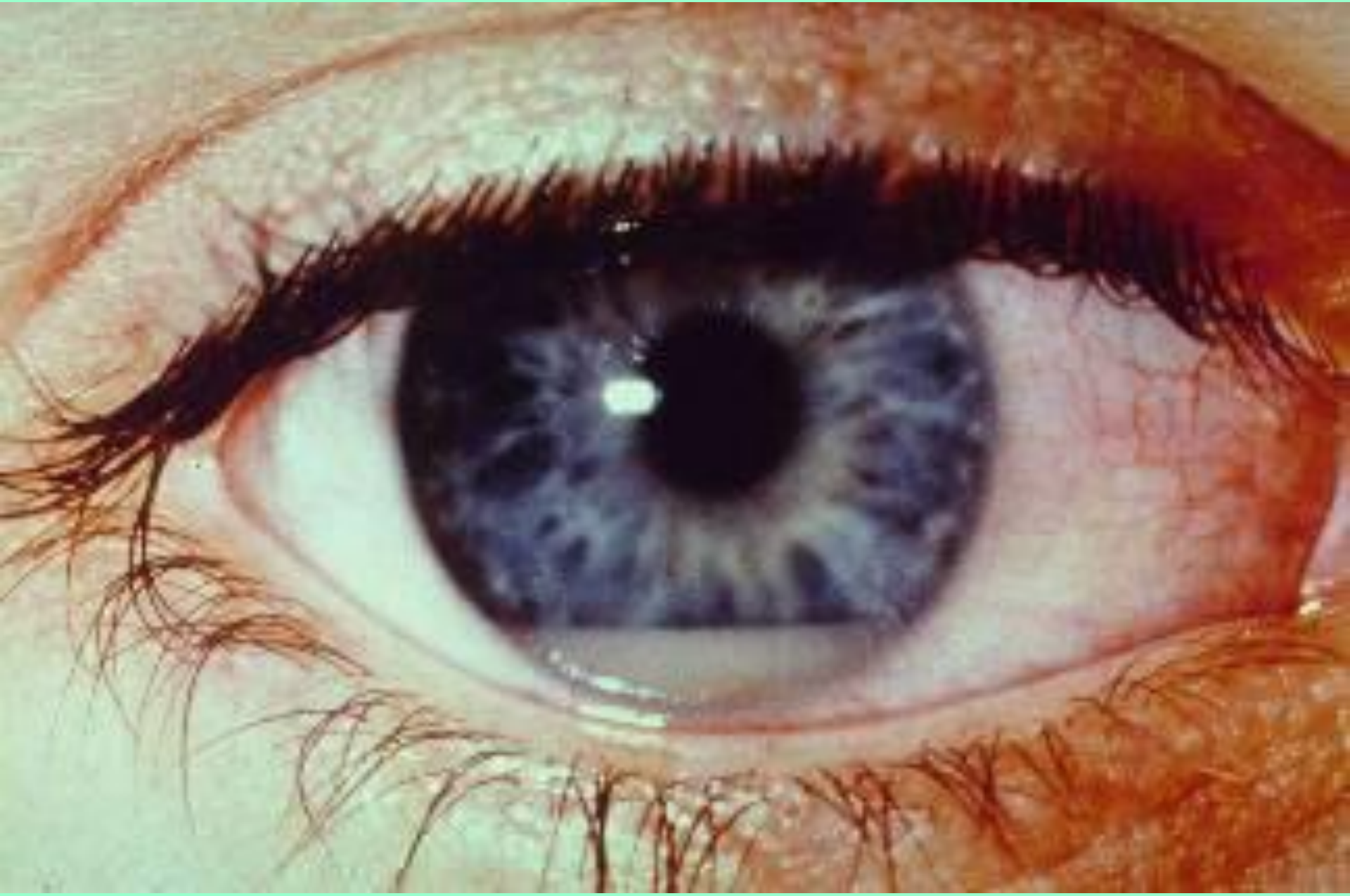




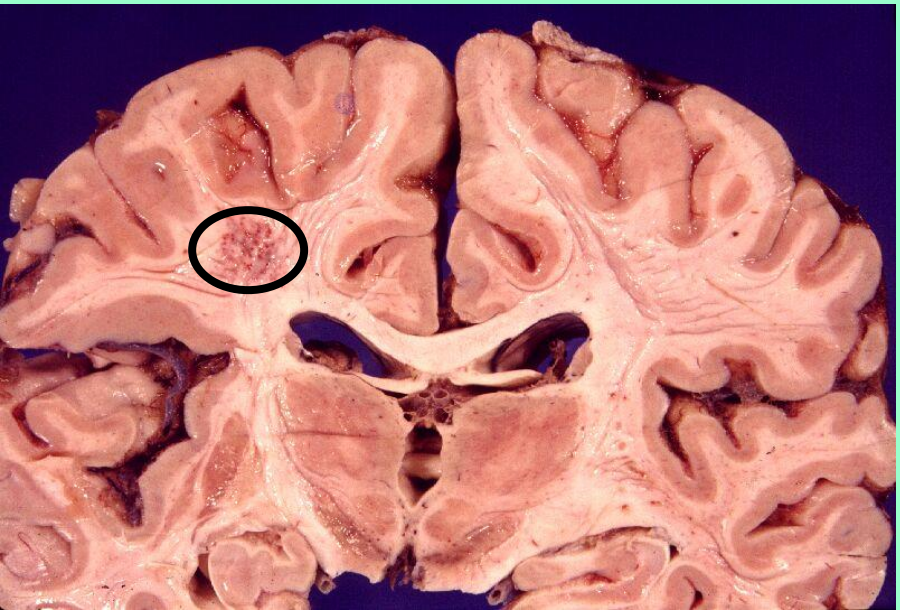
Orale tumoröse Manifestation bei AML







Intrazerebrales leukämisches Infiltrat mit zentraler Fazialisparese



Acute Leukaemia: Morphological Classification*

Myeloid (AML)

M_1: myeloblastic without maturation

M_2: myeloblastic with maturation

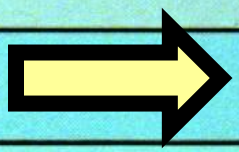
M_3: hypergranular promyelocytic

M_4: myelomonocytic

M_5: monocytic

M_6: erythroleukaemia

M_7: megakaryoblastic



Lymphoblastic

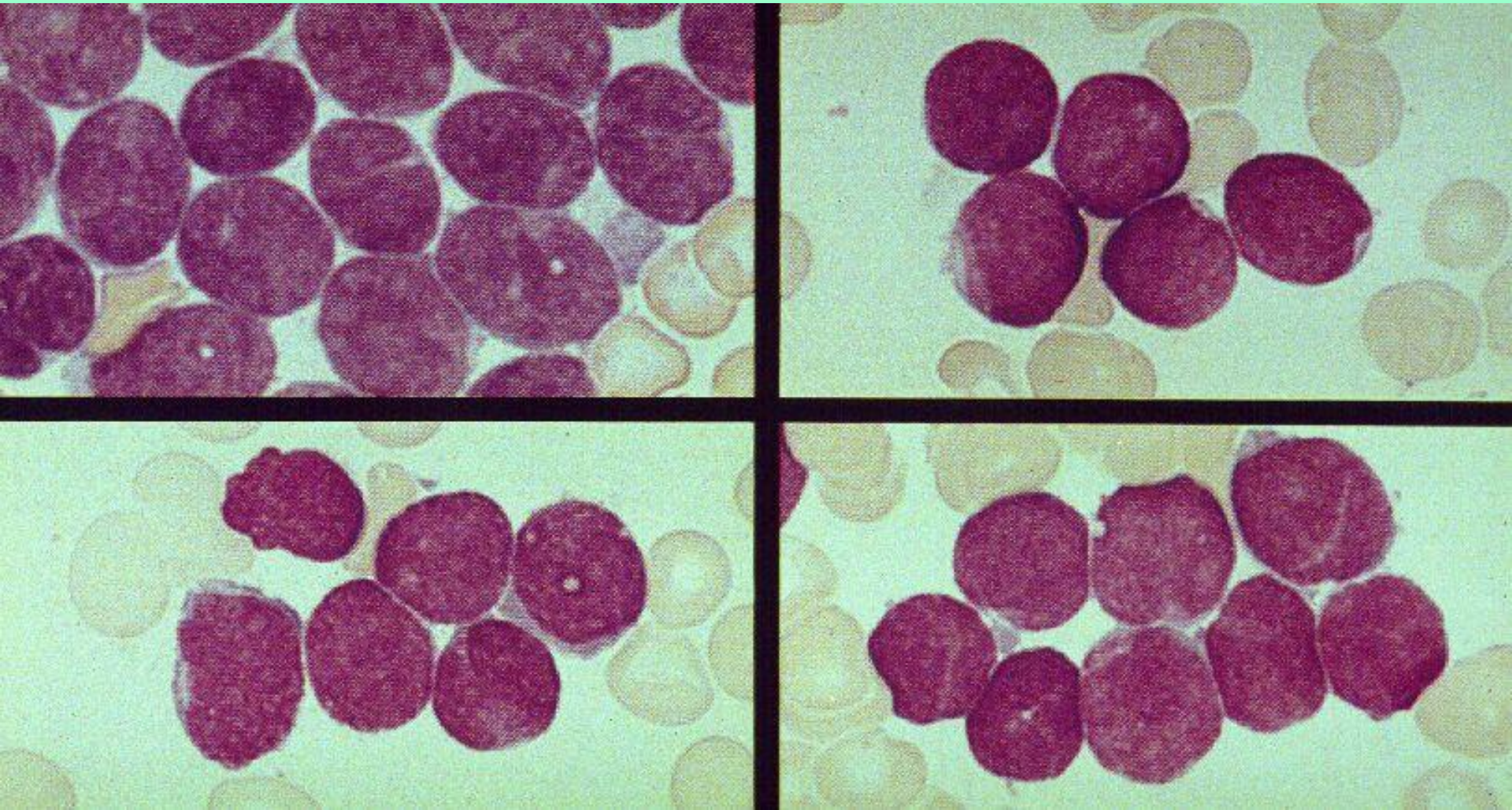
L_1: small, monomorphic

L_2: large, heterogeneous

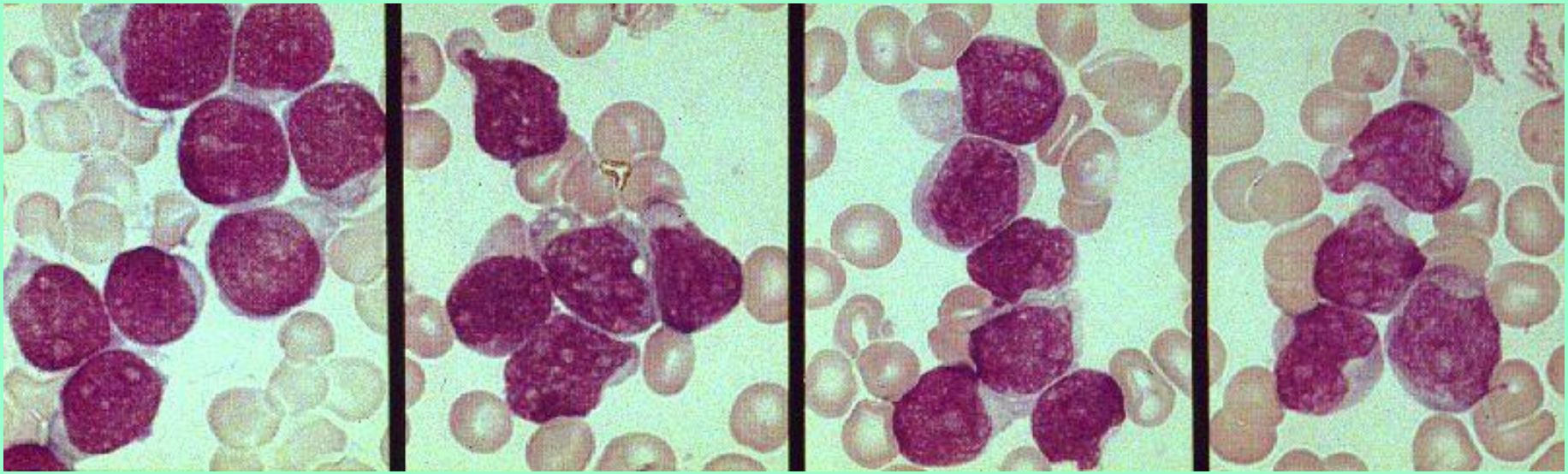
L_3: Burkitt cell-type

*French-American-British (FAB) classification

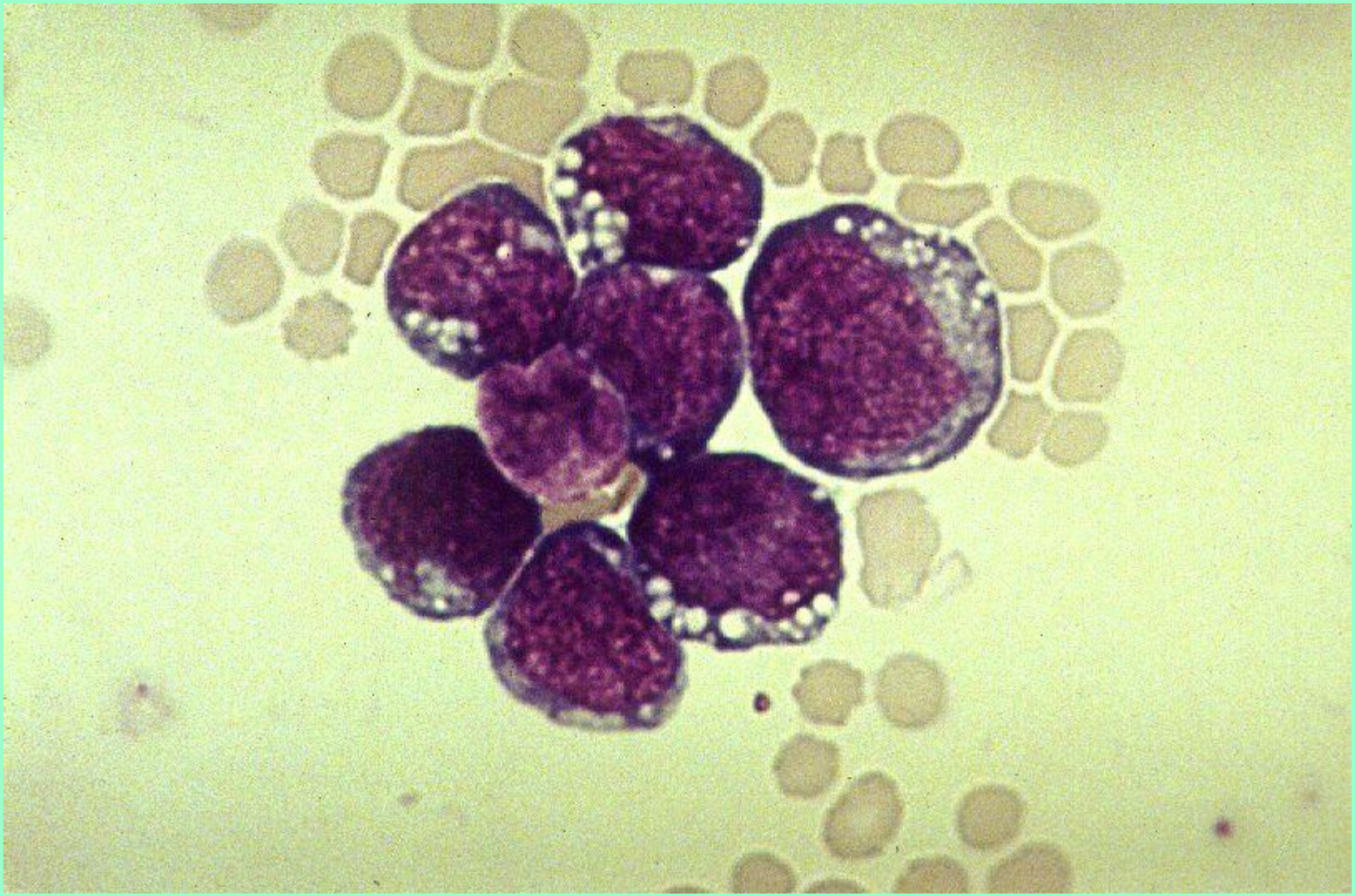
Akute lymphoblastische Leukämie (ALL): kleinzellig-monomorph

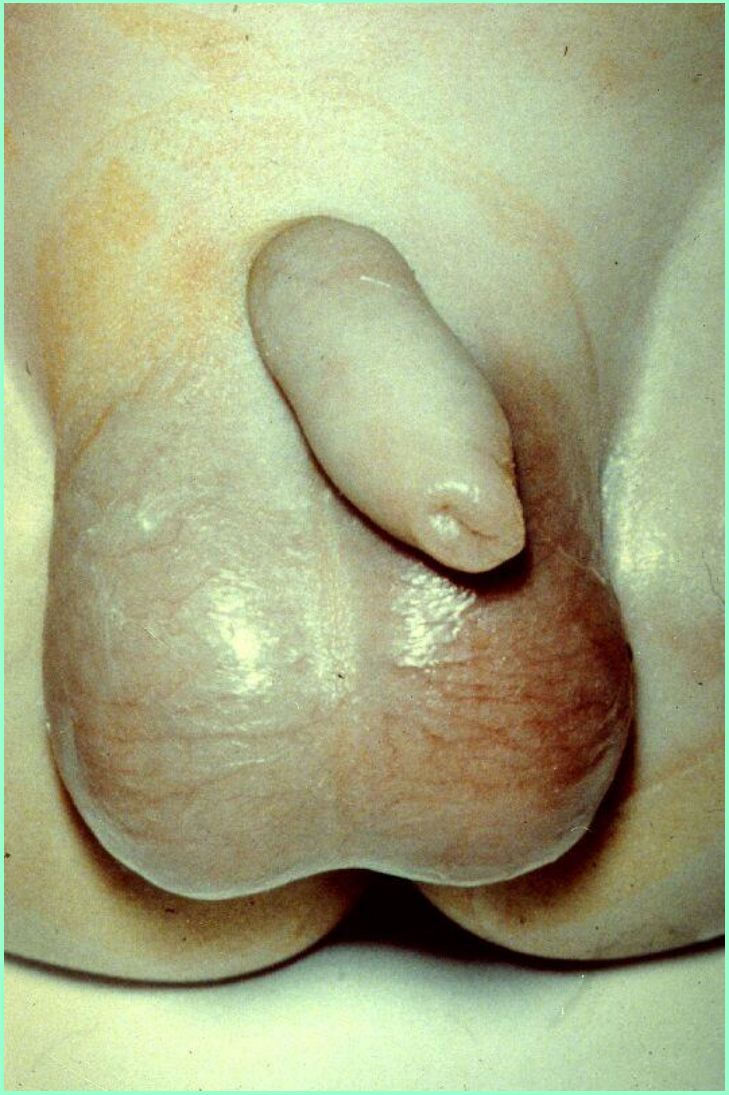


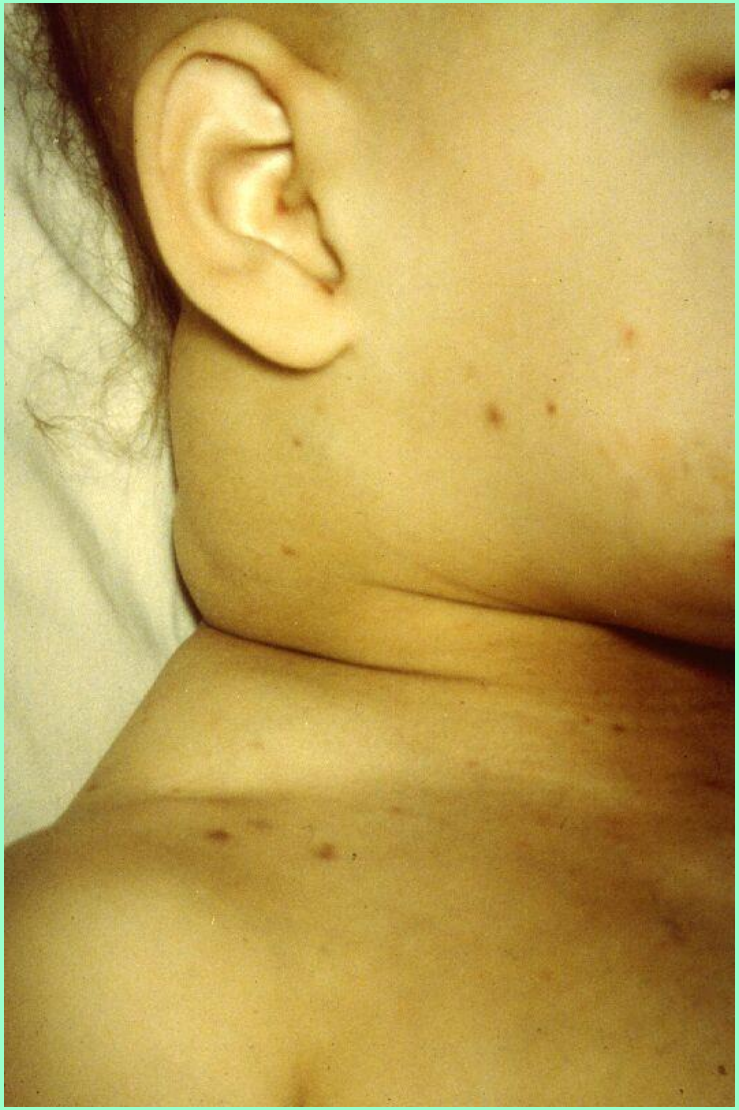
Akute lymphoblastische Leukämie (ALL): großzellig-heterogen

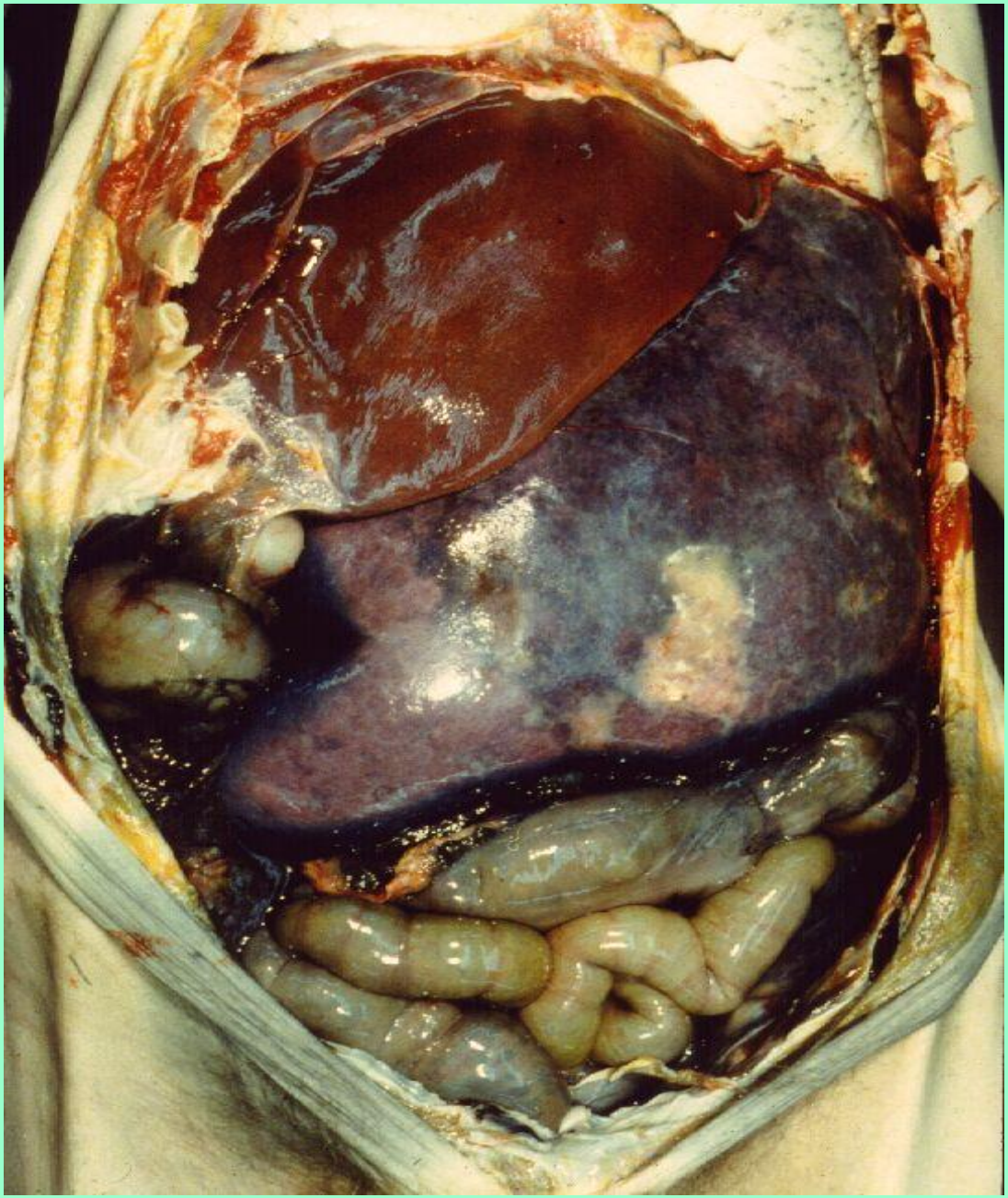


Akute lymphoblastische Leukämie (ALL): Burkitt-Typ

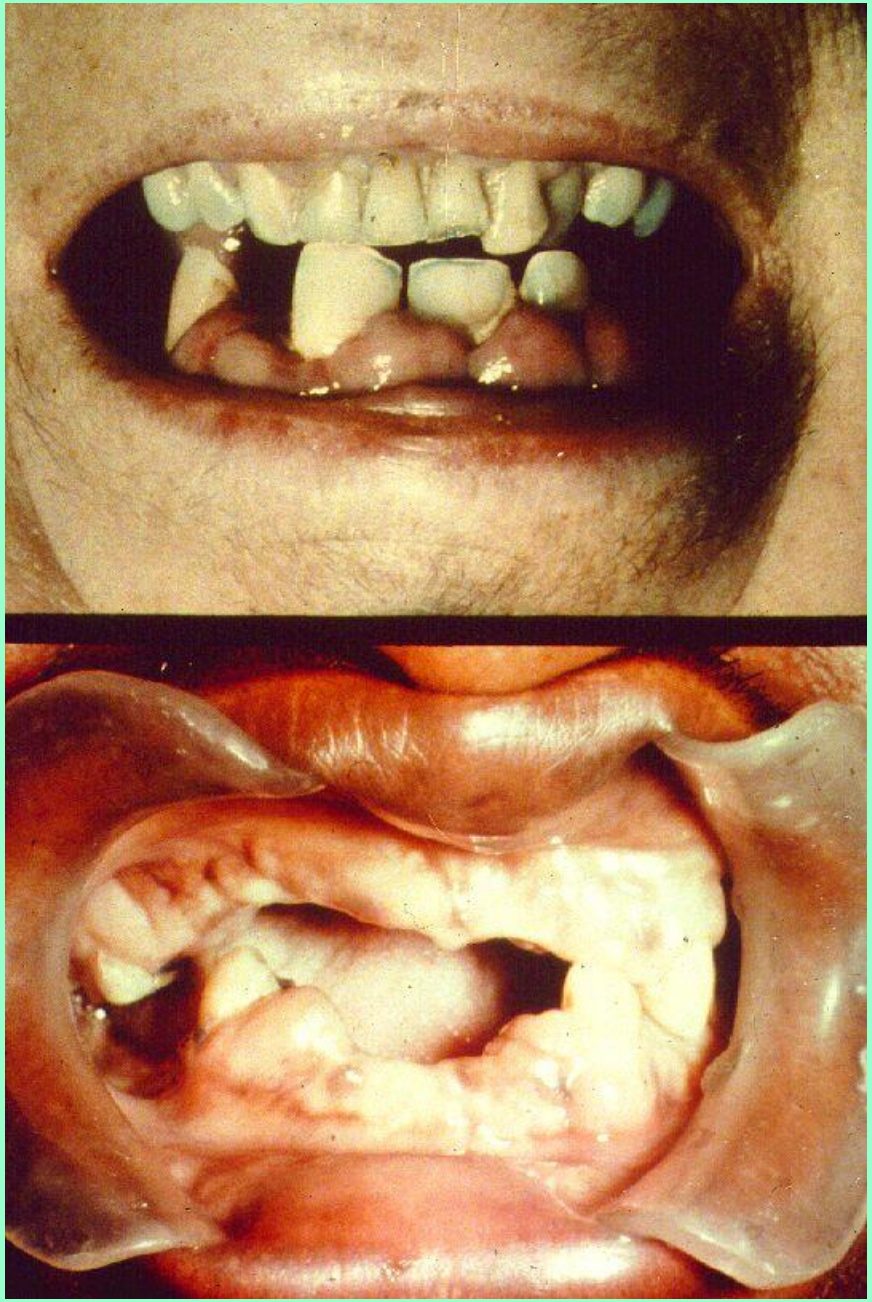


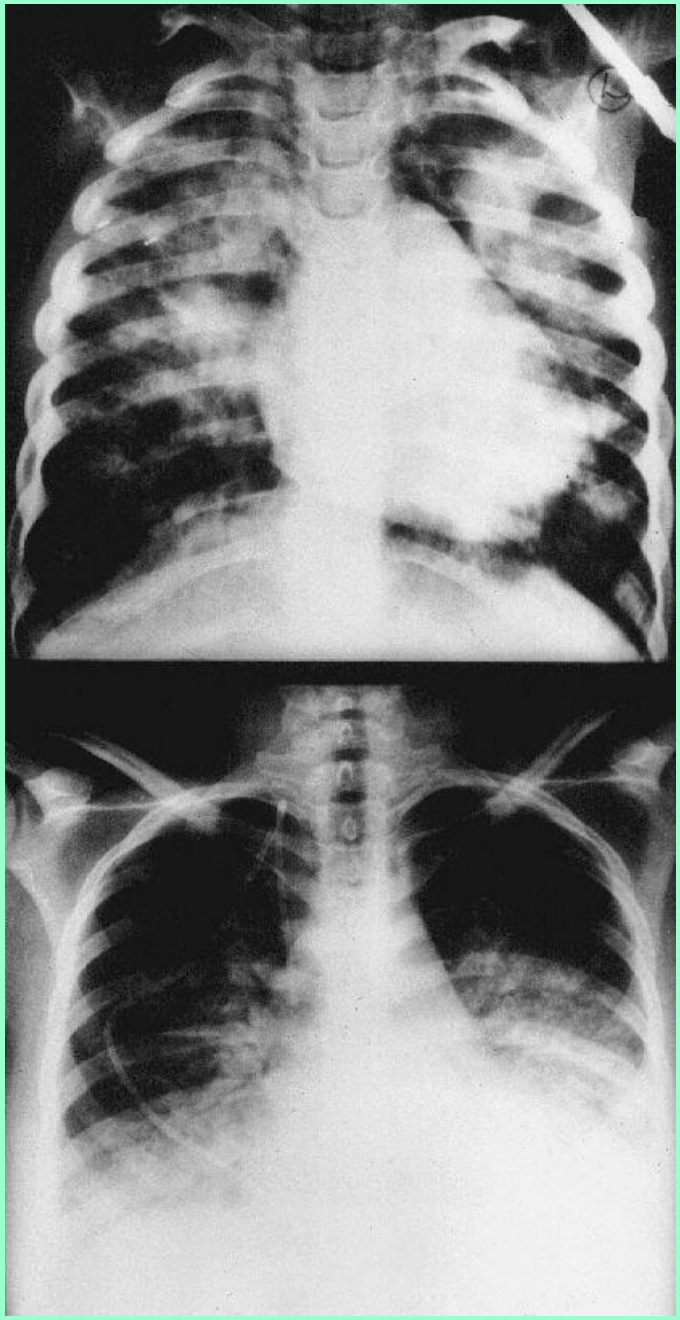


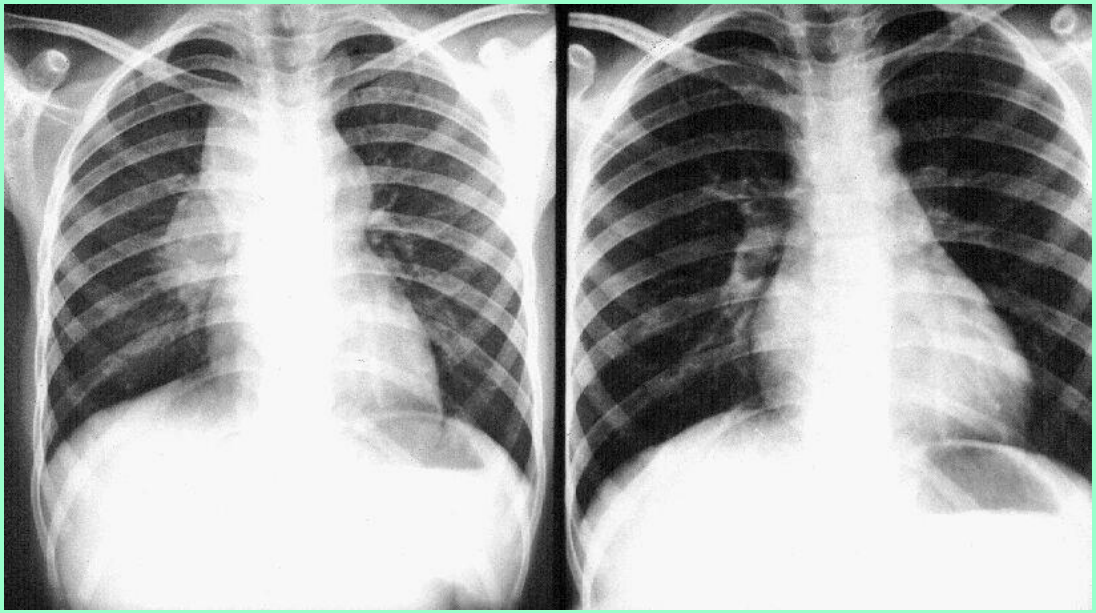




Tumoröse Gingivainfiltrate und Gingivahyperplasie bei AML

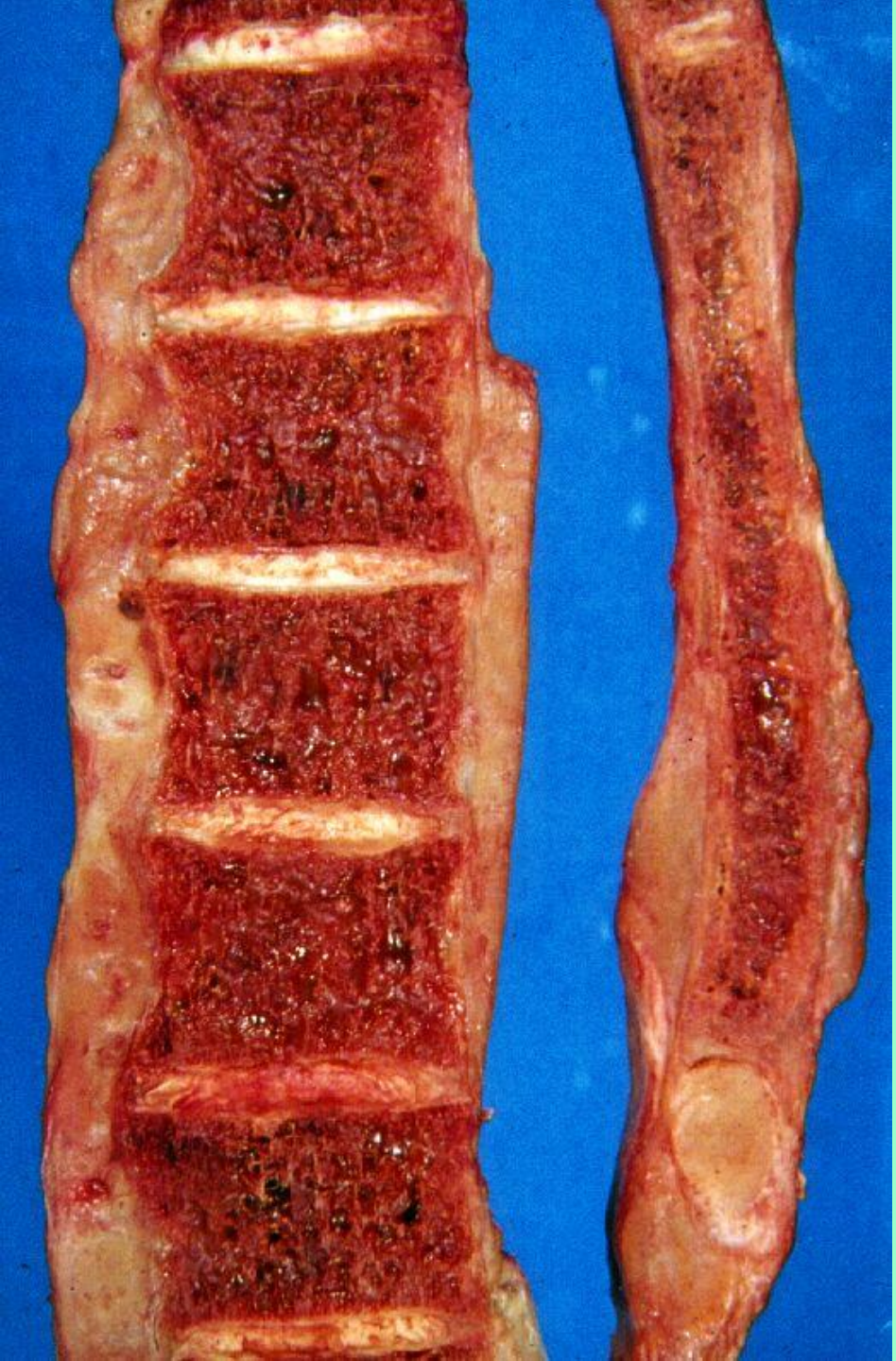


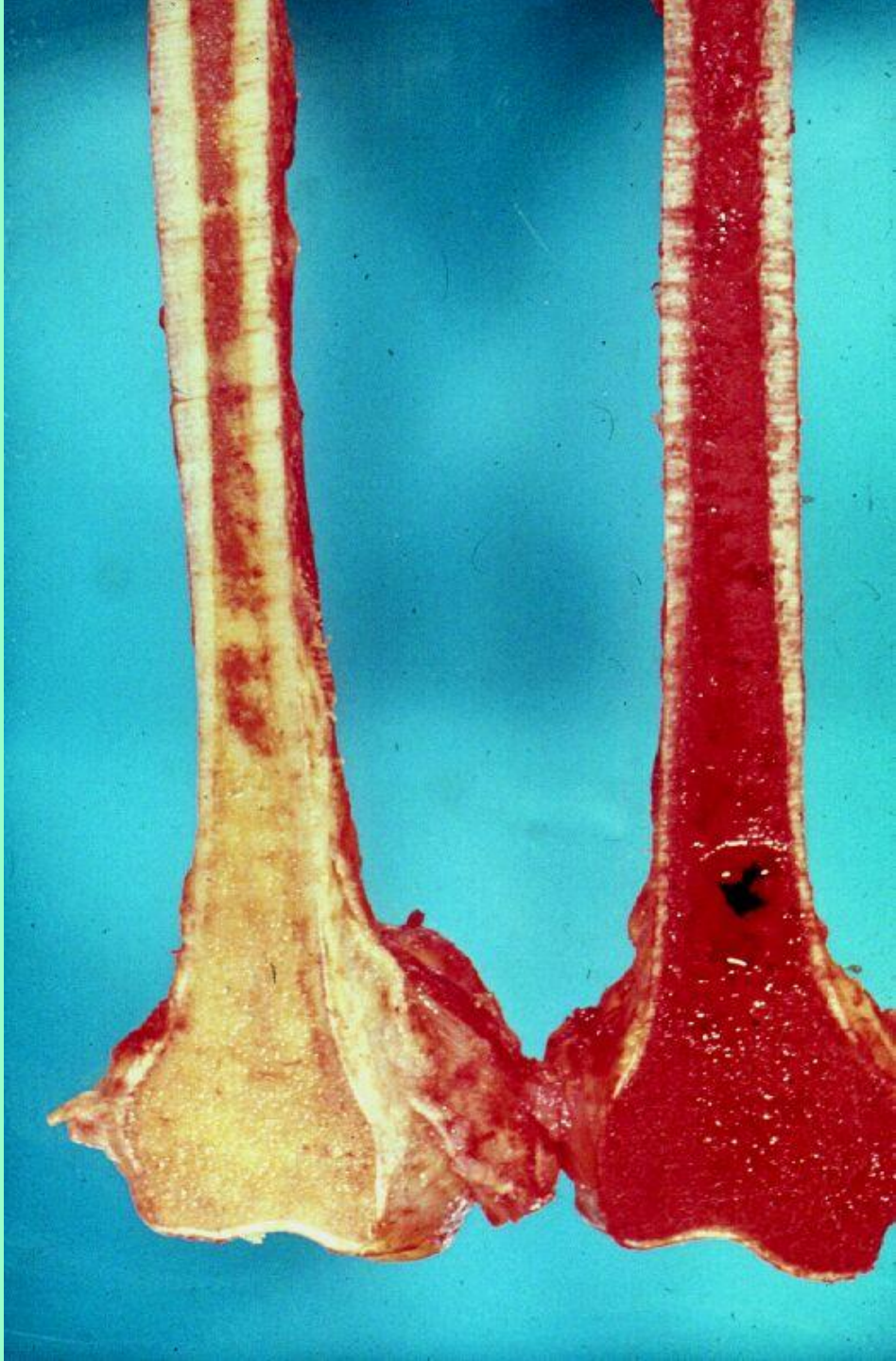


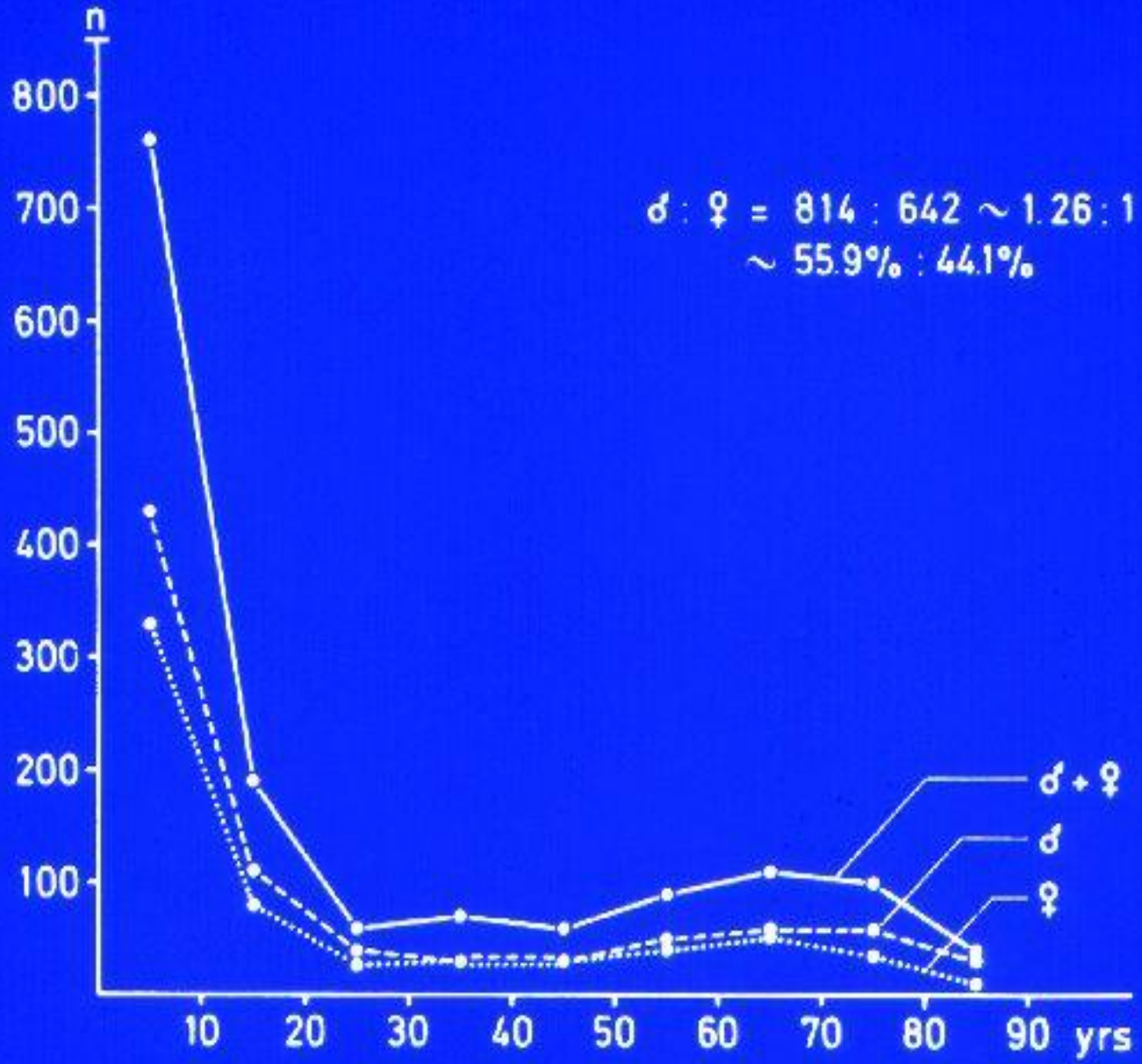


ALL bei einem 7 Jahre alten Jungen

- **links vor Radiatio und Zytostase**
- **rechts oben/links unten 4 Wochen nach Therapie**

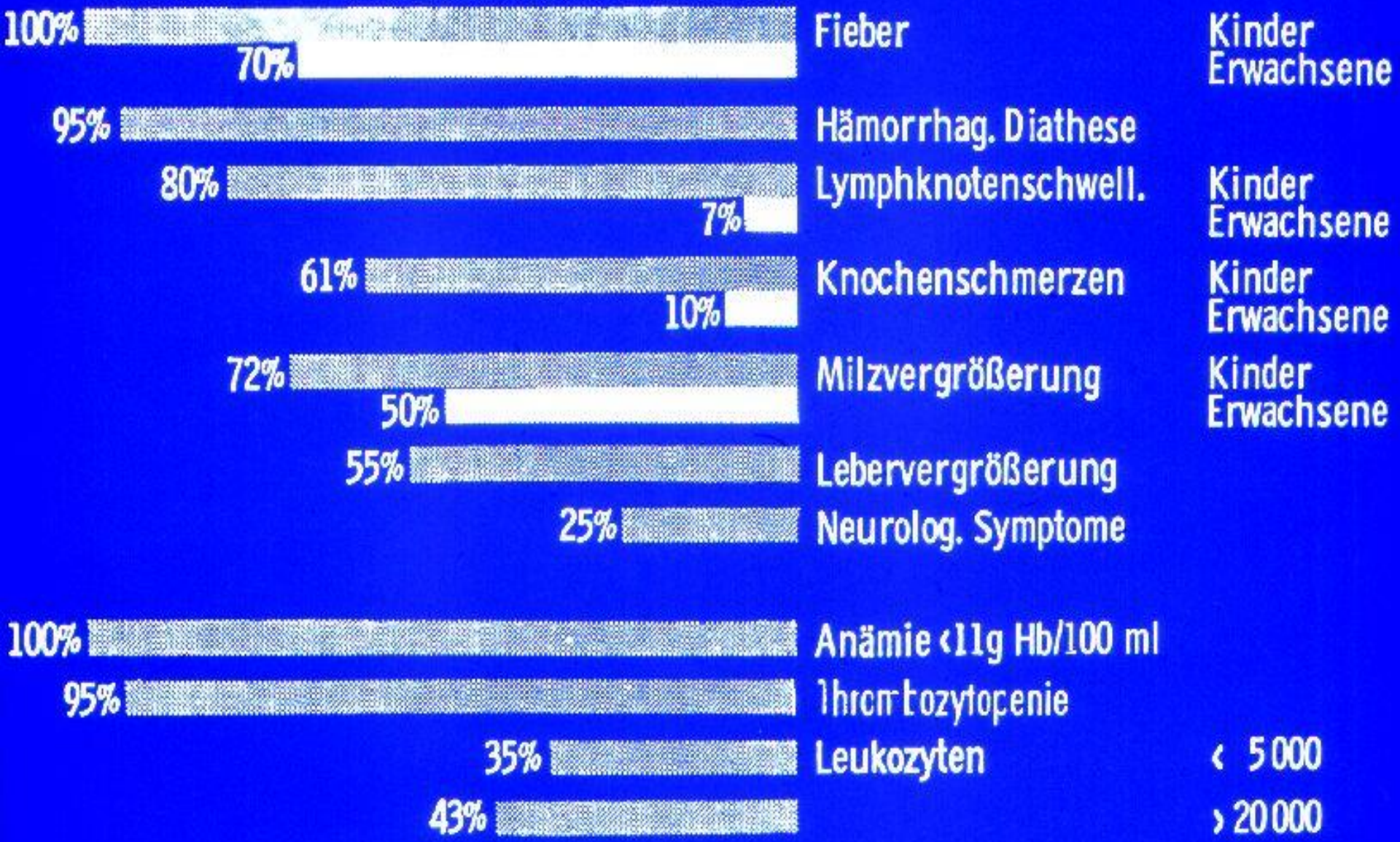


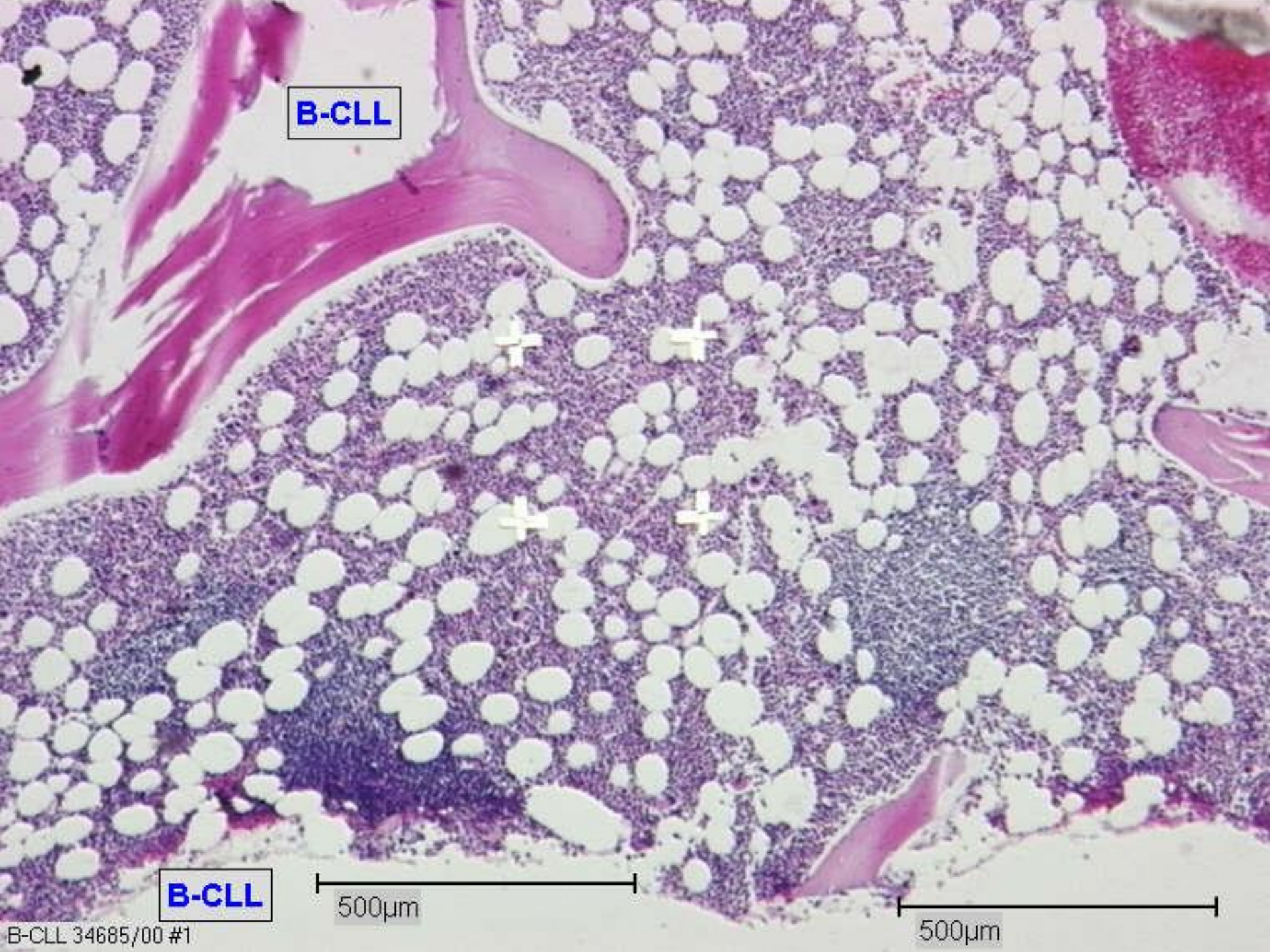


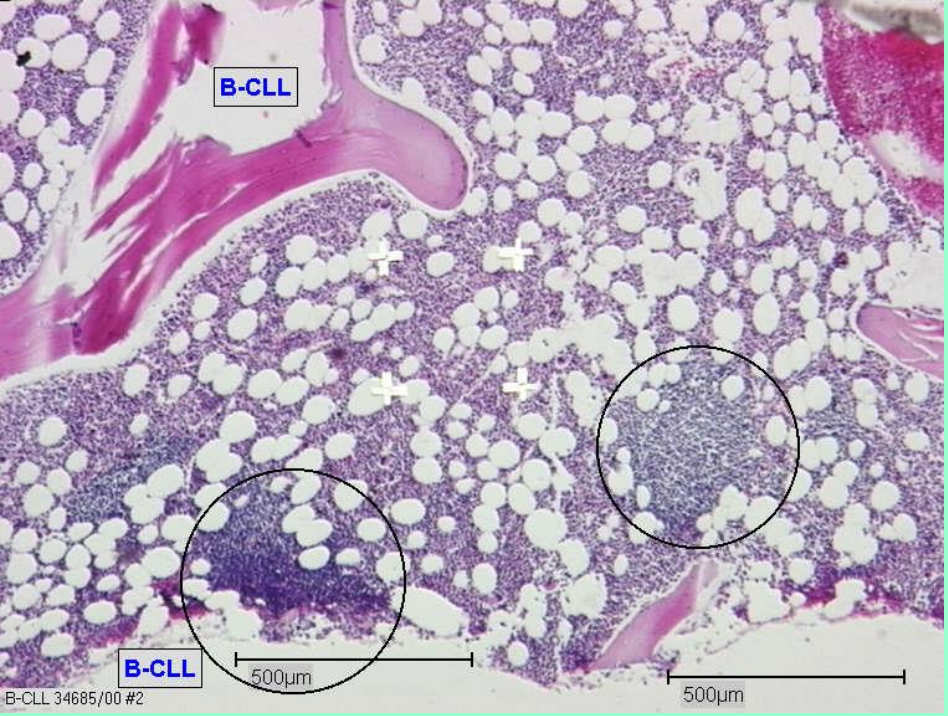


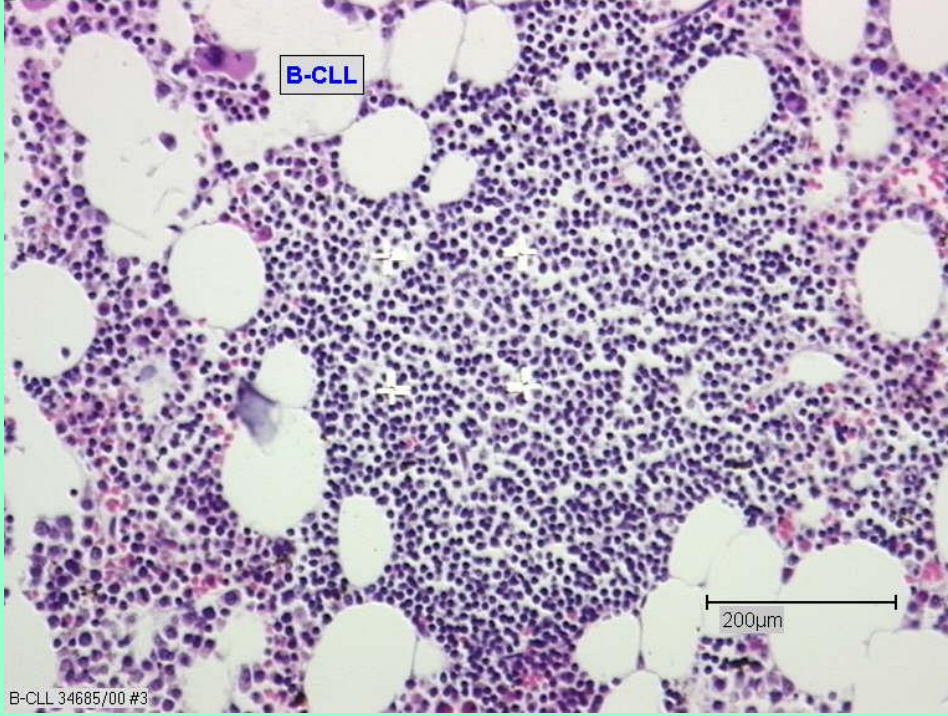
Age distribution and sex ratio of ALL, according to CUTLER, AXTELL and HEISE (1967). 1456 patients, examined between 1940 and 1962

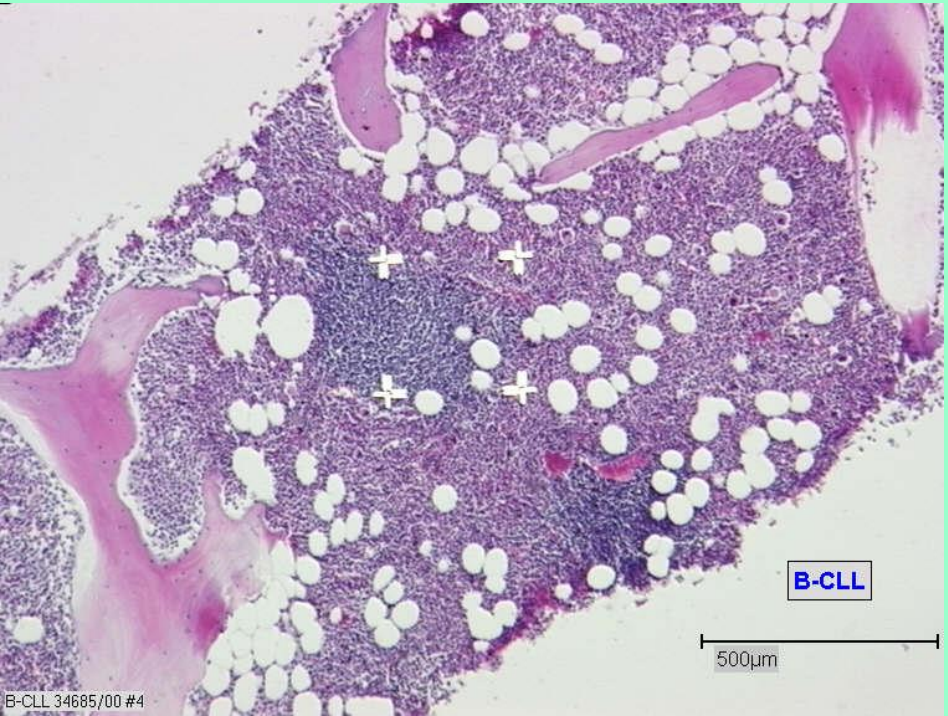
Akute lymphoblastische Leukämien: Symptome

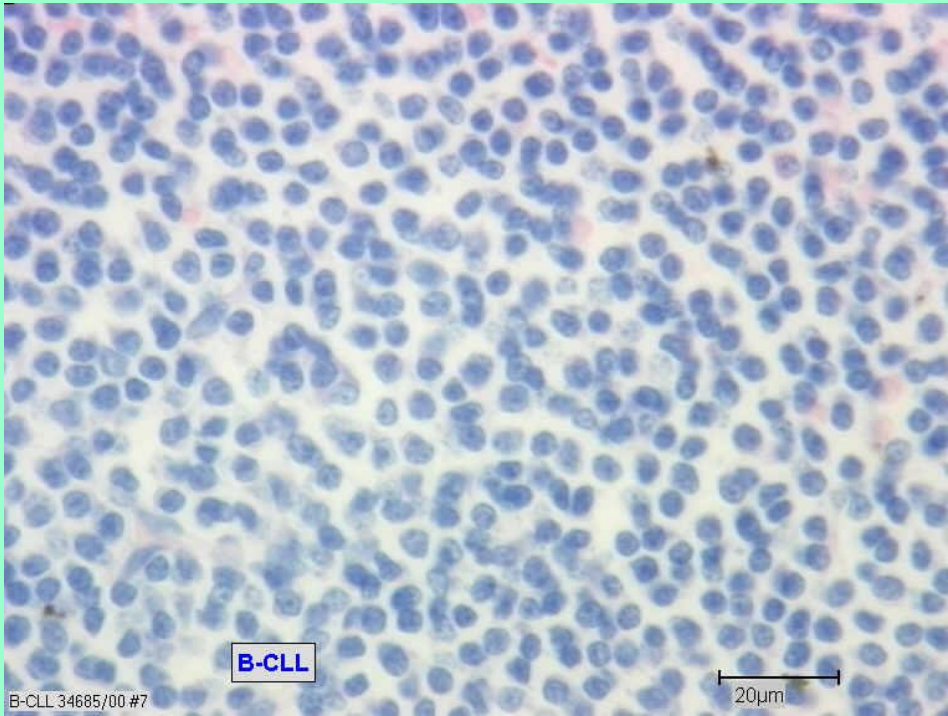


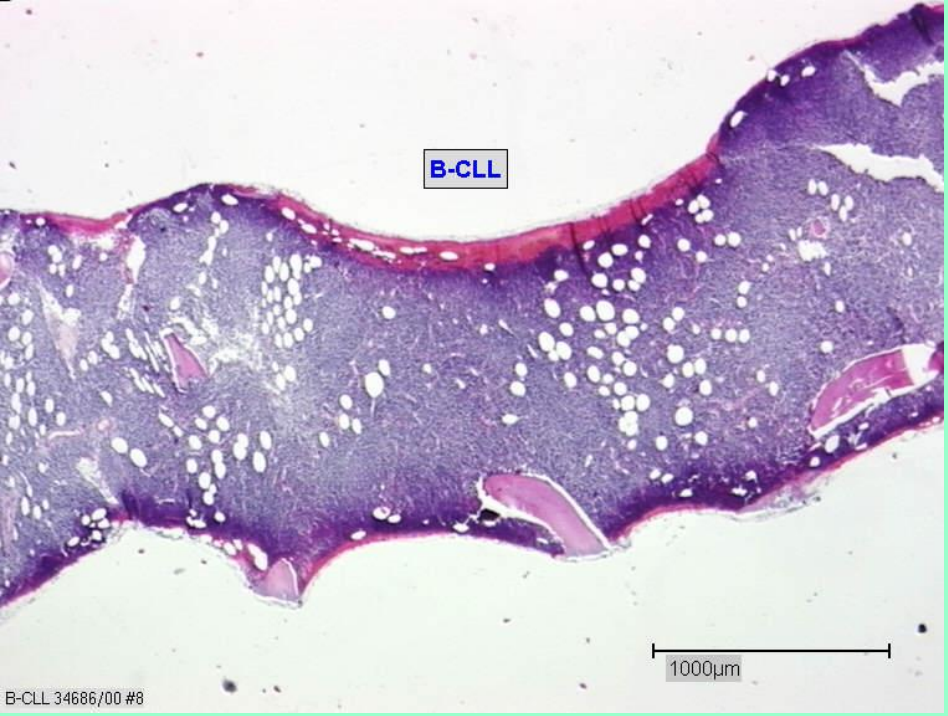

B-CLL
B-CLL
500µm
500µm
B-CLL 34685/00 #1

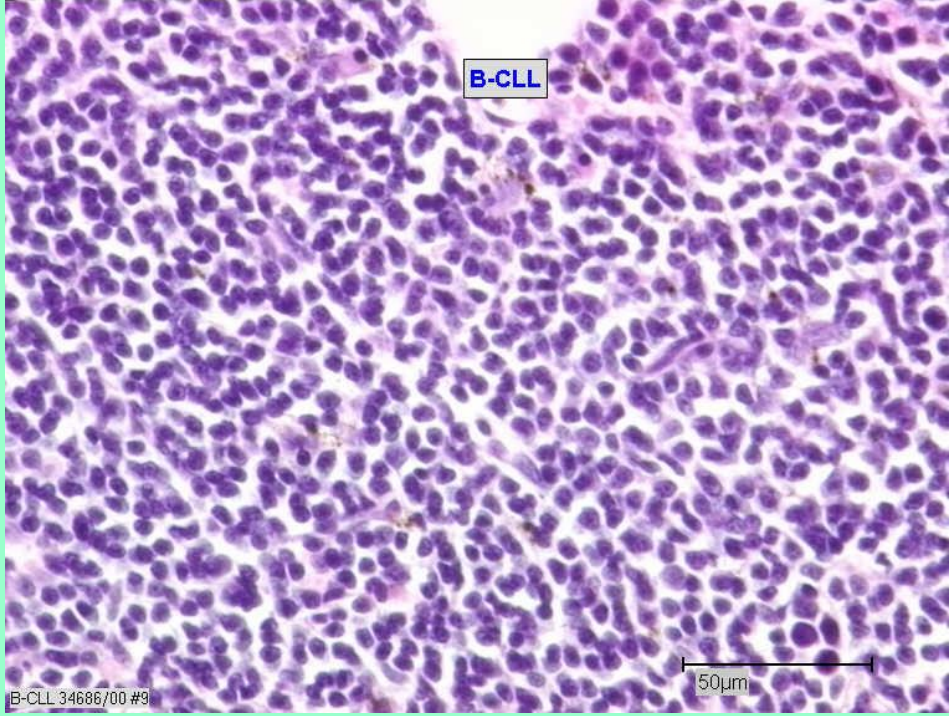

B-CLL
B-CLL
500µm
500µm
B-CLL 34685/00 #2

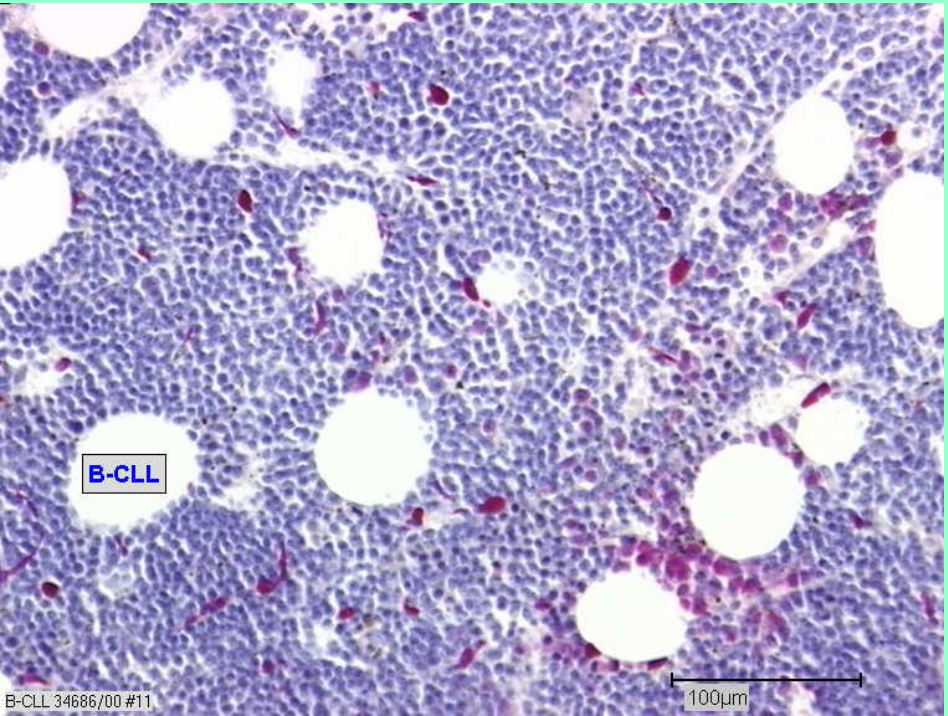

B-CLL
200µm
B-CLL 34685/00 #3

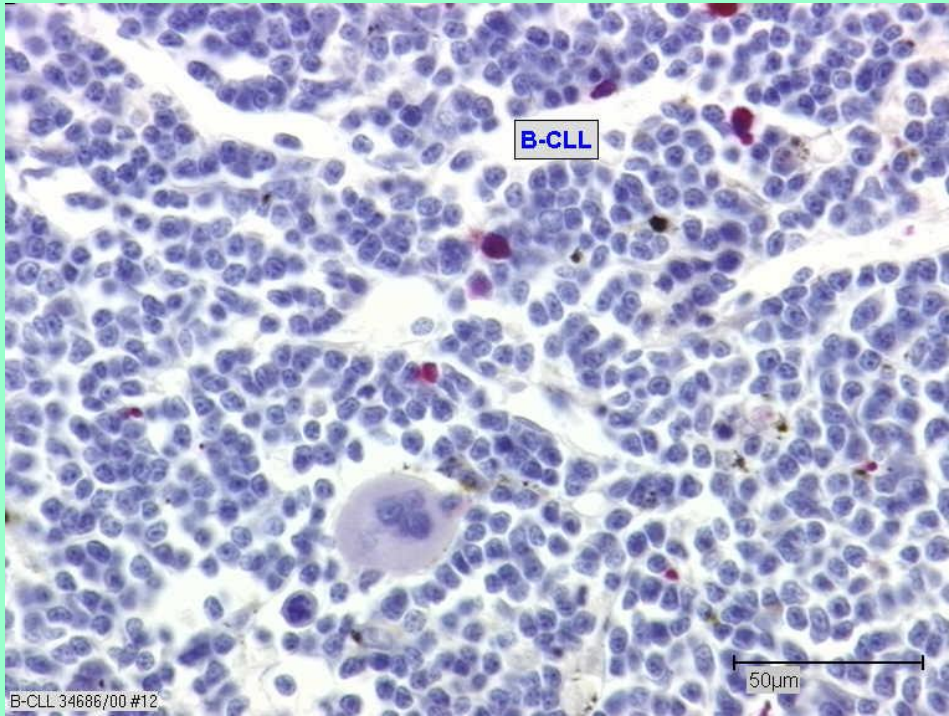

B-CLL
500µm
B-CLL 34685/00 #4


B-CLL
20µm
B-CLL 34685/00 #7


B-CLL
1000µm
B-CLL 34686/00 #8


B-CLL
50µm
B-CLL 34686/00 #9


B-CLL
100µm
B-CLL 34686/00 #11


B-CLL
50µm
B-CLL 34686/00 #12

Common features of B-lineage ALL:	DR+, Tdt+, CD19+, CD34+
Criteria for subclassification:	
Common-ALL or early pre-B-ALL or pre-pre-B-ALL	CD10+, cCD22+, cμIg–, SmIg–, CD20+/–
Pre-B-ALL	CD10+, cCD22+, cμIg+, SmIg–, CD20+/–
CD10– ALL or early pre-B CD10– ALL	CD10–, CD22+, CD20–, cμIg+, SmIg–
B-ALL	Tdt–, CD10+/–, CD22+, CD20+, SIg+

Chromosomale Translokationen in ALL:

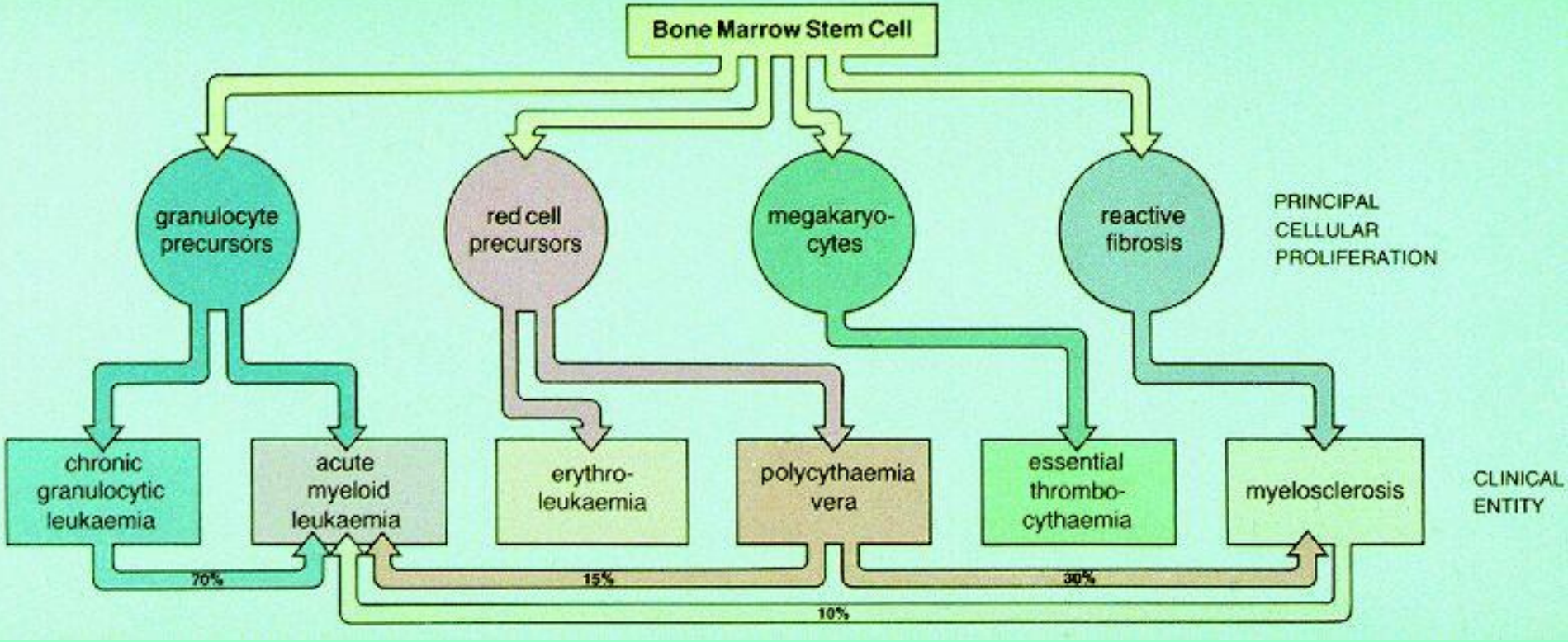
(B-ALL und pre-B-ALL)

Translocation	Involved gene
t(1;19)(q23;p13)	E2A-PBX1
t(2;8)(p12;q24)	c-MYC
t(4;11)(q21;q23)	HRX-FEL
	ALLI-AF4
	MLL-PBMI
t(8;14)(q24;q32)	c-MYC
t(8;22)(q24;q11)	c-MYC
t(17;19)(q22;p13)	E2A-HLF

Chromosomenanomalien:

B-ALL (L3)

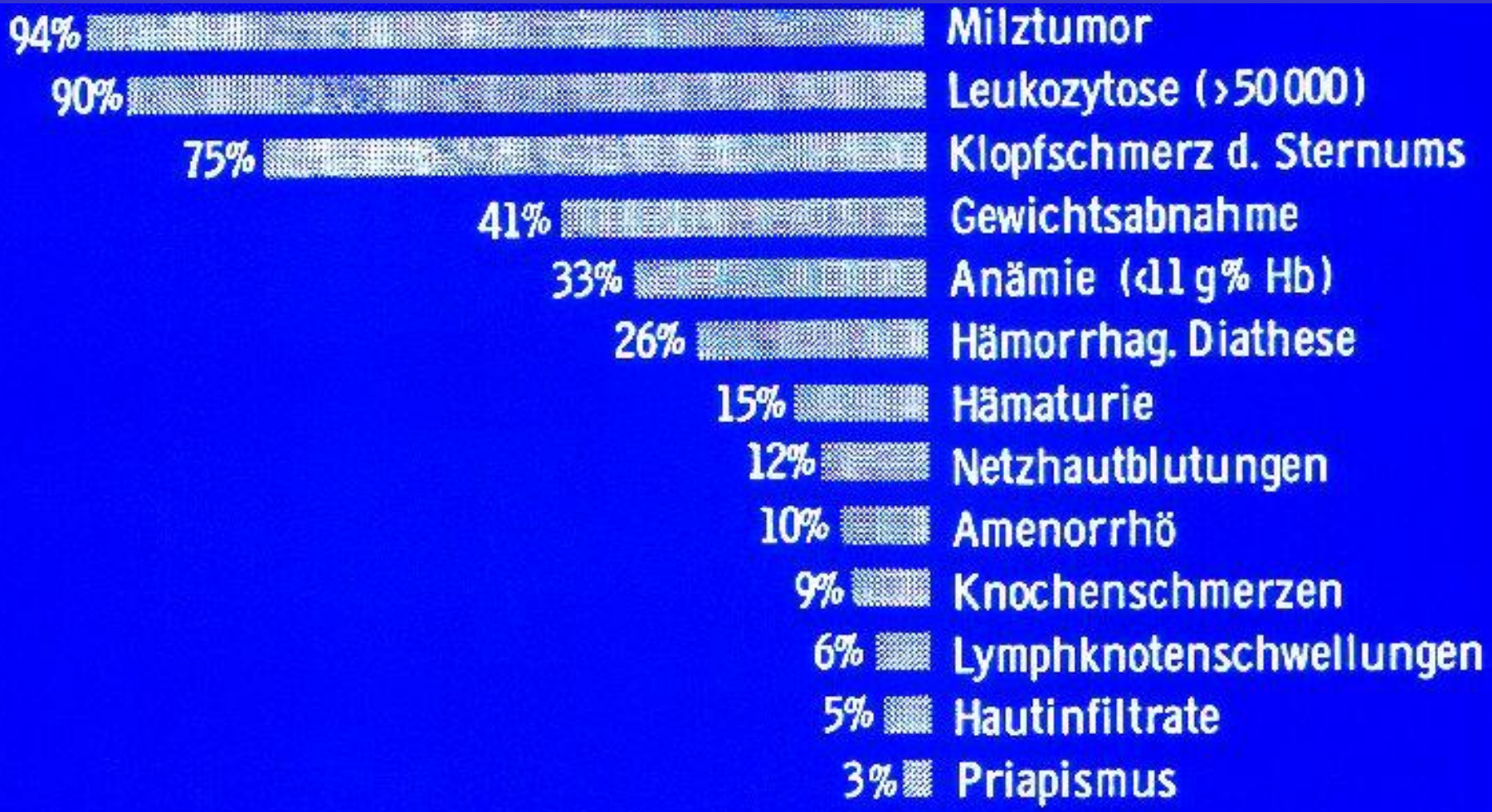
Abnormality	Immunological type
dup(1)(p12–31)	B-ALL
t(2;8)(p12;q24)	B-ALL
t(8;14)(q24;q32)	B-ALL
t(8;22)(q24;q11)	B-ALL


Bone Marrow Stem Cell
granulocyte precursors
red cell precursors
megakaryo-cytes
reactive fibrosis
PRINCIPAL CELLULAR PROLIFERATION
chronic granulocytic leukaemia
acute myeloid leukaemia
erythro-leukaemia
polycythaemia vera
essential thrombo-cythaemia
myelosclerosis
CLINICAL ENTITY
70%
15%
30%
10%

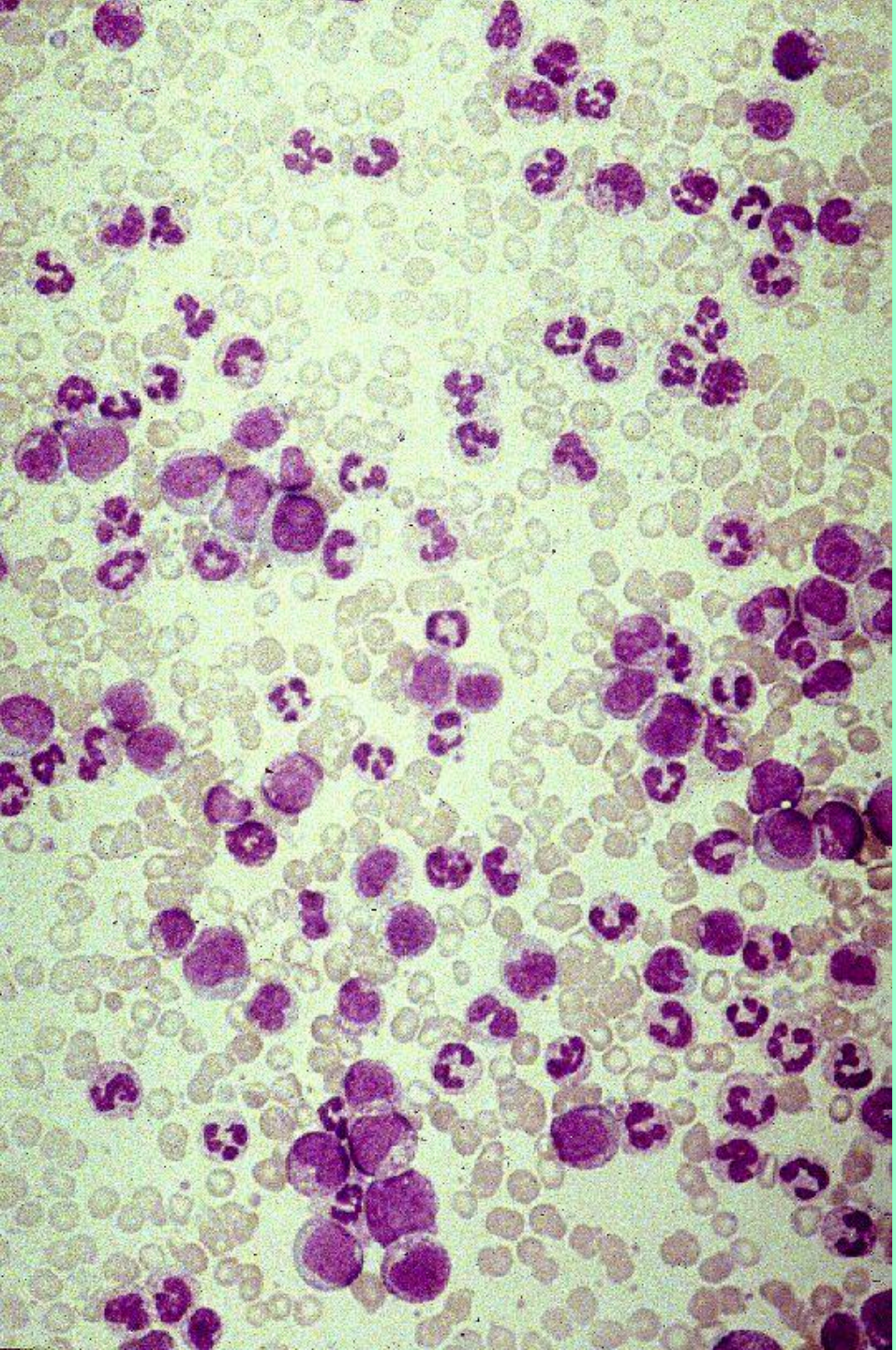
MYELOPROLIFERATIVE Syndrome

1. chron.granulozyt. Leukämie(CGL) und andere chron.Myeloleukämien
2. PCV
3. ETH
4. idiopath.Myelofibrose
5. systemische Mastozytose
6. idiopath. Hypereosinophilen-Syndrom
7. transitionale u.unklassif. myeloprolif. Erkrankungen
8. Overlap-Sydrome

Chronische myeloische Leukämie (CML)

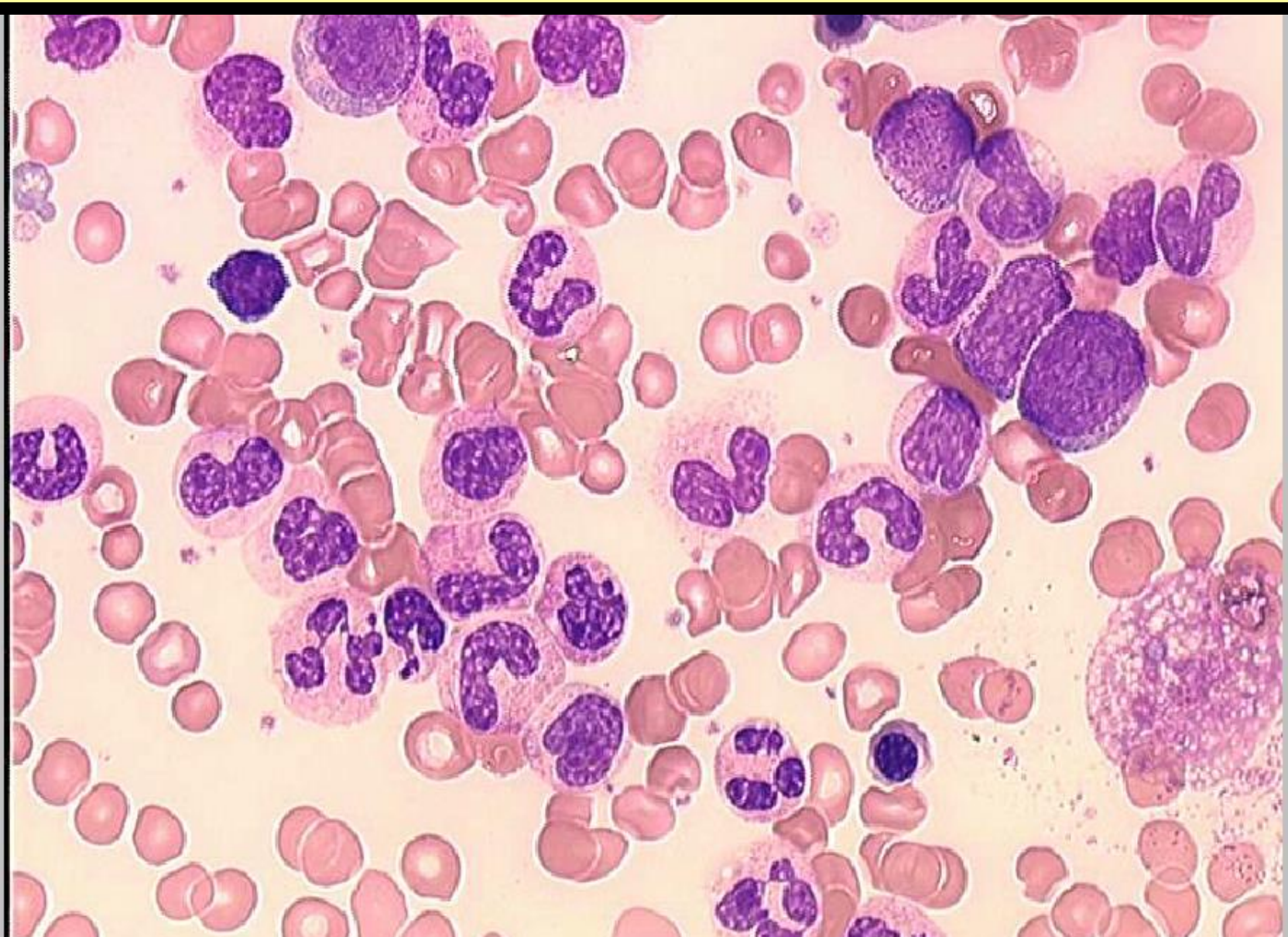


Häufigkeit wichtiger Symptome bei der chronischen myeloischen Leukämie (eigene Beobachtungen und Literaturangaben);



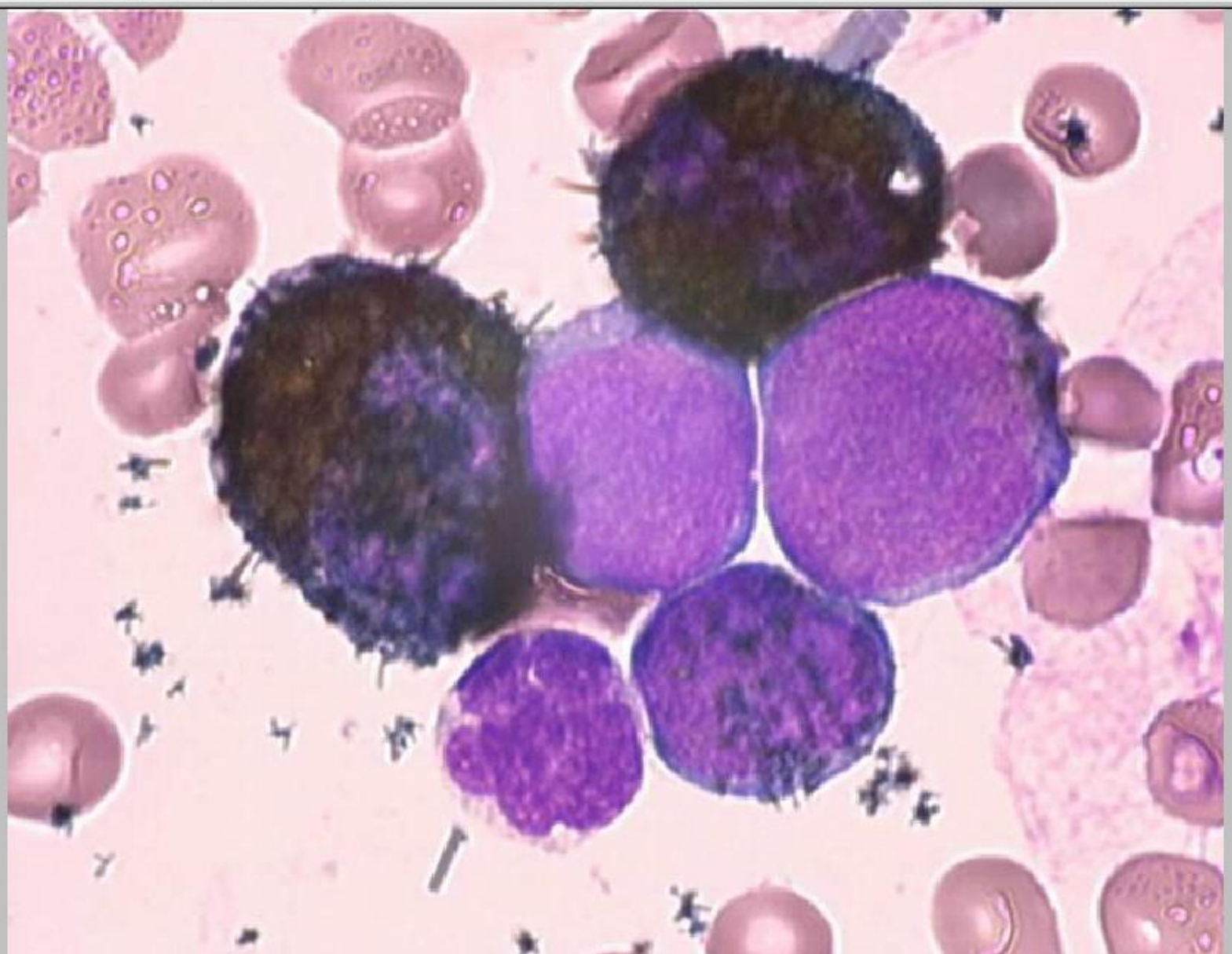
Chronische myeloische Leukämie (CML)

Chronische myeloische Leukämie (CML): 67 Jahre alter Mann



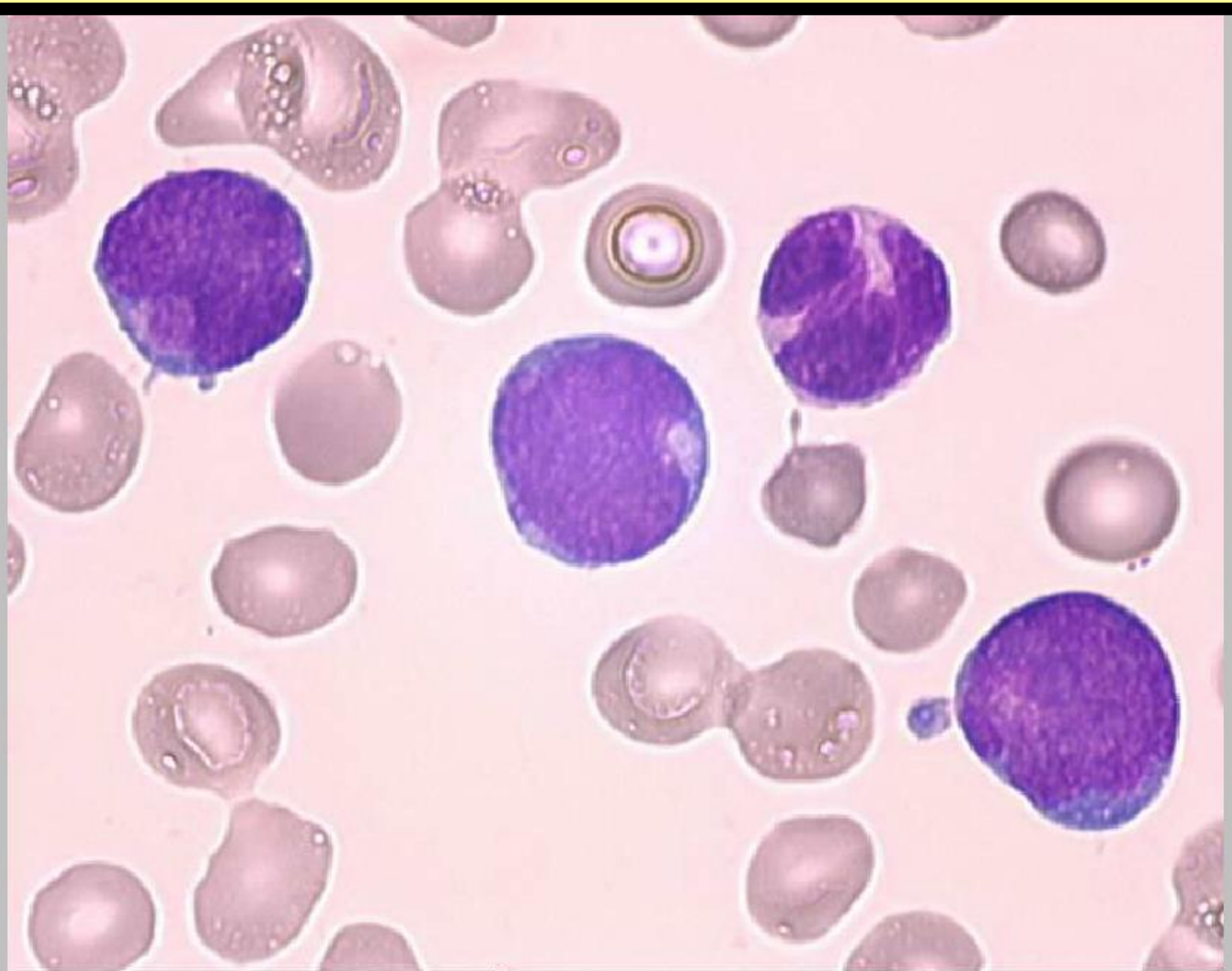
Chronische myeloische Leukämie (CML):

42 Jahre alter Mann - Knochenmark - POX+

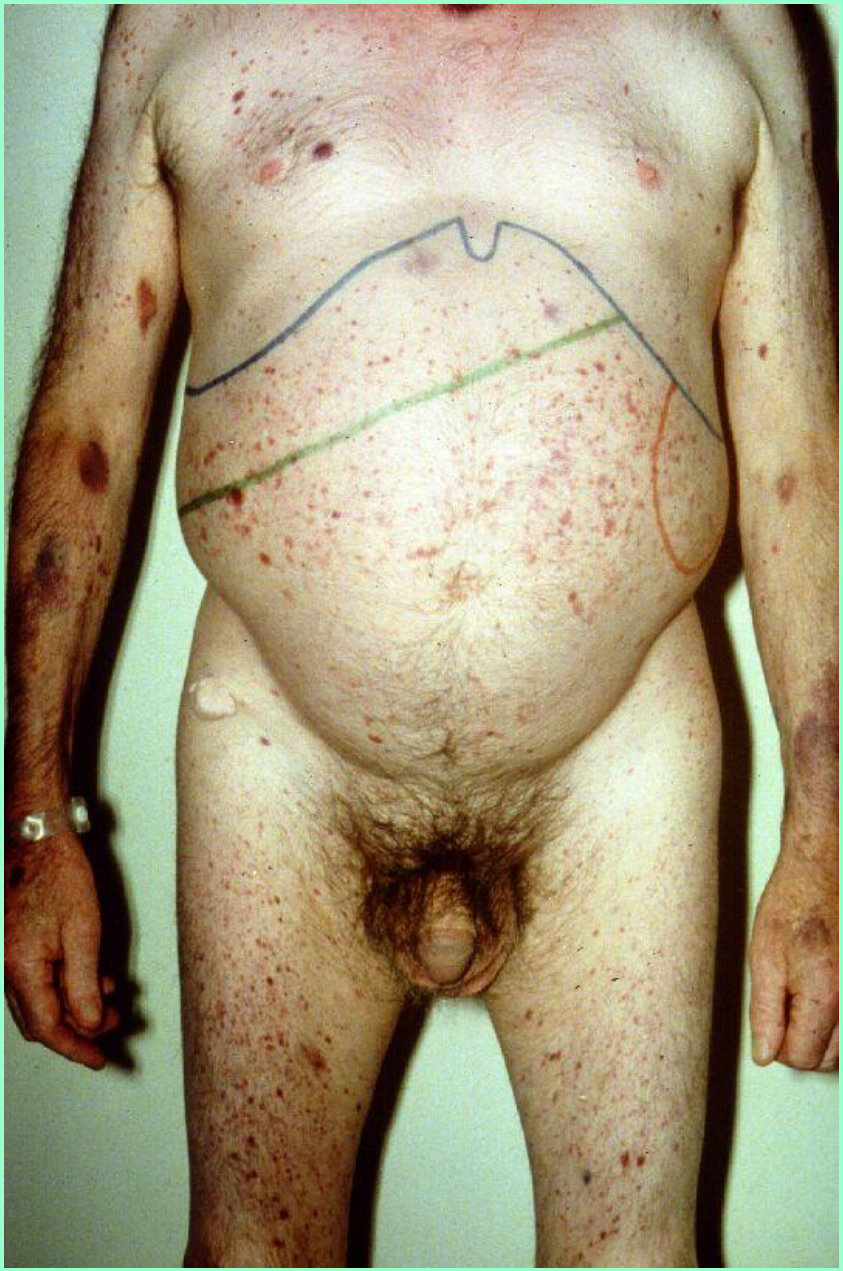


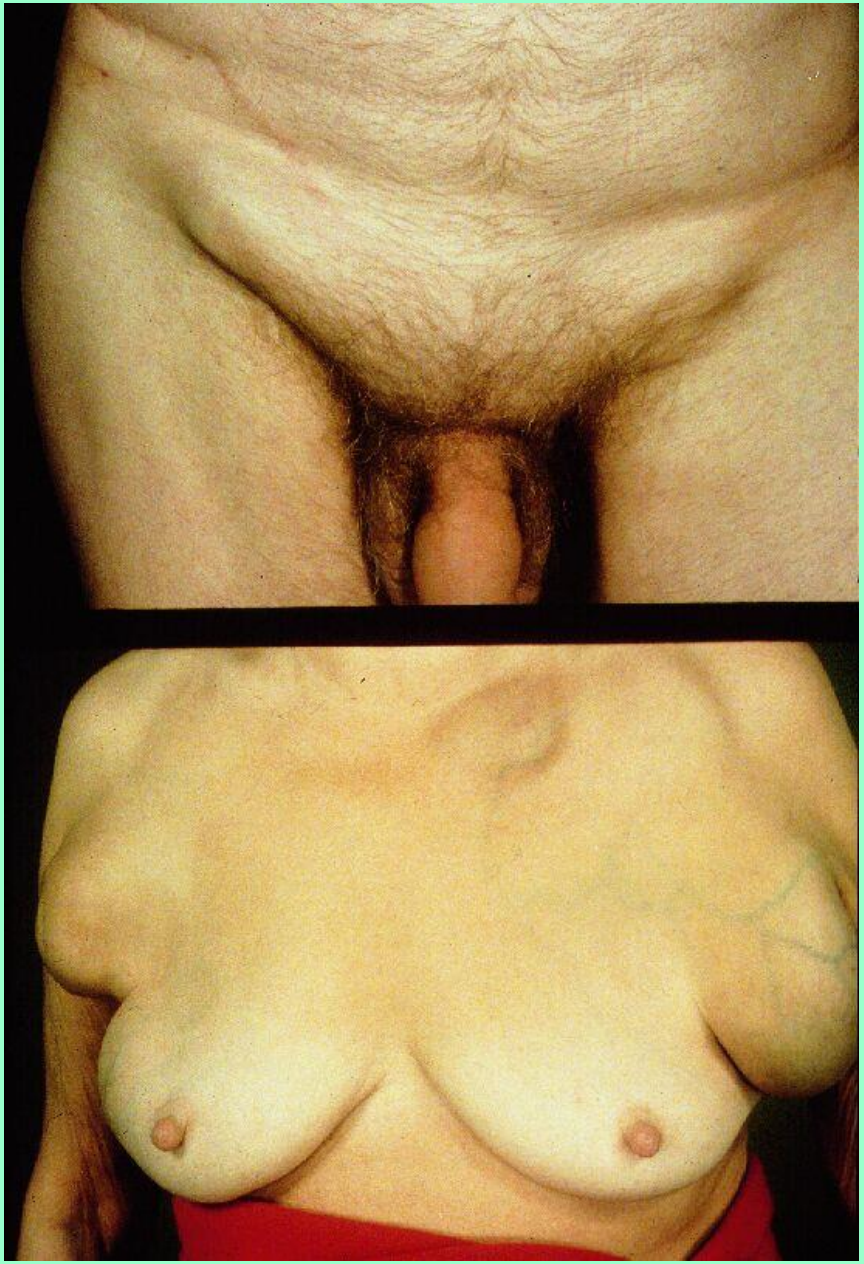
Chronische myeloische Leukämie (CML):

42 Jahre alter Mann - peripheres Blut



Chronische myeloische Leukämie (CML)





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8. Overlap-Sydrome

Causes of Polycythaemia

Primary

Polycythaemia vera

Secondary

Due to compensatory erythropoietin increase in:
- high altitudes;
- heavy smoking;
- cardiovascular disease;
- pulmonary disease & alveolar hypoventilation;
- increased affinity haemoglobins (familial polycythaemia);
- methaemoglobinaemia (rarely)

Due to inappropriate erythropoietin increase in:
- renal diseases:
  - hydronephrosis,
  - vascular impairment,
  - cysts,
  - carcinoma,
- massive uterine fibromyomata;
- hepatocellular carcinoma;
- cerebellar haemangioblastoma

Relative

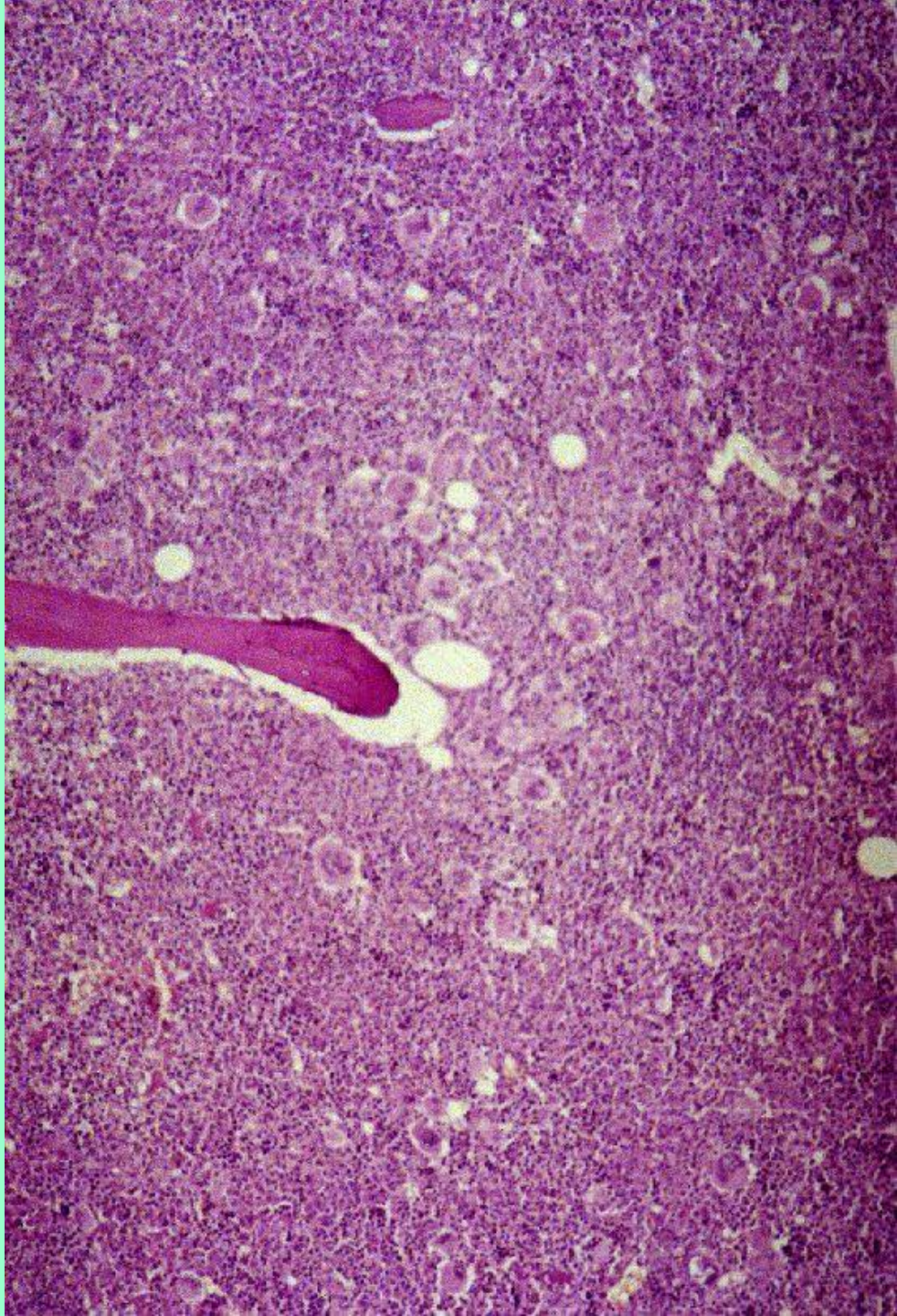
'Stress' or 'spurious' polycythaemia;

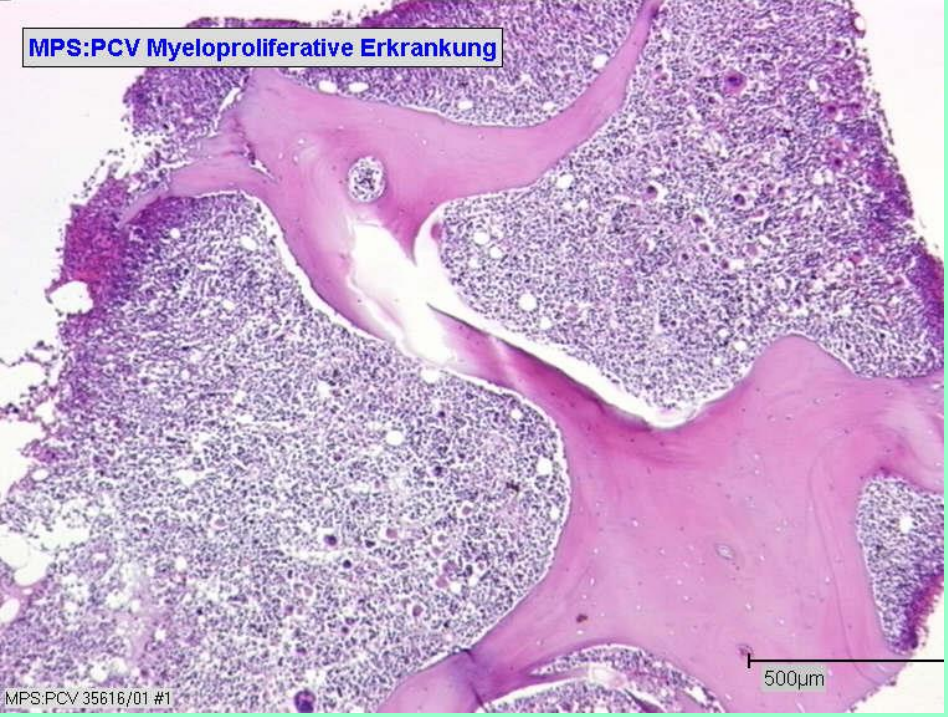
Dehydration:
- water deprivation; vomiting;
- diuretic therapy

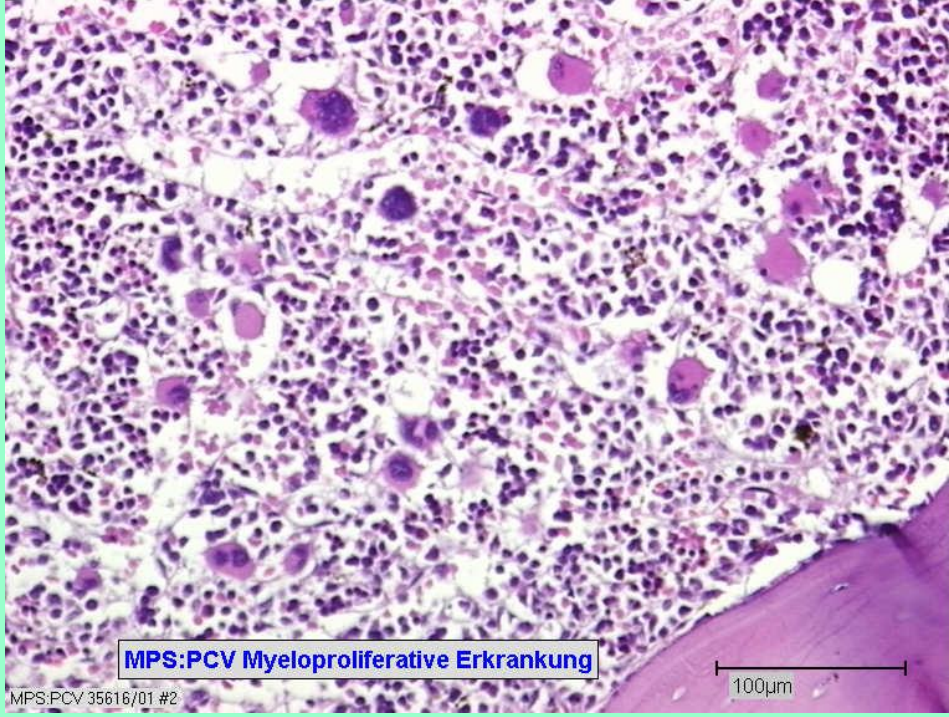
Plasma loss:
- burns;
- enteropathy

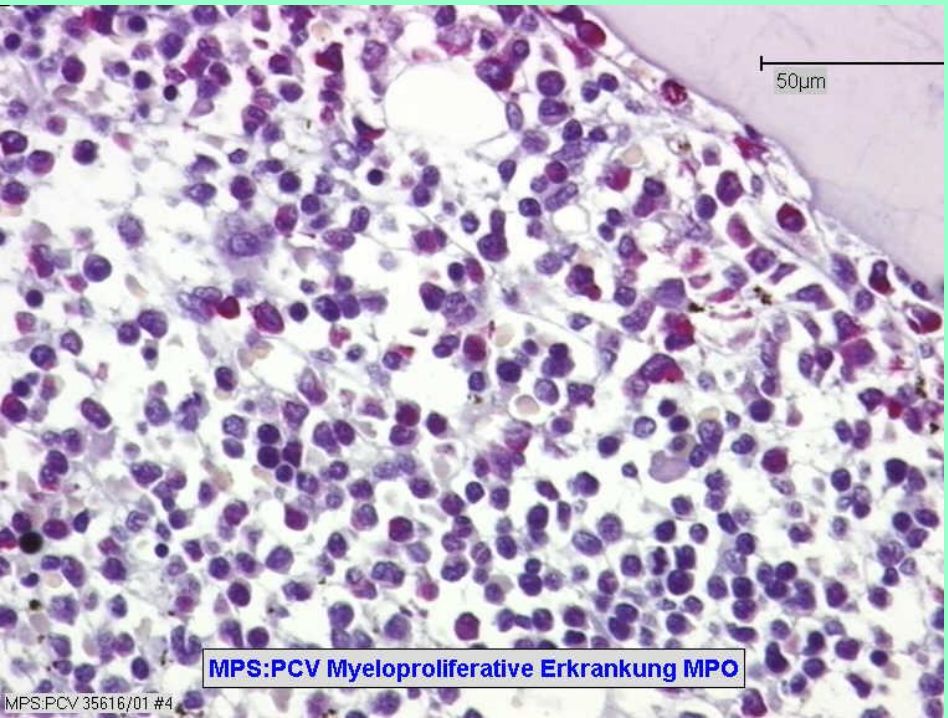
Myeloproliferative Syndrom:
(MPS:PCV)
Polyzythämia vera

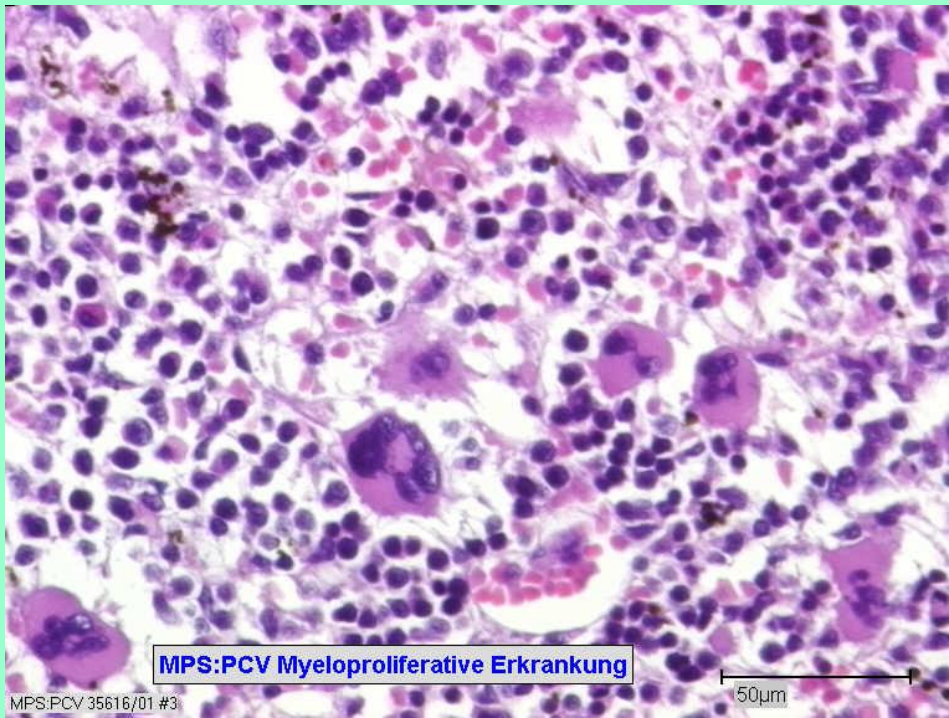
trilineare Proliferation von:
1. Myelozytopoese
2. Erythrozytopoese
3. Megakaryozytopoese

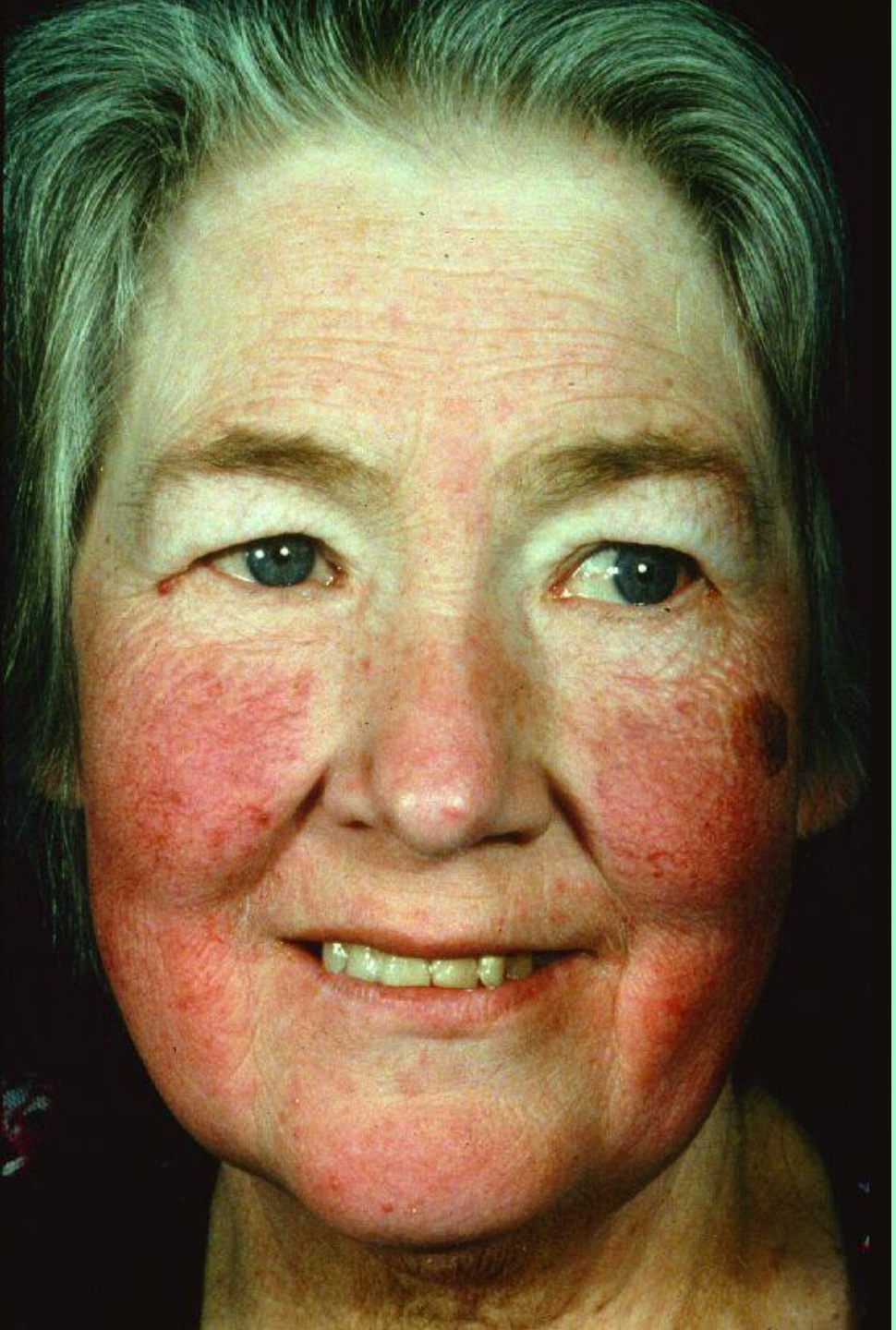


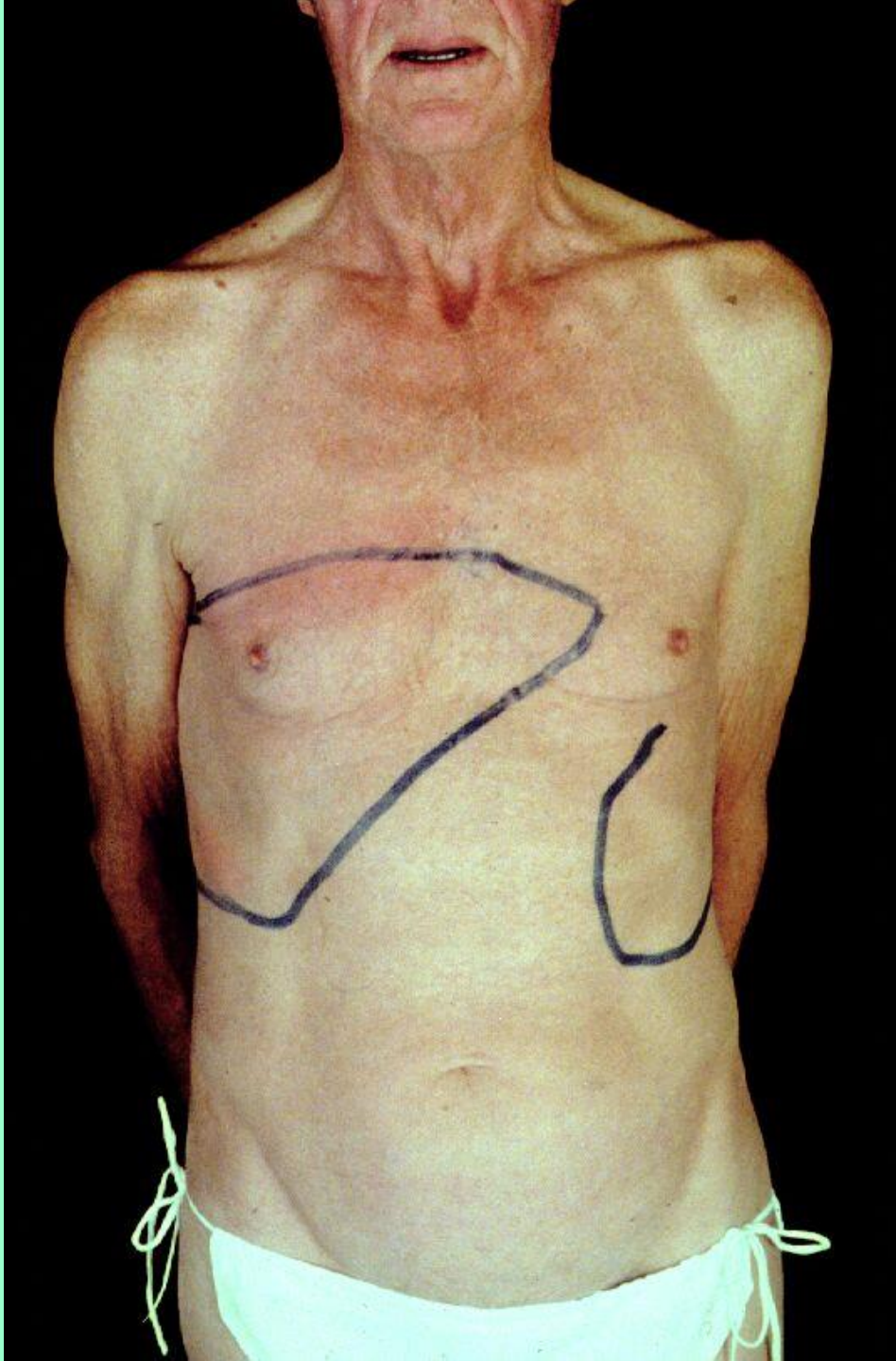

MPS:PCV Myeloproliferative Erkrankung
500µm
MPS:PCV 35616/01 #1


MPS:PCV Myeloproliferative Erkrankung
100µm
MPS:PCV 35616/01 #2


50µm
MPS:PCV Myeloproliferative Erkrankung MPO
MPS:PCV 35616/01 #4


MPS:PCV Myeloproliferative Erkrankung
50µm
MPS:PCV 35616/01 #3





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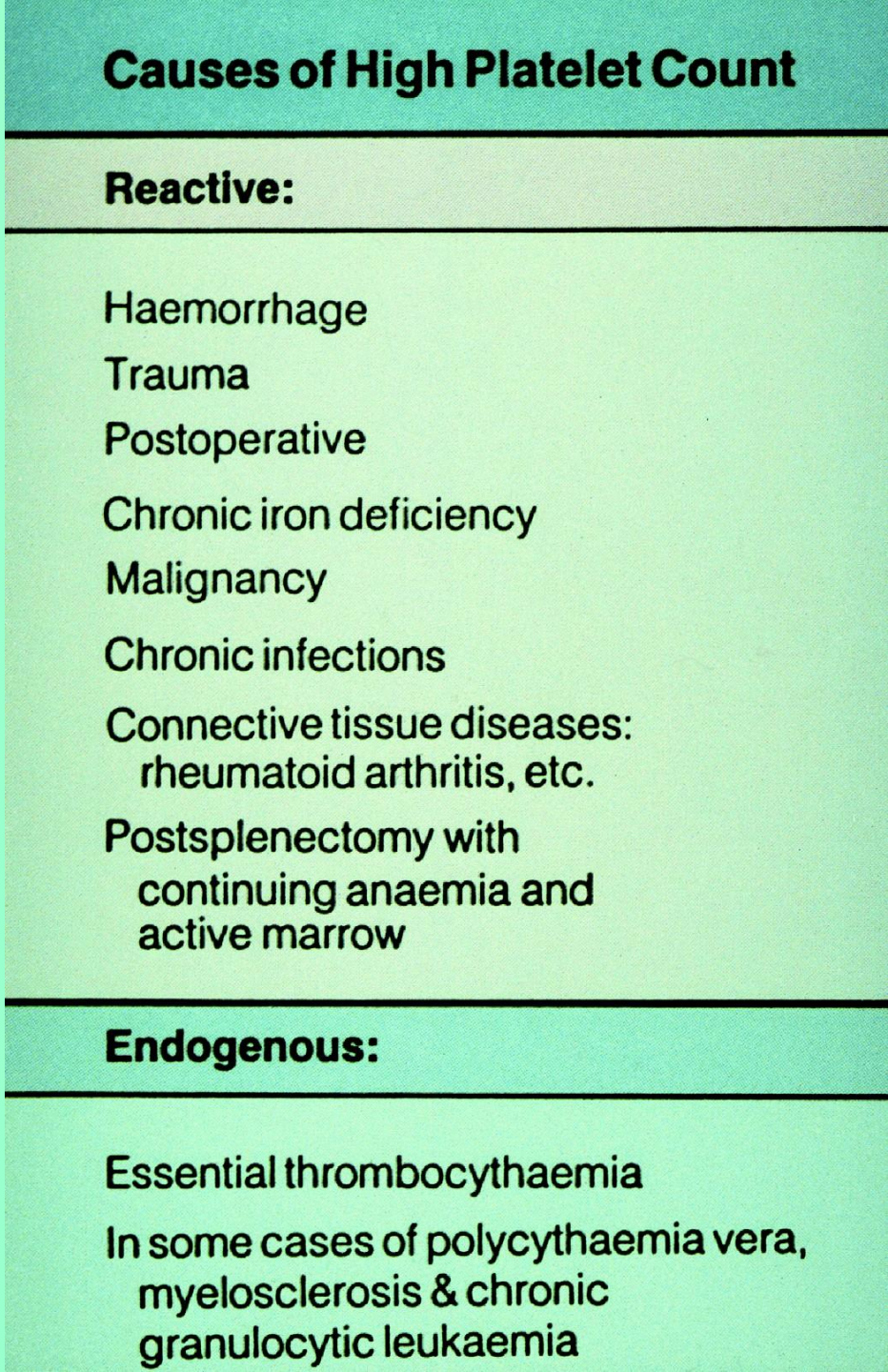
7. transitionale u.unklassif. myeloprolif. Erkrankungen
8. Overlap-Sydrome

Myeloproliferatives Syndrom:
(MPS:ETH)

Essentielle Thrombozythämie:
Proliferation von Zellen der Thrombozytopoese bzw. von atypischen Megakaryozyten



Causes of High Platelet Count

Reactive:

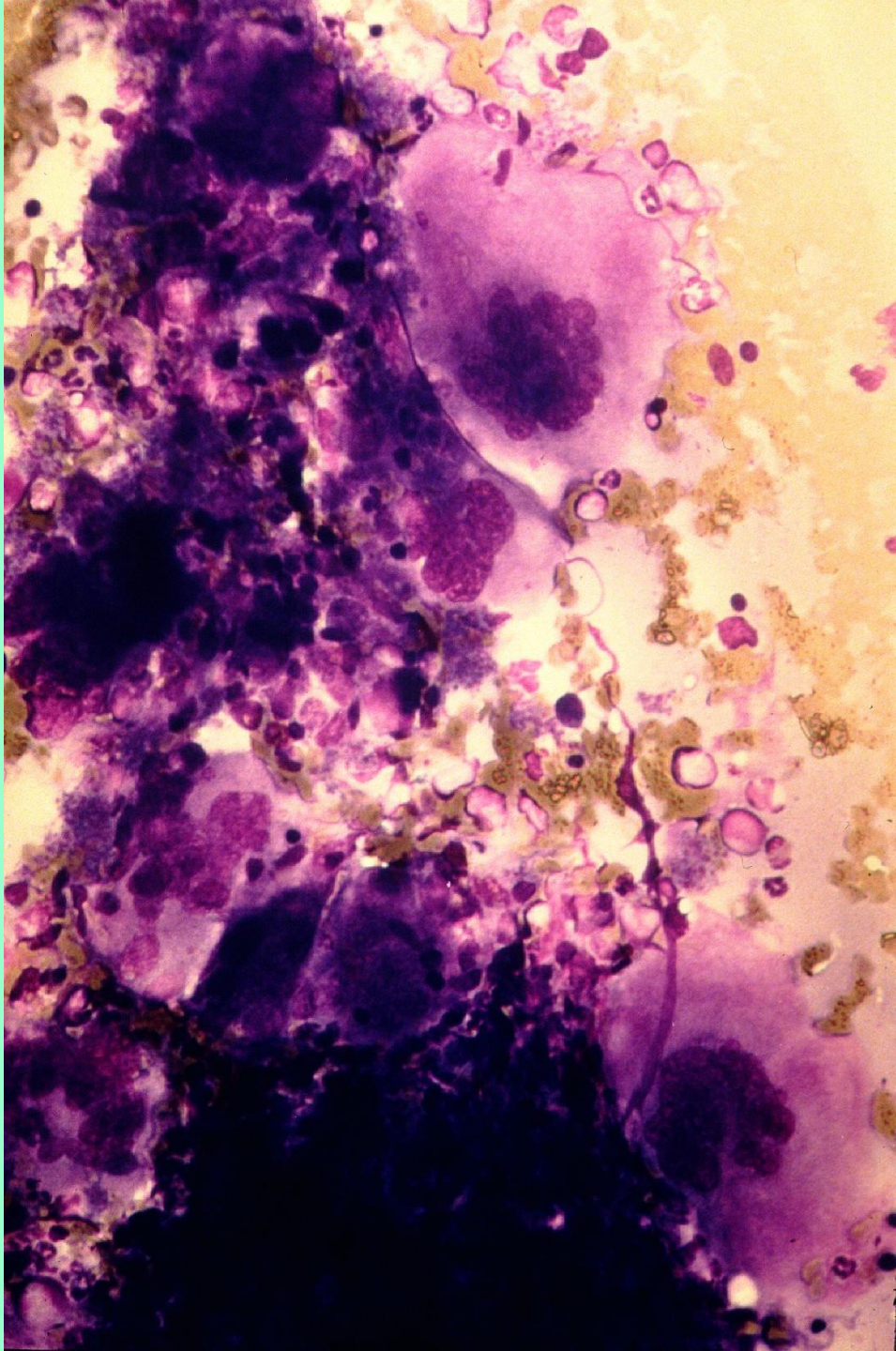
Haemorrhage
Trauma
Postoperative
Chronic iron deficiency
Malignancy
Chronic infections
Connective tissue diseases: rheumatoid arthritis, etc.
Postsplenectomy with continuing anaemia and active marrow

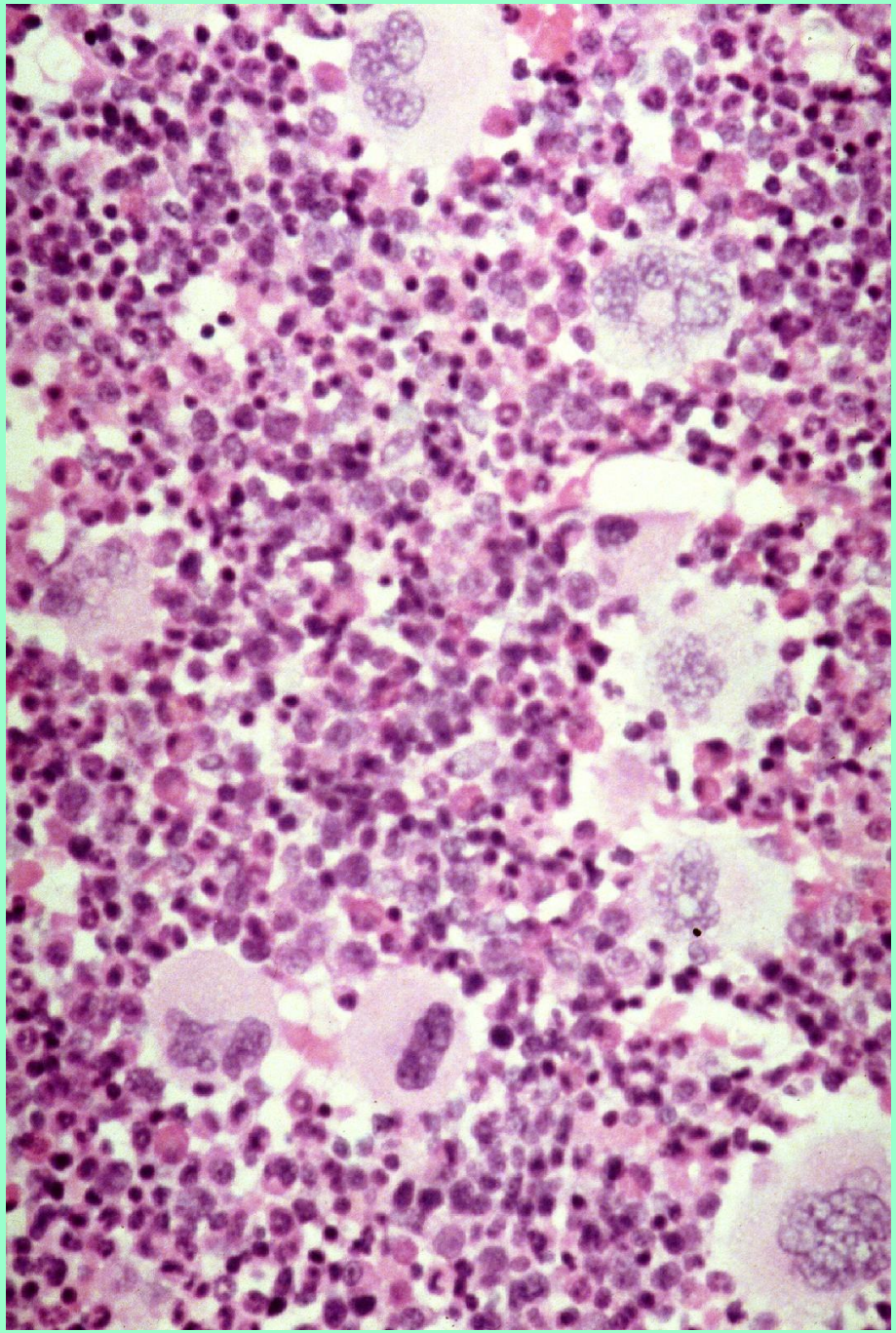
Endogenous:

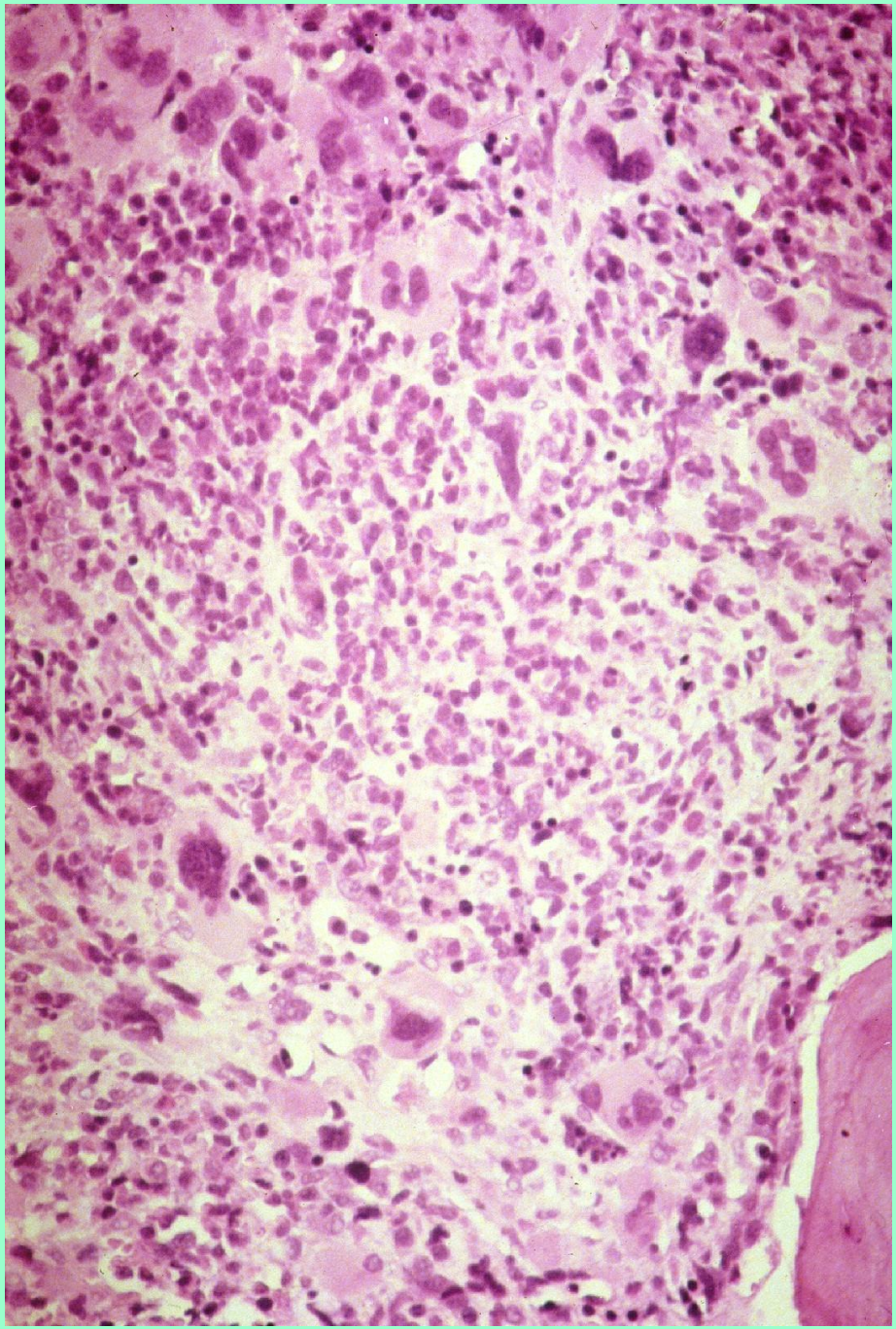
Essential thrombocythaemia
In some cases of polycythaemia vera, myelosclerosis & chronic granulocytic leukaemia

Myeloproliferatives Syndrom:
(MPS:ETH)

Essentielle Thrombozythämie:
Proliferation von Zellen der Thrombozytopoese bzw. von atypischen Megakaryozyten

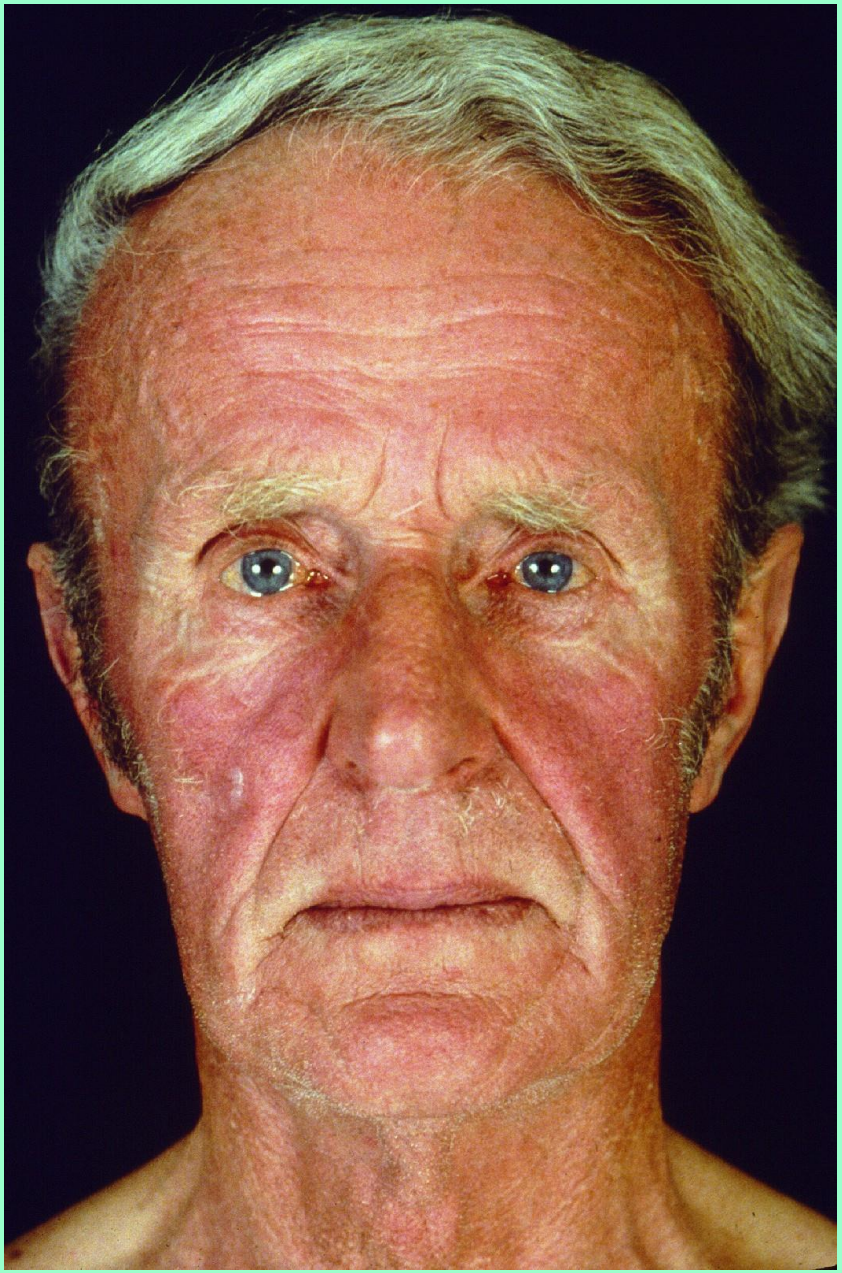






Distinction between ET and reactive thrombocytosis.

ET	Reactive thrombocytosis
Megakaryocytes:	Megakaryocytes:
Giant forms	Normal or small
Clustered	Separate
Paratrabecular	Central
Atypical forms	No atypia
Emperipolesis — occasional	Emperipolesis — common
Erythropoiesis and granulopoiesis are normal	Erythropoiesis and granulopoiesis are right-shifted



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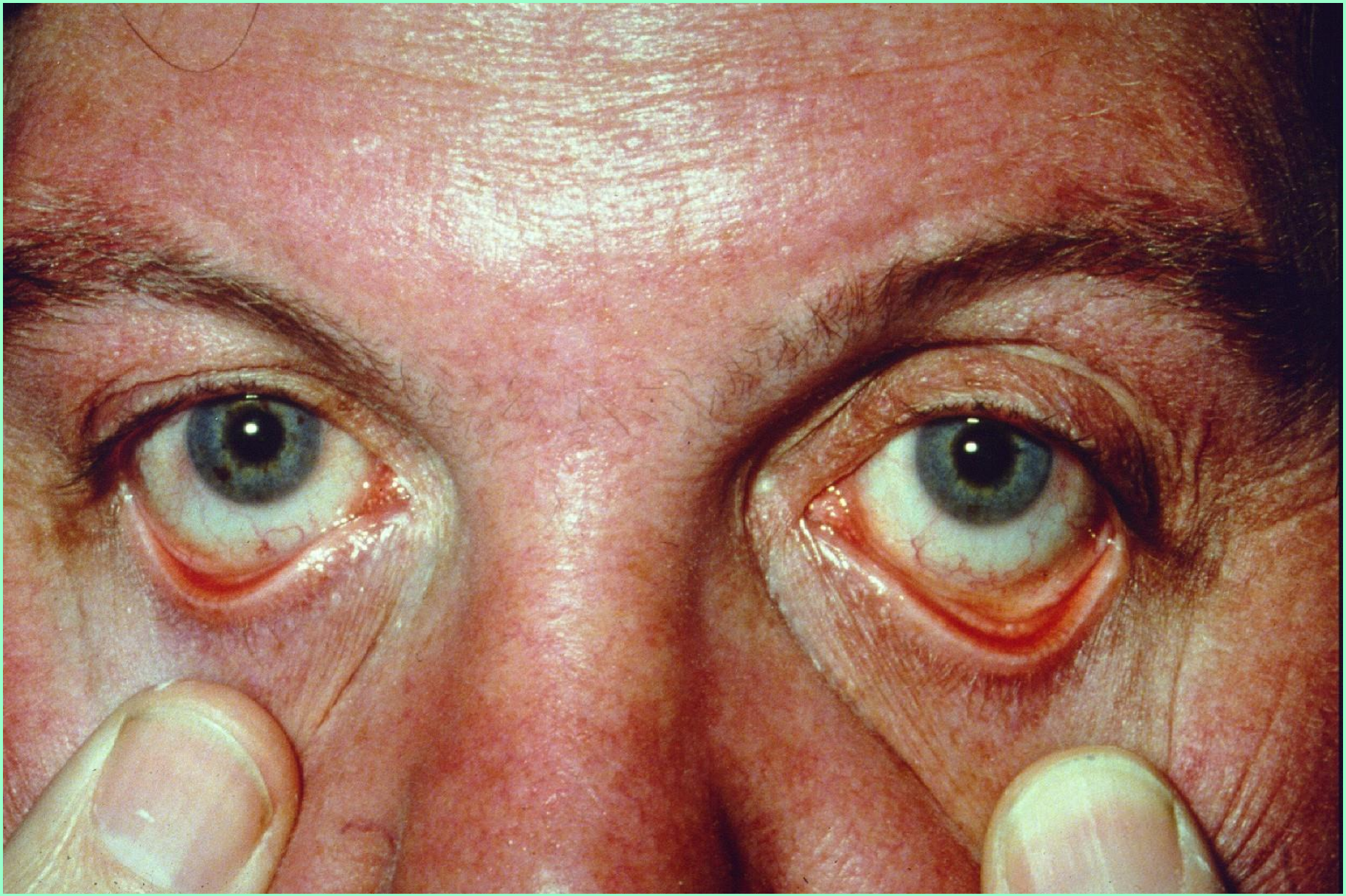
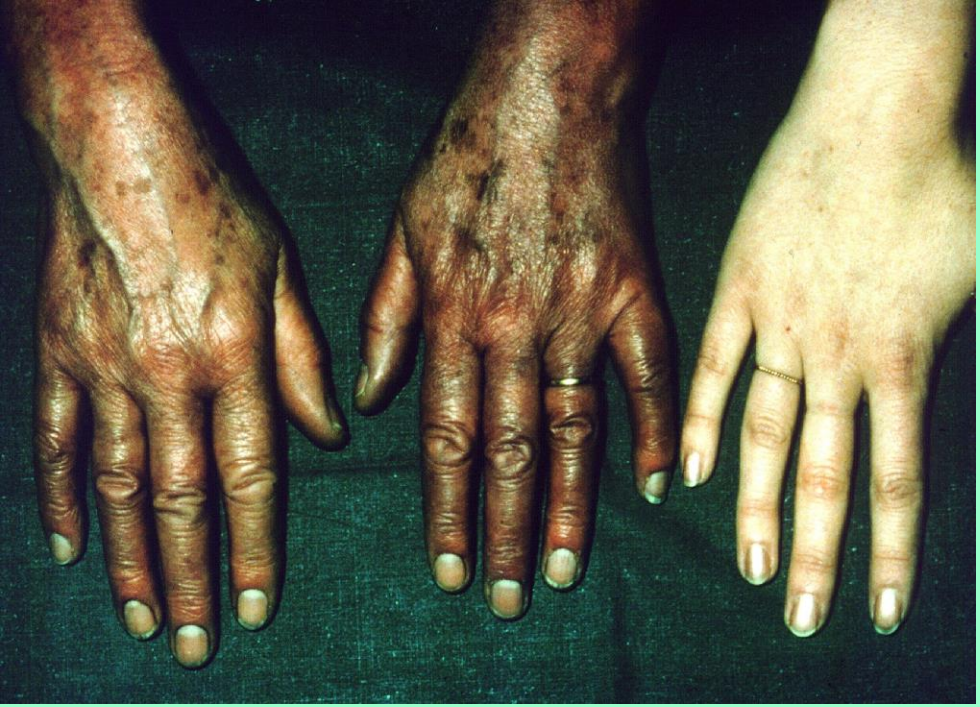
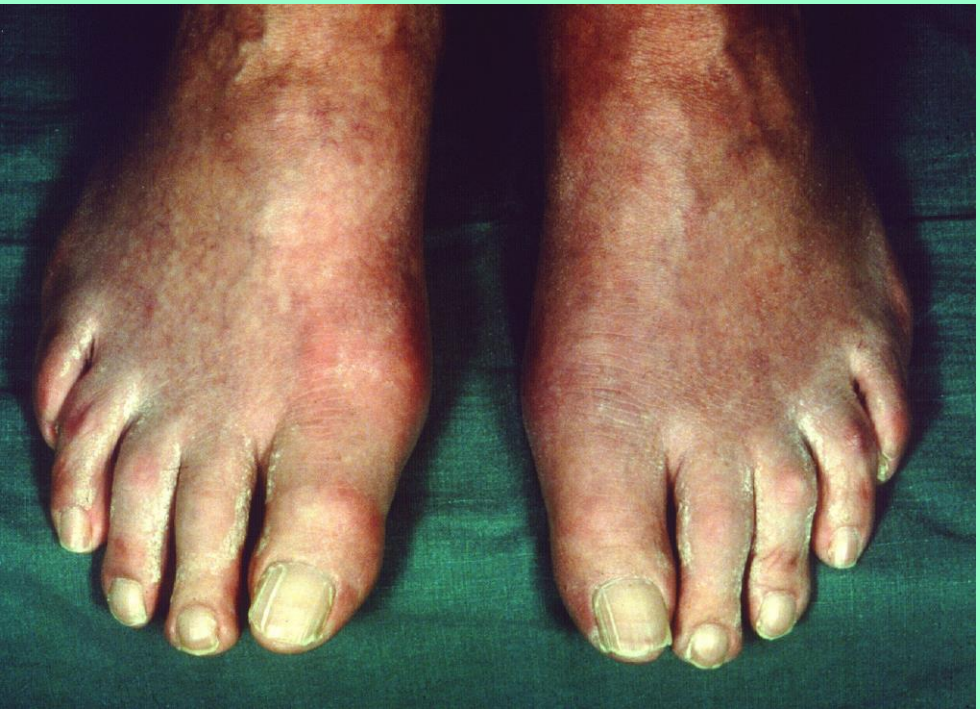
Proliferation von Zellen der Thrombozytopoese bzw. von atypischen Megakaryozyten

klinisch stehen oft die Symptome infolge rheologischer Faktoren im Vordergrund

Myeloproliferatives Syndrom: (MPS:ETH)







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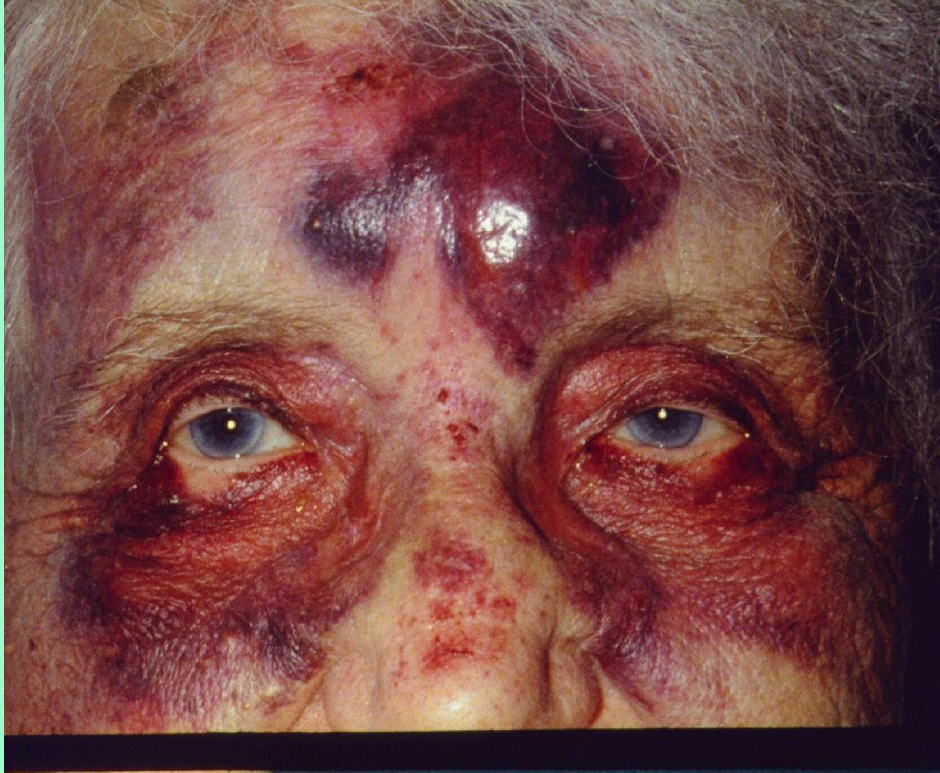
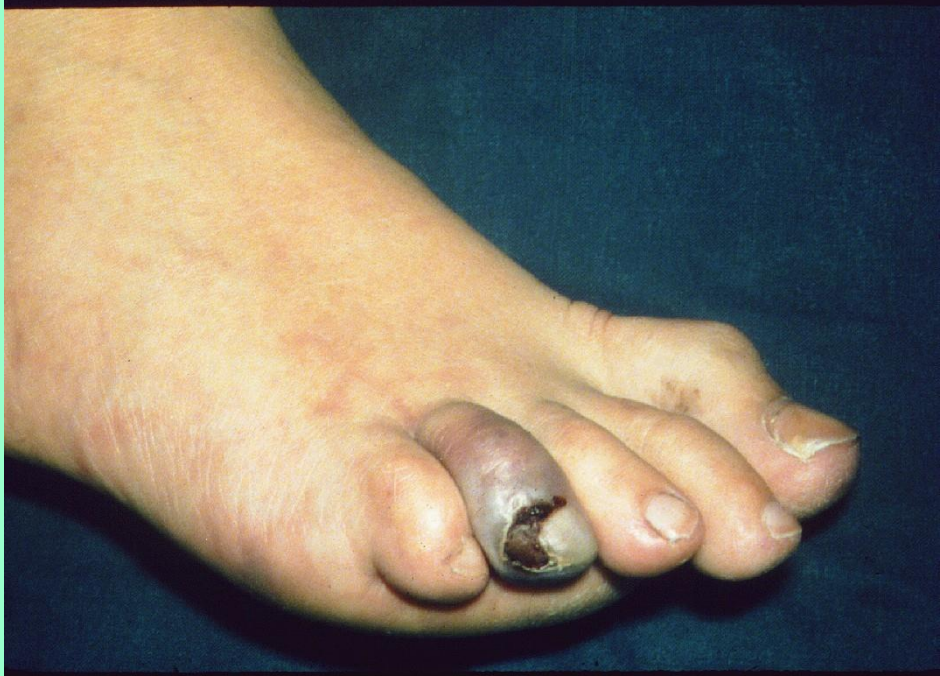
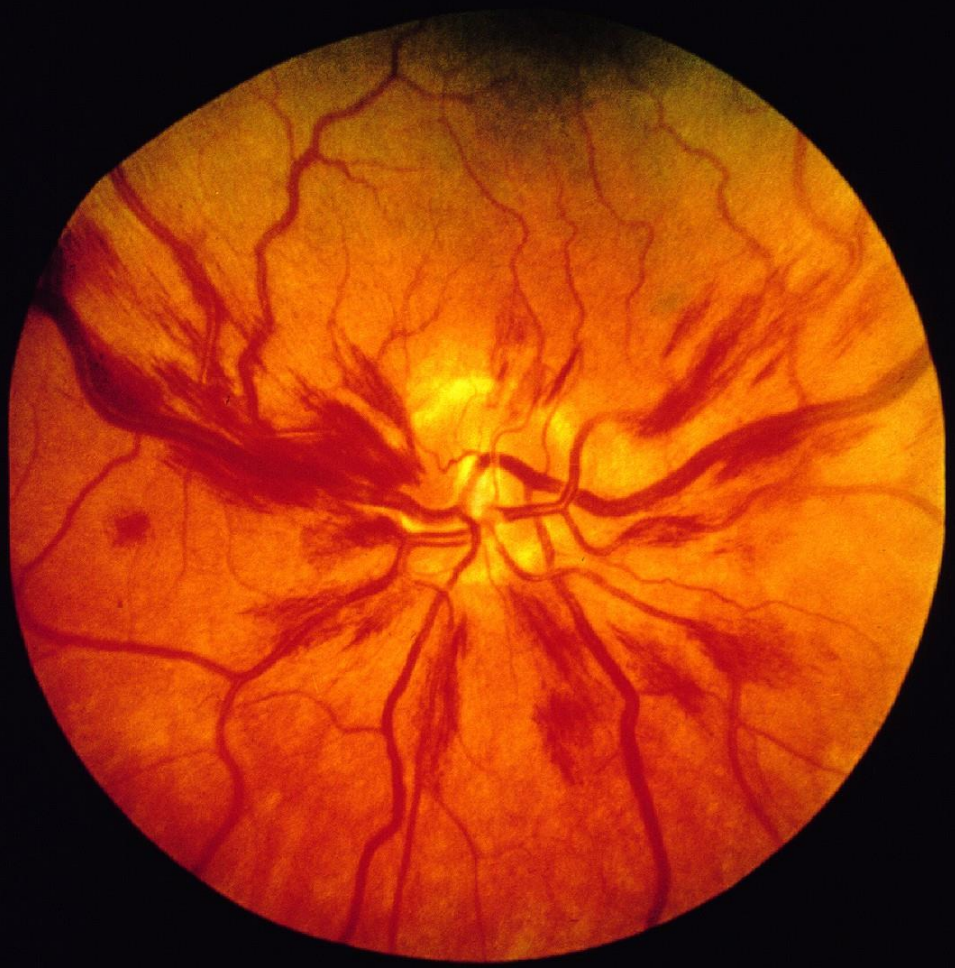






Myeloproliferatives Syndrom:

(MPS:ETH)

klinisch stehen oft die Symptome infolge rheologischer Faktoren im Vordergrund

Causes of megakaryocytic hyperplasia.

Post splenectomy
Haemorrhage
Malignancy
Crohn's disease
Rheumatoid arthritis
Hepatitis
Iron deficiency

MYELOPROLIFERATIVE Syndrome

1. chron.granulozyt. Leukämie(CGL) und andere chron.Myeloleukämien
2. PCV
3. ETH
4. idiopath.Myelofibrose
5. systemische Mastozytose
6. idiopath. Hypereosinophilen-Syndrom
7. transitionale u.unklassif. myeloprolif. Erkrankungen
8. Overlap-Sydrome

Causes of Marrow Fibrosis

Myelosclerosis

Infections:
tuberculosis (see Chapter 15),
osteomyelitis (focal fibrosis)

Malignant lymphoma,
including Hodgkin's disease (see Chapter 10)

Occasionally in chronic granulocytic
leukaemia (see Chapter 9)
& other leukaemias (see Chapter 8)

Metastatic carcinoma,
especially breast & prostate (see Chapter 15)

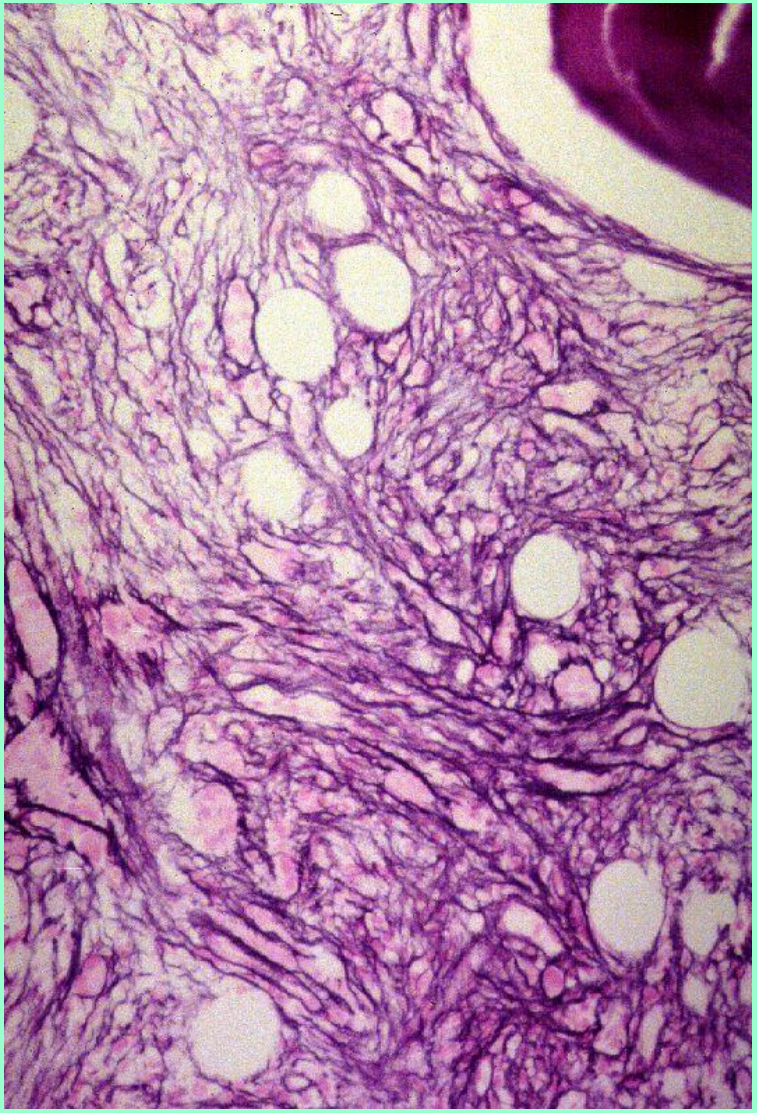
Excess irradiation

Benzene poisoning

Excess fluorine

Paget's disease
(focal fibrosis; see Chapter 15)

Osteopetrosis (see Chapter 15)



Osteomyelofibrose (OMF,OMS)

Causes of secondary diffuse fibrosis in the bone marrow.

All other myeloproliferations
Acute leukaemias other than M7
MDS
Lymphoma: both Hodgkin's and non-Hodgkin's
Myeloma
Carcinoma and sarcoma
TB and other granulomatous disorders
Others including fractures, toxins and irradiation

Experimentelle Möglichkeiten zur Erzeugung einer Osteomyelofibrose

1. **Zirkulationsstörungen** (Arterienligatur, Mikroembolien) (21, 69, 119)
2. **Ionisierende Strahlen** (Ganzkörperbestrahlung, Sr^{-19}) (31, 62, 71, 132)
3. **Chemische Agentien** (Saponin, Bleiazetat) (6, 33, 86, 101)
4. **Hormone** (Östrogene, Hypophysenvorderlappen, PTH) (89, 128, 130)
5. **Entzündungen** (136)
6. **Viren** (44, 139)
7. **Fremdeiweiße** (Ov-Albumin, Rinderserumalbumin, Hühnereiweiß) (48, 72, 104, 110, 137)
8. **Spezifische Antikörper** (60, 97)

Myelodysplastische Syndrome

(MDS)

1. **MDS:RA**
2. **MDS:RAS**
3. **MDS:RAEB**
4. **CMML**
5. **MDS-t**

FAB-Klassifikation der Myelodysplastischen Syndrome

1. **Refraktäre Anämie (RA)**

2. **Refraktäre Anämie mit Ringsideroblasten (Ringsideroblasten > 15%)**

3. **Refraktäre Anämie mit Blastenexzess (RAEB)**
   Blasten 5 - 20 %

4. **Chronische myelomonozytäre Leukämie (CMML)**

5. **RAEB in Transformation (Blasten > 20 - 30 %)**

French
American
British

Classification of MDS

FAB Classification of the Myelodysplastic Syndromes

1 Refractory anaemia (RA)

2 RA with ring sideroblasts (ring sideroblasts > 15%)

3 RA with excess blasts (RAEB; blasts 5-20%)

4 Chronic myelomonocytic leukaemia (CMML)

5 RAEB 'in transformation' (blasts 20-30%)

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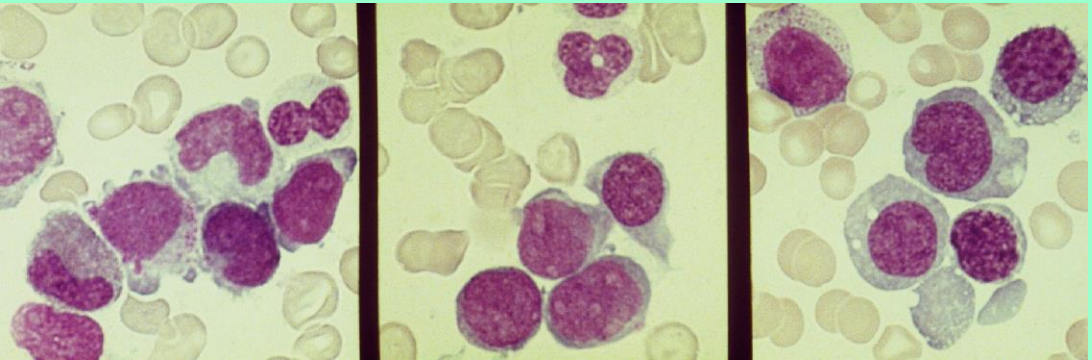
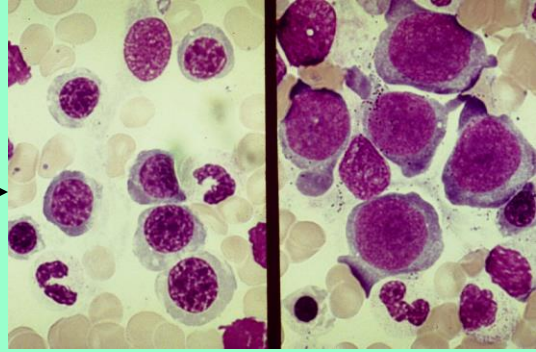
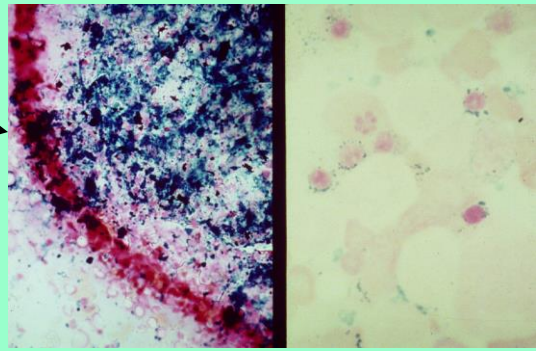
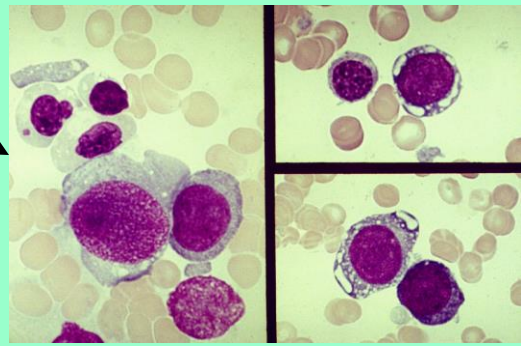
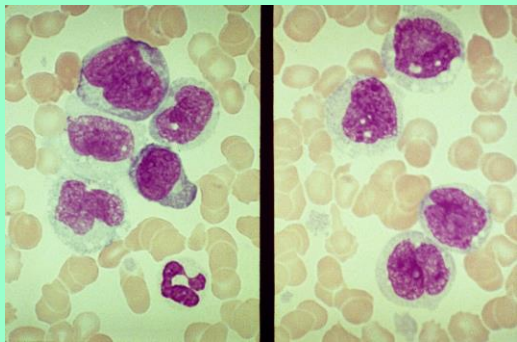
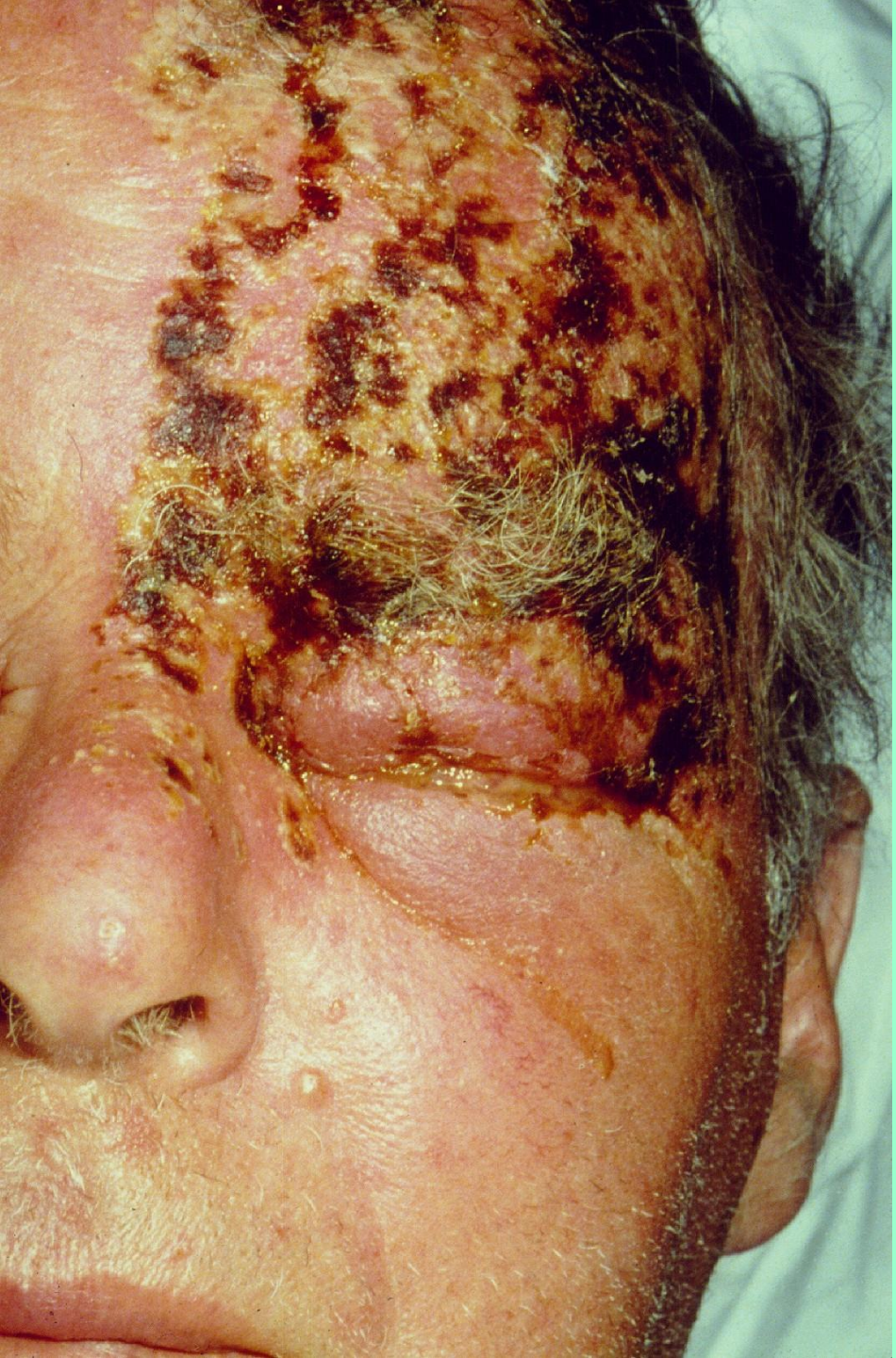


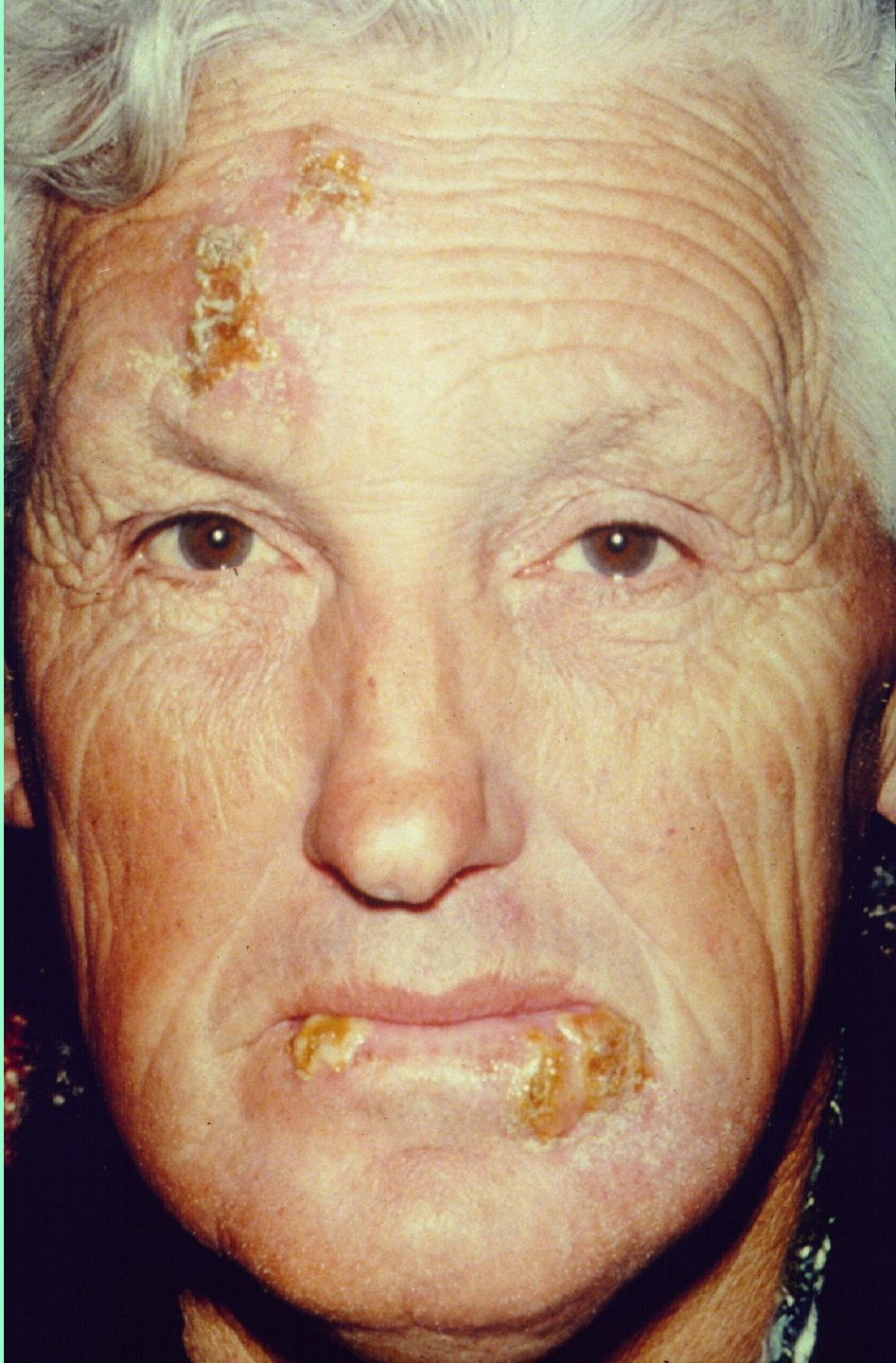




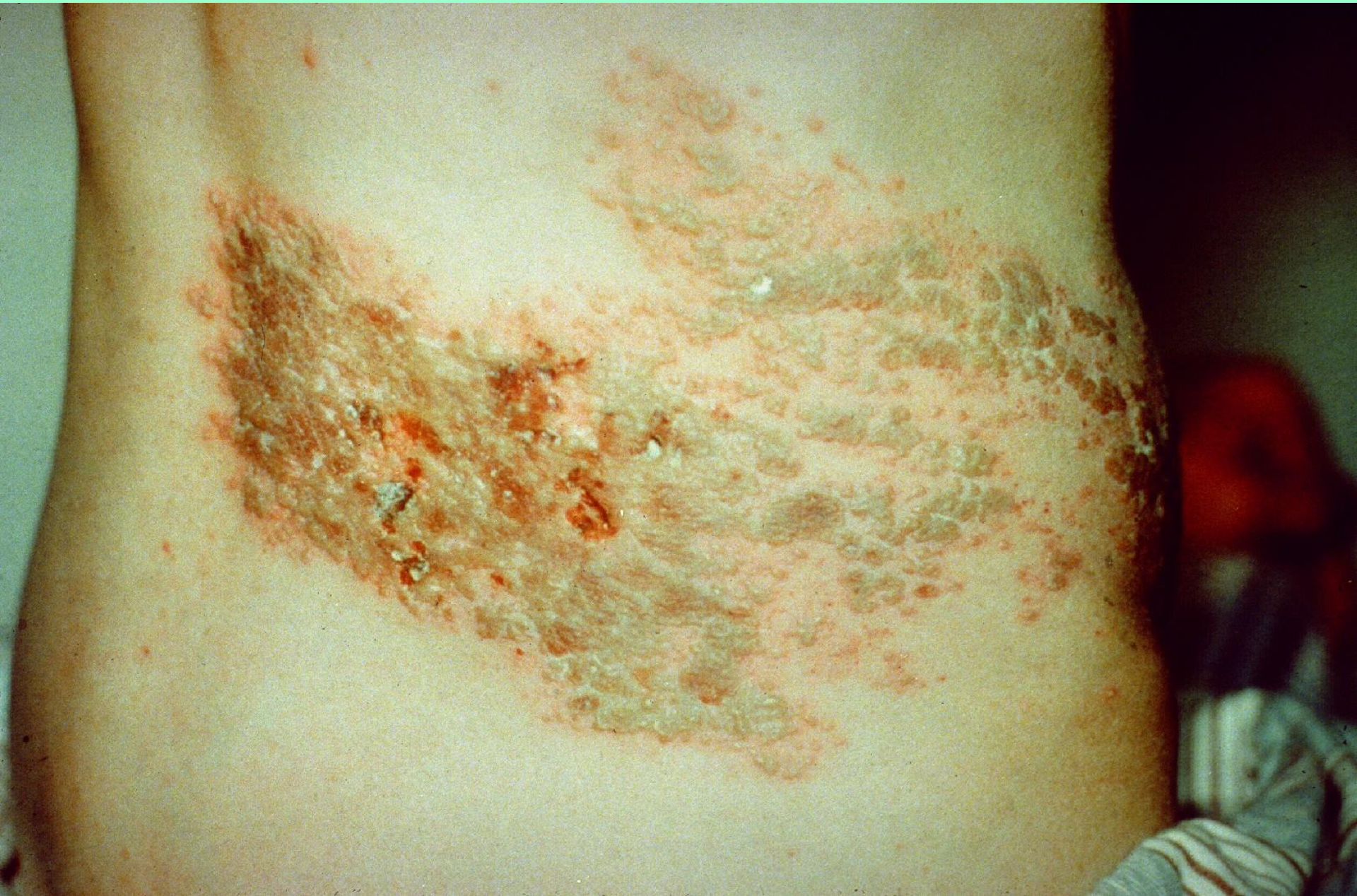


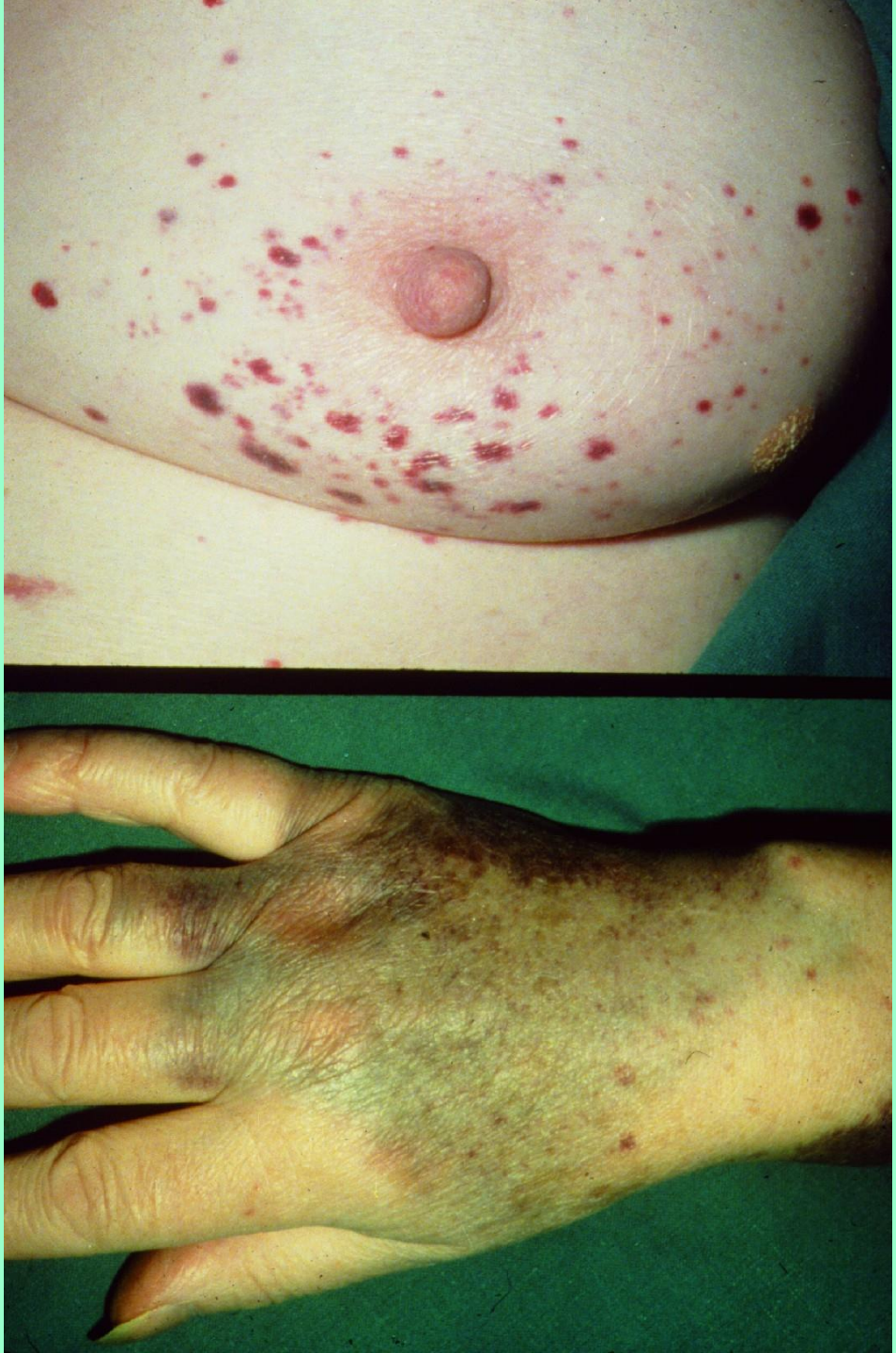




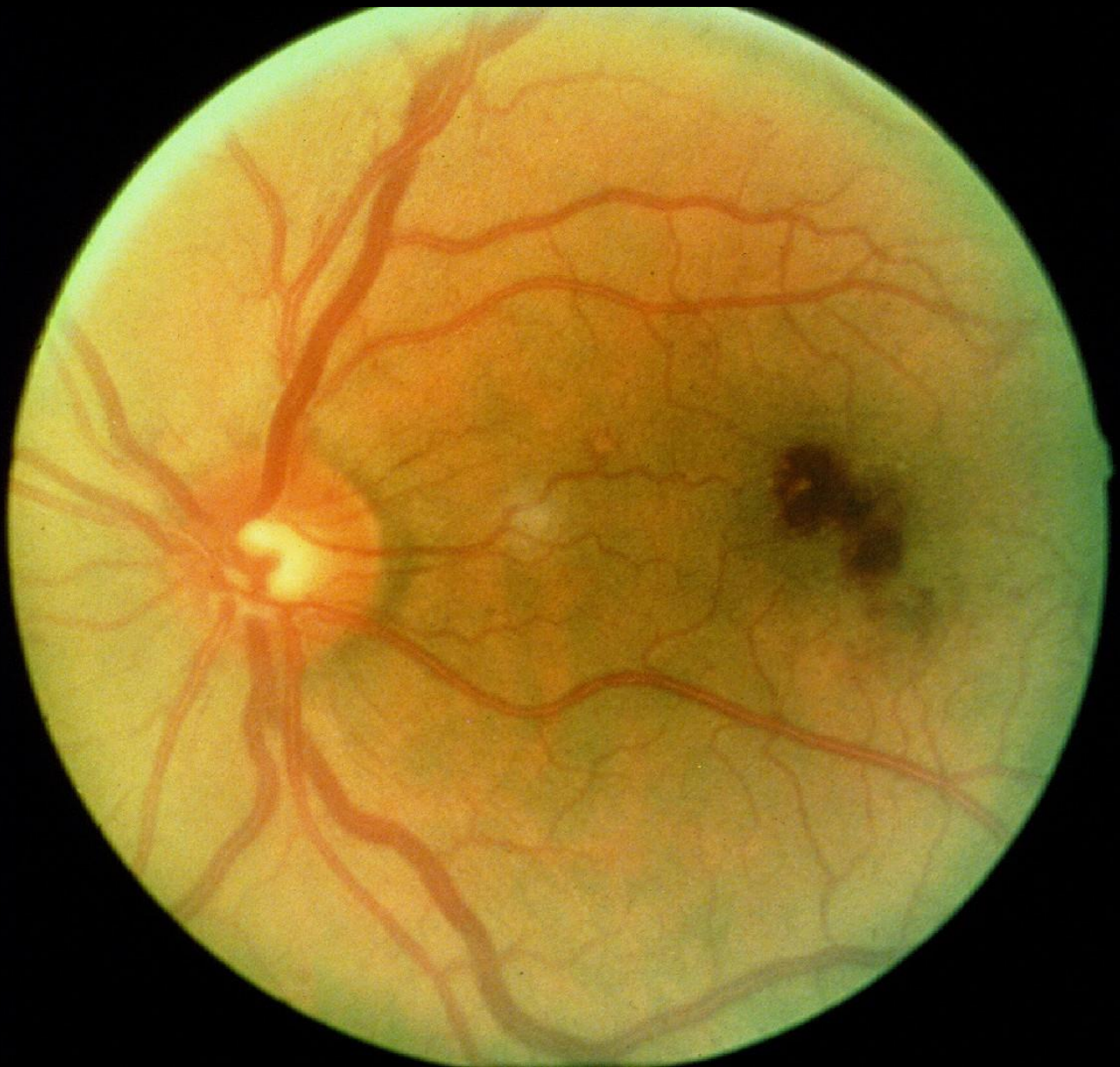


Herpes zoster bei präexistentem MDS





Retinablutungen bei myelodysplastischem Syndrom



MDS	peripheres Blut	Knochenmark
refraktäre Anämie (RA)	Blasten<1%	Blasten<5%
RA mit Ringsideroblasten(RARS)	Blasten<1%	Blasten>5% mit RS>der Erythroblasten
RA mit Blastenexzess(RAEB)	Blasten<5%	Blasten 5-19%
Chronische myelomono- zytäre Anämie (CMML)	Blasten<5% Monozyten>1x10^9/l	Blasten<20%
RAEB in Transformation(RAEB-T)	Blasten>5%	Blasten 20-29% oder Auerstäbchen

MDS subtype and distribution (%)	Cases with chromosomal changes (%)	Cases that evolve to AML (%)	Median survival (months)
RA (30)	48	11	37
RARS (18)	12	5	49
RAEB (25)	57	25	9
RAEB-T (12)	93	50	6
CMML (15)	20	15	22

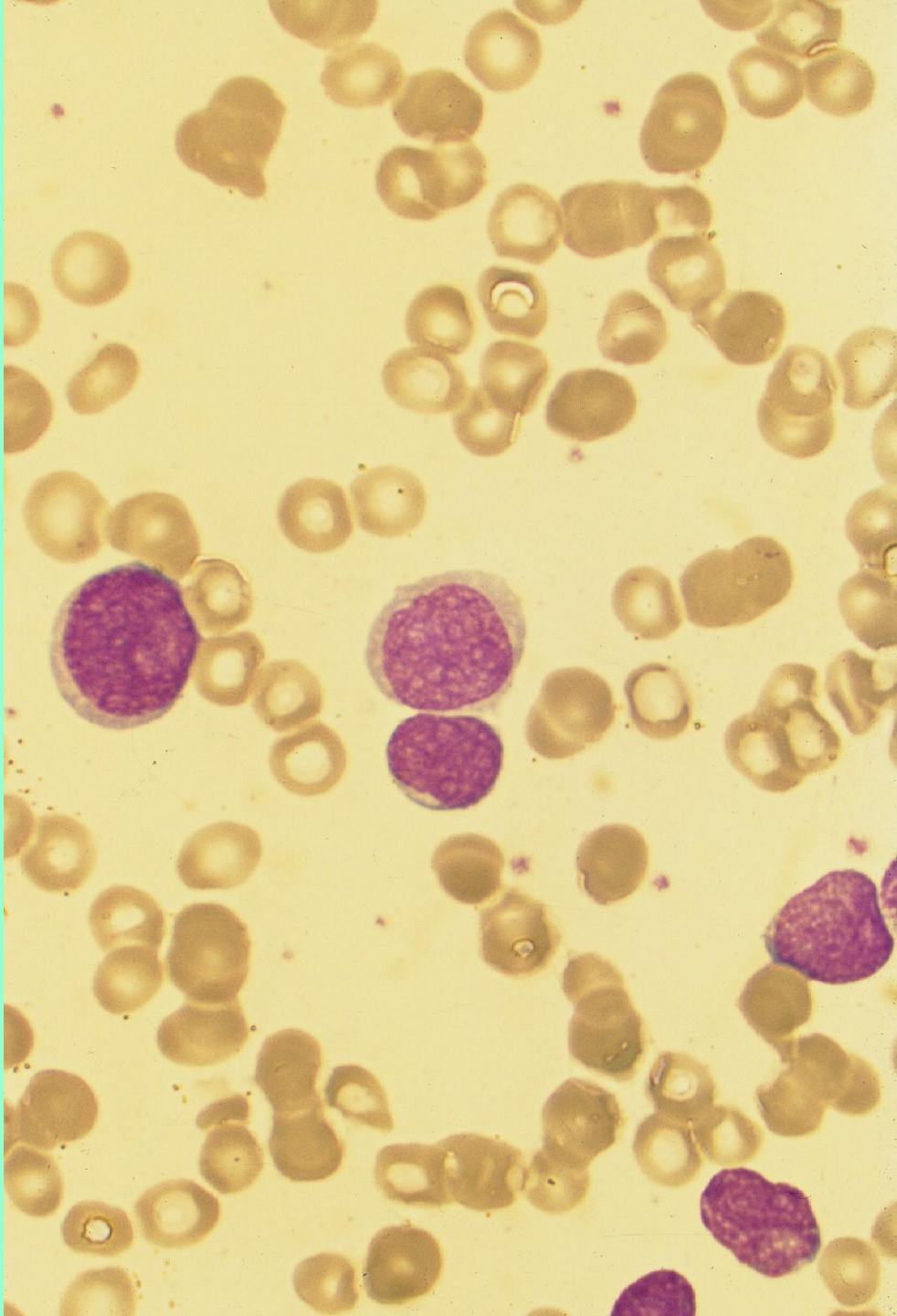
MDS subtype	Number of cases	RAS mutations (%)
RA	78	9 (11.5)
RARS	67	3 (4.5)
RAEB	44	12 (27)
RAEB-T	21	4 (19)
CMML	117	50 (43)
Total	326	78 (24)

Comparison of MDS with MPD.

MDS	MPD
Abnormal topography	Normal topography
Immaturity	Usually full maturity
Ineffective haematopoiesis, i.e. 'paenias'	Effective haematopoiesis, i.e. 'cytosis'
Stem cell defect reflected as premalignant, i.e. dysplastic changes	Stem cell defect reflected as frankly malignant changes

Anamnese :

- 15 Jahre altes Mädchen
- aktive Sportlerin
- „kerngesund“
- Angina tonsillaris
- anschließende unspezifische Prodromi mit Schlappheit, Inappetenz, Mattigkeit, Übelkeit
- Hausarzt aufgesucht
- Blutbild vom Hausarzt angefertigt



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- Hausarzt aufgesucht
- Blutbild vom Hausarzt angefertigt

- Diagnose : akute lymphoblastische Leukämie (ALL)
- Hämatologische Abteilung
- Zytostase, Radiatio („kill or cure“)
- KM-Transplantation
- mehrere längerfristige Remissionen
- exitus letalis an Grundleiden im Alter von 21 Jahren

MDS subtype	Peripheral blood	Bone marrow
Refractory anaemia (RA)	Blasts <1%	Blasts <5%
RA with ring sideroblasts (RARS)	Blasts <1%	Blasts <5% with ring sideroblasts >15% of erythroblasts
RA with excess of blasts (RAEB)	Blasts <5%	Blasts 5–19%
RAEB in transformation (RAEB-T)	Blasts ≥5%	Blasts 20–29% or Auer rods
Chronic myelomonocytic leukaemia (CMML)	Blasts <5% Monocytes >1 × 10^9/l	Blasts <20%

MDS subtype	Number of cases	RAS mutations (%)
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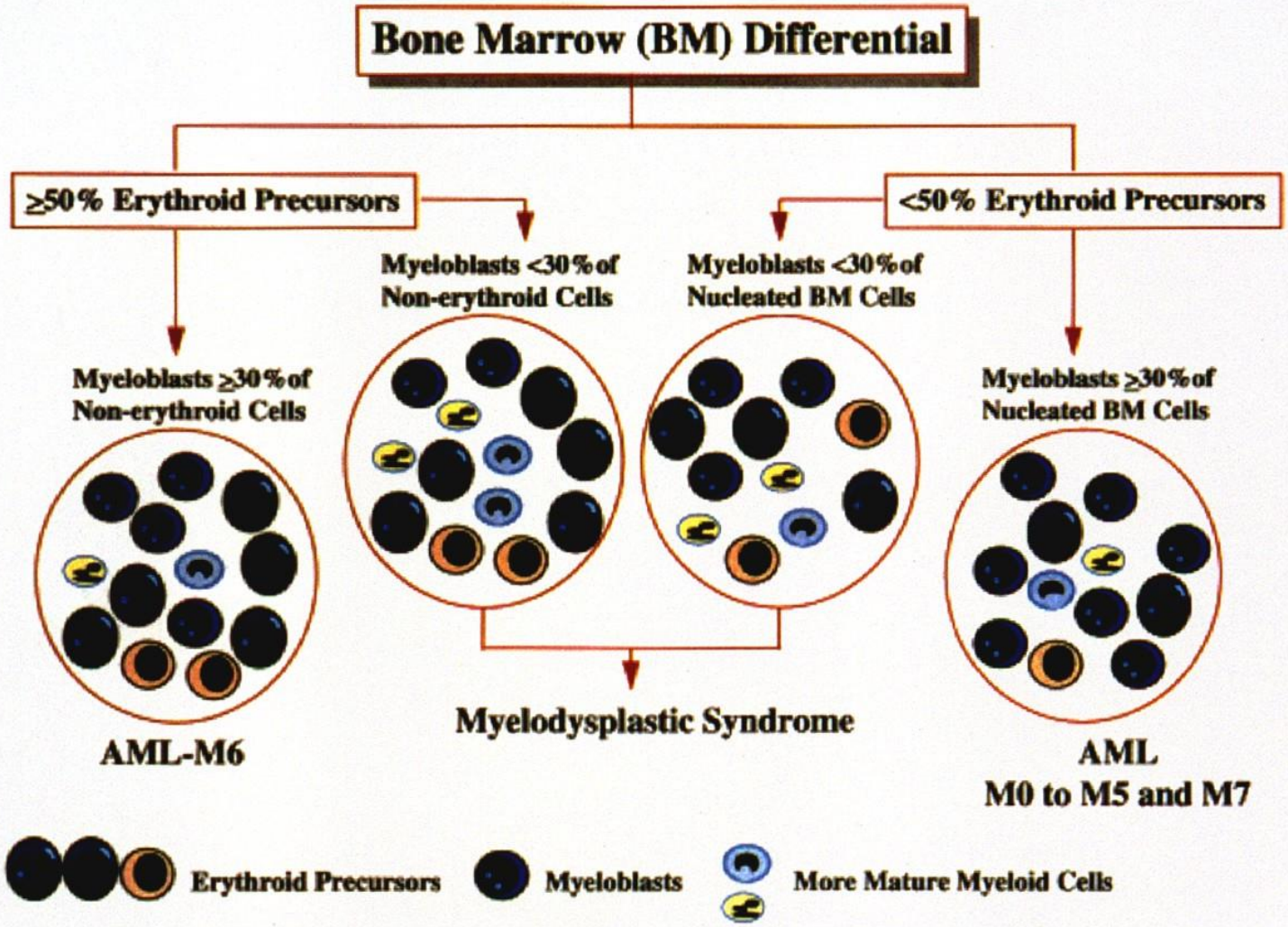
Chromosomale Lokalisationen :

T-Zell-Rezeptor-Gene und Immunglobuline

	Chromosome Number	Band
Immunoglobulin genes		
Heavy chain	14	q32
κ-light chain	2	p12
λ-light chain	22	q11
T-cell receptor genes		
α	14	q11.2
β	7	q34
γ	7	p14–15
δ	14	q11



Schematic demonstration of major differences between erythroleukemia (AML-M6) and myelodysplastic syndrome (RAEB/RAEB-T).

Myeloproliferative Syndrome

Chronic myeloid leukaemia (CML)
BCR–ABL rearrangement positive

Atypical CML (a–CML)
BCR–ABL rearrangement negative

Juvenile CML (jCML)

Chronic neutrophilic leukaemia (CNL)

Chronic myelomonocytic leukaemia (CMML)

Polycythaemia (rubra) vera (PRV)

Primary (idiopathic) myelofibrosis (PMF)

Essential thrombocythaemia (ET)

B-cell leukaemia
Chronic lymphocytic leukaemia (CLL, B-CLL)
Chronic lymphocytic leukaemia/prolymphocytic leukaemia (CLL/PLL)
Prolymphocytic leukaemia (B-PLL)
Hairy cell leukaemia (HCL)
Hairy cell leukaemia variant (HCL-v)

B-cell lymphoma (leukaemic phase)
Splenic lymphoma with villous lymphocytes (SLVL)
Follicular lymphoma (FL)
Mantle cell lymphoma (McL)
Waldenström's macroglobulinaemia (lymphoplasmacytic lymphoma)

T-cell leukaemia
Chronic lymphocytic leukaemia/Large granular lymphocytosis (T-CLL/LGL)
'Prolymphocytic leukaemia (T-PLL)
Sézary's syndrome; mycosis fungoides

T-cell lymphoma (leukaemic phase)
Adult T-cell leukaemia lymphoma (ATLL)
T-non-Hodgkin's lymphoma (T-NHL)

	Multiple myeloma	MGUS
1. Symptoms and signs	Present	Absent
2. Lytic bone lesions	Present	Absent
3. Bone marrow plasmacytosis (%)	>10	<10
4. Monoclonal paraprotein concentration in the serum/ Urinary excretion of Bence Jones protein	IgG (g/l)>30 IgA>10 BJP>1 g/24 hours	IgG<30 IgA<10 <1 g/24 hours
5. Polyclonal immunoglobulins	Decreased	Normal

Epithelial carcinoma	% metastasizing to bone
Prostatic adenocarcinoma	54
Breast adenocarcinoma	27
Gastric adenocarcinoma	19
Bronchogenic carcinoma	8
Follicular carcinoma of thyroid	<2
Renal cell carcinoma	<2
Colonic carcinoma	<2

Drugs which may cause aplasia.

Type of drug	Example
Antibiotic	Chloramphenicol
Anti-inflammatory	Phenylbutazone
Anti-epileptics	Phenytoin
Anti-malarials	Mepacrine
Anti-diabetic	Chlorpropamide

A comparison of the features which may help discriminate between benign lymphoid aggregates in bone marrow and neoplastic involvement.

Benign	Neoplastic
Rounded aggregates	May be irregular
Well circumscribed regular small lymphocytes	Cellular atypia may be present
Elderly population	Wide age range
< 3 mm in diameter	May be > 3 mm diameter
Never paratrabecular	May be paratrabecular
Germinal centres (5% of cases)	No germinal centres
May contain plasma cells and eosinophils	Usually just lymphoid cells
Polyclonal light chain expression	Monoclonal light chain pattern
1–3 aggregates per trephine	> 3 aggregates per trephine

Causes of a reactive plasmacytosis.

HIV

Hepatitis

Systemic lupus erythematosis

Rheumatoid arthritis

Iron and folate deficiency

Alcohol abuse

Hodgkin's disease

A comparison of the histological features of reactive plasmacytosis and multiple myeloma.

Reactive plasmacytosis	Multiple myeloma
Majority are mature plasma cells	Variation in size and differentiation, intermediate forms common
Nucleoli uncommon	Nucleoli often present
No clusters	Clusters common
Single layer around capillaries	Several cells deep around capillaries

A comparison of the histological features of reactive plasmacytosis and multiple myeloma.

Reactive plasmacytosis	Multiple myeloma
Plasma cells usually constitute < 25% of cells	Plasma cells usually constitute > 25% of cells
Majority are mature plasma cells	Greater variation in size
Nucleoli only present in a few plasma cells	Nucleoli often present
Collections, i.e. nodules or sheets of plasma cells, never seen	Often present in large homogeneous groups
Occasional bi-nucleated forms and less mature forms	Plasmablast forms (prominent central nucleoli)
Single layer around capillaries	Several cells deep around capillaries, diffusely distributed amongst fat cells, groups or sheets of plasma cells

Letztes teilweises update im Jahr 2002