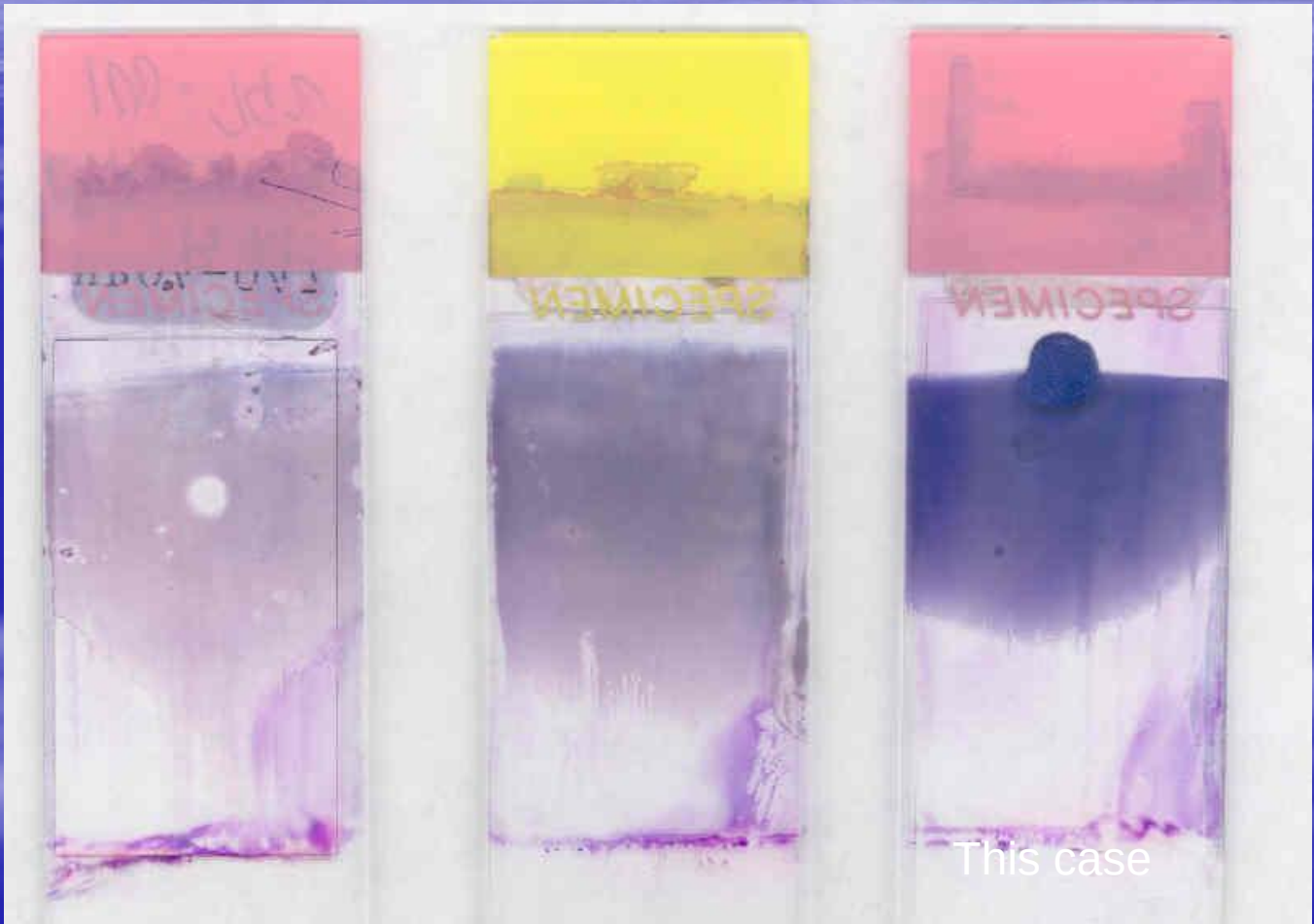
Hematology cases

May 2004

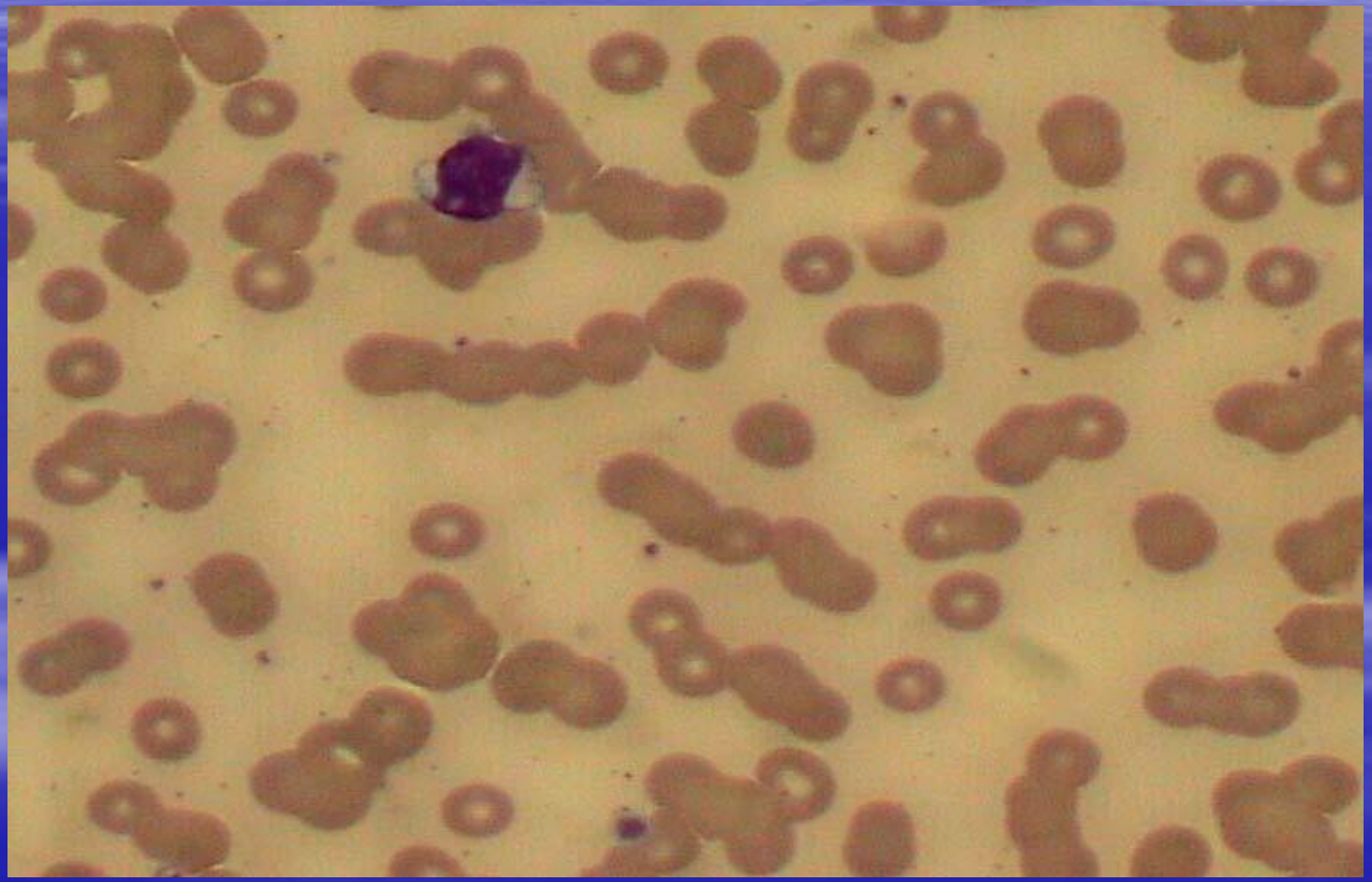
A 89 y.o female with back pain and monoclonal gammopathy

Peripheral smear



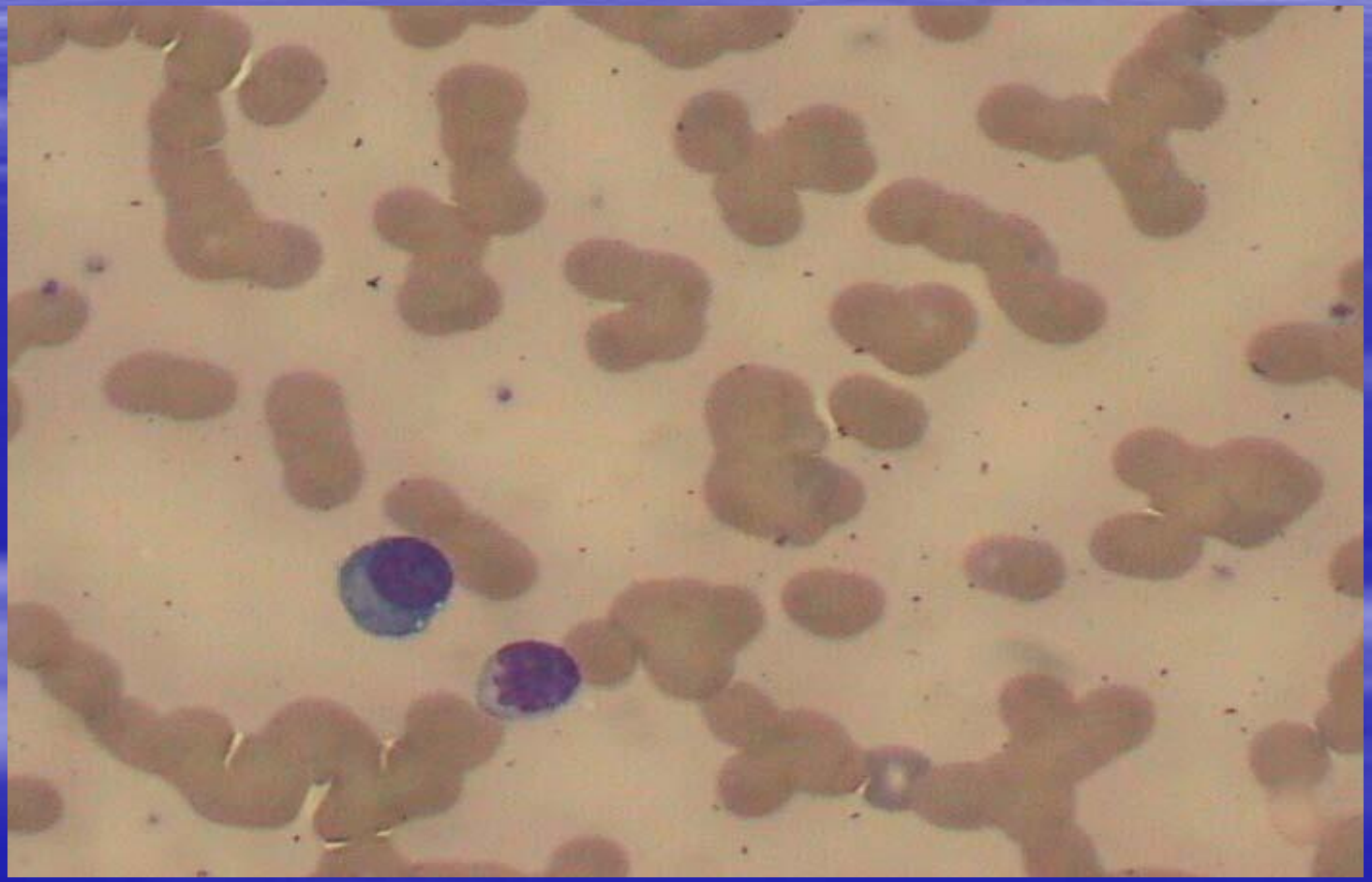
Blue background

Peripheral smear



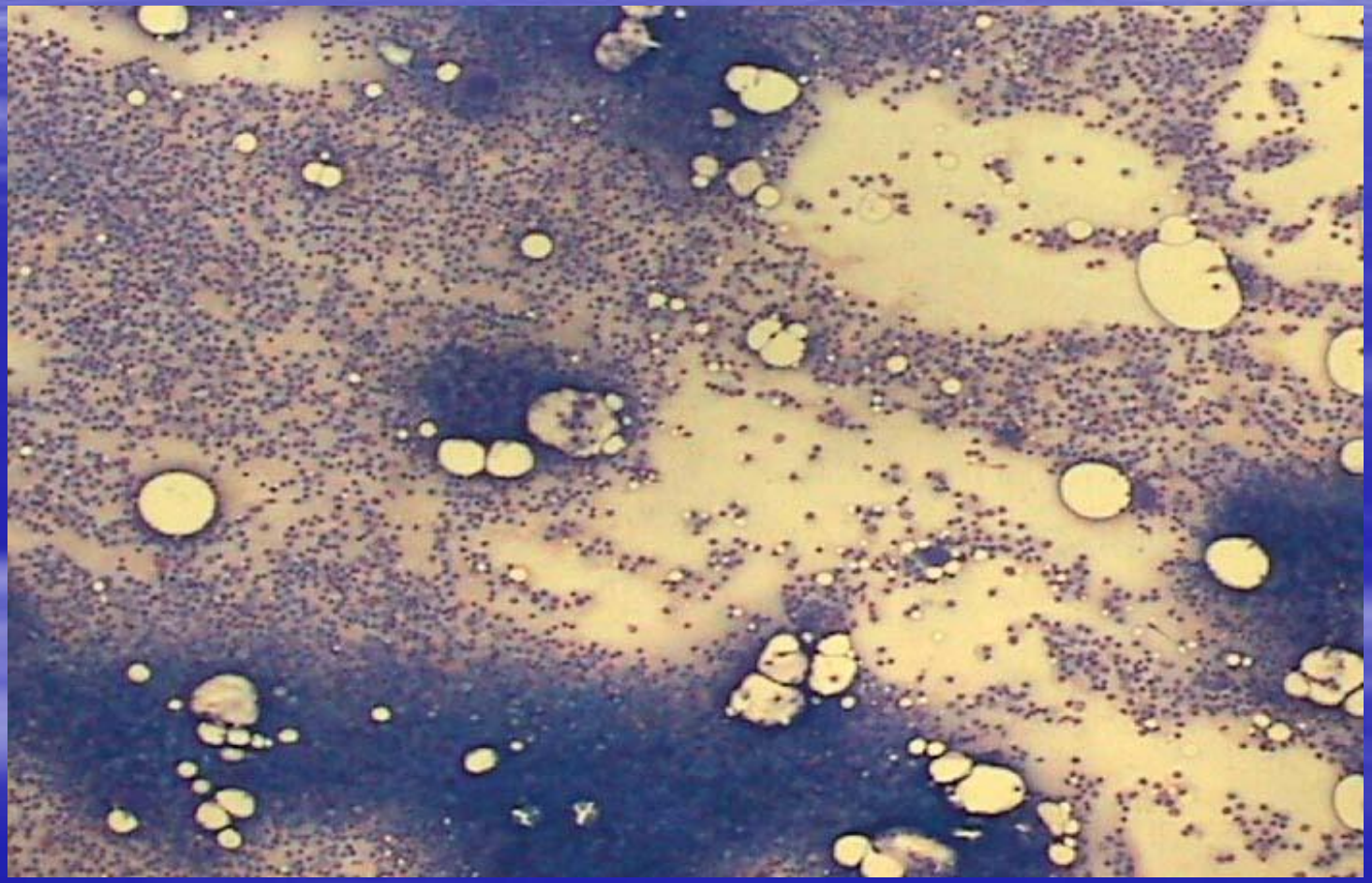
Macrocytic anemia with rouleaux

Peripheral smear



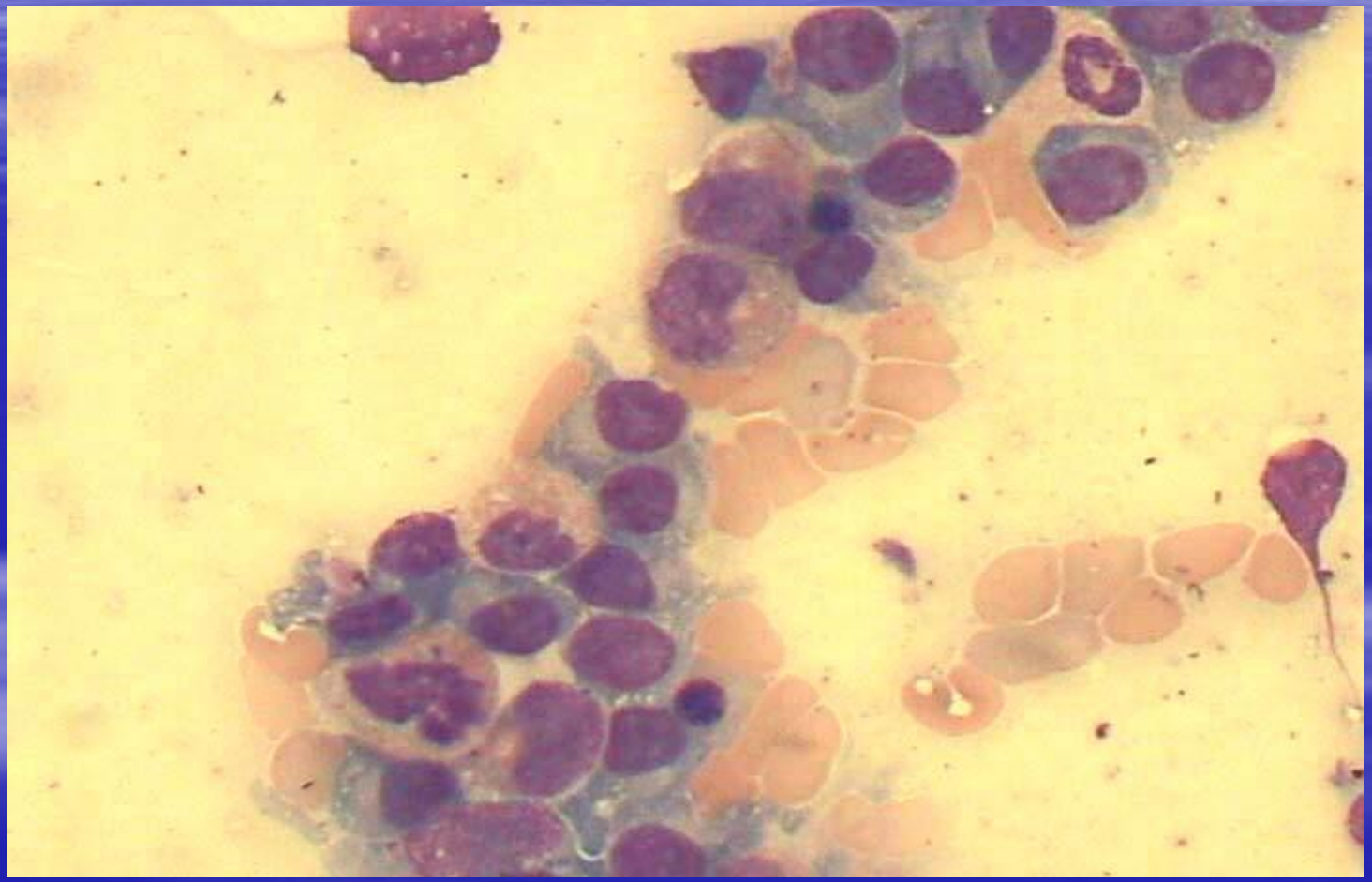
Inc lymphocytes (50% of 12,500) with a few plasmacytoid lymphocytes

Bone marrow

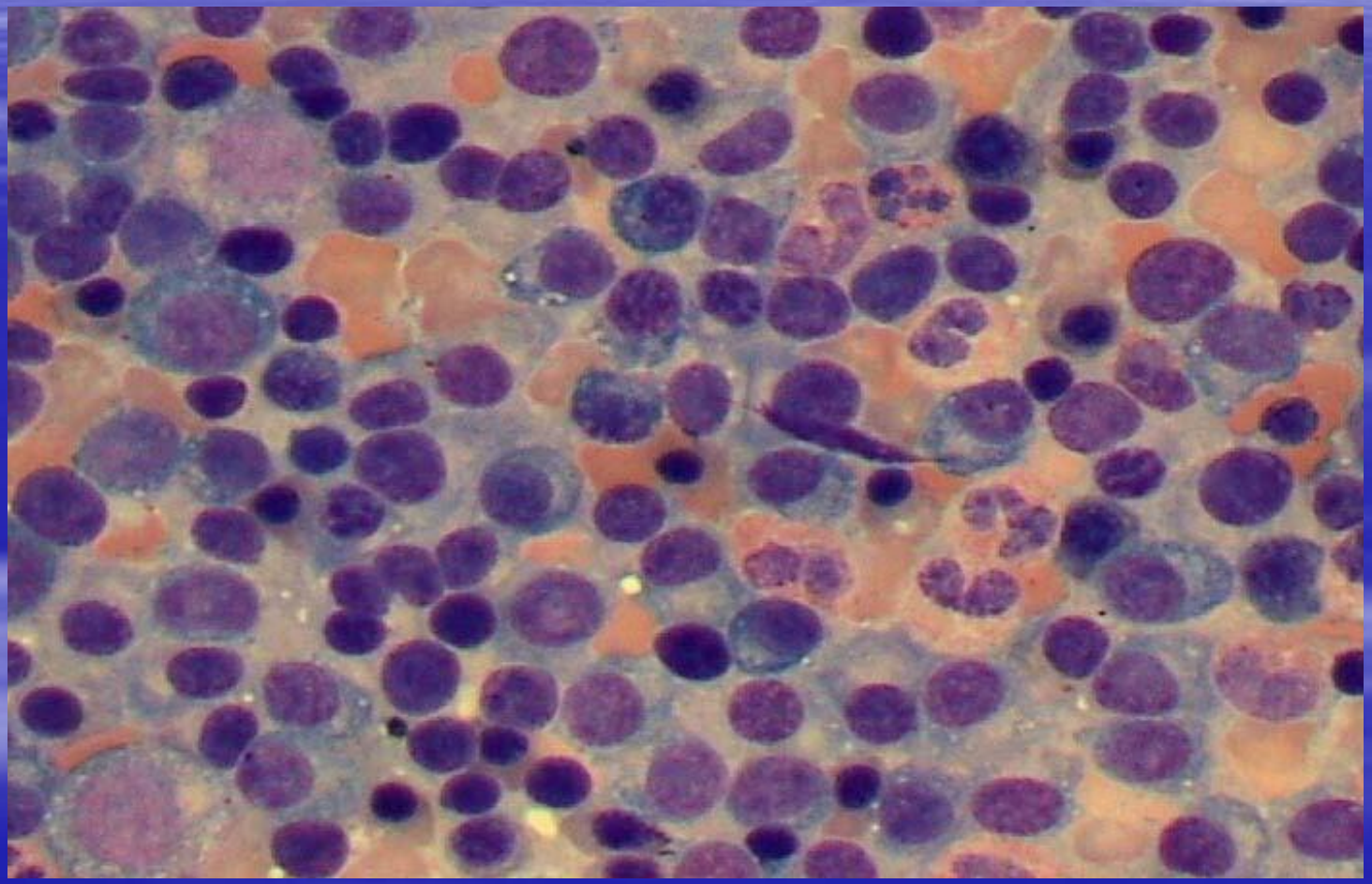


Adequate spicules

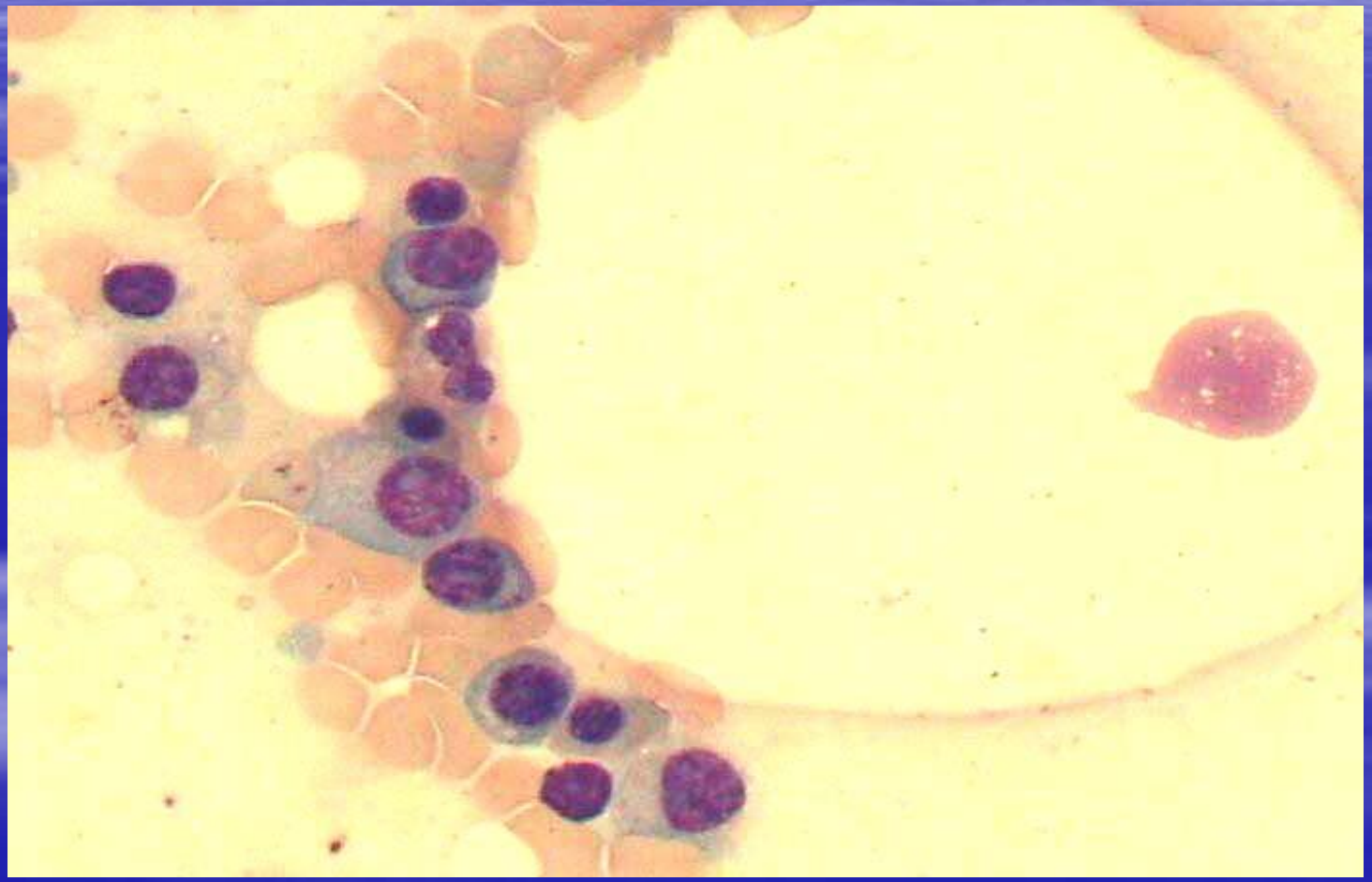
Bone marrow



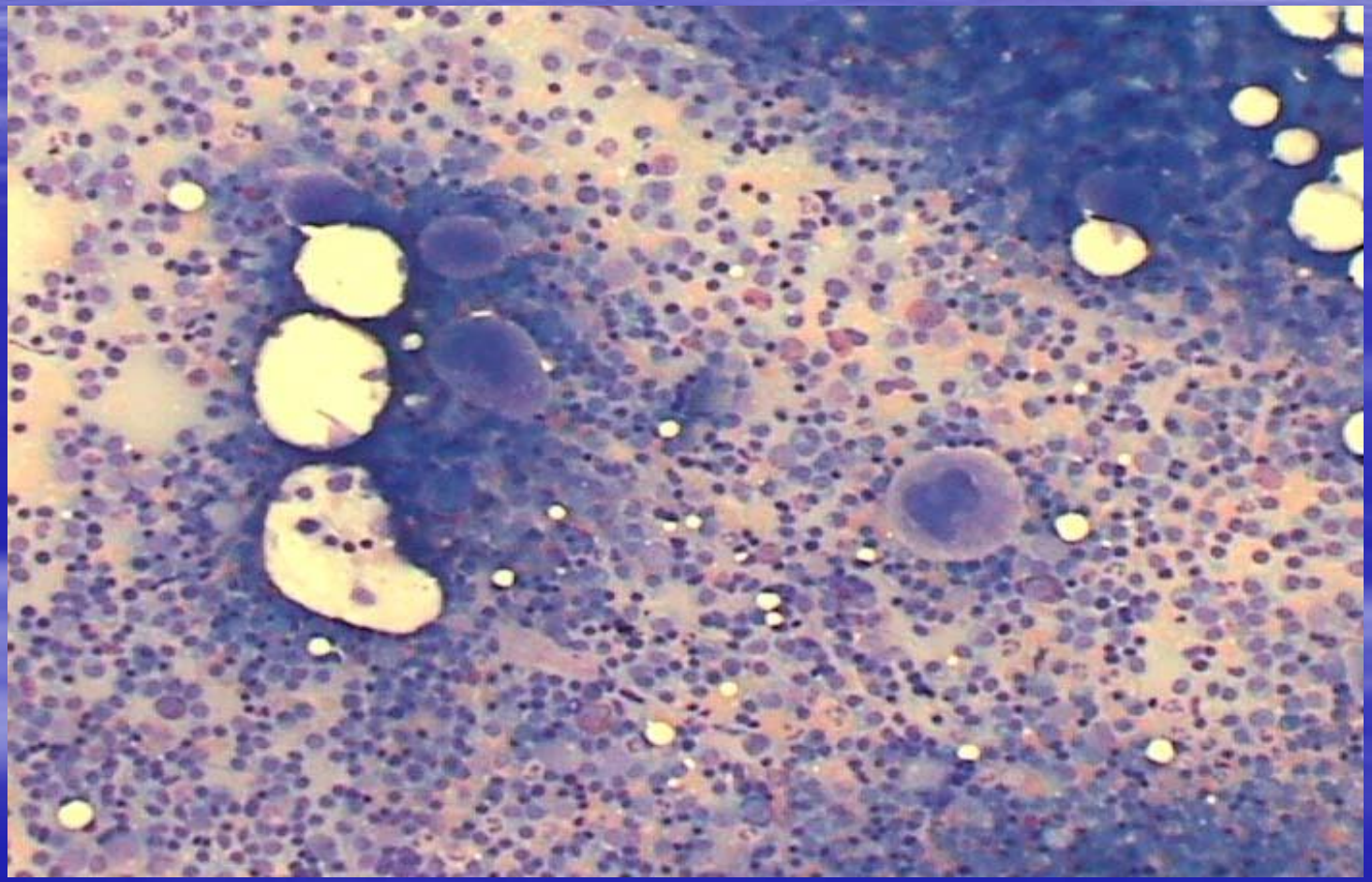
Bone marrow



Plasma cells:36%

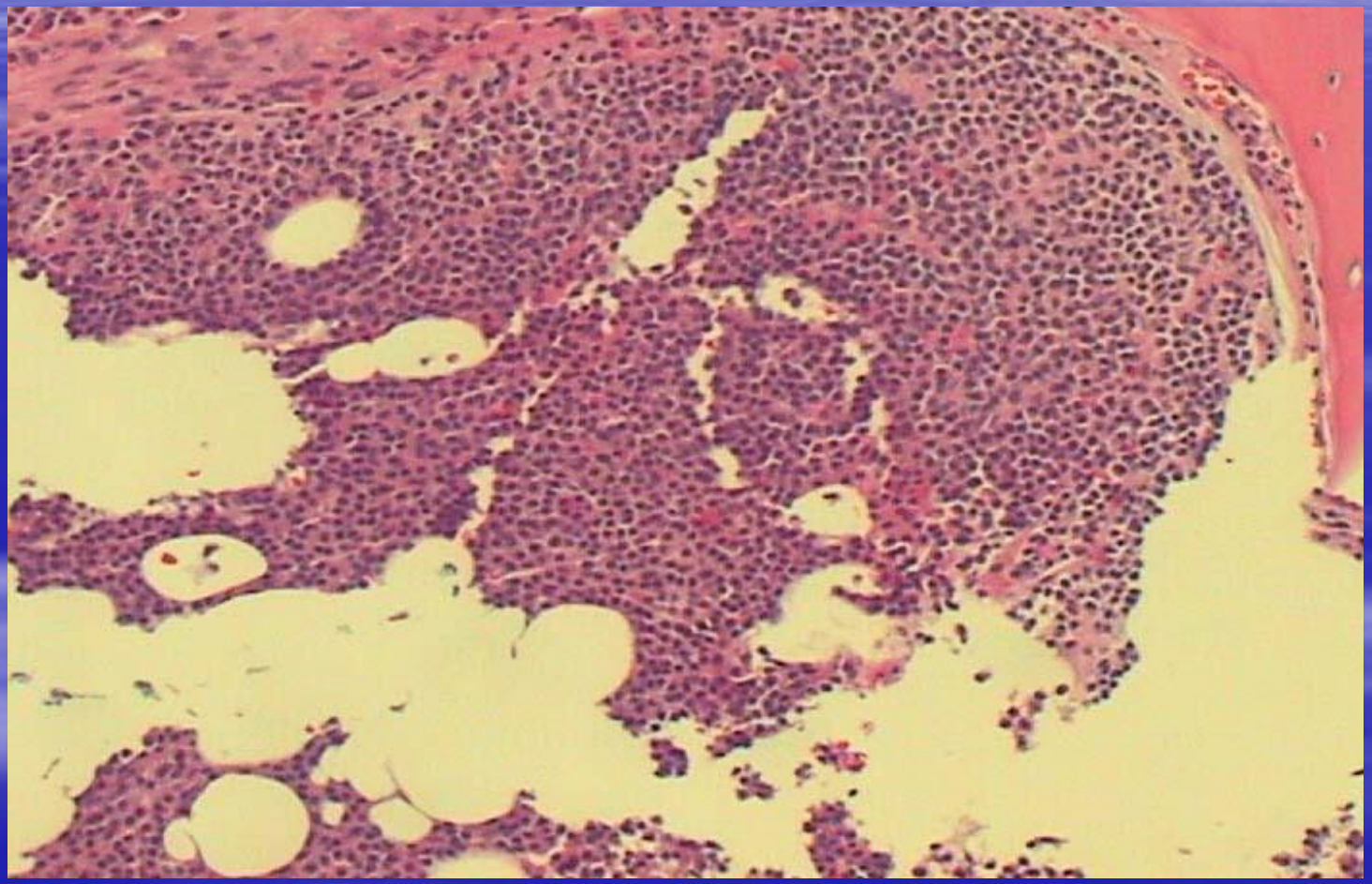


Bone marrow



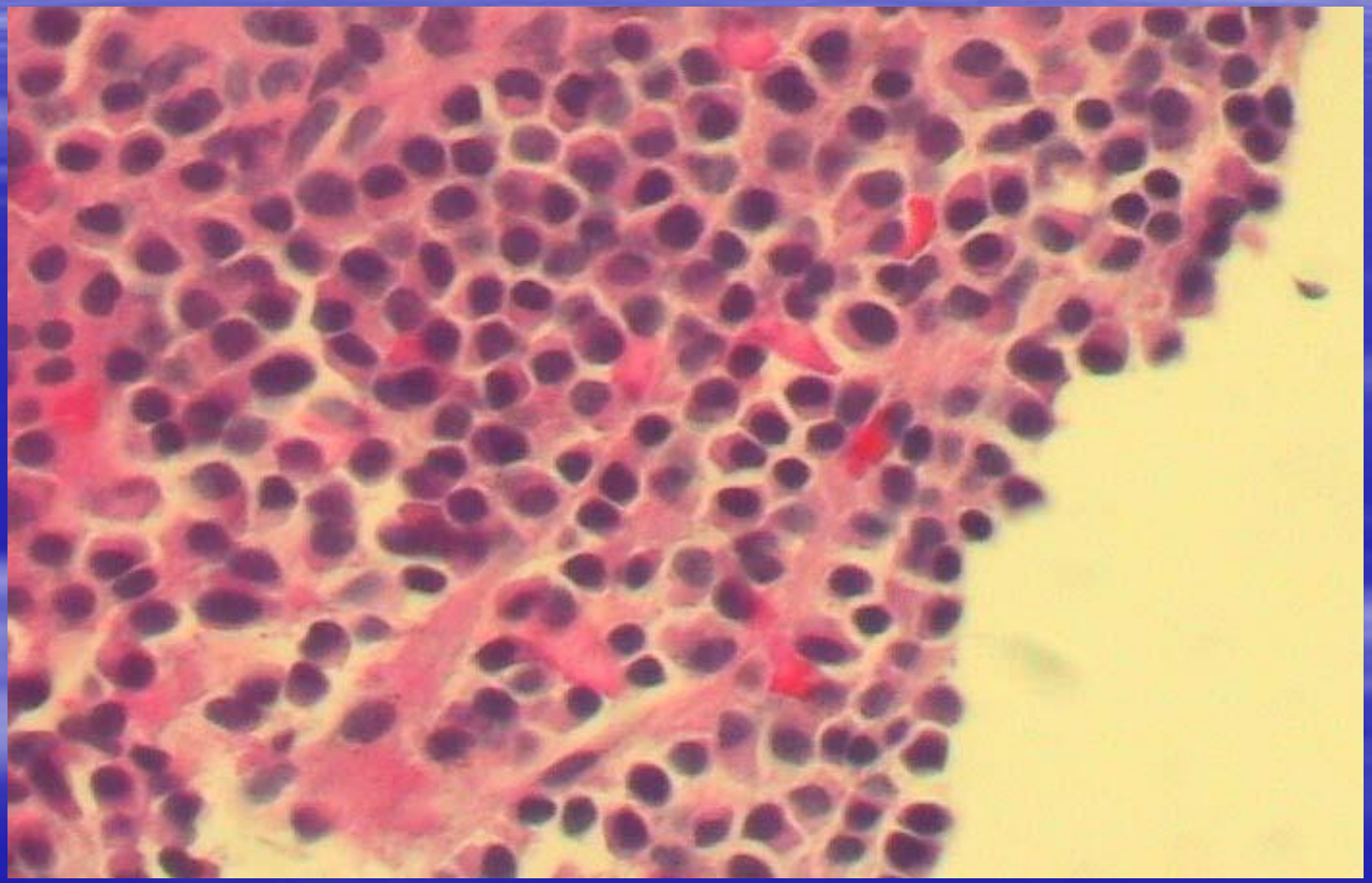
Adequate megs and granulopoiesis; reduced erythropoiesis

Bone marrow

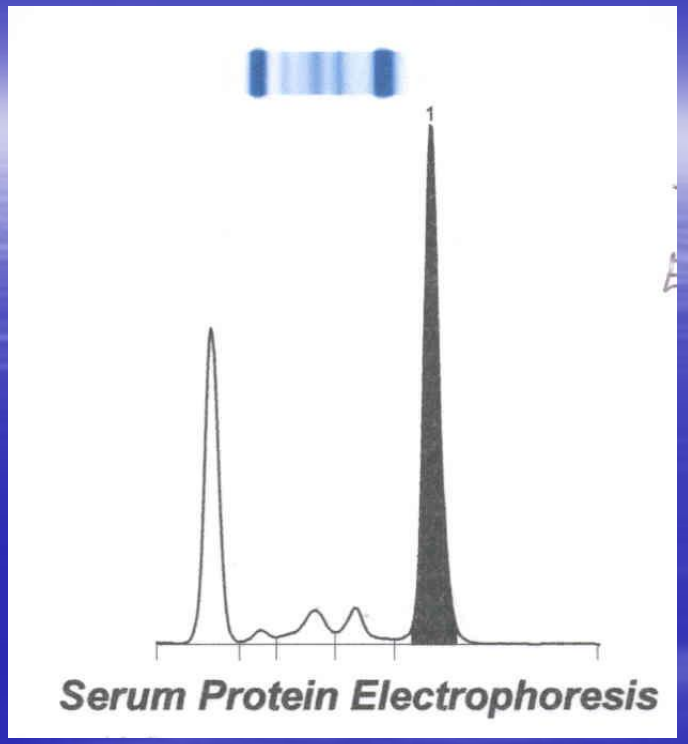


BM cellularity: 80%

Bone marrow



Diffuse infiltration of plasma cells on biopsy



T.P. g/dL : 10.5 A/G: 0.45

Fractions	%	Ref. %	g/dl	Ref. g/dl
Albumin	**31.1** ↓	58.8 - 69.6	**3.27** ↓	3.76 - 5.85
Alpha 1	**1.8**	1.8 - 3.8	**0.19**	0.12 - 0.32
Alpha 2	**6.3**	3.7 - 13.1	**0.66**	0.24 - 1.10
Beta	**5.3** ↓	8.9 - 13.6	**0.56** ↓	0.57 - 1.14
Gamma	**55.5**	8.4 - 18.3	**5.83** +	0.54 - 1.54
1	**53.9**		**5.66**	

- No paraprotein in UPE
- Immunofixation not done

Criteria

Major criteria

I. Plasmacytoma by bx

II. >30% marrow plasmacytosis

III. Monoclonal gammopathy

Serum: IgG>3.5 g/dl, IgA>2 g/dl

Urine: >1 g/day of BJ proteins

Minor criteria

A.10-30% marrow plasmacytosis

B.Monoclonal gammopathies with lower values

C.Lytic bone lesions

D.Suppressed normal immunoglobulins

Diagnosis

One major and one minor criteria or three minor criteria which should include 1 and 2

These criteria should be in symptomatic patients with progressive disease

Multiple myeloma

- Aka Kahler's disease, myelomatosis, medullary plasmacytoma
- 15% of all hematological malignancies
- More common in blacks
- Male to female ratio is 1:1
- Median age of diagnosis 68-70 yrs

Etiology

-Exposure to chemicals

-High dose radiation

-Viruses? (HHV8, HIV)

-Long standing chronic infections

Genetics

-Structural and numerical chromosome abnormalities in 20-60% of new and 60-70%of progressive cases

-Multiple chromosomal gains and losses

-13q14 in 15-40% of new cases

-Translocation t(11;14)(q13;q32)

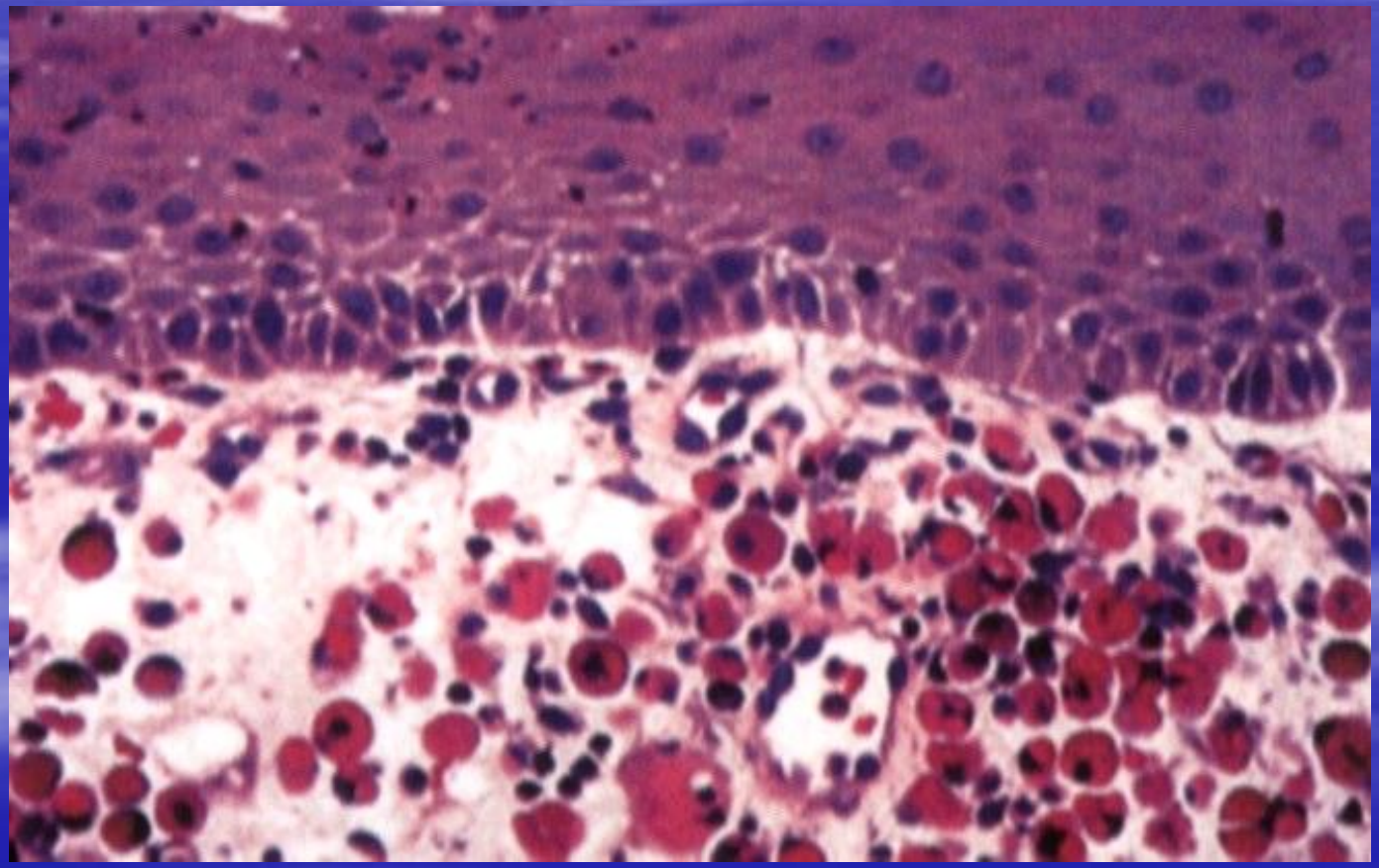
-Deletion of 17p13 in 25% associated with poor outcome

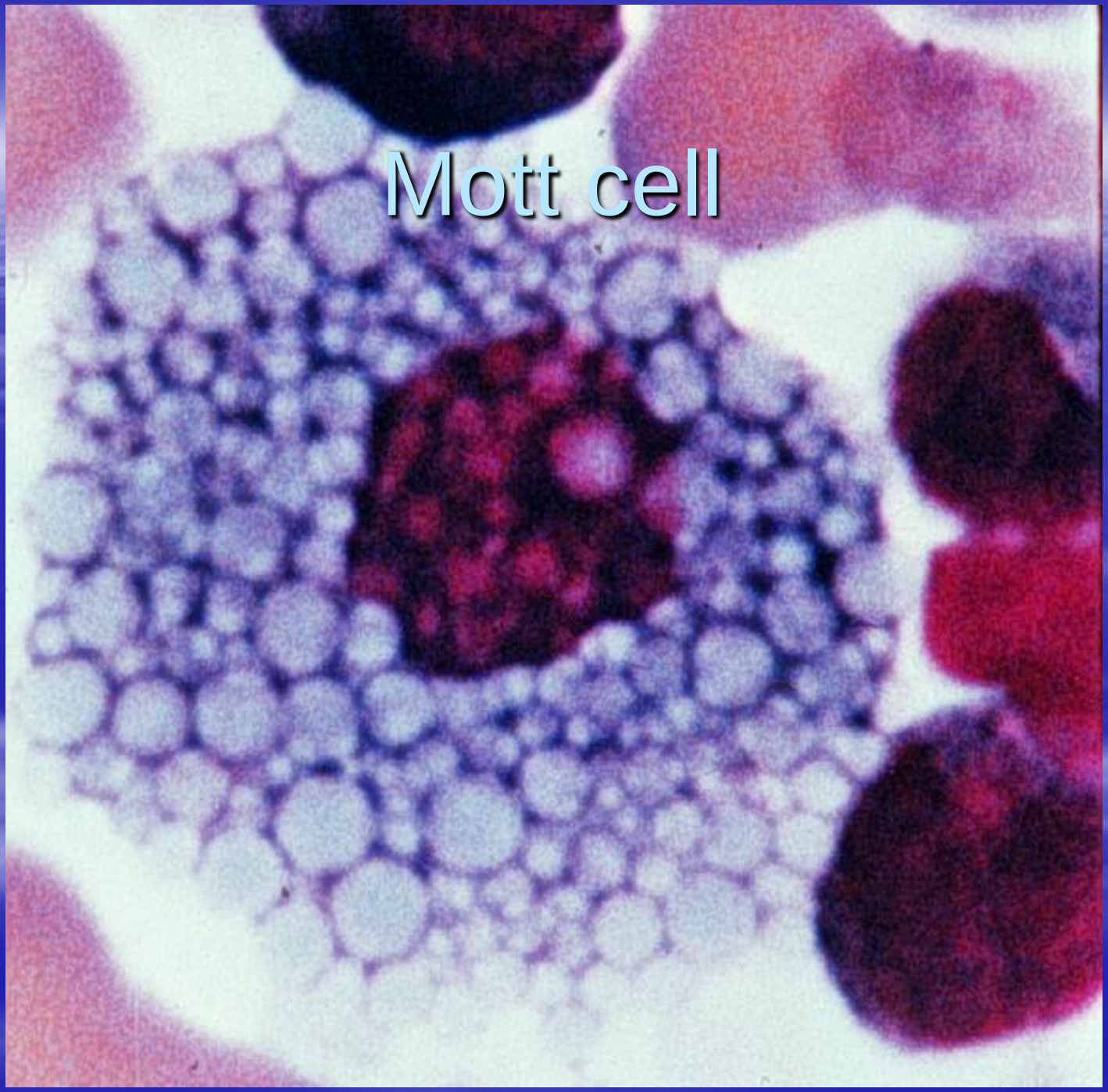
-Deletion of long arm of chromosome 7 associated with increased drug resistance

Clinical features

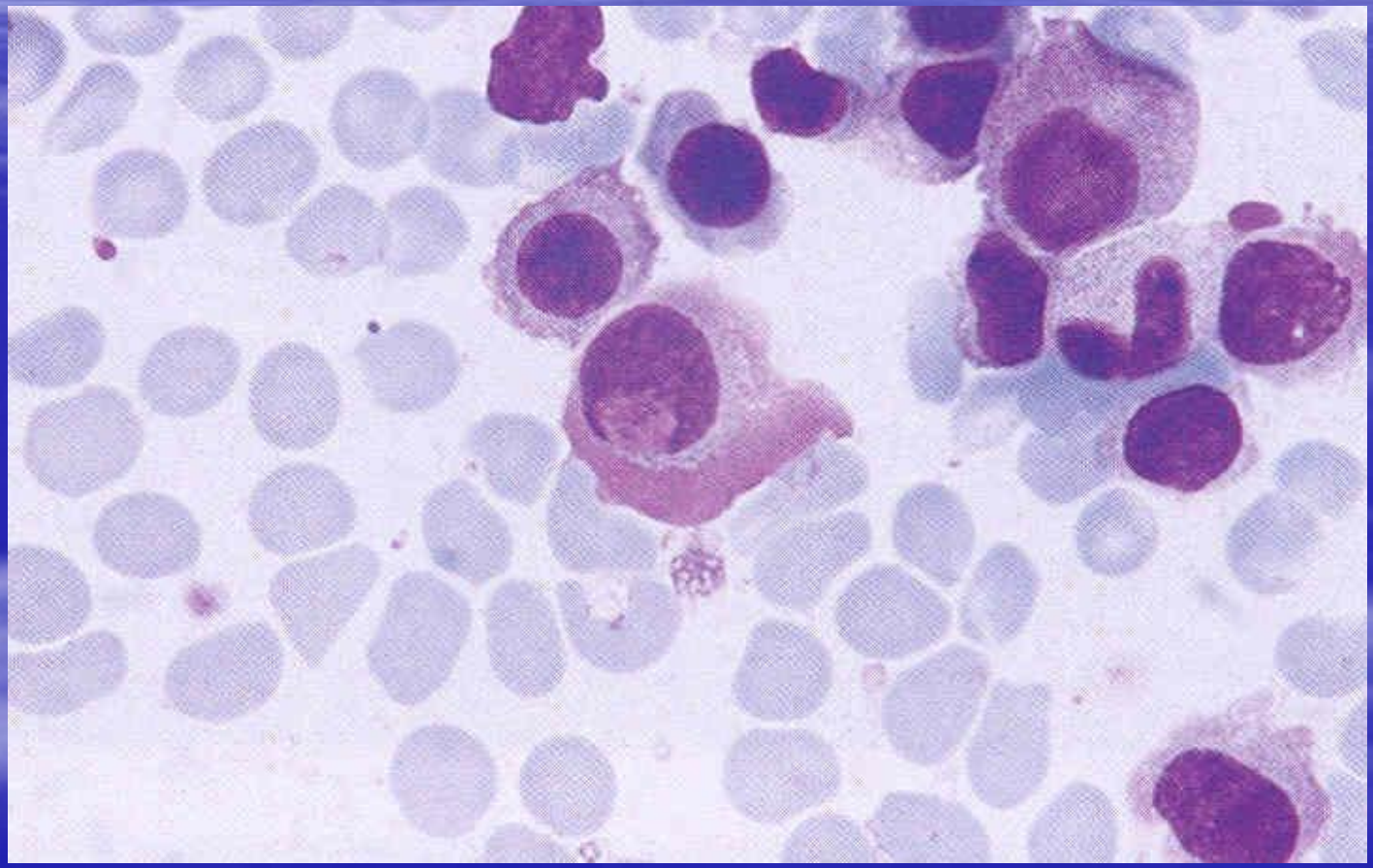
- Bone pain, pathological fractures, hypercalcemia
- Anemia
- Recurrent infections
- Renal failure
- Serum/urine M-component in 99%patients usually accompanied by hypogammaglobulinemia
- IgG-50%, IgA-20%, Light chains-15%, IgD-2% and Biclonal-1%
- Bence Jones proteins in 75% of patients

Russell bodies



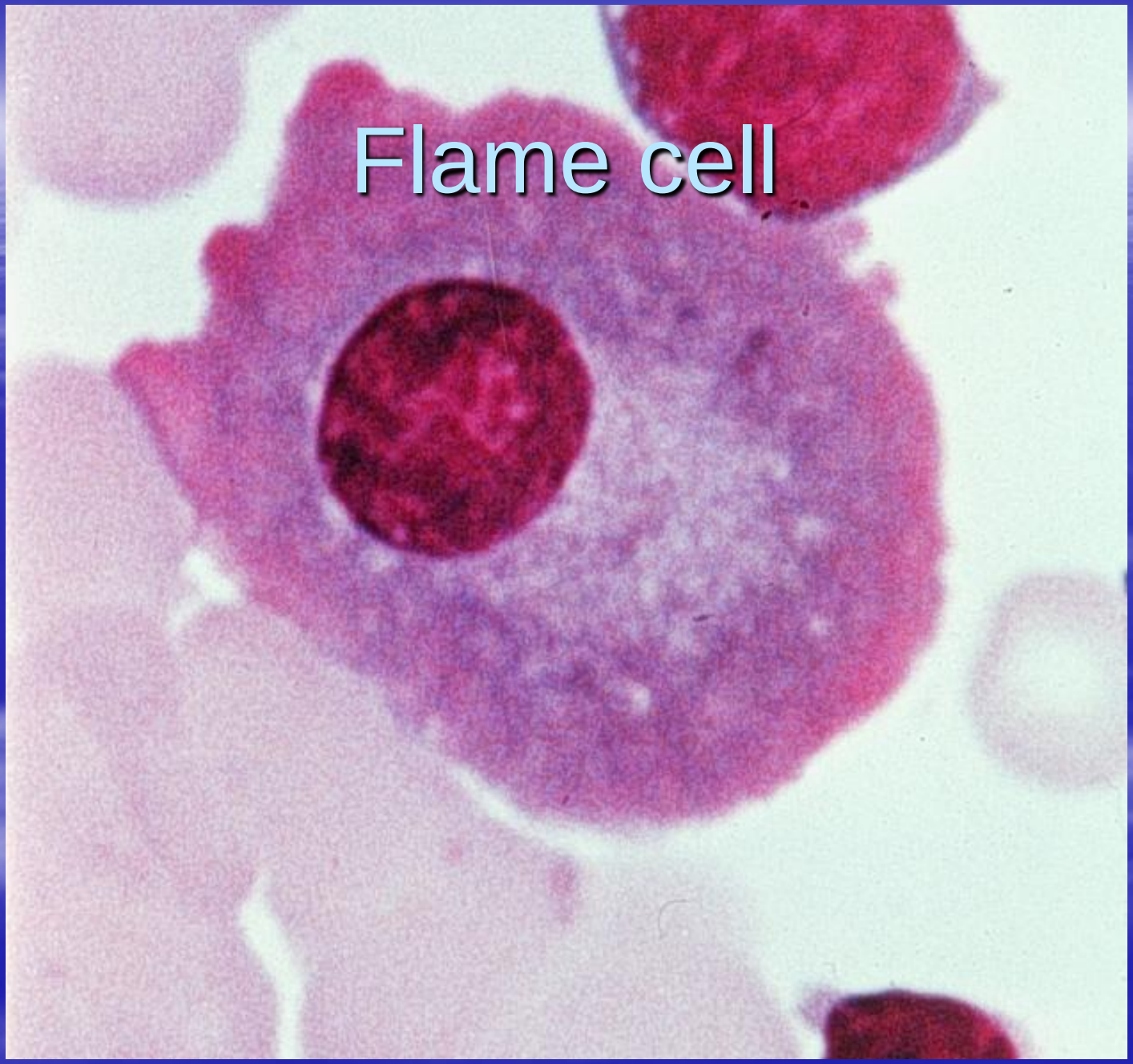

Mott cell

Dutcher bodies

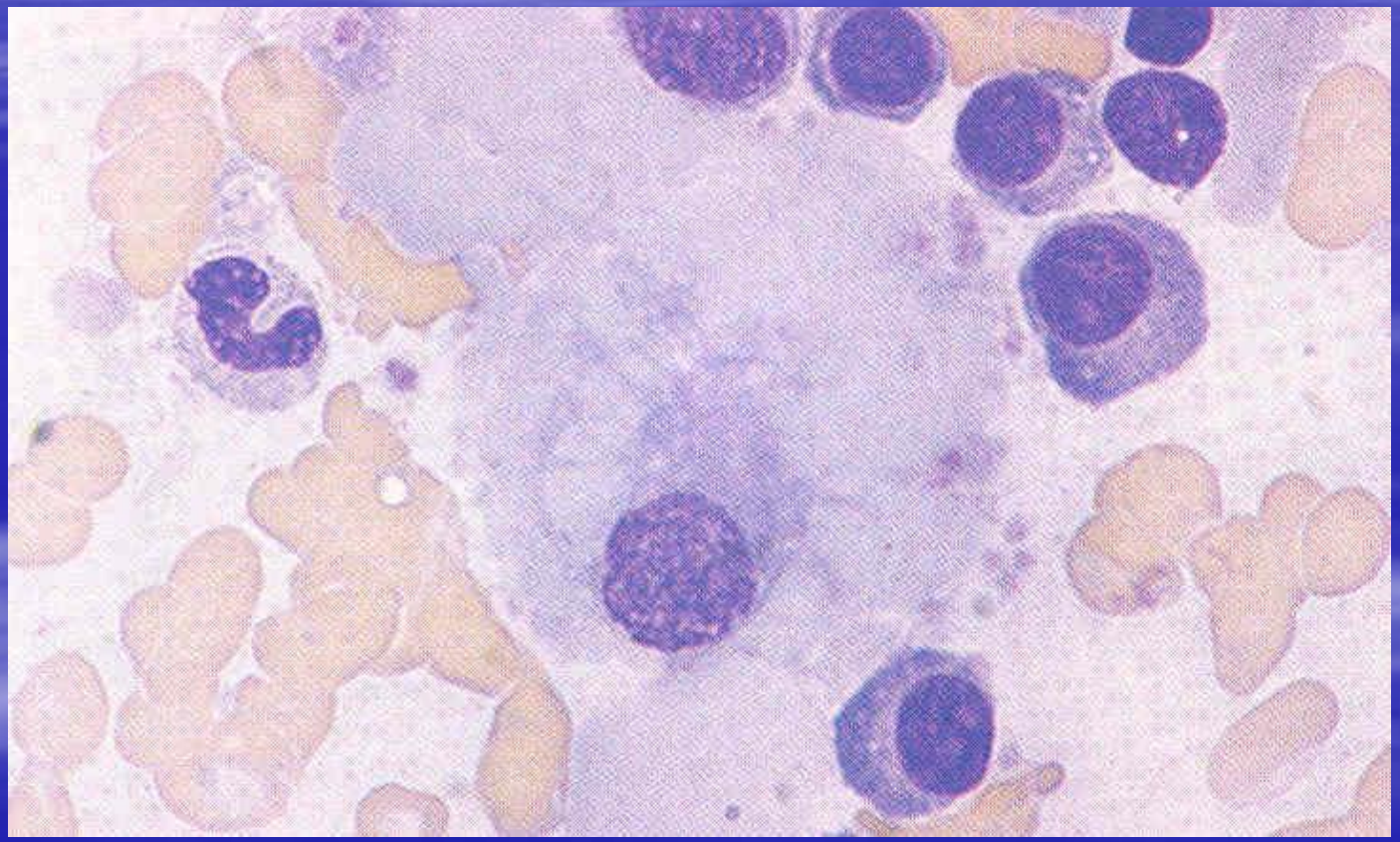


Intranuclear inclusions

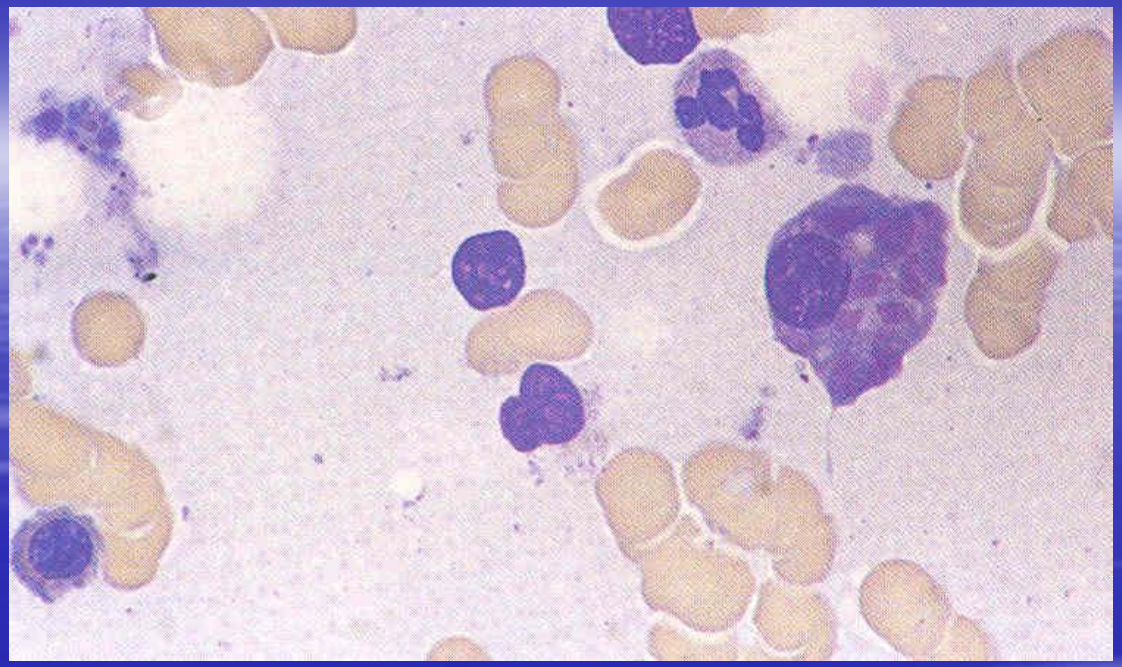
Flame cell



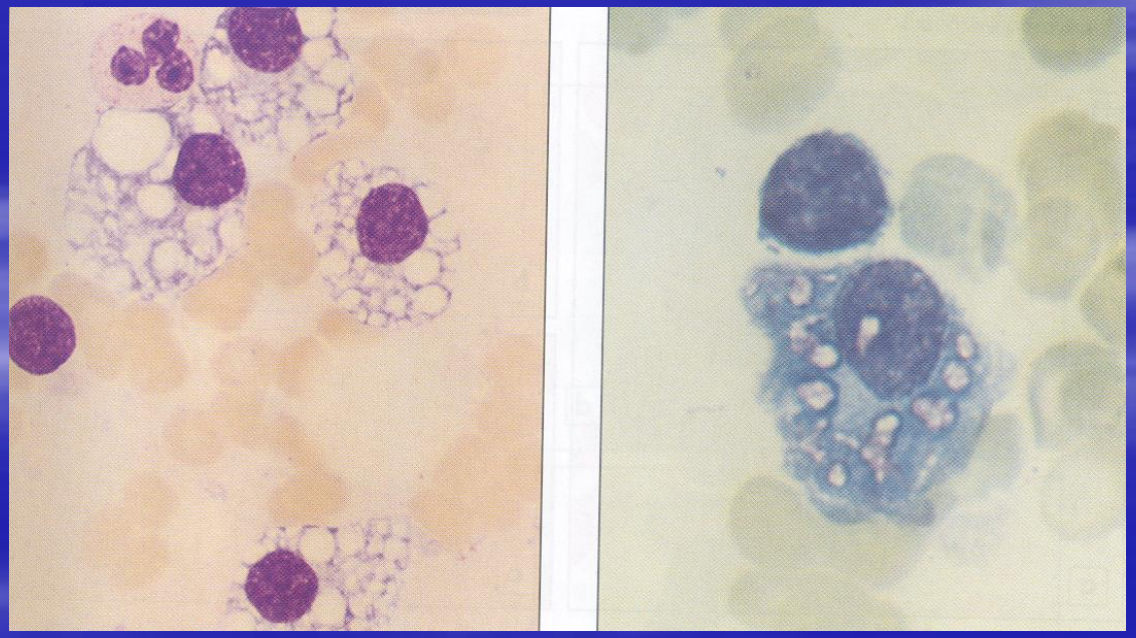
Thesaurocytes



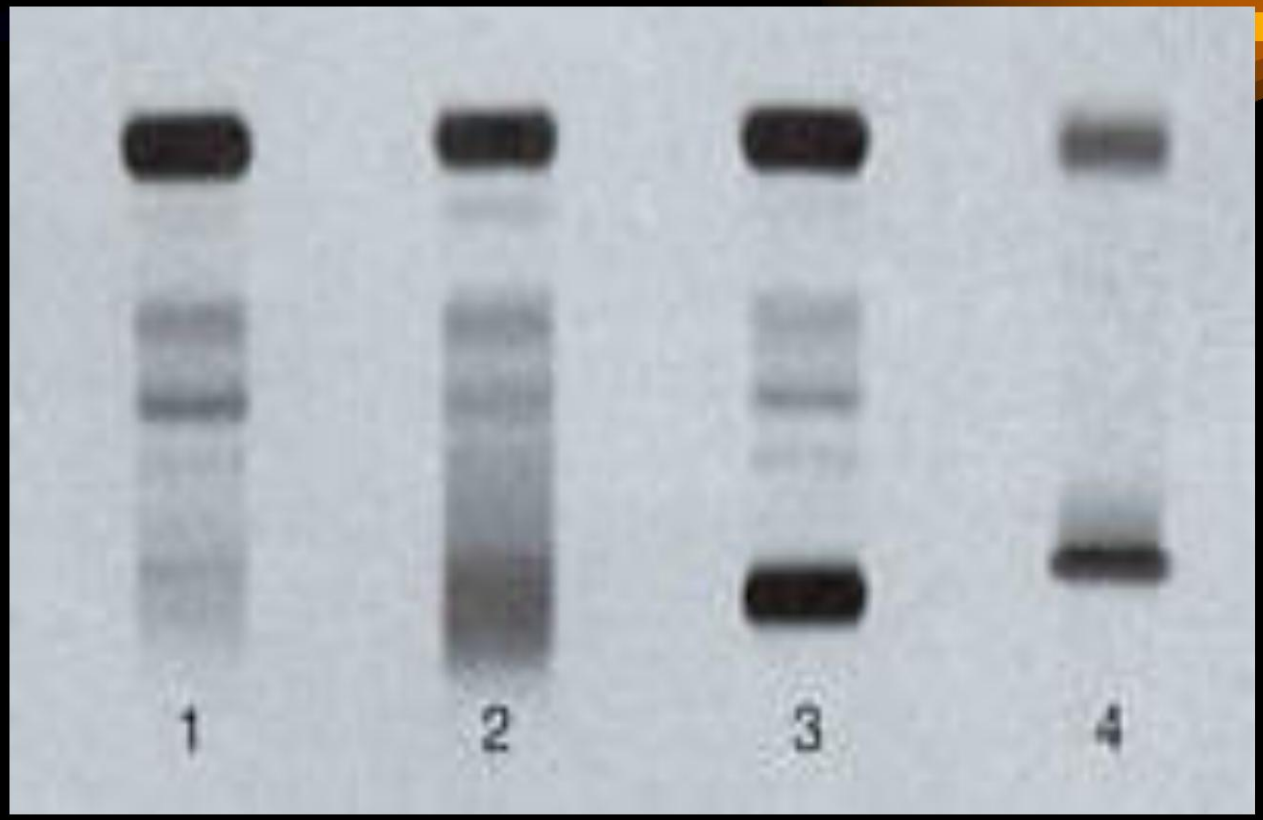
E.R distended with Ig; voluminous ground glass cytoplasm



Ig inclusions



1.Normal Plasma 2.Polyclonal Hyperglobulinemia 3.Monoclonal Spike4.Bence Jones proteins in urine

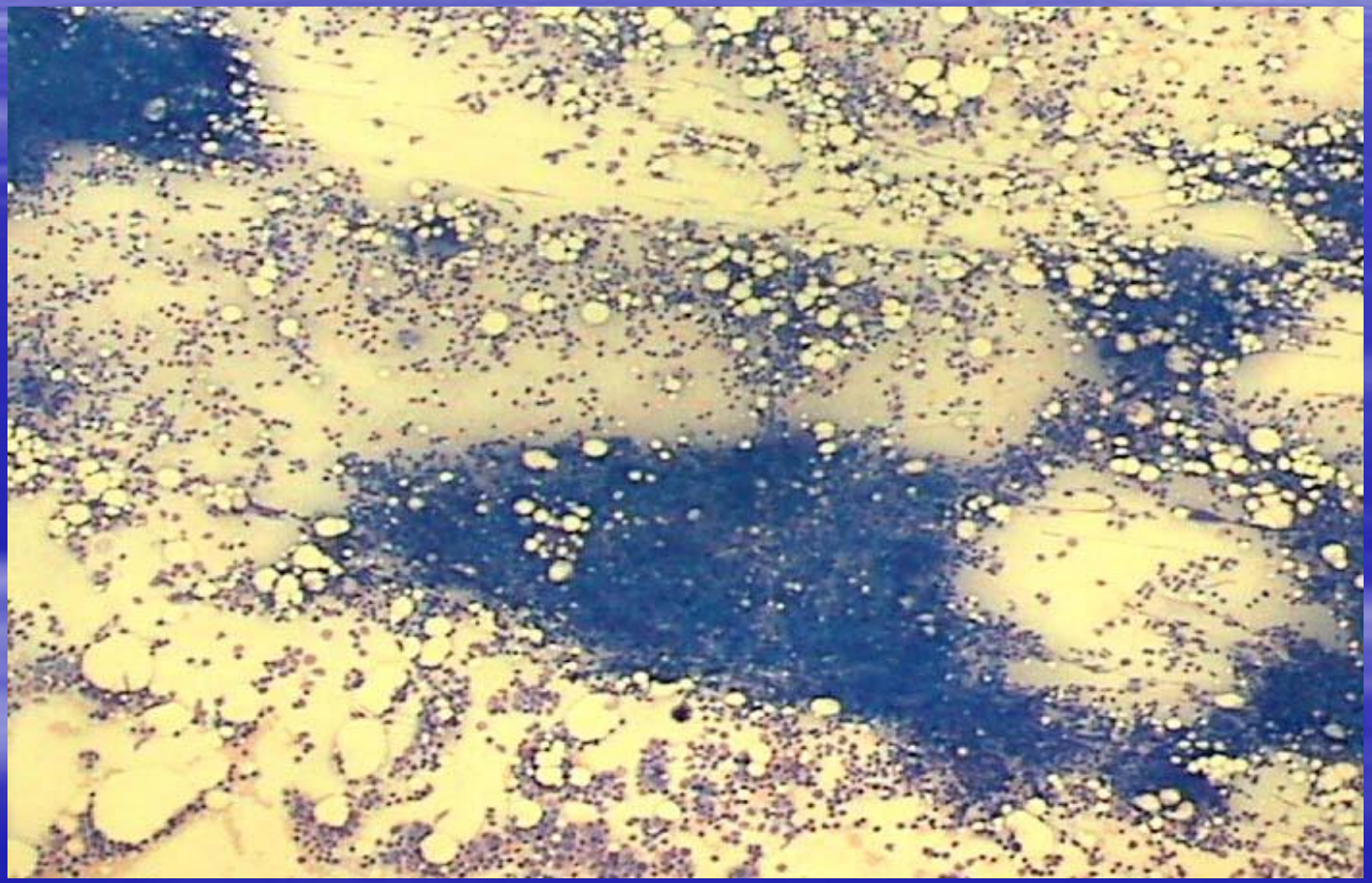


A 57 year old female with H/O MGUS; new neurologic features

CBC and peripheral smear

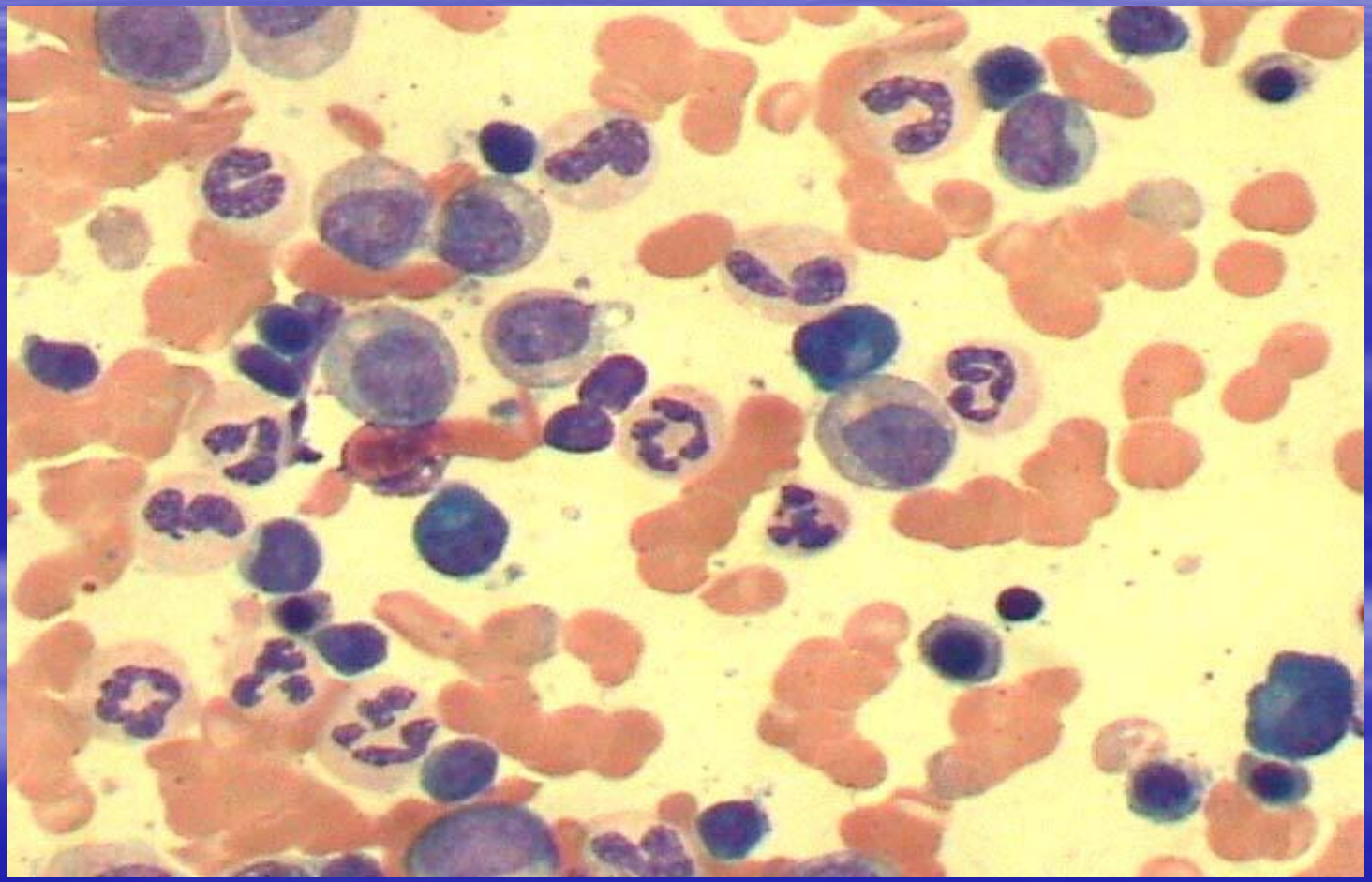
- Mild normocytic normochromic anemia, slight rouleaux formation

Bone marrow



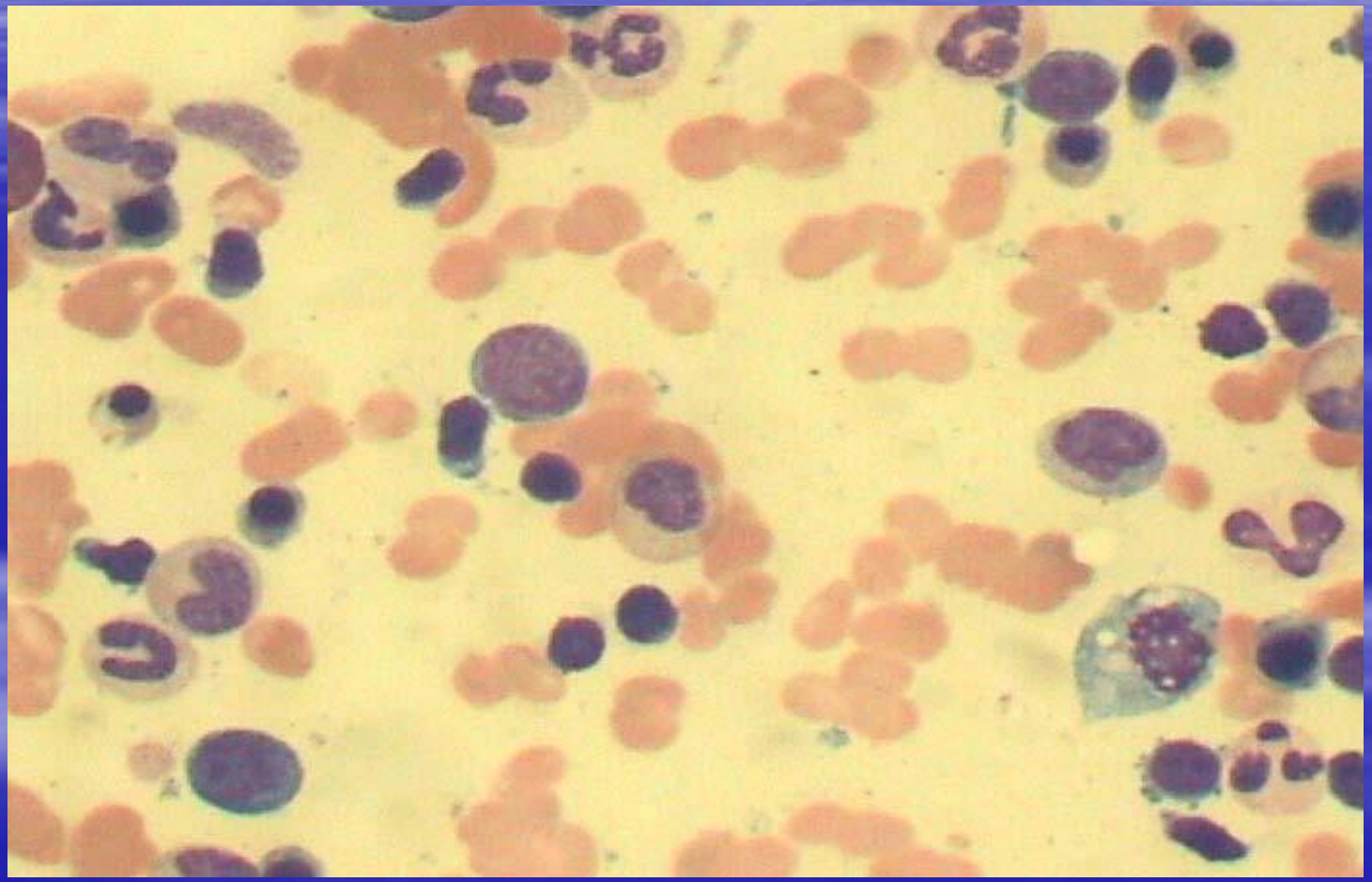
Adequate spicules

Bone marrow



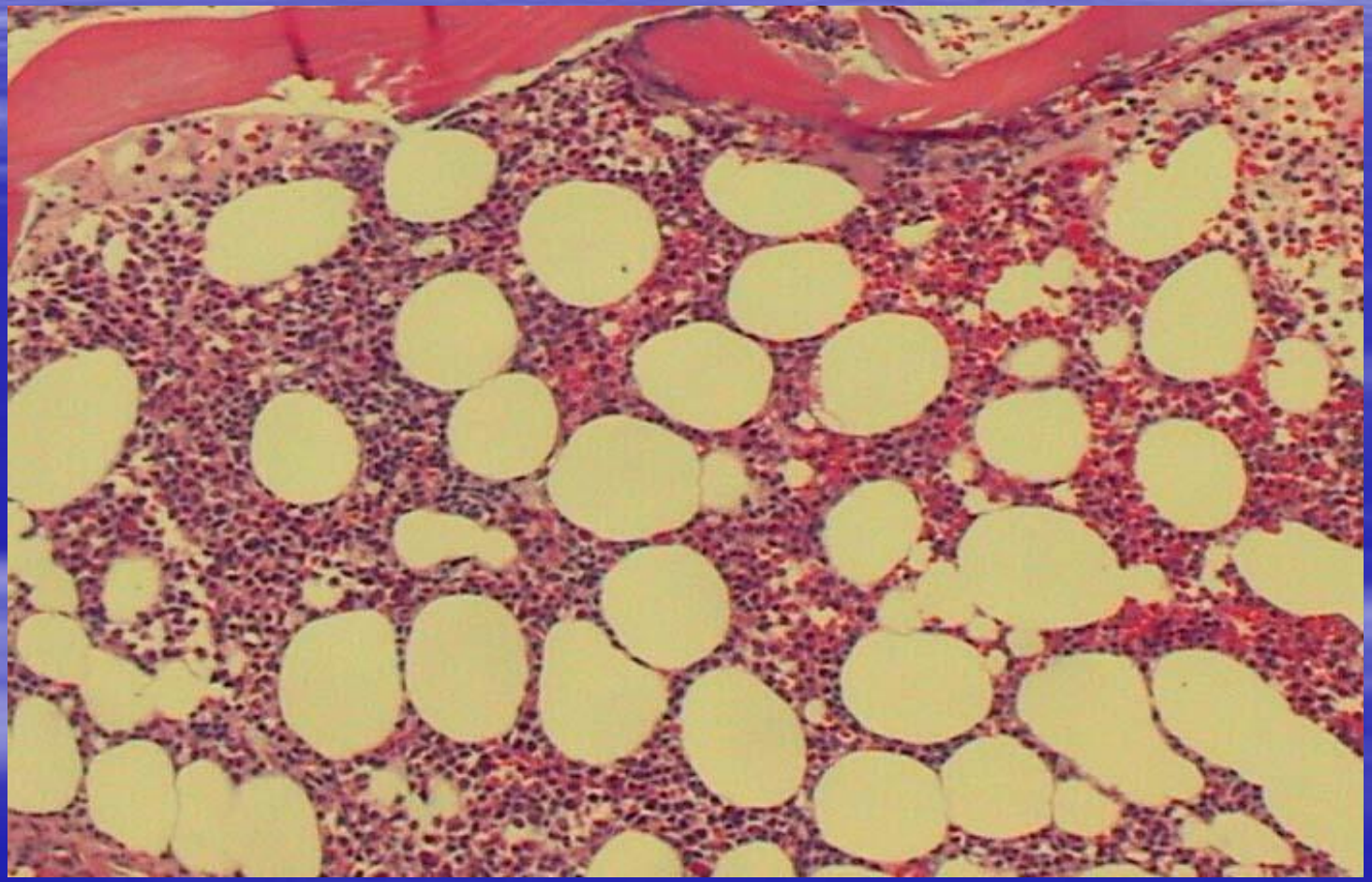
Plasma cells :3%, normal morphology

Bone marrow

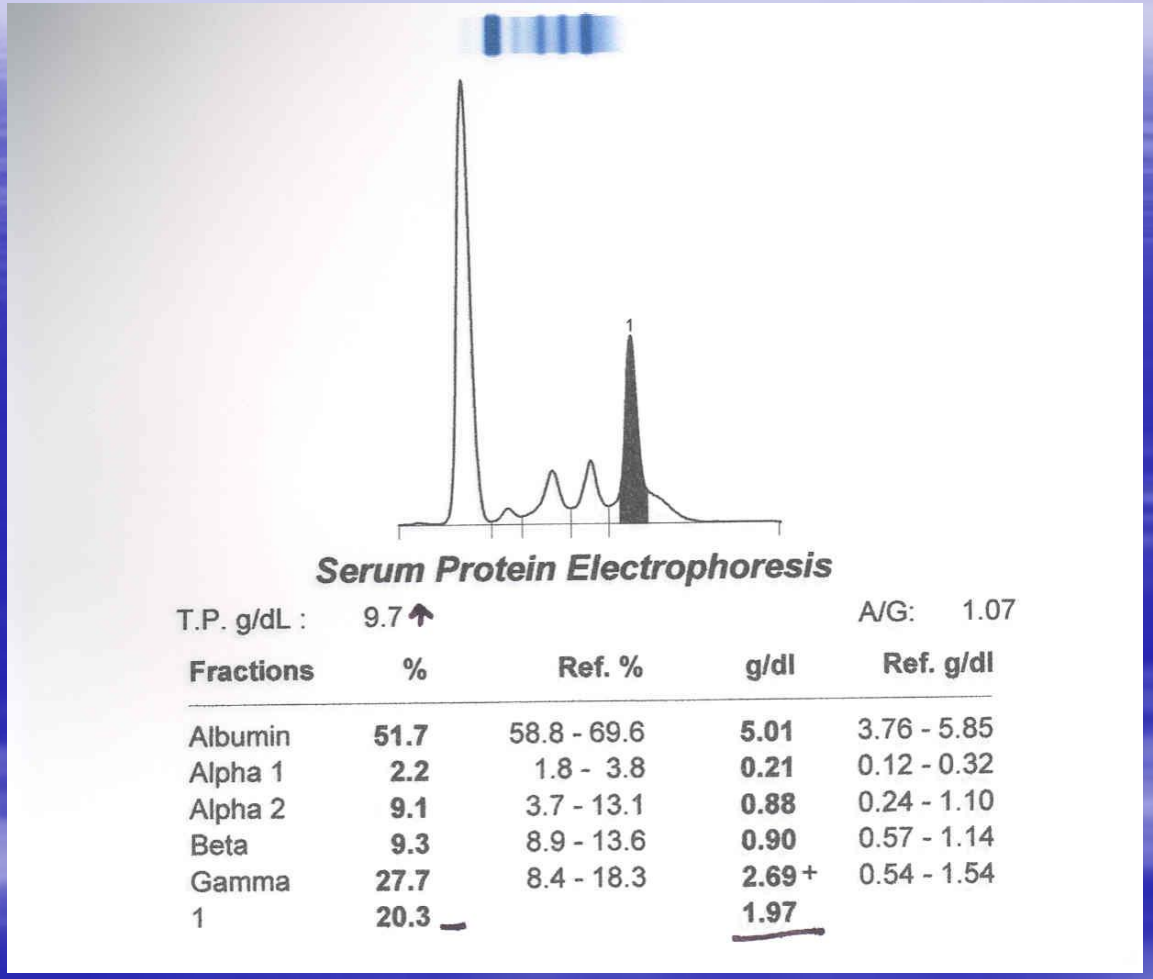


20% lymphocytes

Bone marrow



40% cellularity



Serum Protein Electrophoresis

T.P. g/dL : 9.7 ↑ A/G: 1.07

Fractions	%	Ref. %	g/dl	Ref. g/dl
Albumin	**51.7**	58.8 - 69.6	**5.01**	3.76 - 5.85
Alpha 1	**2.2**	1.8 - 3.8	**0.21**	0.12 - 0.32
Alpha 2	**9.1**	3.7 - 13.1	**0.88**	0.24 - 1.10
Beta	**9.3**	8.9 - 13.6	**0.90**	0.57 - 1.14
Gamma	**27.7**	8.4 - 18.3	**2.69** +	0.54 - 1.54
1	**20.3**		**1.97**	

- Immunofixation: not done
- 1998: IgM kappa

MGUS

- Monoclonal gammopathy of undetermined significance
- Presence of a monoclonal protein without evidence of MM, macroglobulinemia, amyloidosis or lymphoproliferative disorder
- M-protein in serum< 30 g/l
- Bone marrow clonal plasma cells< 10% and low level of plasma cell infiltration on Bx
- No related organ or tissue impairment (ROTI)

- Progression to multiple myeloma documented
- 12%, 25% and 30% probability of progression at 10, 20 and 25 yrs respectively

Risk factors for progression

-IgM and IgA M-proteins

-Concentration of serum M-protein

-Plasma cell morphology

Life-long follow up required

Non-secretory Myeloma

Rare variant (1%)

No monoclonal protein in serum or urine

M-protein identified in plasma cells by immunoperoxidase or IF

Renal insufficiency less common

Lower level of plasmacytosis

Less depression of normal Ig

Smoldering myeloma

- M-protein in serum > 30 g/l
- Bone marrow plasma cells 10-30%
- No ROTI (asymptomatic)
- Not treated unless progression occurs

Indolent Myeloma

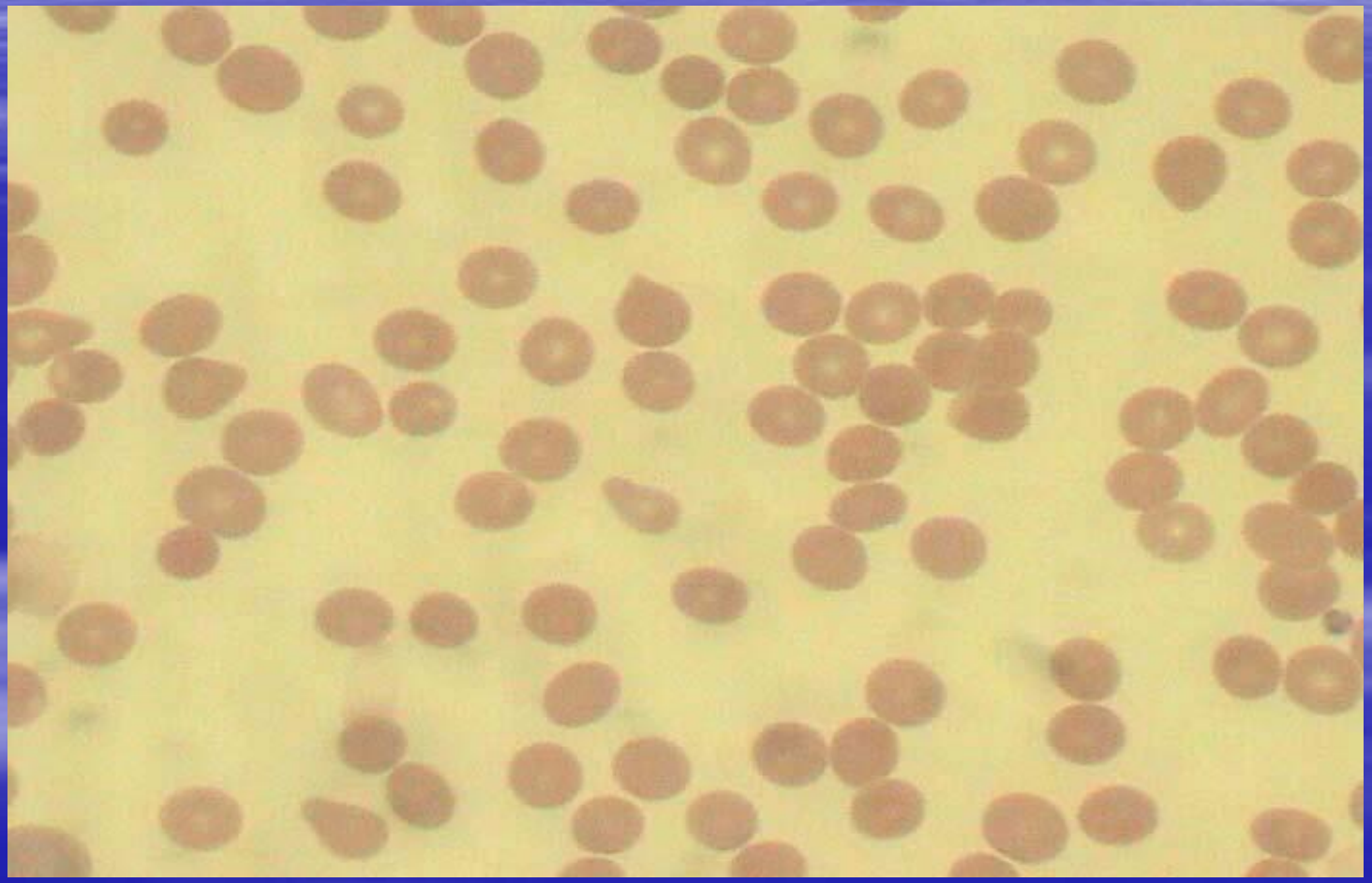
- Serum M-component at intermediate levels
- Up to 3 lytic bone lesions
- Normal Hb, Ca and creatinine
- No infections

Plasma cell leukemia

- Rare (2%)
- Peripheral blood plasma cells > $2x10^9$ or 20% of white cells
- Primary or secondary
- More common in light chain, IgE and IgD
- Osteolytic lesions less
- More frequent organomegaly, lymphadenopathy and renal failure
- Aggressive disease

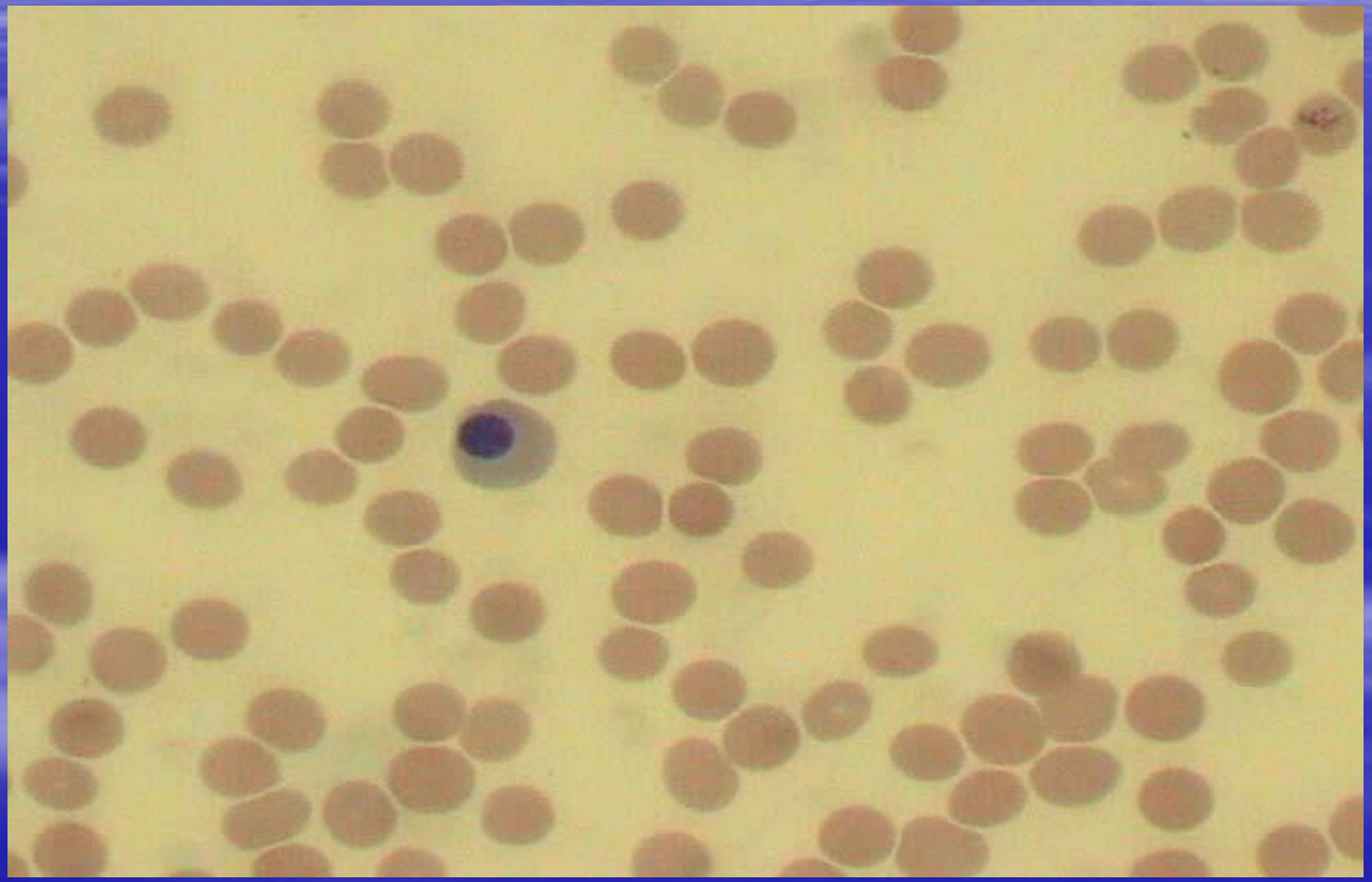
A 46 y.o female with pancytopenia

Peripheral blood



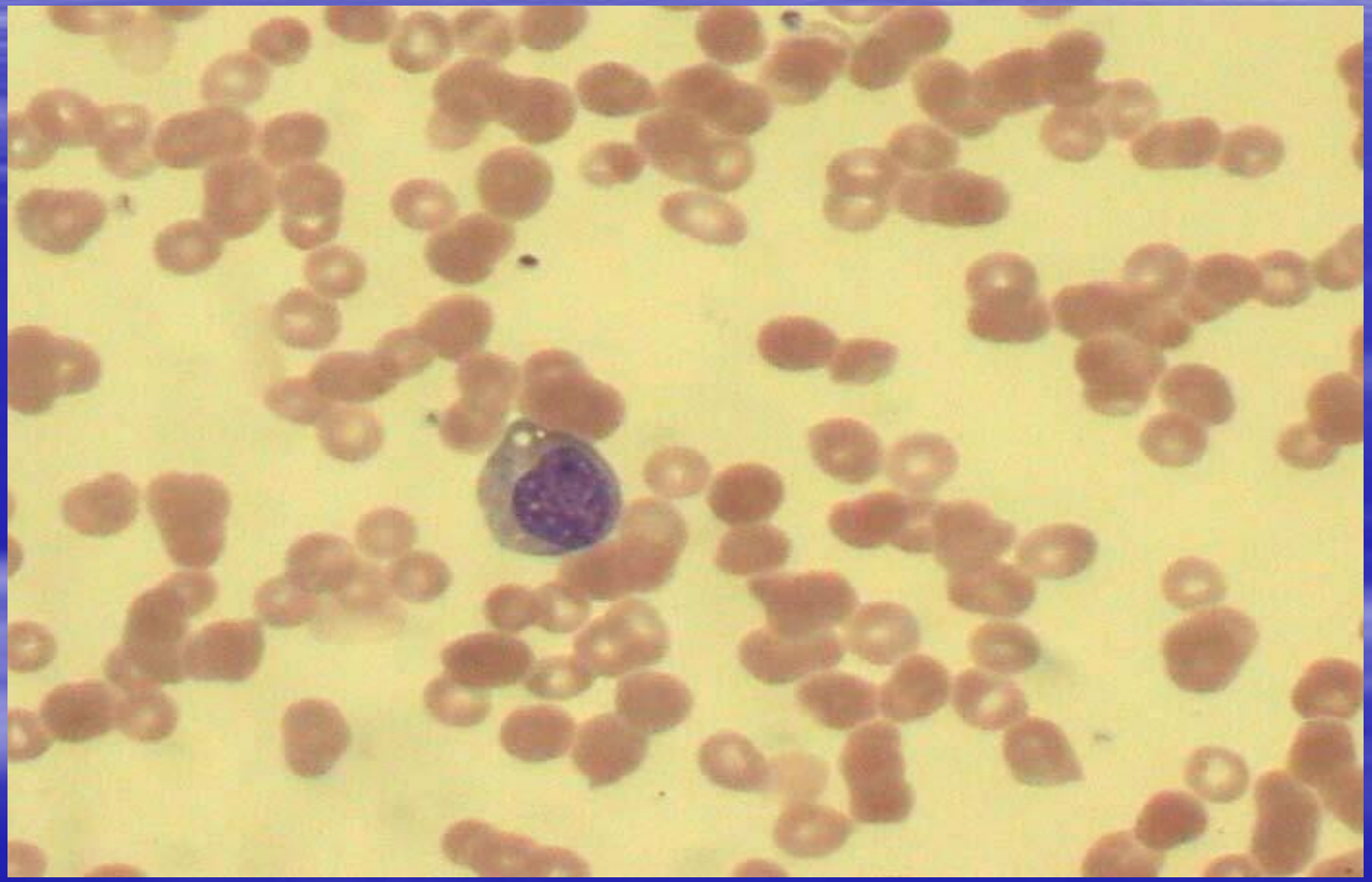
Normocytic normochromic anemia with anisocytosis; few dacrocytes

Peripheral blood



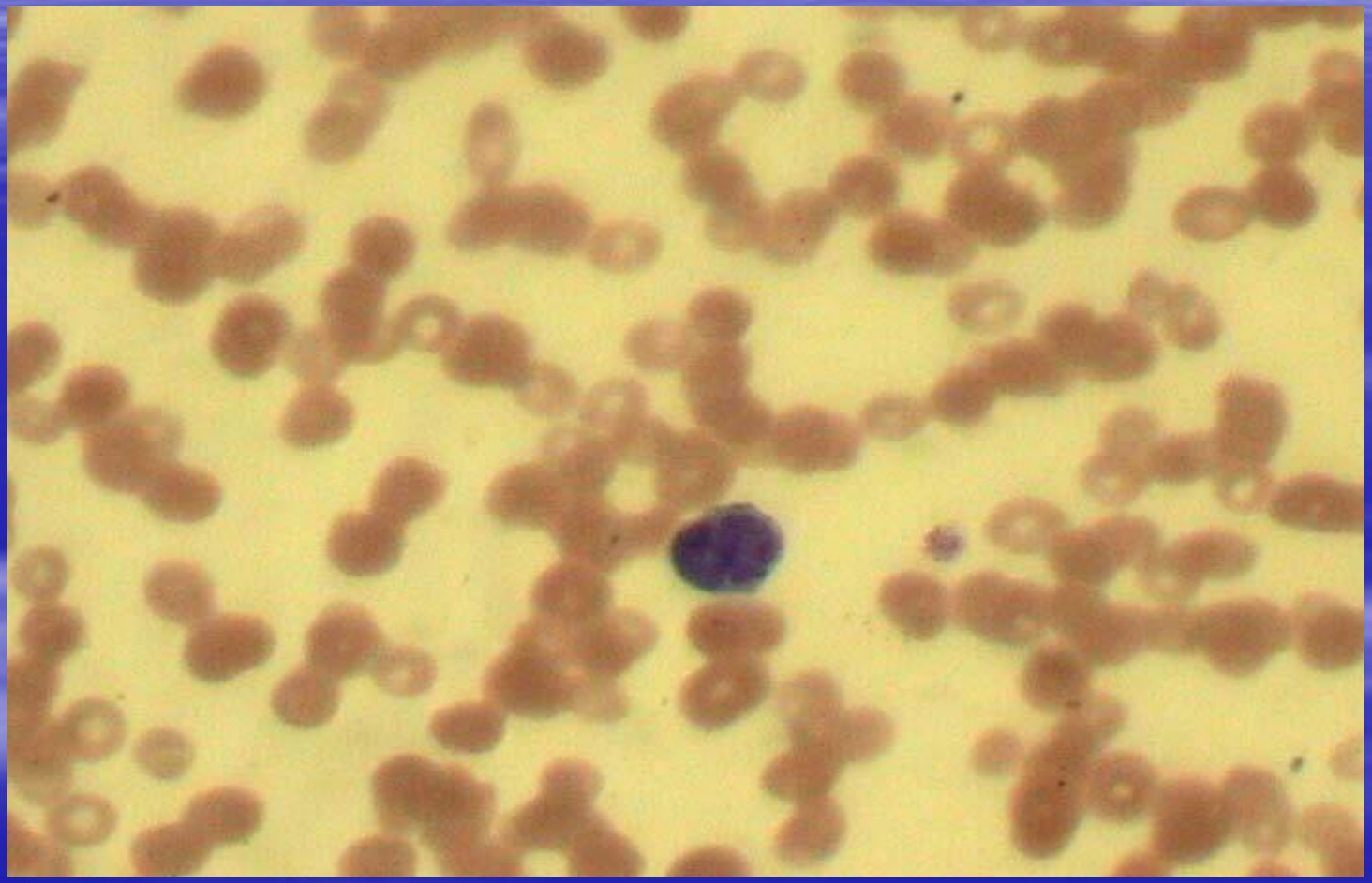
Nucleated red cells

Peripheral blood



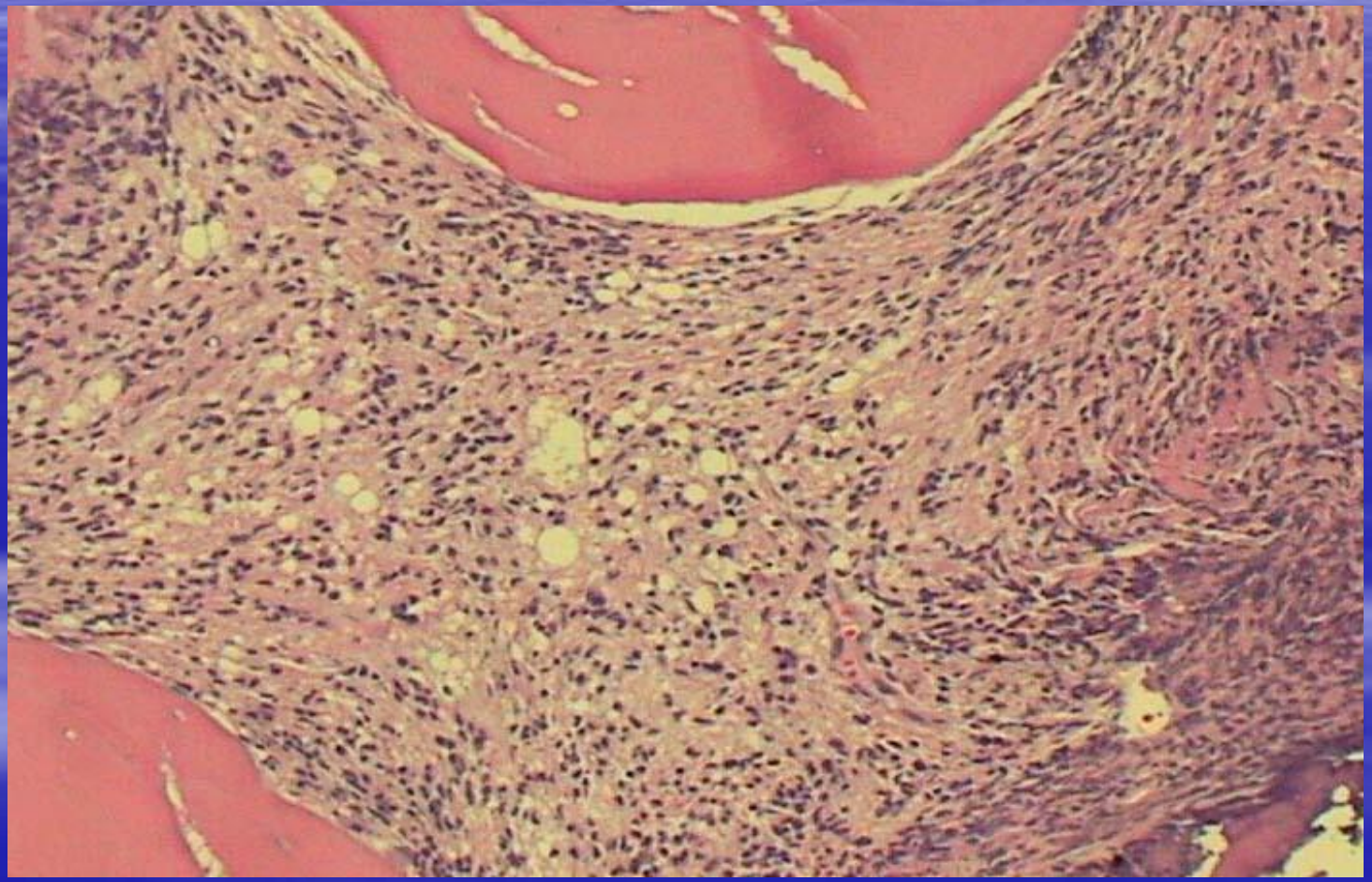
Rare myelocytes; monocytes: 0%

Peripheral blood

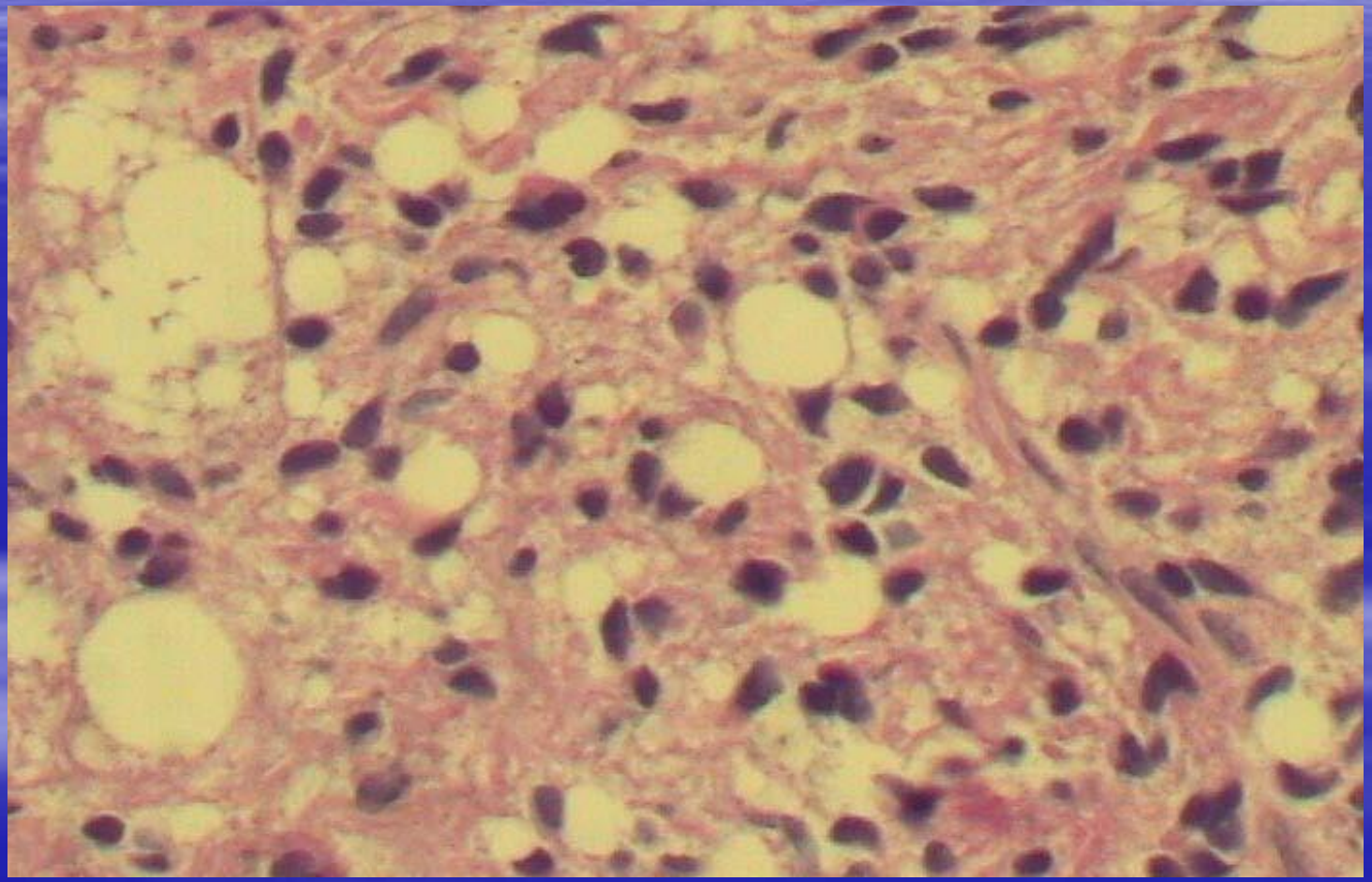


Rare atypical lymphocytes

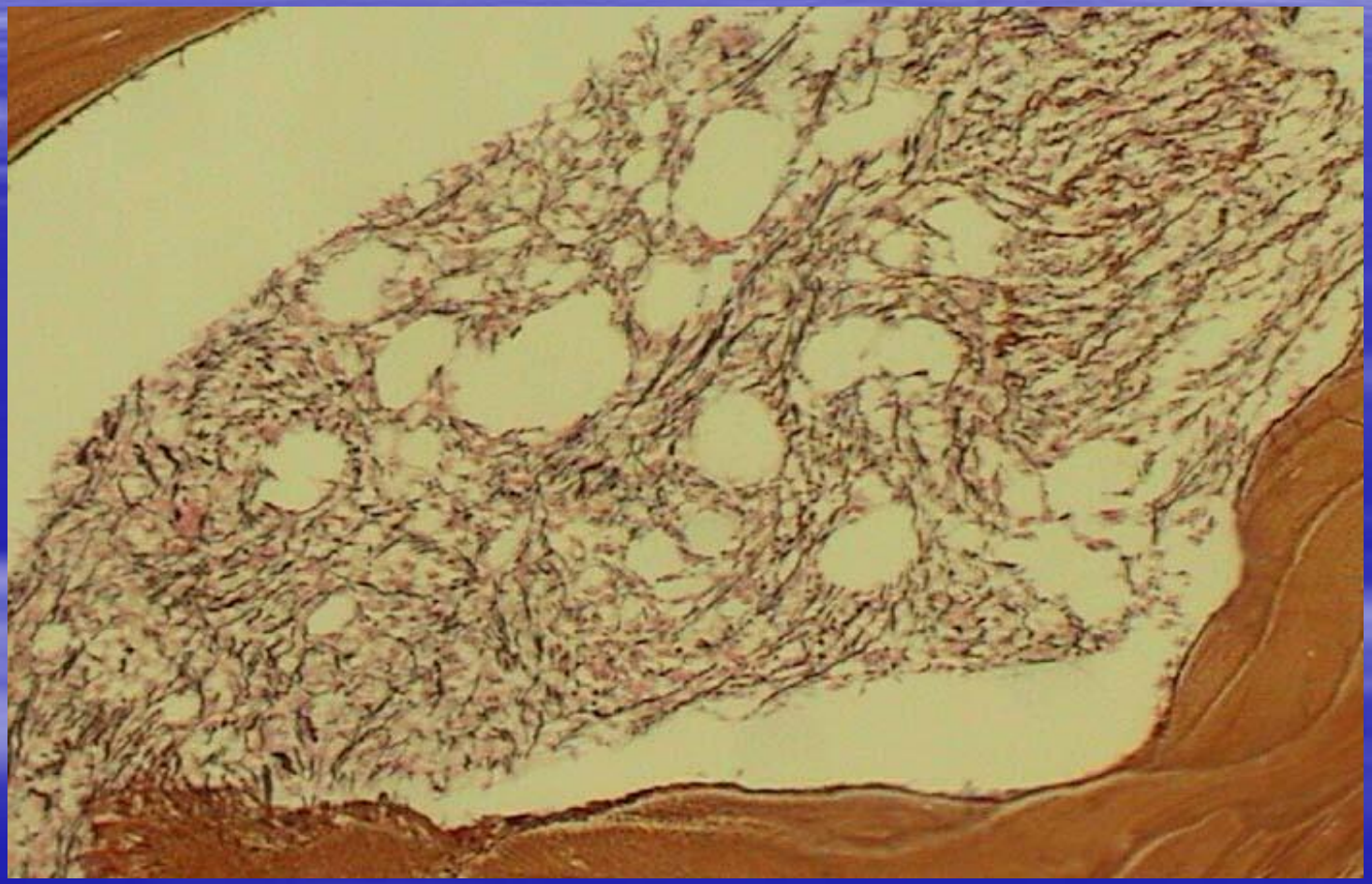
Bone marrow



Bone marrow

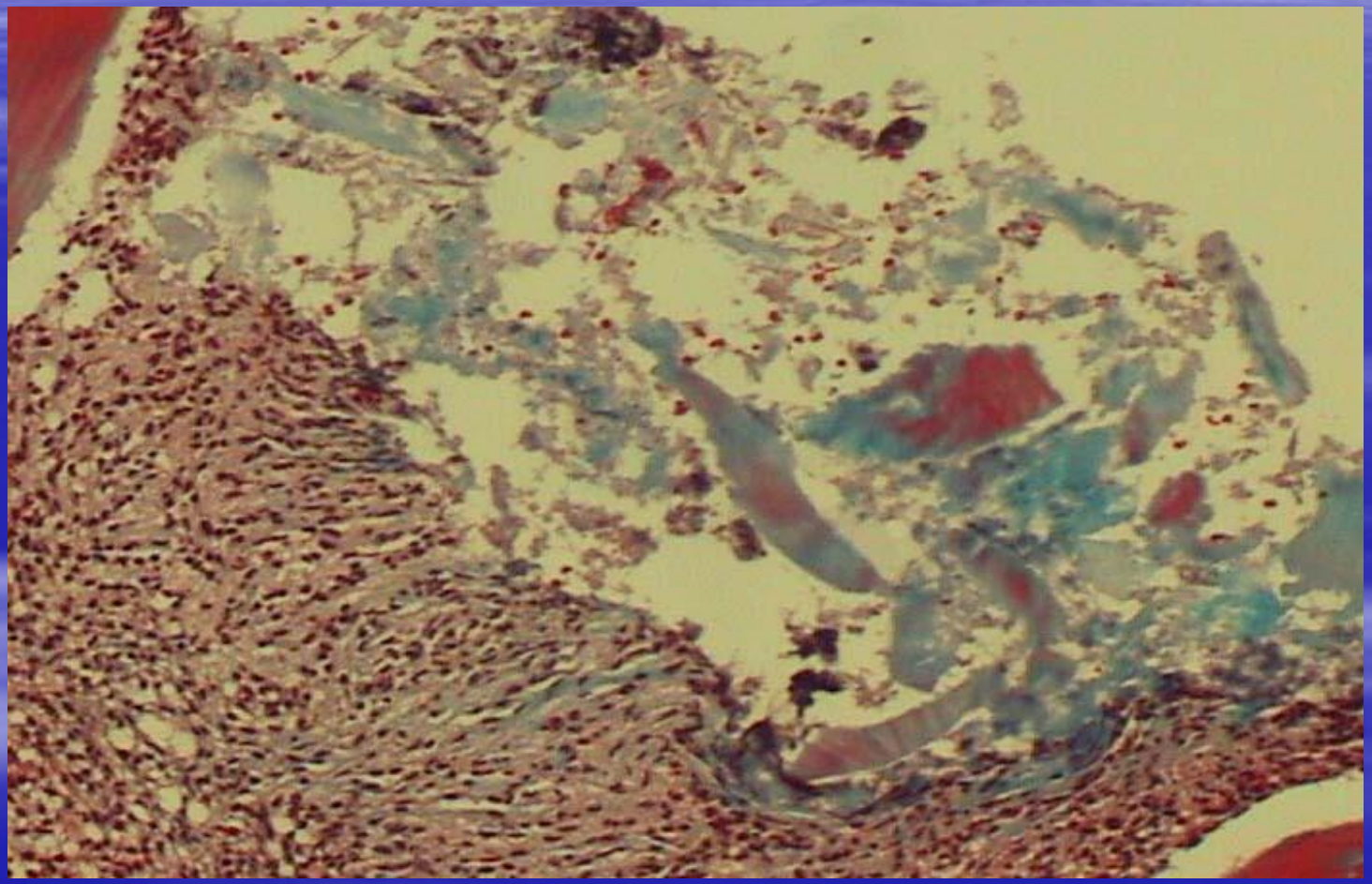


Bone marrow



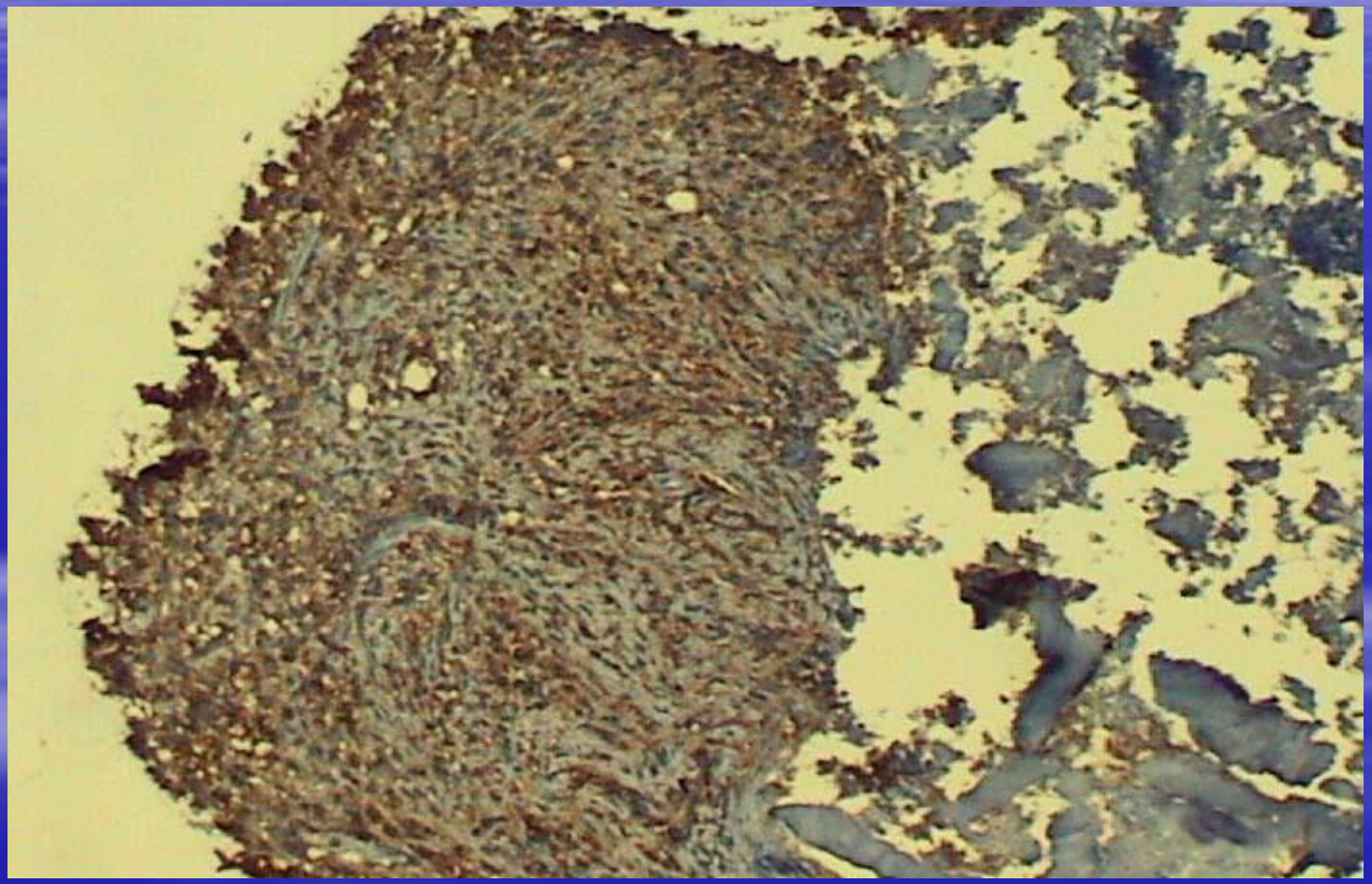
Marked increase in reticulin fibrosis

Bone marrow



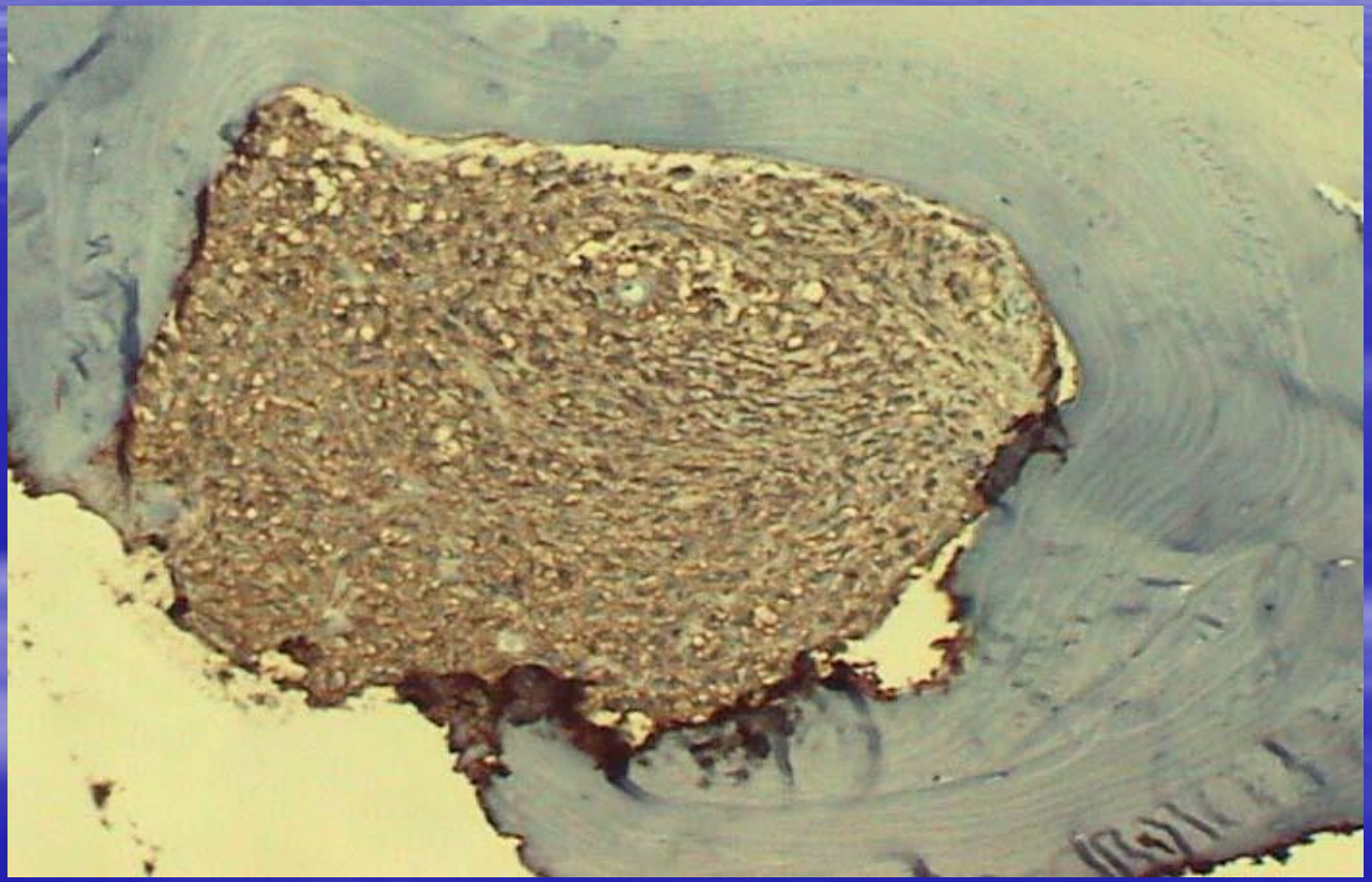
Trichrome stain with focal positivity

Bone marrow



CD 45

Bone marrow



CD 20

Flow on peripheral blood

- CD 19, 20: 6% each
- Negative for hairy cell leukemia markers

Immunostains on biopsy

- TRAP: negative
- DAB44: positive

- Subsequent bone marrow procedure yielded adequate aspirate for flow cytometry study
- The B cell population is positive for: CD11c, CD22, CD25, CD103

Hairy cell leukemia

- Pancytopenia and splenomegaly without lymphadenopathy
- Neutropenia and monocytopenia, particularly severe
- Dry tap due to reticulin fibrosis

Hairy cell

- Round eccentric nucleus, without nucleoli
- Moderate pale blue-gray cytoplasm; sometimes rod shaped inclusions (EM: ribosomal-lamella complex)
- Cytoplasmic outline: fine hair like villi or broader ruffles

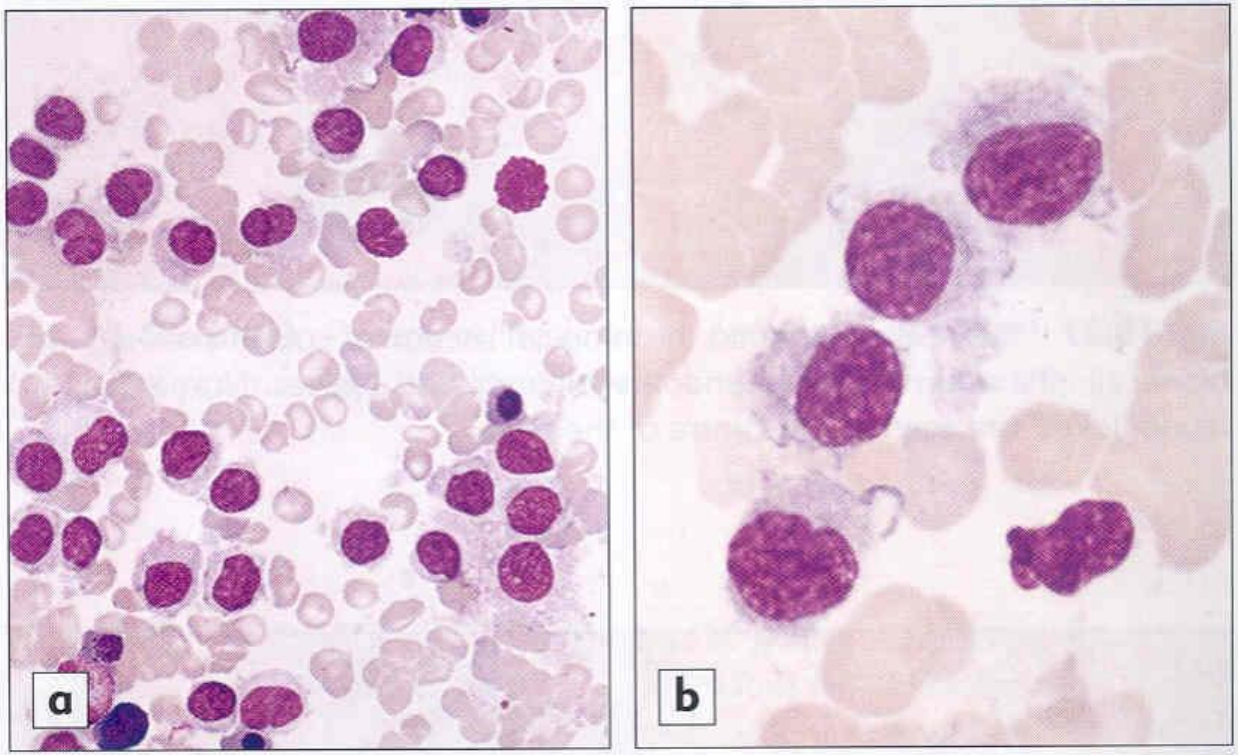
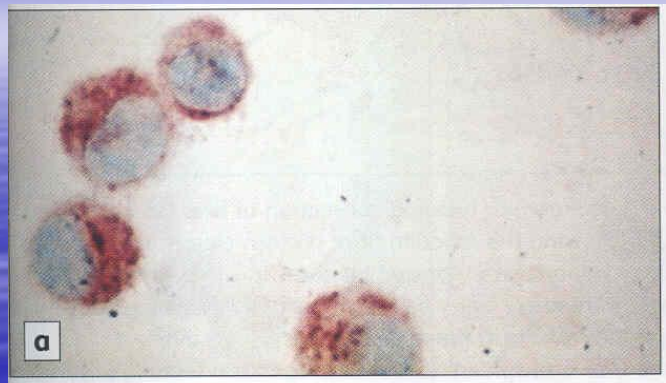


Fig. 10.33a and b Hairy cell leukaemia: (a) bone marrow aspirate showing a predominance of hairy cells in the cell trail; (b) splenic imprints showing typical nuclear and cytoplasmic features of the abnormal hairy cells.



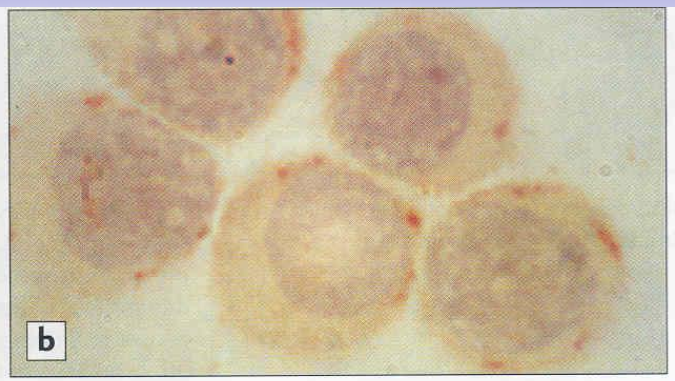


Fig. 10.34a and b Hairy cell leukaemia: typical cytochemical findings of hairy cells include (a) a strongly positive reaction to tartaric acid-resistant acid phosphatase (TRAP) and (b) a fine granular positivity with crescentic accumulation at one side of the nucleus following alpha-naphthyl butyrate esterase staining.

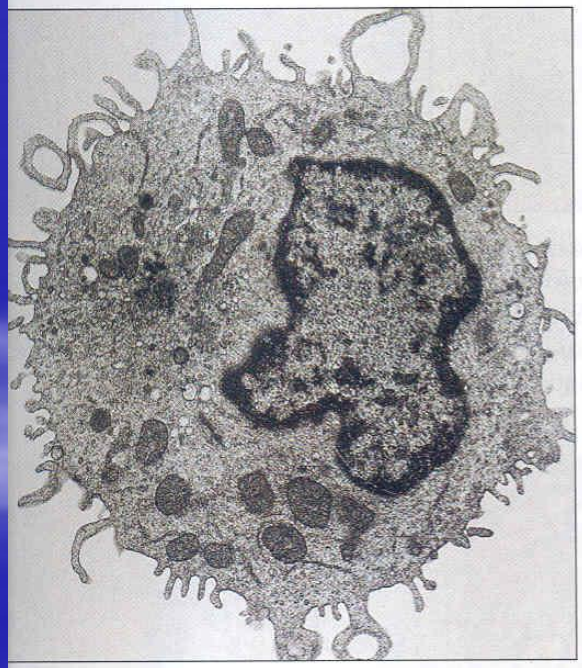


Fig. 10.32 Hairy cell leukaemia: hairy cell from the peripheral blood. Typical features are the abundant cytoplasm, low N/C ratio and cytoplasmic projections or villi that give the cell a 'hairy' appearance. (× 9200; courtesy of Mrs D Robinson and Prof. D Catovsky.)

BM and Hairy cell leukemia

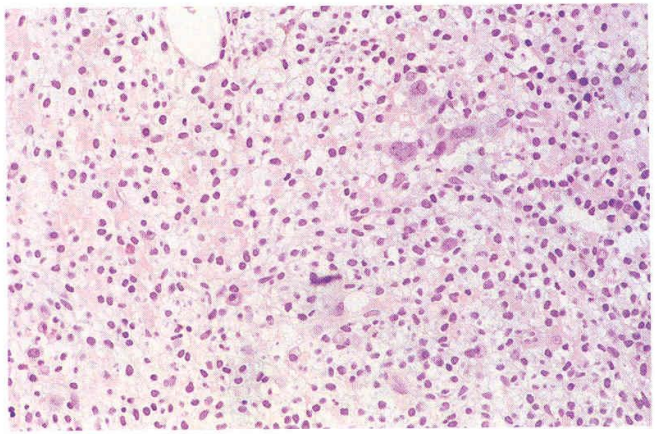


Fig. 6.24 BM trephine biopsy section, hairy cell leukaemia, showing diffuse infiltration by 'hairy cells'; note the characteristic 'spaced' arrangement of the cells. Plastic-embedded, H&E ×188.

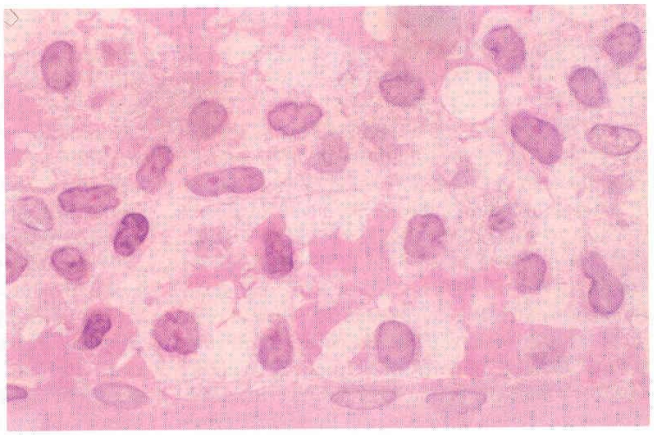


Fig. 6.25 BM trephine biopsy section, hairy cell leukaemia, showing bland nuclei of various shapes surrounded by shrunken cytoplasm with irregular margins; clear spaces surround the cells. Plastic-embedded, H&E ×970.

Bone marrow

- Angiomatous vascular lakes
- Increased mast cells

Membrane markers in chronic B-cell leukaemias

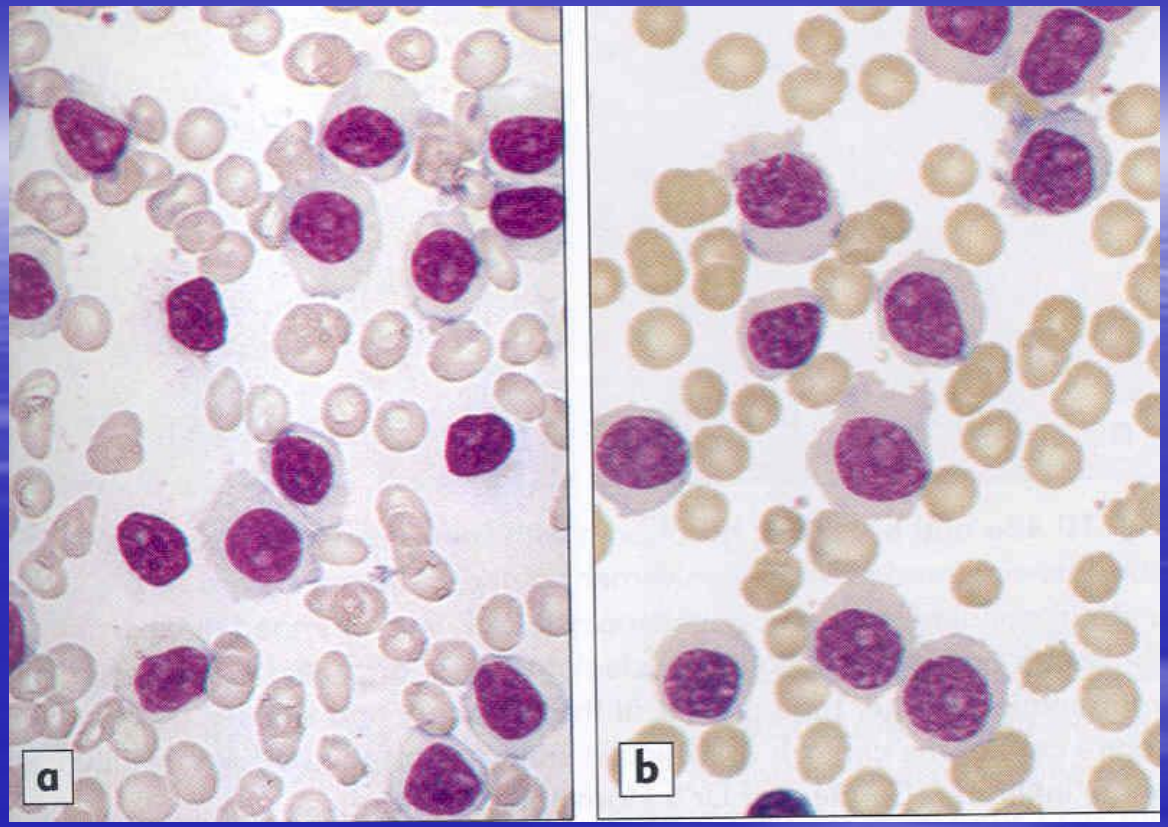
	CLL	PLL	HCL	HCL-V	SLVL	FL	MZL	PCL
SIg	+/–	++	++	++	++	+	+	– (cyt Ig$^+$)
CD5	+	–	–	–	–	–	+	–
CD19/CD20/37	+	+	+	+	+	+	+	–
FMC7/CD22	–/+	+	+	+	+	+	+	–
CD23	+	–/+	++	++	–/+	–/+	–/+	–
CD11c/25	–	–	++	+	+	?	?	–
CD25	–	–	++	–	–/+	–	–	–
CD38	–	–	–/+	–/+	–	–/+	–	++
CD103	–	–	+	+/–	–	–	–	–
HC2/CD103	–	–	+	–	–	–	–	–
HLA-DR	+	+	+	+	+	+	+	–
CD79b	–	++	–/+	?	++	++	++	?

SIg, surface immunoglobulin
CLL, B-cell chronic lymphocytic leukaemia
PLL, prolymphocytic leukaemia
HCL-V, hairy cell leukaemia variant
SLVL, splenic lymphoma with villous lymphocytes
FL, follicular lymphoma
MZL, mantle zone lymphoma
PCL, plasma cell leukaemia

Fig. 10.21 Membrane markers in chronic B-cell leukaemias.

Immnuophenotype

- B-cell markers
- CD11c, CD25 (IL-2 R), CD103 (an alpha subunit of the alpha beta integrin molecule)
- Negative for CD5, CD23, CD10

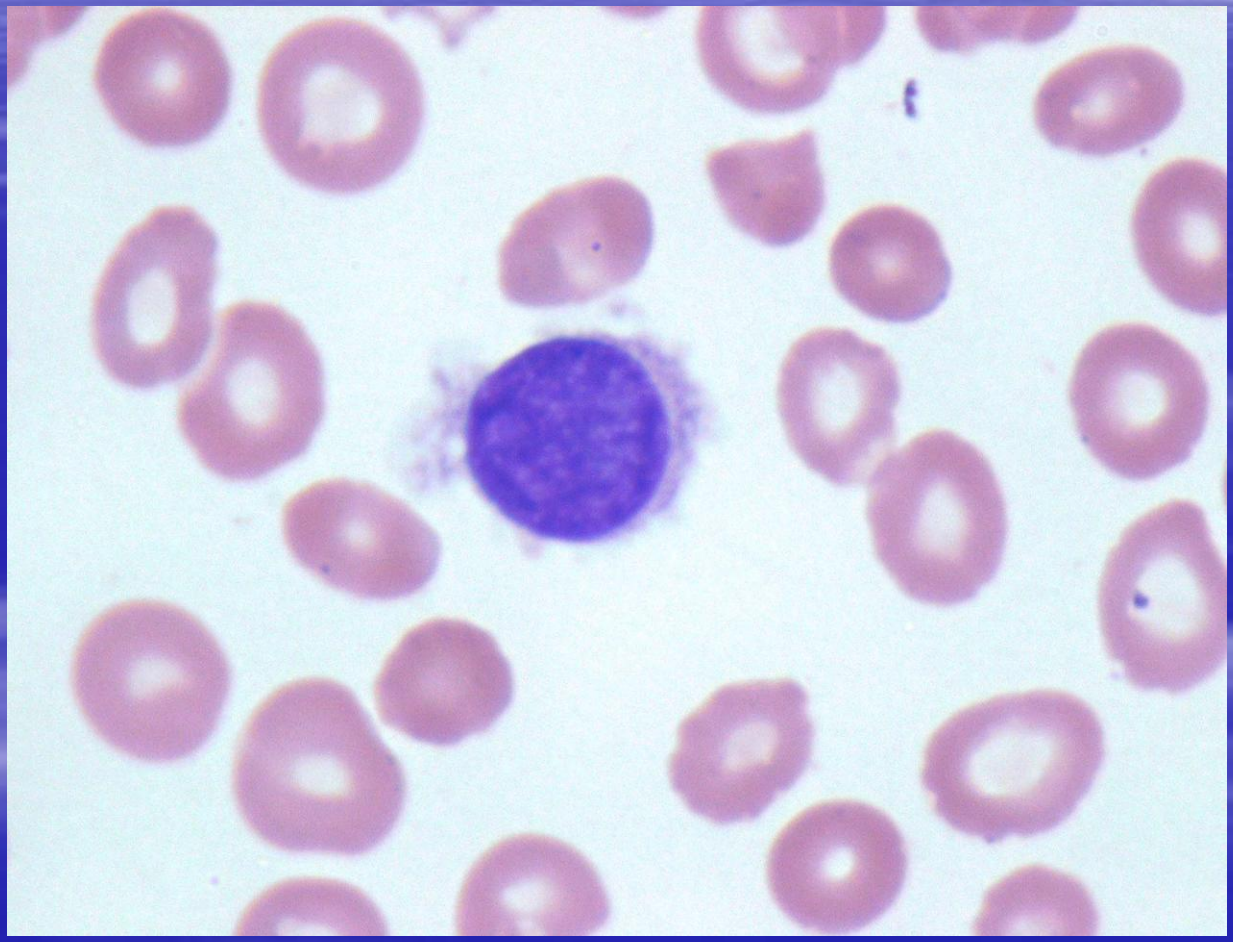


Hairy cell variant: elevated WBC count; neutropenia and monocytopenia not seen
CD 25- , CD103- and TRAP-; prominent nucleolus

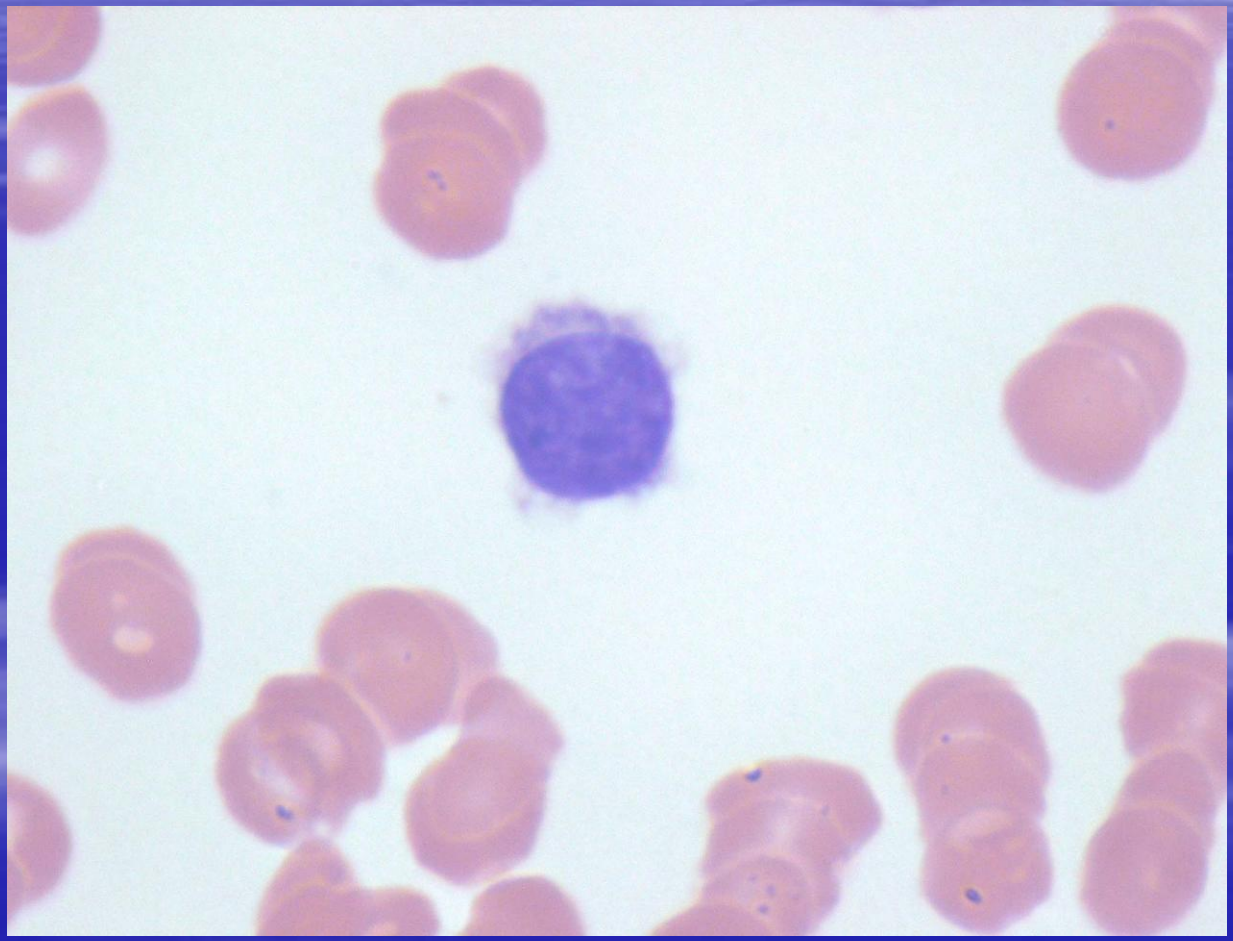
Associations

- Malignancy (eg Multiple myeloma, lymphoma)
- Autoimmune disorders

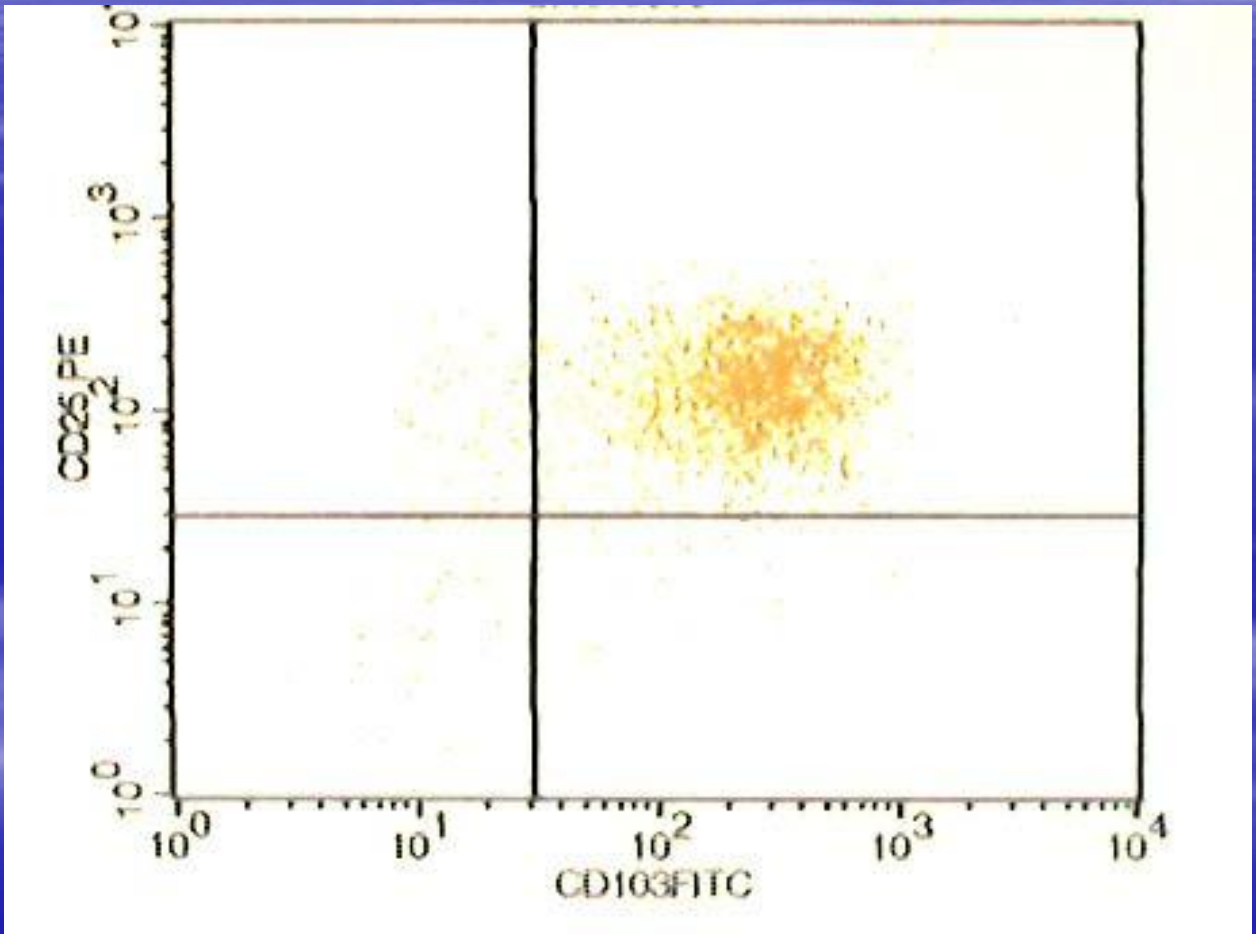
Peripheral Blood Smear



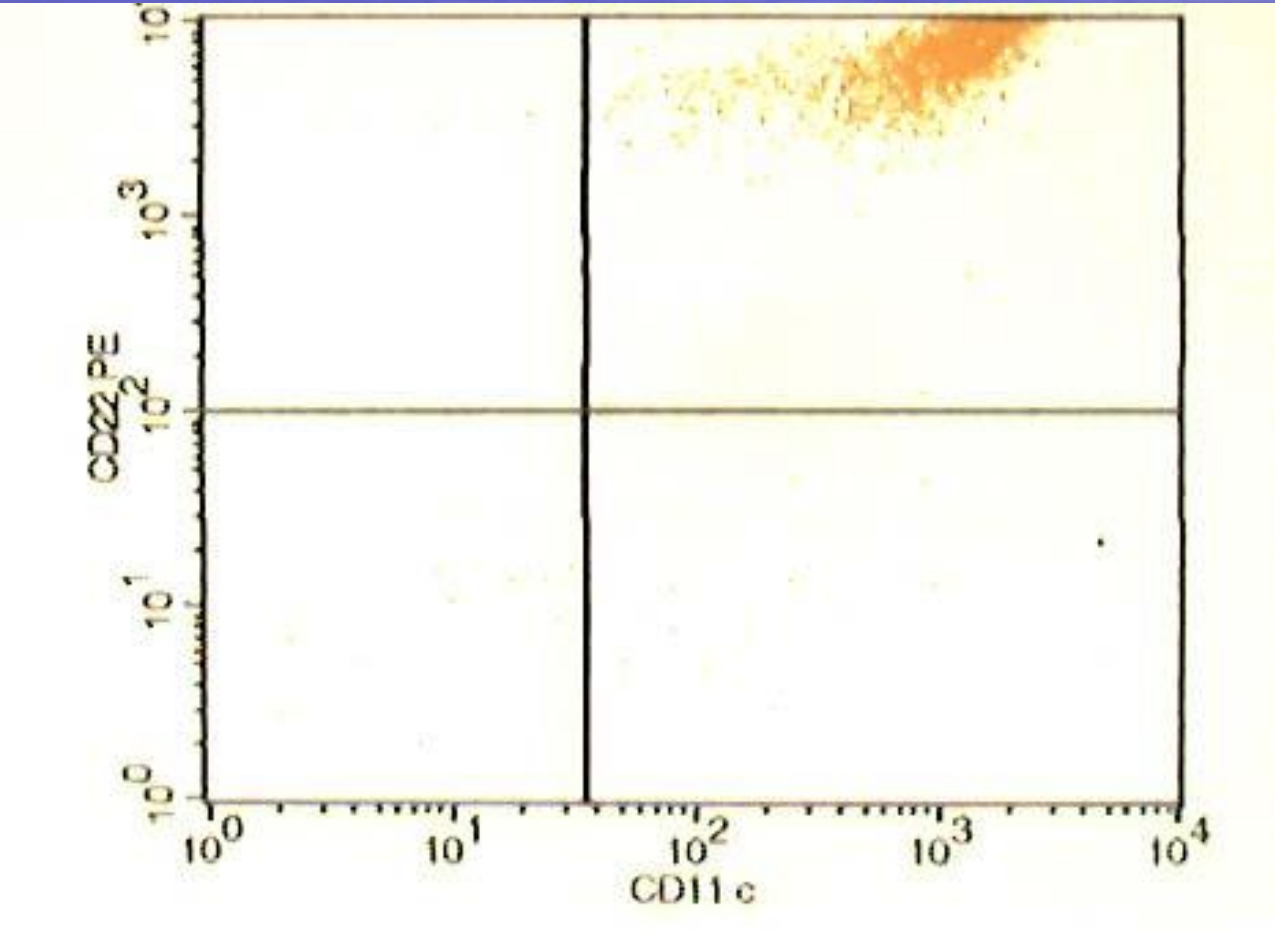
Peripheral Blood Smear



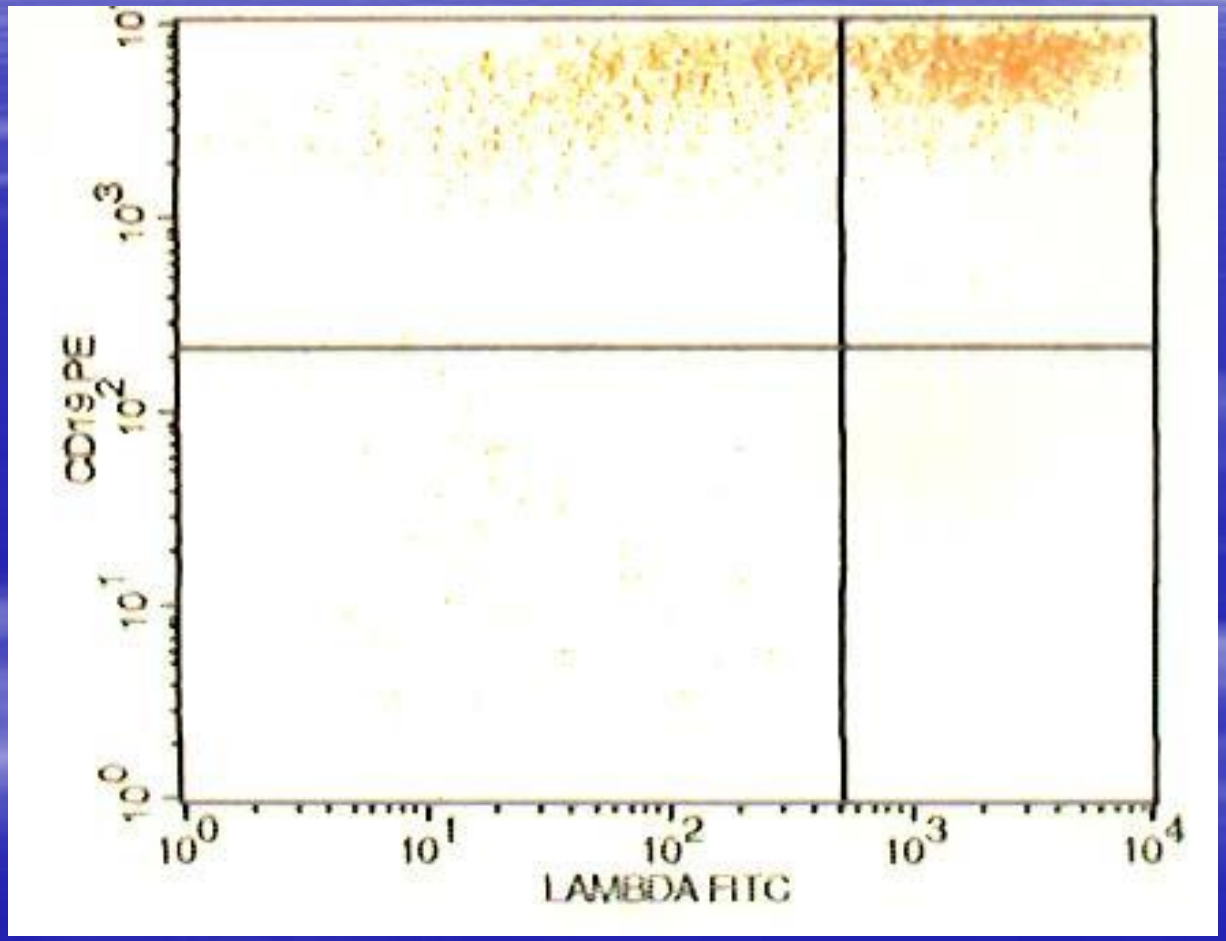
Flow Cytometry Study



Flow Cytometry Study



Flow Cytometry Study



Flow Cytometry Study