

Case II

History I

- 80-year-old Caucasian female, retired architect July 2007
 - difficulty walking, and breathless on exertion, weight loss, change in bowel habits
- Investigations from the 20/07/2007 to the 31/07/2007 as an inpatient at the Royal Free Hospital
- LDH > 1000 iu/l
 - CT head: lacunar infarcts, small vessel disease
 - CT abdomen/pelvis booked as outpatient
- Diagnosis on discharge:
- Vascular dementia, Iron deficiency anaemia

FBC 20/07/2007

Date of Birth:	02/05/1925
Sex:	F
Laboratory Number:	07H173326
Ref. Lab. Details:	Specimen Received: 20/07/07 at 11:46

<u>Test Name</u>	<u>Results</u>		<u>Units</u>	<u>Reference Range</u>
FULL BLOOD COUNT				
Hb	11.0	L	g/dL	11.5-15.5
WBC	7.22		10 ⁹ /L	3.5-11
Platelets	204		10 ⁹ /L	140-400
RBC	4.24		10 ¹² /L	3.9-5.6
HCT	0.333	L	L/L	0.35-0.47
MCV	78.7	L	fL	80-98
MCH	26.1	L	pg	27-33
MCHC	33.1		g/dL	31-37
Neutrophils	4.60		10 ⁹ /L	1.7-8.0
Lymphocytes	0.79	L	10⁹/L	1.0-3.5
Monocytes	0.86		10 ⁹ /L	0.1-1.0
Eosinophils	0.26		10 ⁹ /L	0.0-0.46
Basophils	0.04		10 ⁹ /L	0.00-0.20
ESR	104	H	mm/h	0-30

History II

Re-admitted August 2007

confusion, hallucination

Investigations from the 01/08/2007 to the 14/08/2007
as an inpatient at the Royal Free Hospital

- LDH > 1500 iu/l
- Neurology and Occupational therapy review
- CT abdomen/pelvis not performed, again booked as an outpatient

Diagnosis on discharge:

- Vascular dementia
- Iron deficiency anaemia - treated with oral iron supps.

FBC 03/08/2007

		Date of Birth:	02/05/1925
		Sex:	F
Laboratory Number:	07H185866	Specimen Received:	03/08/07 at 20:29
Ref. Lab. Details:			

<u>Test Name</u>	<u>Results</u>		<u>Units</u>	<u>Reference Range</u>
FULL BLOOD COUNT				
Hb	9.4	L	g/dL	11.5-15.5
WBC	6.19		10 ⁹ /L	3.5-11
Platelets	224		10 ⁹ /L	140-400
RBC	3.65	L	10¹²/L	3.9-5.6
HCT	0.281	L	L/L	0.35-0.47
MCV	77.0	L	fL	80-98
MCH	25.7	L	pg	27-33
MCHC	33.3		g/dL	31-37
Neutrophils	3.96		10 ⁹ /L	1.7-8.0
Lymphocytes	1.05		10 ⁹ /L	1.0-3.5
Monocytes	0.50		10 ⁹ /L	0.1-1.0
Eosinophils	0.12		10 ⁹ /L	0.0-0.46
Basophils	0.06		10 ⁹ /L	0.00-0.20
Film Report	Microcytic hypochromic blood film			

History III

Re-admitted August 2007

confusion, hallucination

Investigations from the 21/08/2007 to the 03/10/2007
as an inpatient at the Royal Free Hospital

- LDH > 2000 iu/l
- Neurology review: for brain biopsy
- CT pneumocolon showed diverticulitis, but no malignancy; incidental finding of splenomegaly of 16 cm

FBC 24/08/2007

Date of Birth:	02/05/1925
Sex:	F
Laboratory Number:	07H202902
Ref. Lab. Details:	Specimen Received: 24/08/07 at 12:44

<u>Test Name</u>	<u>Results</u>		<u>Units</u>	<u>Reference Range</u>
FULL BLOOD COUNT				
Hb	9.2	L	g/dL	11.5-15.5
WBC	5.79		$10^9/L$	3.5-11
Platelets	244		$10^9/L$	140-400
RBC	3.57	L	$10^{12}/L$	3.9-5.6
HCT	0.278	L	L/L	0.35-0.47
MCV	77.7	L	fL	80-98
MCH	25.9	L	pg	27-33
MCHC	33.3		g/dL	31-37
Neutrophils	3.94		$10^9/L$	1.7-8.0
Lymphocytes	0.70	L	$10^9/L$	1.0-3.5
Monocytes	0.57		$10^9/L$	0.1-1.0
Eosinophils	0.22		$10^9/L$	0.0-0.46
Basophils	0.03		$10^9/L$	0.00-0.20
ESR	116	H	mm/h	0-30

History IV

- Brain biopsy showed some lymphocytic infiltrates, but insufficient for a diagnosis
- CSF: WBC 2, RBC 695, Protein 1.24 g/l, Glucose 3 mmol/l

Diagnosis on discharge:

- Vascular dementia
- Iron deficiency anaemia - treated with oral iron supplements

History V

Re-admitted 05/11/2007

confusion, pyrexia, tachycardia

Investigations

- LDH > 2500 iu/l
- USS abdomen: splenomegaly 18 cm

Diagnosis:

- Anaemia of chronic disease
- Haematological malignancy?

FBC 06/11/2007

Date of Birth: 02/05/1925	
Sex: F	
Laboratory Number: 07H266763	Specimen Received: 06/11/07 at 14:45
Ref. Lab. Details:	

<u>Test Name</u>	<u>Results</u>		<u>Units</u>	<u>Reference Range</u>
FULL BLOOD COUNT				
Hb	10.1	L	g/dL	11.5-15.5
WBC	5.93		10 ⁹ /L	3.5-11
Platelets	157		10 ⁹ /L	140-400
RBC	3.50	L	10¹²/L	3.9-5.6
HCT	0.292	L	L/L	0.35-0.47
MCV	83.4		fL	80-98
MCH	28.8		pg	27-33
MCHC	34.5		g/dL	31-37
Neutrophils	4.28		10 ⁹ /L	1.7-8.0
Lymphocytes	0.58	L	10⁹/L	1.0-3.5
Monocytes	0.39		10 ⁹ /L	0.1-1.0
Eosinophils	0.05		10 ⁹ /L	0.0-0.46
Basophils	0.03		10 ⁹ /L	0.00-0.20

Film Report Polychromasia , Platelets Anisocytosis

Examination I

- Confused, but obeying commands
- Pale
- Pyrexial at 38.5 C°
- HR 92 BPM, BP 130/50
- RR 20/min, O² Sats 93% on 2l O²
- Heart sounds clear on auscultation
- Inspiratory crepitations at the left lung base
- Abdomen: splenomegaly of 10 cm below the left costal margin
- Cervical, axillary and inguinal lymphnodes are not enlarged

Investigations I

- FBC
 - Blood film
 - Bone marrow aspirate & trephine
(H&E, DE, SBB, and Immunohistochemistry)
 - Flowcytometry
- What is the likely diagnosis?

Full Blood Count

Laboratory Number: 07H282397		Date of Birth: 02/05/1925
Ref. Lab. Details:		Sex: F
		Specimen Received: 23/11/07 at 13:36

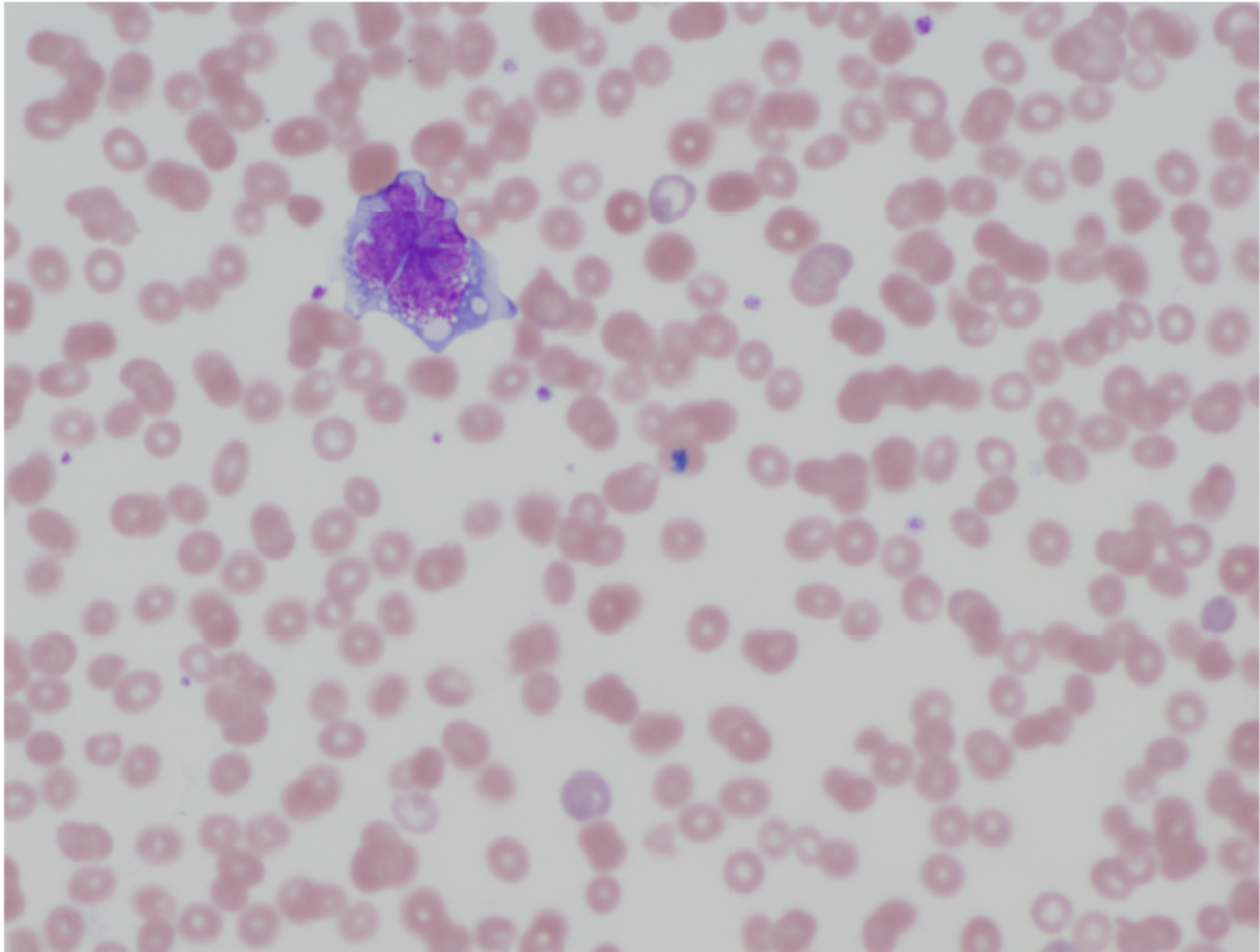
Test Name	Results	Units	Reference Range
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FULL BLOOD COUNT

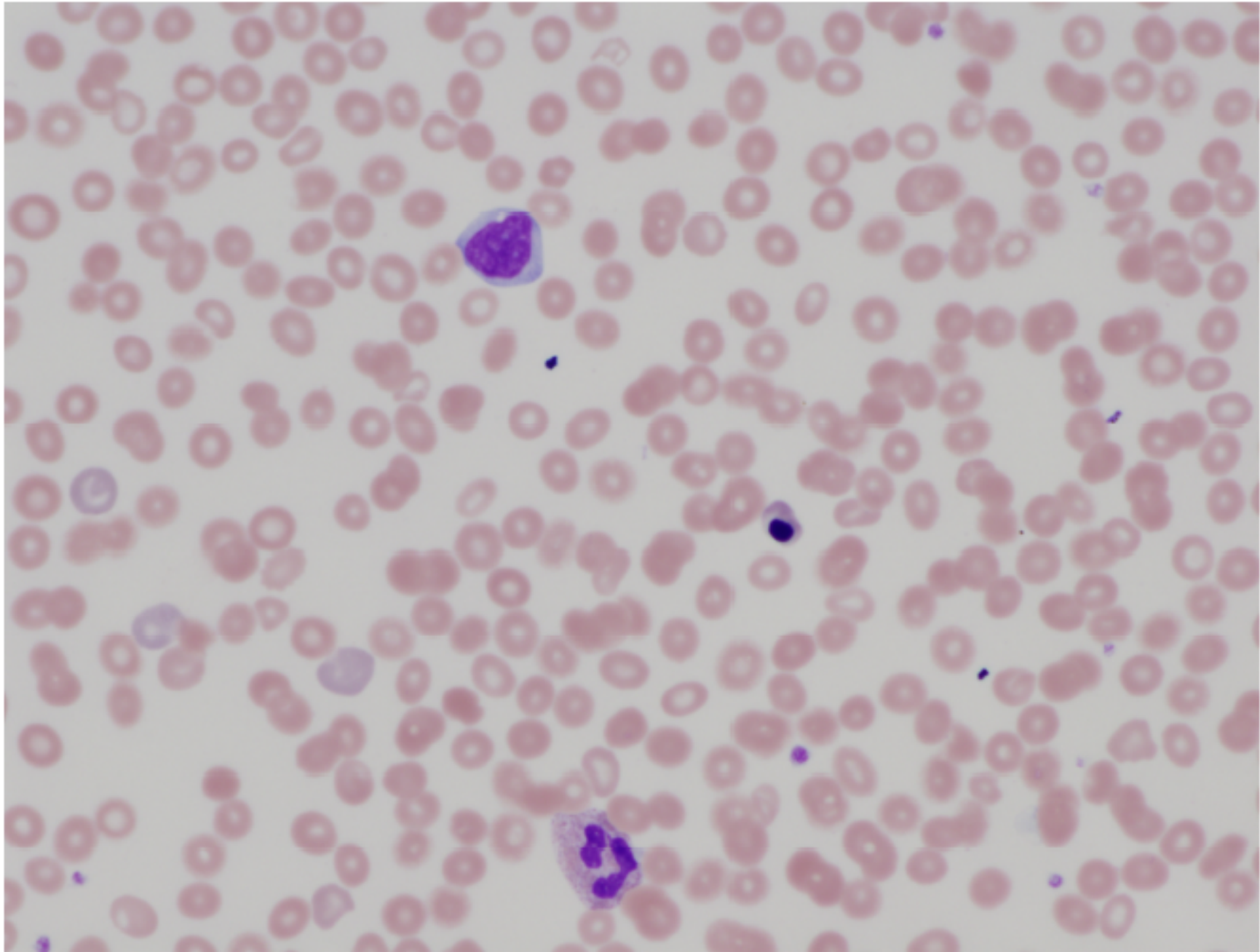
Hb	10.9	L	g/dL	11.5-15.5
WBC	10.63		10⁹/L	3.5-11
Platelets	70	L	10⁹/L	140-400
RBC	4.01		10¹²/L	3.9-5.8
HCT	0.330	L	L/L	0.35-0.47
MCV	82.4		fL	80-98
MCH	27.1		pg	27-33
MCHC	32.8		g/dL	31-37
Neutrophils	8.19	H	10⁹/L	1.7-8.0
Lymphocytes	2.34		10 ⁹ /L	1.0-3.5
Monocytes	0.11		10 ⁹ /L	0.1-1.0
Eosinophils	0.00		10 ⁹ /L	0.0-0.46
Basophils	0.00		10 ⁹ /L	0.00-0.20
Blast cells	0.00		10 ⁹ /L	
Promyelocytes	0.00		10 ⁹ /L	
Myelocytes	0.00		10 ⁹ /L	
Metamyelocytes	0.00		10 ⁹ /L	

Film Report	Polychromasia , Nucleated red cells , Platelet anisocytosis seen , Thrombocytopenia
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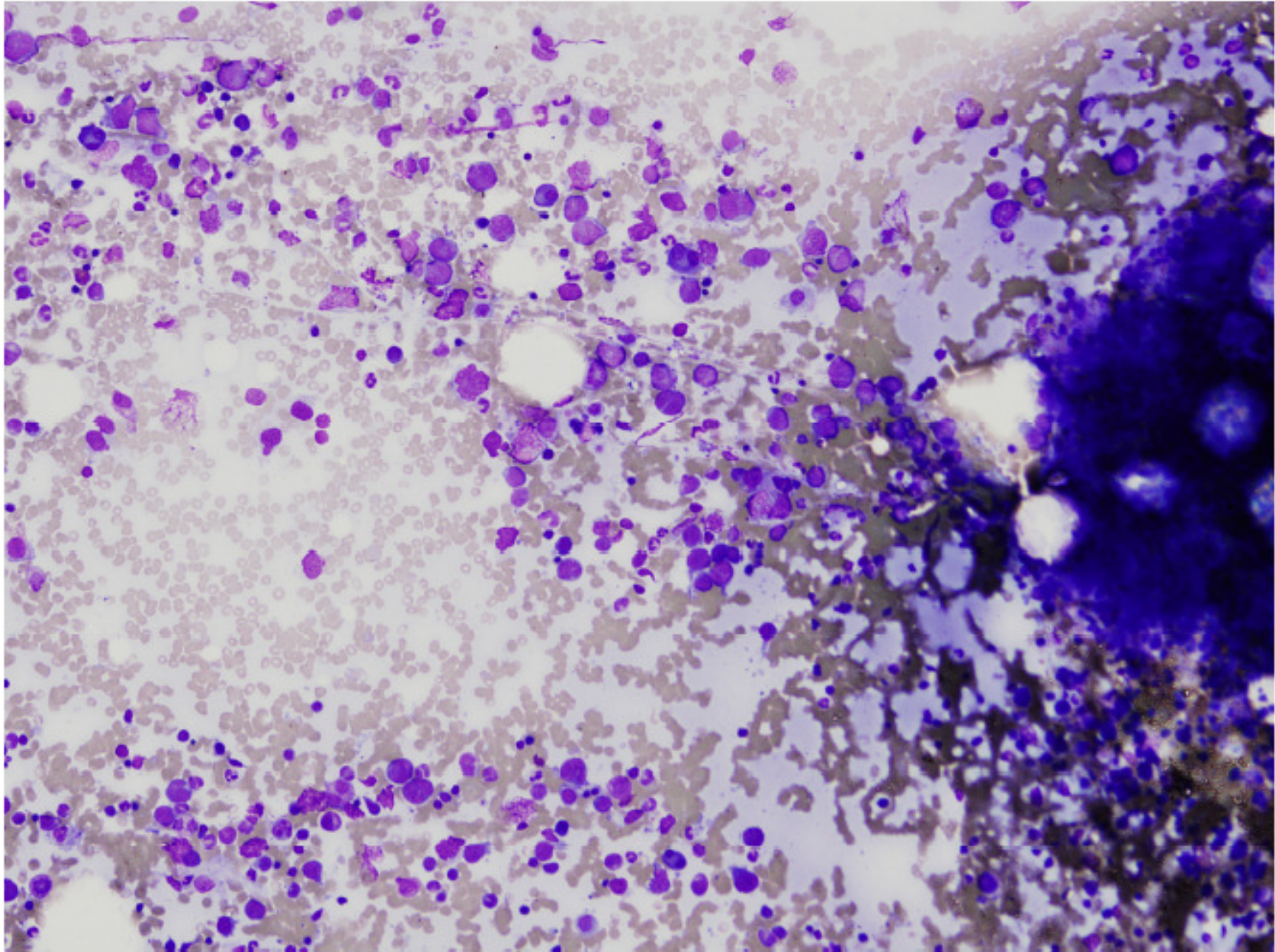
Blood Film I



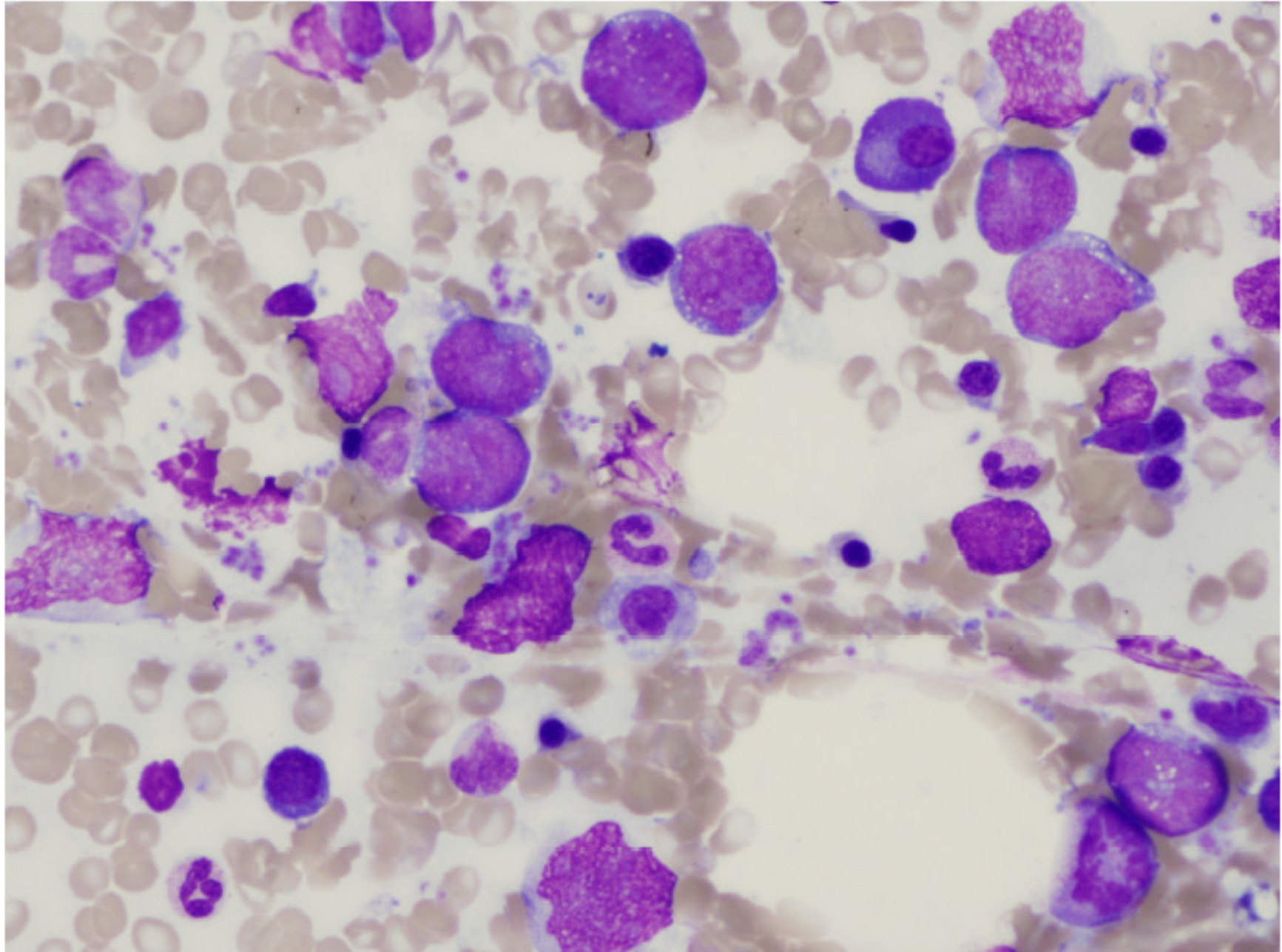
Blood Film II



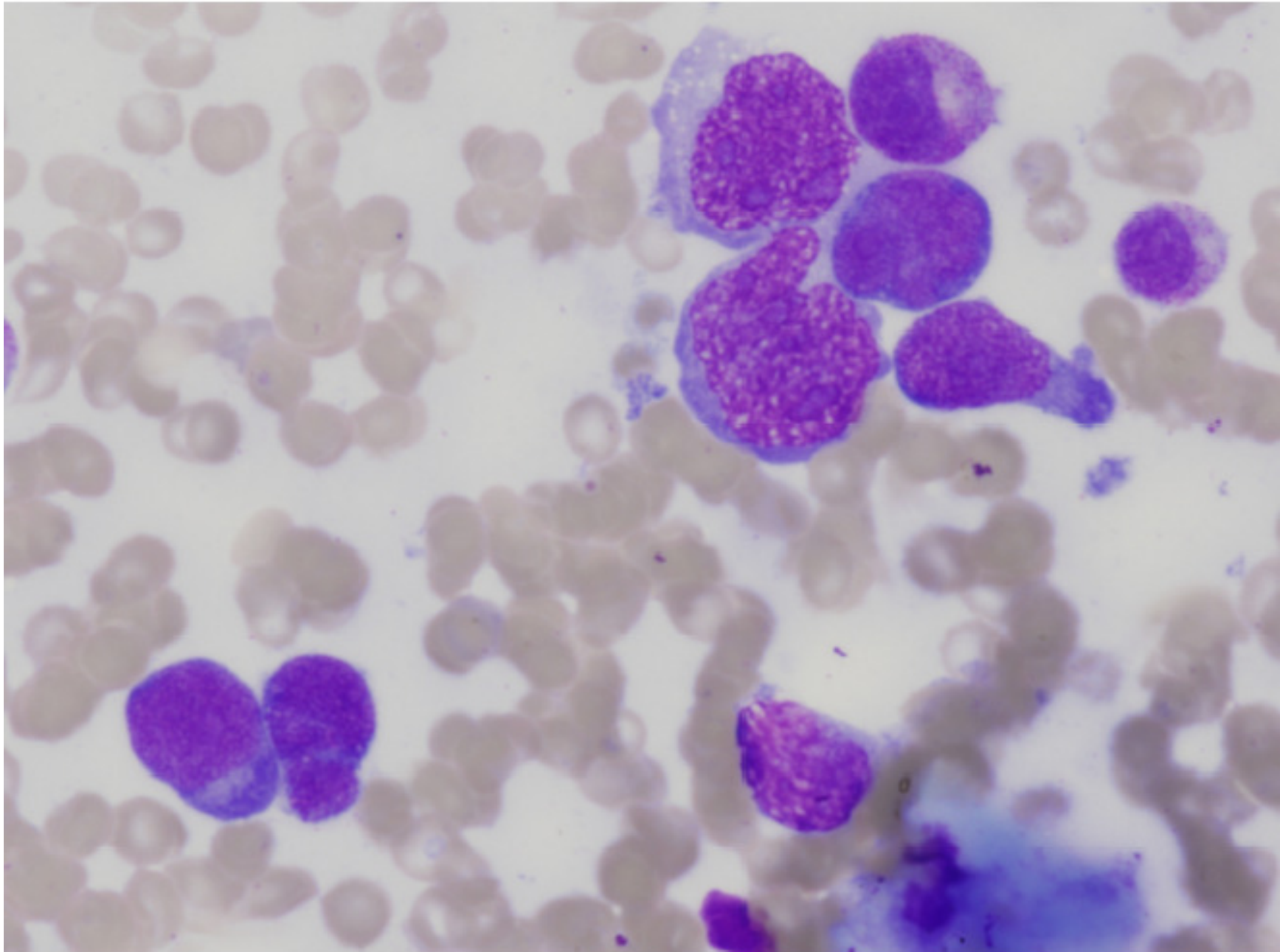
Bone Marrow aspirate H&E x100



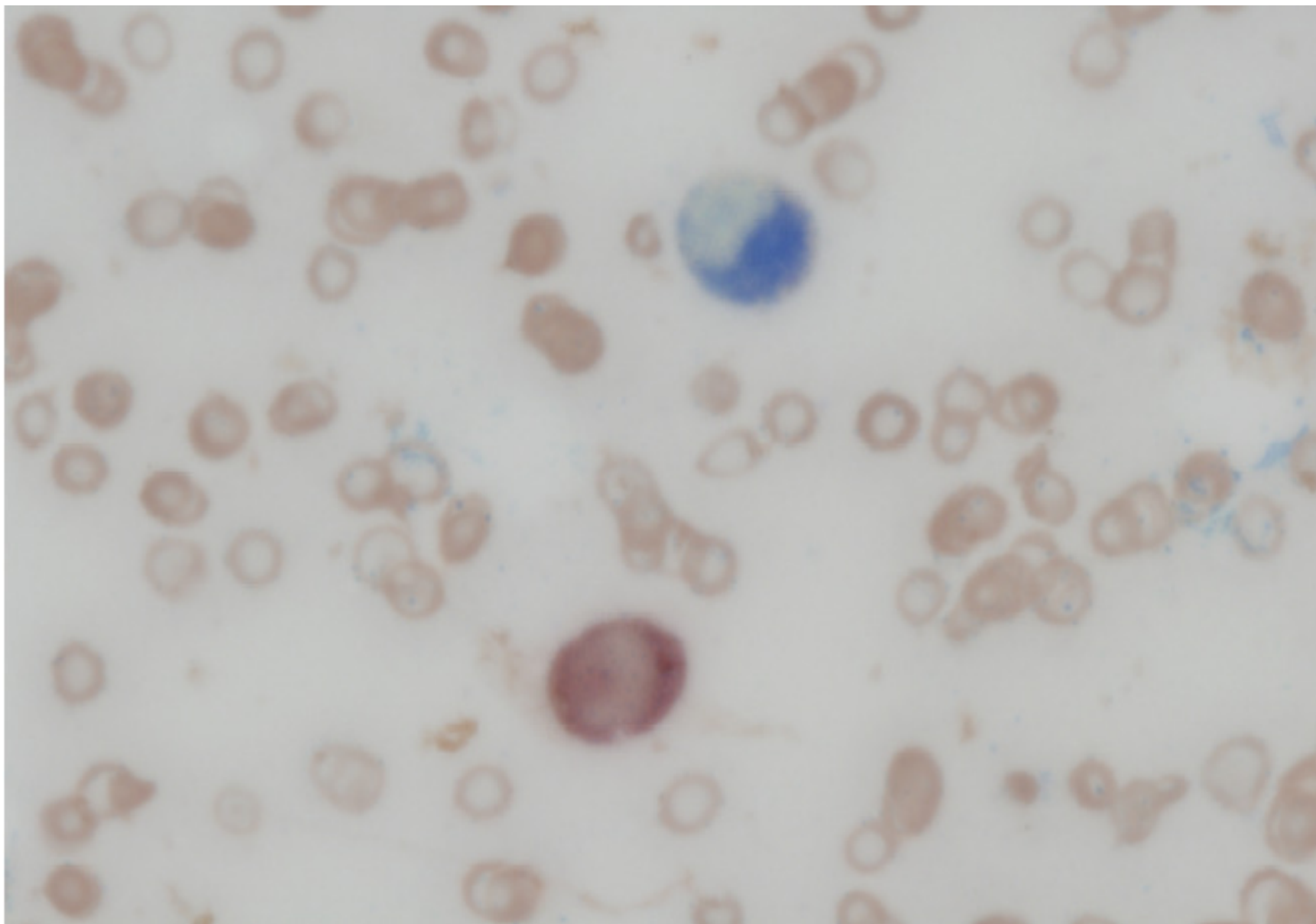
Bone Marrow aspirate H&E x400



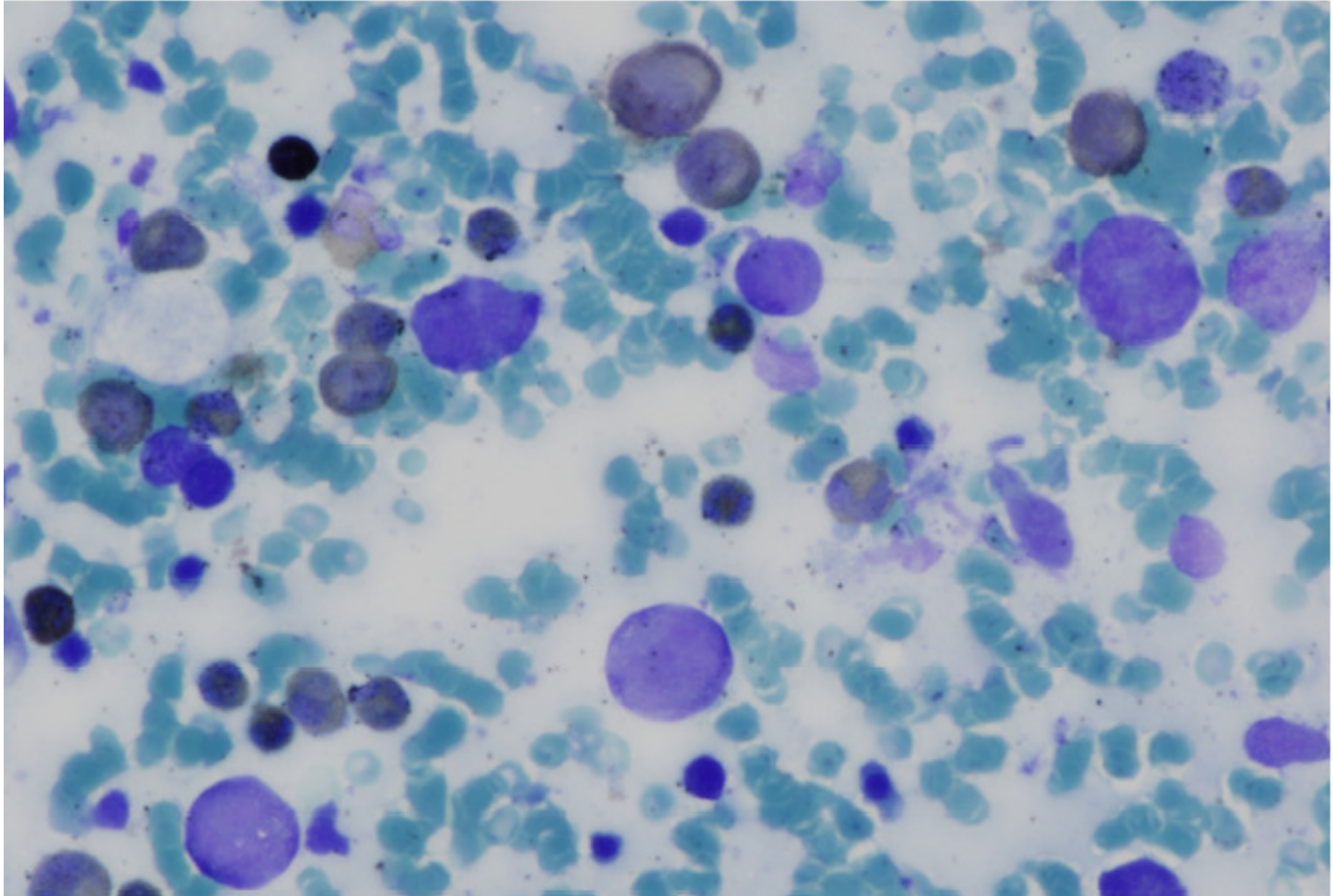
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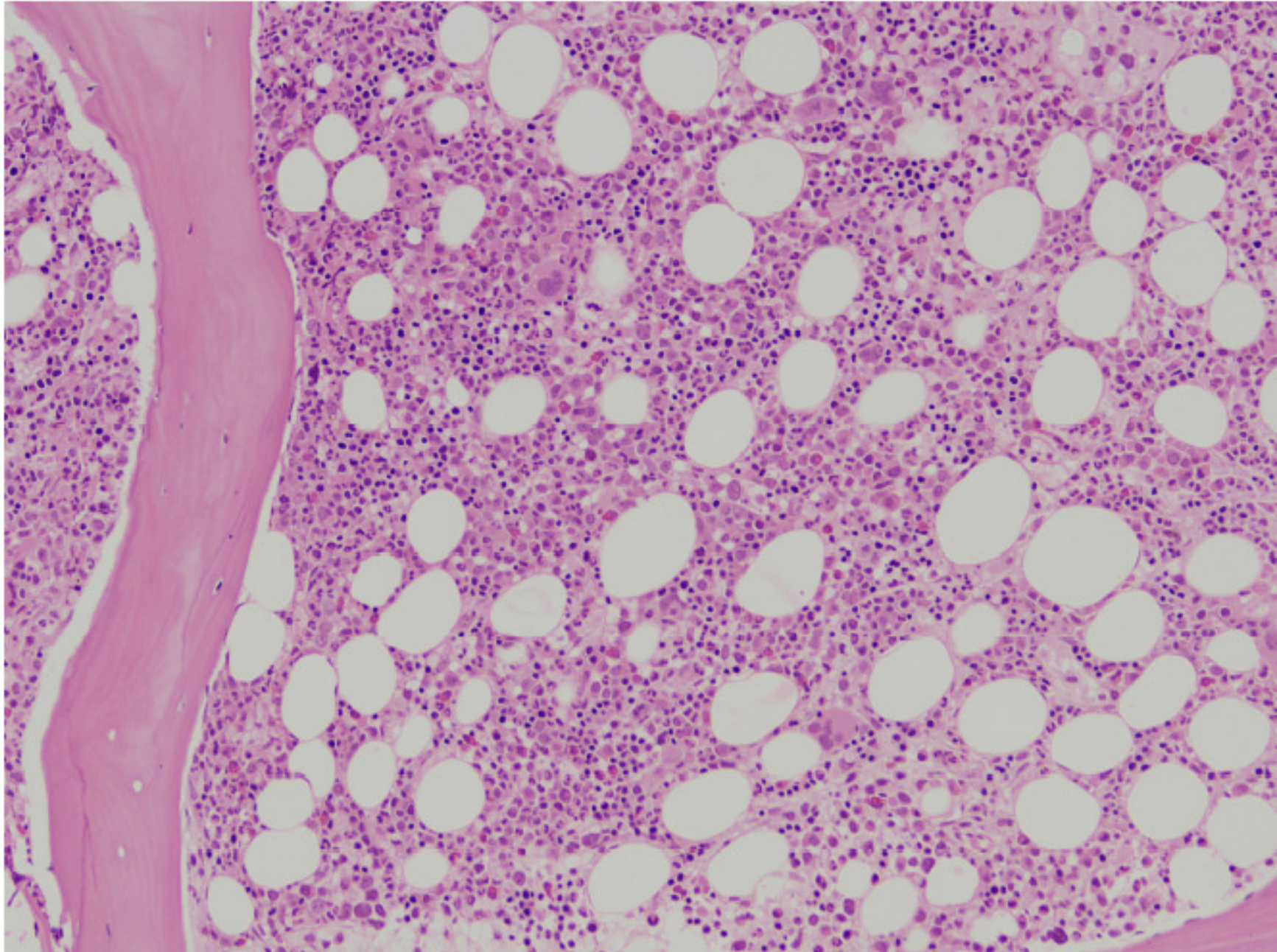
Bone Marrow aspirate Dual Esterase x400



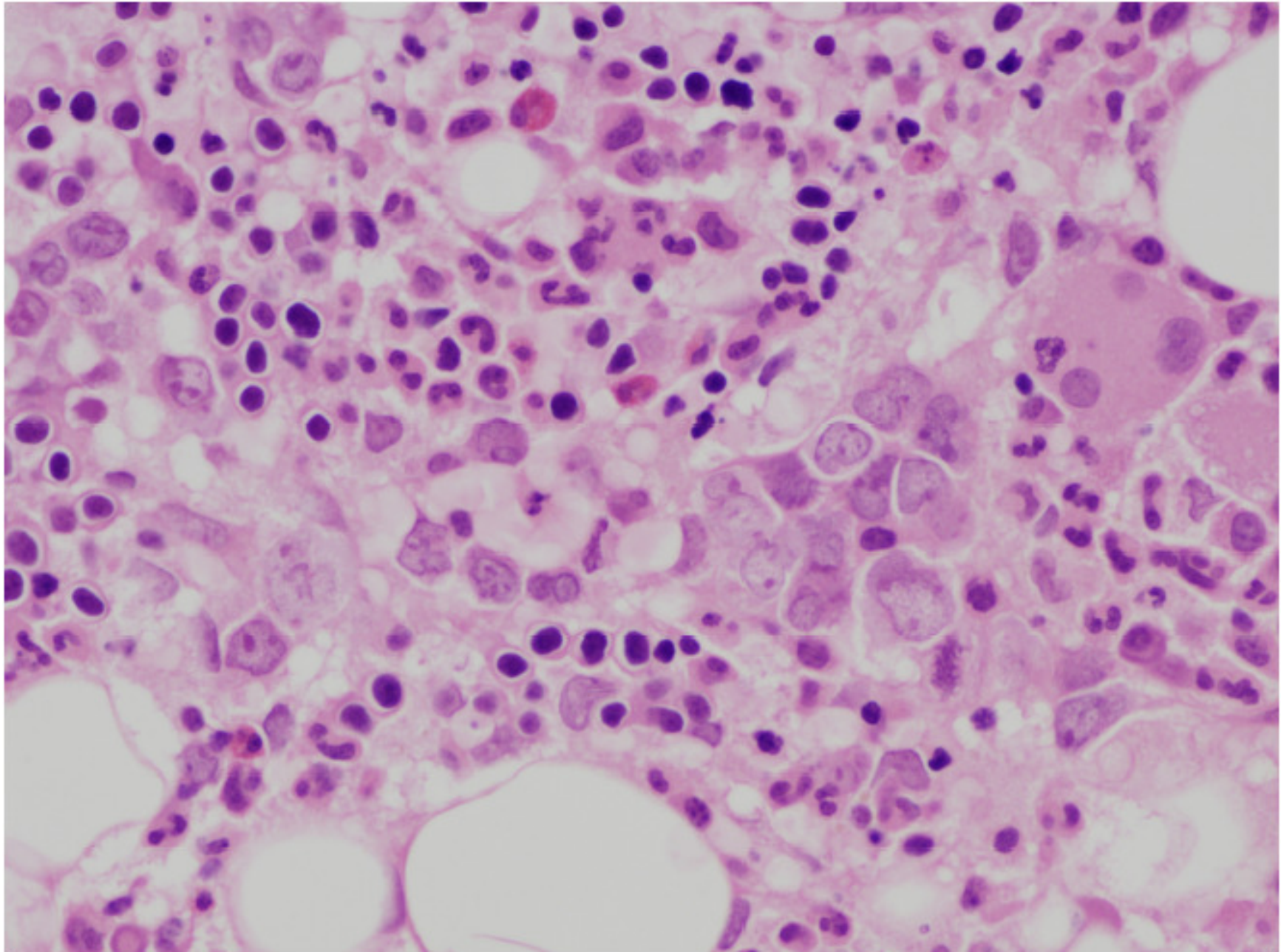
Bone Marrow aspirate Sudan Black B x400



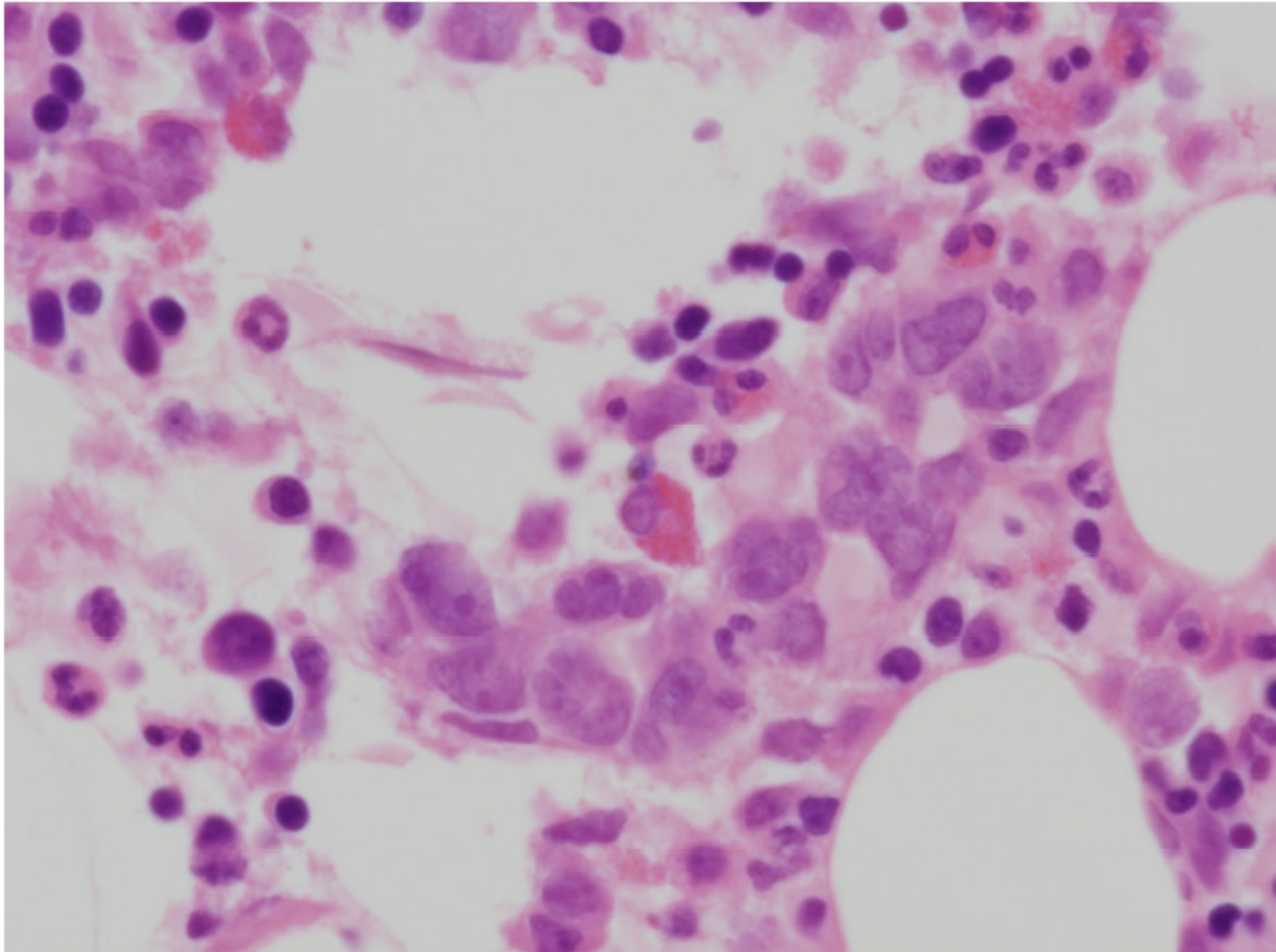
Bone Marrow trephine H&E x100



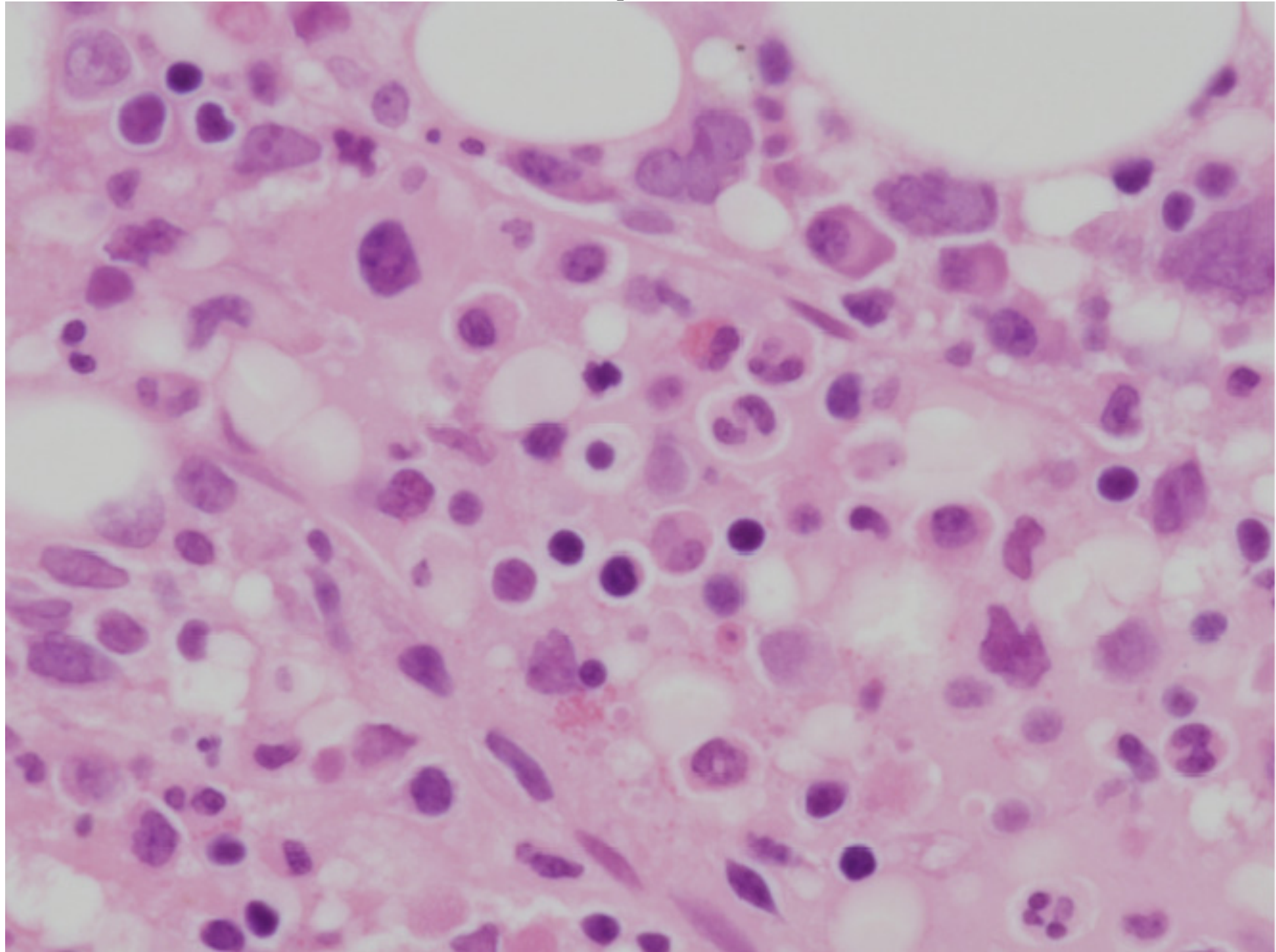
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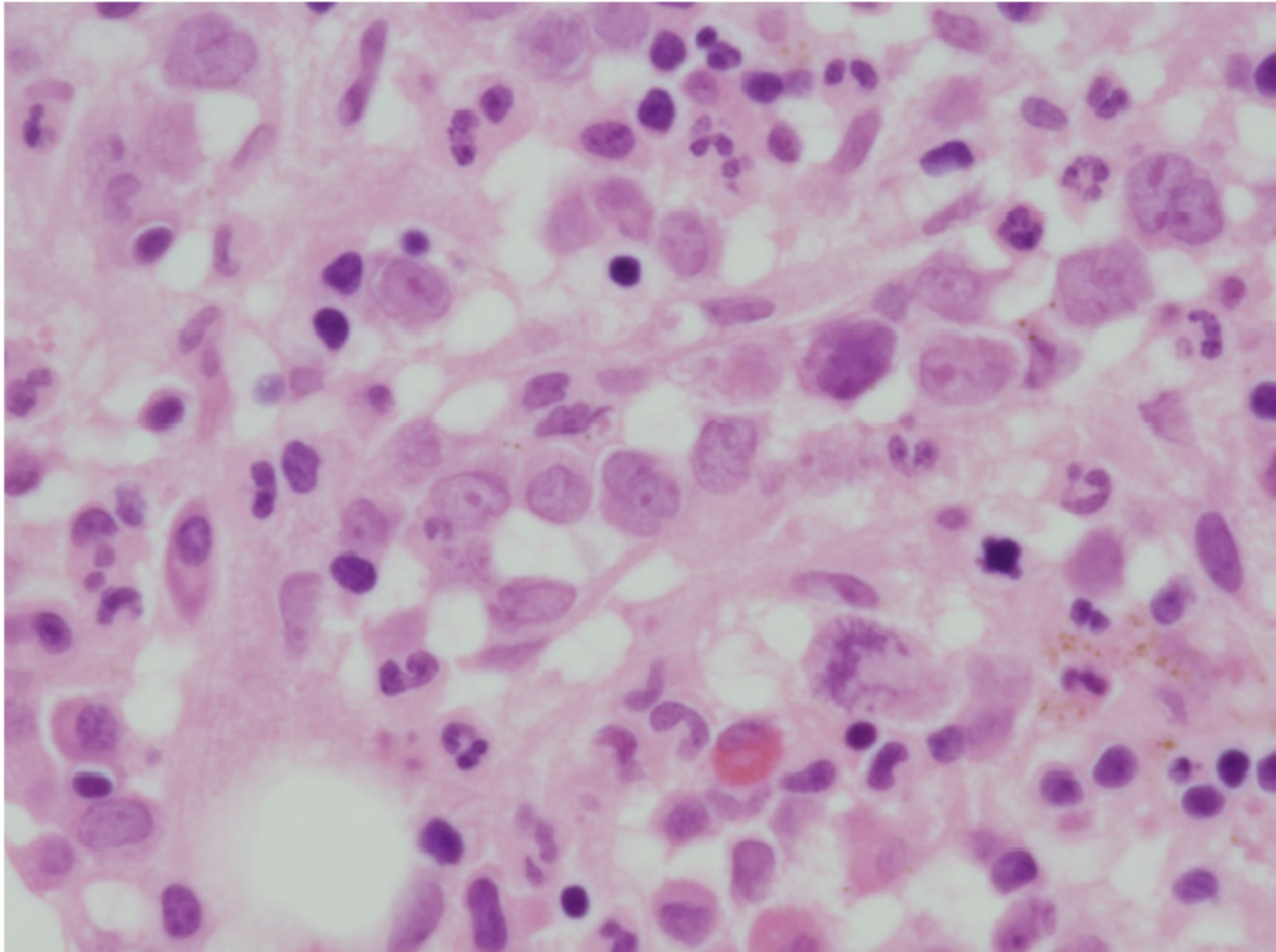
Bone Marrow trephine H&E x600a



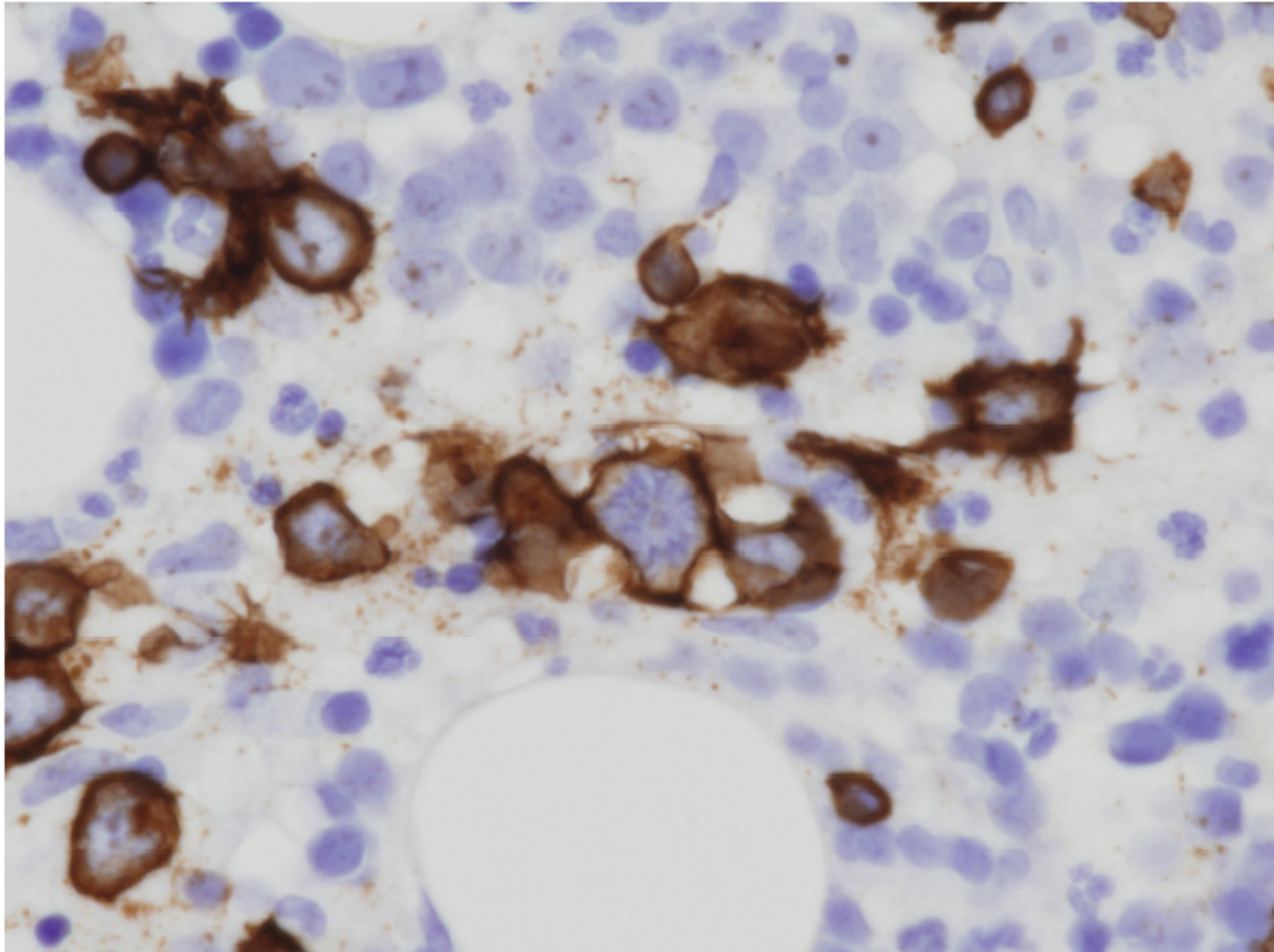
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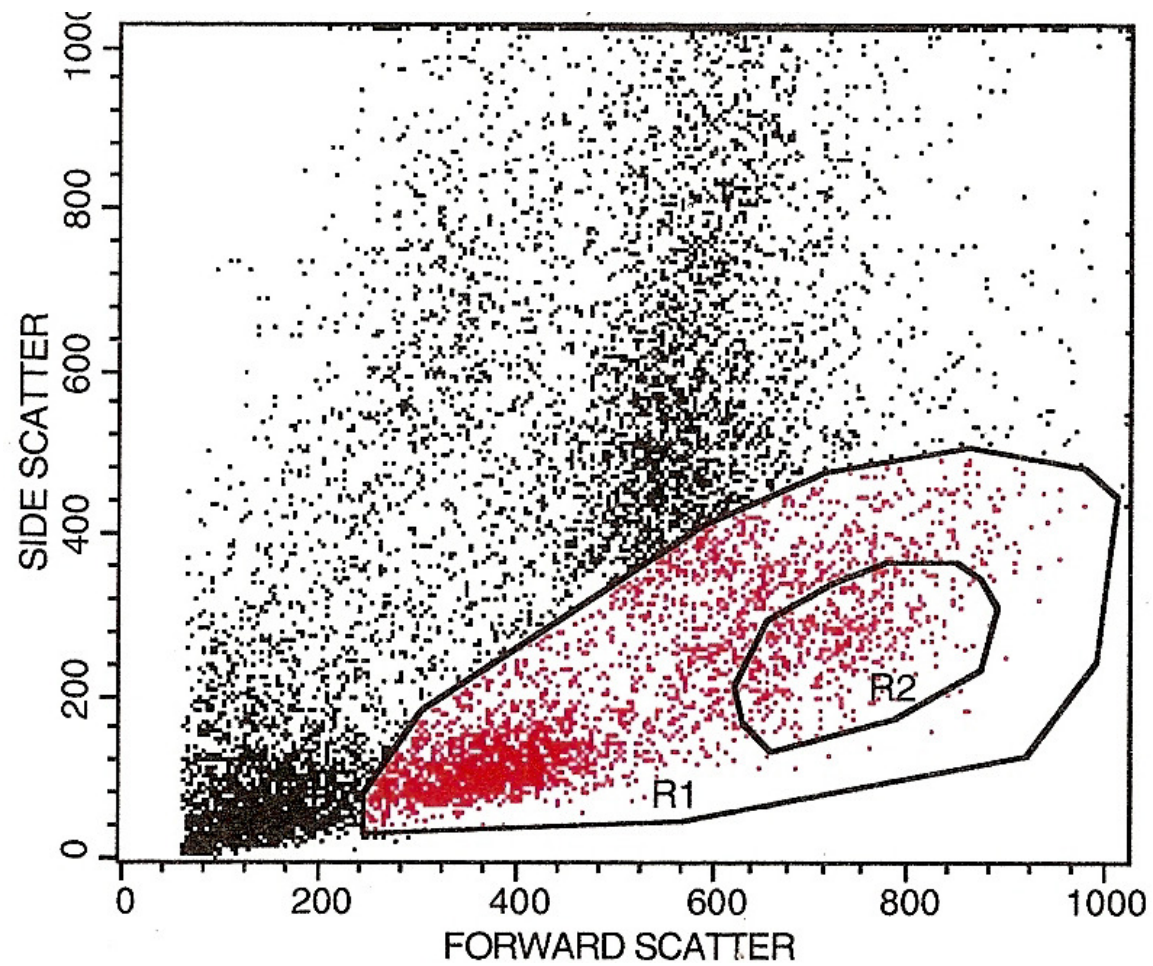
Bone Marrow trephine H&E x600c



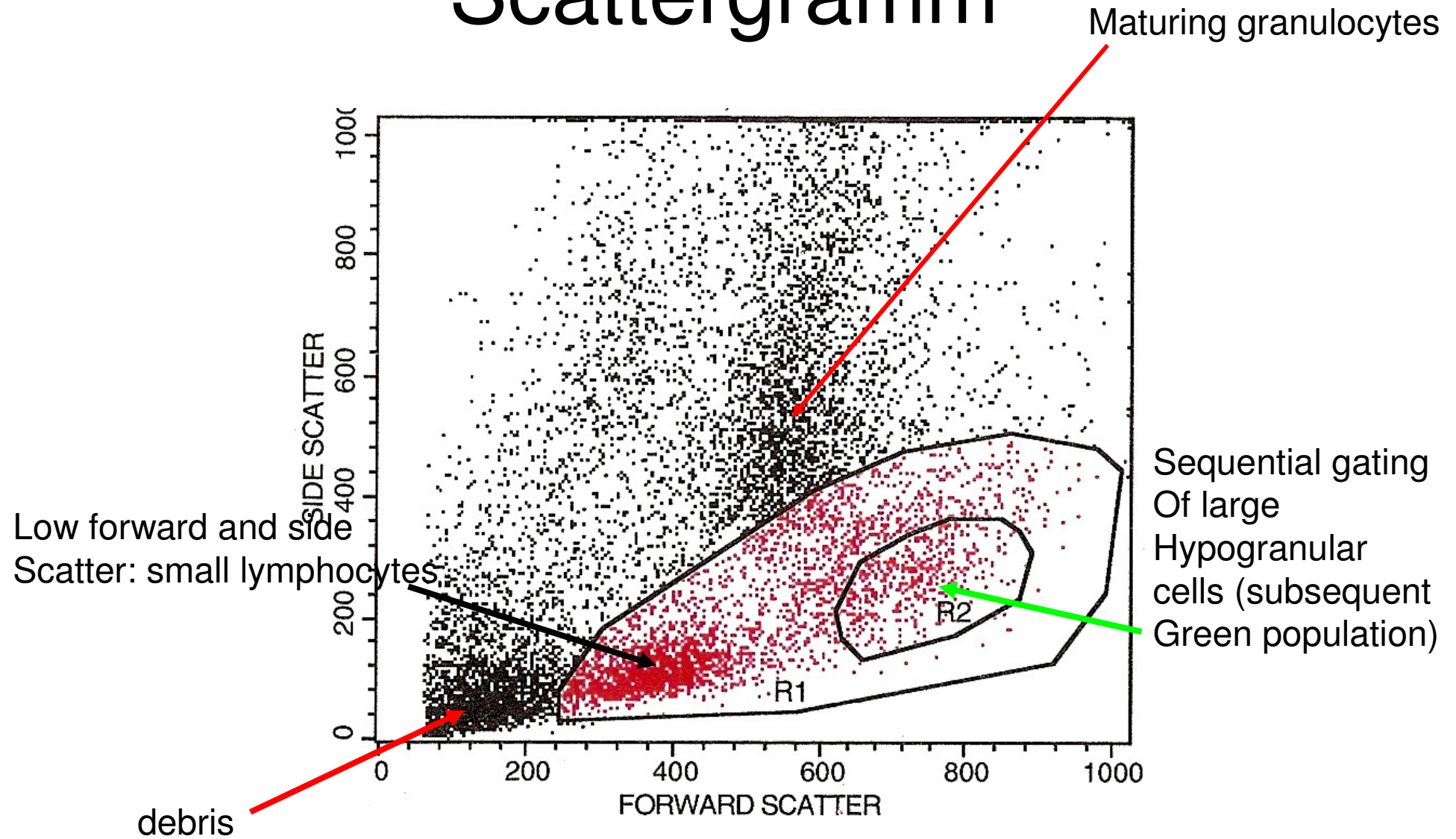
Bone Marrow trephine CD20 x600



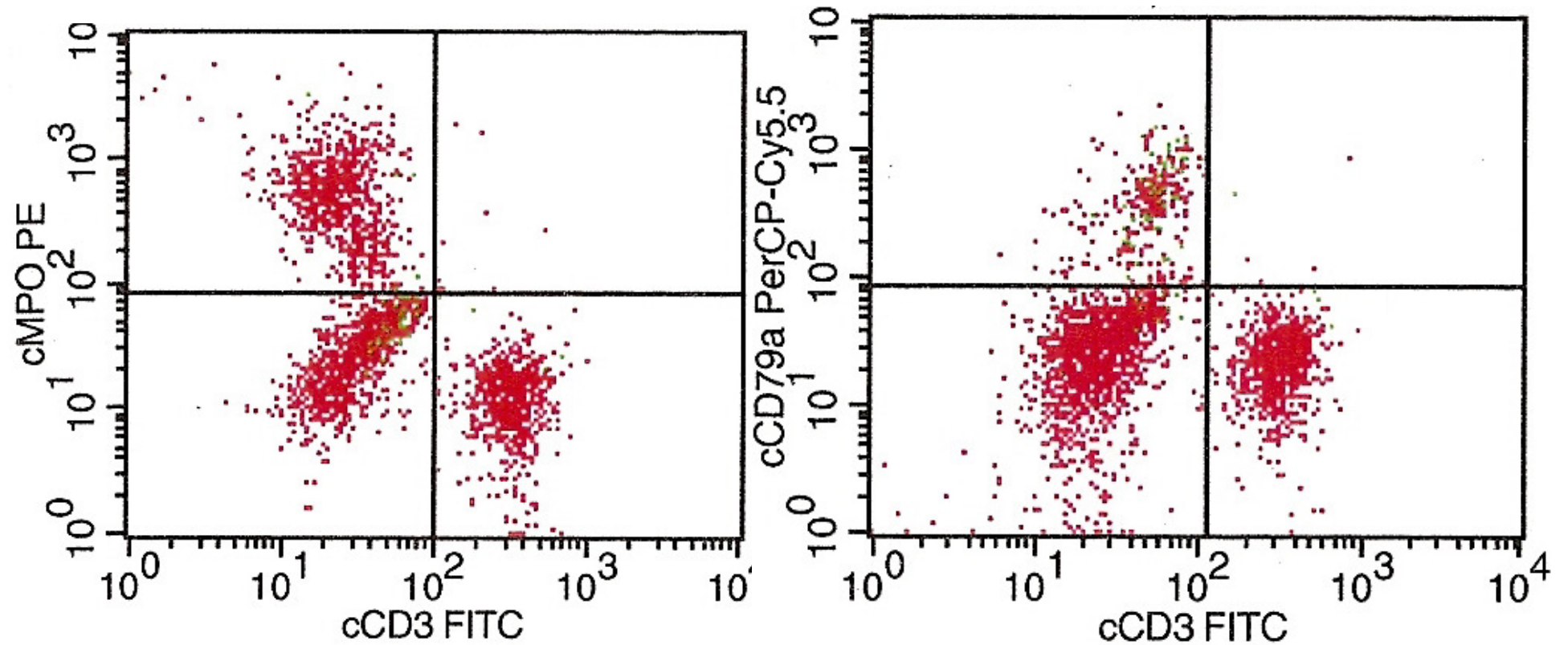
Scattergram



Scattergram

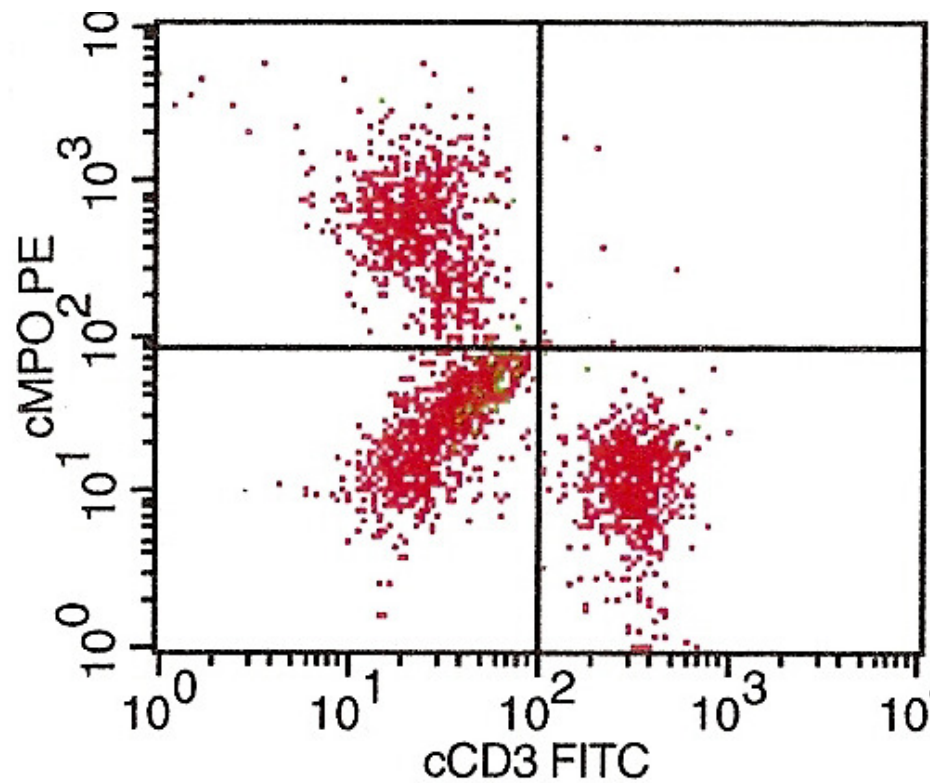


MPO/CD3 – CD79a/CD3



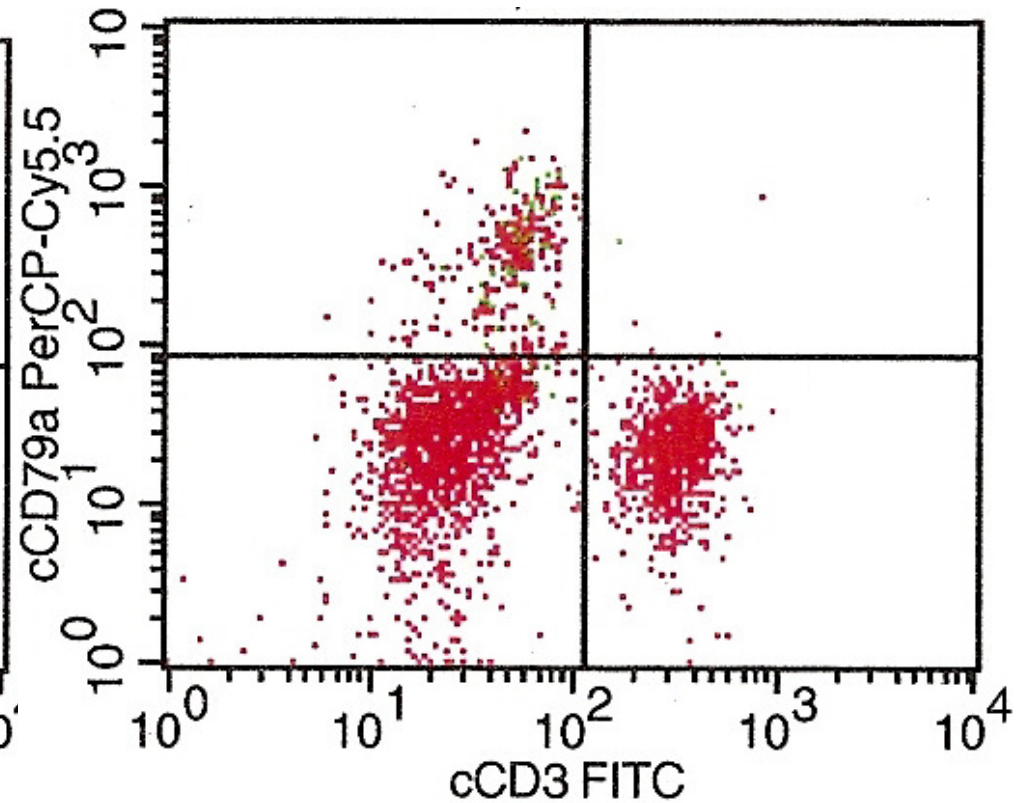
MPO/CD3 – CD79a/CD3

Plots myeloid marker against T-cell marker



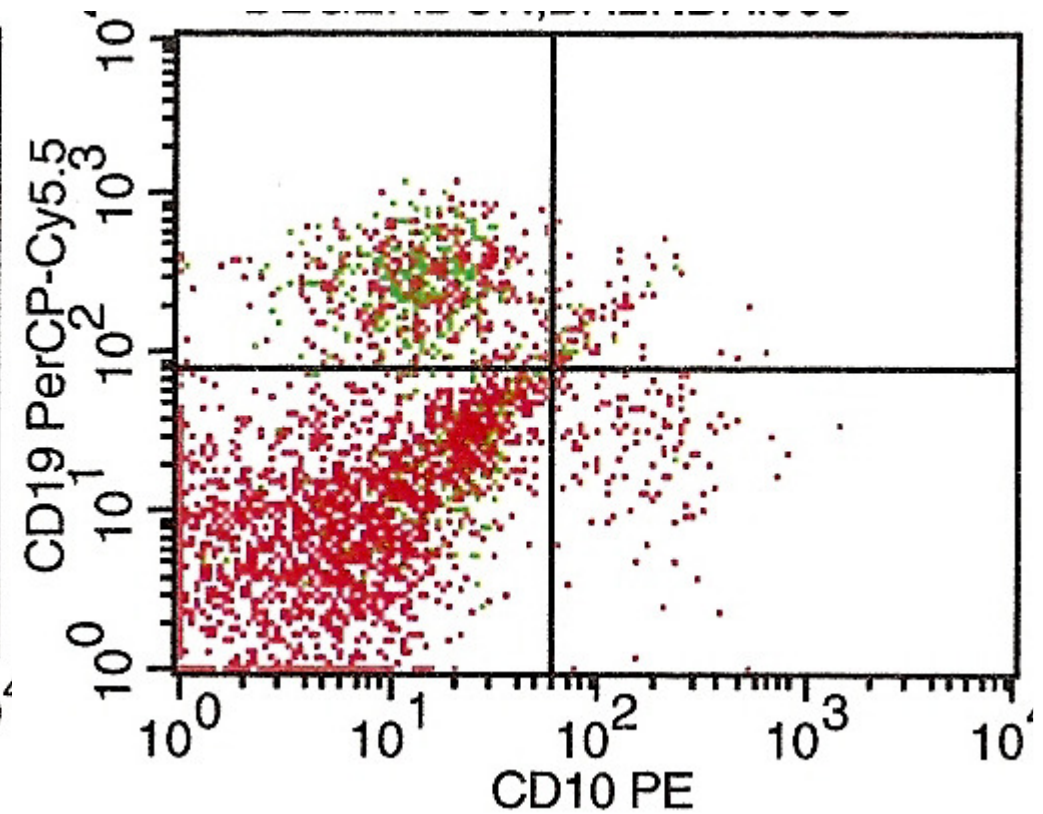
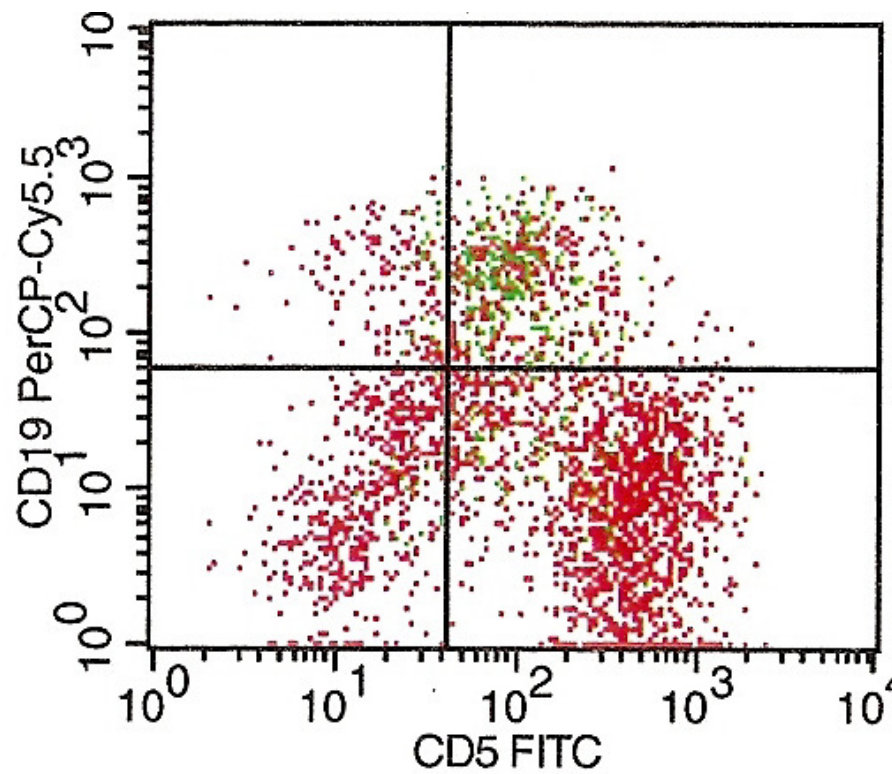
Green cell population is MPO negative

Plots B-cell against T-cell marker



B-cell : T-cell ratio is 1:2 (NR up to 4:1)

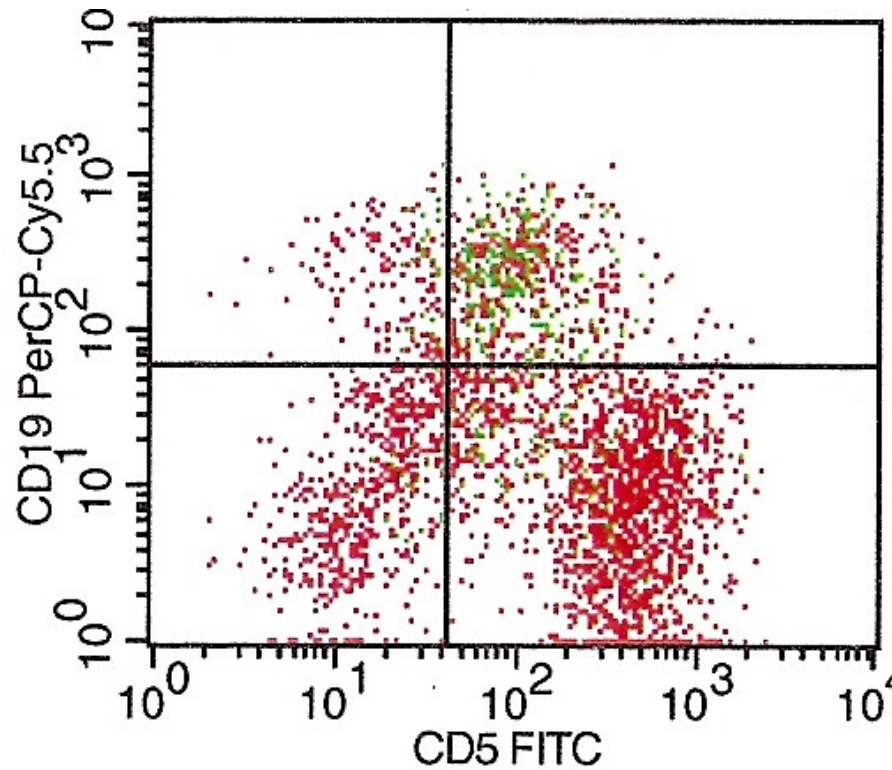
CD19/CD5 – CD19/CD10



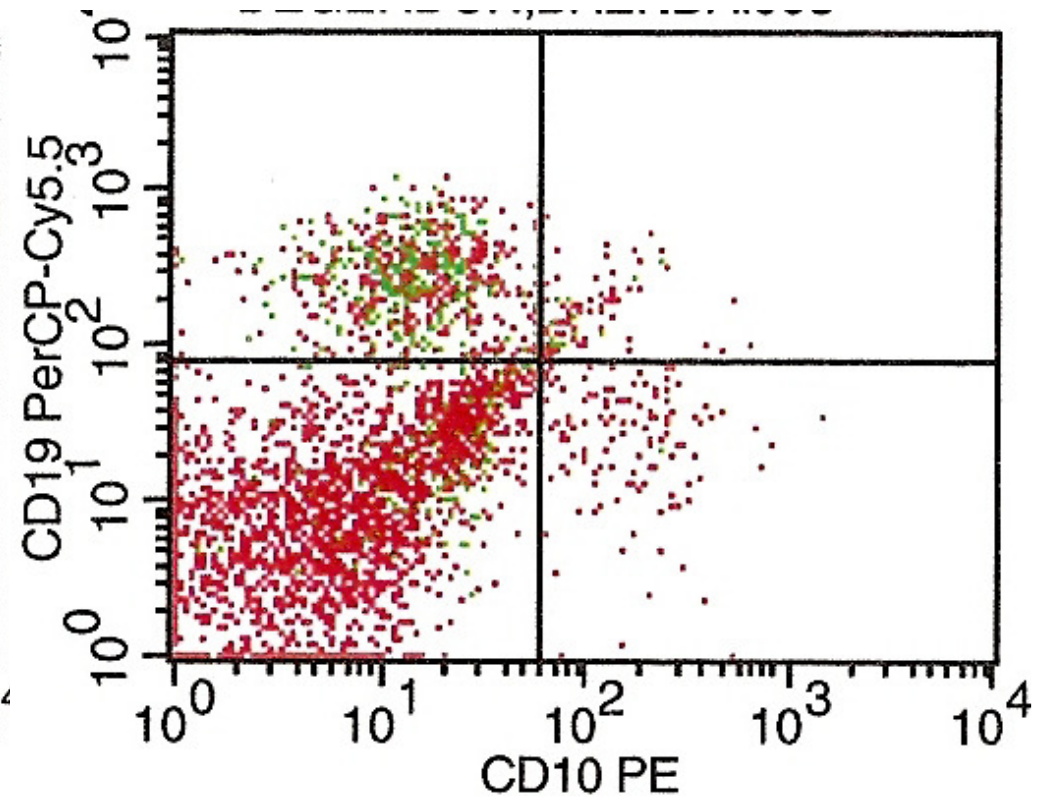
CD19/CD5 – CD19/CD10

Plots B-cell marker against T-cell marker

Lymphoid differentiation markers

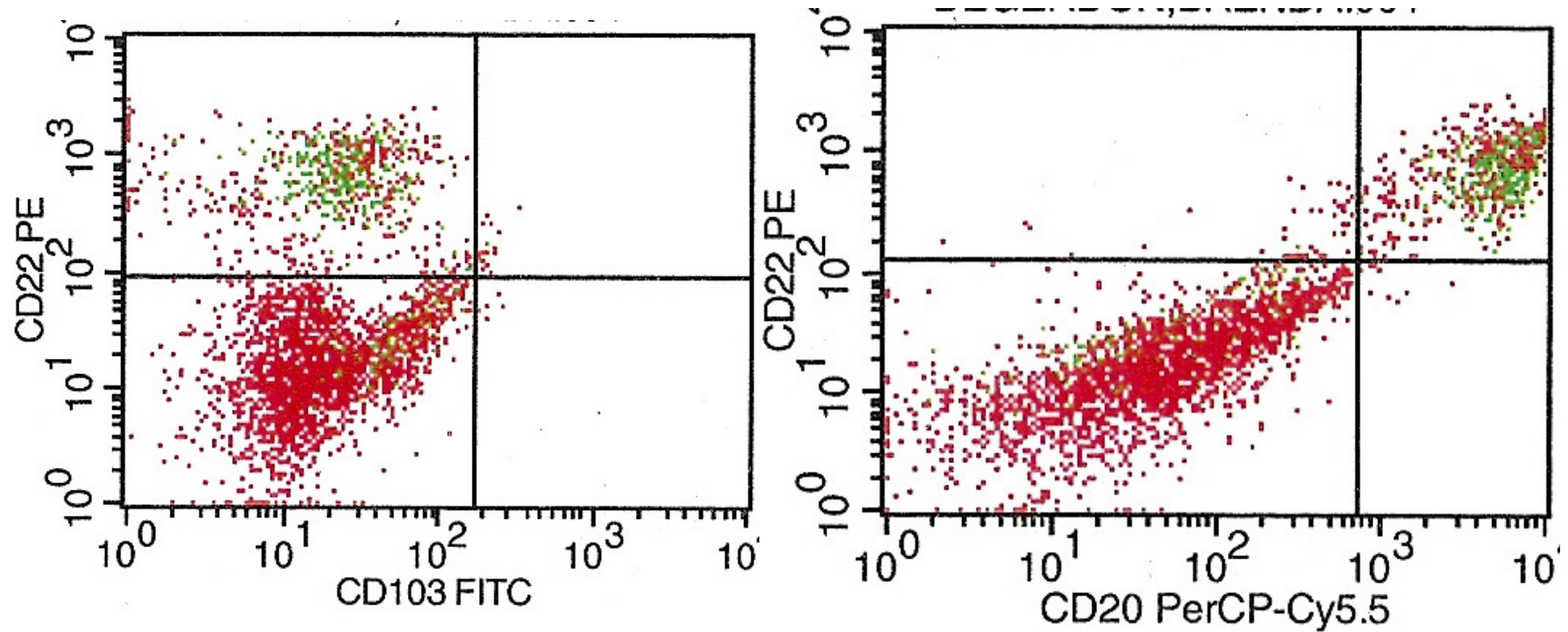


Aberrant co-expression CD5/CD19



Cells carry CD19

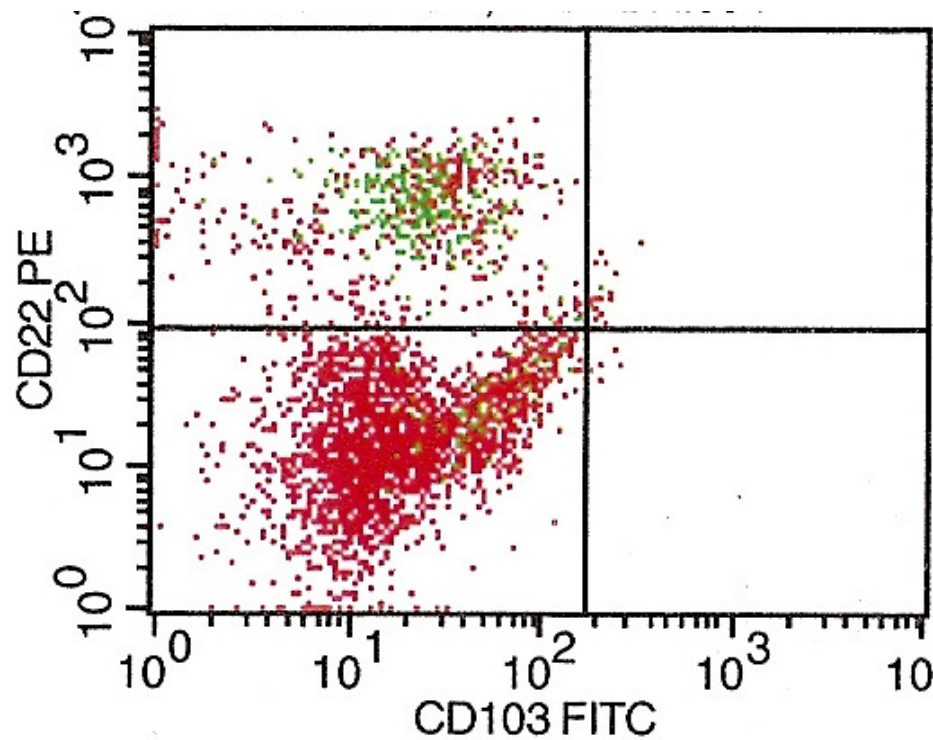
CD22/CD103 – CD22/CD20



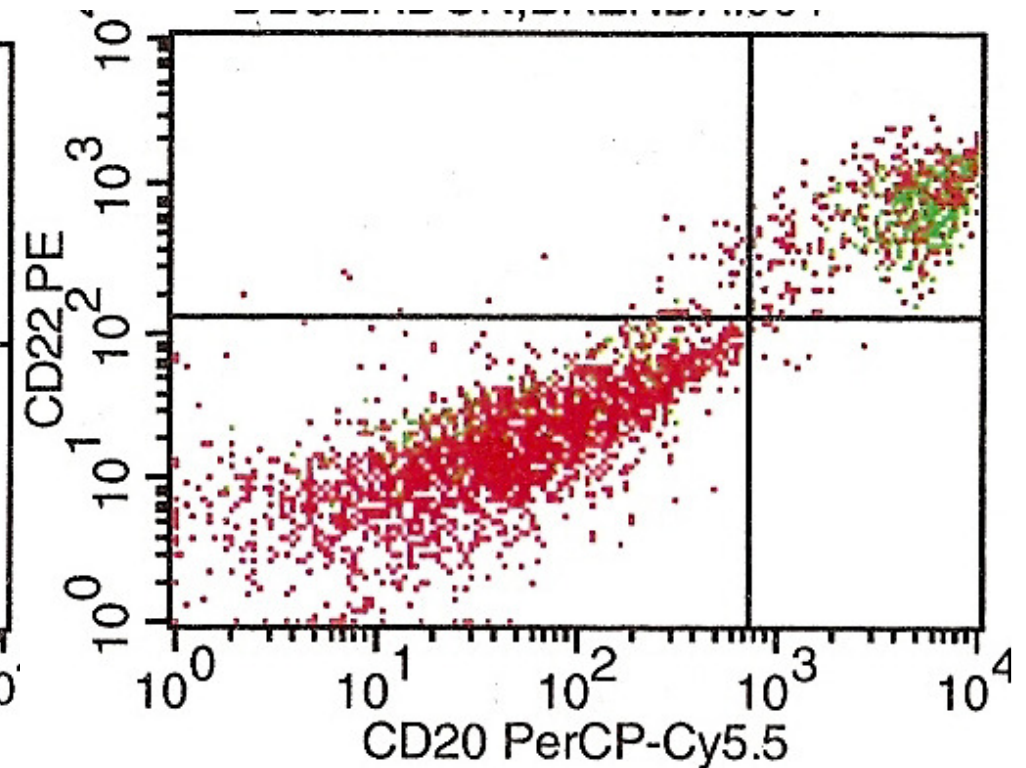
CD22/CD103 – CD22/CD20

CD103 – hairy cell marker

CD22 – early B-cell marker

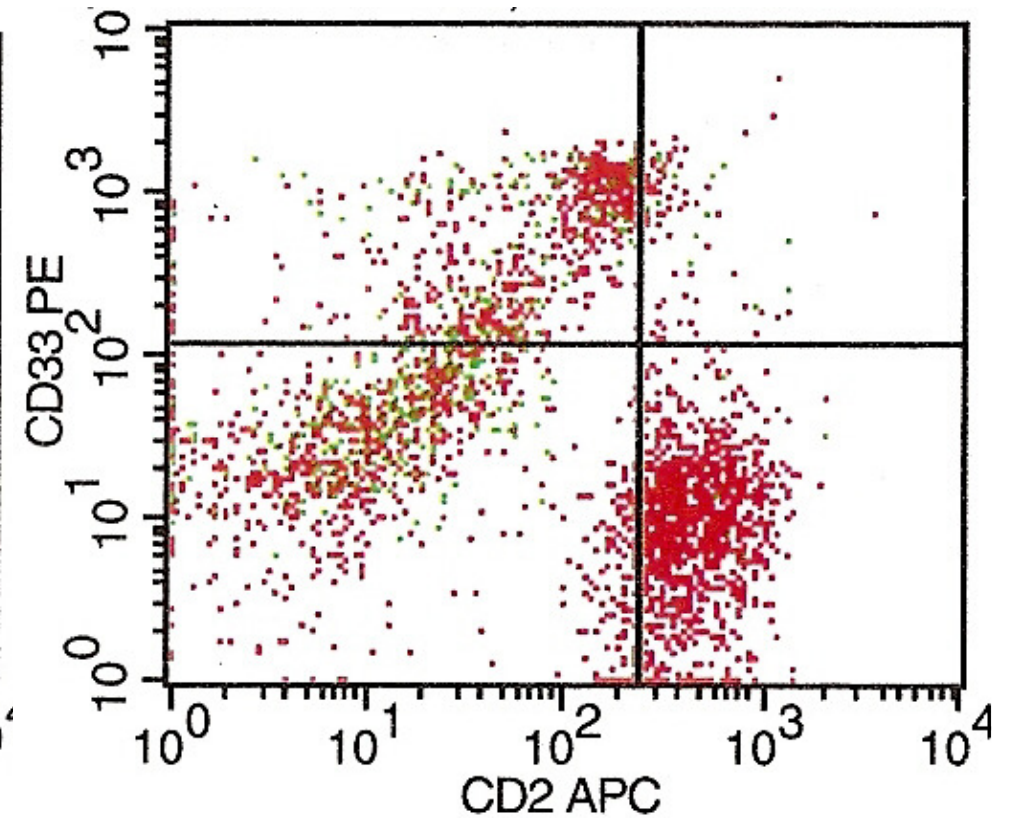
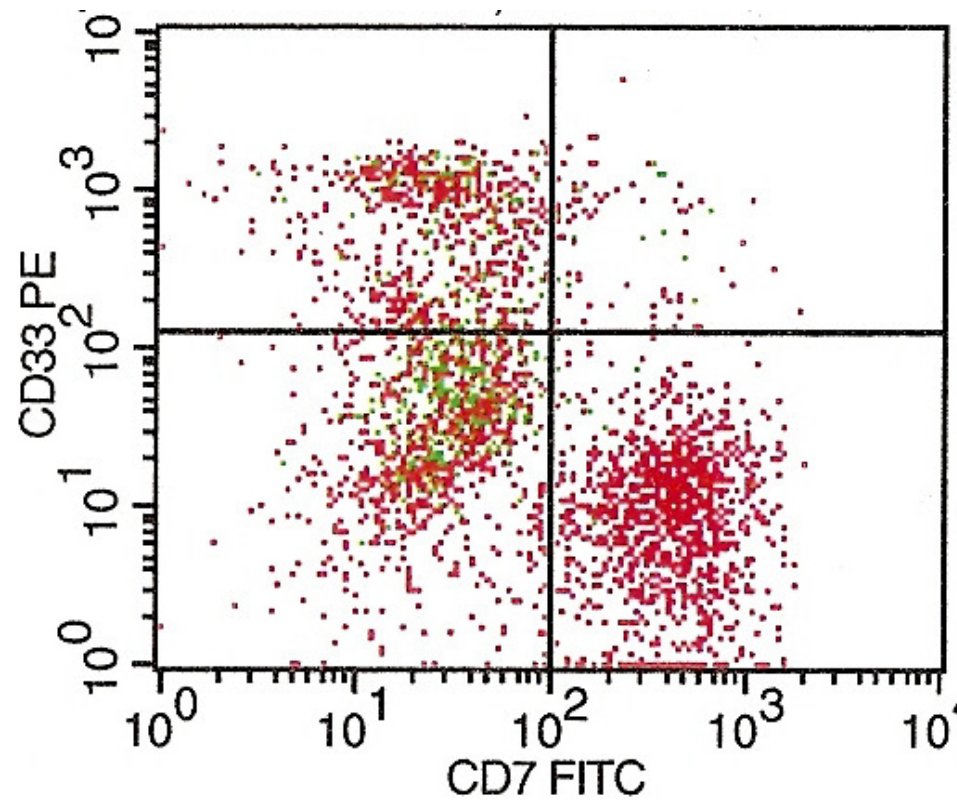


Not HCL



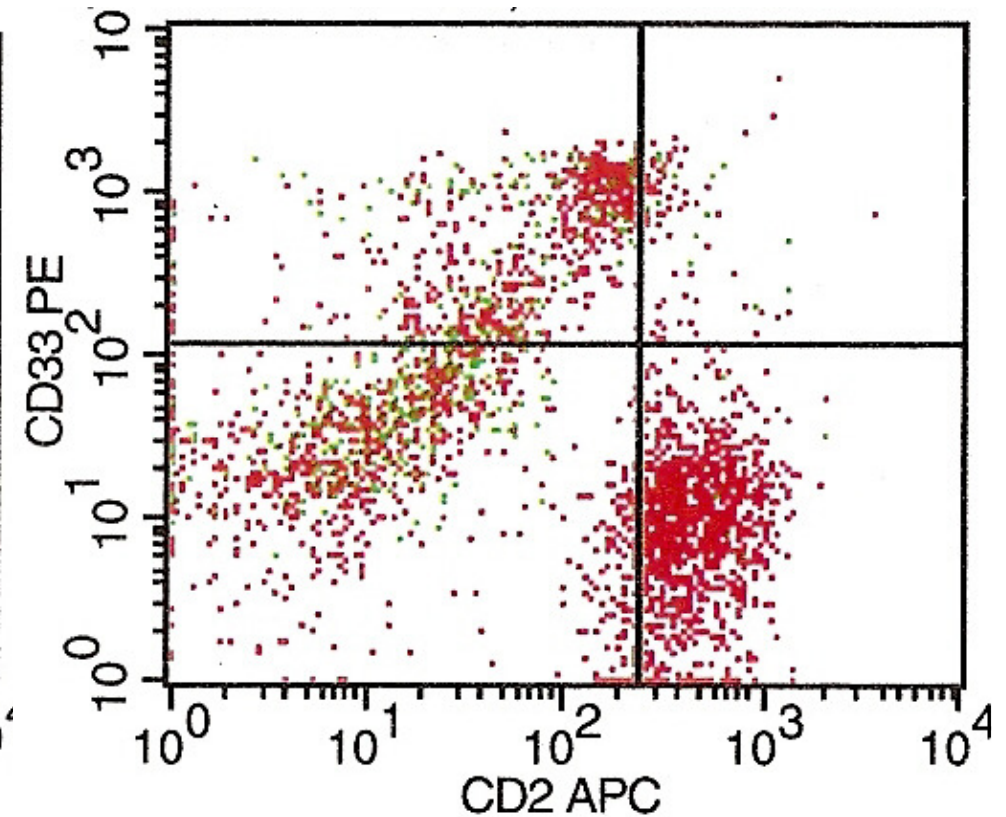
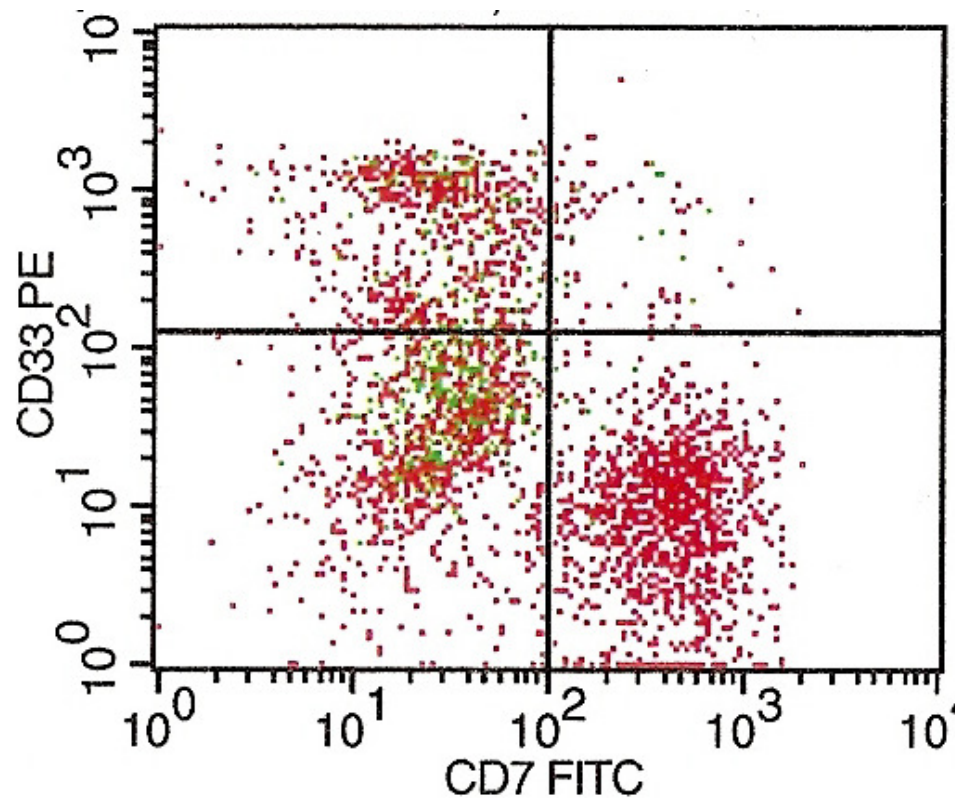
CD20 and CD22 positive cells

CD33/CD7 – CD33/CD2



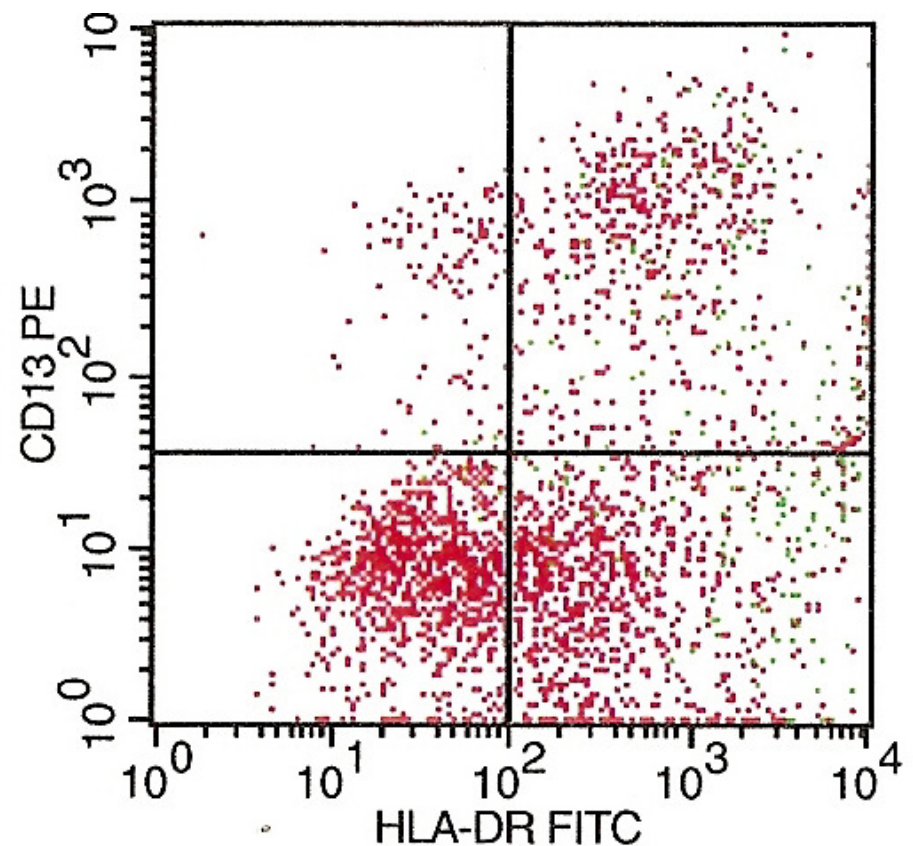
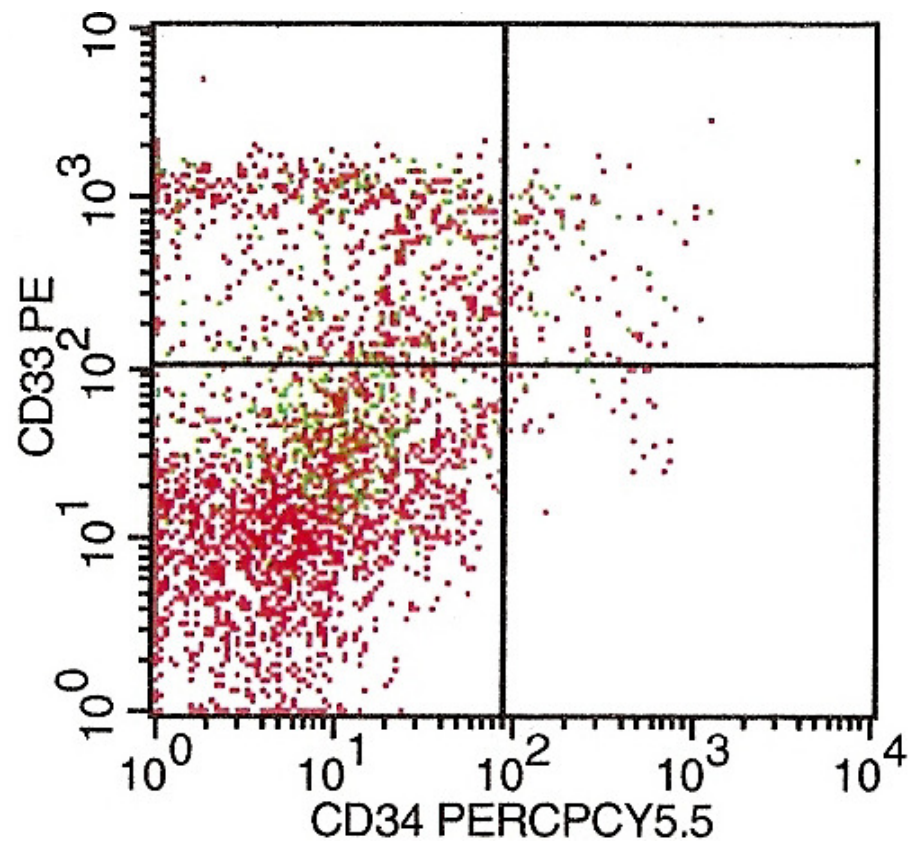
CD33/CD7 – CD33/CD2

Early Myeloid marker CD33



Not carrying the CD33 myeloid marker

CD33/CD34 – CD13/HLA-DR

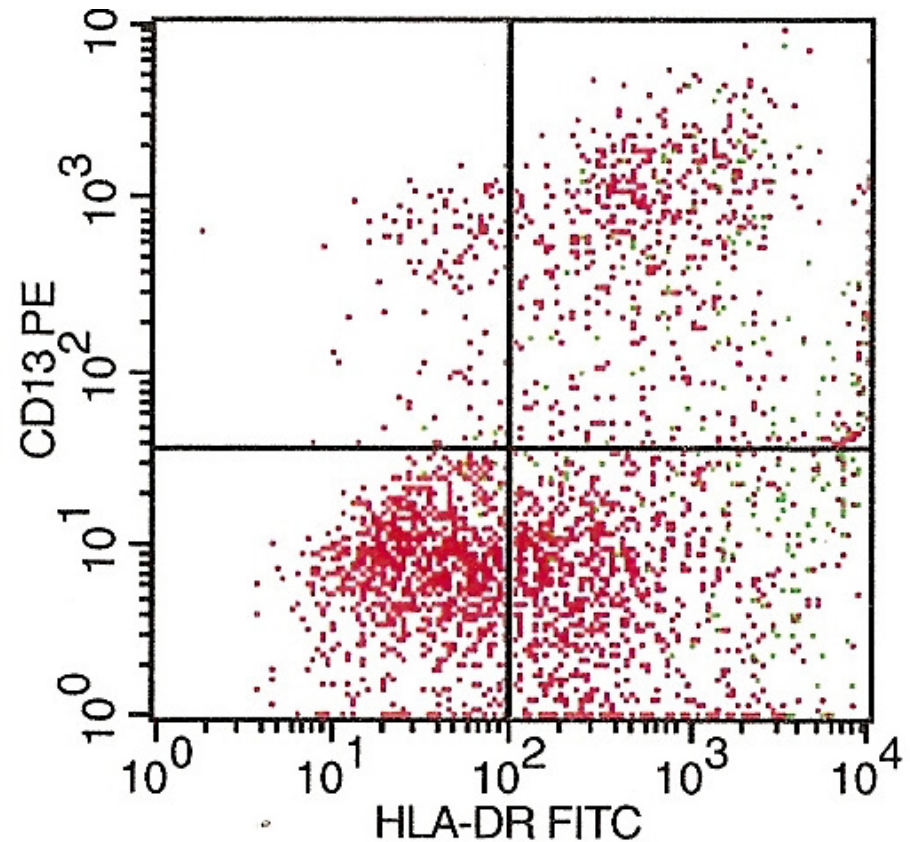
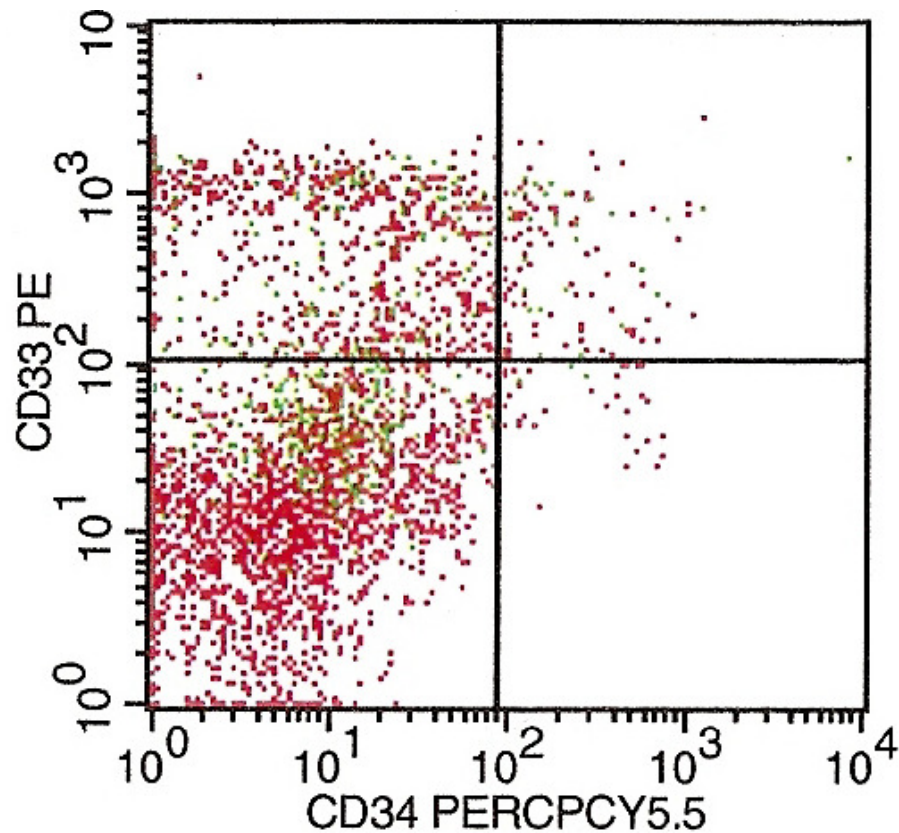


CD33/CD34 – CD13/HLA-DR

CD34 – stem cell marker

CD13 – early myeloid marker

HLA-DR – immature cells

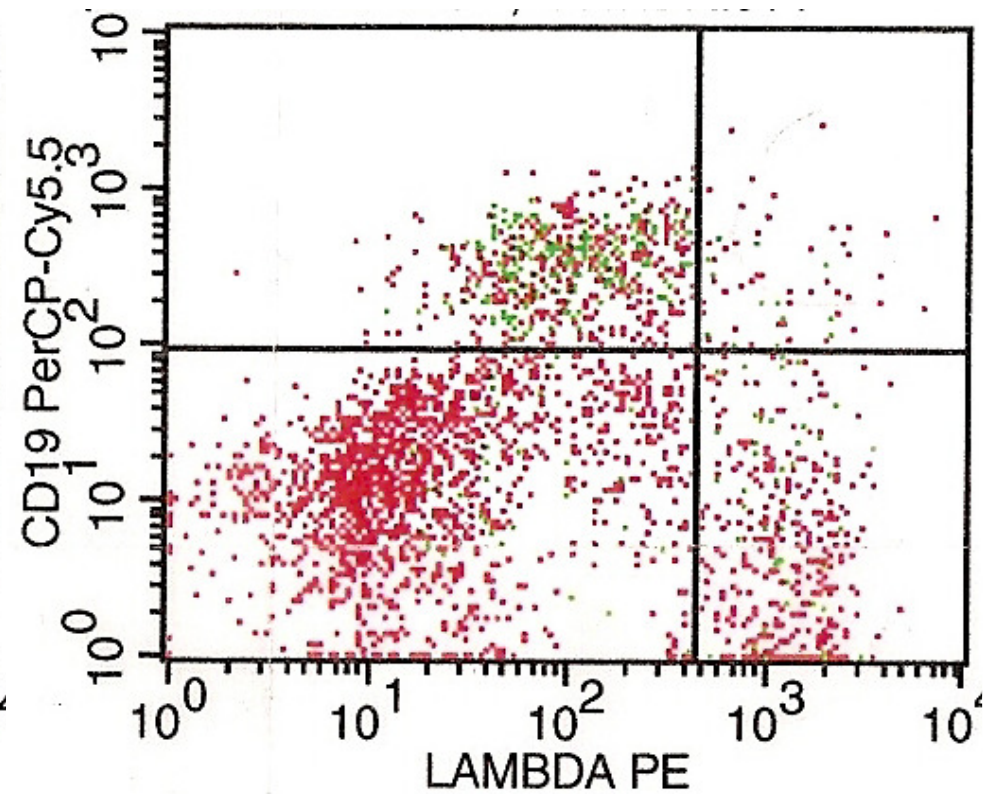
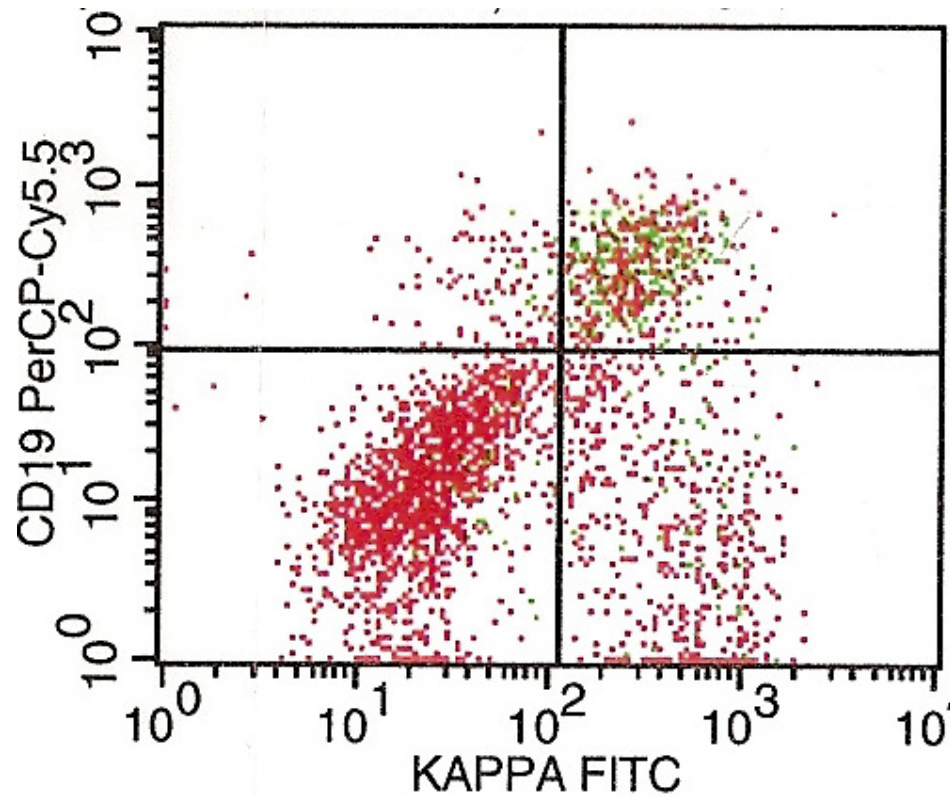


Not carrying CD34, but HLA-DR

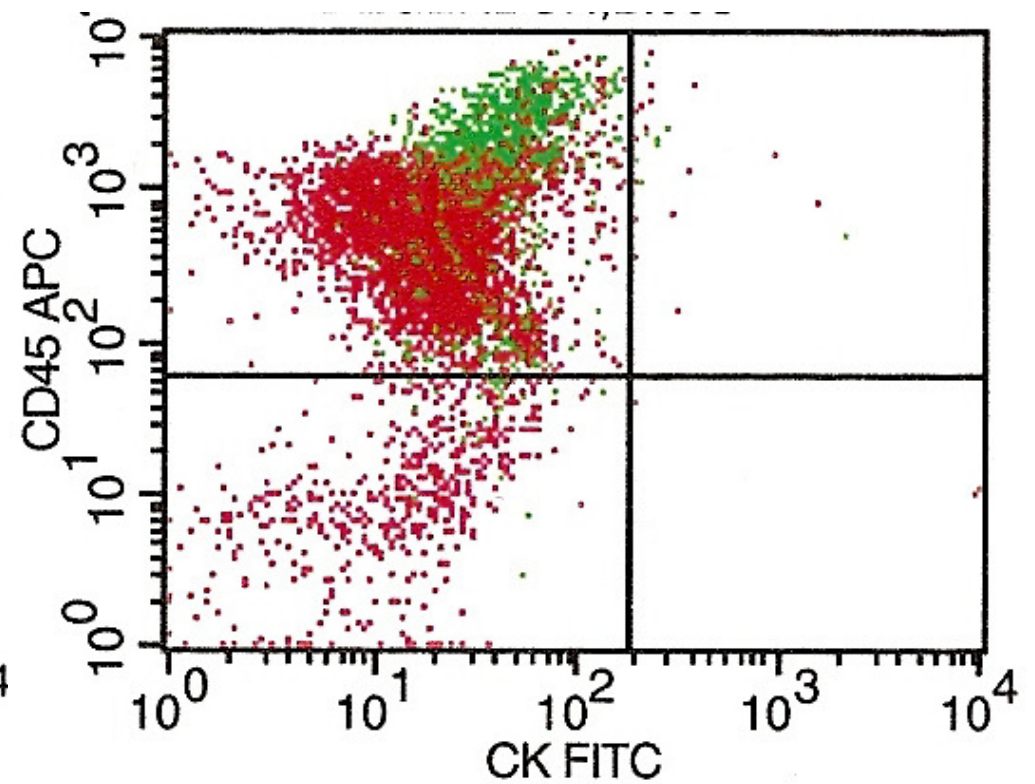
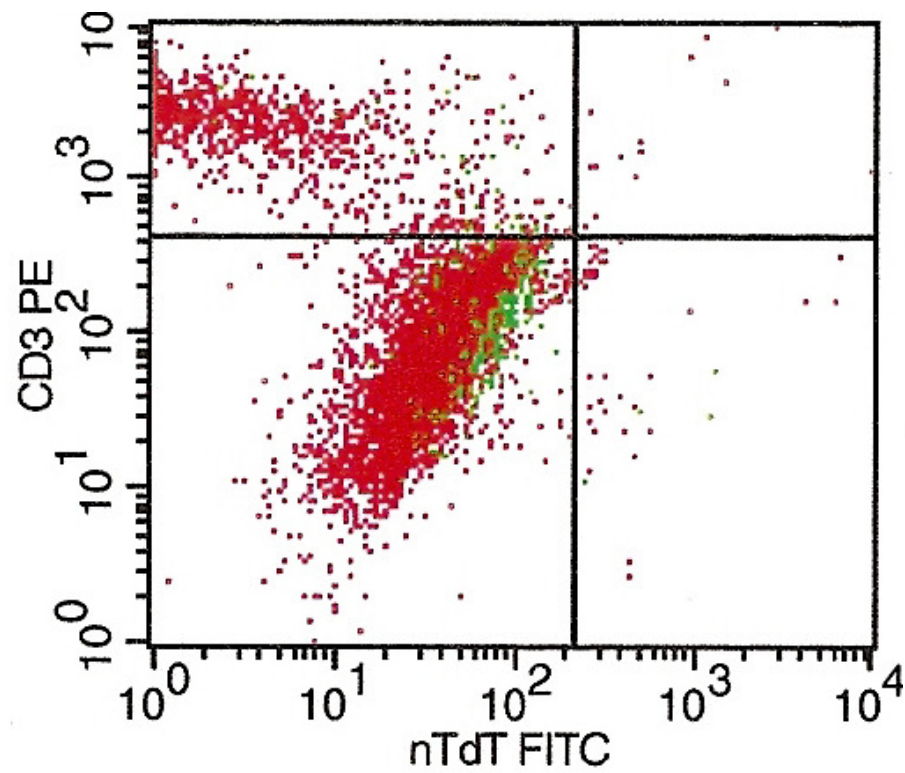
CD19/ κ – CD19/ λ

Kappa Light chains at 5.29%

Lambda Light chains at 0.63%



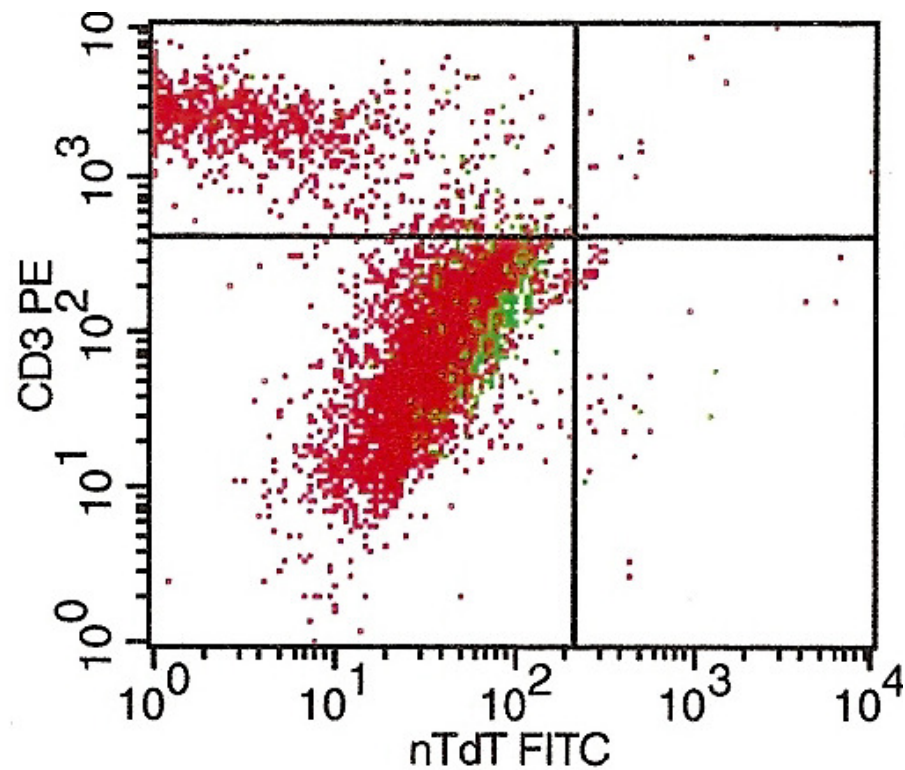
CD3/TdT – CD45/CK



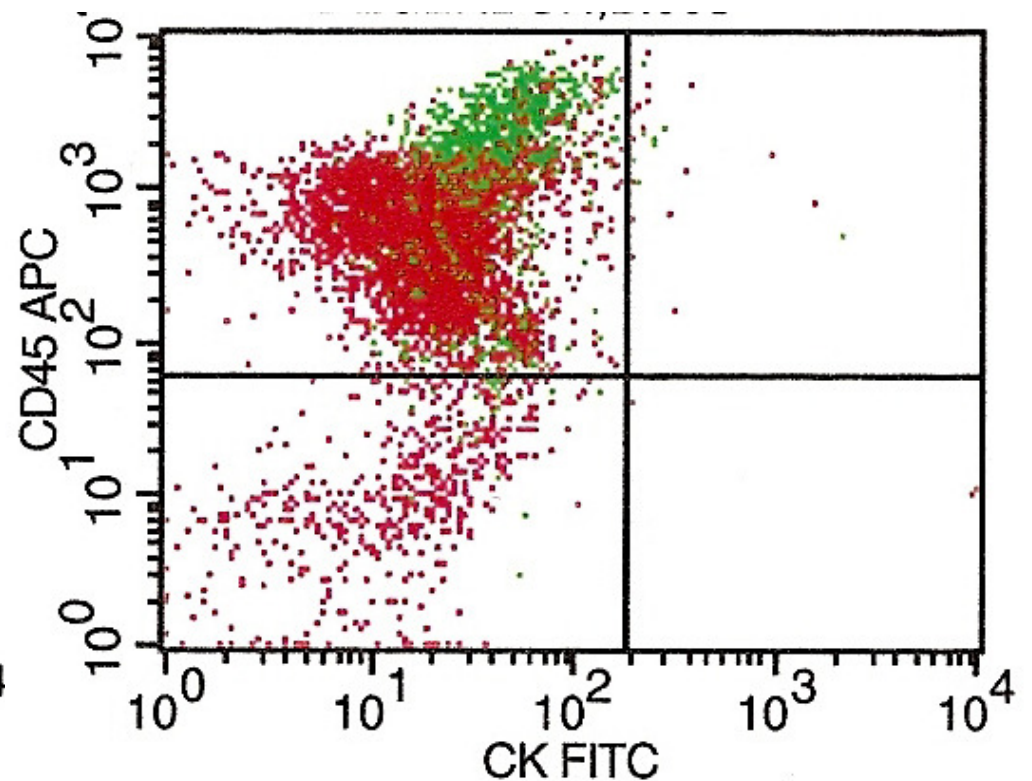
CD3/TdT – CD45/CK

CD3 – early T-cell marker
TdT – immature marker, for ALL

Cytokeratin – carcinoma
CD45 – most haematopoietic cells

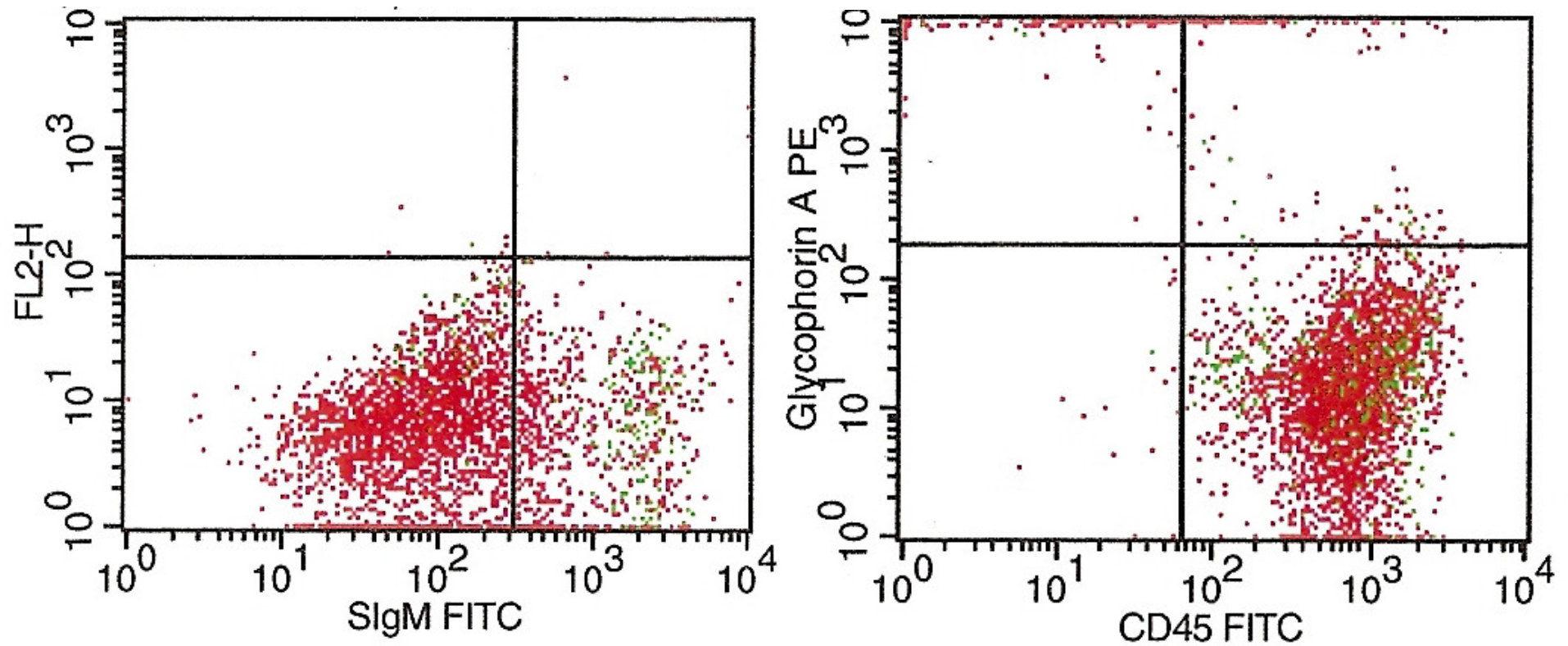


Not ALL



Not epithelial tumour

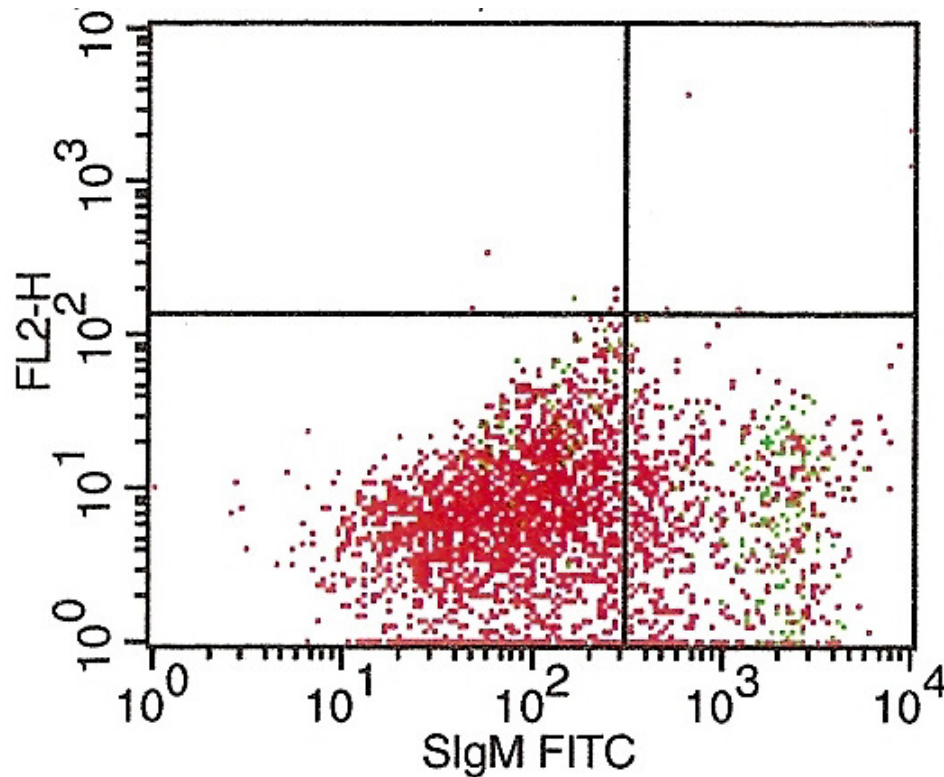
Surface IgM - Glycophorin



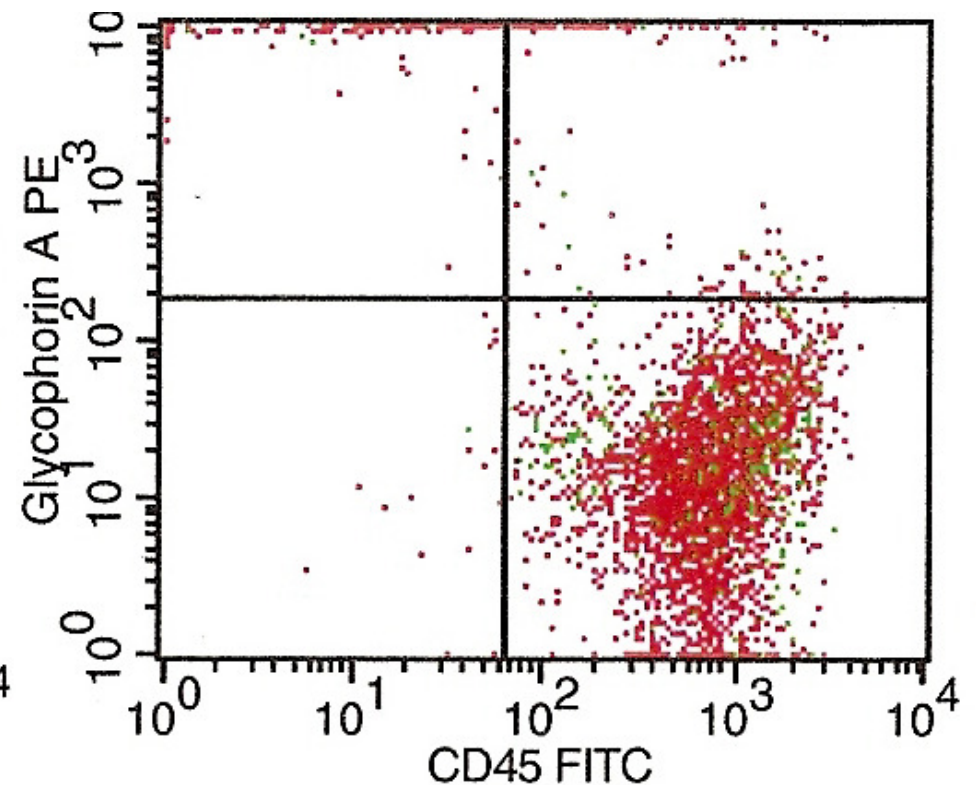
Surface IgM - Glycophorin

Surface IgM

Glycophorin A

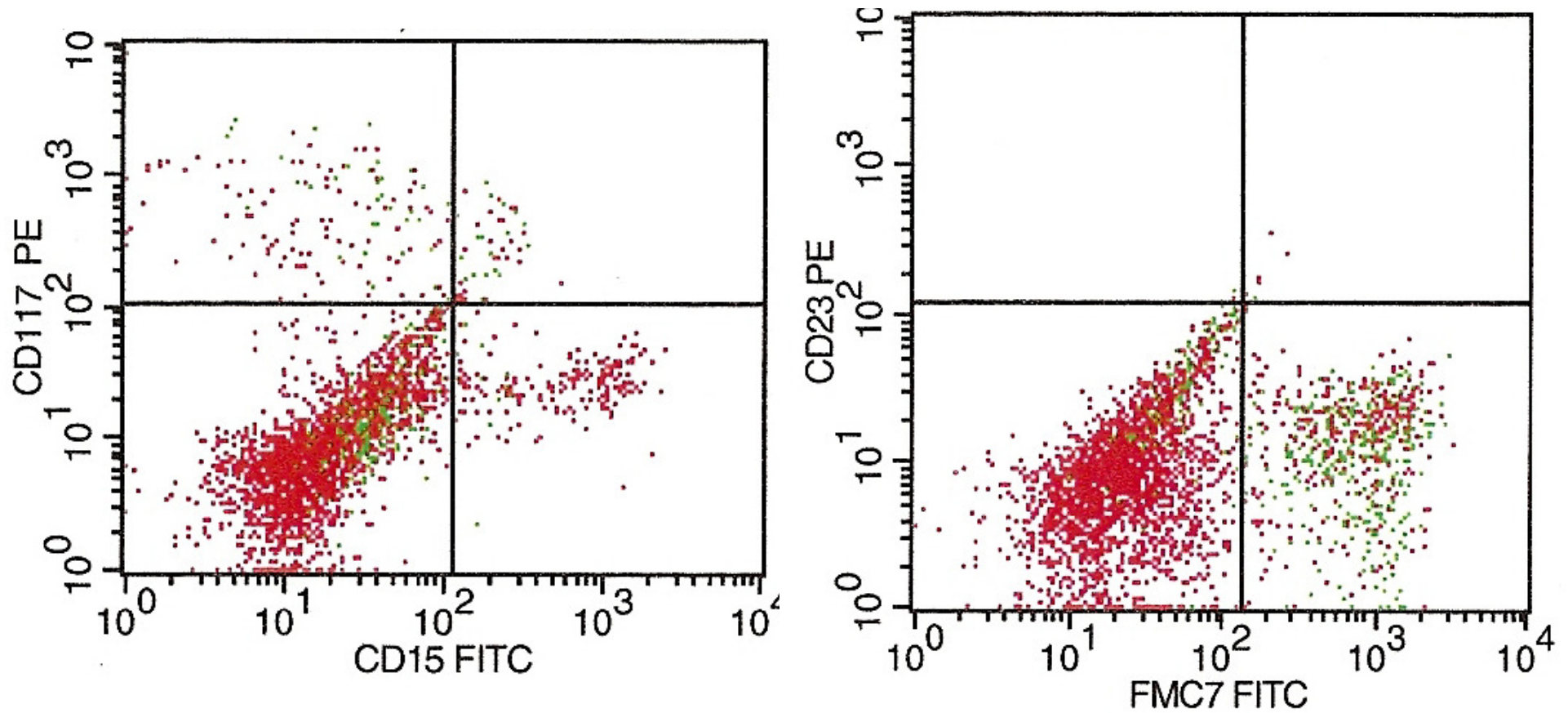


Carries surface IgM Antibodies



Not erythroid leukaemia

CD117/CD15 – CD23/FMC7

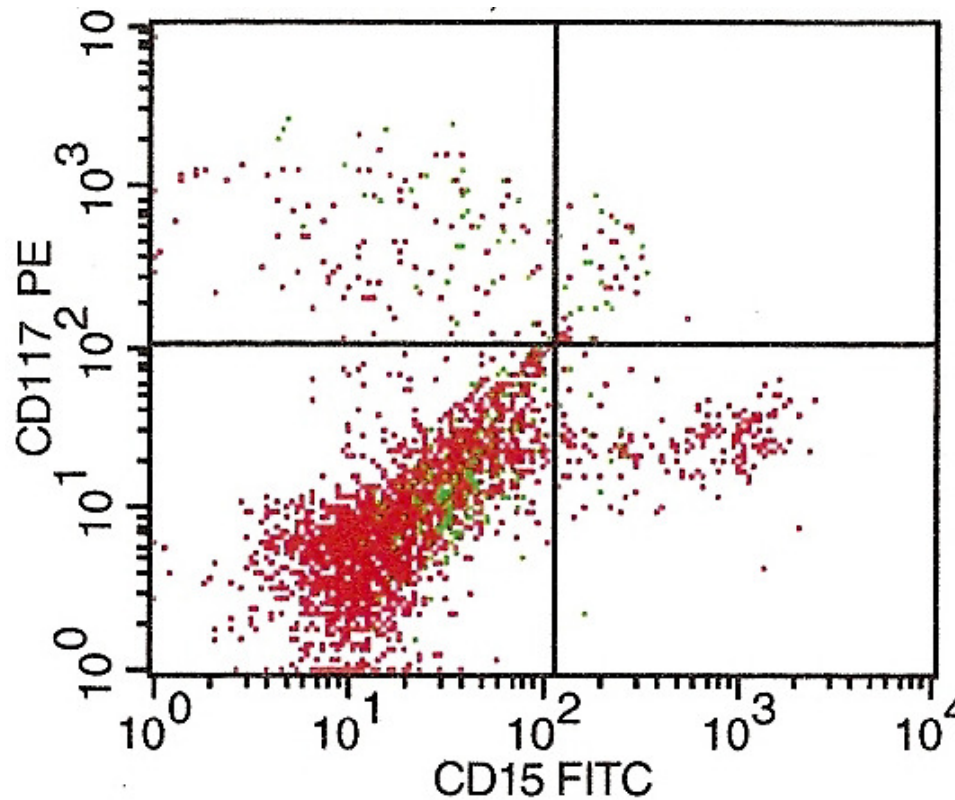


CD117/CD15 – CD23/FMC7

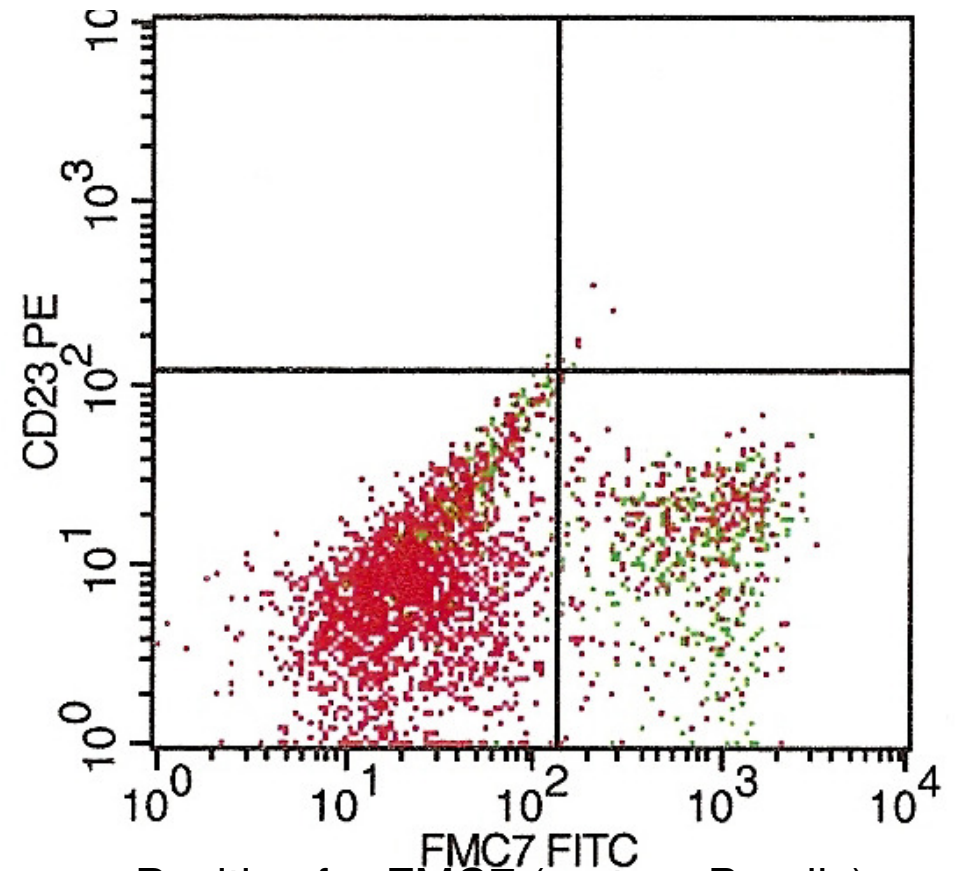
CD117 – immature myeloid cells

CD23 – B-cell marker

FMC7 – in B-NHL, but not CLL



Negative for CD117



Positive for FMC7 (mature B-cells)

Flowcytometry

T-LYMPHOID MARKERS

Cell Marker - CD2	38	%
Cell Marker - cCD3	29	%
Cell Marker - CD5	74	%
Cell Marker - CD7	40	%

B-LYMPHOID MARKERS

Cell Marker - CD10	3	%
Cell Marker - CD19	26	%
Cell Marker - CD20	20(ST)	%
Cell Marker - CD22	23(M)	%
Cell Marker - CD23	<1	%
Cell Marker - cCD79a	12	%
Cell Marker - FMC7	21	%
Cell Marker - sIgM	26(ST)	%
Cell Marker - Kappa:Lambda	10K:1L	

MYELOID MARKERS

Cell Marker - CD13	29	%
Cell Marker - CD14	15	%
Cell Marker - CD33	27	%
Cell Marker - cMPO	31	%
Cell Marker - CD64	25	%
Cell Marker - Glycophorin A	9	%
Cell Marker - CD41A	9	%

IMMATURE STEM CELL MARKERS

Cell Marker - CD117	4	%
Cell Marker - nTdT	<1	%
Cell Marker - CD34	5	%

DOUBLE CELL MARKERS

Cell Marker - CD5:CD19	20	%
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OTHERS

Cell Marker - CD45	95	%
Cell Marker - CD103	<1	%
Cell Marker - HLA-DR	60	%

Conclusion

- Interstitial and intrasinusoidal infiltrate of large lymphoblasts, suggestive of a diffuse large B-cell lymphoma with high proliferation index (> 90%)
 - CD19 pos, CD20 pos, CD22 pos, IgM pos, Kappa light chain restricted, FMC-7 pos, aberrant expression of CD5
- The possibility of an intravascular lymphoma with possible cerebral involvement should be raised