INTERESTING CASES IN HEMATOLOGY

February 16, 2012

1. What is the specificity of DCIP test in screening for HbE?

	DCIP+	DCIP-	
HbE	185	15	200
Not HbE	20	80	100
	205	95	300

- A. 80%
- B. 84.2%
- C. 88.3%
- D. 90.2%
- E. 92.5%

Diagnostic accuracy of test

	Disease+	Disease-	
Test+	TP	FP	TP+FP
Test-	FN	TN	FN+TN
	TP+FN	FP+TN	Total

- Sensitivity = TP/TP+FN
- Specificity = TN/TN+FP
- PPV = TP/TP+FP
- NPV = TN/TN+FN
- Accuracy = TP+TN/total

Diagnostic accuracy of DCIP test

	DCIP+	DCIP-	
HbE	185	15	200
Not HbE	20	80	100
	205	95	300

- Sensitivity = 185/200 = 92.5%
- Specificity = 80/100 = 80%
- PPV = 185/205 = 90.2%
- NPV = 80/95 = 84.2%
- Accuracy = 88.3%

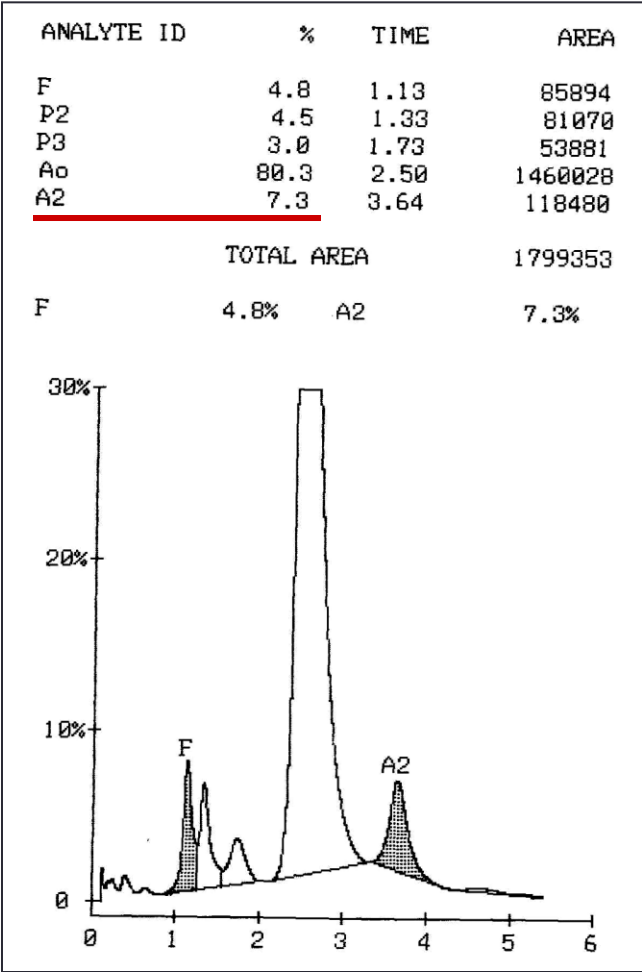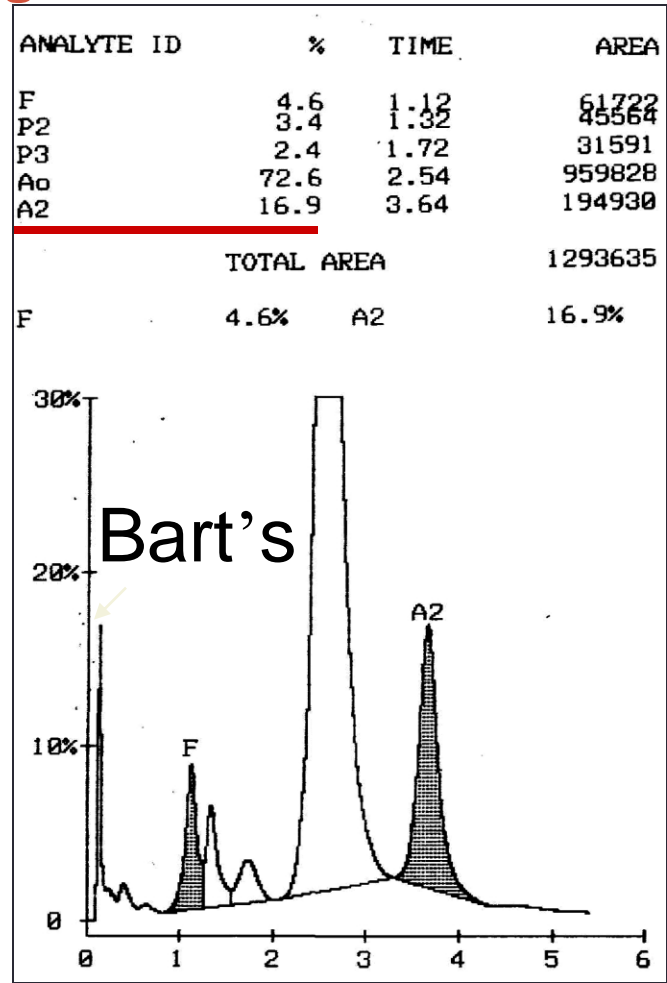# 2. A 5 yr boy of parents with α^0-thalassemia carriers

ANALYTE ID	%	TIME	AREA
F	0.3	1.10	6209
P2	4.8	1.32	86891
P3	3.2	1.70	57290
Ao	88.8	2.48	1593268
A2	2.7	3.60	43974
TOTAL AREA			1787632
F	0.3%	A2	2.7%
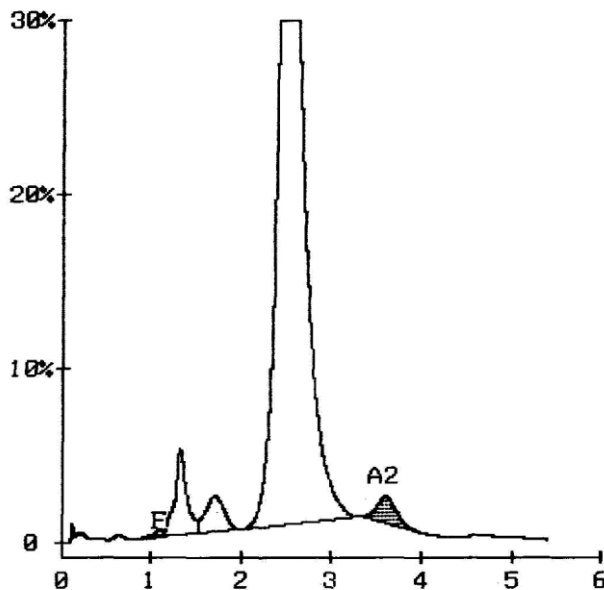
- What is a risk of α^0-thalassemia carrier of this child?
- A. 0%
- B. 25%
- C. 33%
- D. 50%
- E. 67%

3. A couple came to pre-natal diagnosis clinic. Their Hb analysis were shown. They had a fetus with Hb Bart's hydrops fetalis at previous gestation.

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ANALYTE ID        %     TIME          AREA
F                4.6    1:12         61722
P2               3.4    1:32         45564
P3               2.4    1.72         31591
Ao              72.6    2.54        959828
A2              16.9    3.64        194930

                TOTAL AREA          1293635

F        4.6%    A2              16.9%
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Bart's

A2

F

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ANALYTE ID        %     TIME          AREA
F                4.8    1.13         85894
P2               4.5    1.33         81070
P3               3.0    1.73         53881
Ao              80.3    2.50       1460028
A2               7.3    3.64        118480

                TOTAL AREA          1799353

F        4.8%    A2               7.3%
```

F

A2

Risk of Hydrops?

A. 0%

B. 25%

C. 50%

D. 75%

E. 100%

Hb 8.9 g/dL MCV 66 fL RDW 20%

Hb 11.2 g/dL MCV 68 fL RDW 14.5%
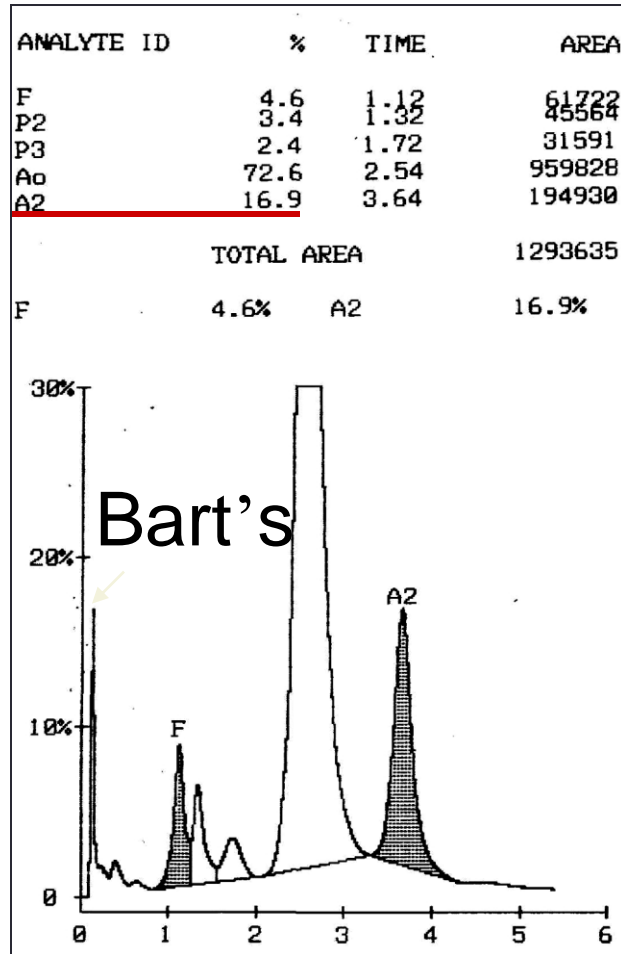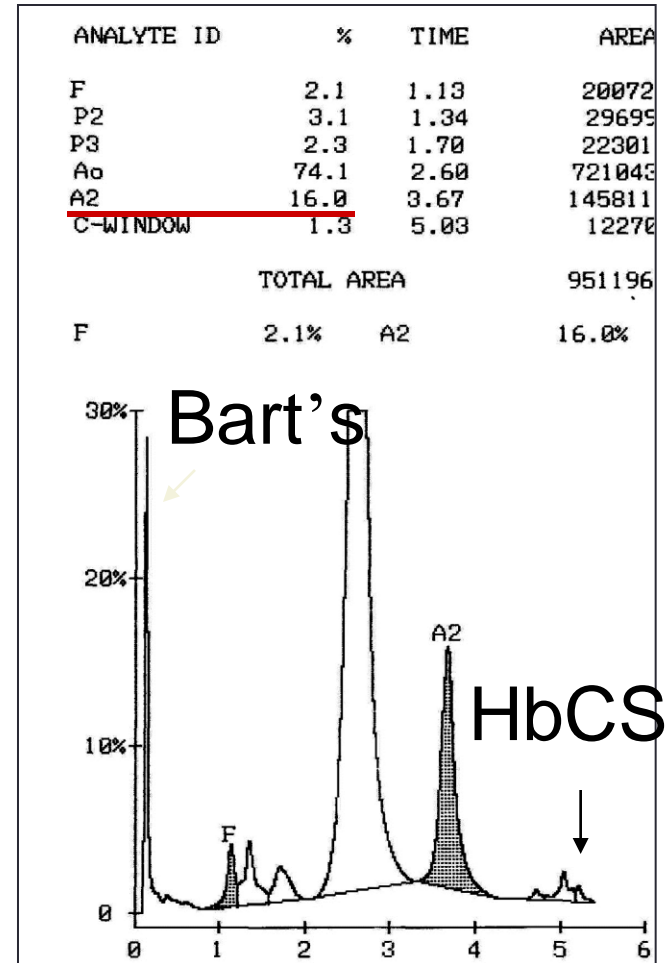
Hb A_2 < 3.5%

Hb E syndromes

E < 25%
Suggests
α-thal
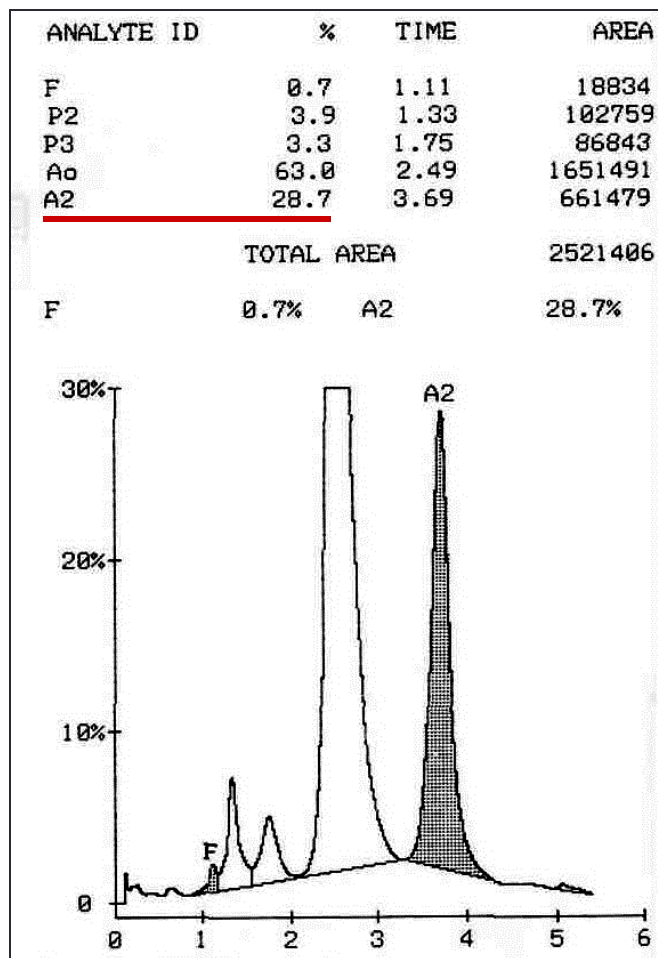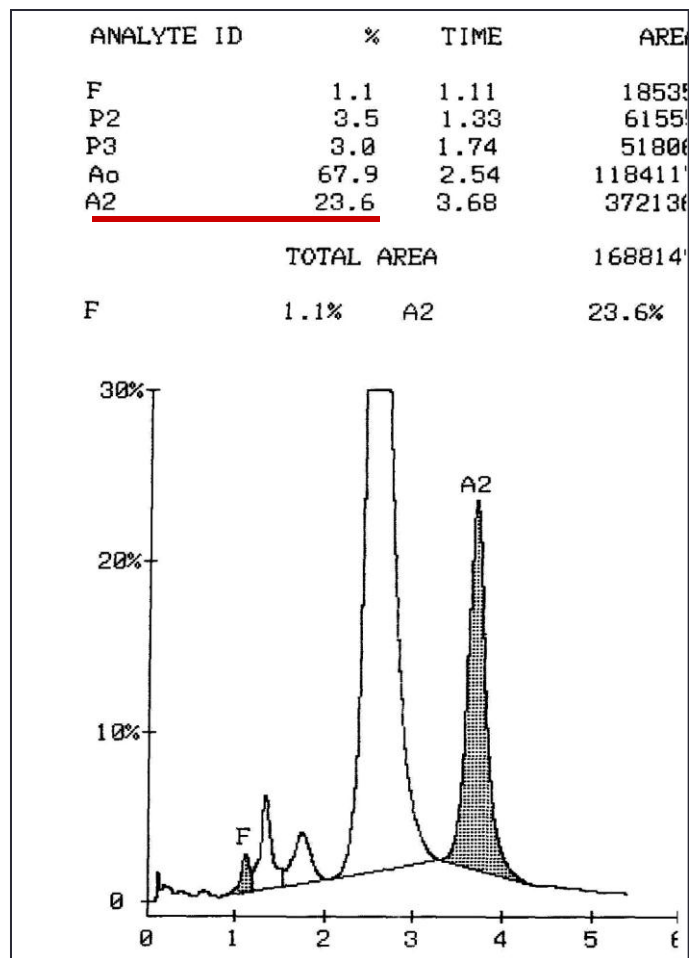
HbE trait

HbE with α-thal-1

Hb E trait with α thalassemia

AEBart's disease
(HbH+HbE trait)

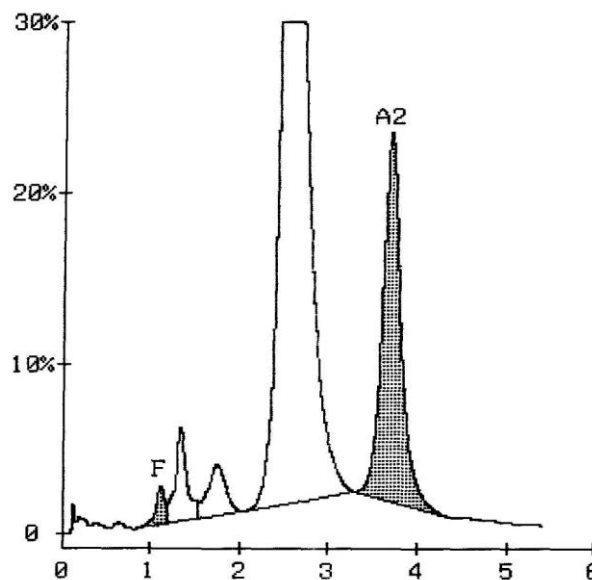

AEBart's with HbCS
(HBHCS+HbE trait)

EFBart's diseases

ANALYTE ID	%	TIME	AREA
F	11.4	1.16	241249
P3	3.4	1.77	71494
Ao	3.8	2.27	78951
A2	84.6	3.72	1623735
	TOTAL AREA		2015429

F   11.4%   A2   84.6%

Bart's

HbH

ANALYTE ID	%	TIME	AREA
F	28.4	1.16	265747
P3	1.9	1.76	18001
Ao	2.5	2.24	23616
A2	65.1	3.68	545550
	TOTAL AREA		852914

F   28.4%   A2   65.1%

Bart's

HbH
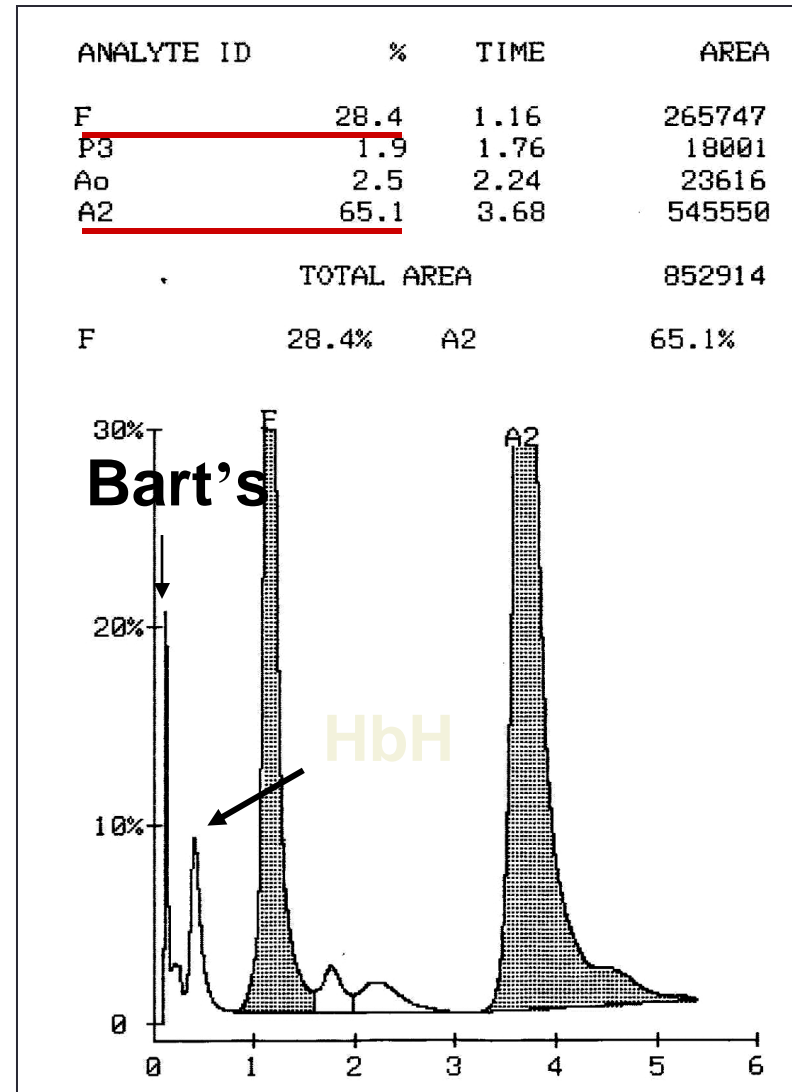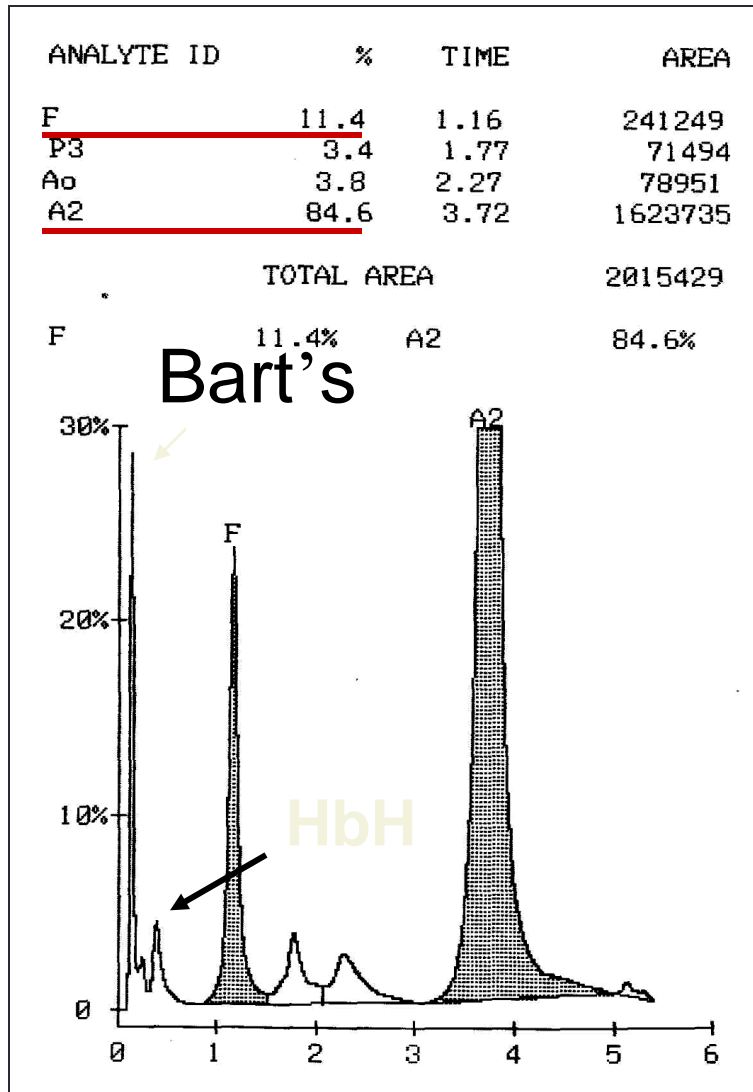
HbH + HomoE or β^0-thal/HbE

4. A couple came to pre-natal diagnosis clinic. Their Hb analysis were showed.

ANALYTE ID	%	TIME	AREA
F	1.1	1.11	18535
P2	3.5	1.33	61559
P3	3.0	1.74	51800
Ao	67.9	2.54	1184111
A2	23.6	3.68	372136

TOTAL AREA   1688141

F   1.1%   A2   23.6%

ANALYTE ID	%	TIME	AREA
F	3.1	1.13	45372
P2	3.9	1.33	53239
P3	2.3	1.71	32015
Ao	86.2	2.55	1184654
A2	2.1	3.61	24735
C-WINDOW	2.3	5.04	31089

TOTAL AREA   1371104

F   3.1%   A2   2.1%

Bart's   HbCS

Risk of Hydrops?

A. 0%
B. 25%
C. 50%
D. 75%
E. 100%

Hb 13.9 g/dL MCV 70 fL
RDW 14.9%
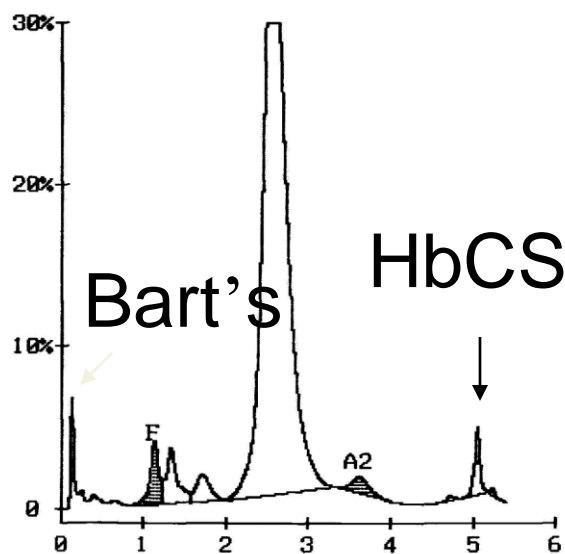
Hb 10.4 g/dL MCV 77 fL
RDW 14%

Hb CS syndromes

ANALYTE ID	%	TIME	AREA
P2	3.9	1.32	69273
P3	2.2	1.71	39968
Ao	90.5	2.48	1626171
A2	2.2	3.60	35116
C-WINDOW	1.1	5.05	20539
TOTAL AREA			1791067

F   0.0%   A2   2.2%
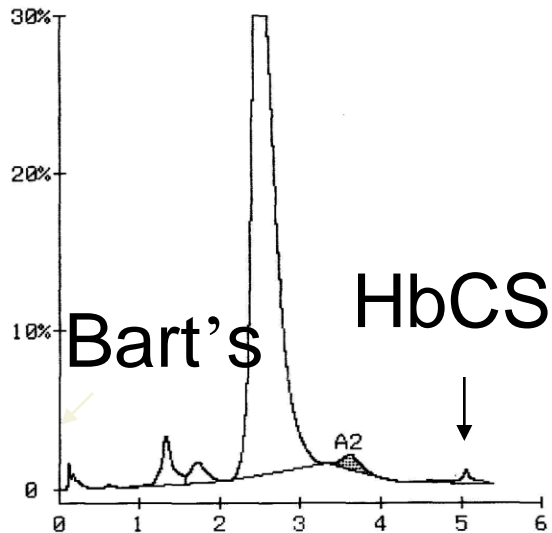
ANALYTE ID	%	TIME	AREA
F	3.1	1.13	45372
P2	3.9	1.33	53239
P3	2.3	1.71	32015
Ao	86.2	2.55	1184654
A2	2.1	3.61	24735
C-WINDOW	2.3	5.04	31089
TOTAL AREA			1371104

F   3.1%   A2   2.1%
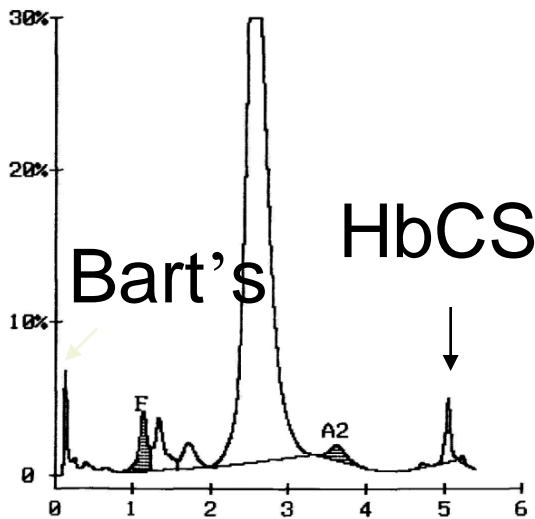
ANALYTE ID	%	TIME	AREA
F	0.3	0.94	2780
P2	3.3	1.32	30244
P3	2.5	1.70	22474
Ao	89.1	2.55	811499
A2	3.5	3.59	27378
C-WINDOW	1.4	5.04	12449
TOTAL AREA			906824

F   0.3%   A2   3.5%
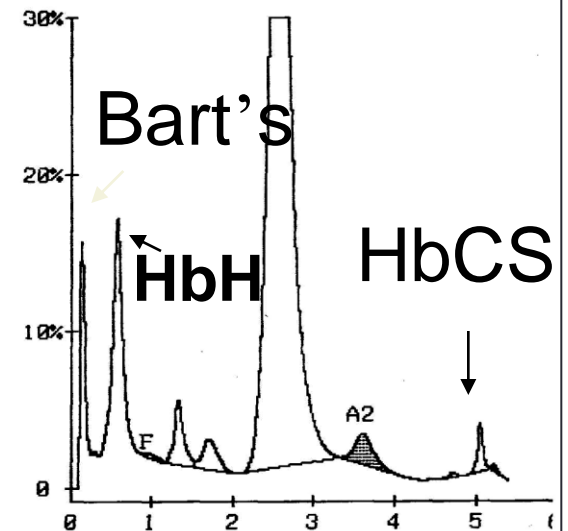
HbCS trait   **Homozygous HbCS**   **HbHCS**

5. What is your diagnosis?
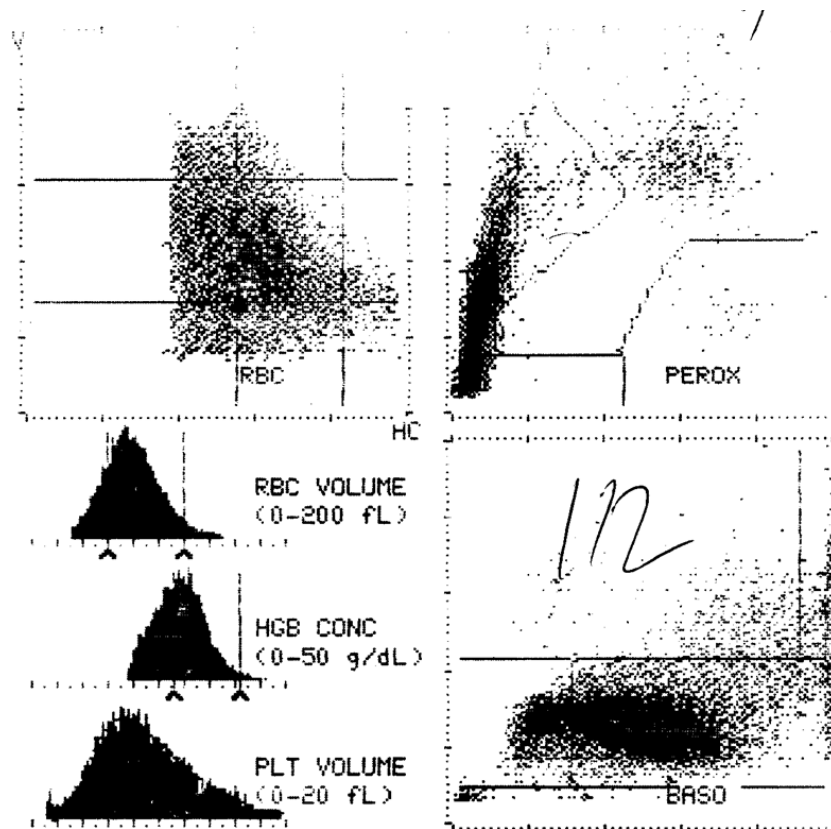
A. AIHA

B. Hereditary spherocytosis

C. Thalassemia post-splenectomy

D. Acute myeloid leukemia

E. Chronic lymphocytic leukemia

6. What is your diagnosis?
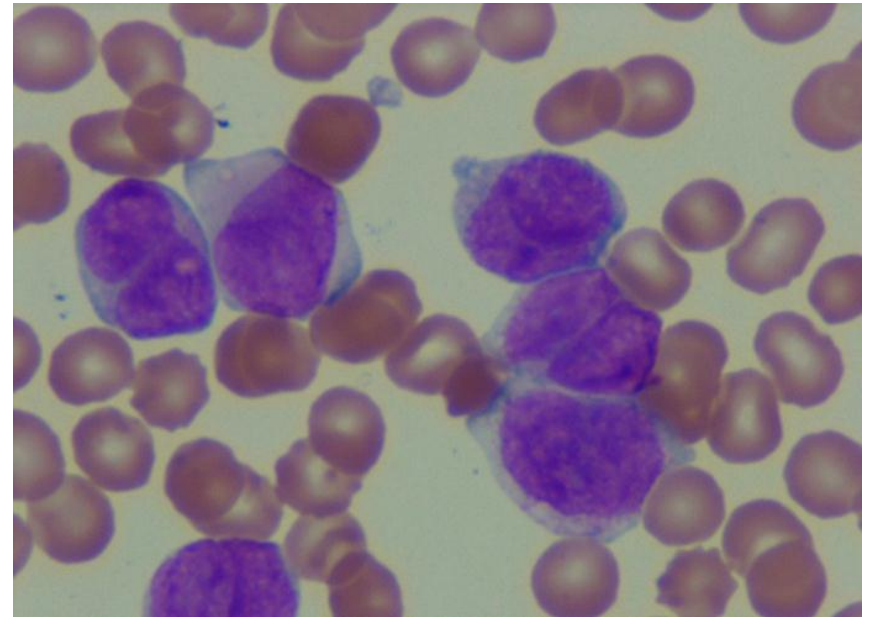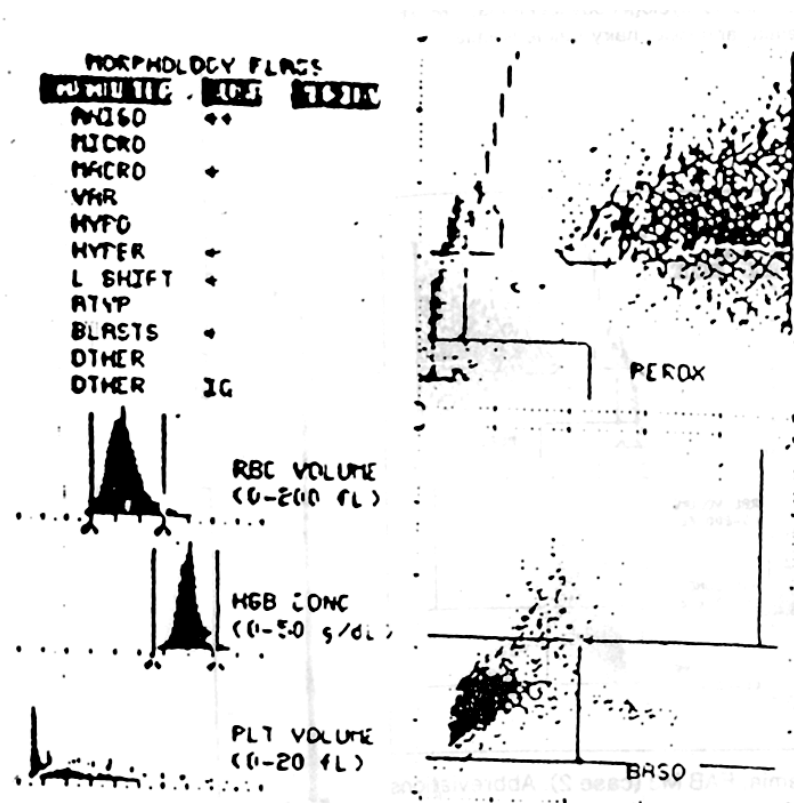
A. Acute promyelocytic leukemia
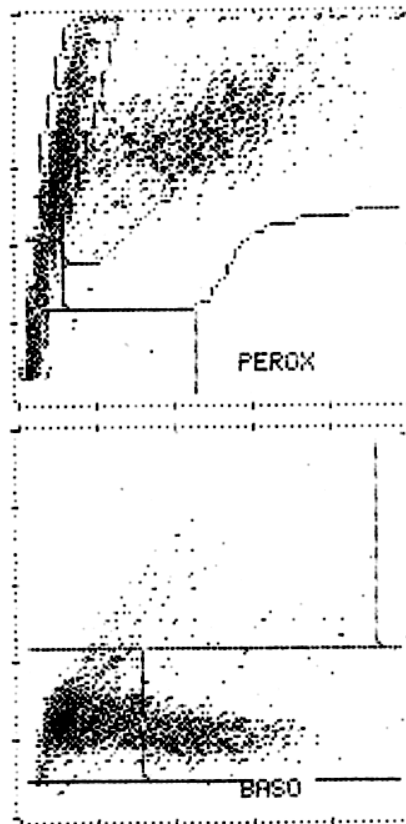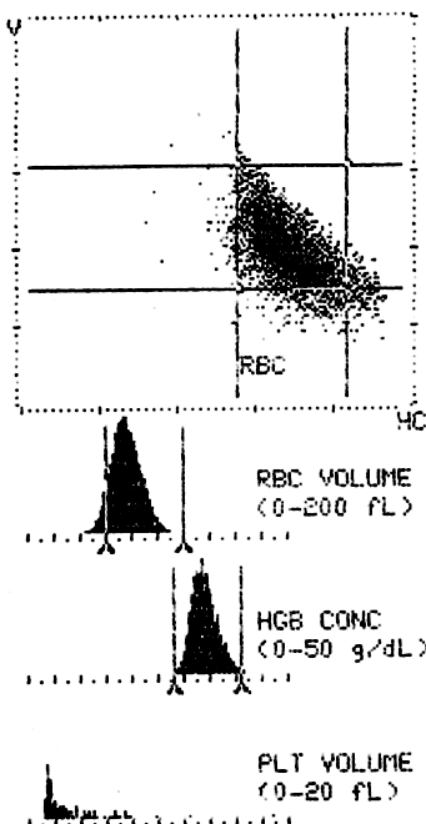C. Chronic myelomonocytic leukemia
E. Mantle cell lymphoma

B. Acute myelomonocytic leukemia
D. Acute lymphoblastic leukemia

APL vs CML

AML M2 vs AML M4

7. A 30 y/o Thai mail with HbHCS.

- A. Postthrombotic syndrome
- B. Chronic leg ulcer
- C. Pythiosis
- D. Cutaneous lymphoma
- E. *Mycobacterium* infection

8. A 25-yr-old man, a known case of thalassemia major post splenectomy receiving irregular transfusion, complains dyspnea and back pain for 2 months.

A. Extramedullary hematopoiesis
B. TRALI
C. Germ cell tumor
D. Mesothelioma
E. Pulmonary aspergillosis
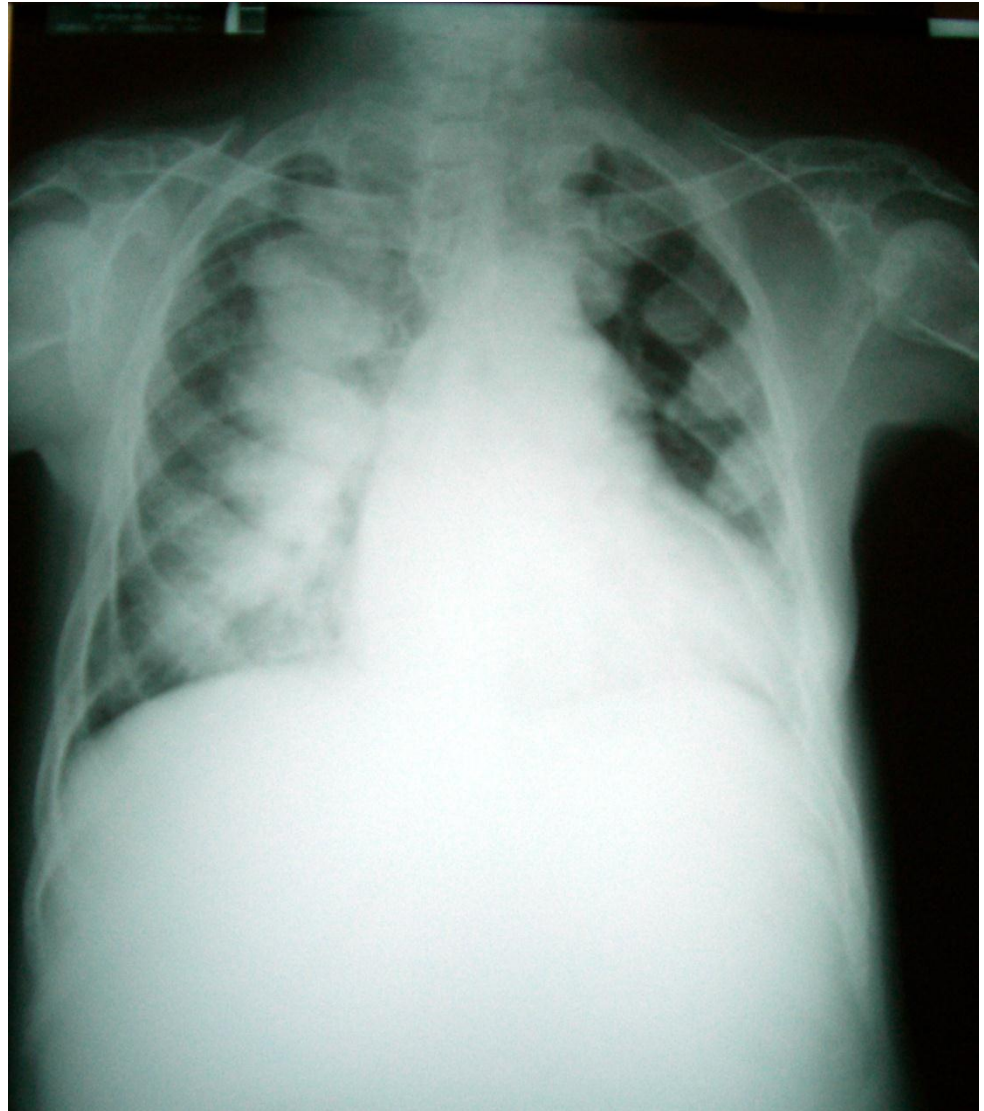
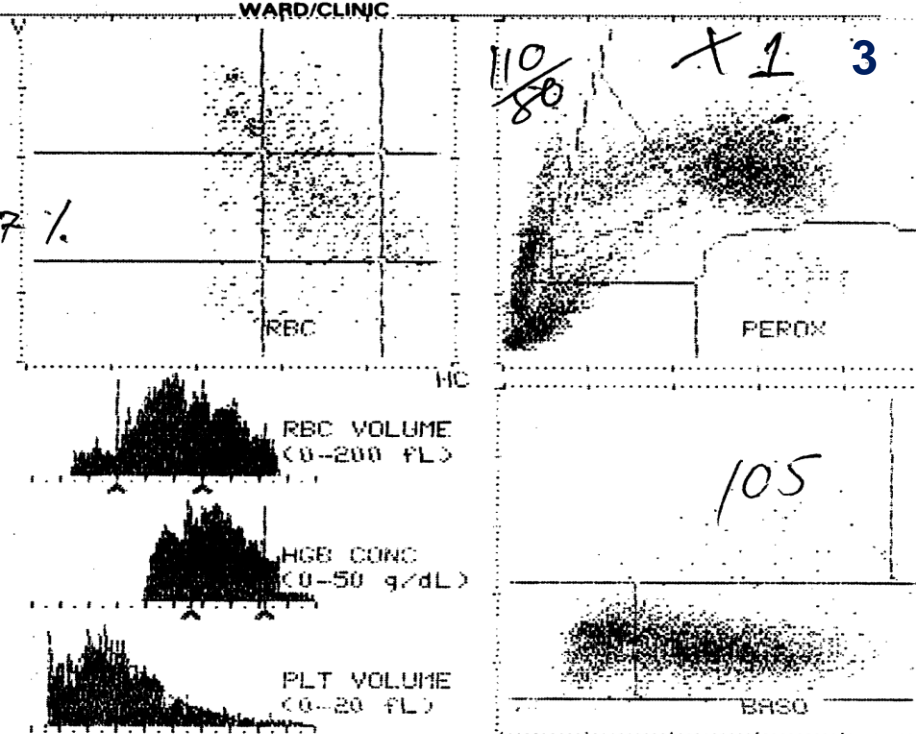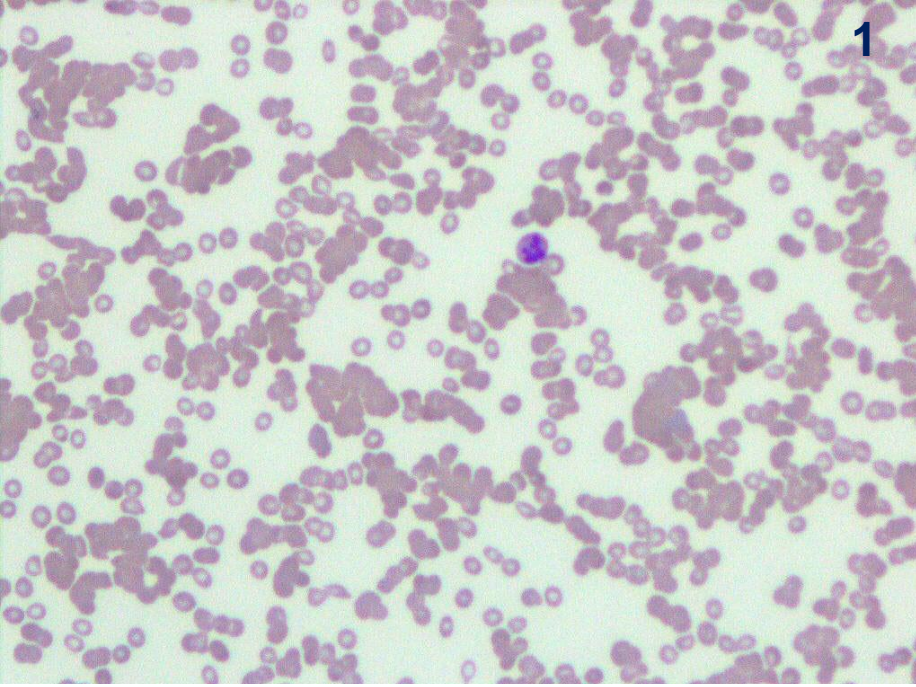# 9. A 50-yr-old woman with fever and rashes for 5 days

- CBC: RBC 0.51 x10^9/L Hb 5 g/dL Hct 4.9 % MCV 126 fL MCH 102 pg MCHC 106 g/dL RDW 25 %

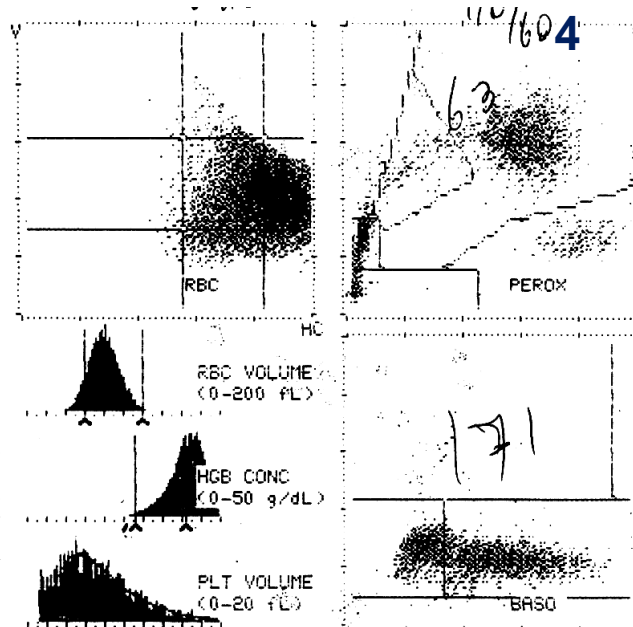
- What is the most useful investigation?

A. OF test

B. Serum B12 and folate level

C. Bone marrow study

D. Coombs' test

E. Flow cytometry for PNH

1

2

WARD/CLINIC

3

RBC

HC

10/80   X 1

PEROX

7 %

105

RBC VOLUME
(0-200 fL)

HGB CONC
(0-50 g/dL)

PLT VOLUME
(0-20 fL)

BASO

4

SEQ#	0000171	
TIME	10:13 07/03/96	
SYS#	001	
ID	000000000171	
	CBC	
WBC	7.94*	x10³/µL
RBC L	3.10*	x10⁶/µL
HGB L	9.7*	g/dL
HCT L	25.2*	%
MCV	81.1*	fL
MCH H	31.2*	pg
MCHC H	38.5*	g/dL
RDW H	19.8	%
HDW H	4.93	g/dL
PLT	216	x10³/µL
MPV	7.2	fL
PDW	54.2	%
PCT	.16	%
RBC FLAGS		2632
DIFF	%	x10³/µL
NEUT	57.7*	4.58*
LYMP	28.2*	2.24*
MONO	4.2*	.33*
EOS	6.3*	.50*
BASO	.9*	.07*
LUC	2.7*	.21*
LI	2.04	
MPXI	1.1	
WBC FLAGS	0000	

RBC

HC

PEROX

RBC VOLUME
(0-200 fL)
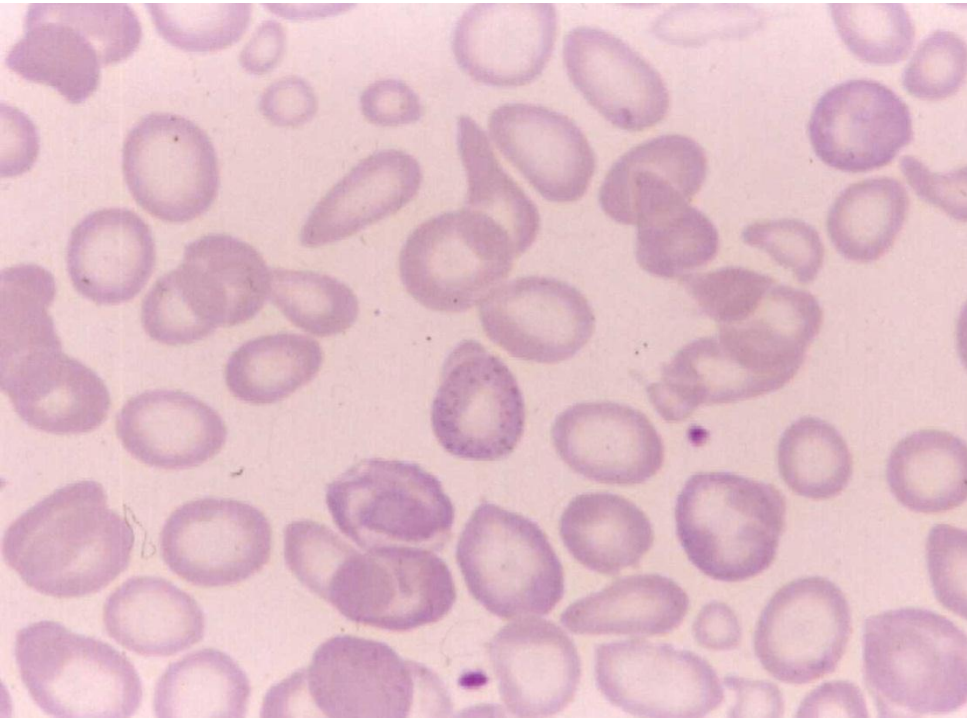
HGB CONC
(0-50 g/dL)

PLT VOLUME
(0-20 fL)

BASO

1,2, 3 Cold agglutinin and 4 HS

10. A 26-yr-old woman with fever, seizure, and petechia. What is the most appropriate management?
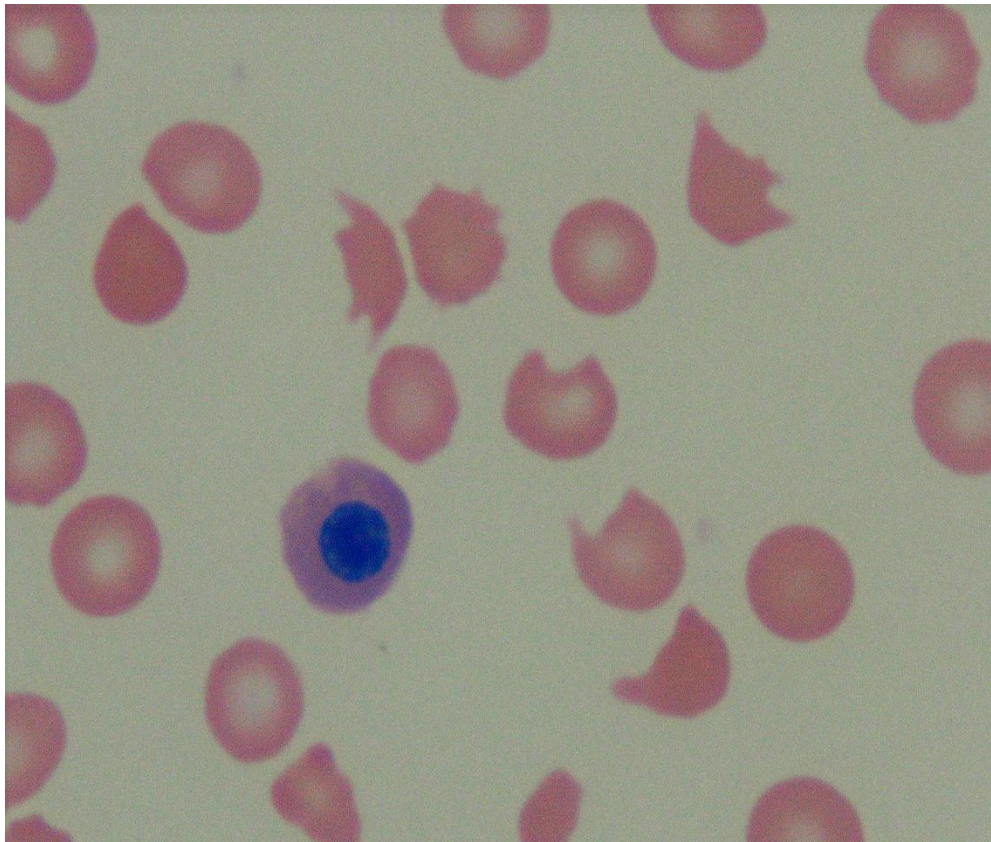
A. Platelet transfusion
B. Emergency Splenectomy
C. IVIG
D. FFP infusion
E. Plasma pheresis
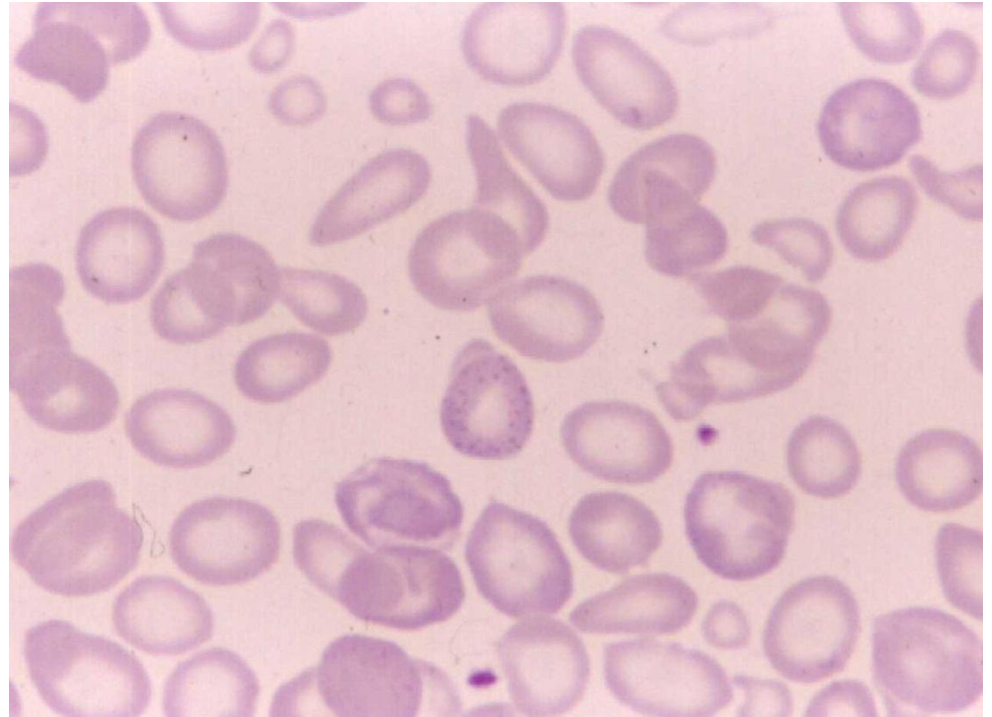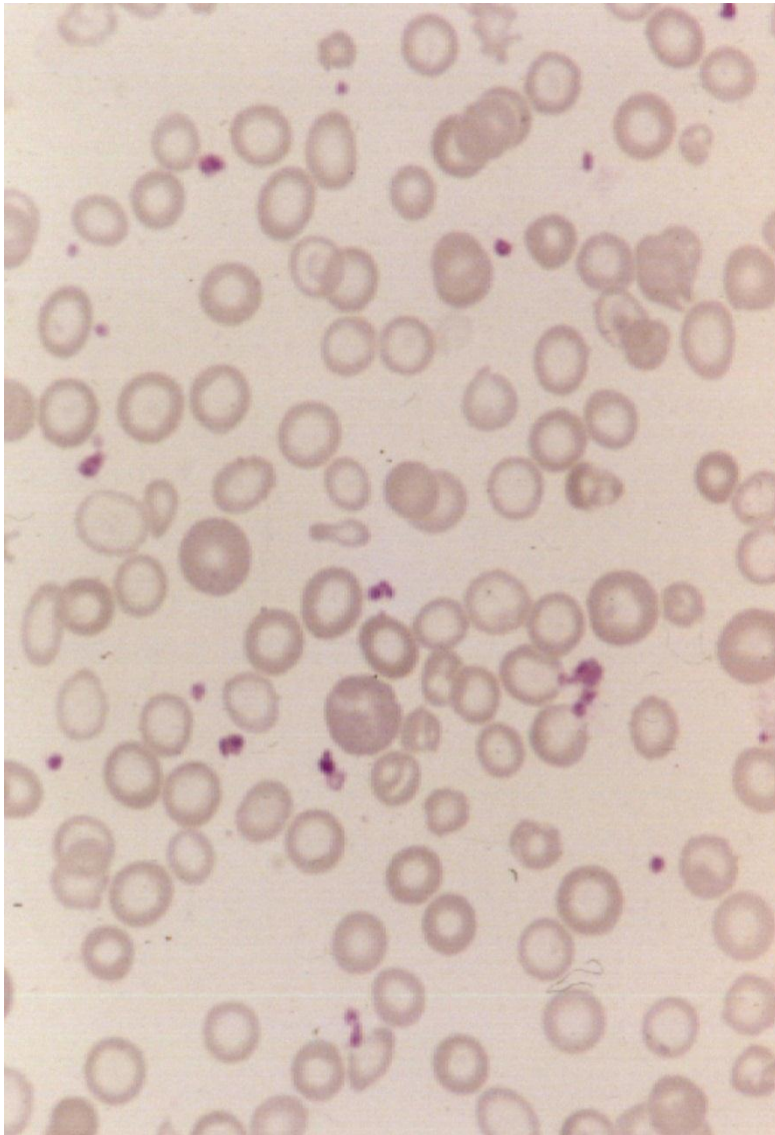
11. 20-yr-old woman with anemia

A. Hemoglobin electrophoresis
B. Stool exam
C. Kidney function test
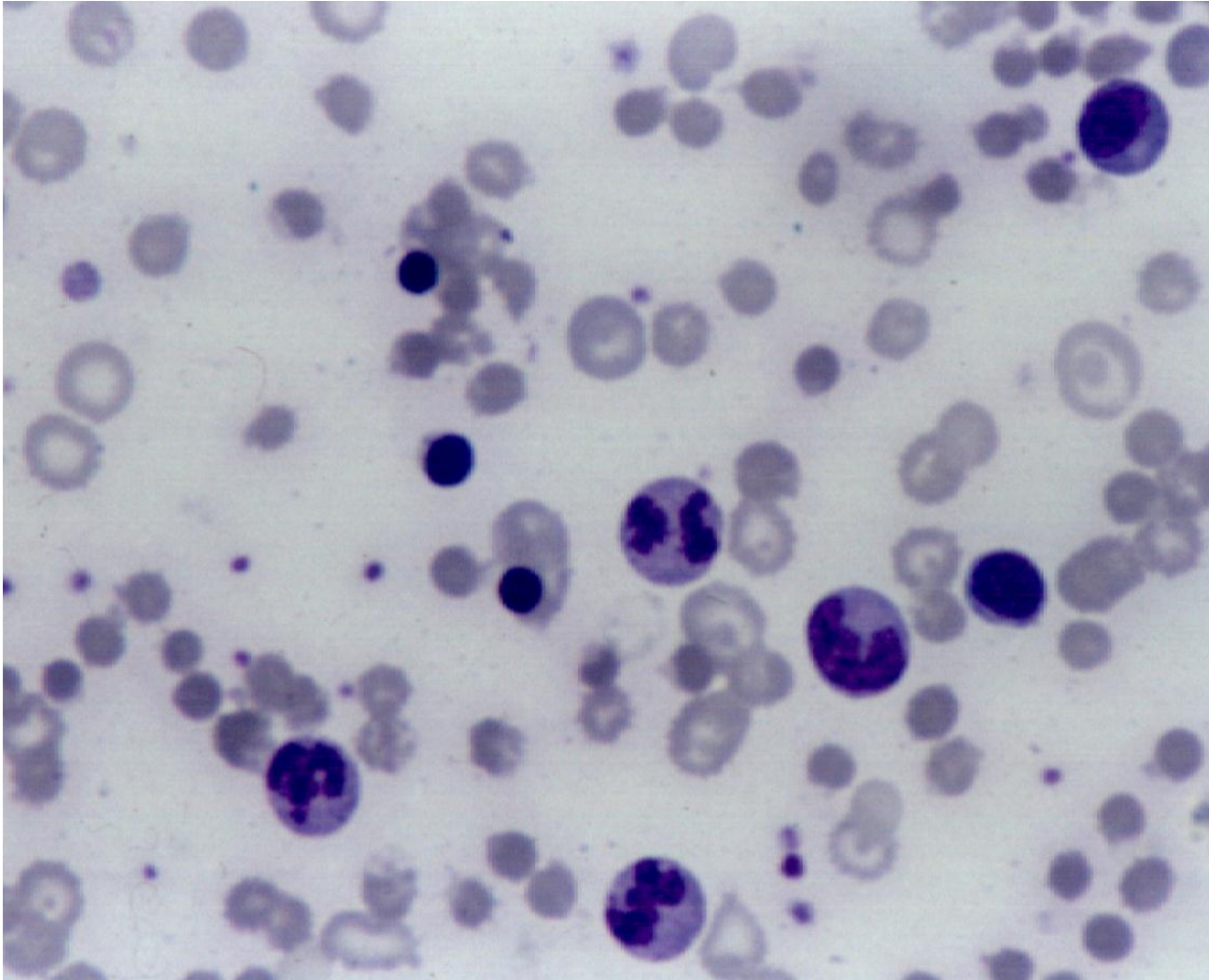D. Bone marrow iron stain
E. Bone marrow biopsy

Iron deficiency vs. thalassemia
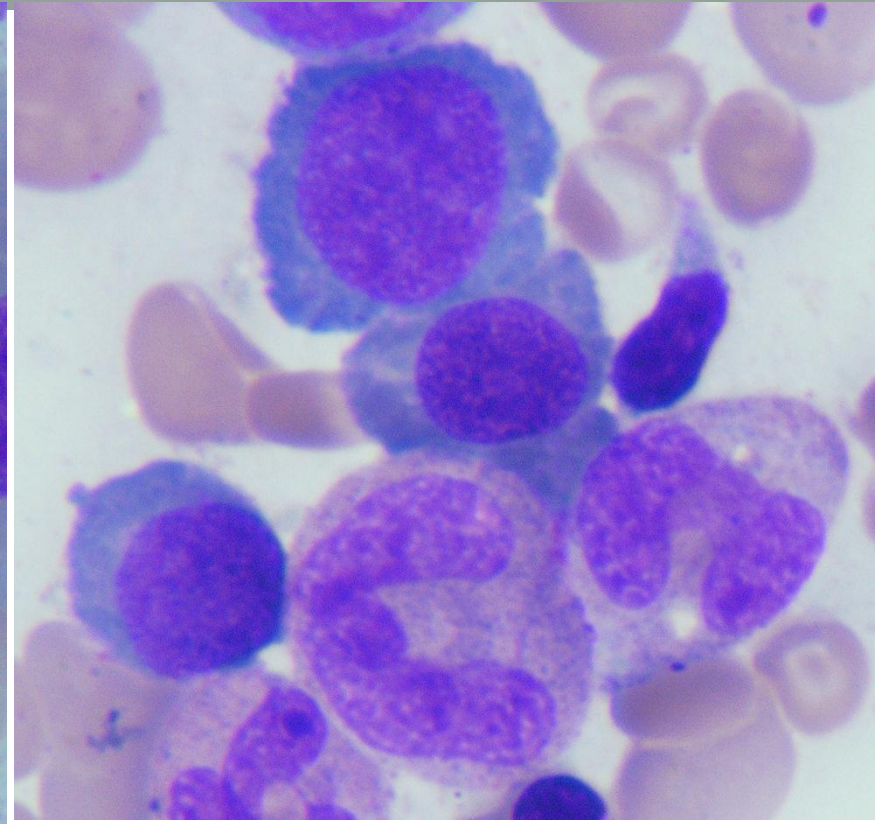

Marked poikilocytosis
Polychromasia
Basophilic stippling
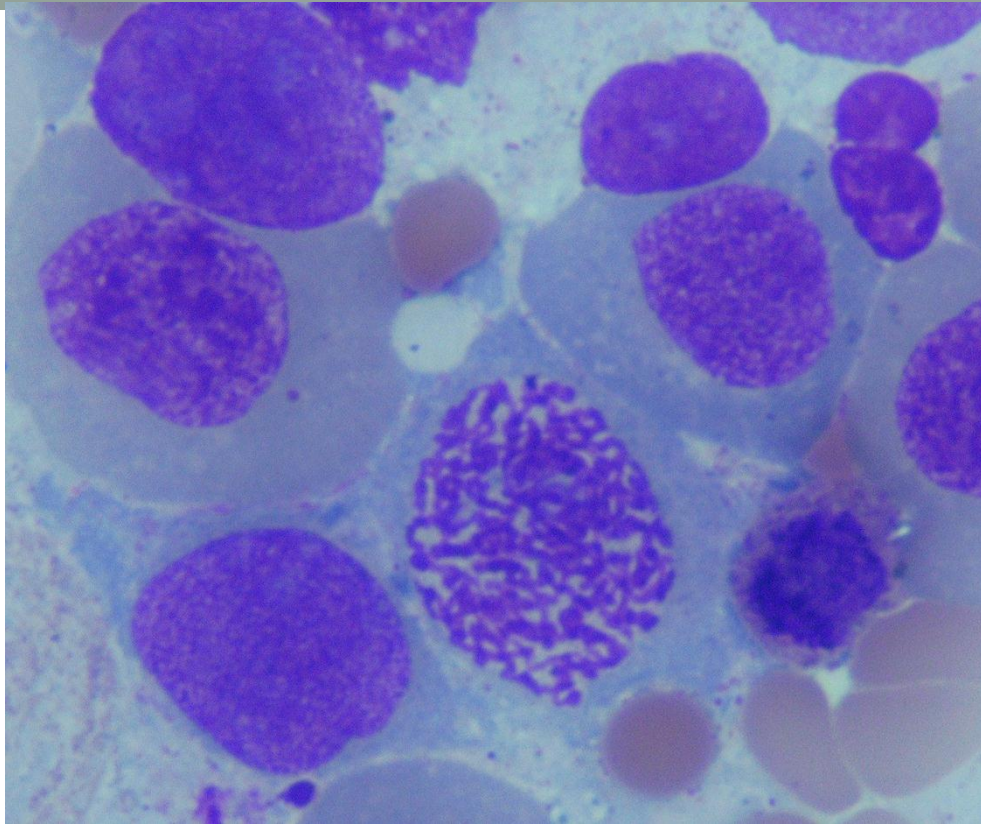
12. ผู้ป่วยชายอายุ 16 ปี มีไข้ 5 วัน 3 วันมีอาการเหนื่อย 1 วัน ปัสสาวะลดลง

A. TTP/HUS

B. G-6-PD deficiency

C. AIHA

D. DHF

E. HS

|	HbH	G-6PD	HS	PNH	AIHA
Sex	both	**M**>F	both	both	both
Baseline	asymptomatic/ mild	asymptomatic	asymptomatic /mild	Various degree (rarely aysmptomatic)	asymptomatic
Splenomegaly *	**++**	**-**	**++**	**-**	**+/-**
Dark urine	+/-	++ (black urine)	+/-	++ (black urine)	+/-
MCV*	**low**	**normal**	**normal**	**normal (low or high)**	**normal**
PBS*	**poikilocytosis, target cell, basophilic stippling**	**Hb leak cells, bite cells**	**spherocytes**	**no specific morphology**	**spherocytes varying in sizes**
Family history	+	+	+	-	-
Gall stone	**+**	**-**	**+**	**+**	**-**
Stress	+	+	+	+/-	-/+ (2-3 wks before on set of hemolysis)

13) ผู้หญิงอายุ 70 ปี มาด้วยซีดอ่อนเพลียมา 3 เดือน
จงให้การวินิจฉัยจากไขกระดูก

A. Large cell lymphoma   B.   Megaloblastic anemia
C. Myelodysplastic syndrome   D.   Erythroleukemia
E. Acute myeloid leukemia with myedysplasia-related changes
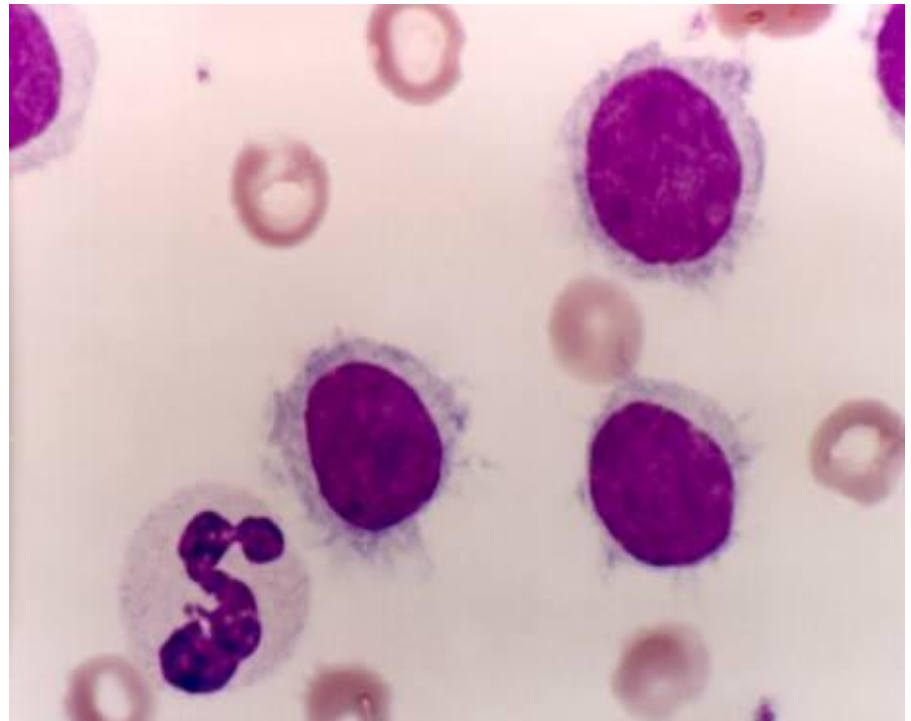
Causes of Megaloblastic Anemia
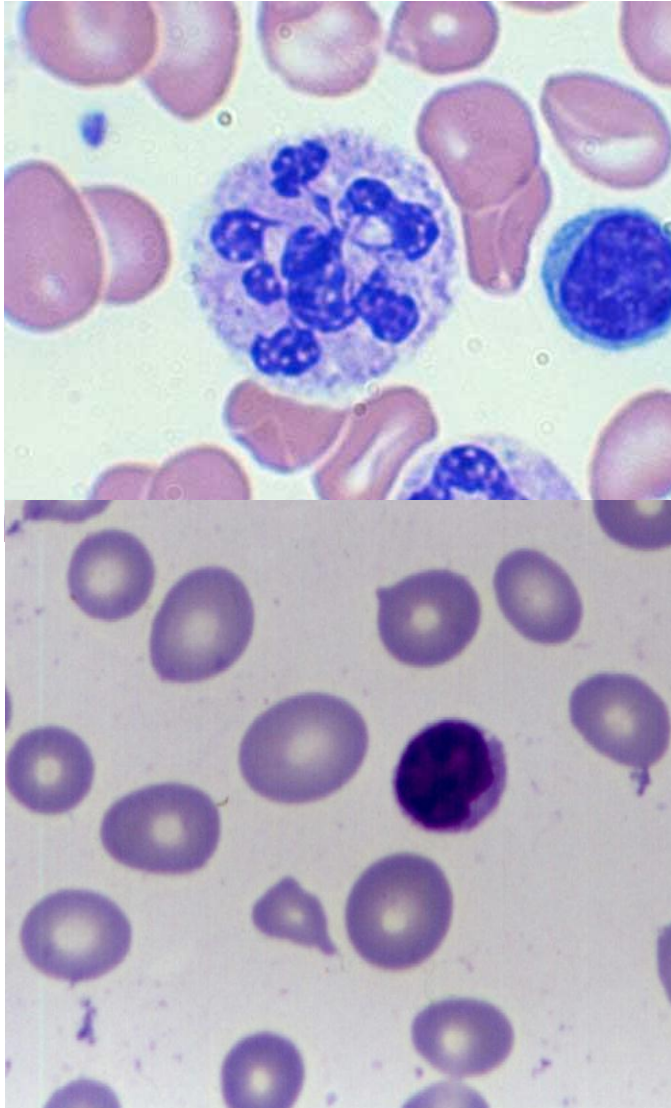
- Vitamin B12 deficiency
- Folate deficiency
- Drug-induced
  - Antimetabolites
  - Antiretroviral
  - Anti-cancer
  - Anesthesia (nitrous oxide)

14) ผู้ป่วยชาย 50 ปีมาด้วยแน่นอึดอัดท้อง PE: huge splenomegaly
CBC: Hb 8 g/dl, MCV 95 fl, WBC 3,400/mm^3, N 30, L 65%, platelet 80,000/mm^3
ข้อใดไม่ใช่ immunophenotype ของเซลล์ผิดปกตินี้
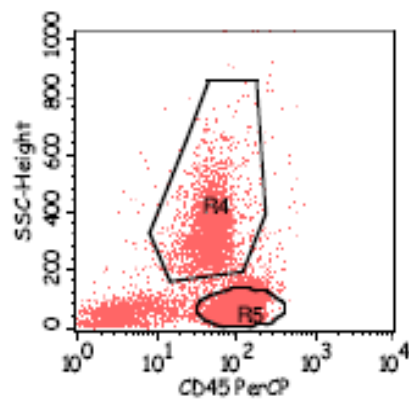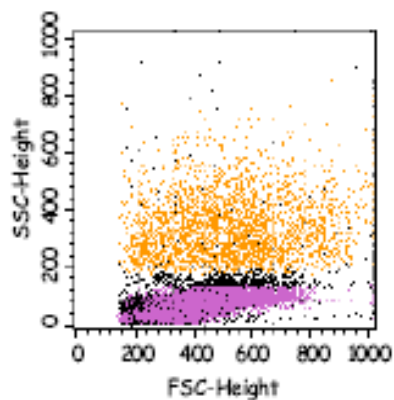
A. CD5+
B. CD20+
C. CD11C+
D. CD25+
E. CD103+

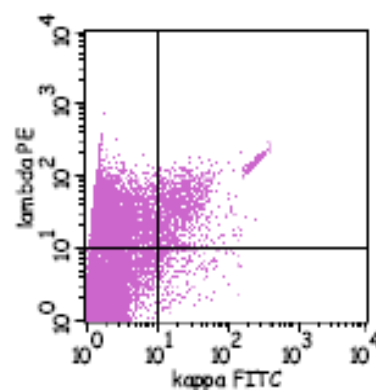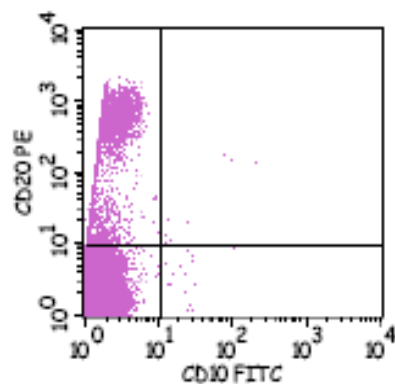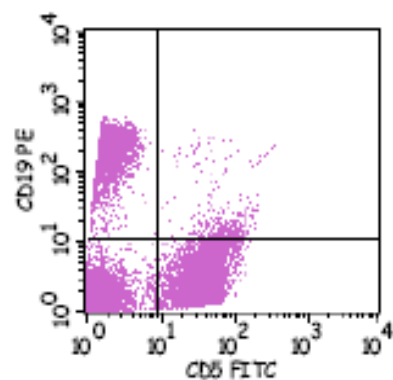# Lymphocyte with cytoplasmic projection
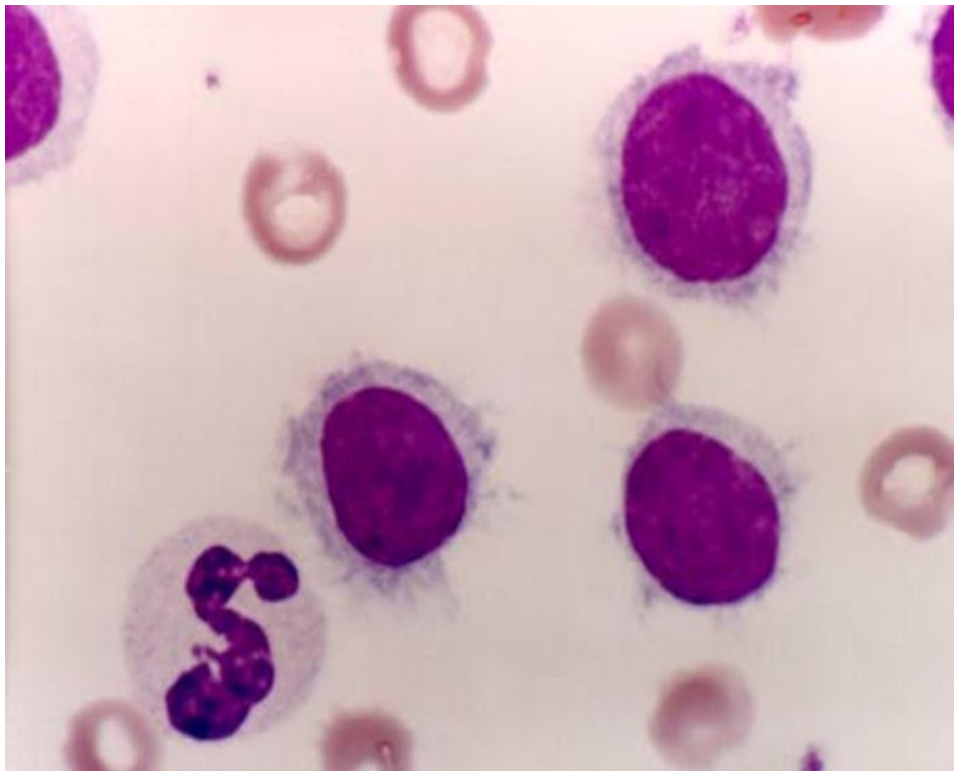
Hairy cell leukemia
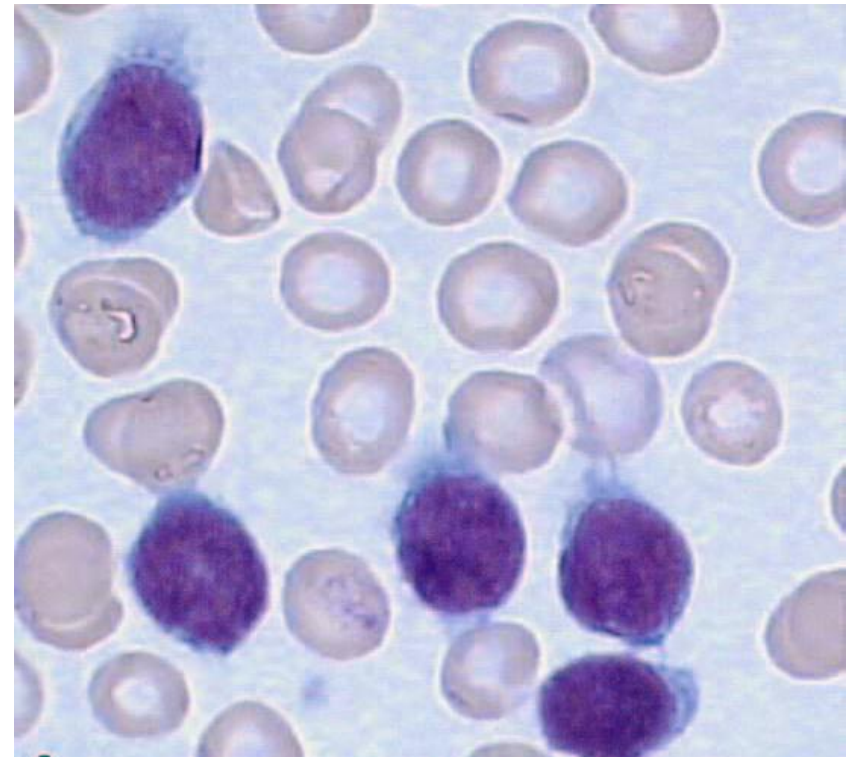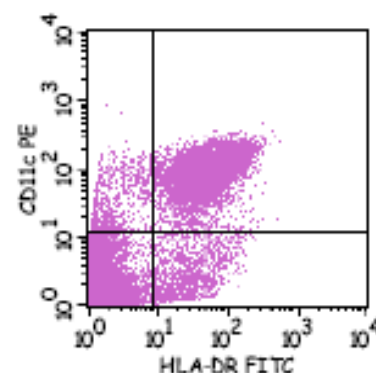

Splenic marginal zone lymphoma with villous lymphocytes

Region	Events	% Gated	% Total
R4	9636	19.27	19.27
R5	32288	64.58	64.58

FLOW CYTOMETRY LAB

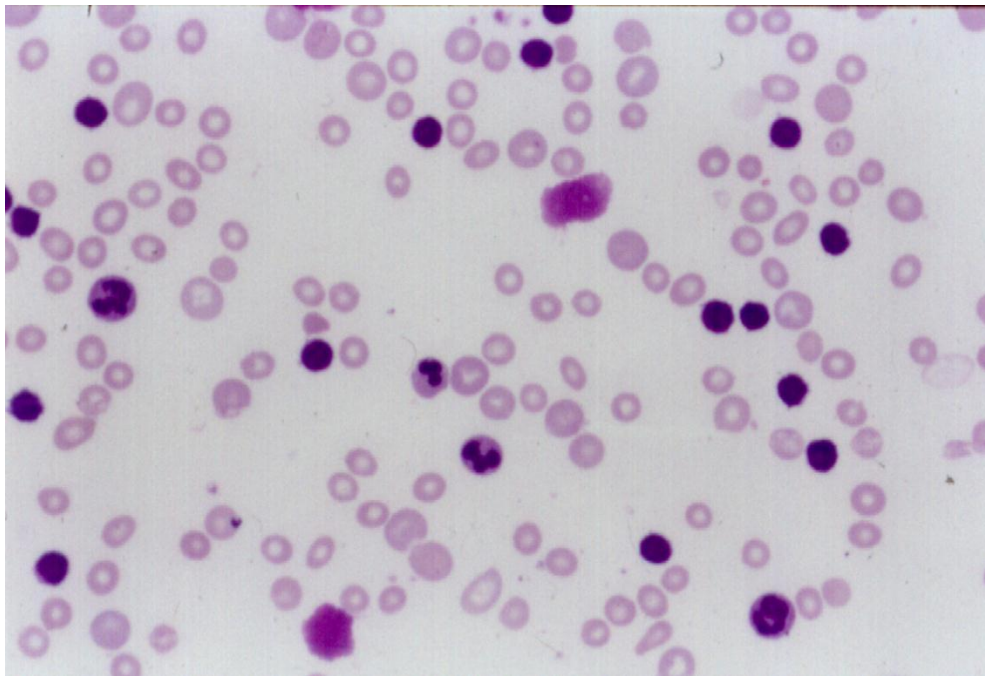**DIVISION OF HEMATOLOGY**

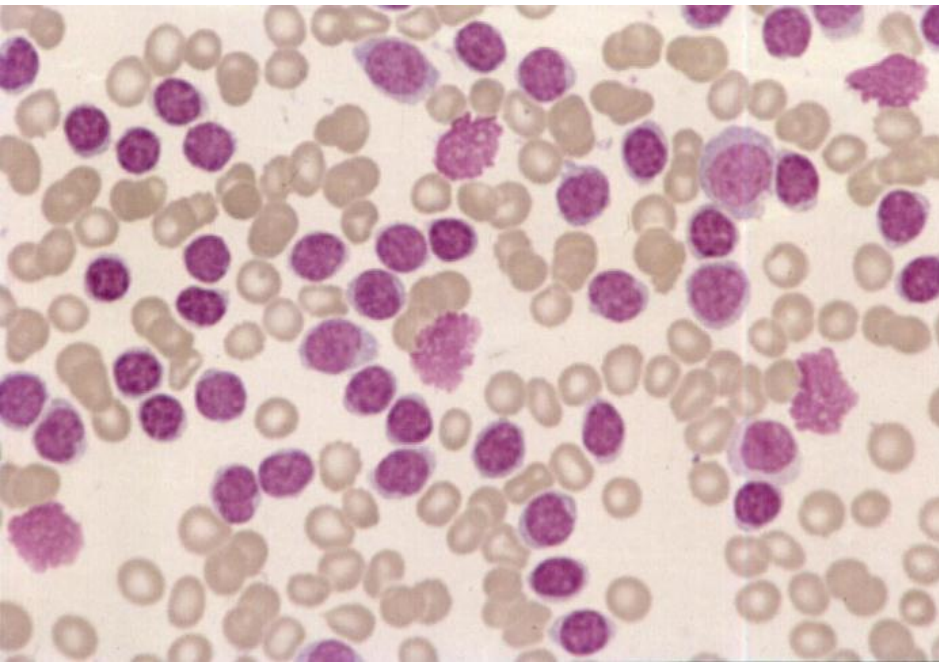**CHULALONGKORN UNIVERSITY**

R5 (lymphoid) gate
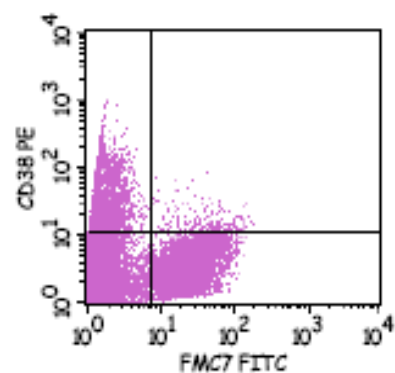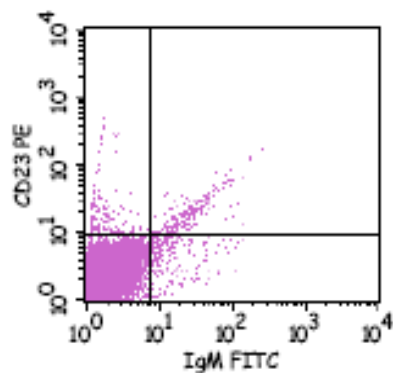
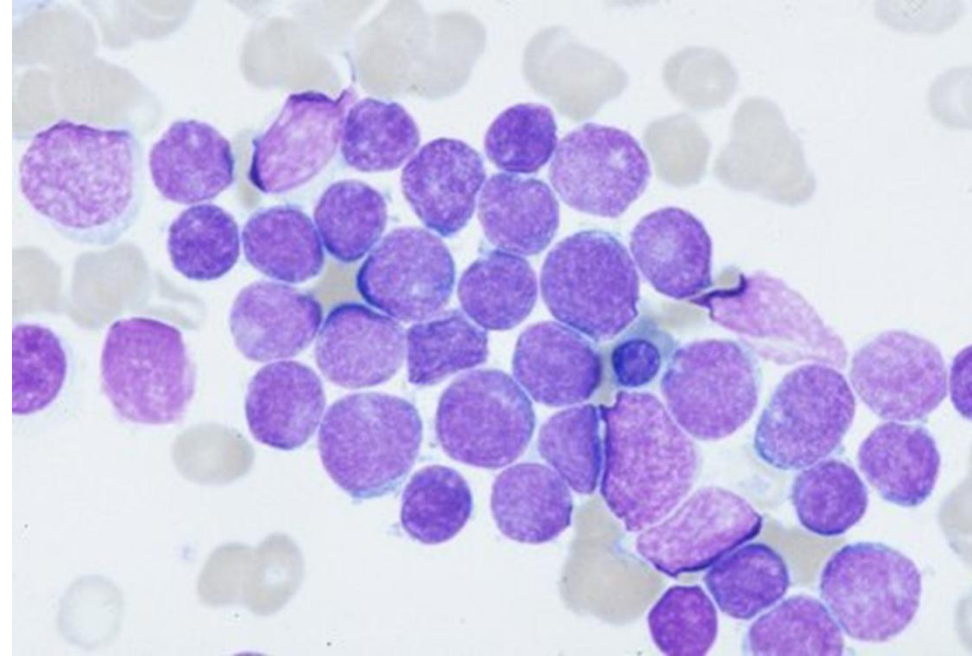**Hairy cell leukemia CD25+ and CD103+**

15. A 70 yr man with anemia

- **A. Acute lymphoblastic leukemia**
- **B. Chronic lymphocytic leukemia**
- **C. Mantle cell lymphoma**
- **D. Follicular cell lymphoma**
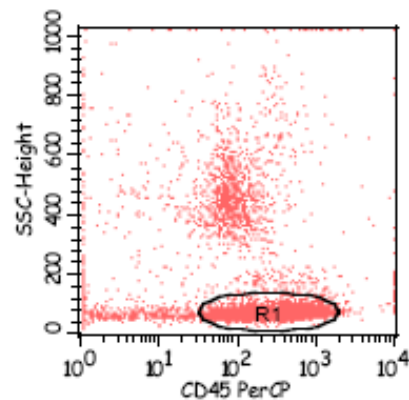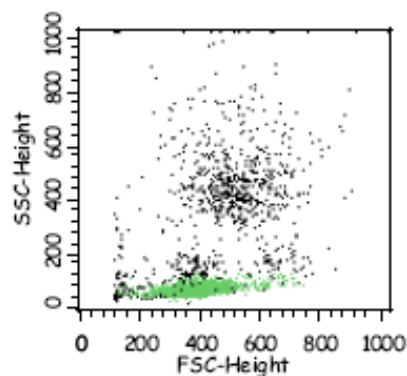- **E. Prolymphocytic leukemia**

mature lymphocyte *vs.* lymphoblast

CLL

ALL

File: In 05/08/05.001

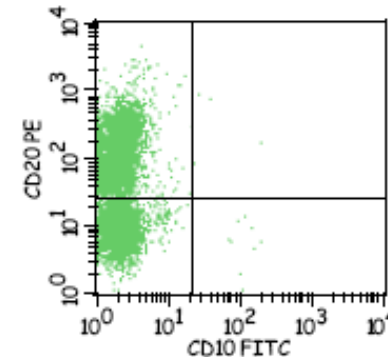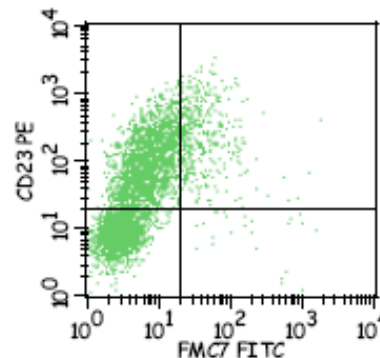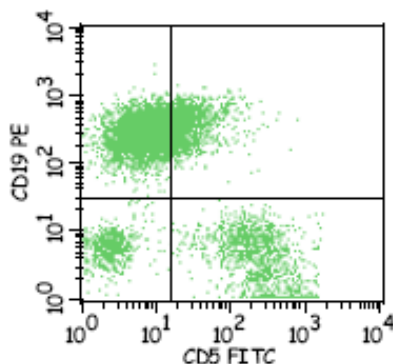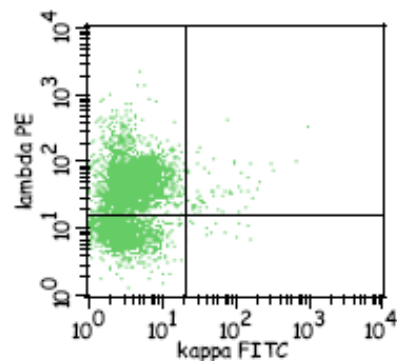| Region	Events	% Gated	% Total
R1	11642	73.15	73.15

R1 (Lymphocyte) gate

FLOW CYTOMETRY LAB

DIVISION OF HEMATOLOGY

CHULALONGKORN
UNIVERSITY

File: In 05/08/05.001

Quad	Events	% Gated	% Total
UL	8276	71.09	52.00
UR	121	1.04	0.76
LL	3222	27.68	20.25
LR	23	0.20	0.14

File: In 05/08/05.002

Quad	Events	% Gated	% Total
UL	6404	51.32	42.40
UR	2633	21.10	17.43
LL	1008	8.08	6.67
LR	2433	19.50	16.11

File: In 05/08/05.003

Quad	Events	% Gated	% Total
UL	3829	48.12	35.06
UR	792	9.95	7.25
LL	3291	41.36	30.14
LR	45	0.57	0.41

File: In 05/08/05.006

Quad	Events	% Gated	% Total
UL	4266	56.85	42.20
UR	4	0.05	0.04
LL	3225	42.98	31.90
LR	9	0.12	0.09

Scoring System for B-CLL

Marker	CLL	Score
sIg (kappa or lambda)	weak	1
CD5	pos	1
CD23	pos	1
CD79b/CD22 (CD20)	weak	1
FMC7	neg	1

16. A 60-yr-man with tonsillar mass
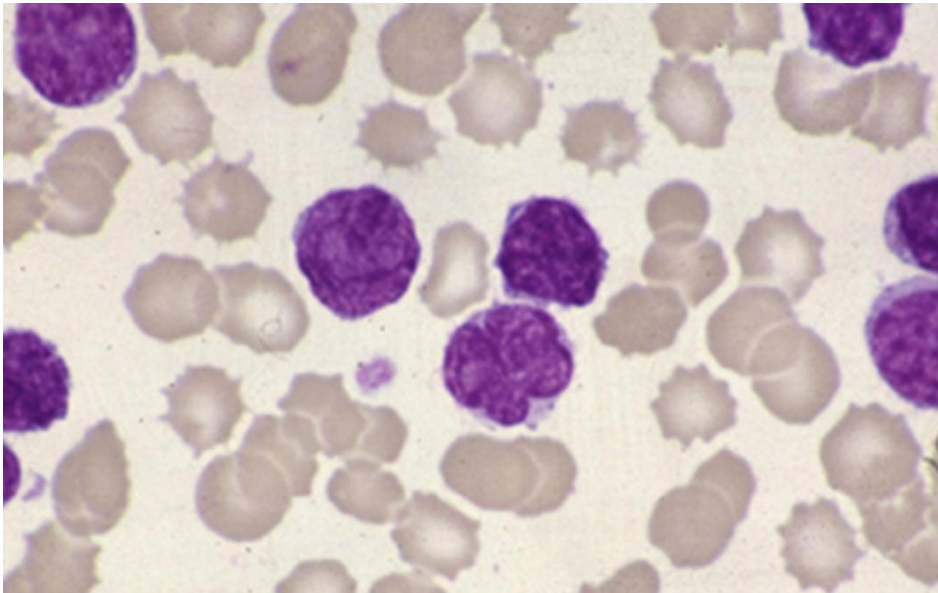
- A. Mantle cell lymphoma
- B. Plasma blastic lymphoma
- C. Small lymphocytic lymphoma
- D. Aggressive NK/T cell lymphoma
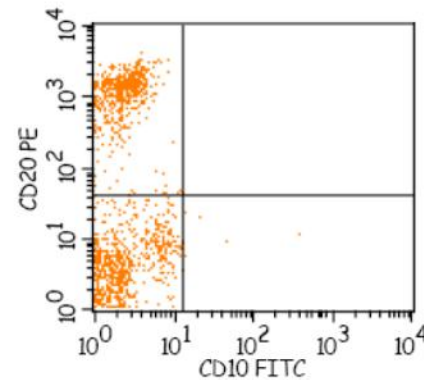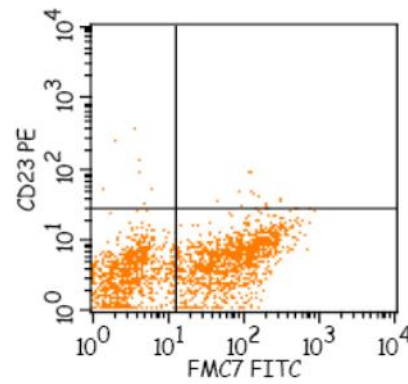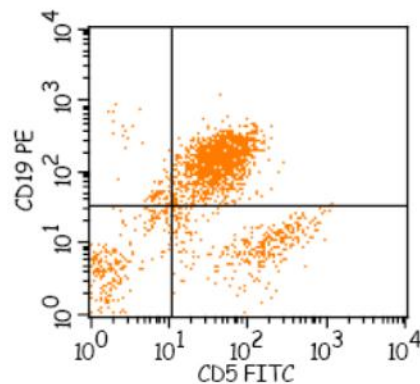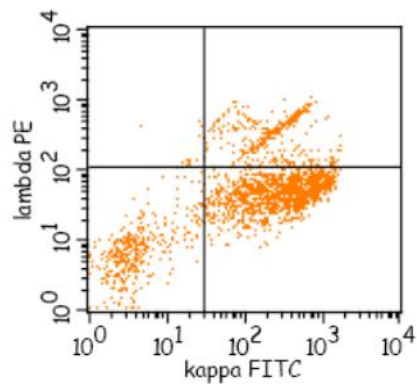- E. Diffuse large B-cell lymphoma
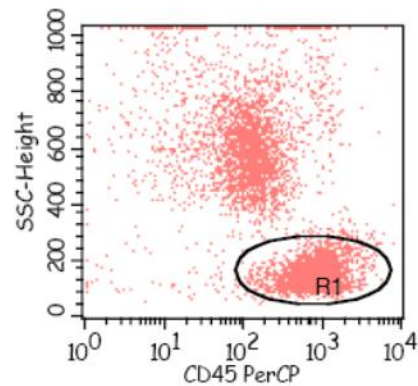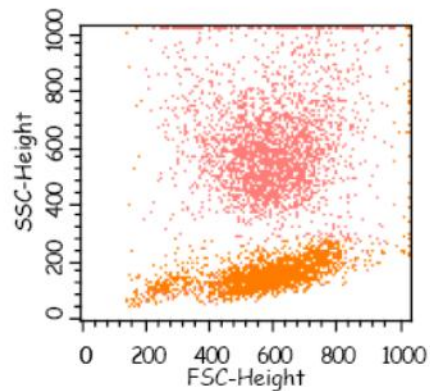
File: Komsan 07/01/22.001

Region	Events	% Gated	% Total
R2	19676	100.00	98.38
R1	8467	43.03	42.34

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R1 (Lymphocyte) gate

File: Komsan 07/01/22.001

Quad	Events	% Gated	% Total
UL	74	0.87	0.37
UR	1466	17.22	7.33
LL	1475	17.32	7.38
LR	5499	64.59	27.50

File: Komsan 07/01/22.002

Quad	Events	% Gated	% Total
UL	293	3.60	1.47
UR	5581	68.66	27.91
LL	817	10.05	4.08
LR	1437	17.68	7.18

File: Komsan 07/01/22.003

Quad	Events	% Gated	% Total
UL	21	0.27	0.10
UR	53	0.68	0.27
LL	3331	42.85	16.66
LR	4368	56.19	21.84

File: Komsan 07/01/22.005

| Quad	Events	% Gated	% Total
UL	2227	46.36	11.13
UR	6	0.12	0.03
LL	2550	53.08	12.75
LR	21	0.44	0.10

Diagnostic approach to LPD

- First step – look at CBC if there is lymphocytosis
- Second step – assess morphology of lymphocytes in blood smear
  - Small, non-cleaved, few cytoplasm with many smudge cells → B-CLL
  - Large lymphocytes with prominent nucleolus → PLL (either B or T-cell), blastoid variant of mantle cell lymphoma (MCL), large B-cell lymphoma
  - Lymphoplasmacytic cells → LPL, CLL, MZL, plasma cell leukemia
  - Medium size lymphocyte with projection → SMZL/VL, Hairy cell leukemia and variants
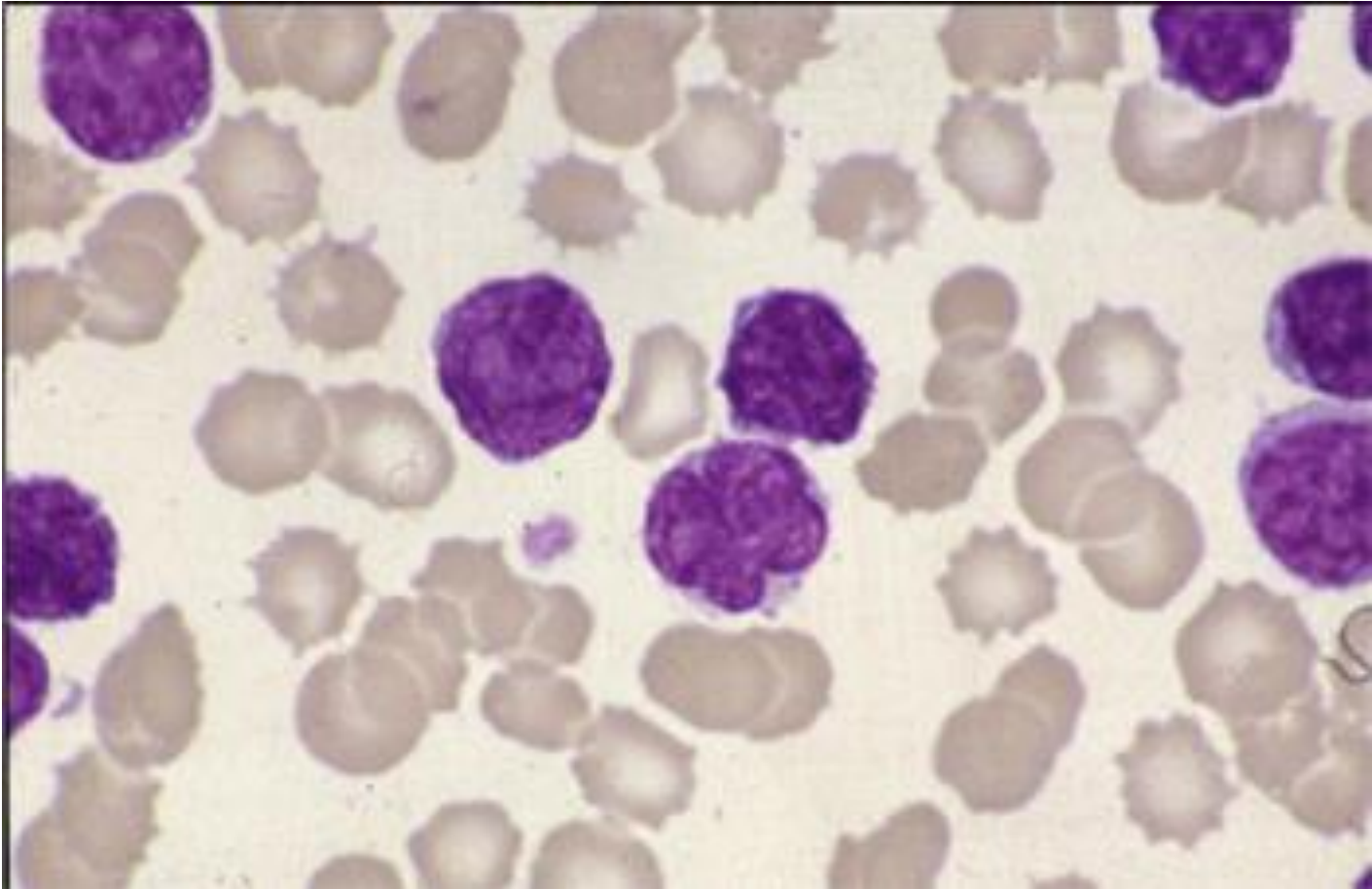
Diagnostic approach to LPD

- Large granular lymphocytes → LGL, NK-cell leukemia
- Small, cleaved lymphocytes → atypical CLL/SLL, MCL, follicular and marginal zone lymphoma (MZL), T-ALL/LBL, ATLL, CTCL or PTCL-U
- Blasts → ALL (precursor T or B), AML-M0

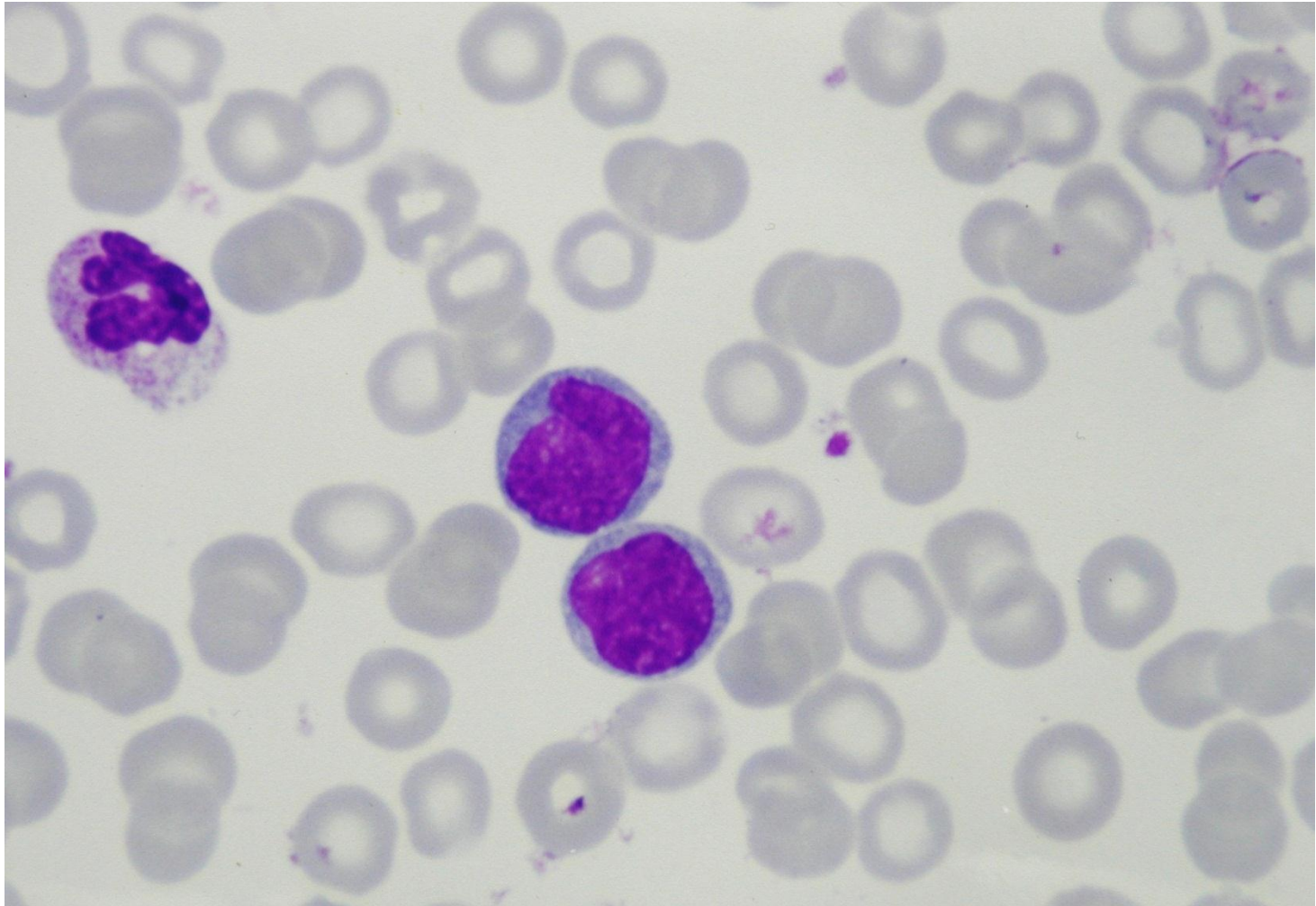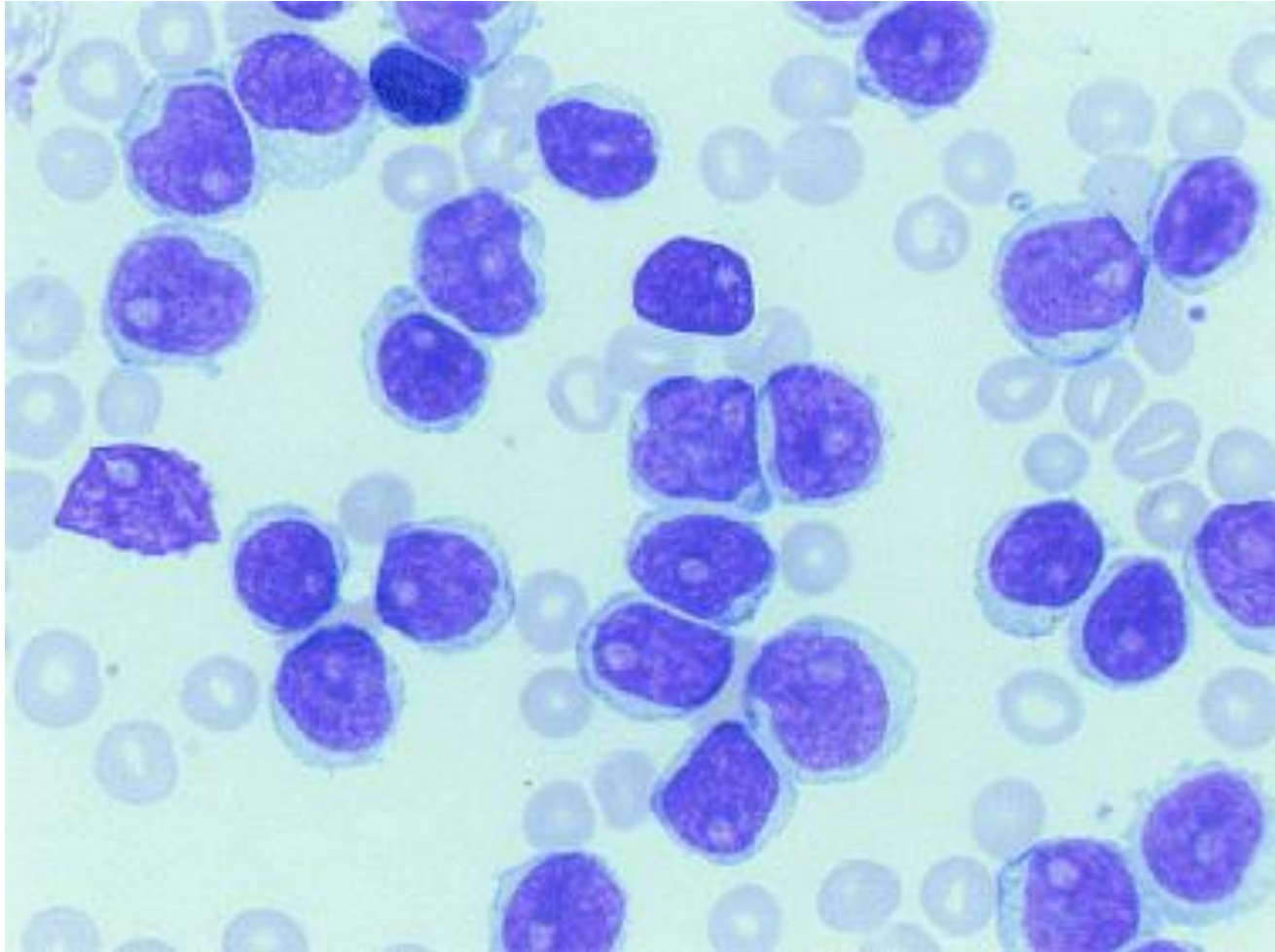# Acute lymphoblastic leukemia
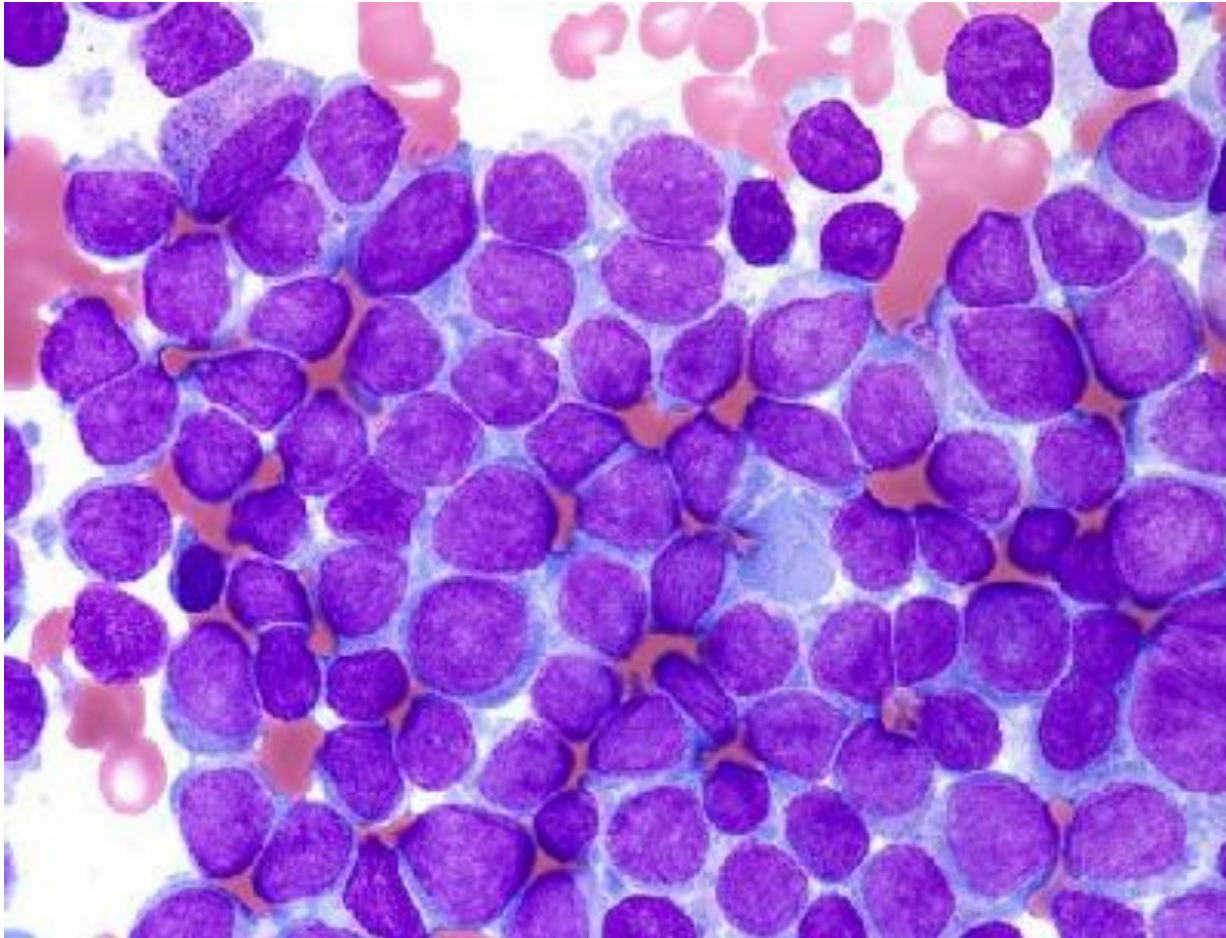
Mantle cell lymphoma
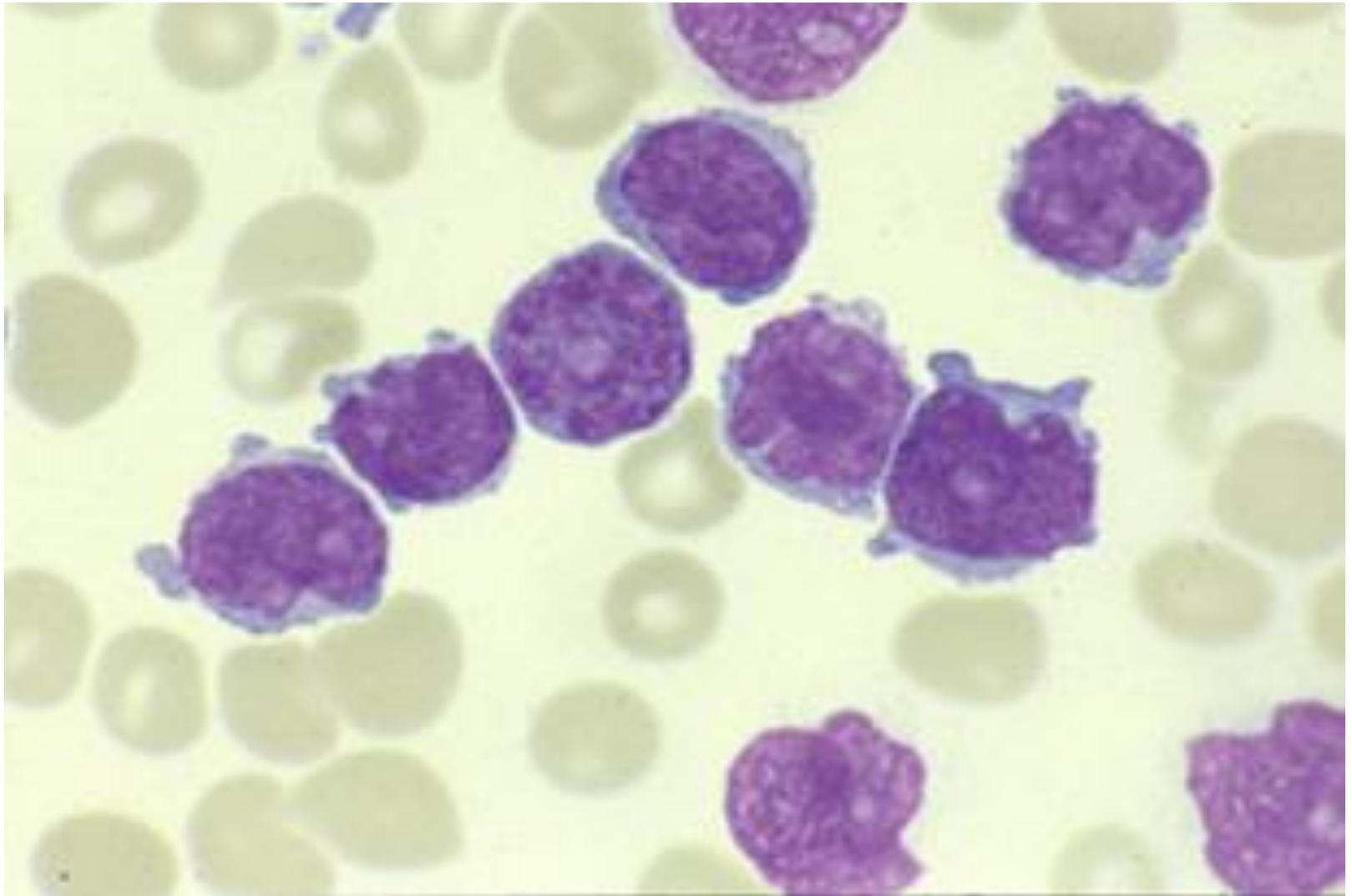
Follicular lymphoma

B-Prolymphocytic Leukemia

T-Prolymphocytic Leukemia (T-PLL)

BSCH Recommendation for flow cytometry diagnosis of LPD

Assess morphology, apply the first line Ab panel (CD19, CD22, CD23, FMC7, sIgM, kappa, lambda, CD2, CD5) and assign CLL score
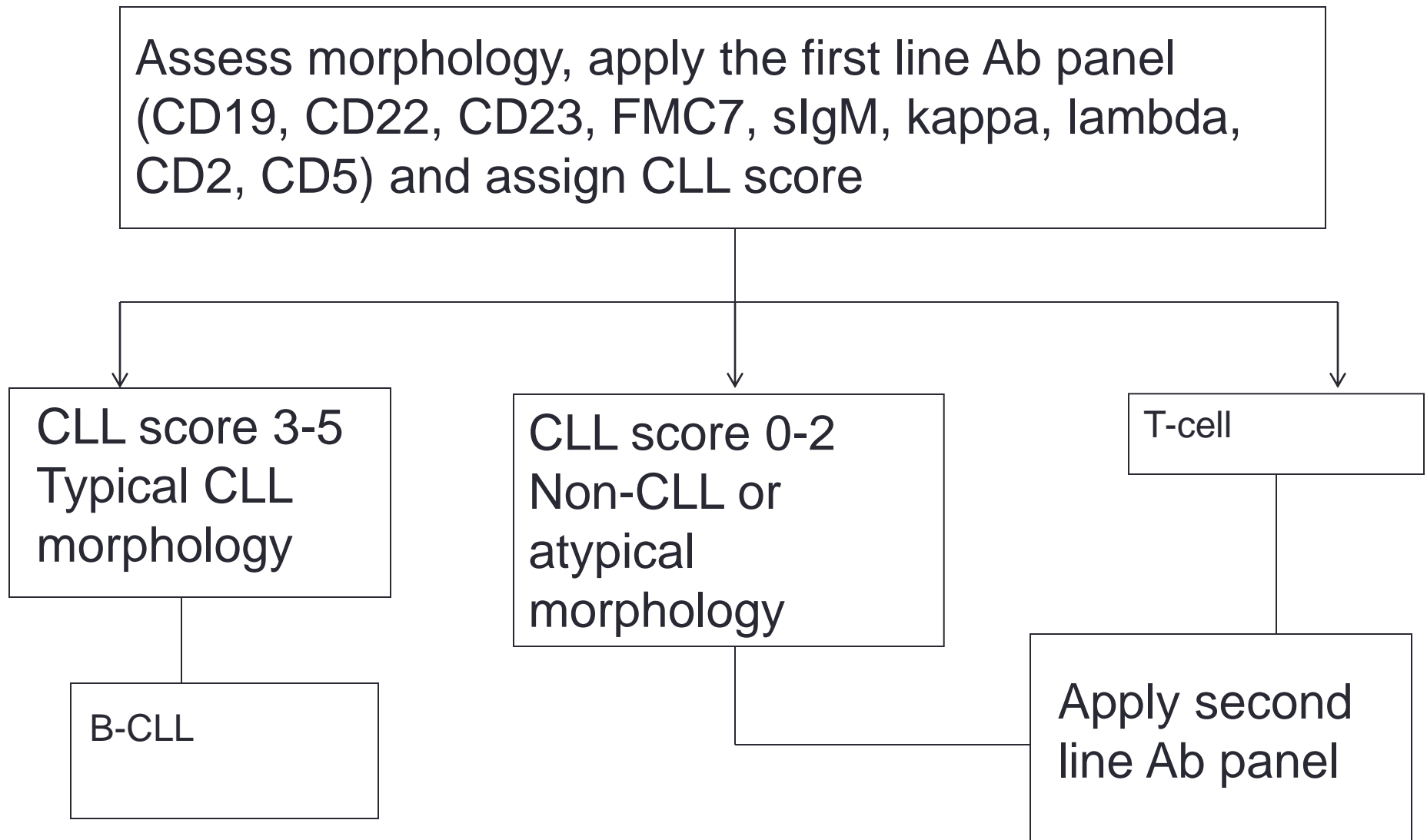
CLL score 3-5
Typical CLL morphology

CLL score 0-2
Non-CLL or atypical morphology

T-cell

B-CLL

Apply second line Ab panel

DDx of B-cell lymphocytosis