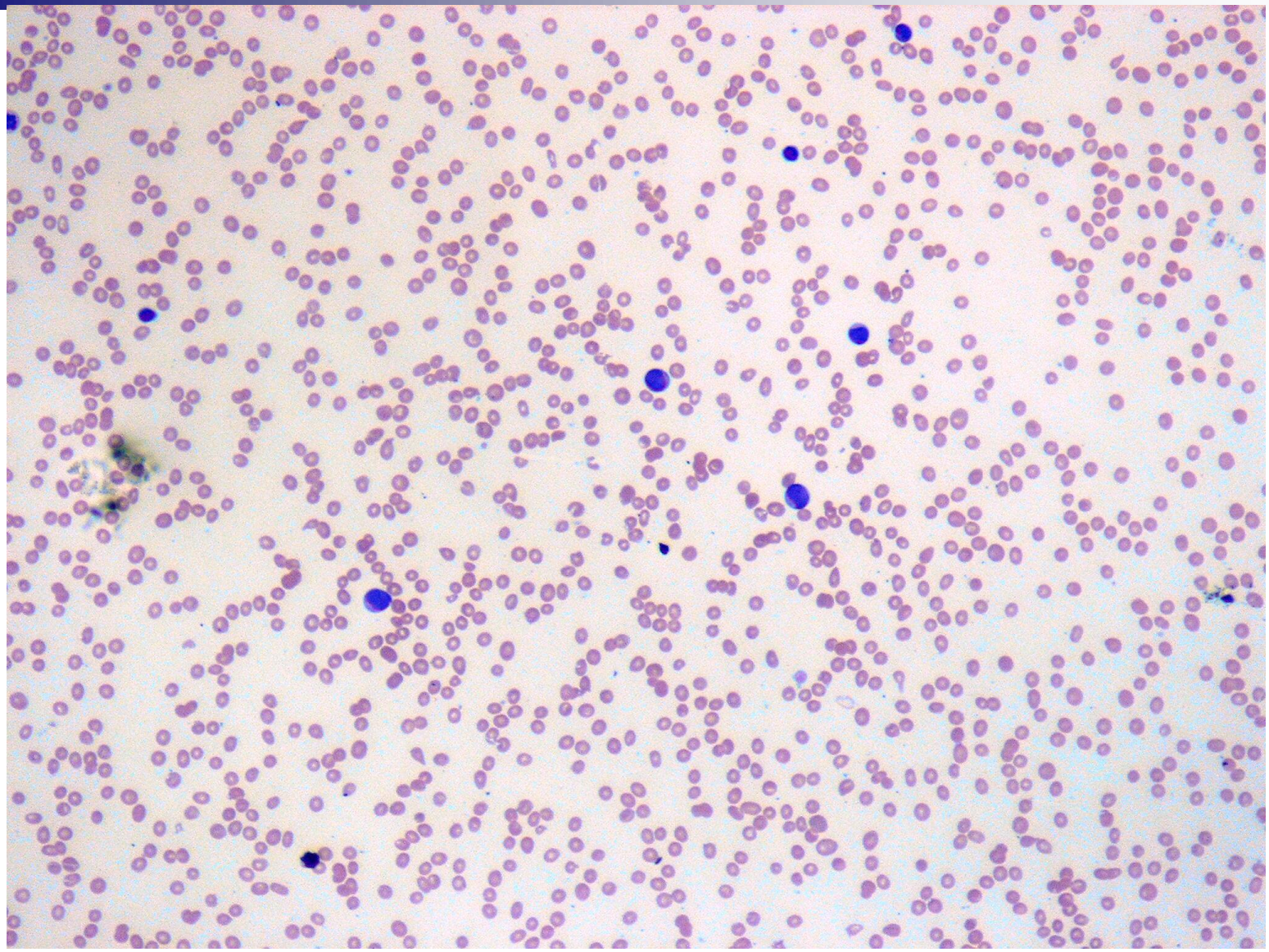
Hematology Case Conference

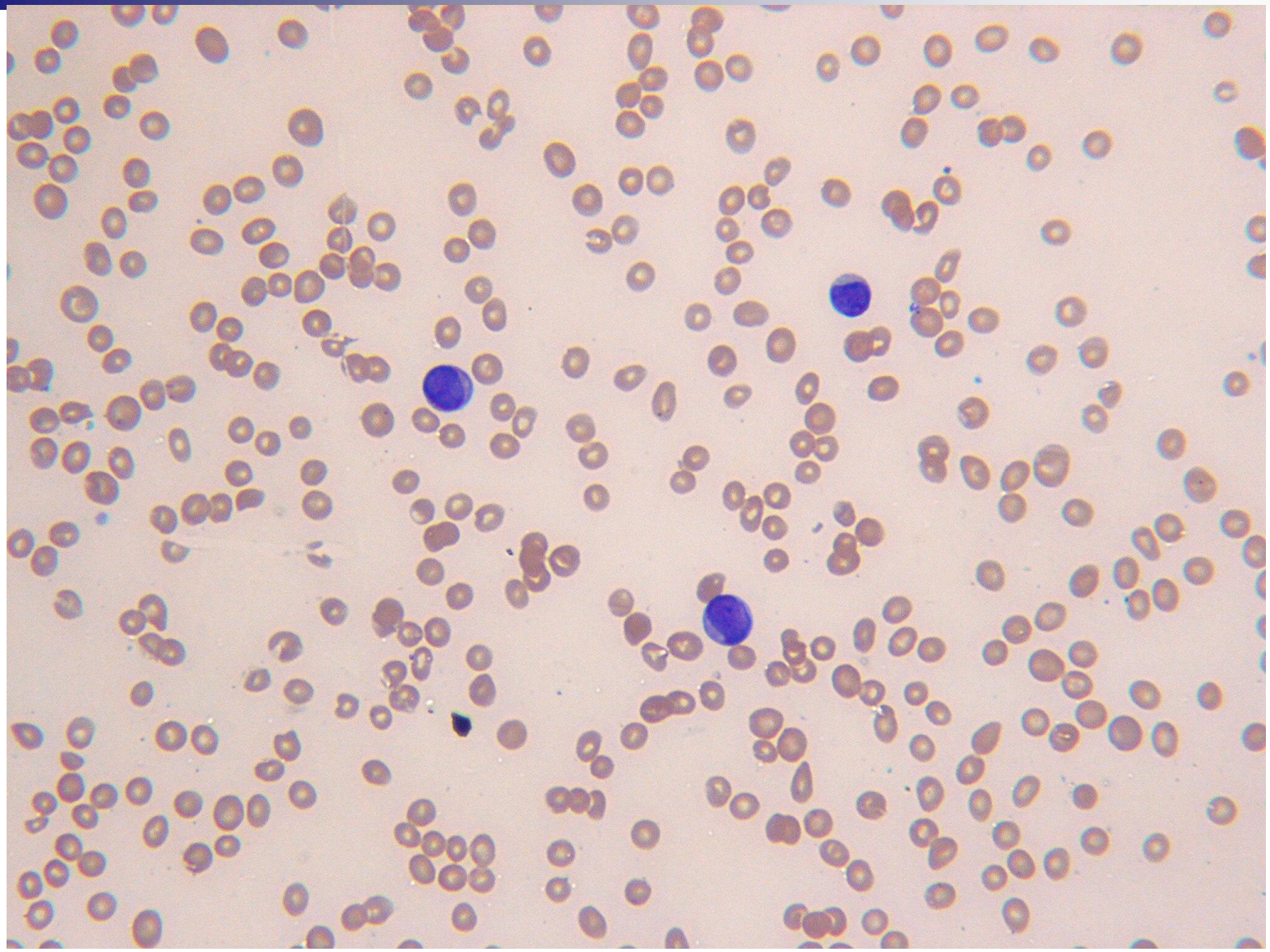
11/4/03

Bone Marrow Case
Patient: Jexx Thxxx

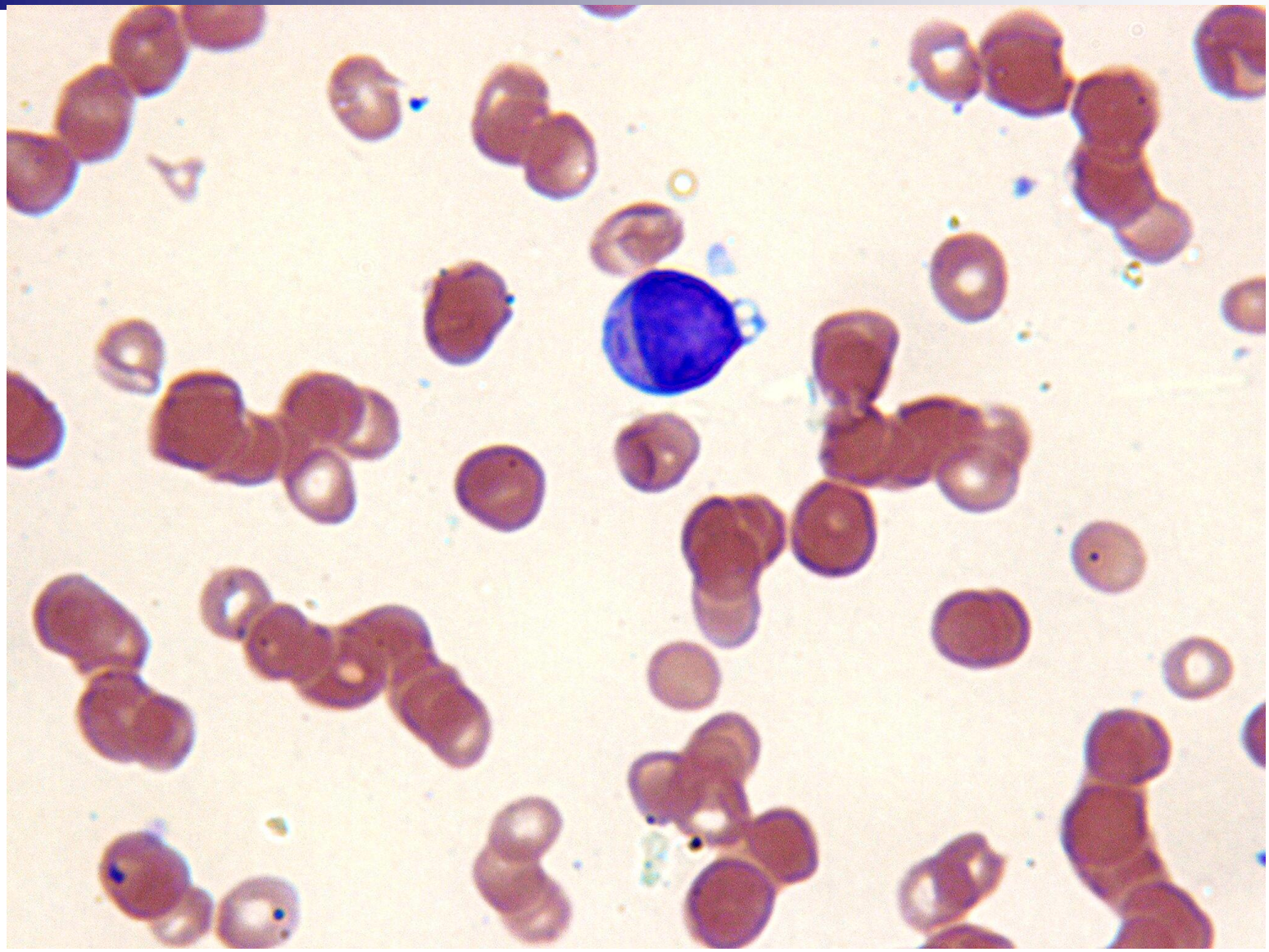
- 38 year old AA female presented in ER with dizziness, syncopy, tachycardia, recent Hx of gingivitis
- WBC= 18.2, Hgb=5.4, Plt=23, Retic 0.5%, MCV 94.5 Rare NRBCs



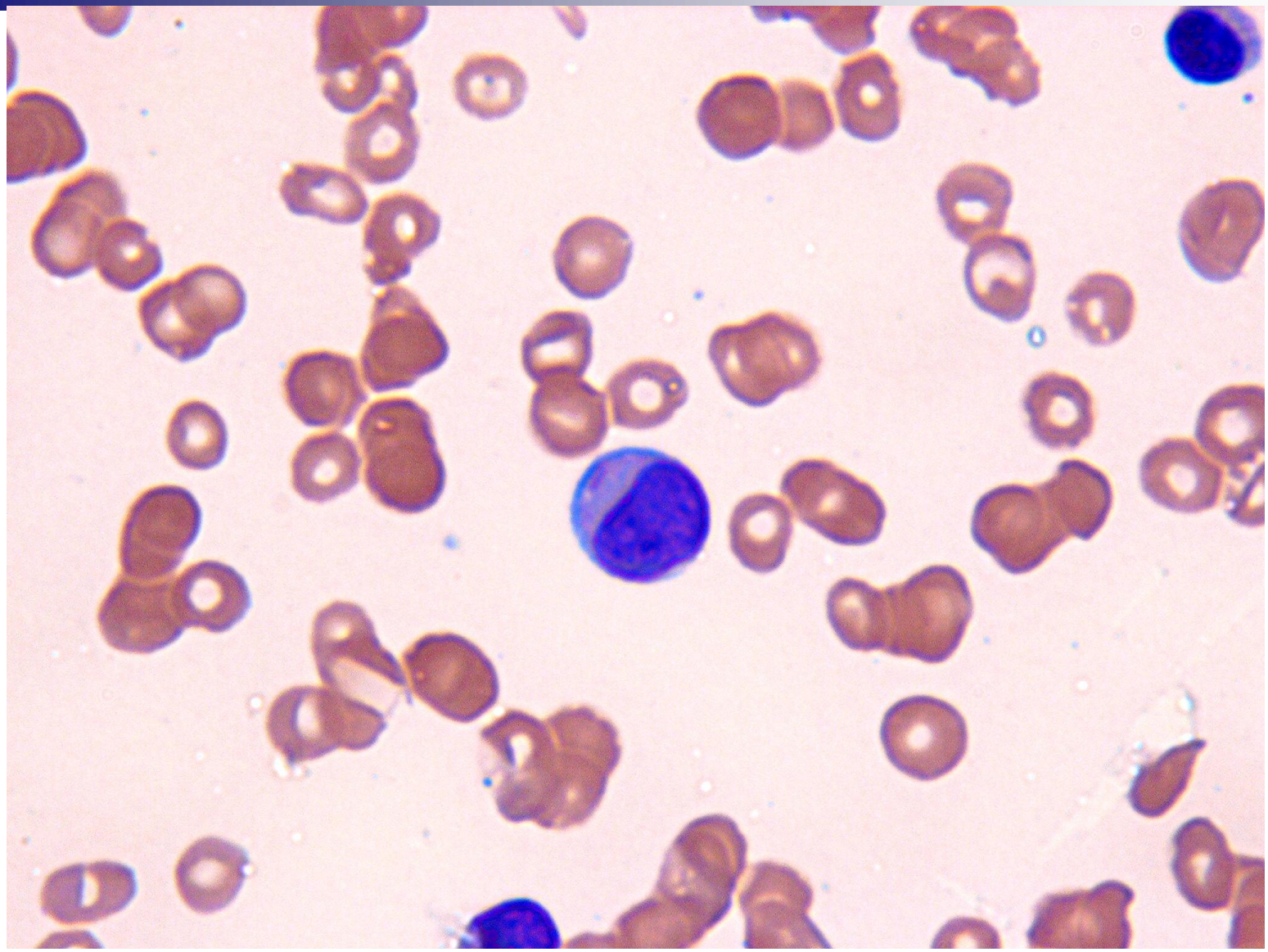
Peripheral blood smear



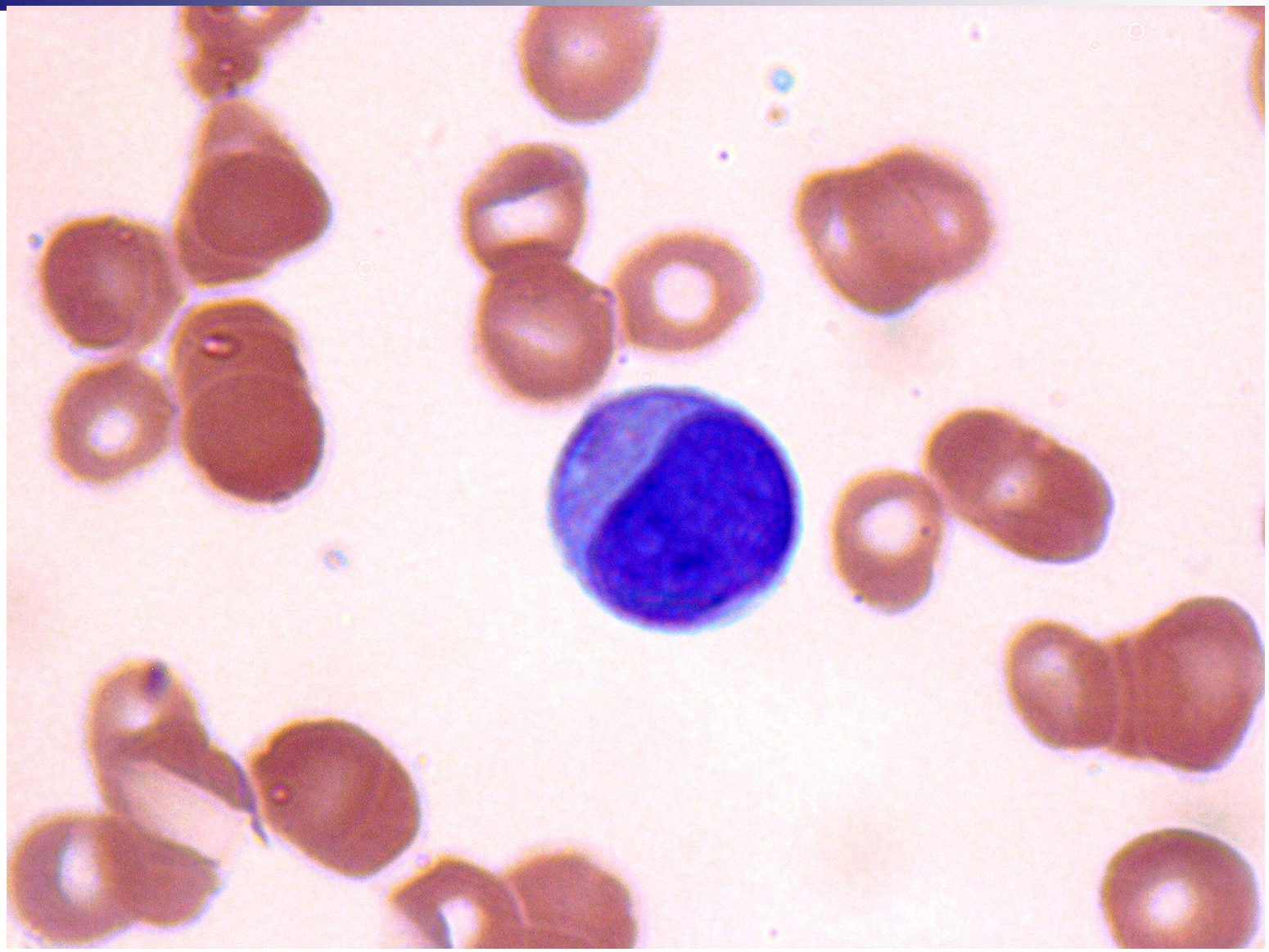
Peripheral blood smear, cont’d



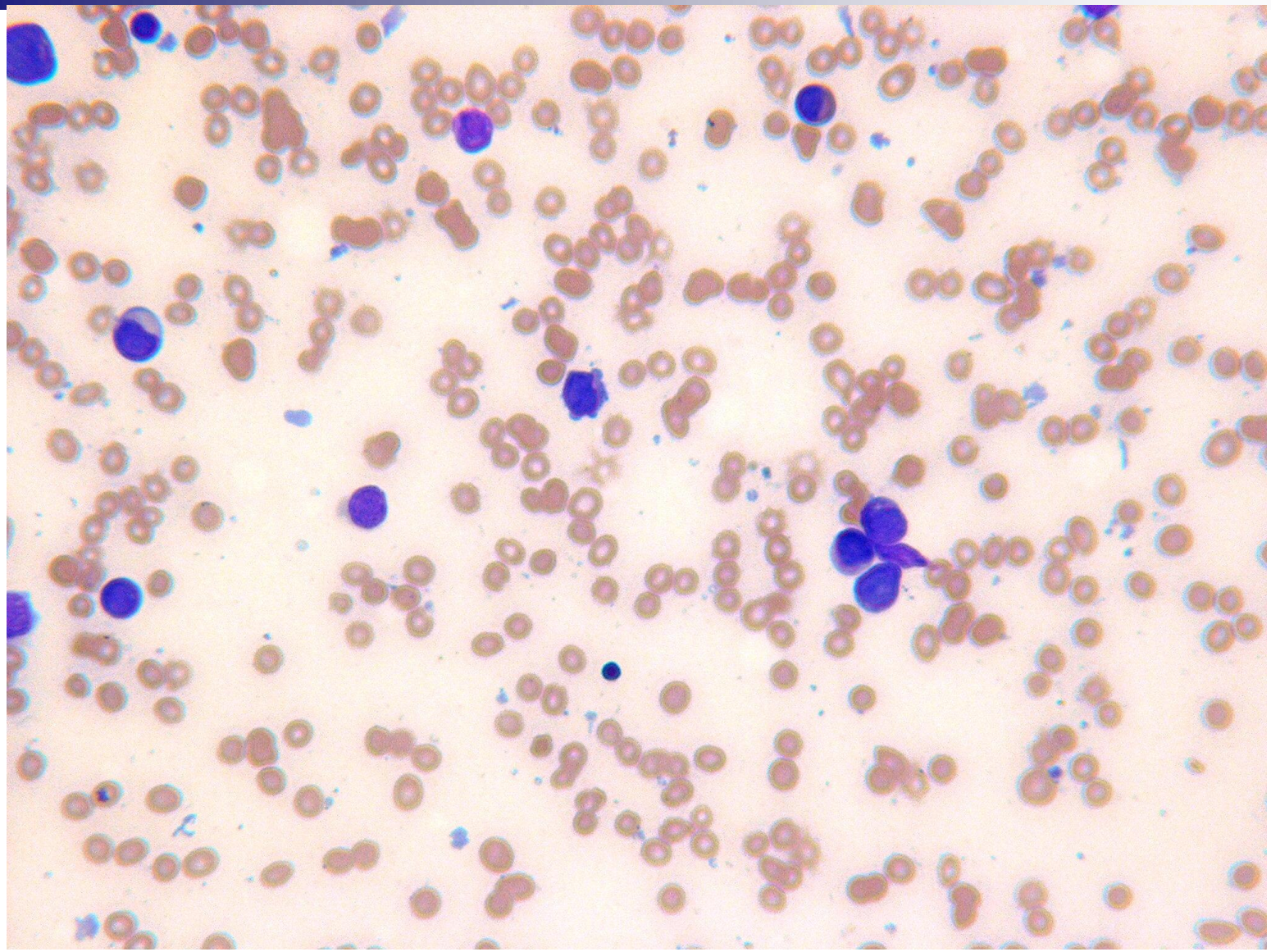
Peripheral blood smear, cont'd
69% blasts, some with auer rods



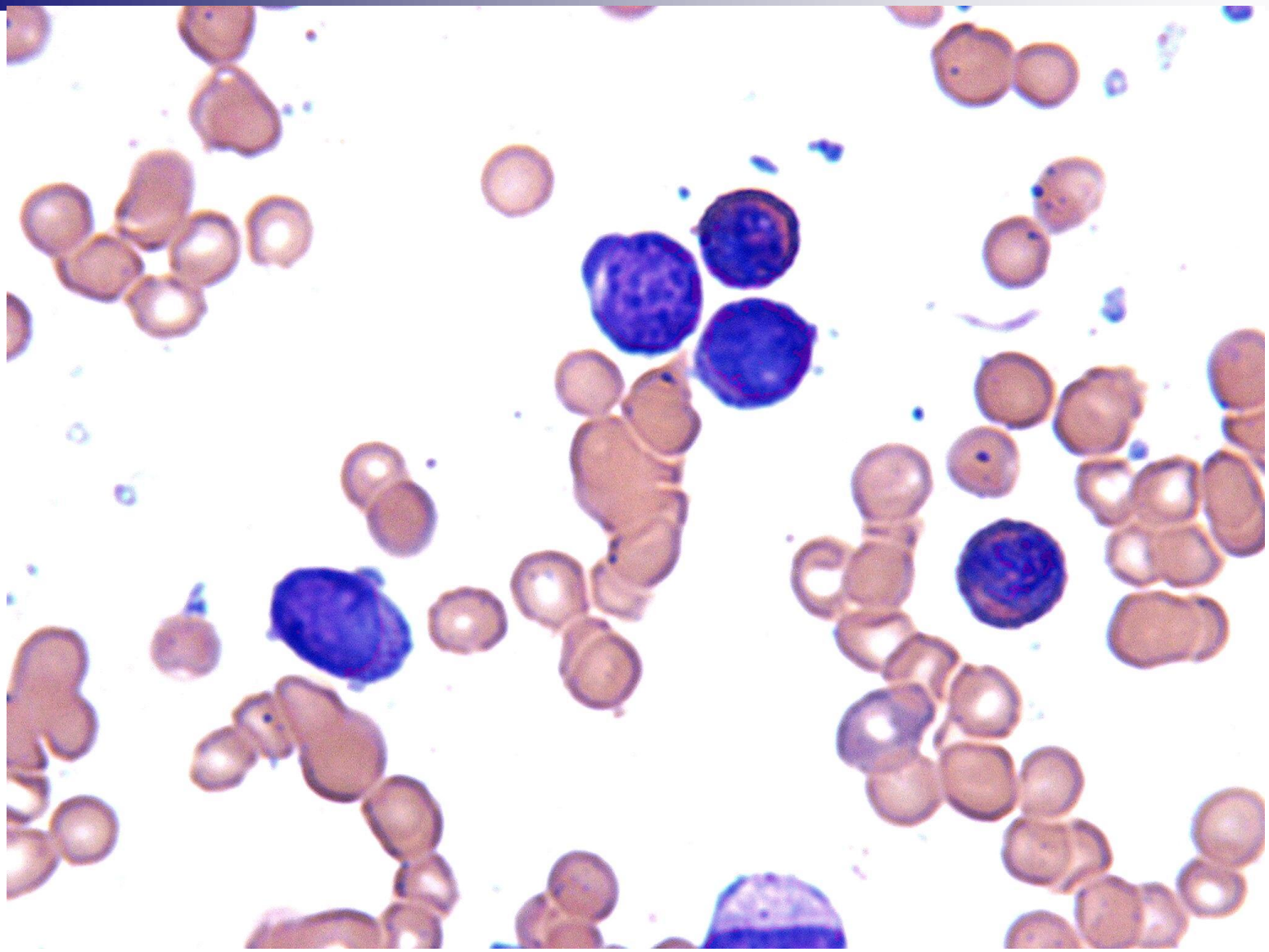
Peripheral blood smear, cont’d



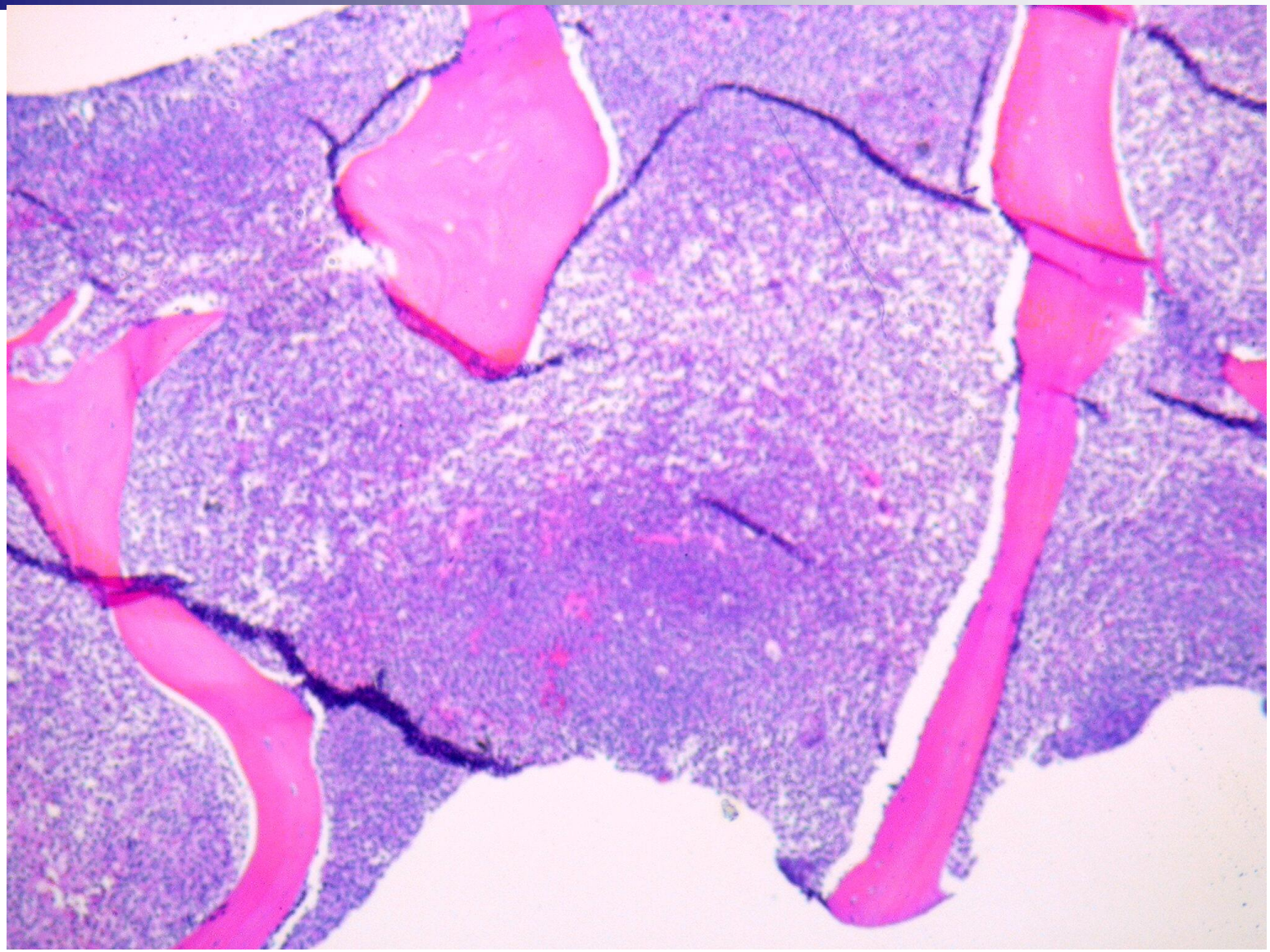
Peripheral blood smear, cont’d



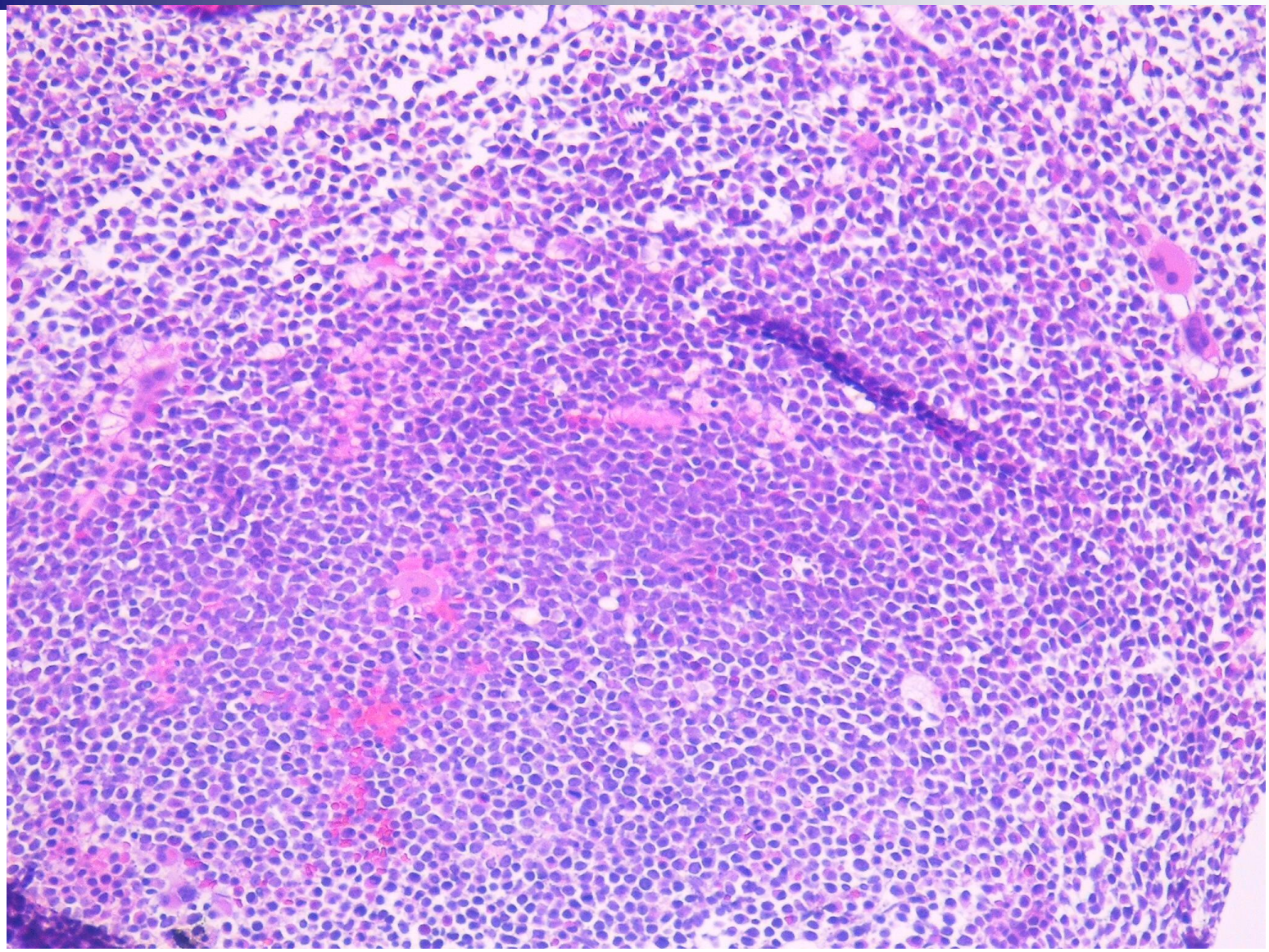
Bone marrow aspirate: hypocellular
60% blasts



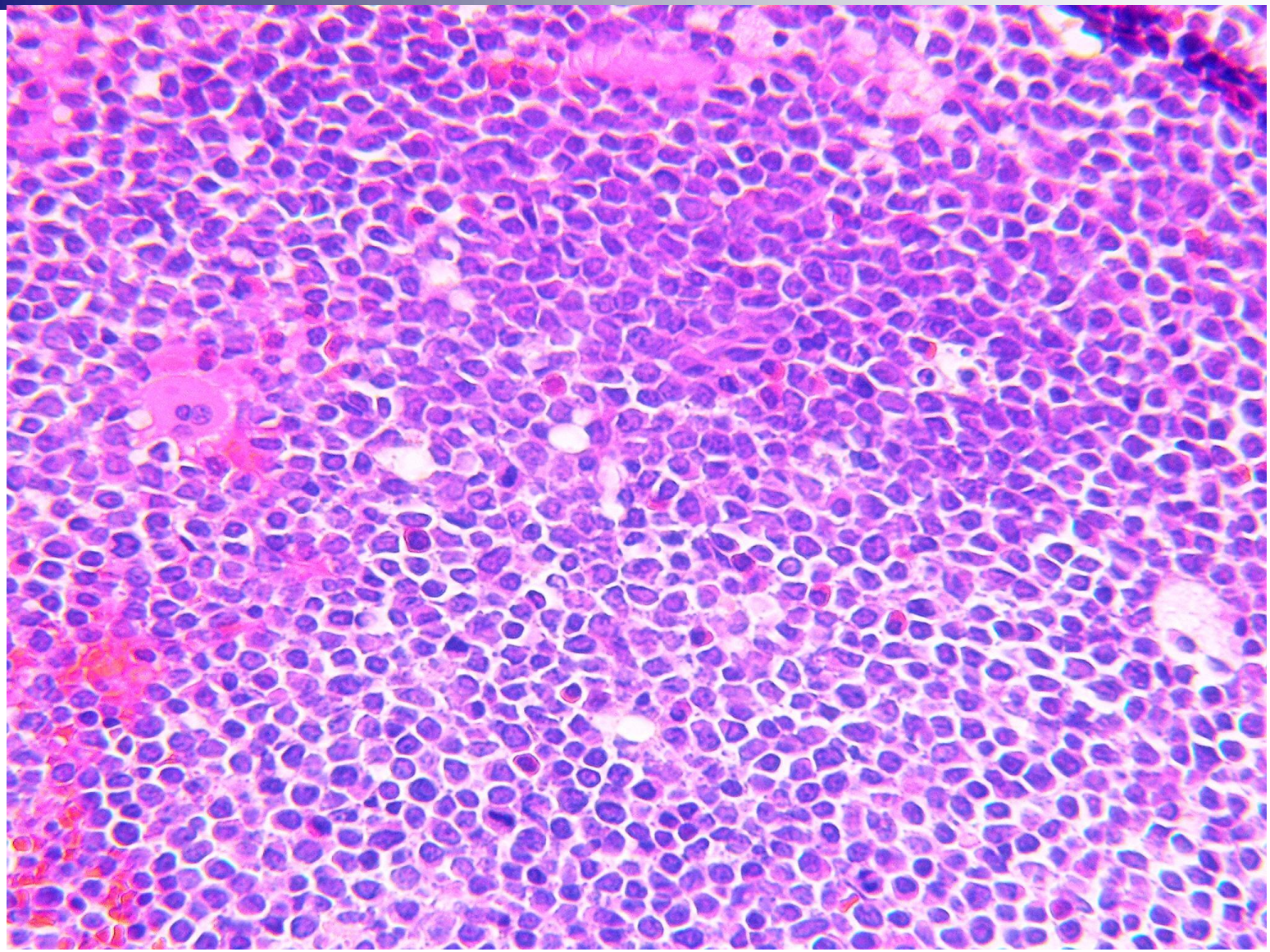
Bone marrow aspirate, cont'd



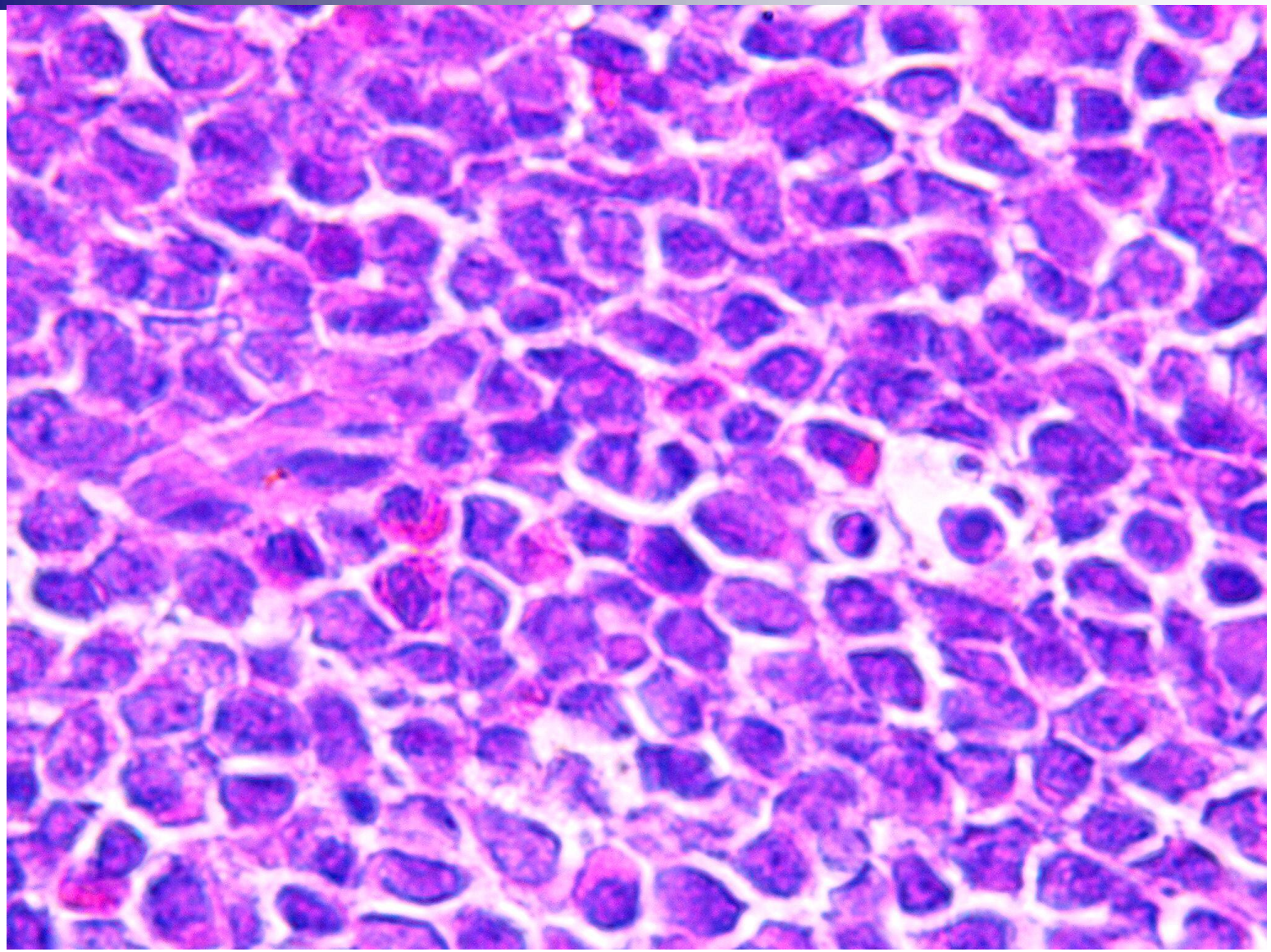
Bone marrow biopsy



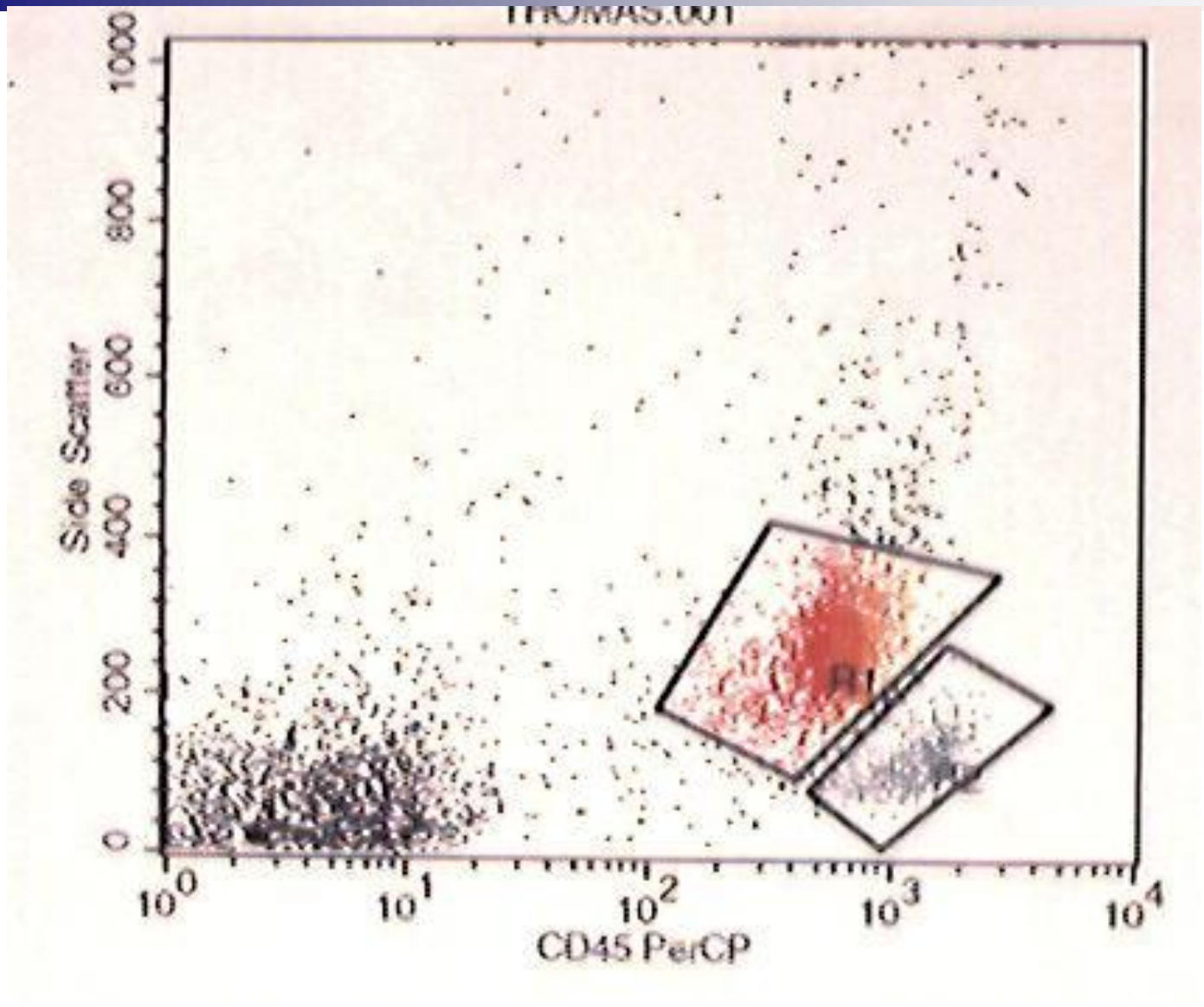
Bone marrow biopsy, cont'd



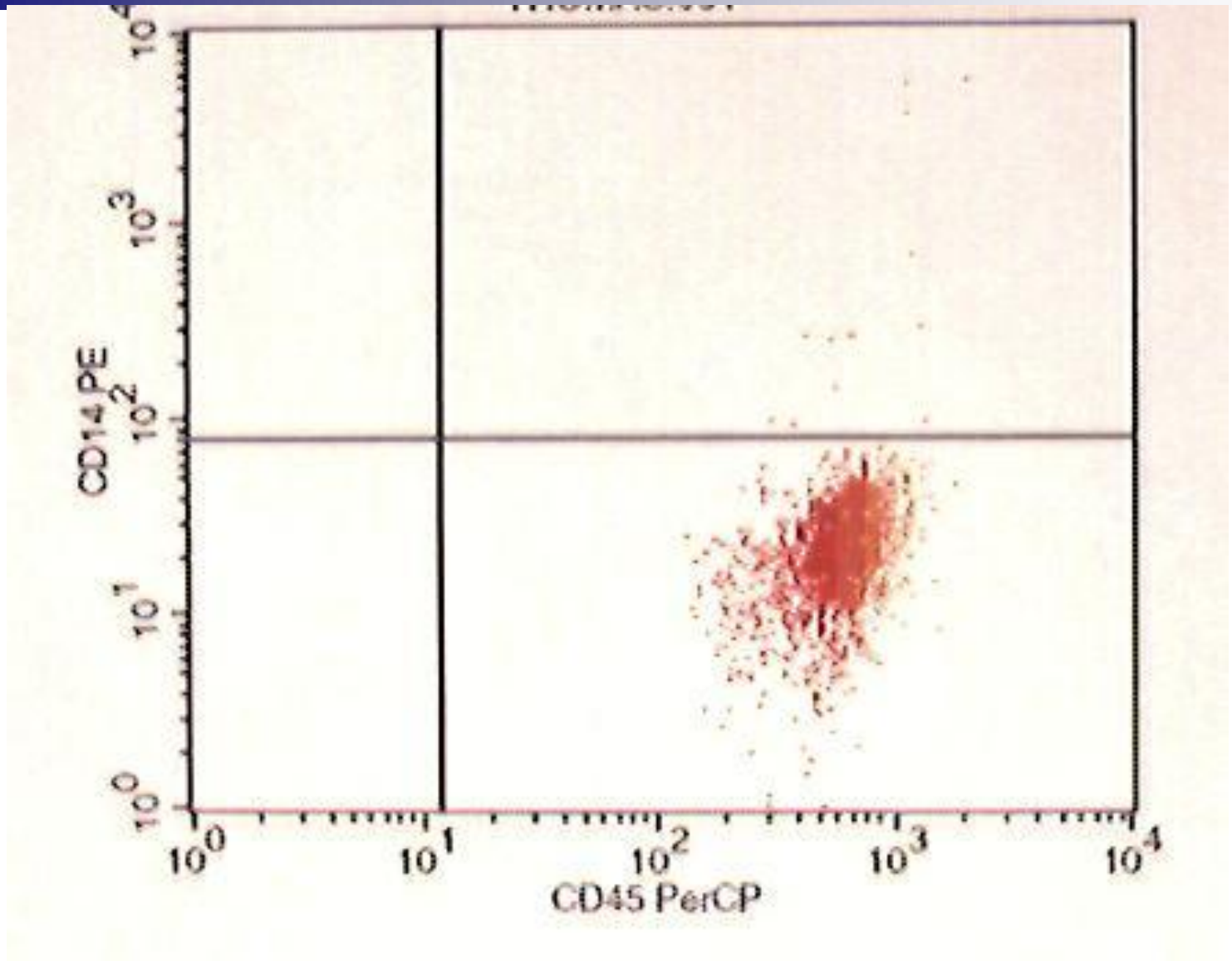
Bone marrow biopsy, cont'd



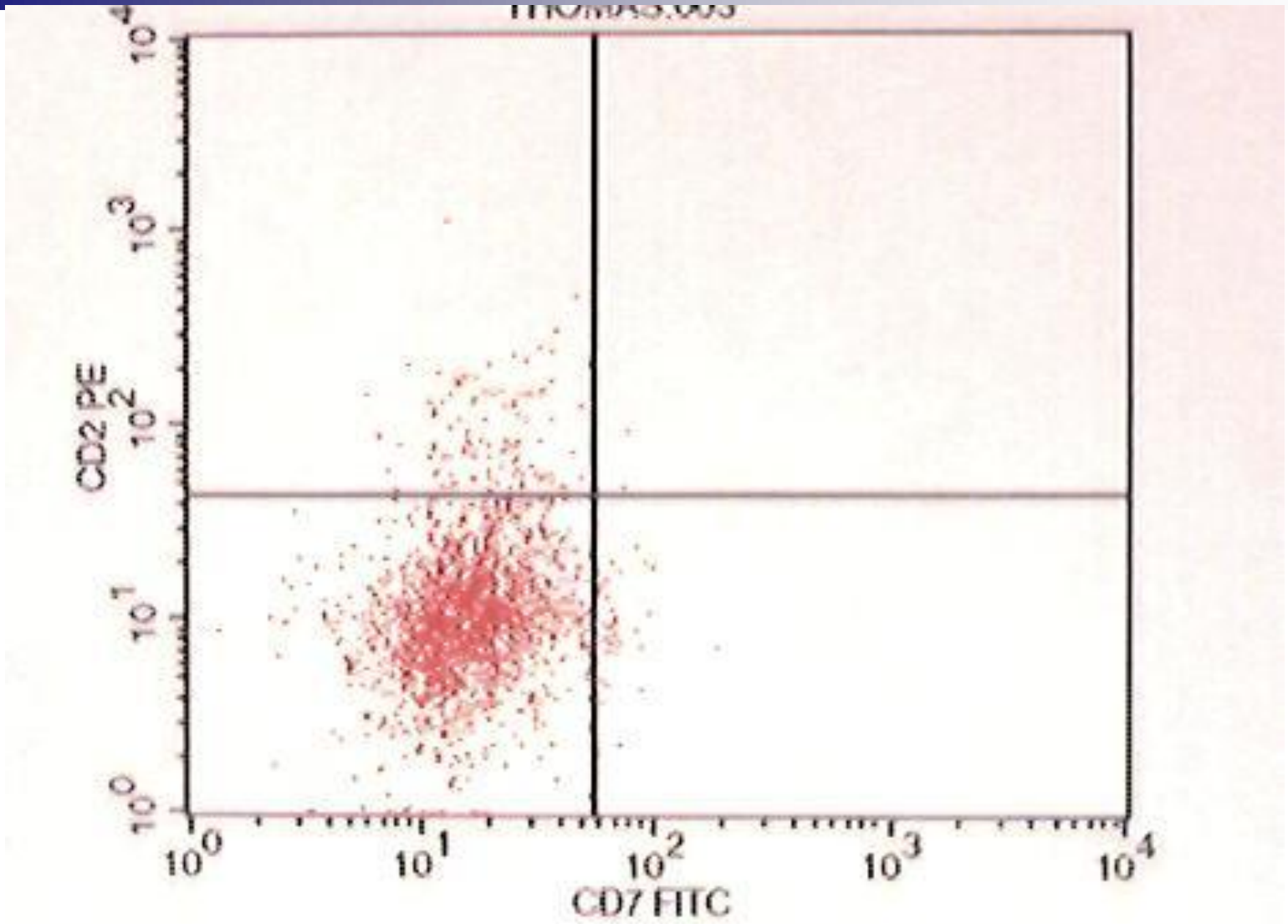
Bone marrow biopsy, cont'd



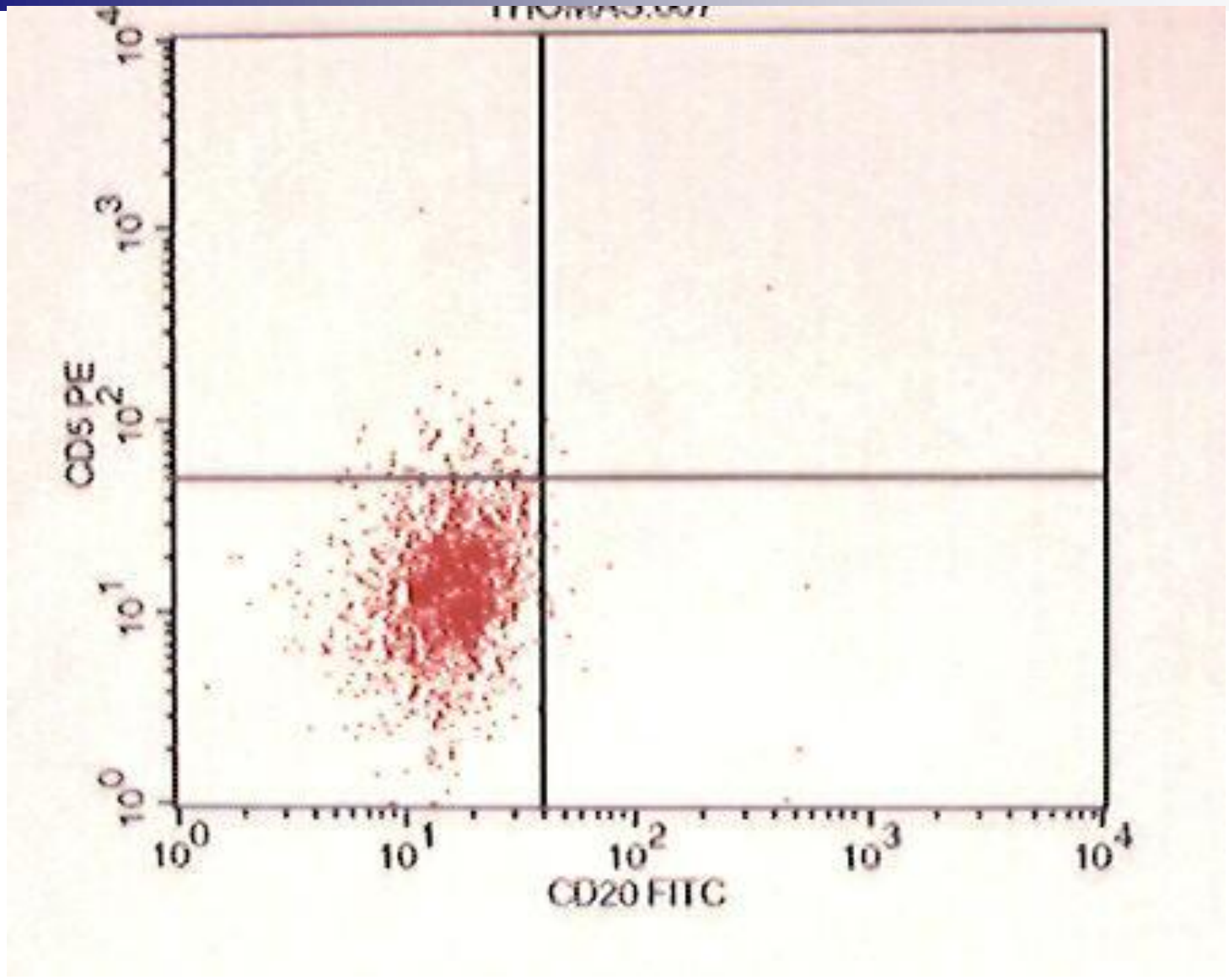
Flow cytometry with peripheral blood, gating



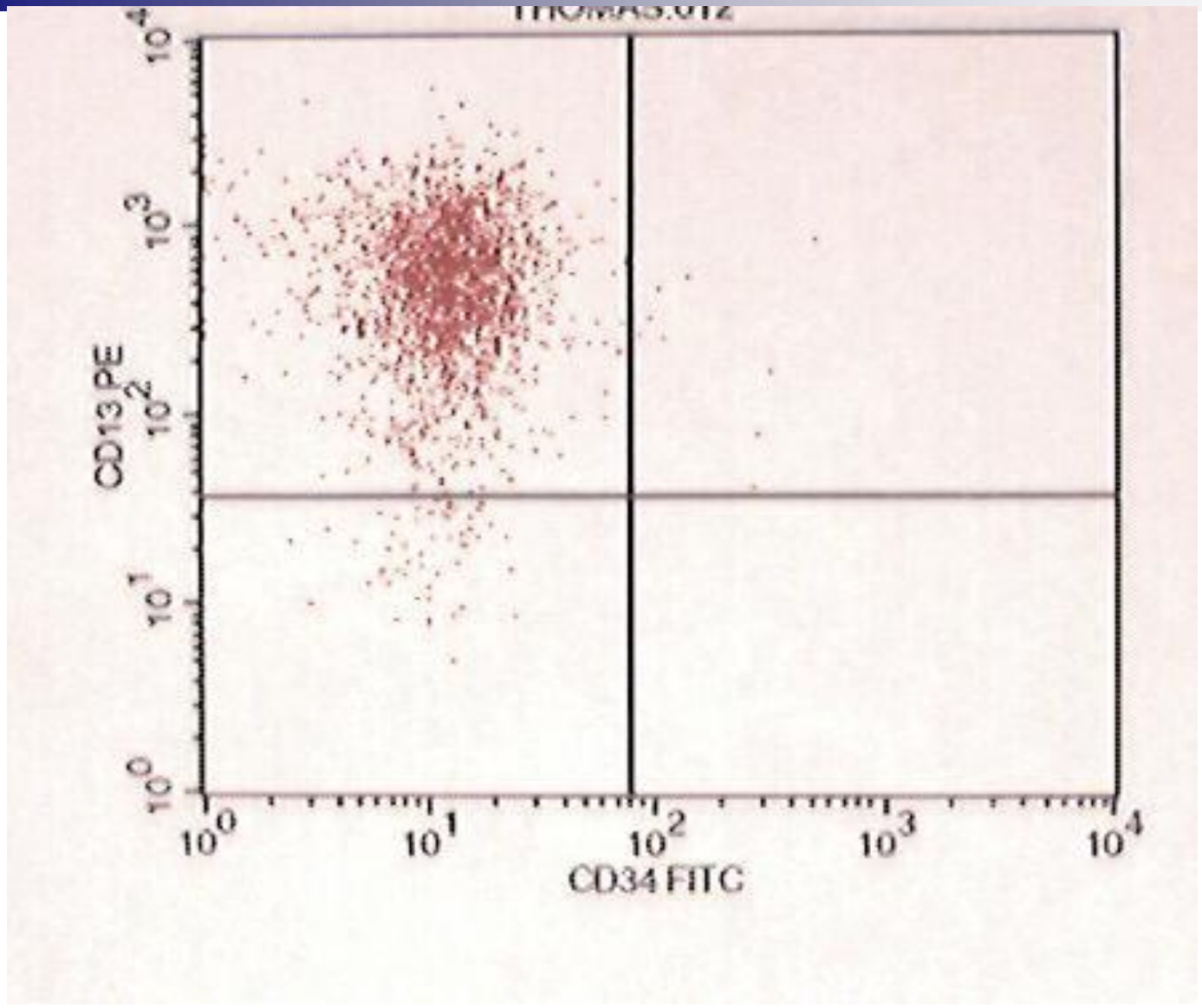
Flow cytometry, CD45-CD14



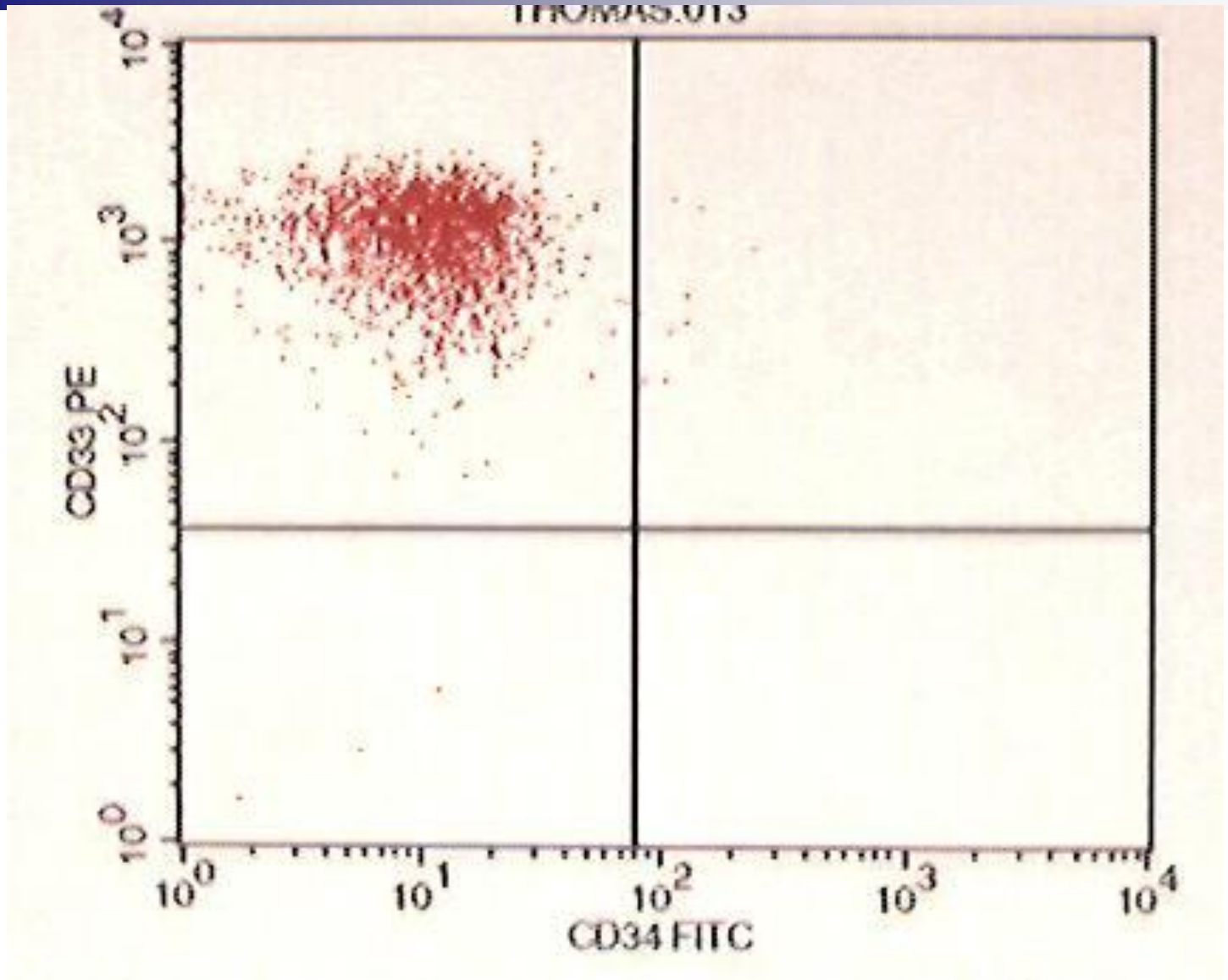
Flow cytometry, CD7-CD2



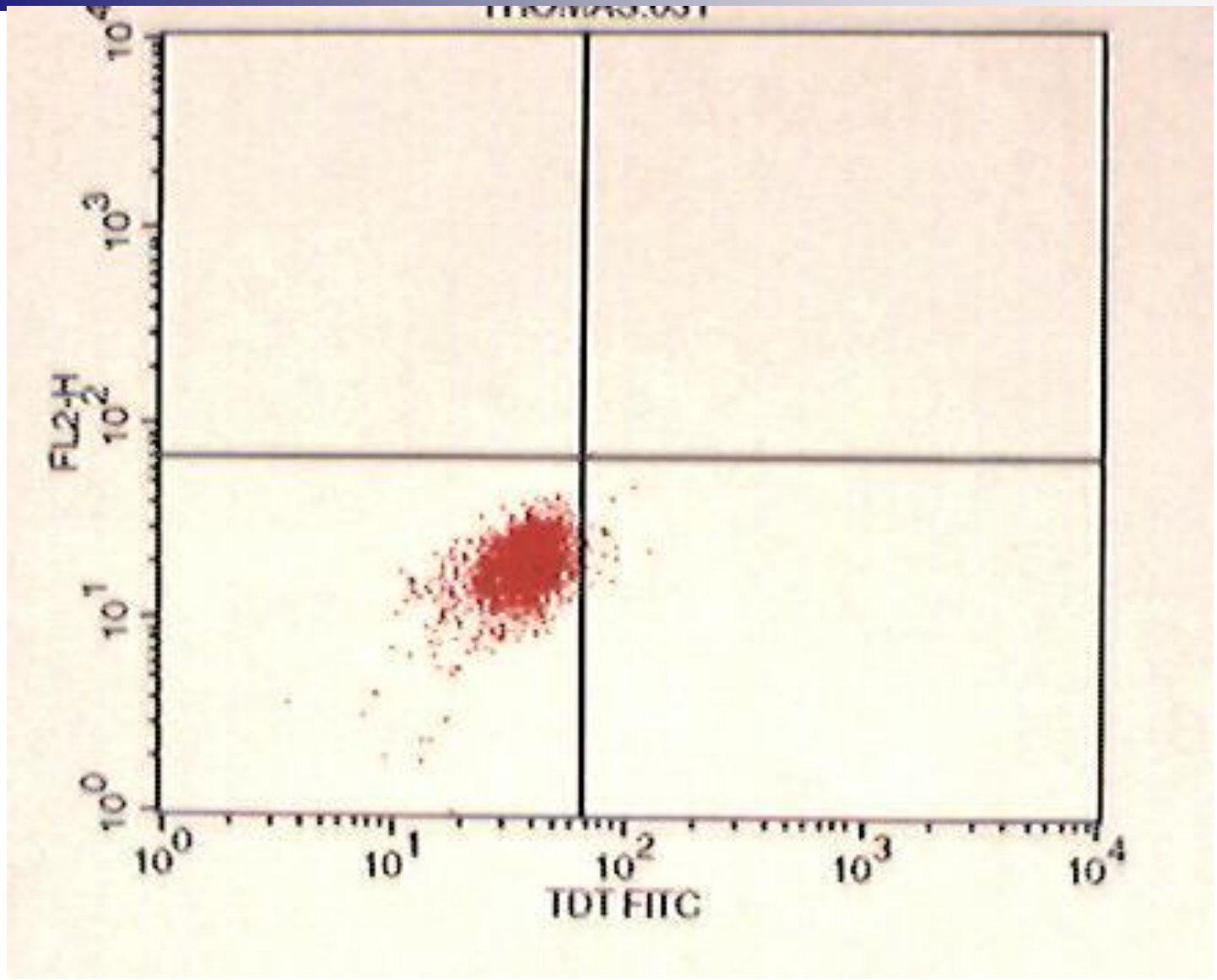
Flow cytometry, CD20-CD5



Flow cytometry, CD34-CD13



Flow cytometry, CD34-CD33



Flow cytometry, TdT

Diagnosis

- Flow cytometry results: a large blast population that is
  (+) CD13, CD33
  (-) CD14

- DX; Acute myeloblastic leukemia with maturation
  (FAB: AML-M2)

- Cytogenetics (bone marrow biopsy):
  (a) –X : loss of one copy of X chromosome
  (b) +8 : trisomy 8, a common abnormality in myeloid leukemia
  (c) add(18)(q2) : addition of unknown chromatin on 18q

Acute myeloblastic leukemia with maturation

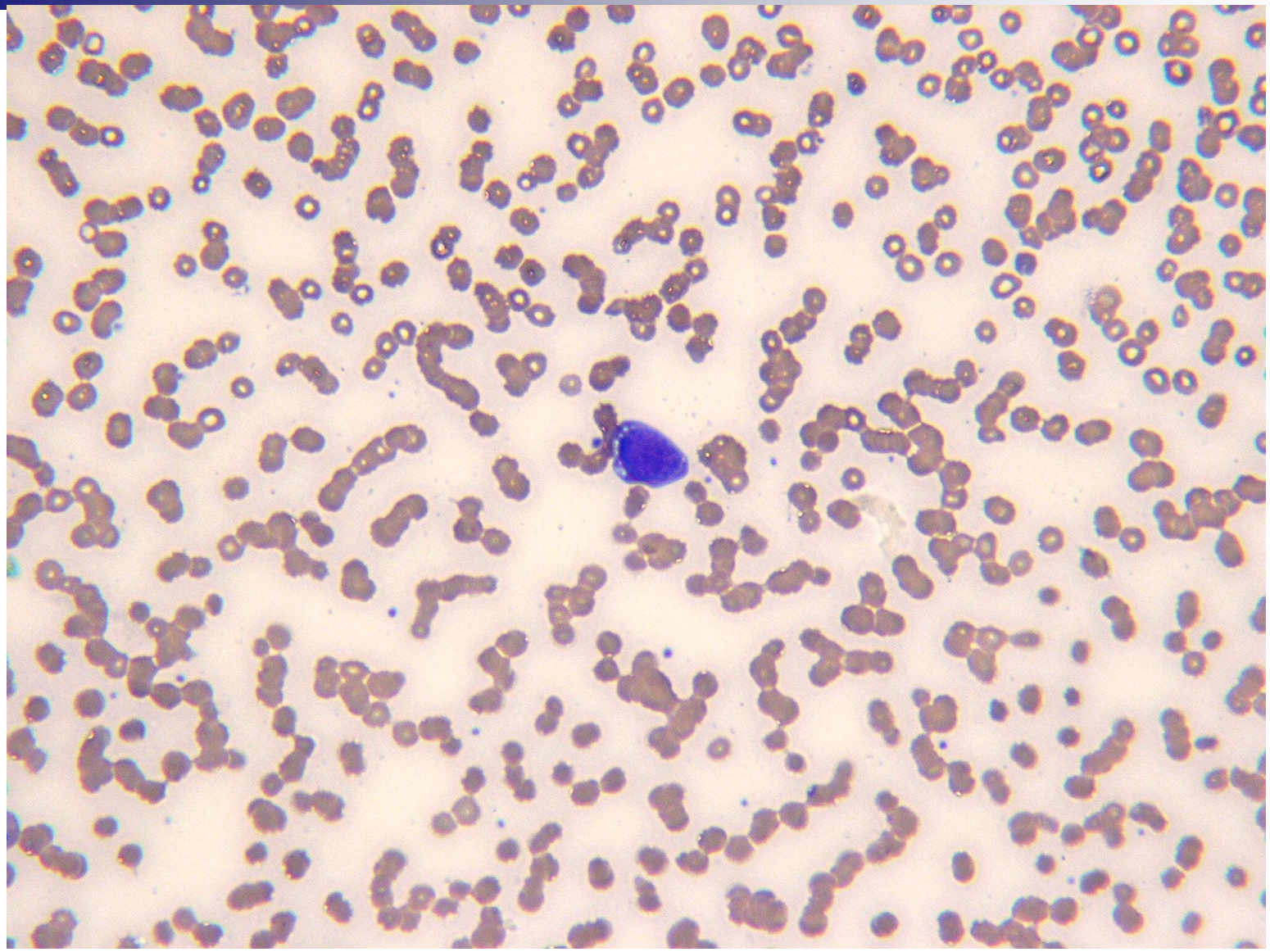
- (1) More than 20% of myeloblasts in bone marrow
  (2) Evidence of granulocytic maturation
  (Promy+myel+meta+band+PMN >10%)
  (3) Less than 20% monocytic cells

- 30-45% of AML cases
  20% of pts below 25 y/o
  40% of pts above 60 y/o

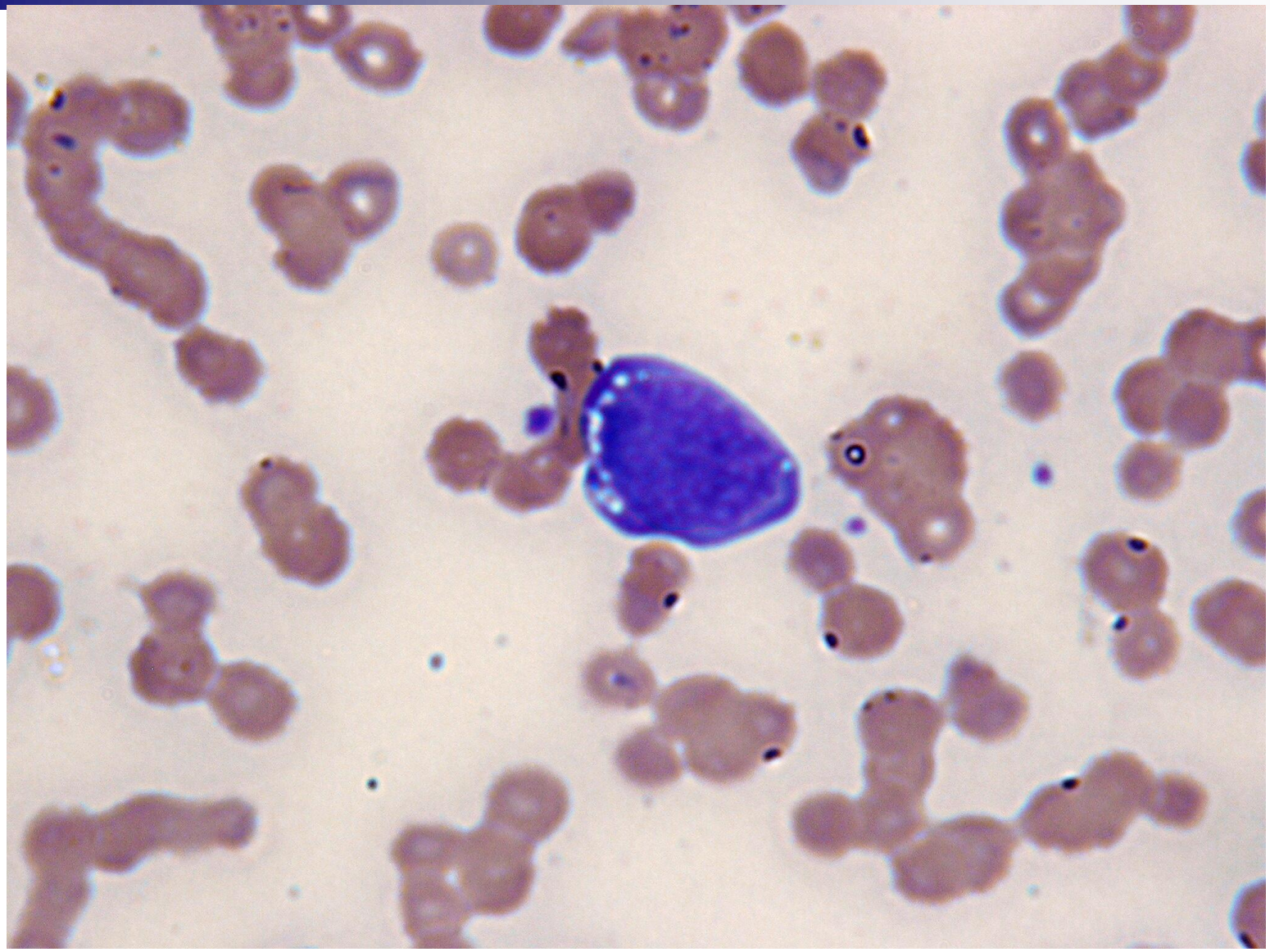
- Cytogenetics:
  (a) t(8;21) -> favorable prognosis, classified under AML with recurrent cytogenetic abnormalities (WHO)
  (b) del 12
  (c) t(6;9)-> poor prognosis
  (d) t(8;16)

Bone Marrow Case
Patient: Tlxx Shxxx

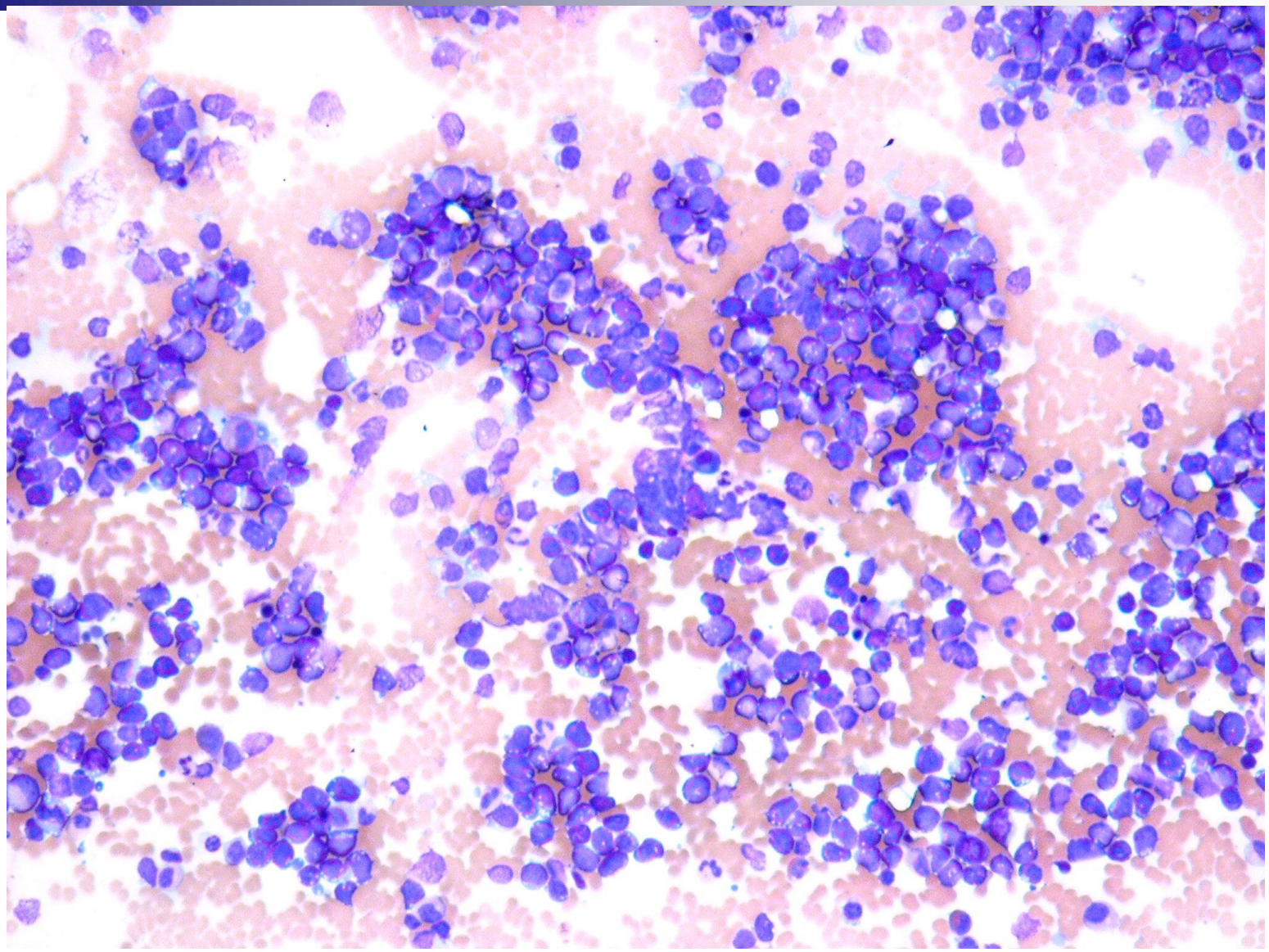
- 45 year old male HIV(+), with fever (T104), biliary duct obstruction, S/P ERCP
- WBC= 3.7, Hgb=6.5, Plt=40, Retic 0.7%, MCV 80.3 seg 66, lymph 17, mono 1, myelo 2, rare atypical cells
- GOT 55, GPT 72, AP 341, T bili 6.0



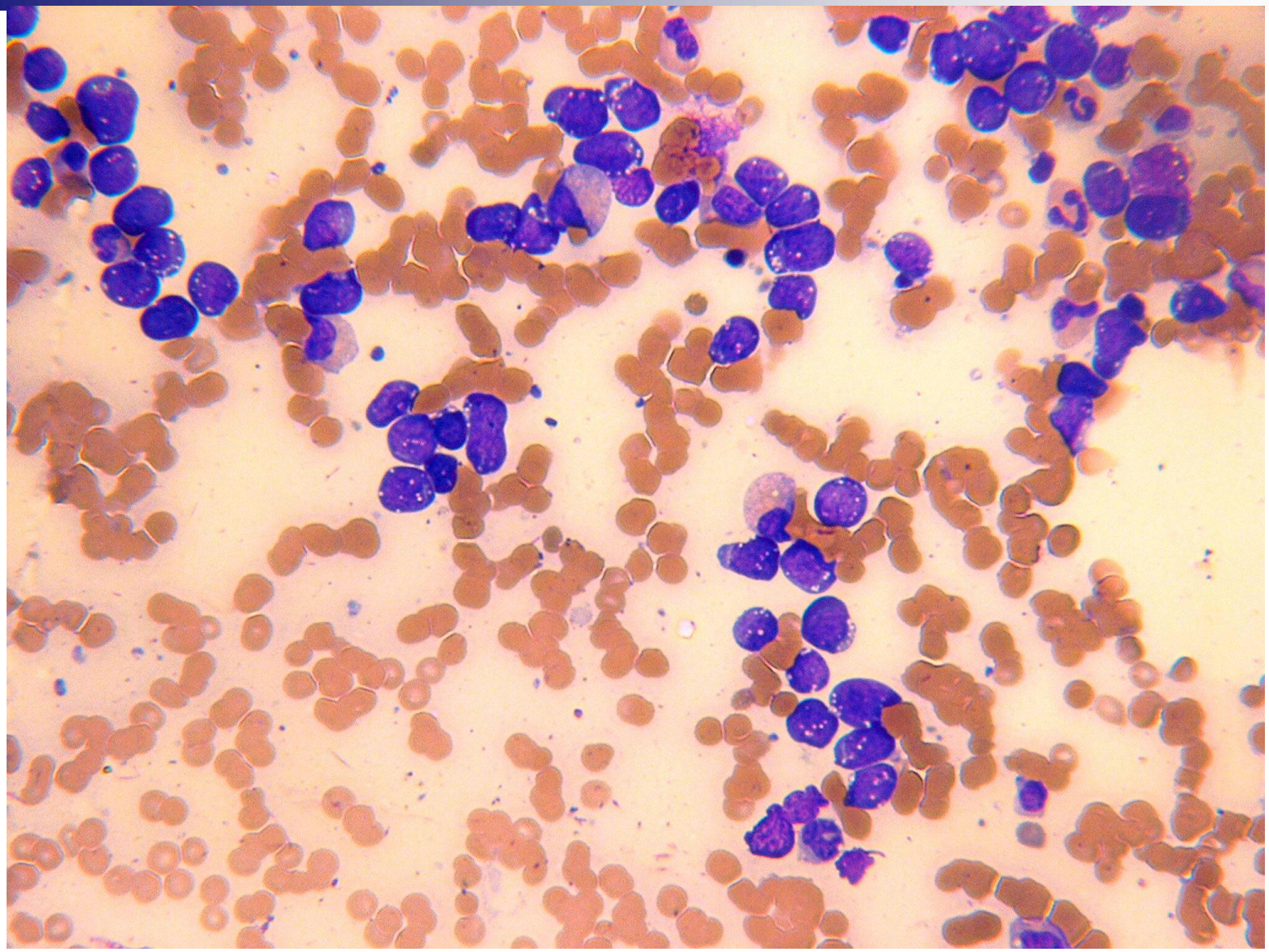
Peripheral blood smear



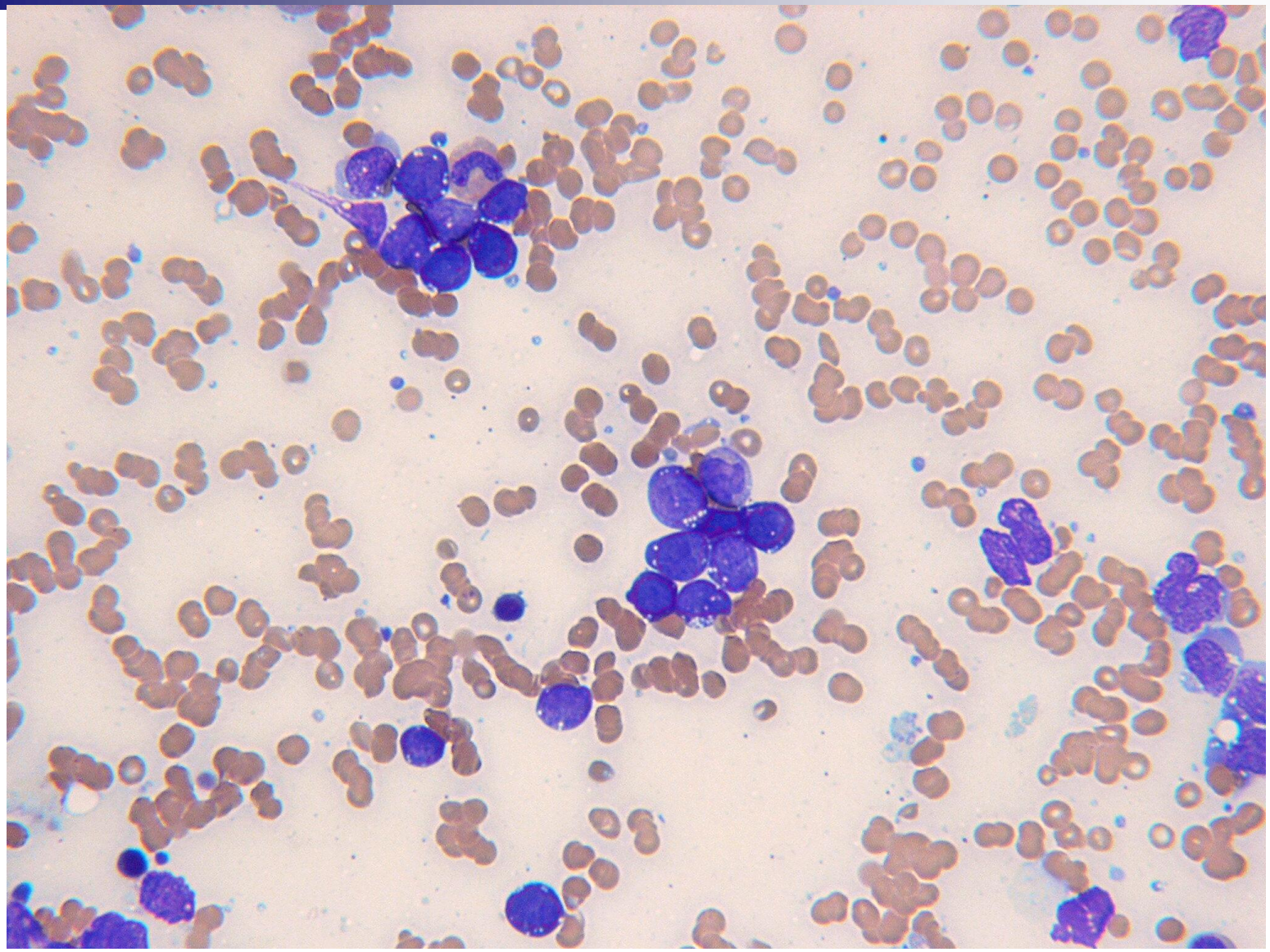
Peripheral blood smear, cont’d



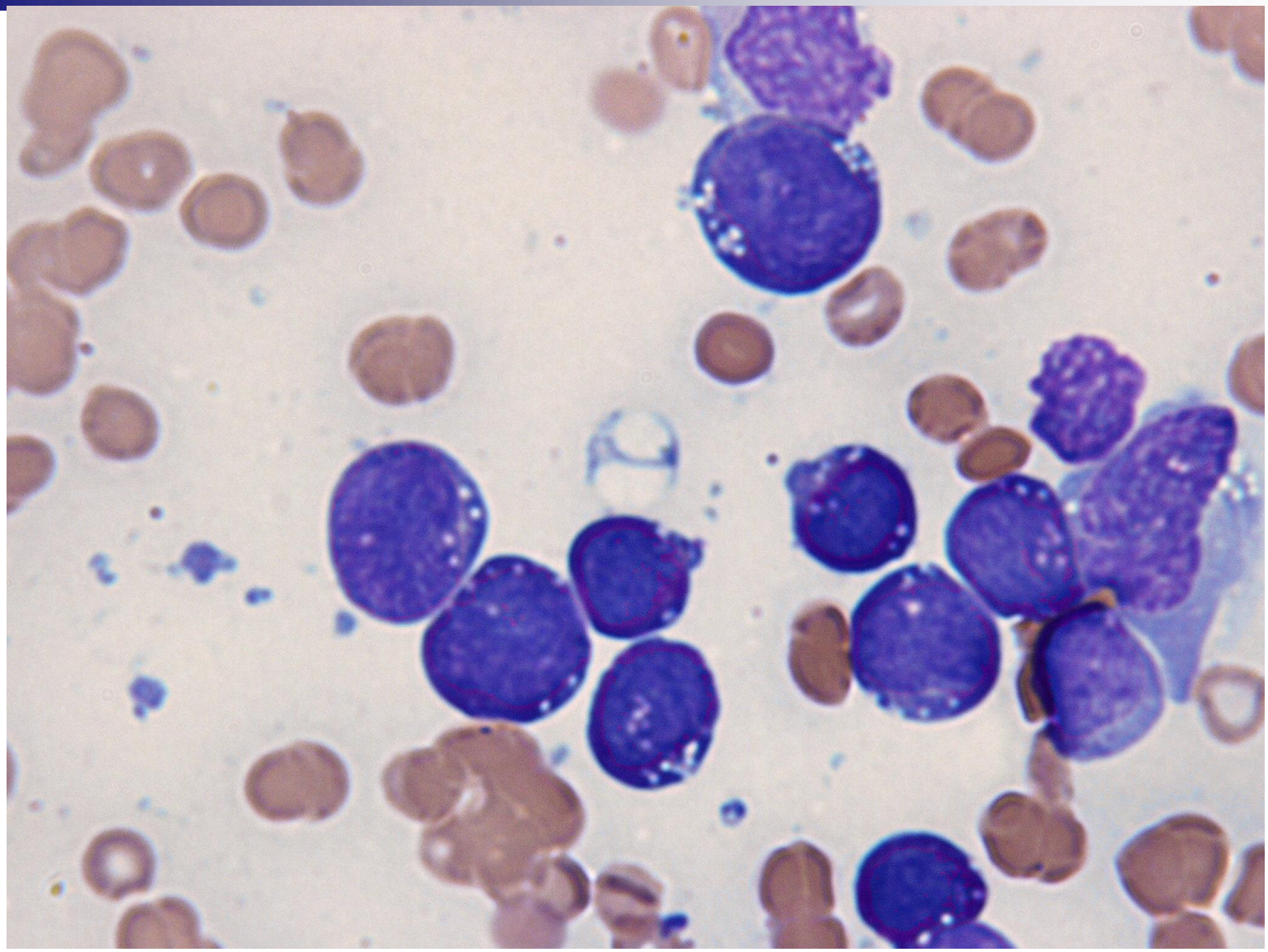
Bone marrow aspirate



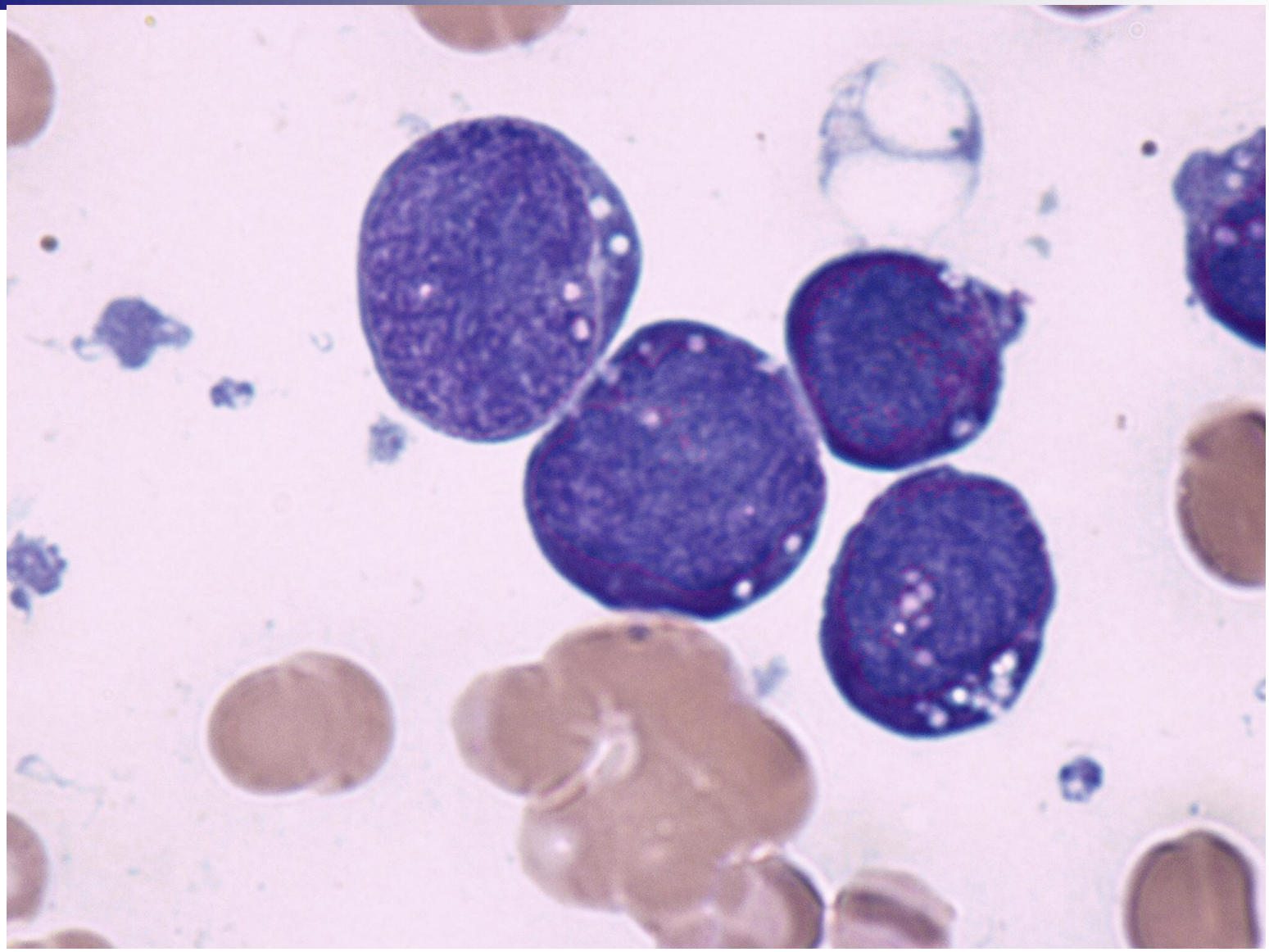
Bone marrow aspirate, cont'd
88% lymphoblasts



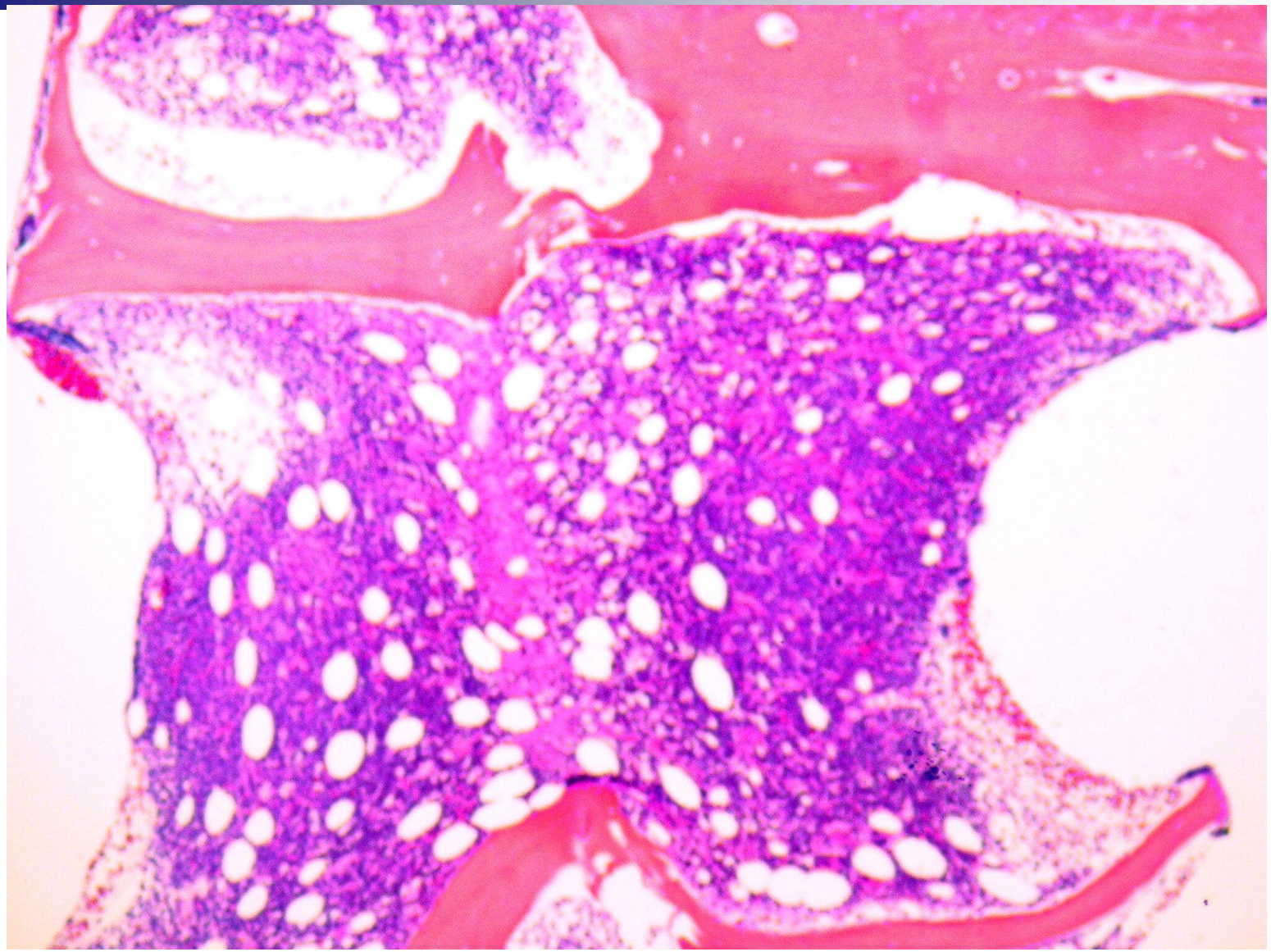
Bone marrow aspirate, cont’d



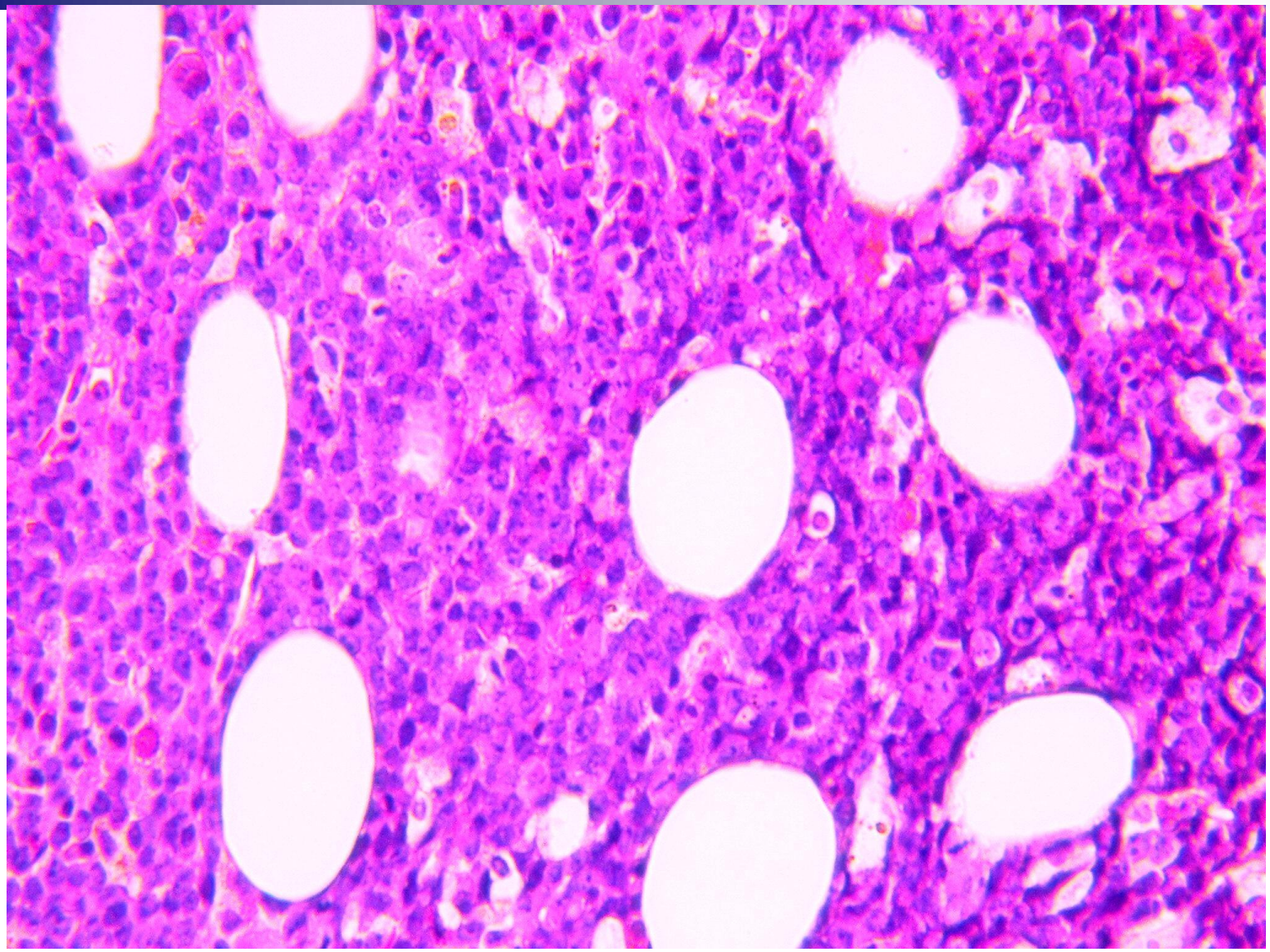
Bone marrow aspirate, cont’d



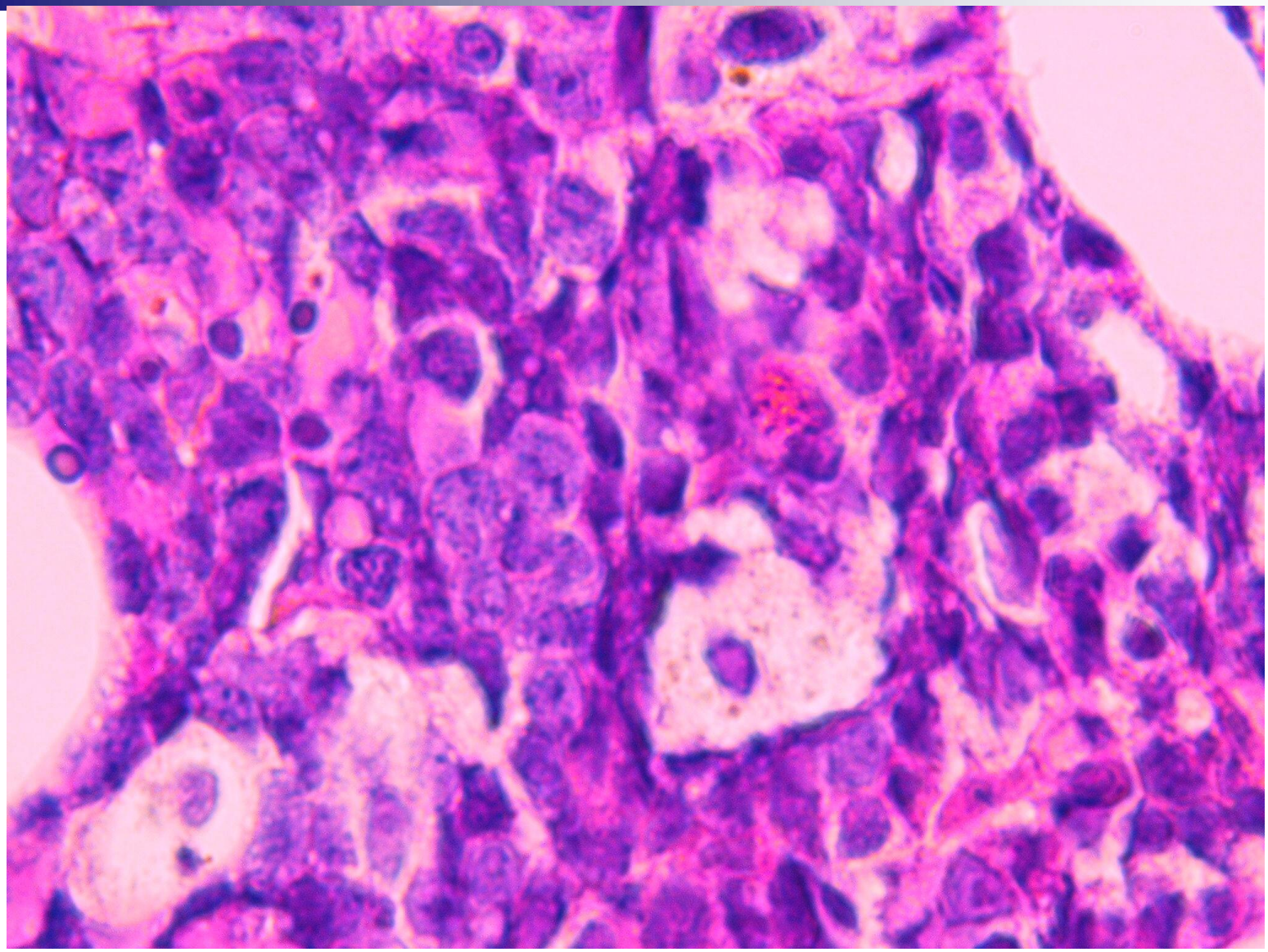
Bone marrow aspirate, cont’d



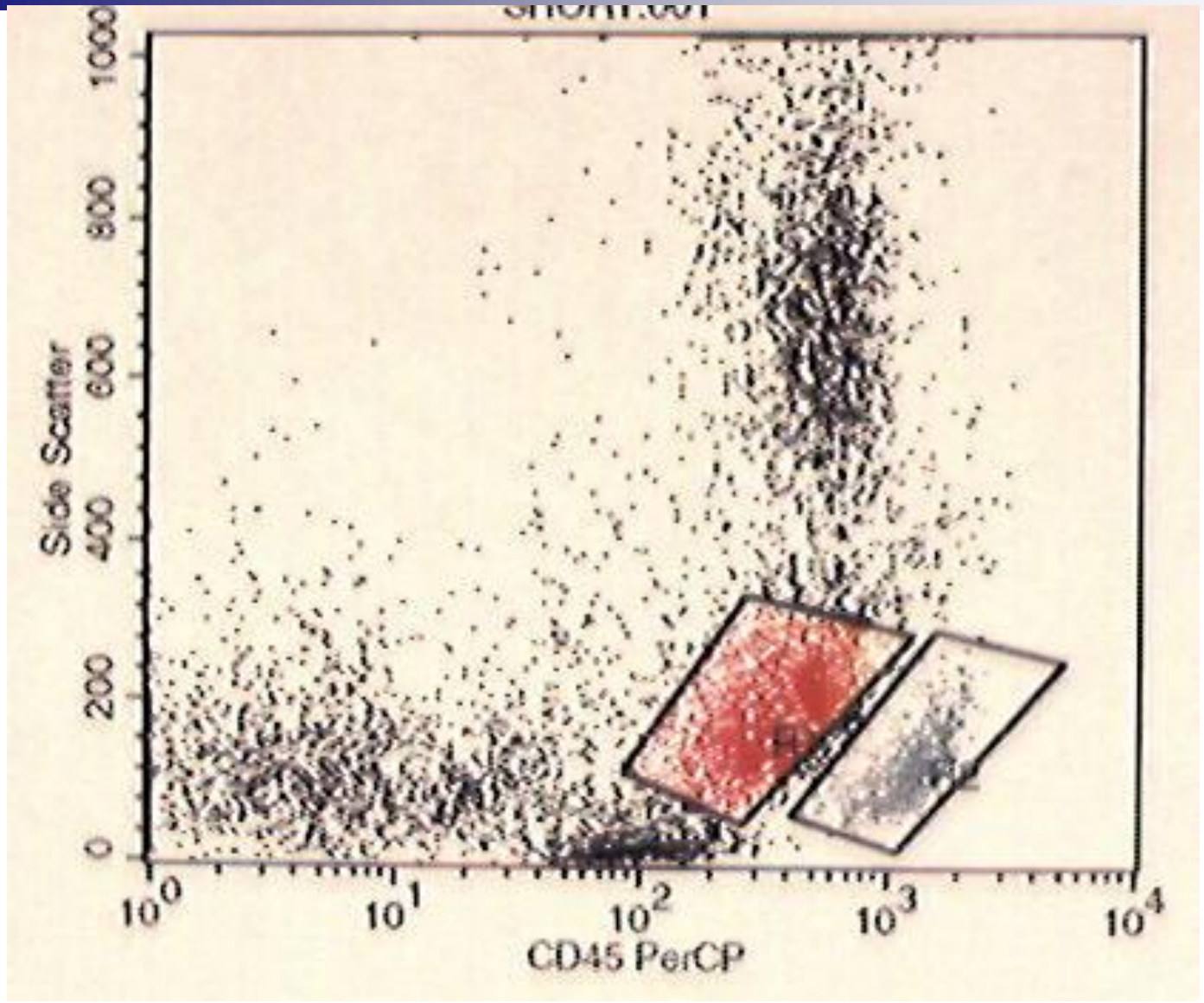
Bone marrow biopsy



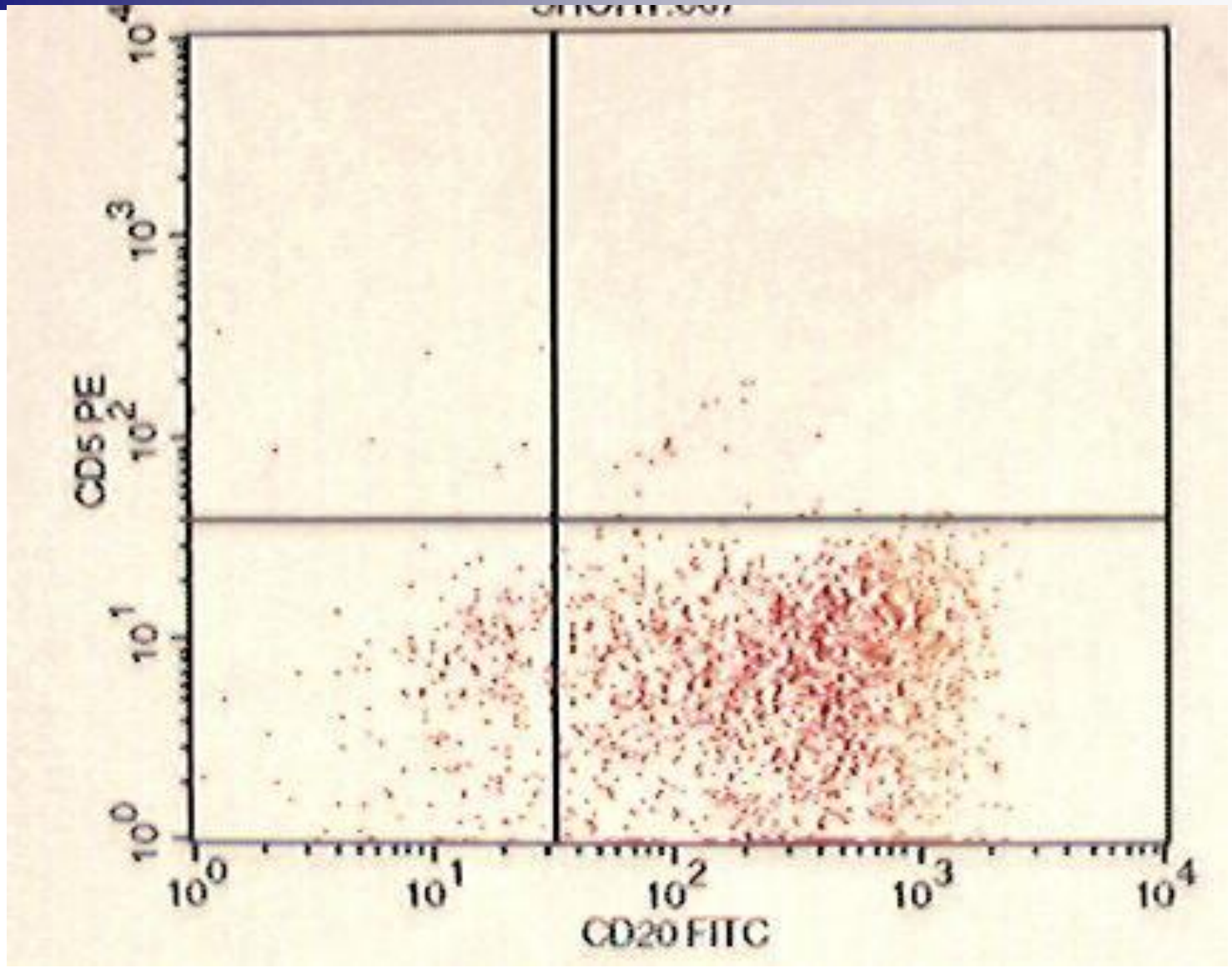
Bone marrow biopsy, cont’d



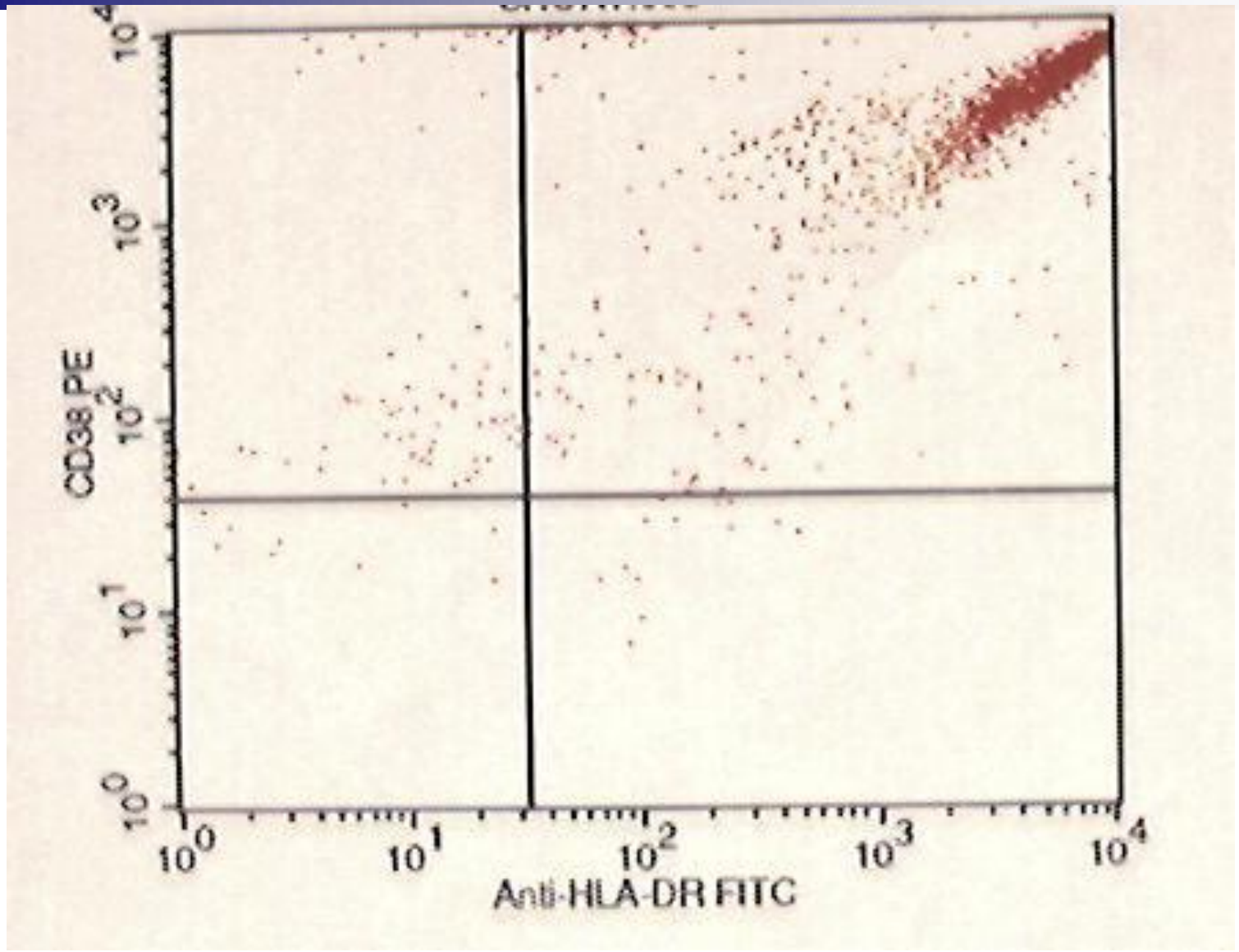
Bone marrow biopsy, cont’d



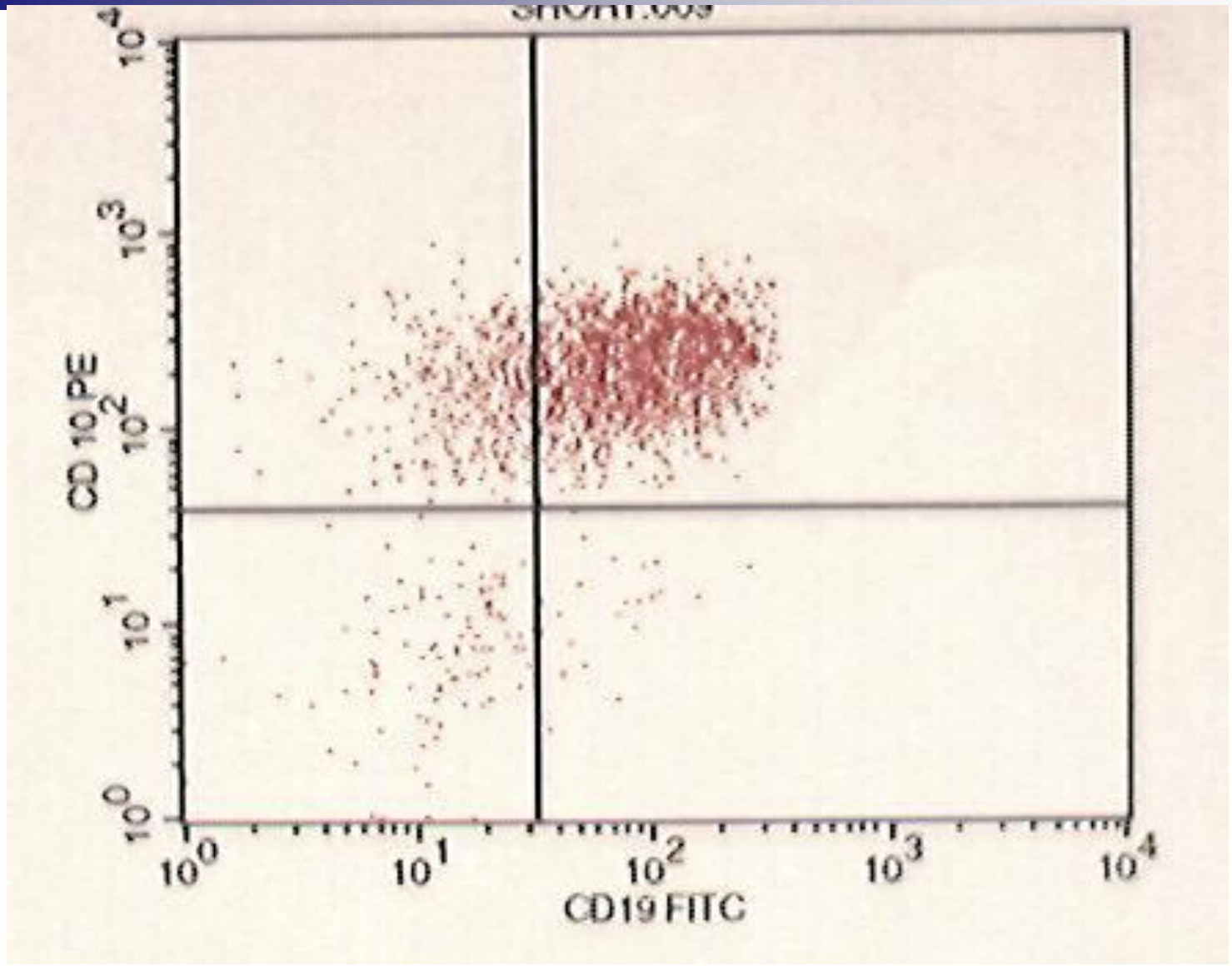
Flow cytometry, gating



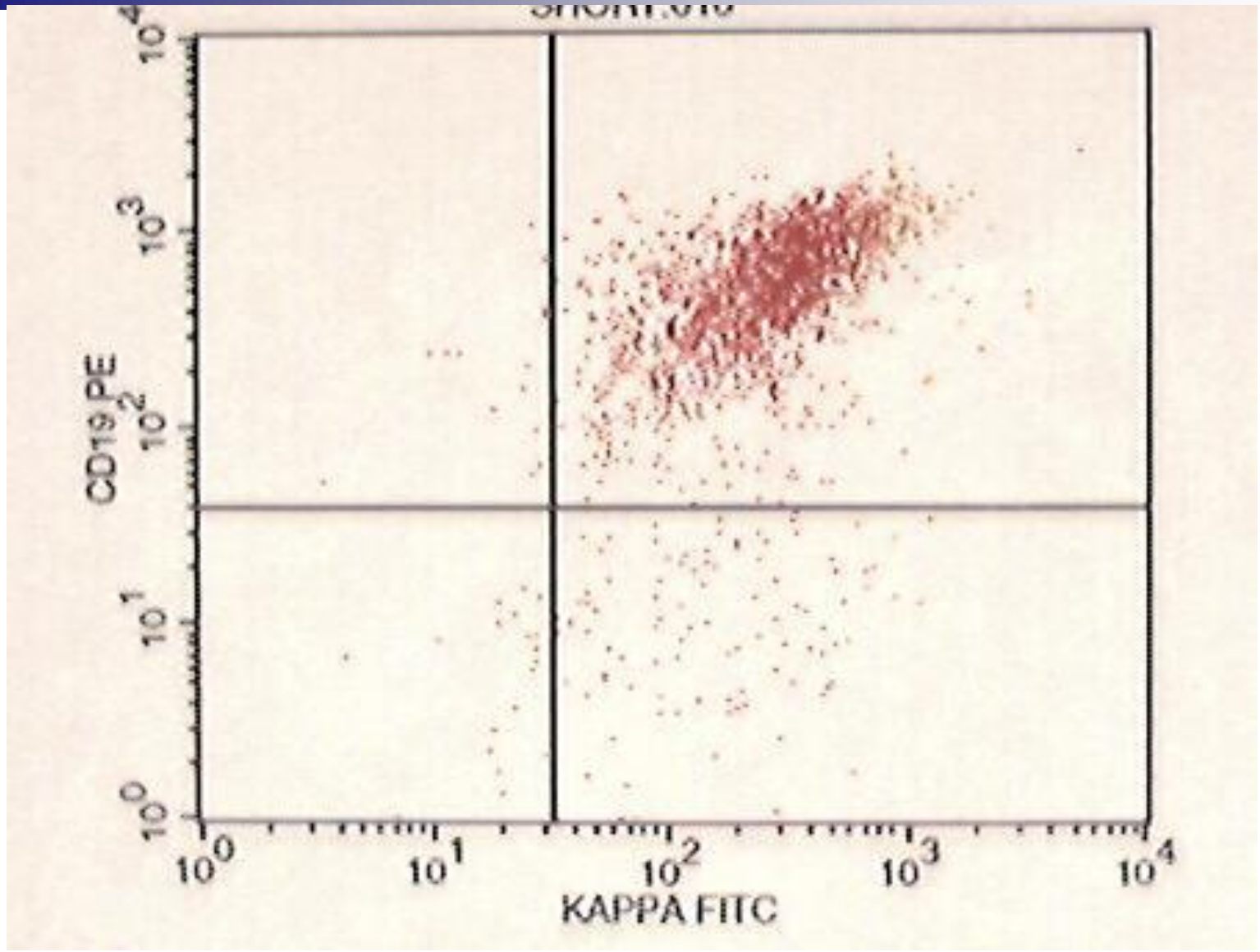
Flow cytometry, CD20-CD5



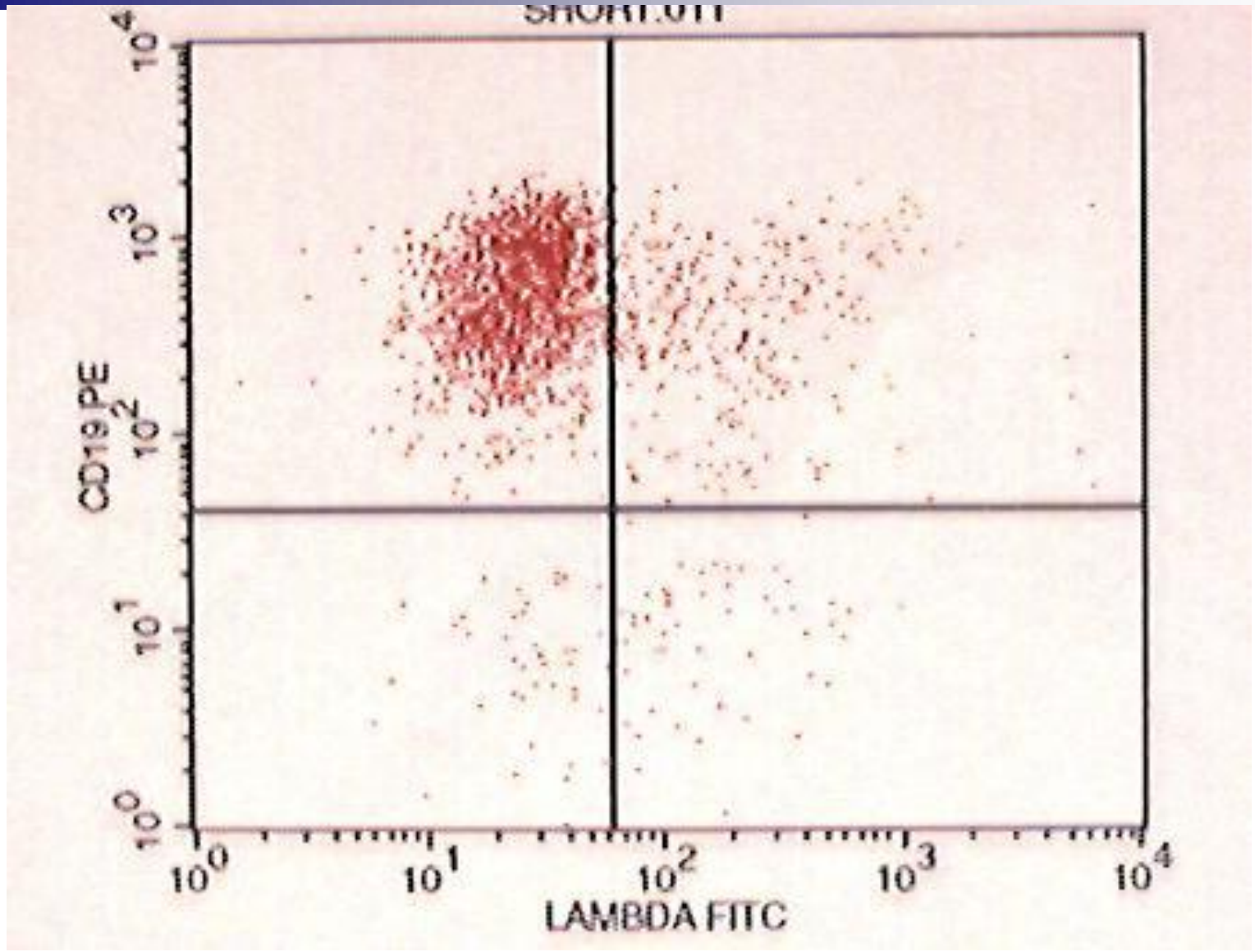
Flow cytometry, HLA DR-CD38



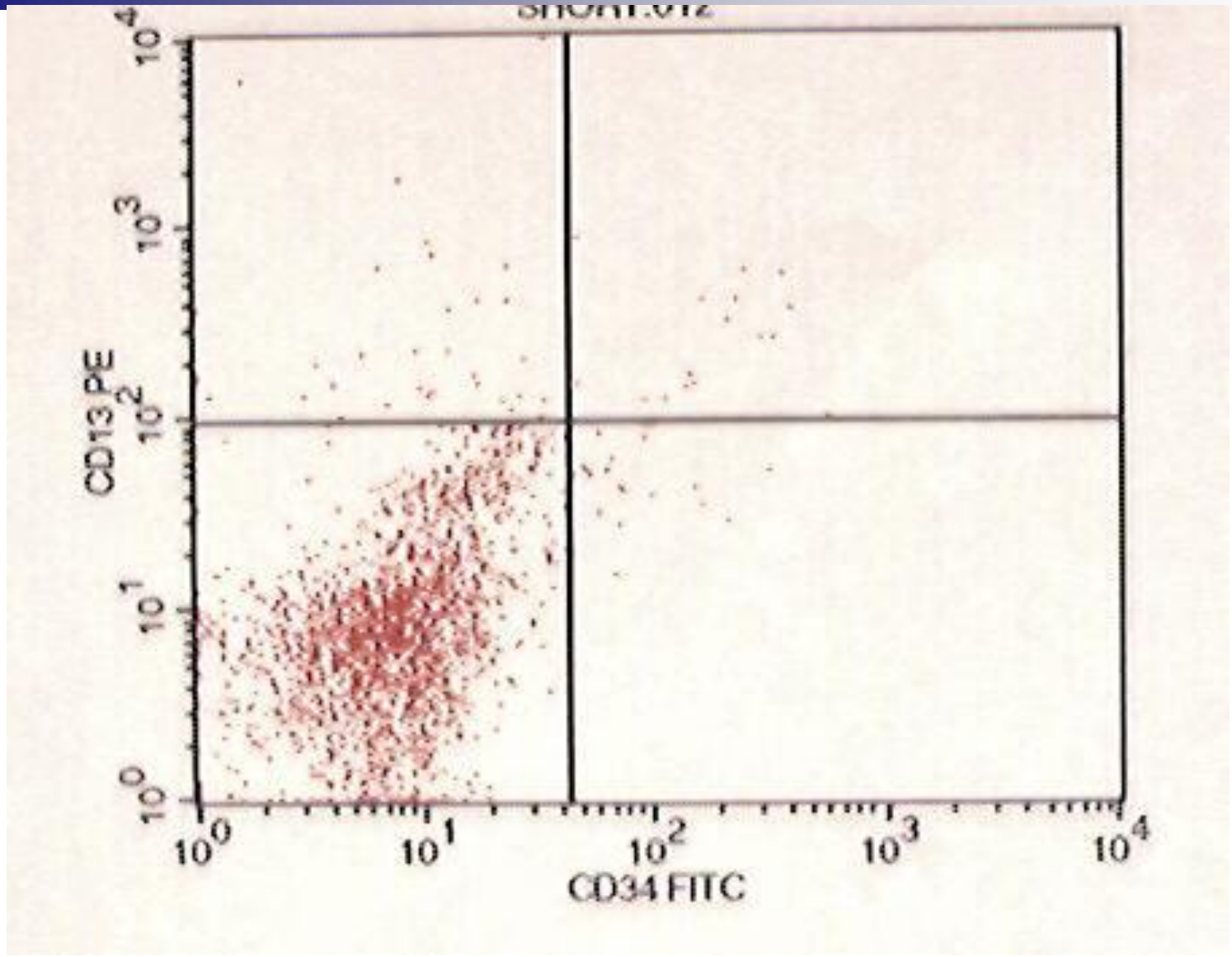
Flow cytometry, CD19-CD10



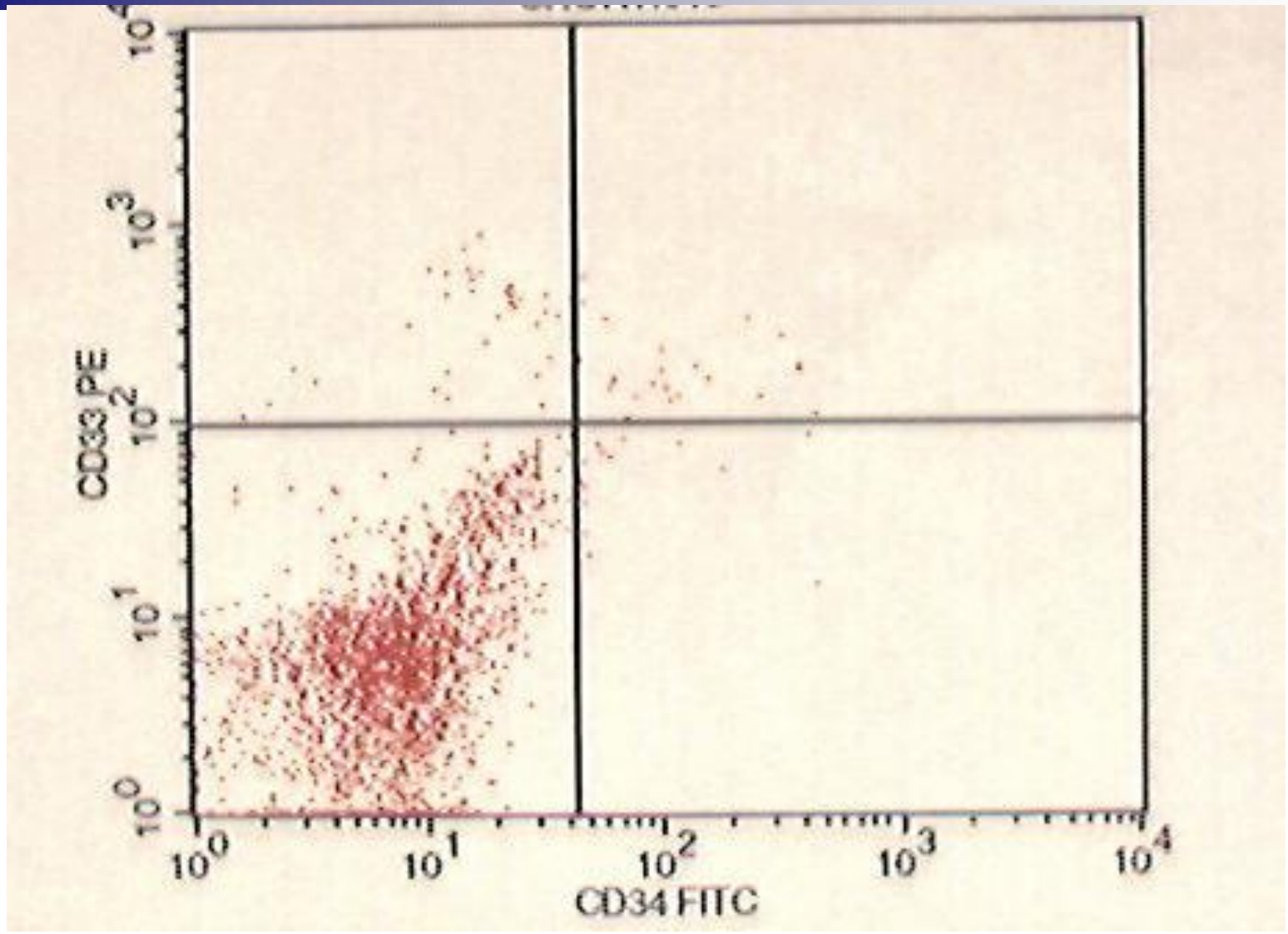
Flow cytometry, Kappa-CD19



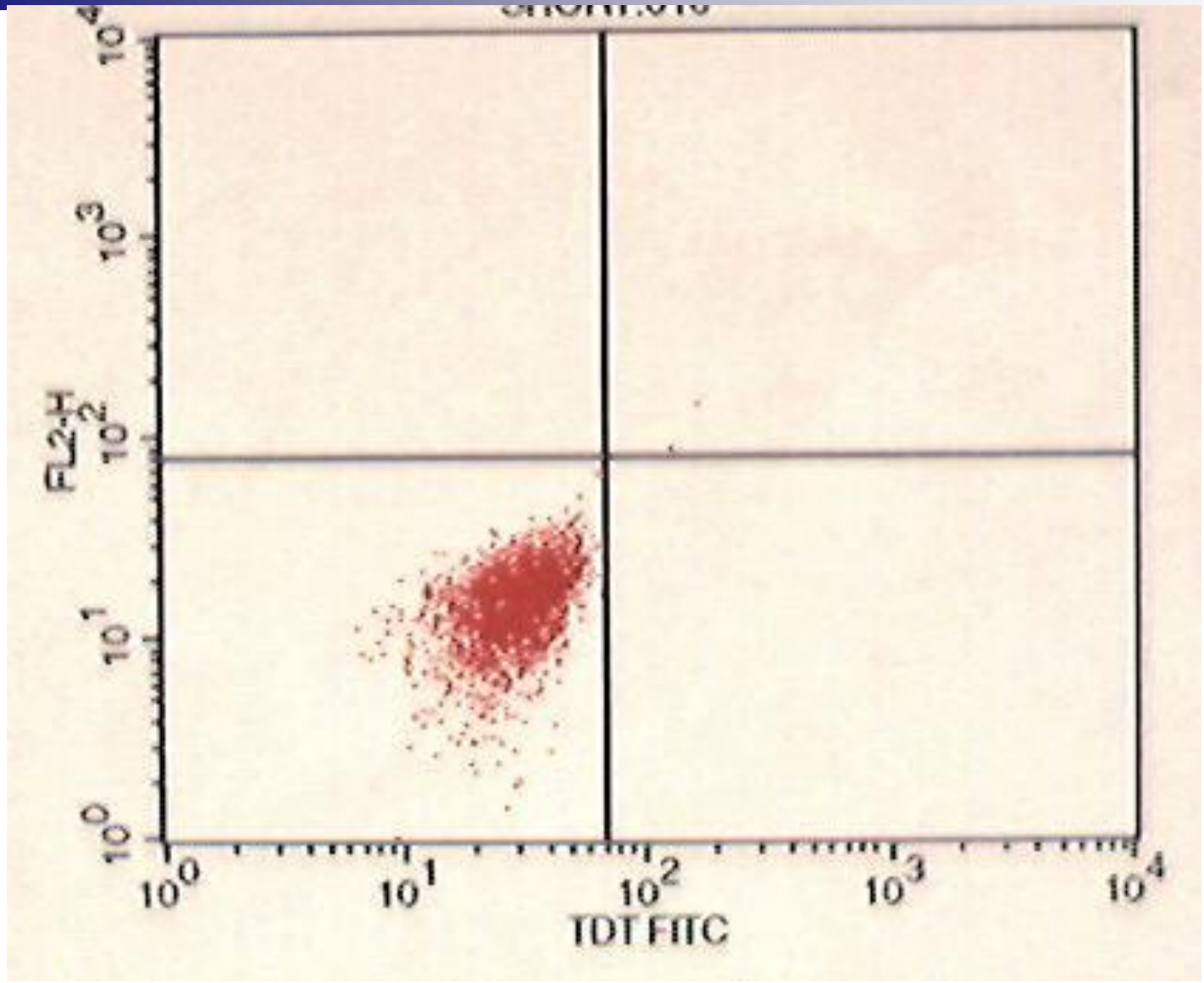
Flow cytometry, Lambda-CD19



Flow cytometry, CD34-CD13



Flow cytometry, CD34-CD33



Flow cytometry, TdT

Diagnosis

- Flow cytometry results: a large blast population that is
  (+) CD10, CD19, CD20, HLA-DR, surface Kappa light chain restriction,
  (-) CD5, TdT

- Cytogenetics (bone marrow biopsy):
  (a) t(8;14) (q24.1; q32) : typ for Burkitt lymphoma
  (b) der(1;13) (q10;q10) : derivative chromosome composed of the long arms of chromosomes 1 and 13, usu seen in lymphoma

- DX: Burkitt lymphoma

Burkitt Lymphoma

- (1) Endemic variant:
  equatorial Africa, the most common childhood malignancy, incidence peak at 4-7 y/o, M:F 2:1, involving jaw/facial bones/CNS. EBV seen in 100% of cases.

- (2) Sporadic variant:
  throughout the world, mainly children& young adults, 1-2% of lymphomas, 30-50% of childhood lymphomas, M:F 2 - 3:1, involving ileo-coecal region/CNS. EBV seen in 30% of cases.

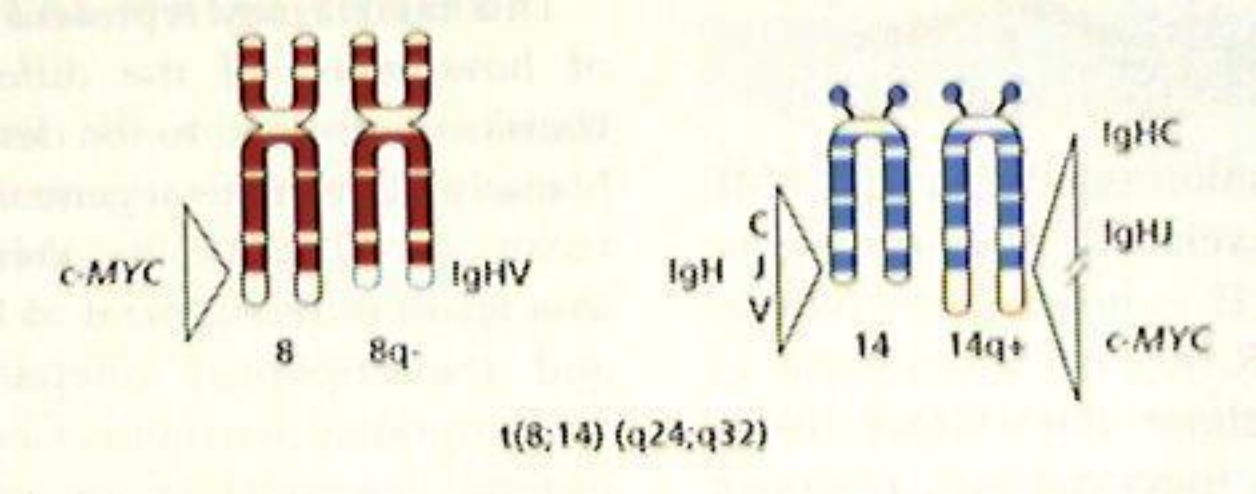
- (3) Immunodeficiency-associated variant:
  primarily with HIV infection, involving lymph nodes/CNS/bone marrow. EBV seen in 25-40% of cases.

Burkitt Lymphoma, cont'd

- Disseminated stages in 70% of pts at presentation

- EBV infection-> defective T-cell regulation-> abnormal B-cell expansion (exact role of EBV is unknown)
- Cytogentics:
  (1) t(8;14): MYC gene on 8q24; Ig heavy chain gene on 14q32
  (2) t(2;8): MYC gene on 8q24; Kappa light chain gene on 2q11
  (3) t(8;22): MYC gene on 8q24; Lambda chain gene on 22q11

Translocation t(8;14)

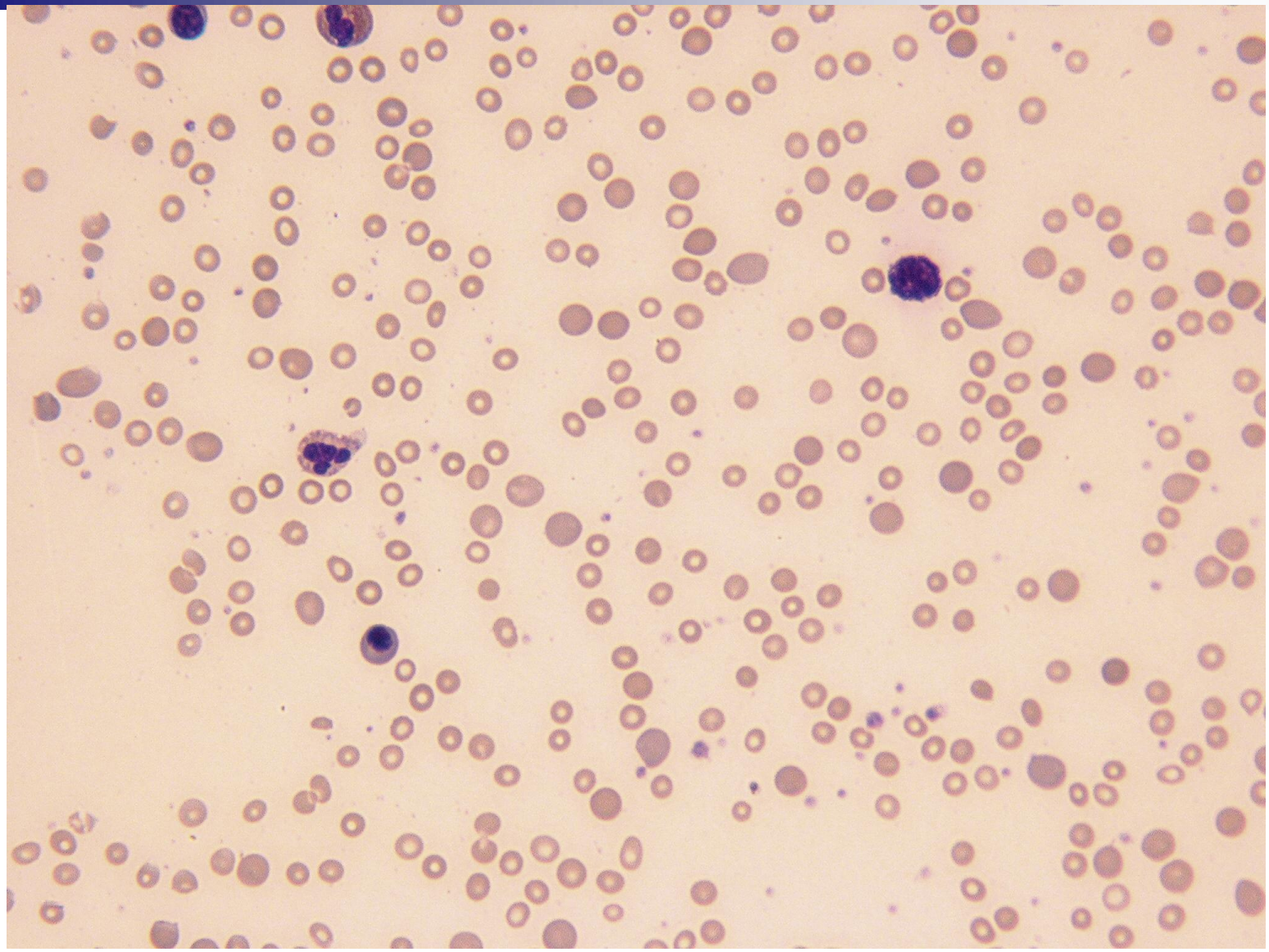


Peripheral Blood Smear Case
Patient: Drxx Arxxx

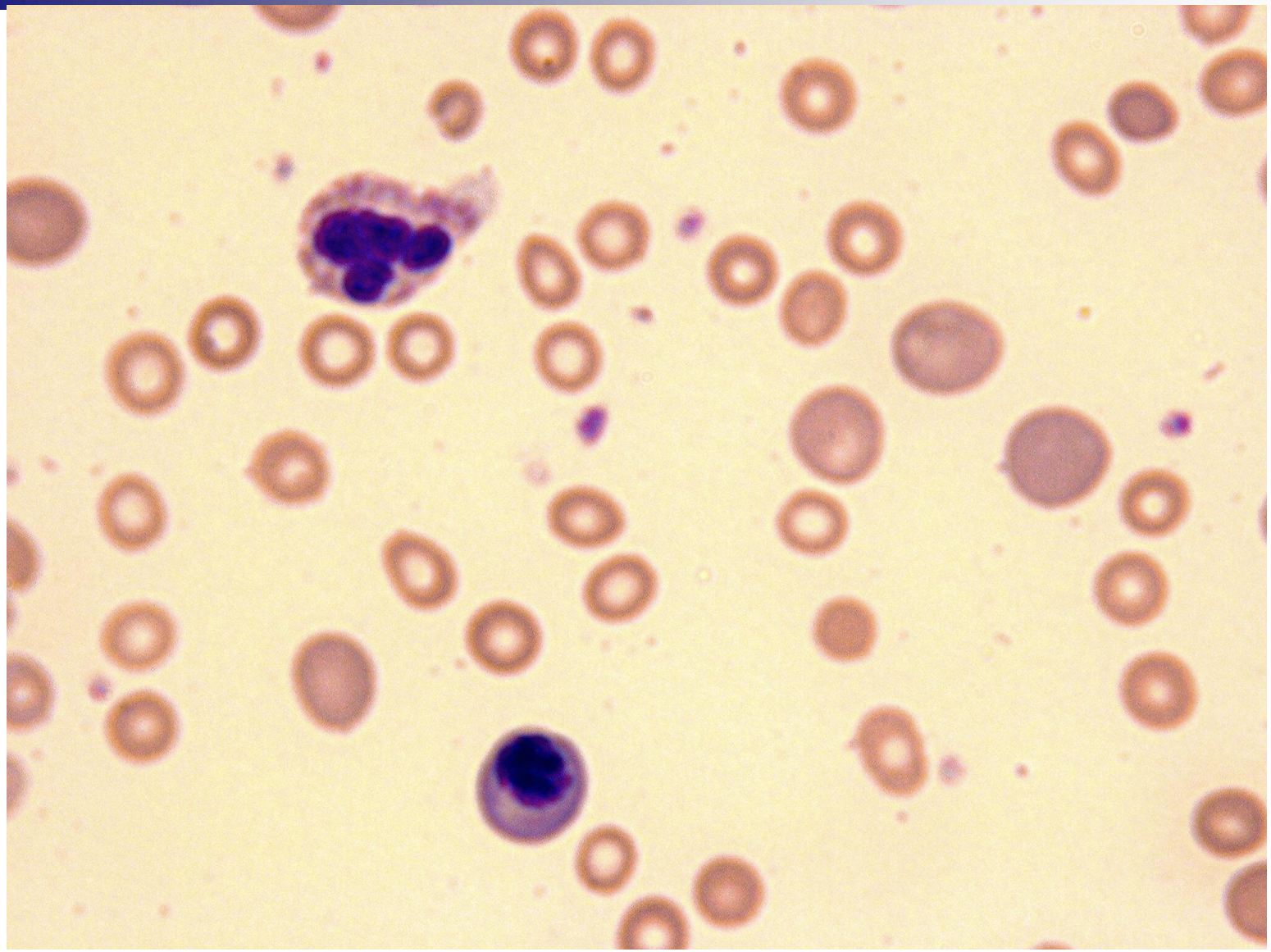
- 2 year old male presented in ER with severe anemia (Hgb 4.7), recent Hx of poor diet (drinking milk only)
- No family Hx of hematologic disorders
- PE: slightly enlarged spleen
- No evidence of bleeding
- WBC= 21.8, Hgb=4.7, Plt=354, Retic 15.3%, MCV 68.7, MCH 22
  A few NRBCs
  Leukocytes with left shift

Additional Tests

- LDH 450, haptoglobin <6, DAT (IgG, C3) negative
  normal Hgb electrophoresis, DIC panel
- Serum iron 367 (ref 30-160)
  TIBC 383 (ref 228-428)
  Iron sat 96 (ref 12-57)
- G6PD 24.8 u/g Hgb (ref 7.0-20.5)
- Pyruvate Kinase 16.3 u/g Hgb (ref 9-22)



Peripheral blood smear

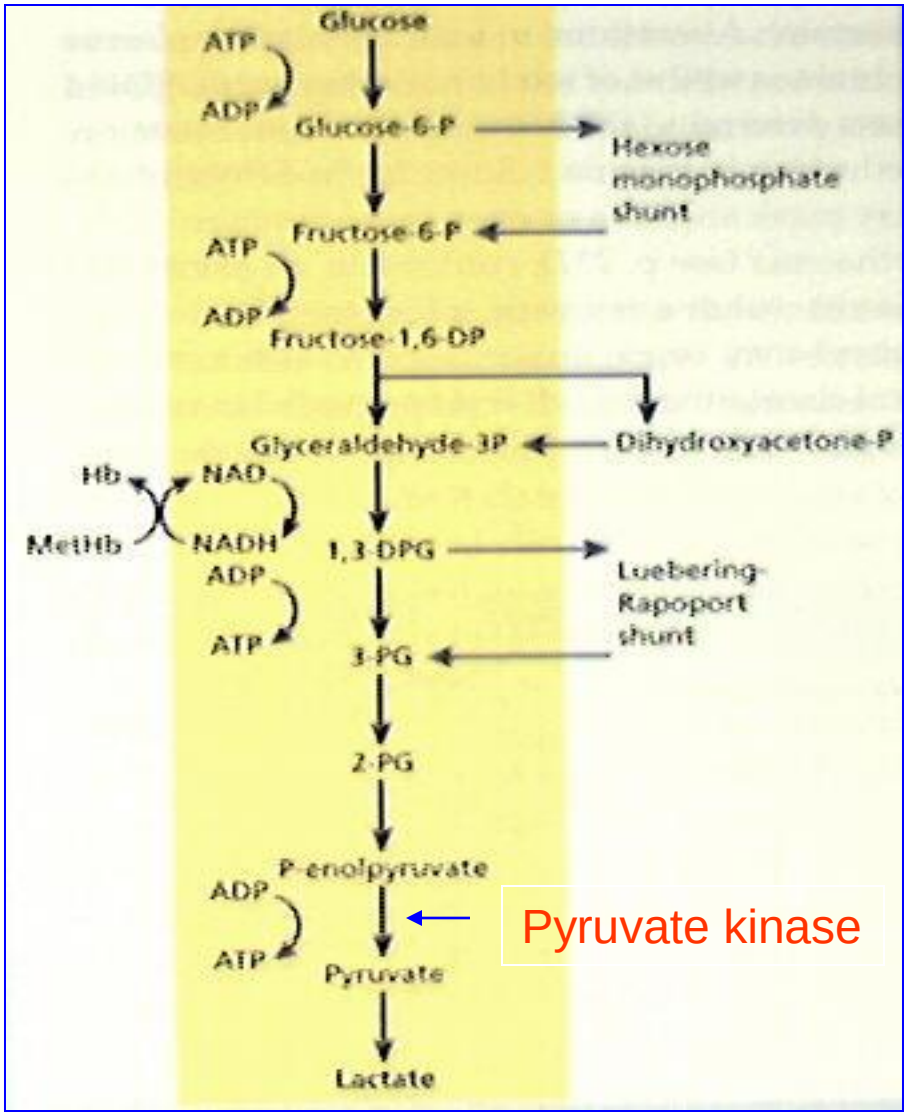


Peripheral blood smear, cont'd

Workup for anemia

- Negative for:
  - Iron deficiency (normal iron panel, increased retic)
  - Immune hemolysis (negative DAT)
  - Hemoglobinopathy, Thal (normal Hgb electrophoresis)
  - G6PD deficiency (elevated G6PD)
- Pyruvate kinase deficiency could not be ruled out (normal PK level with marked reticulocytosis)
- Patient was discharged and will be retested for PK for baseline

Embden Meyerhof glycolytic pathway



Embden Meyerhof glycolytic pathway

- Glucose-> lactate
  each molecule of glucose-> 2 molecules of ATP
  ATP provides energy for red cell membrane ATPase sodium pump
- Disruption of ATP formation-> disrupt membrane flexibility

Pyruvate Kinase Deficiency

- Autosomal recessive (affected pt being homozygous)
- Pyruvate kinase deficiency -> reduce ATP production-> red cell membrane becomes rigid -> red cells unable to pass through splenic microcirculation and taken out by spleen-> hemolysis
- Jaundice, gallstones
- Splenectomy may alleviate anemia
- Blood smear shows poikilocytosis, no microspherocytes (nonspherocytic anemia)