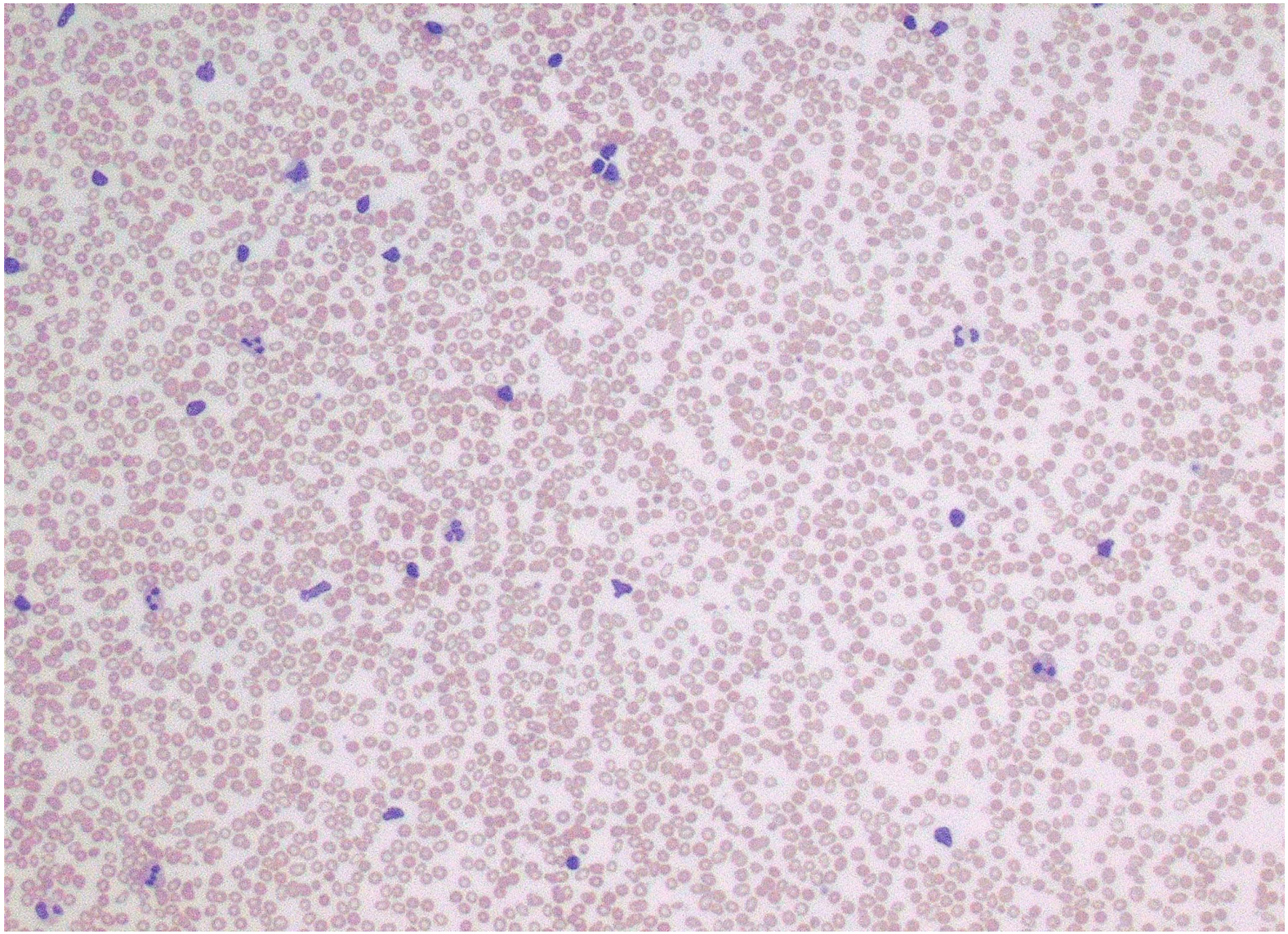
Hematology Case Conference

5/27/03

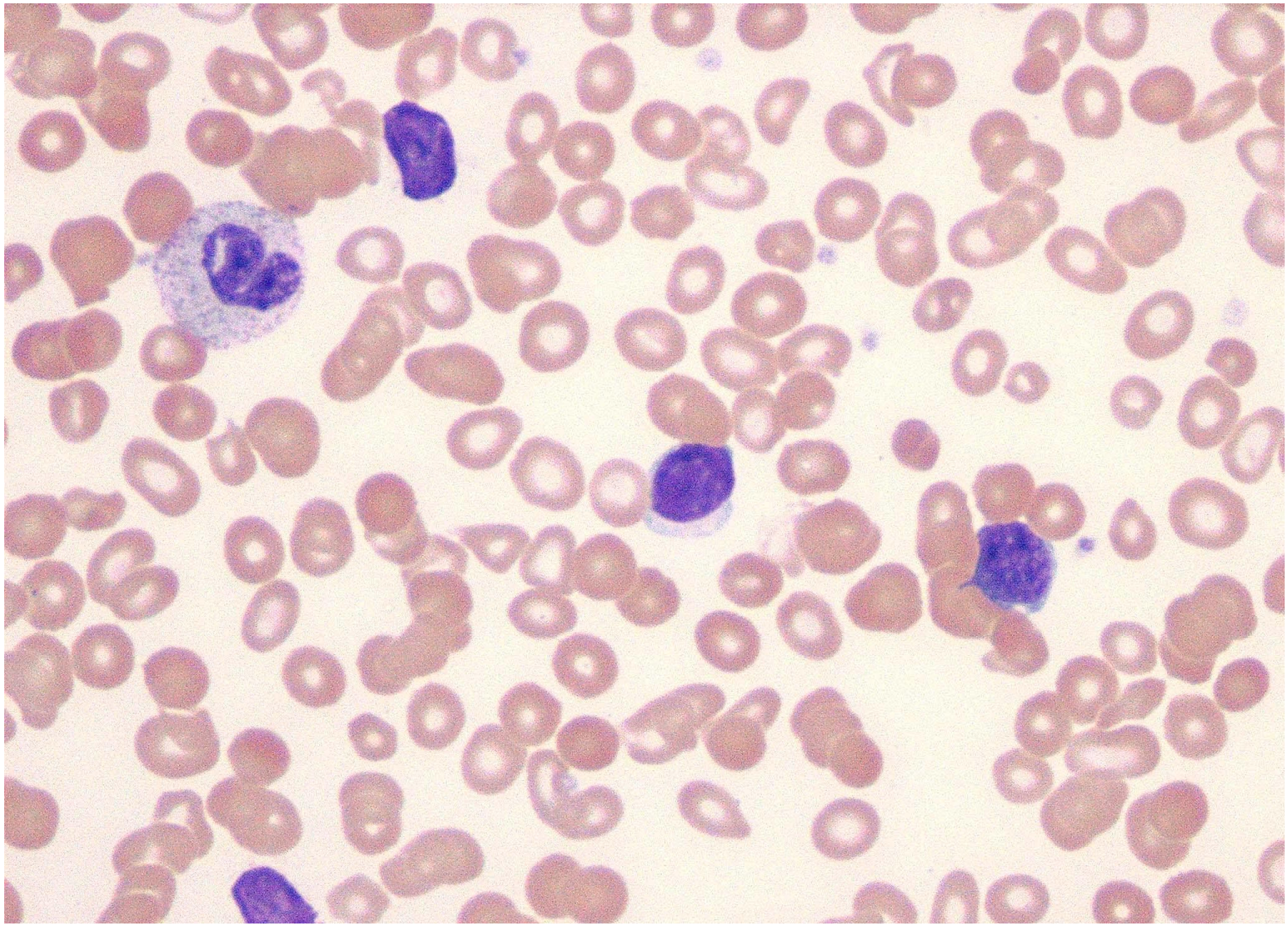
Flow Cytometry Case: 03-120-0366
Patient: Rxxx L Mxxx

- 56-year-old male with Hx of HIV (+) x 9 years, presented with H/A, ® hand abscess
- WBC= 37.9, Hgb=11.2.0, Plt=135,000, MCV= 73.7
  Seg 45, Lymph 55

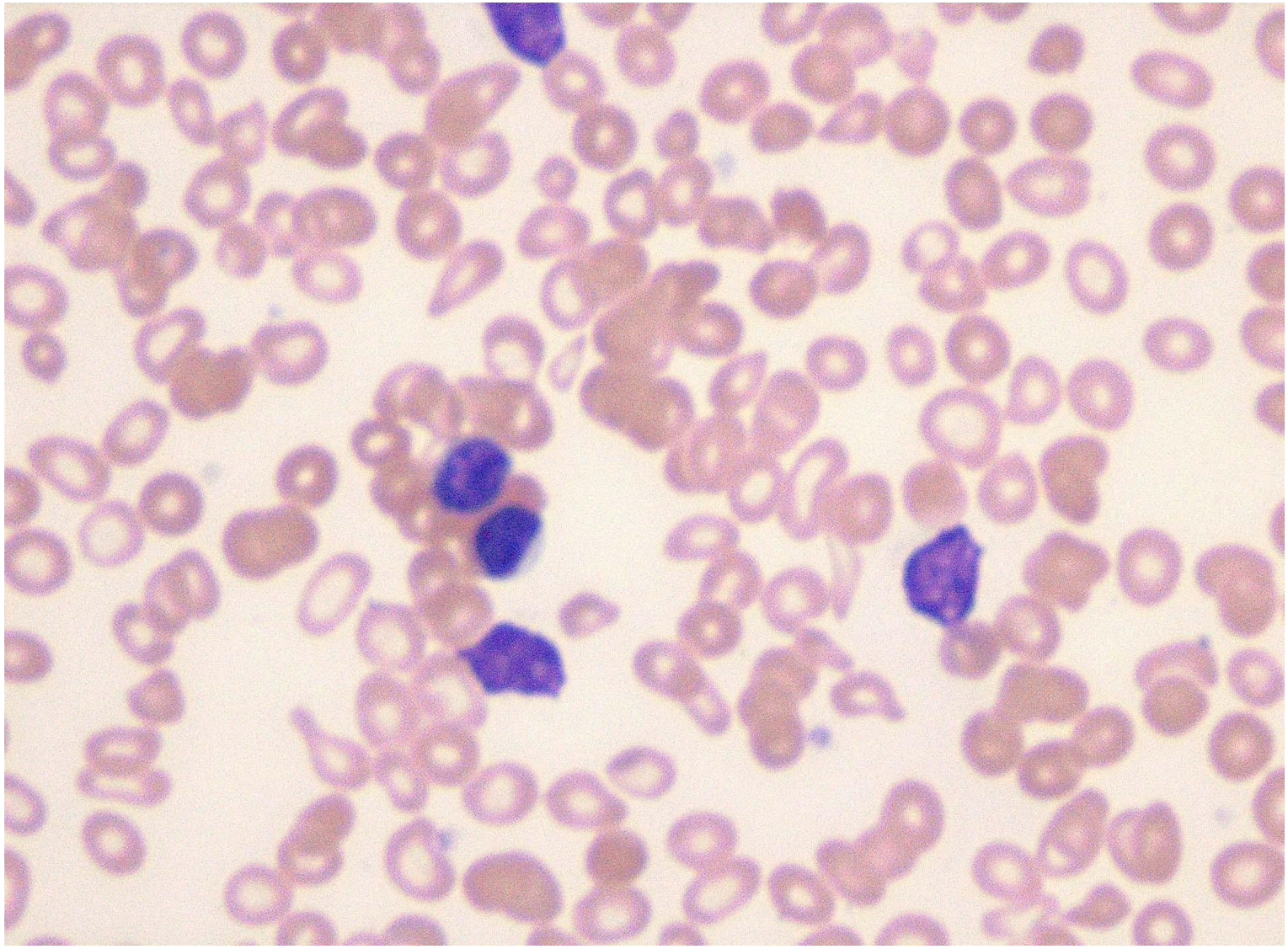
Peripheral Blood Smear



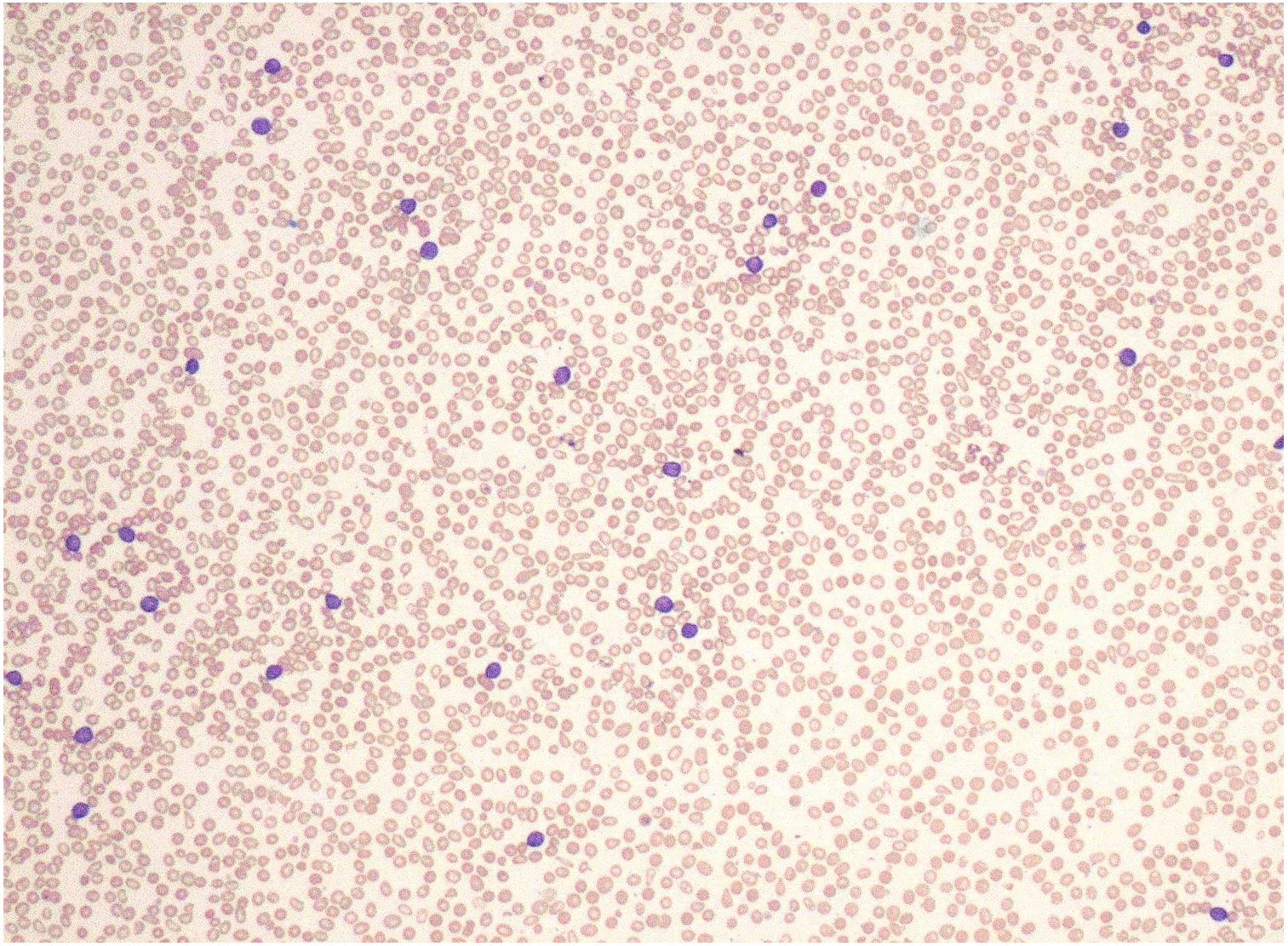
Peripheral Blood Smear (cont'd)



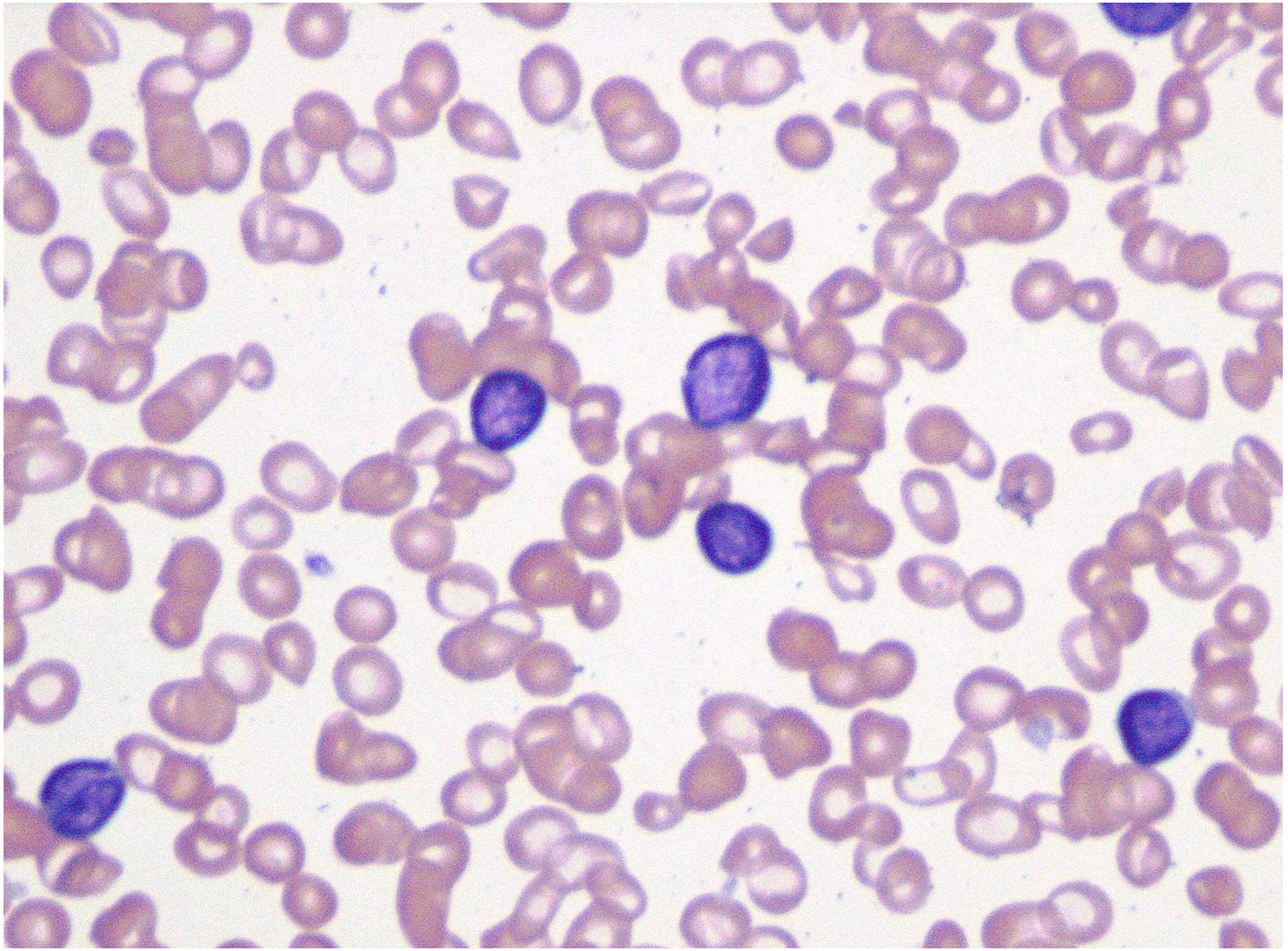
Peripheral Blood Smear (cont'd)



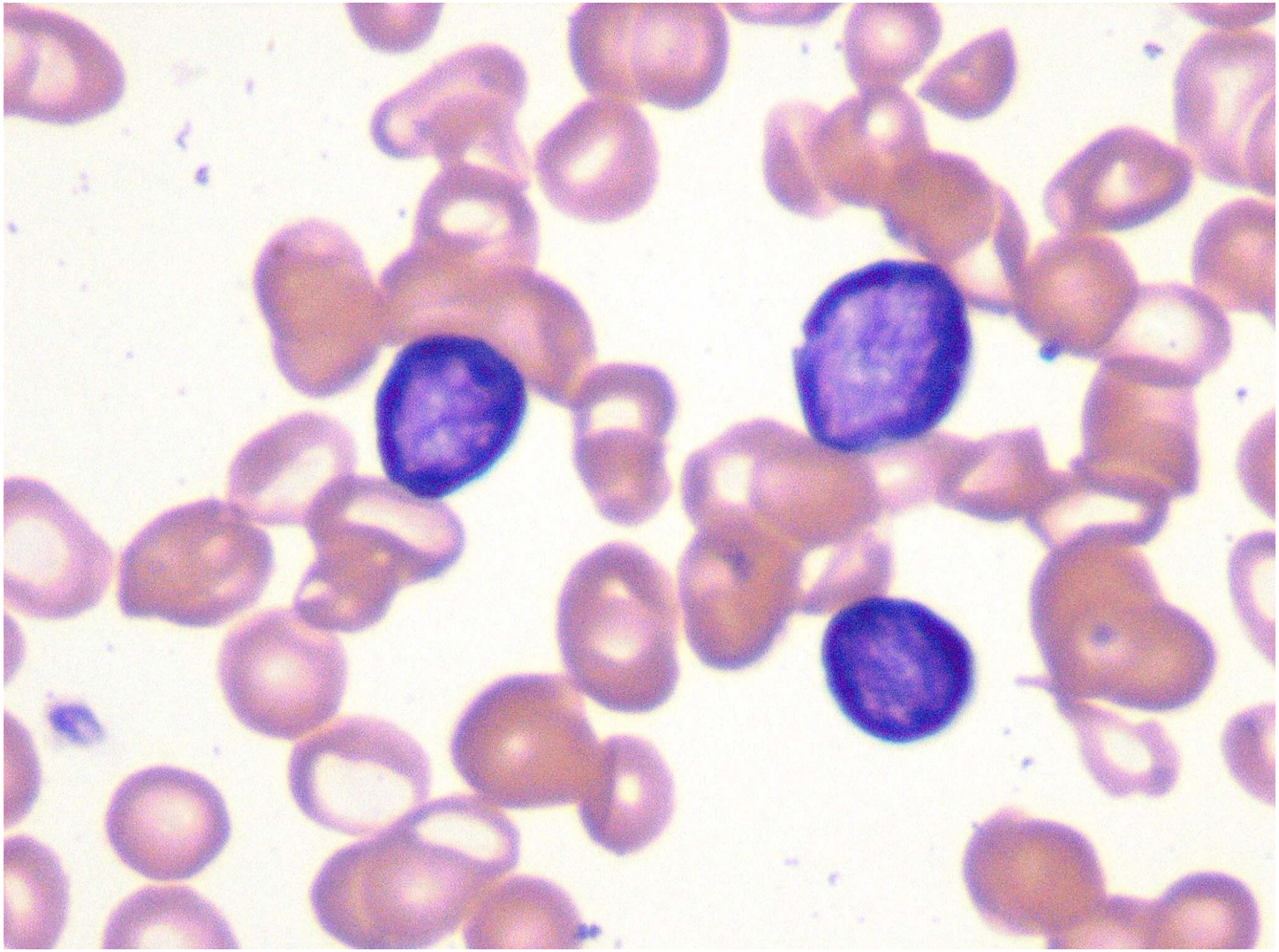
Peripheral Blood Smear (with Albumin)



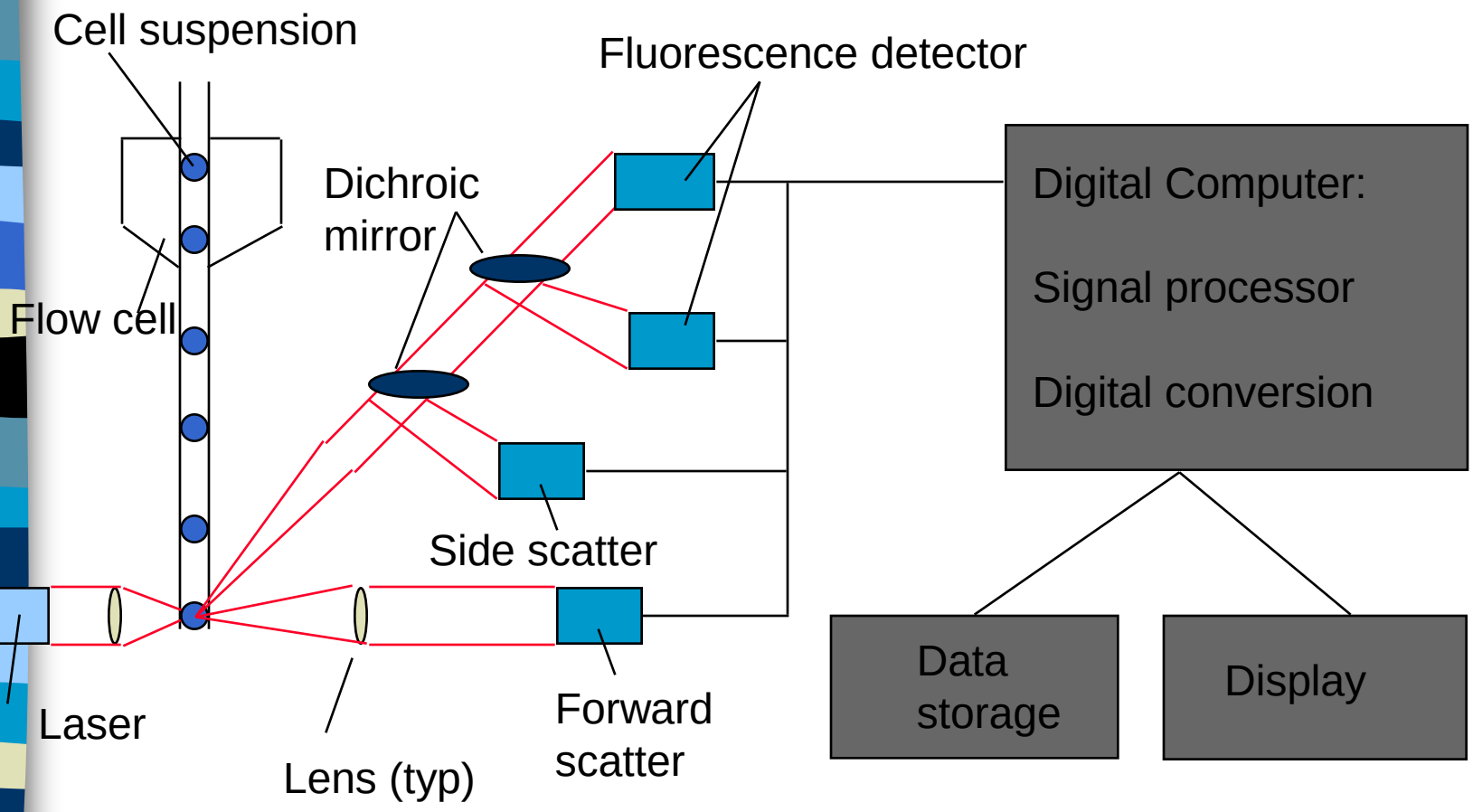
Peripheral Blood Smear (with Albumin), cont'd



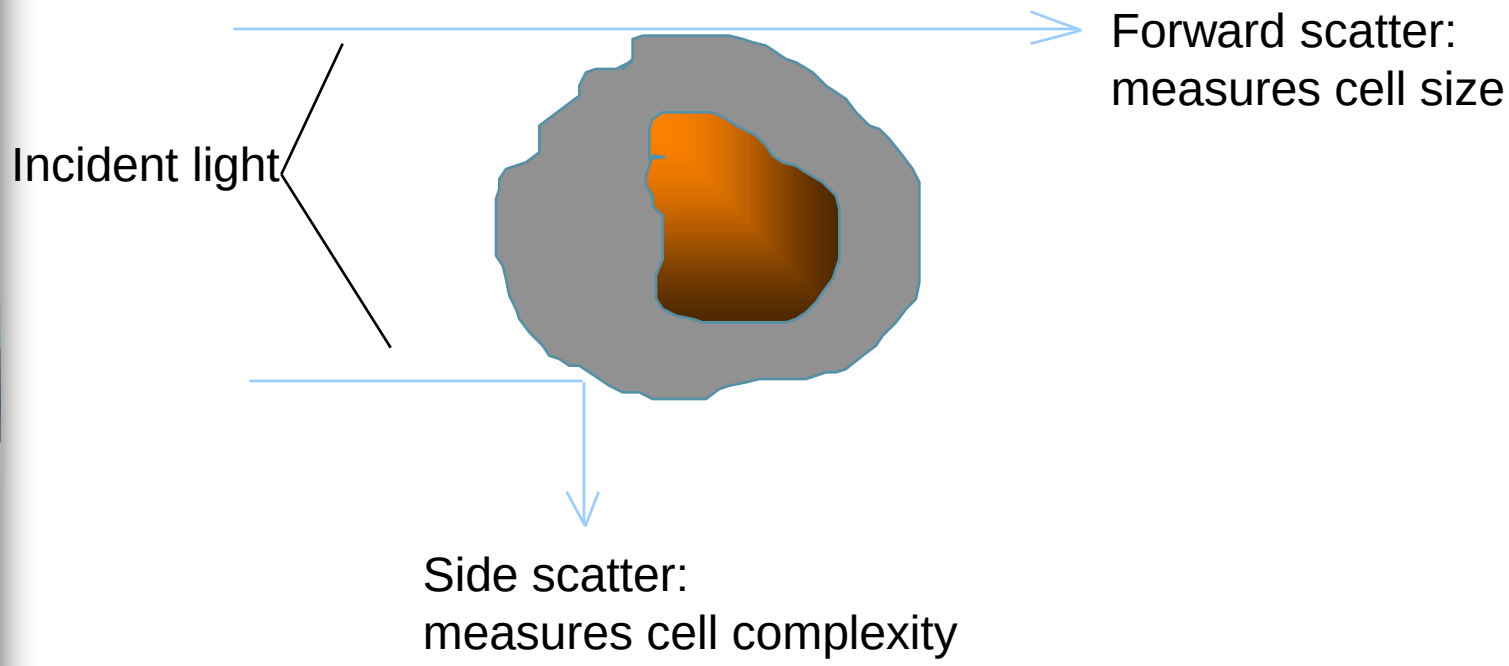
Peripheral Blood Smear (with Albumin), cont'd



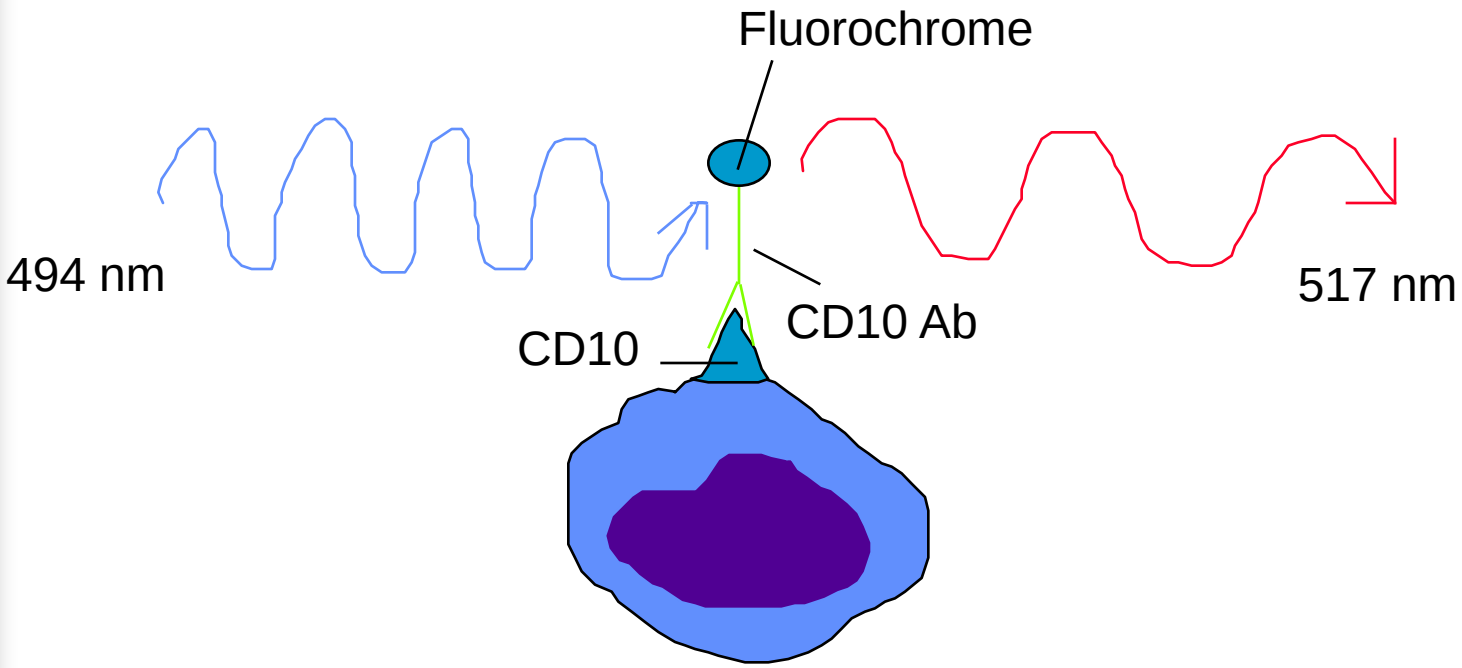
Basic Components of Flow Cytometry



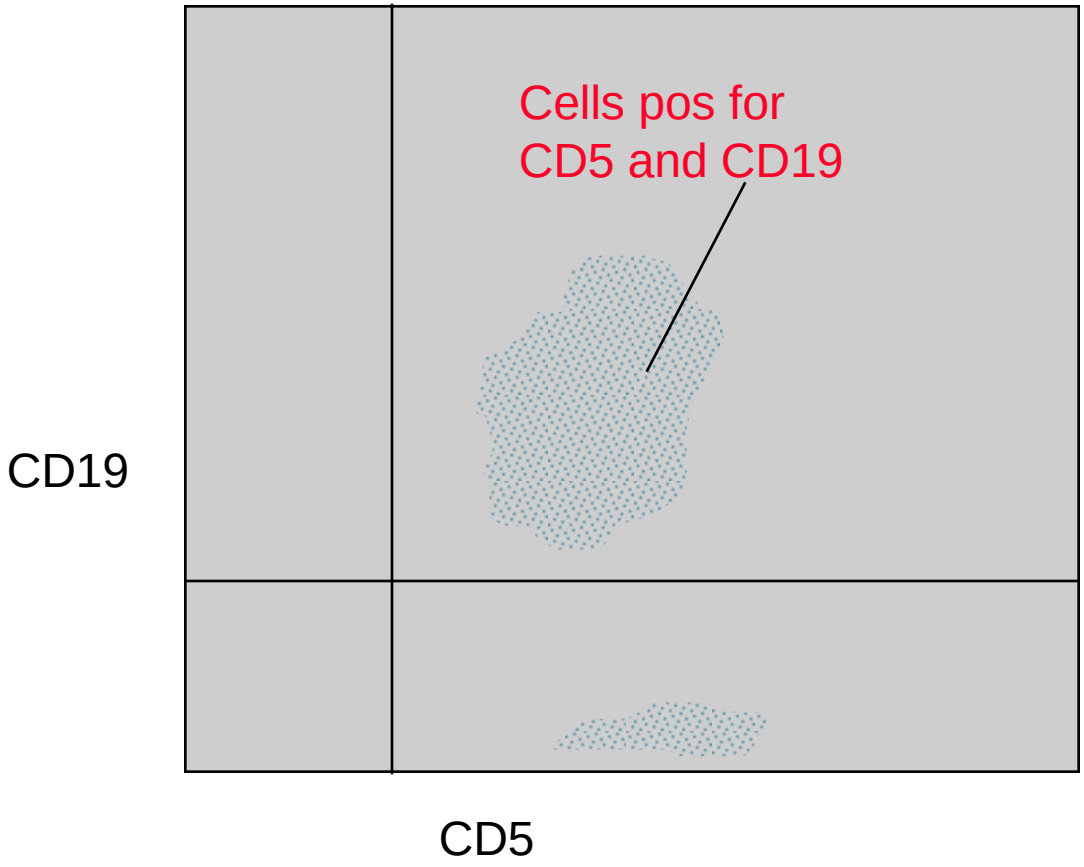
Light Scattering



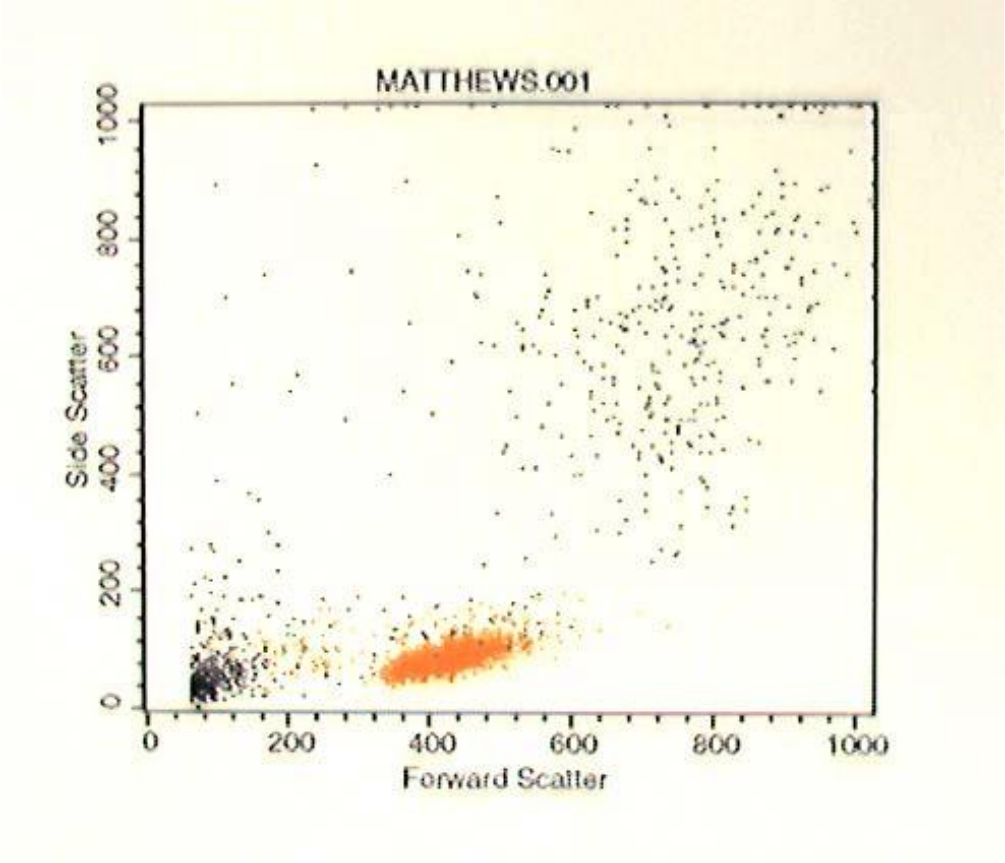
Antigen Detection



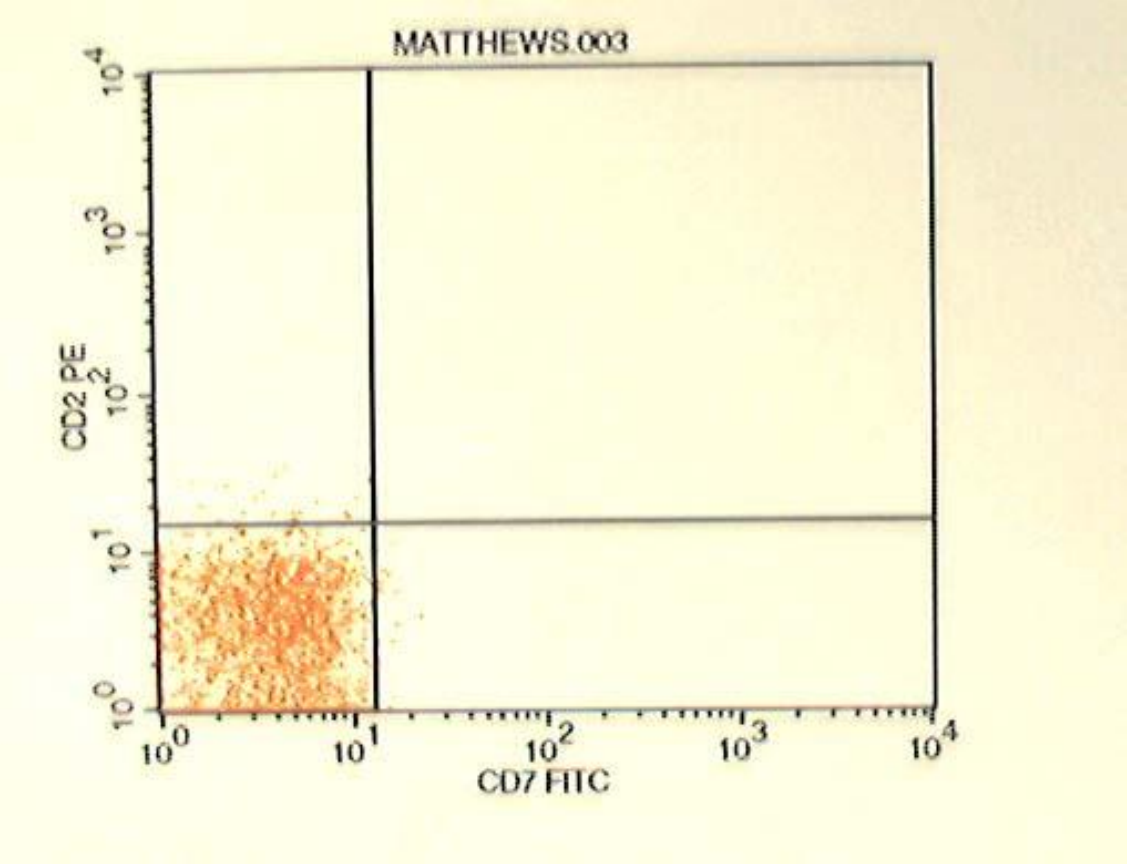
Plotting of Marker Results



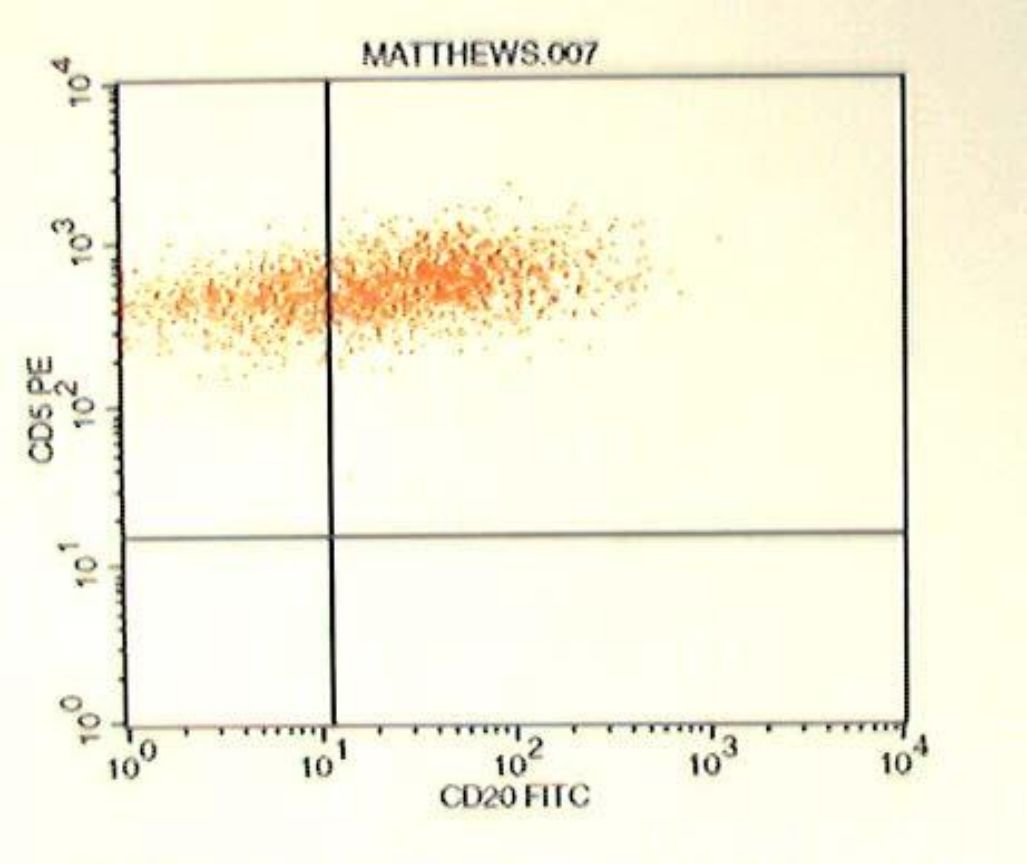
Flow Cytometry



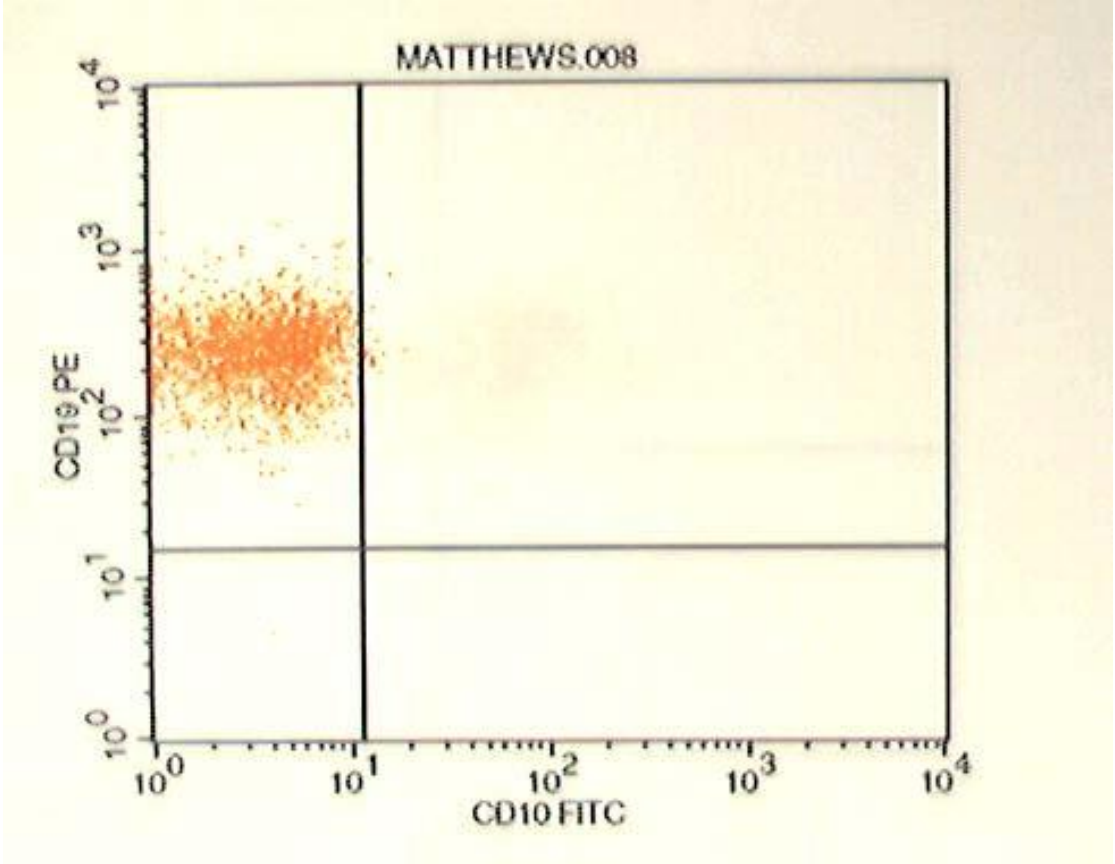
Flow Cytometry (cont'd)



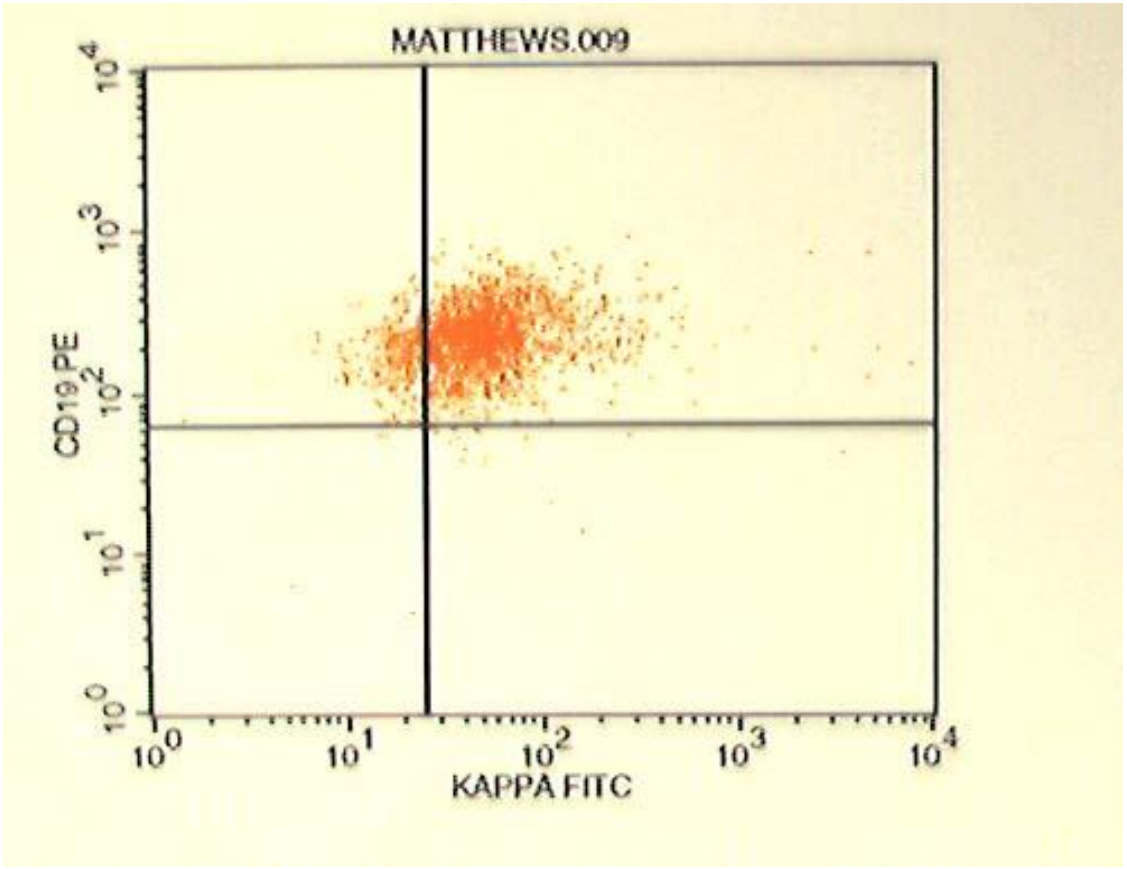
Flow Cytometry (cont'd)



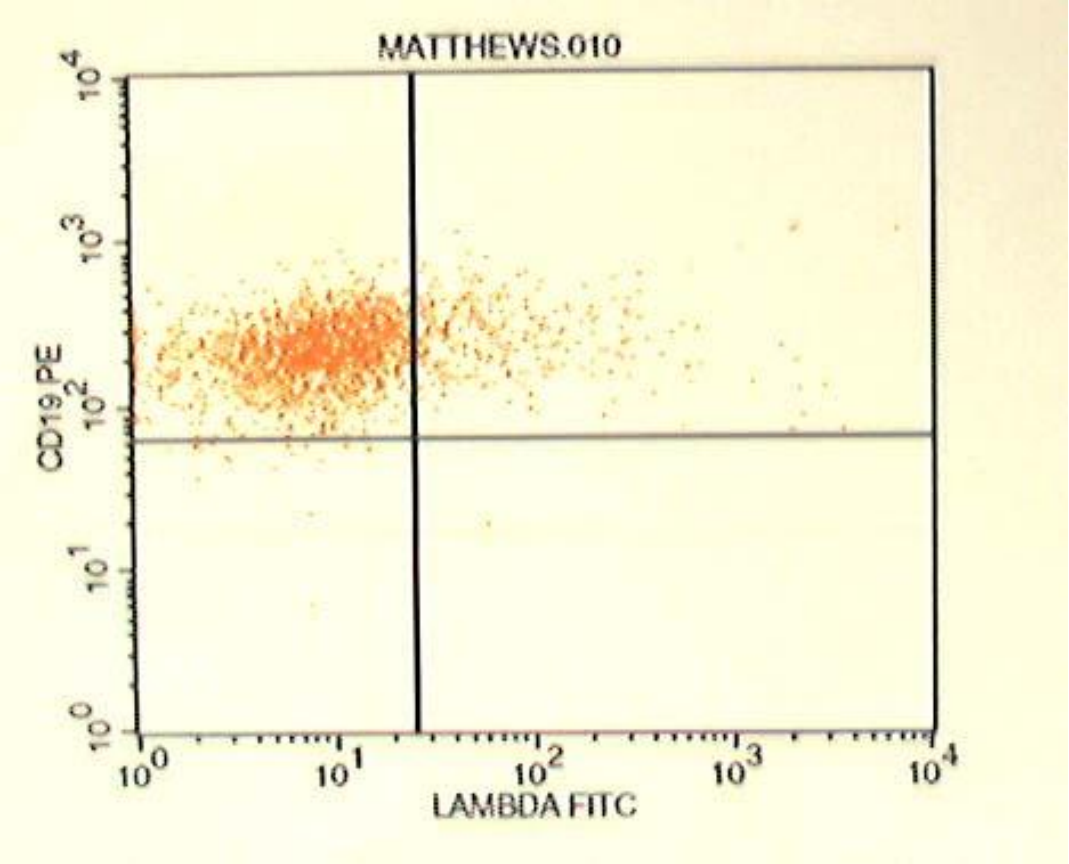
Flow Cytometry (cont'd)



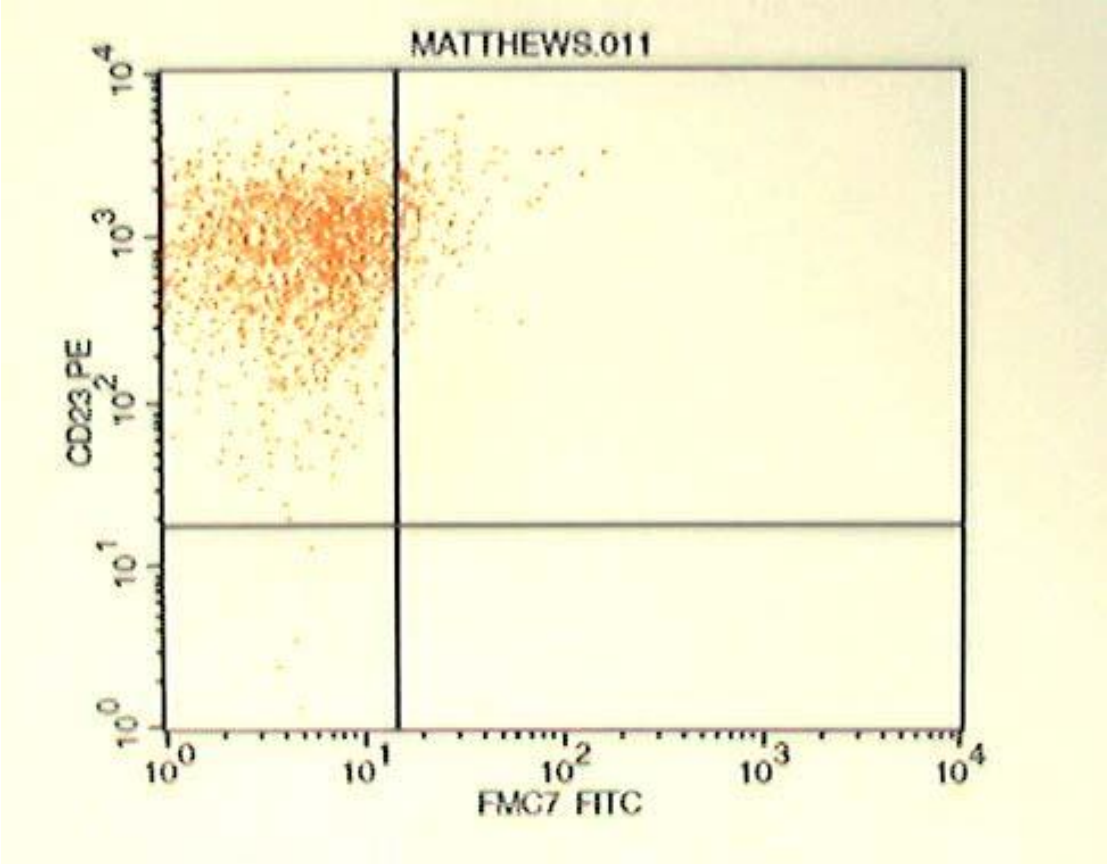
Flow Cytometry (cont'd)



Flow Cytometry (cont'd)



Flow Cytometry (cont'd)



Diagnosis

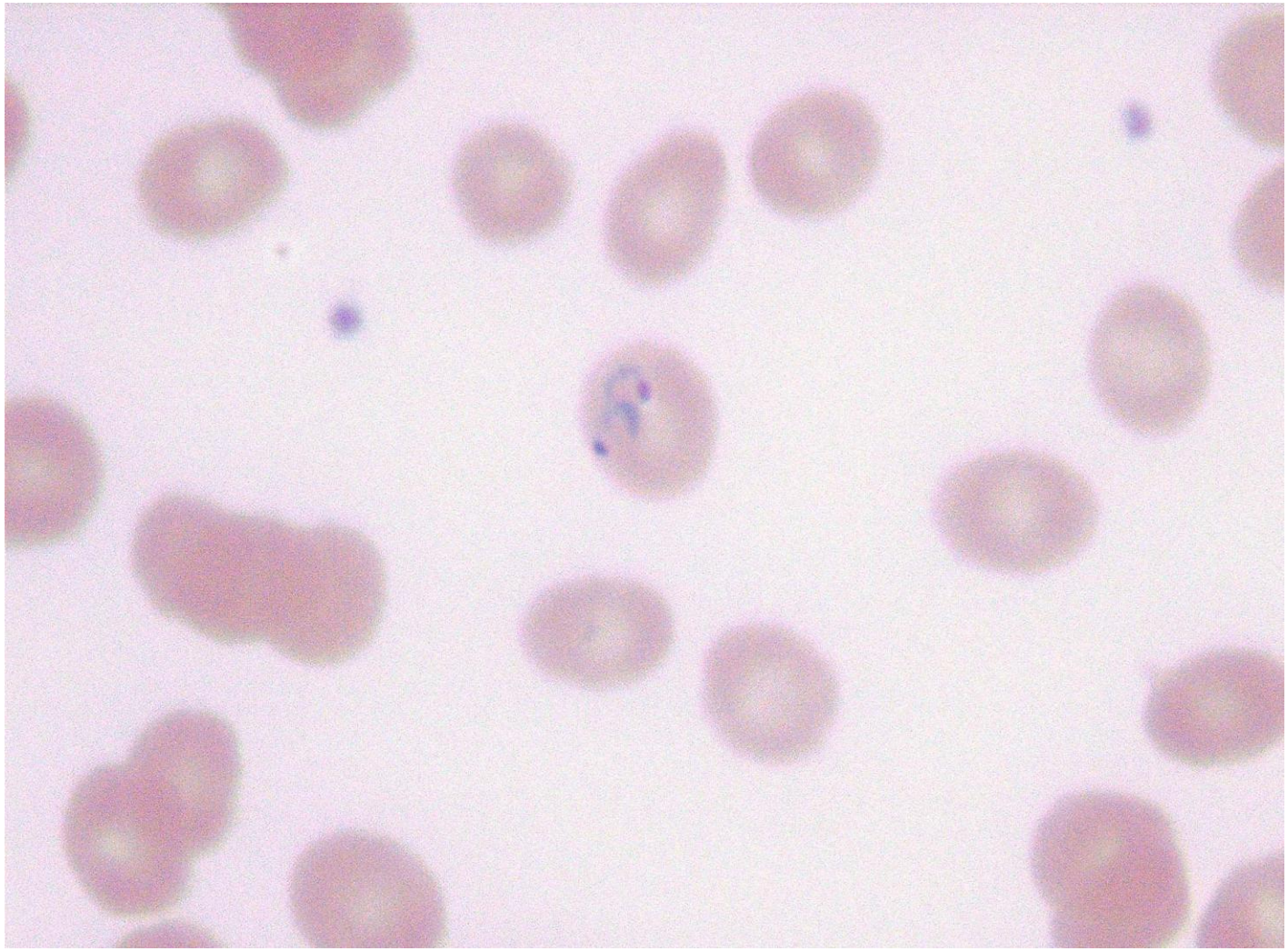
- Flow cytometry:
  -Pos: CD5, CD20, CD23, kappa light chain restriction
  -Neg:CD10, FMC7

- DX: chronic lymphocytic leukemia

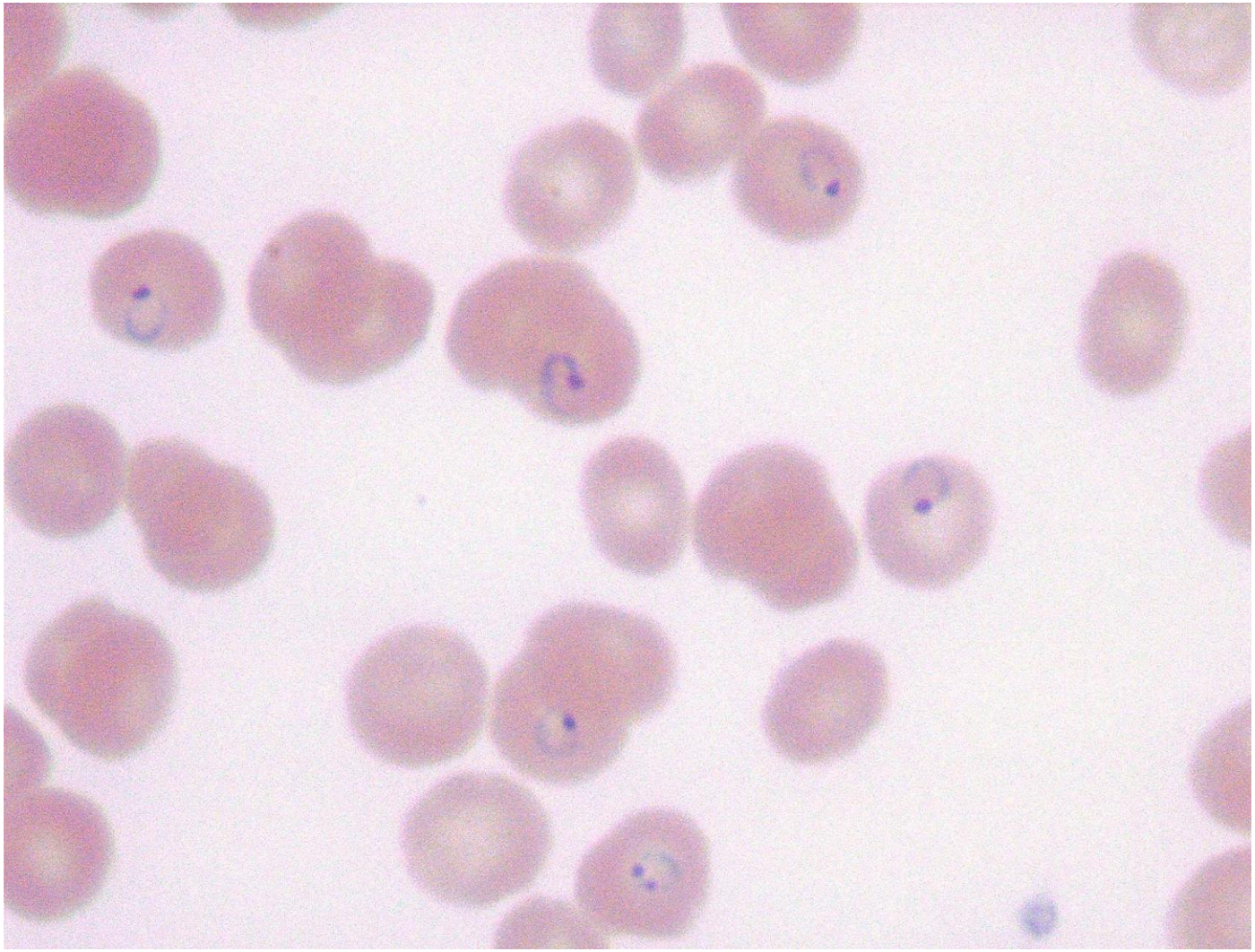
03-113-0227
Patient Name: Yxxx, Fxxx

- 69 y/o male with anemia, thrombocytopenia
  WBC=5, Hgb=5.1, Plt=89K, LDH=253
- Peripheral blood smear shows Plasmodium falciparum, parasitic load 17%.
- Underwent red cell exchanges
- Gametocytes seen in blood smear 6 days after treatment

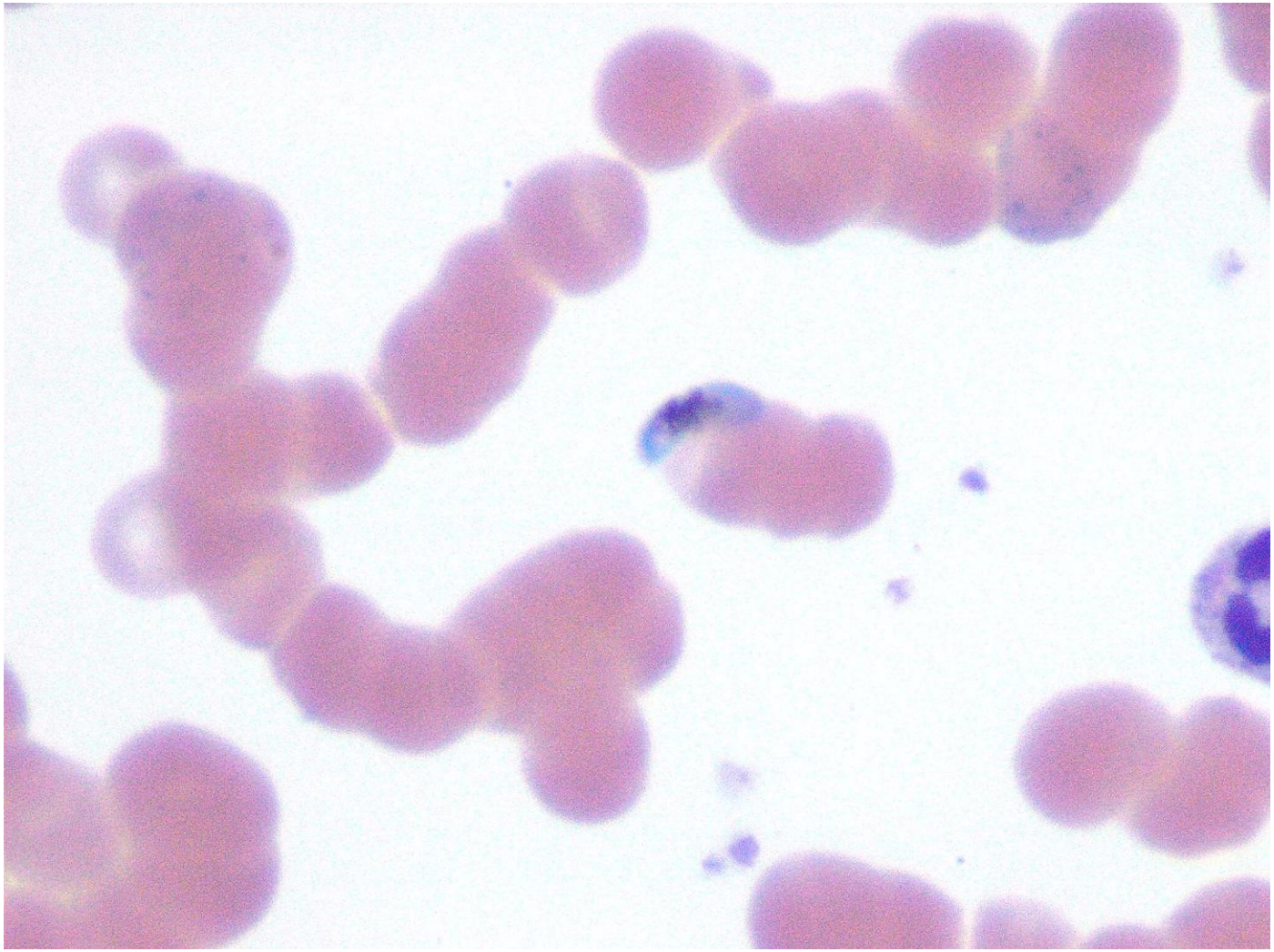
Peripheral Blood Smear



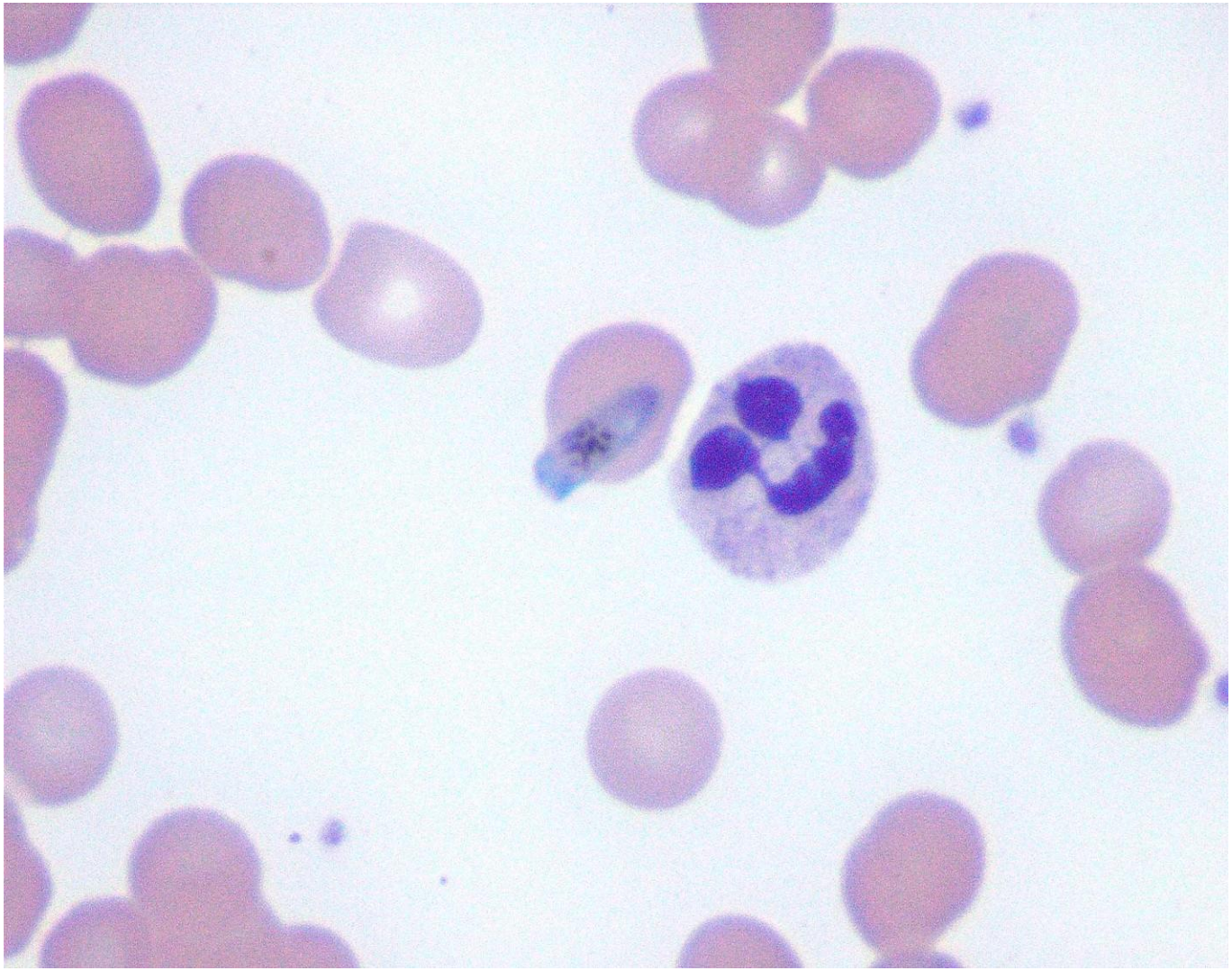
Peripheral Blood Smear (cont'd)



Peripheral Blood Smear, 6 days after tx



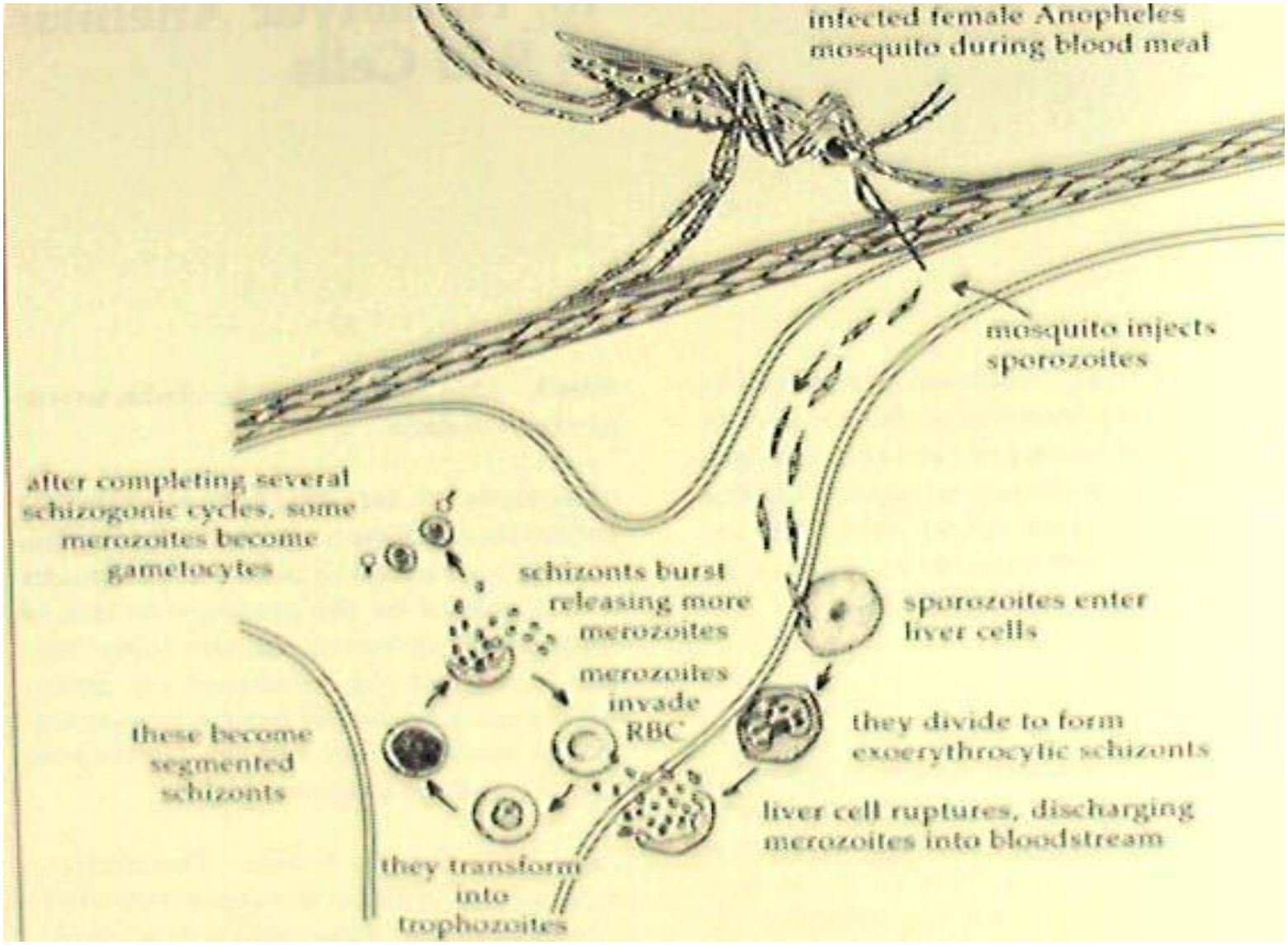
Peripheral Blood Smear, 6 days after tx, cont'd



Gametocytes

- Some individual intracellular merozoites assume sexual forms (gametocytes). These do not lyse red cells and do not divide while in blood. They will proliferate only if ingested by a female anopheles mosquito (fertilization occurs in the mosquito's abdominal cavity to prduce sporozoites)
- Gametocytes are sometimes seen after treatment. Peripheral blood should be monitored only for asexual forms.

Plasmodial Life Cycle



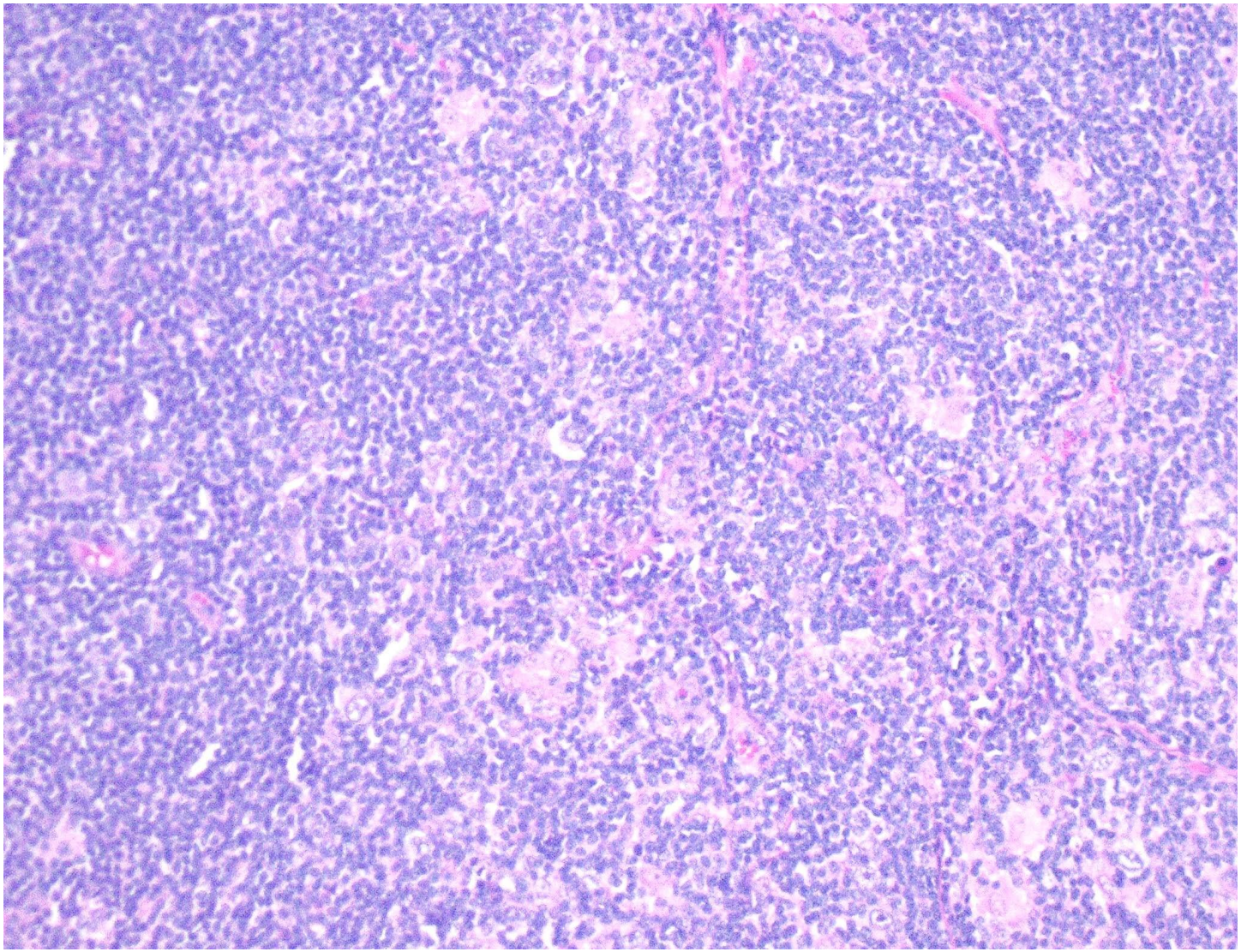
Treatment

- Uncomplicated malaria infection: chloroquine
- Resistance P. Falciparum: quinine or quinidine
- Severe P. Faliciparum:
  - Cerebral malaria (coma, seizure), renal failure, resp distress, DIC-> quinidine gluconate IV
  - Red cell exchange if parasitic load > 10% (5-10% may be considered in pts with severe Sx). Typ 4-17 units of RBCs. Note that patients in endemic areas may develop semi-immune status and do not have severe Sx with high parasitic load

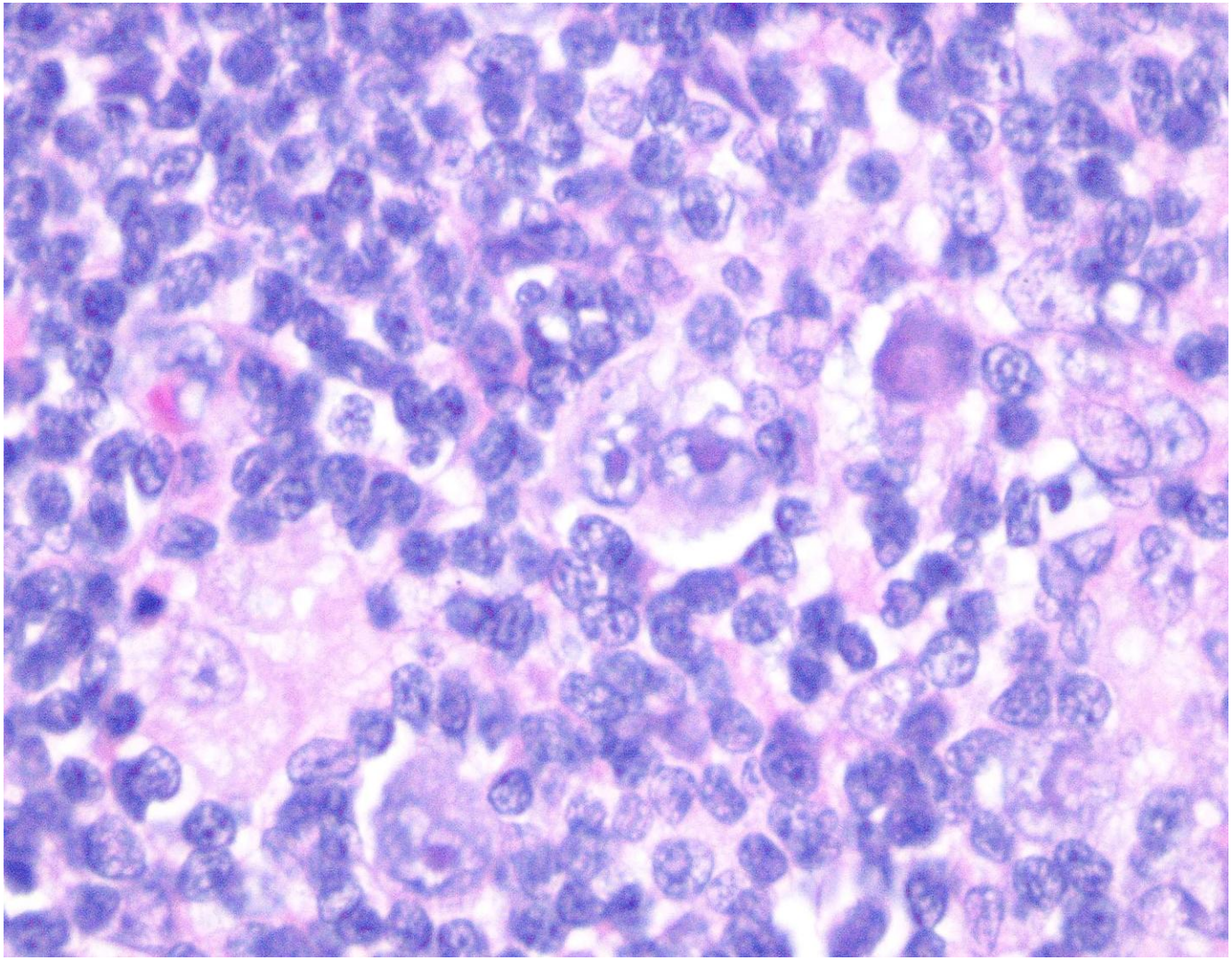
HS-03-2902
Patient Name: Dxxx Oxxx

- 8 y/o male with (L) neck mass
- Tissue submitted: (L) cervical lymph node

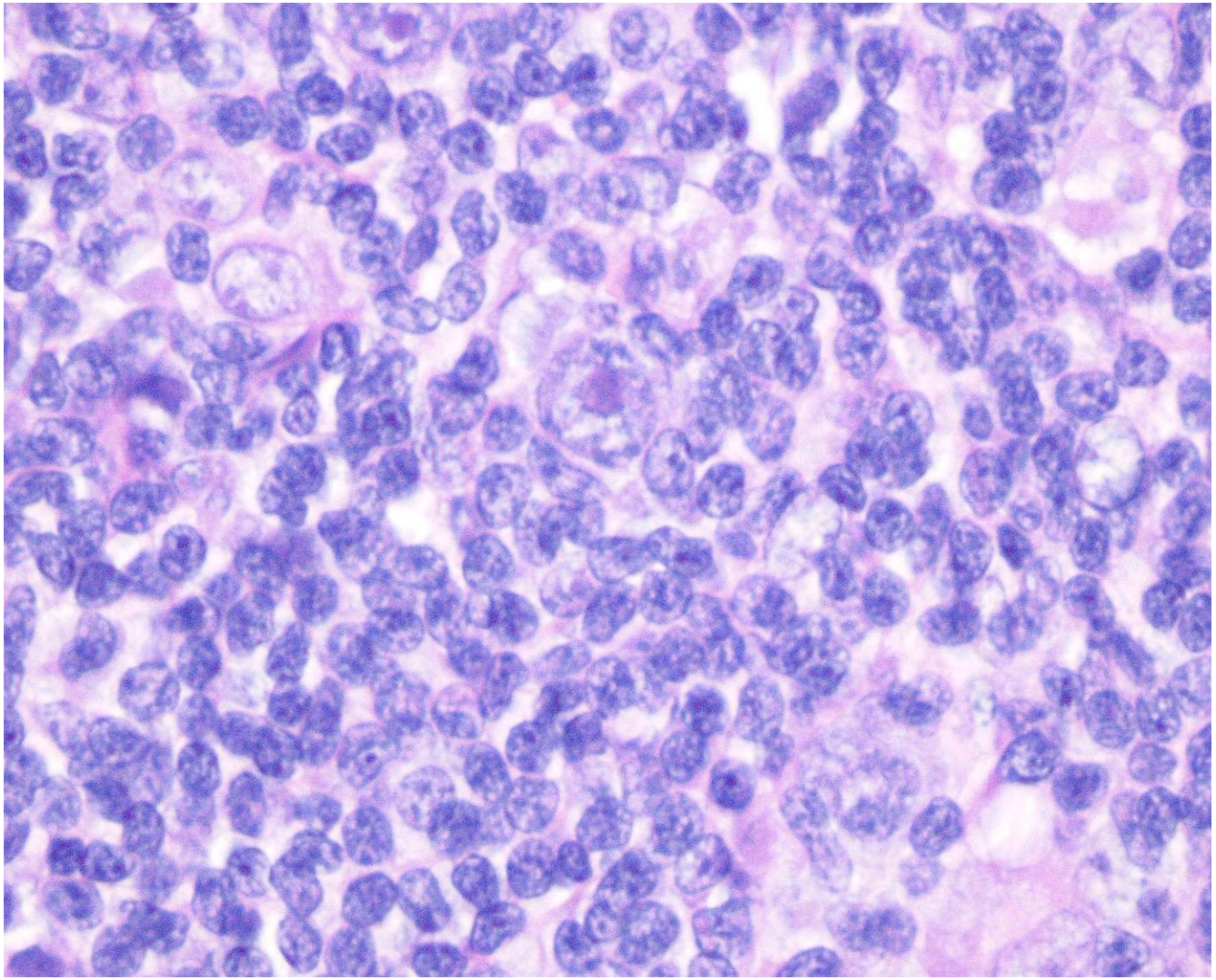
Lymph Node biopsy



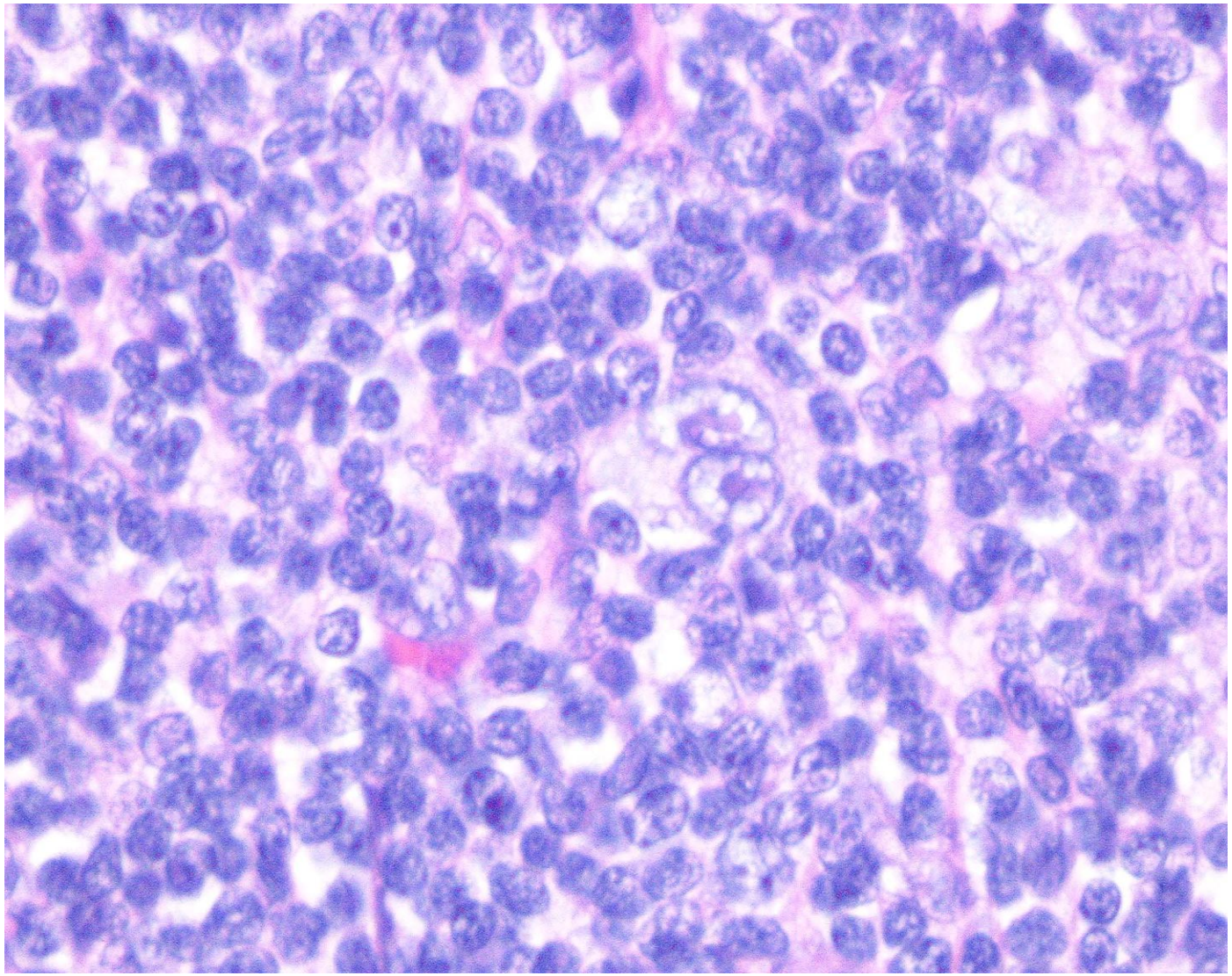
Lymph Node biopsy (cont'd)



Lymph Node biopsy (cont'd)



Lymph Node biopsy (cont'd)



Diagnosis

- Immunostains:
  R-S cells and Hodgkin cells are
  -Pos: CD15, CD30
  -Neg: CD20, CD45 (LCA)

- Flow cytometry: T cells with no aberrant expression, B cells without light-chain restriction

- Numerous lymphocytes, moderate R-S cells, no lacunar cells, no fibrotic septa -> Classic Hodgkin lymphoma, lymphocyte-rich

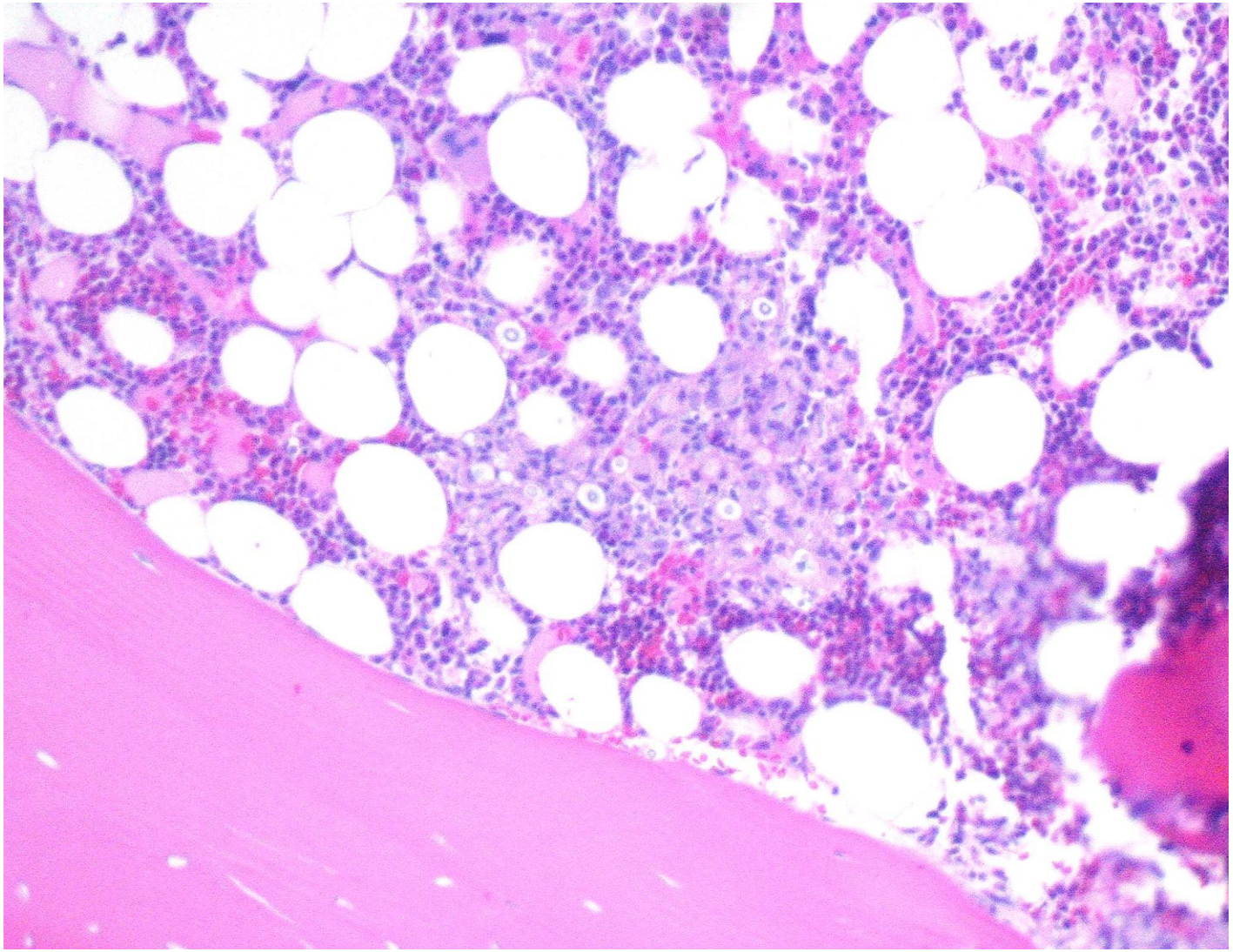
Diagnosis (cont'd)

- Classic Hodgkin lymphoma :
  -95% of all Hodgkin lymphoma
  -Bimodal age: peak at 15-35, second peak in late life
  -Involves cervical LN (75%), followed by mediastinal, axilliary, and para-aortic LN
  -EBV is postulated to play a role in pathogeneis
  -Subtypes:
  (1) Nodular sclerosis: 70%
  (2) Mixed cellularity: 20-25%
  (3) Lymphocyte-rich: 5% (median age is higher than in other subtypes)
  (4) Lymphocyte-depleted: < 5%

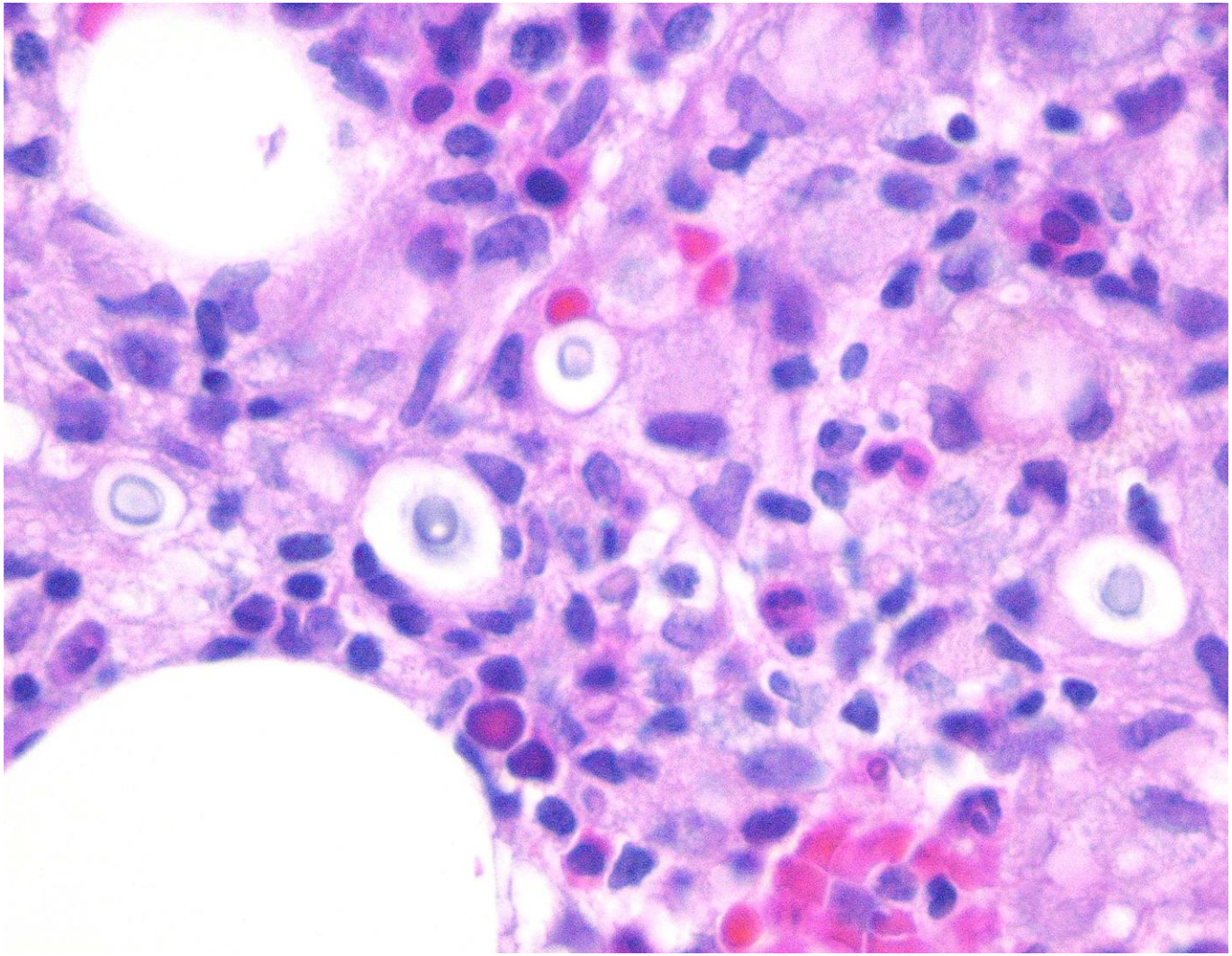
HB-03-55
Patient Name: Hxxx, Yxxx

- 54 year old Hispanic female newly diagnosed with HIV, cryptococcal meningitis.
- CBC: WBC=6.3, Hgb=11.1, Plt=74k, rare NRBCs
- Bone marrow to investigate thrombocytopenia: bx 40% cellularity, increase in megakaryocytes

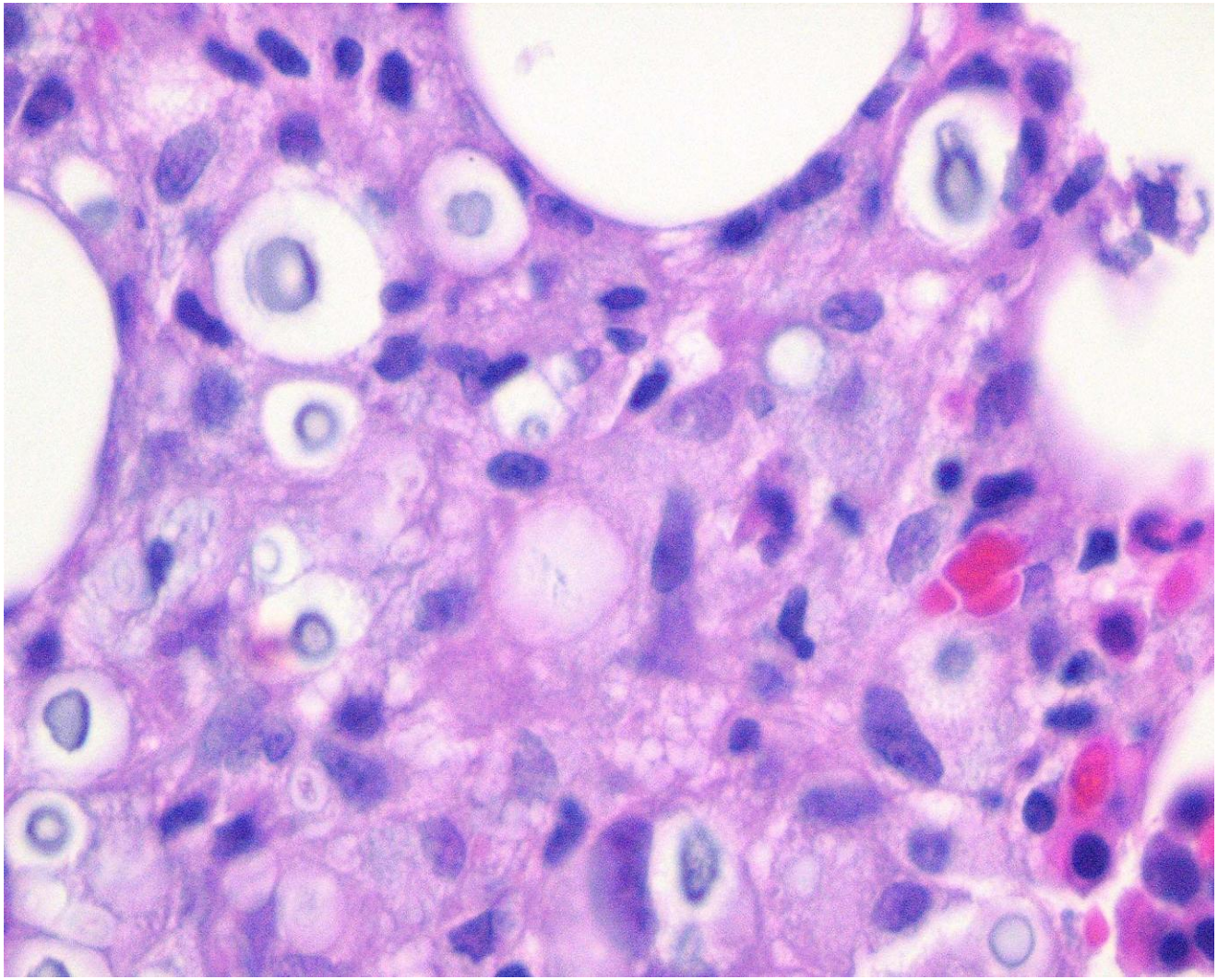
Bone Marrow Biopsy



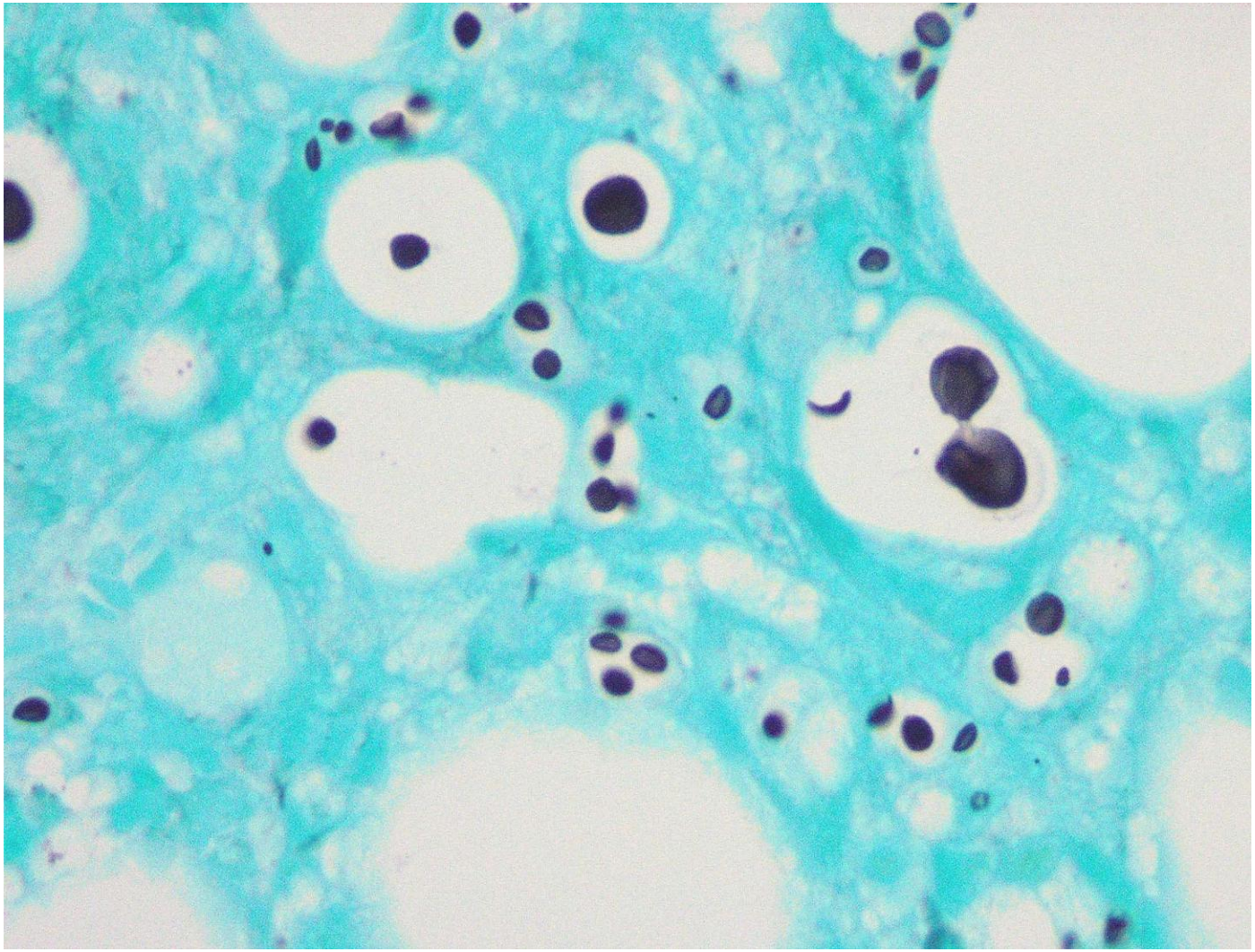
Bone Marrow Biopsy (cont'd)



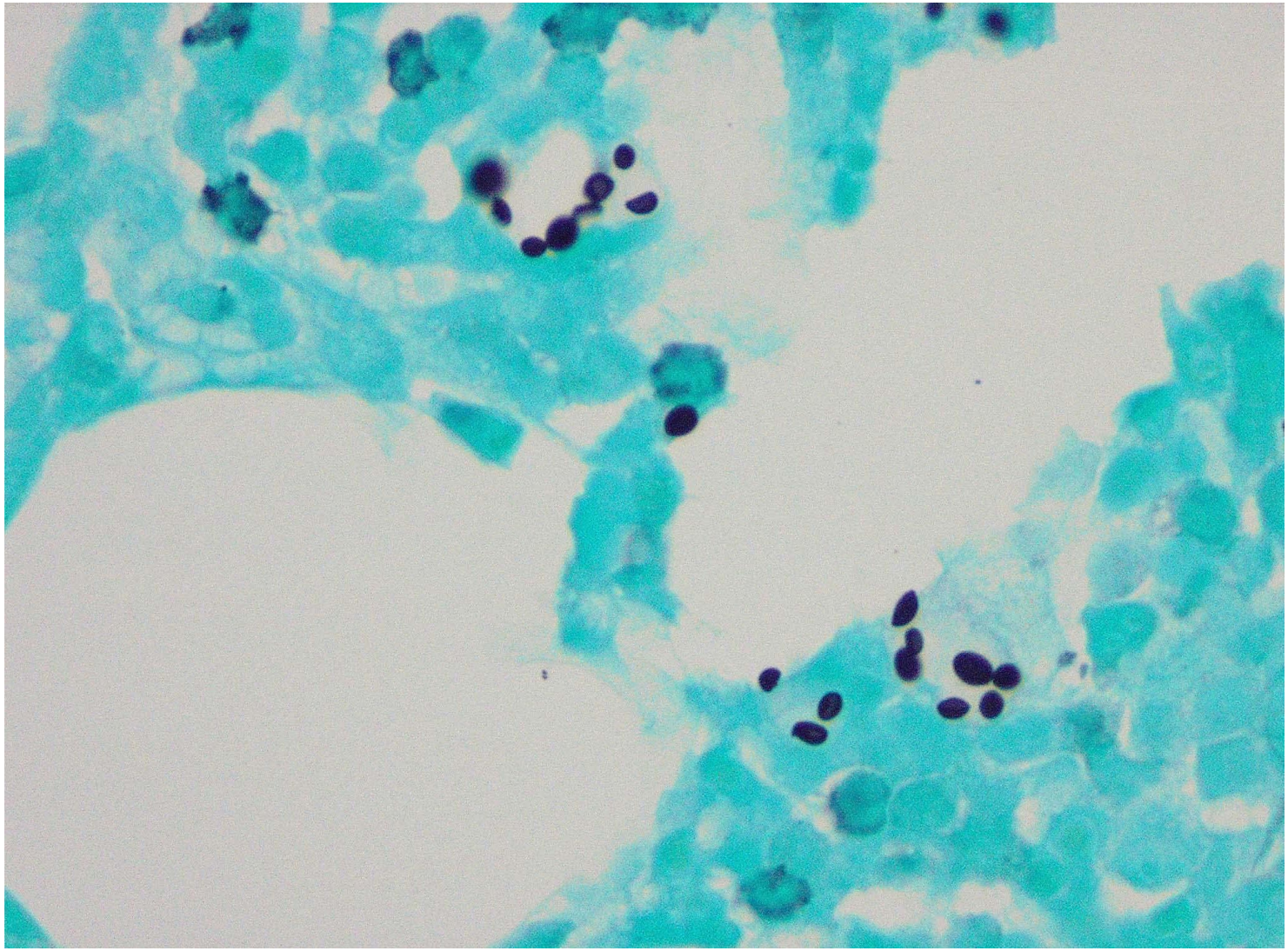
Bone Marrow Biopsy (cont'd)



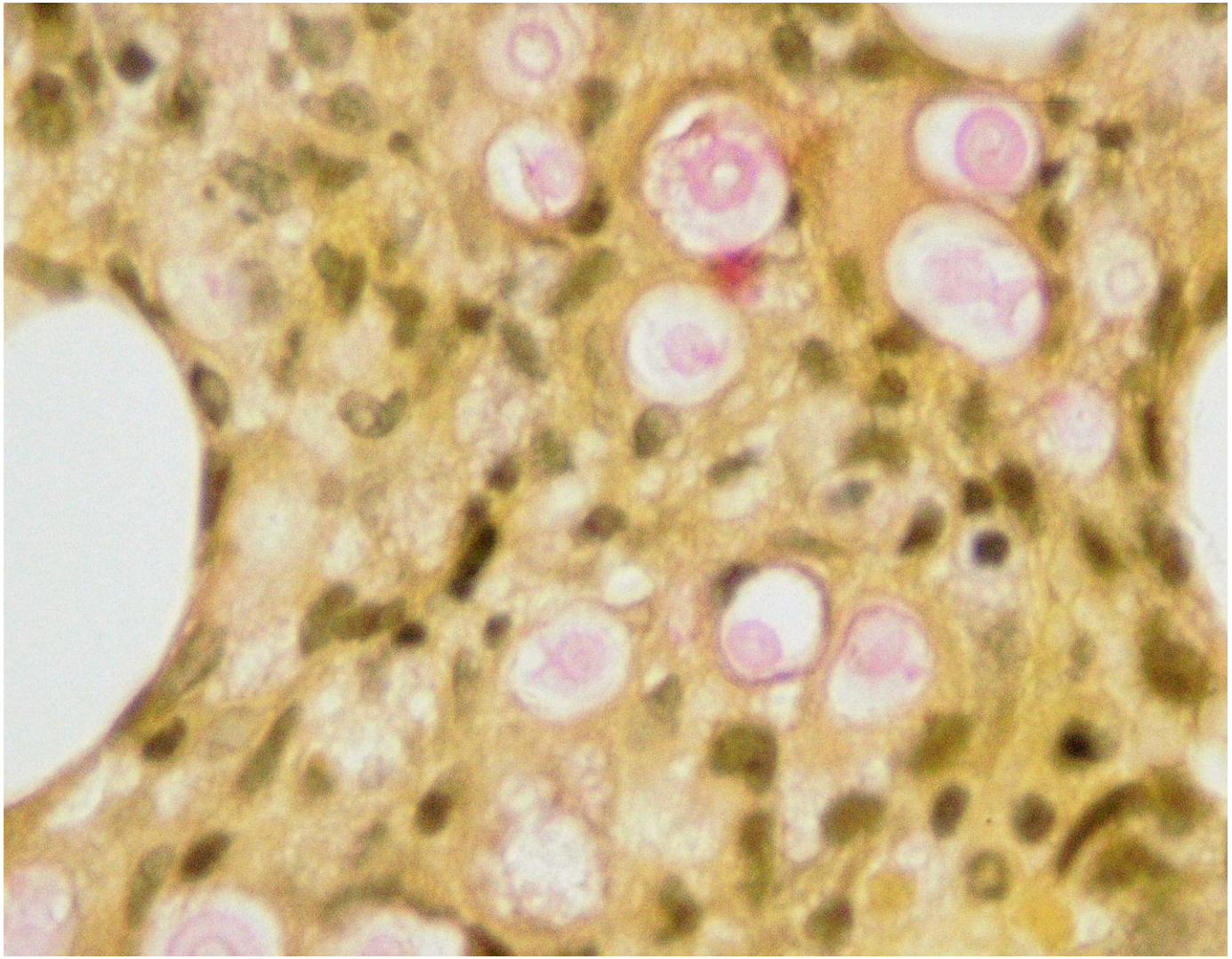
Bone Marrow Biopsy-Gomori Methenamine Silver Stain



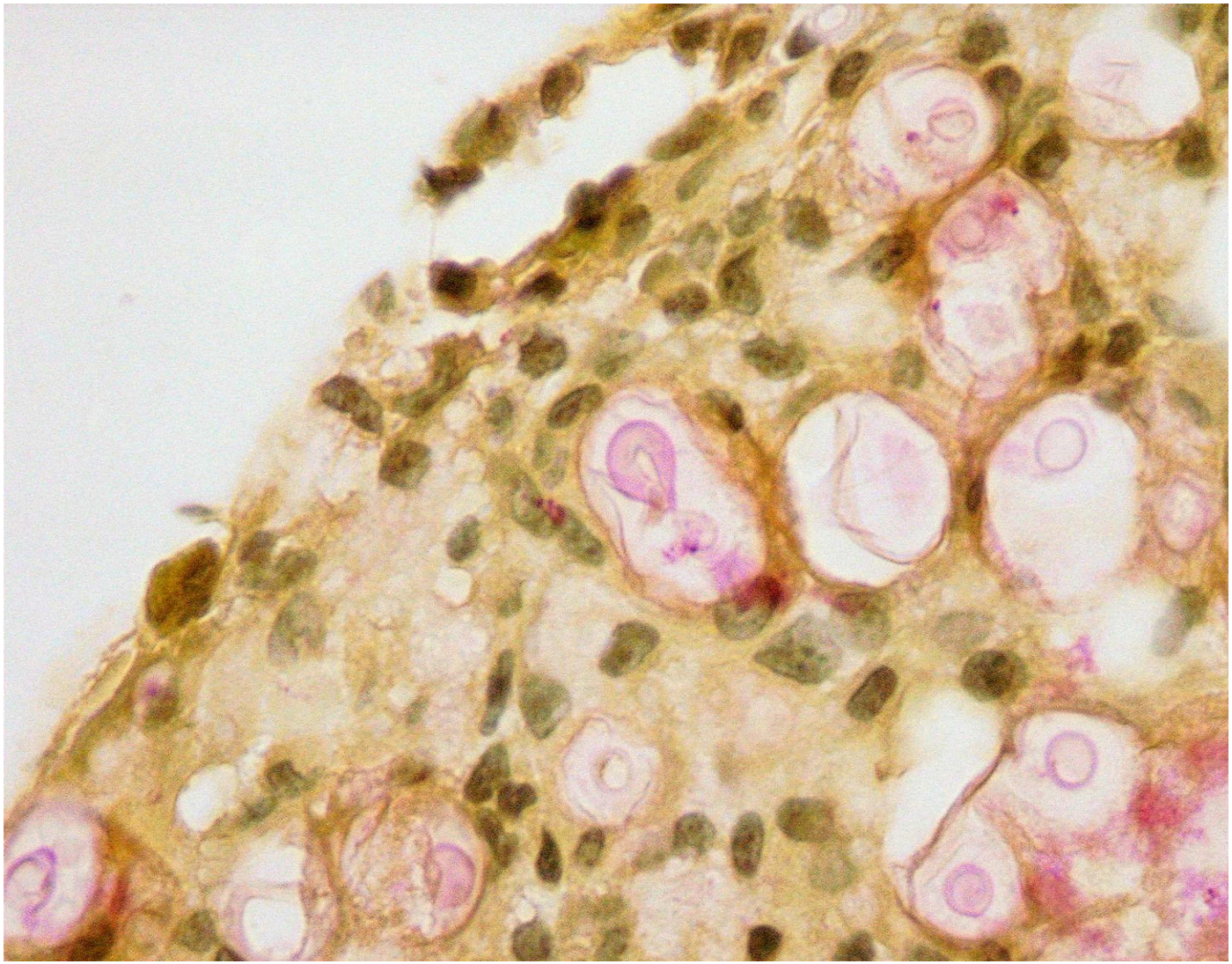
Bone Marrow Biopsy-GMS Stain, cont'd



Bone Marrow Biopsy- Mucin Stain



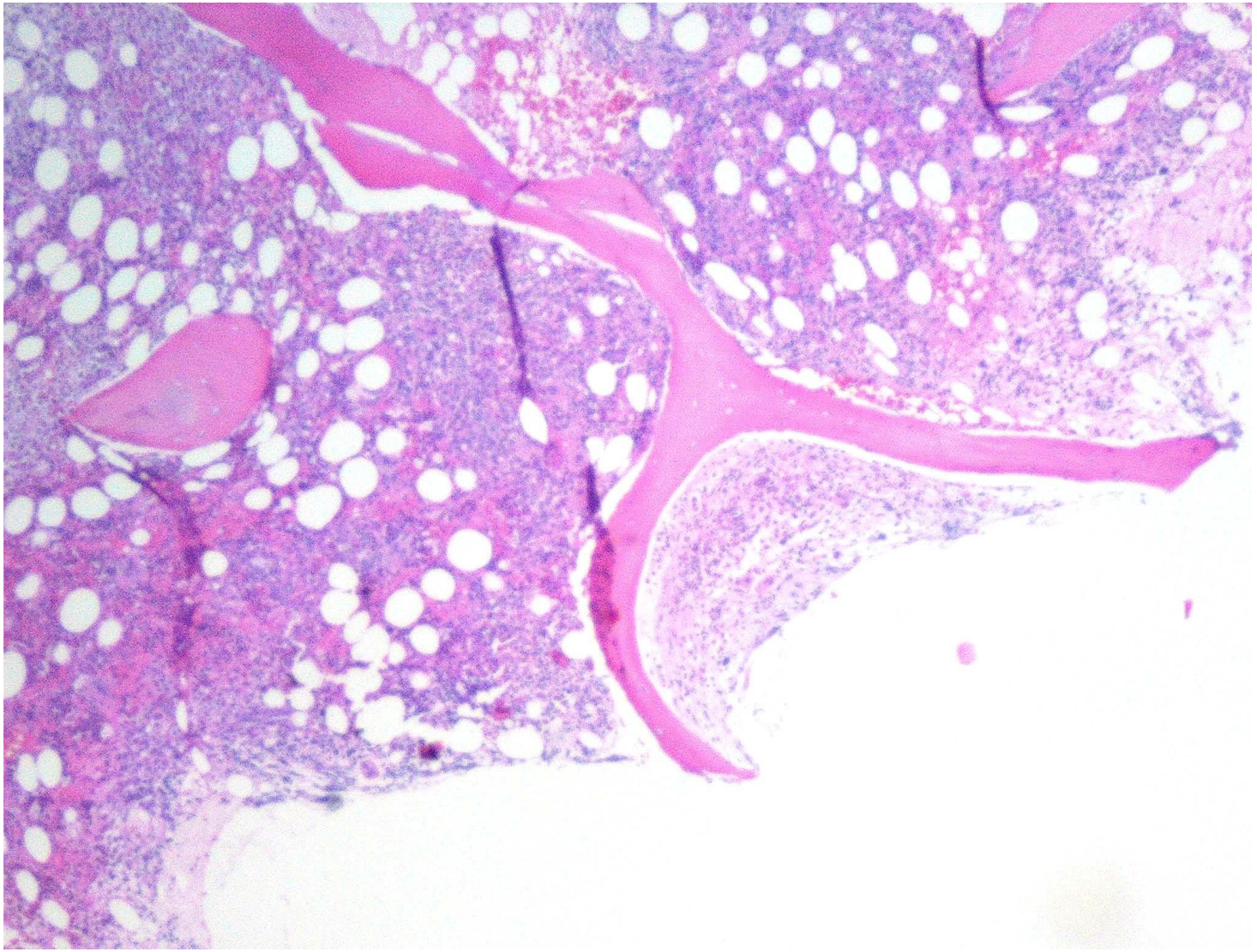
Bone Marrow Biopsy- Mucin Stain, cont'd



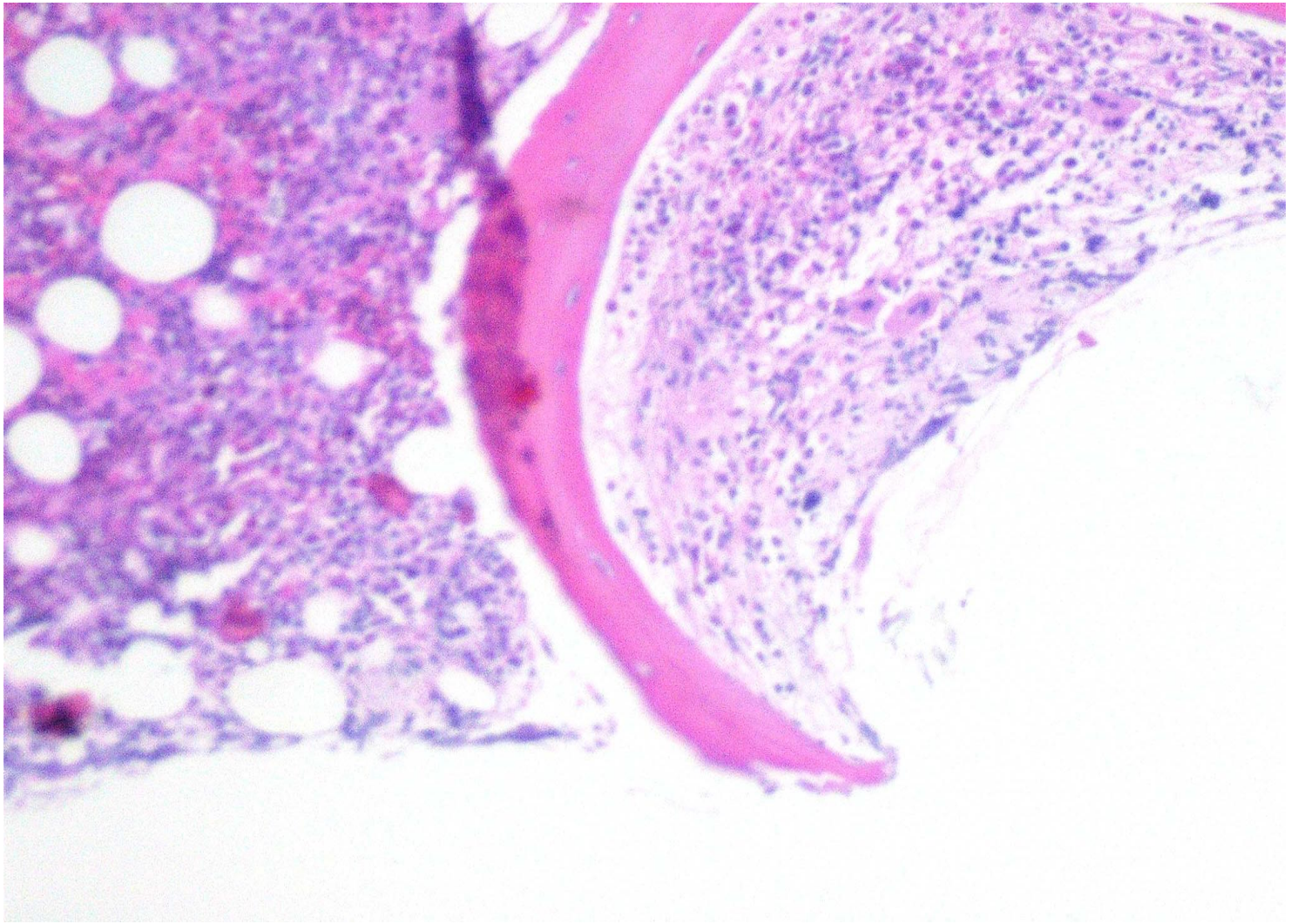
HB-03-58
Patient Name: Sxxx, Bxxx

- 31 year old white female with AIDS and persistent fever. Patient had been diagnosed with MAI in sputum (1/03). Now sputum, CSF and blood cultures are negative
- CBC: WBC=3, Hbg=7, Plt=403k
- Bone marrow was requested by ID: bx 75% cellularity

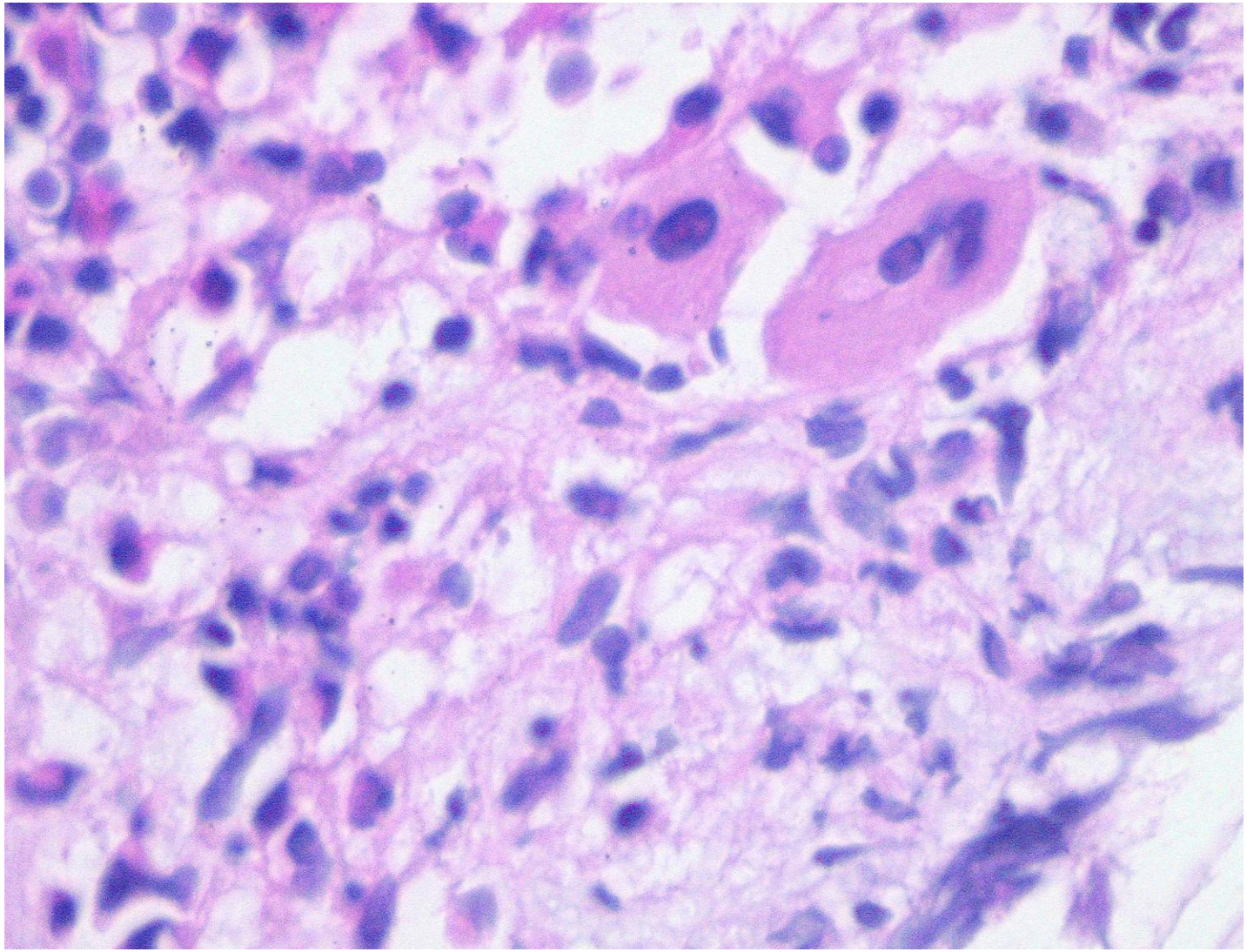
Bone Marrow Biopsy



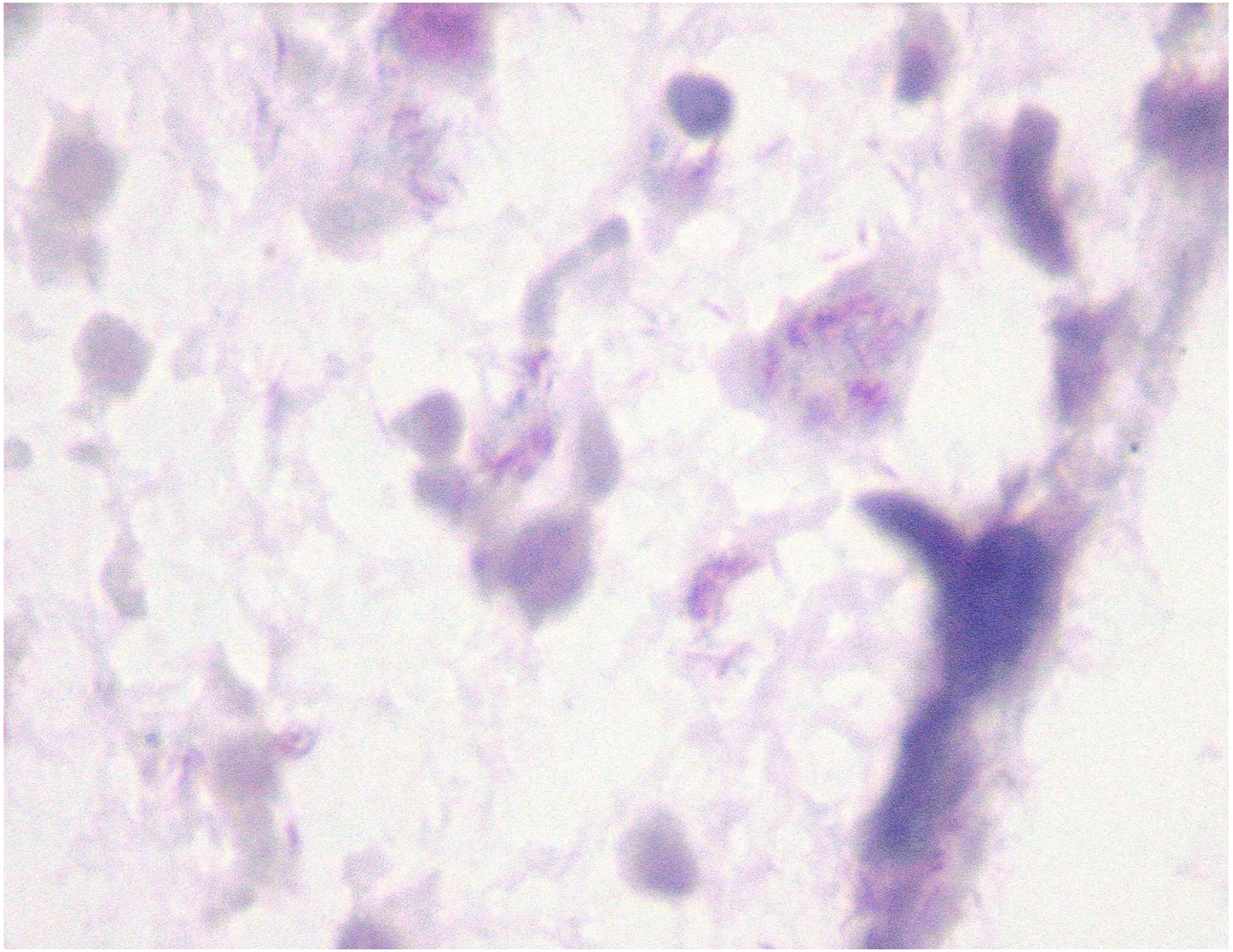
Bone Marrow Biopsy (cont'd)



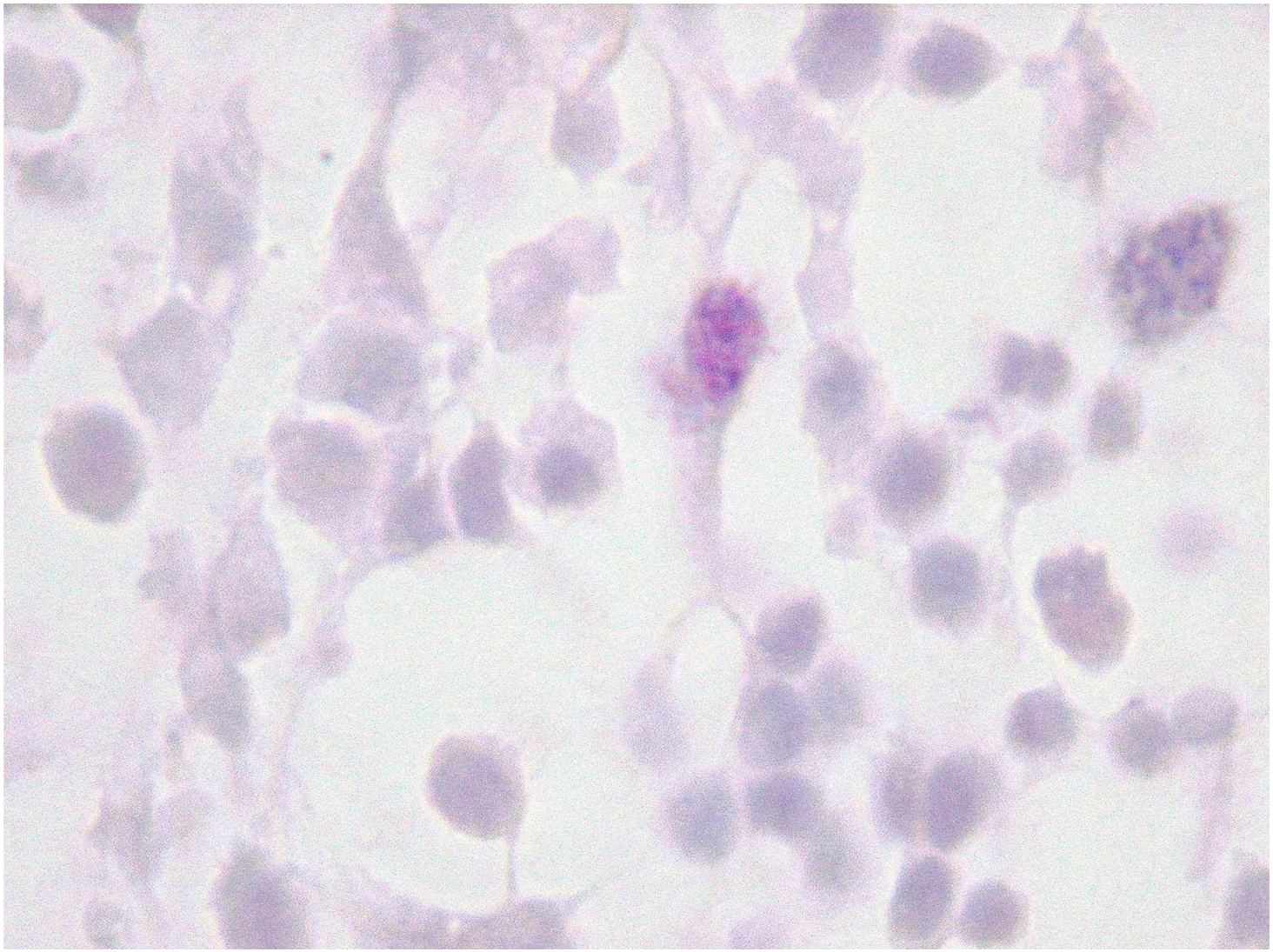
Bone Marrow Biopsy (cont'd)



Bone Marrow Biopsy-AFB Stain



Bone Marrow Biopsy-AFB Stain



03-108-0589
Patient: Axxx, Mxxx

- 50 y/o Iranian male who was evaluated for cholecystectomy at Memorial City Hospital. Patient allegedly has a Hx of hemophilia A with no Hx of frank bleeding tendency. Patient had also been told to have von Willebrand disease.
- Past medical history: in 1982, patient underwent toot extraction at which time he was given some type of fluid (?) to prevent bleeding.
- Family Hx: mother and sister (in Iran) with hemophilia (?)

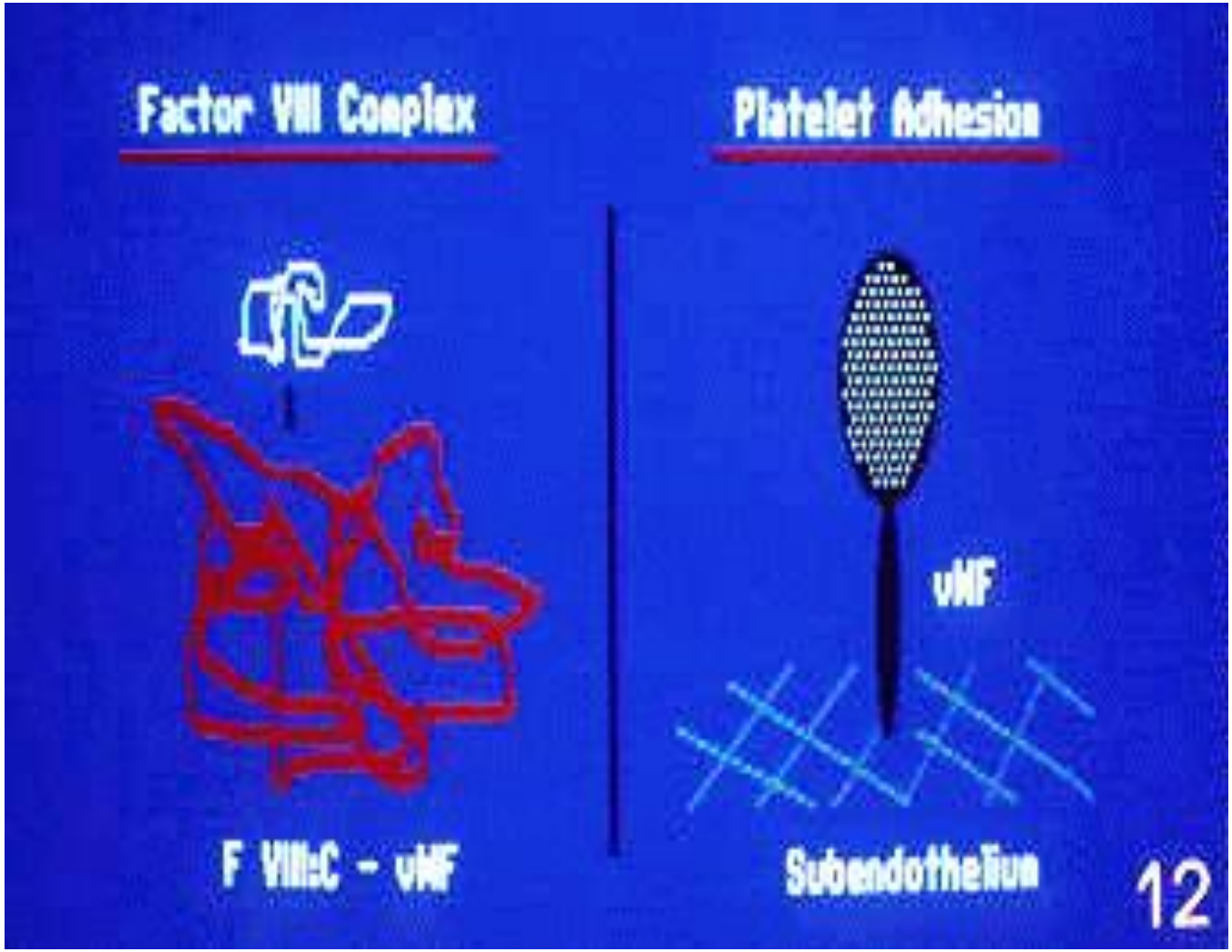
Laboratory Tests

- PT= 11.0 sec (ref 8-11.5)
  PTT= 45.9 sec (ref 24.0-37.5)

- F VIII=8% (ref 46-182)
  vWF:RCo=31% (ref 45-140%)
  vWF:Ag=35% (ref 45-165%)

- Differential diagnosis:
  (1) Hemophilia A: low vWF (?), Hx of hemophilia in mother, and sister (?)
  (2) vWD: low F VIII (?)

F VIII-vWF Complex



2N-von Willebrand Disease

- A rare subtype 2 of vWD. “N” stands for Normandy, France where the first case was described in 1989
- In 2N-vWD, vWF does not bind adequately to FVIII. As a result, F VIII level is low due to a shorter half-life
- vWF level can be normal or moderately low
- 2N-vWD is frequently misdiagnosed as hemophilia A in a male patient. Subsequent family studies show autosomal-recessive inheritance (not sex-linked as in hemophilia)
- At least 5 coding defects of vWF gene (Gene map locus 12p 13.3) has been found to be a/w 2N-vWD
- In several family studies showed compound heterozygous with both type I and and type 2N

2N-von Willebrand Disease: Laboratory Tests

- F VIII level is disproportinally depressed compared to vWF level which is either normal or moderately depressed
- F VIII-vWF Binding Assay (Blood Center, Milwaukee, WI, $275):
  - Capturing pt's vWF in a microtiter well coated with monoclonal Ab to vWF
  - Strip off pt's F VIII with 0.4M Calcium chloride
  - Allow pt's vWF to bind to recombinant F VIII
  - The bound F VIII is quantitated by chromogenic assay
  - Reported ratio of (bound F VIII / pt's vWF)

  Typical ref range: >60%

2N-von Willebrand Disease: Treatment

- 2N-vWD patient has very short correction of F VIII in response to F VIII replacement or DDAVP.
- Optimal therapy: F VIII/vWF concentrates (Humate P, Alphanate, Koate HP)
- Patient responded well to Tx:
  F VIII= 156%
  vWF:RCo=214%