HP education conference
6.21.2011
SH

- **history:** 54 year-old woman with > 5 year history of lymphocytosis
- **past medical history:** hypothyroidism
- **surgical history:** hysterectomy, tubal ligation, appendectomy, knee replacement
- **medications:** Synthroid, Zoloft, Premarin, Chantix
- **social history:** has smoked 1.5 packs per day for 30 years
- **physical exam:** splenomegaly
- **CT abdomen:** splenomegaly (19 cm), no hepatomegaly or lymphoadenopathy

lab

- CBC

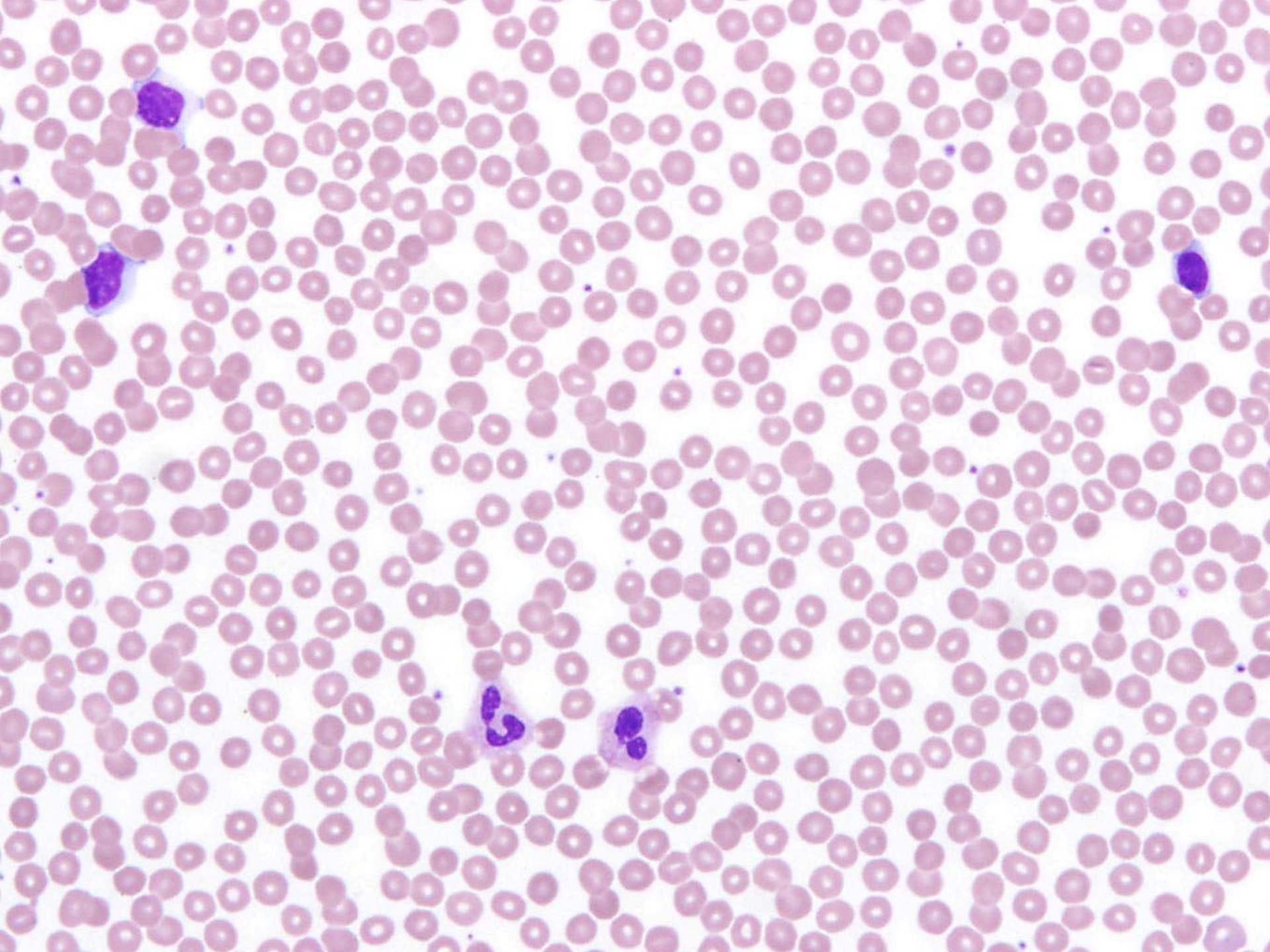
	14.7	neutrophils	30 %
17.4	133	lymphocytes	66 % **ALC 11.5**
		monocytes	4 %

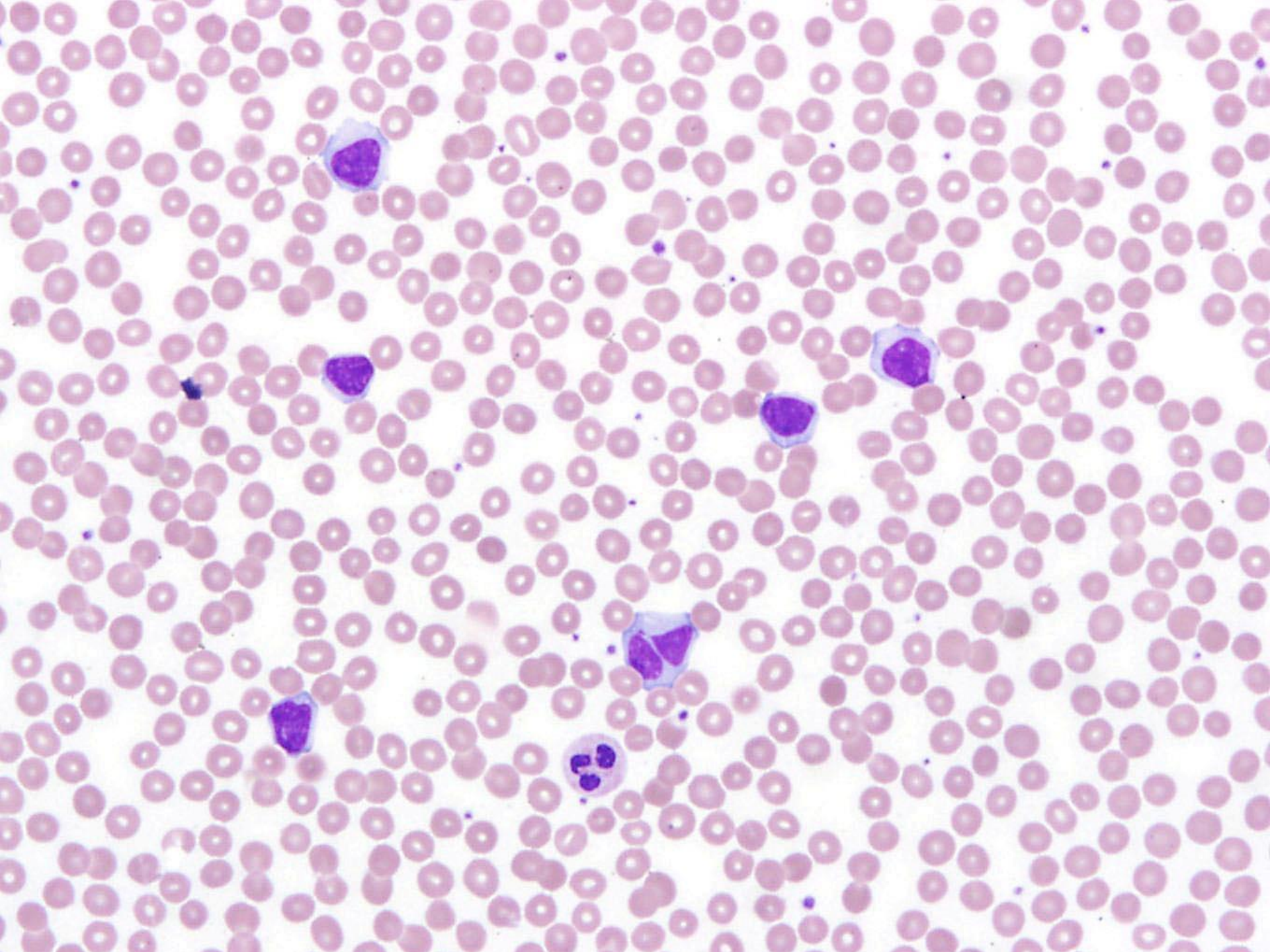
- immunoglobulins

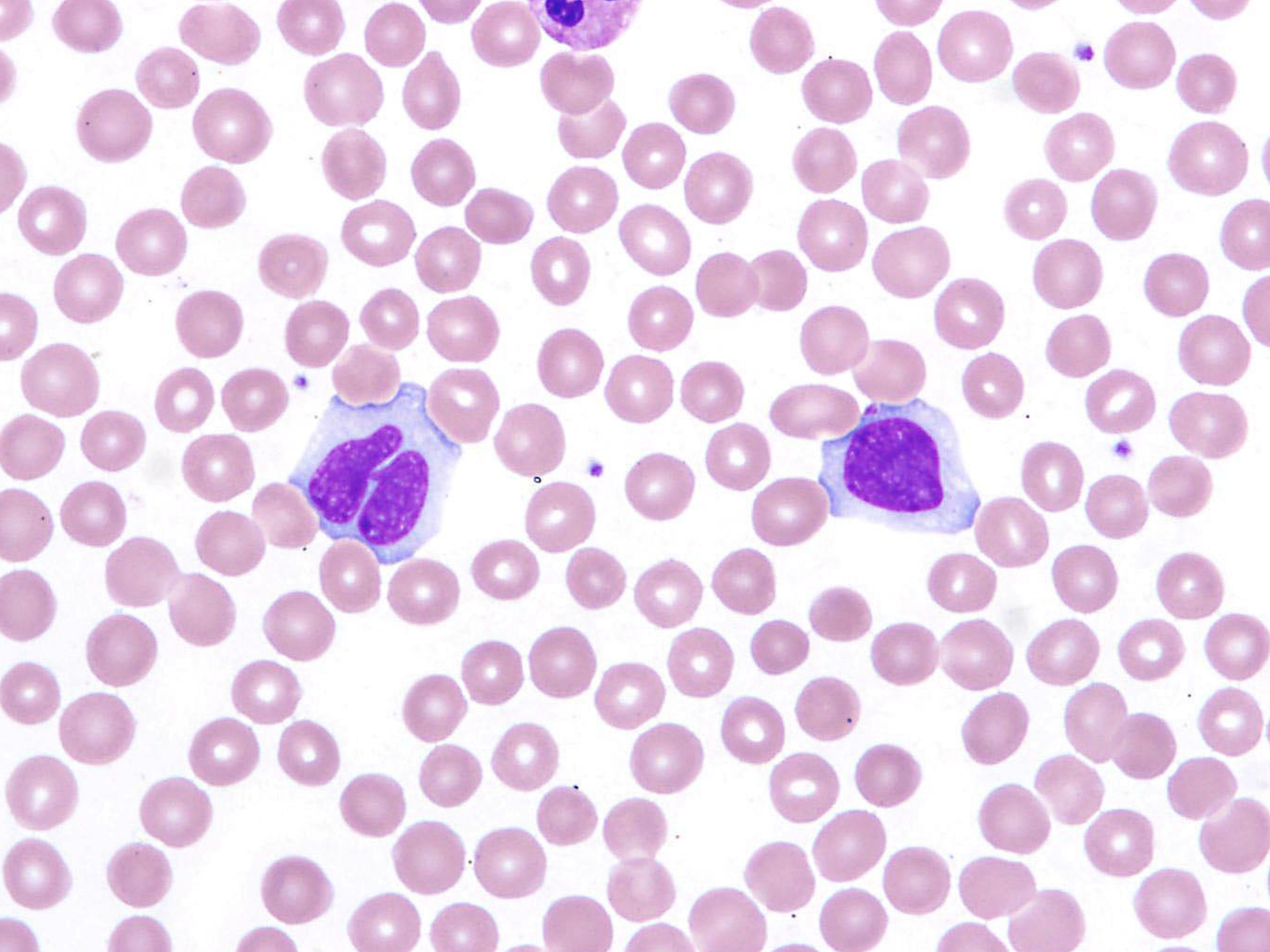
  IgG 583 mg/dL
  IgA 125 mg/dL
  IgM 1440 mg/dL

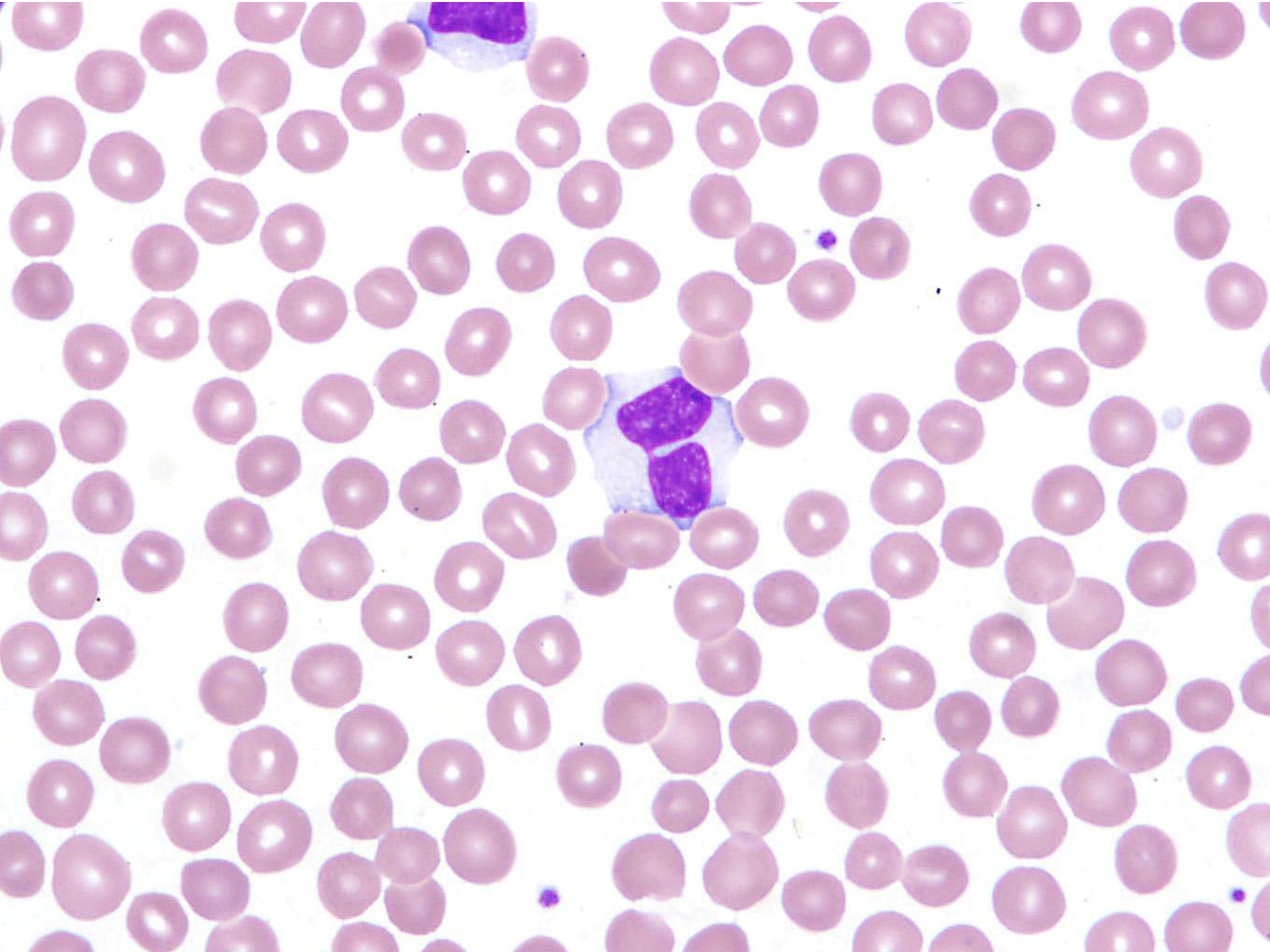
- SPE, IFIX

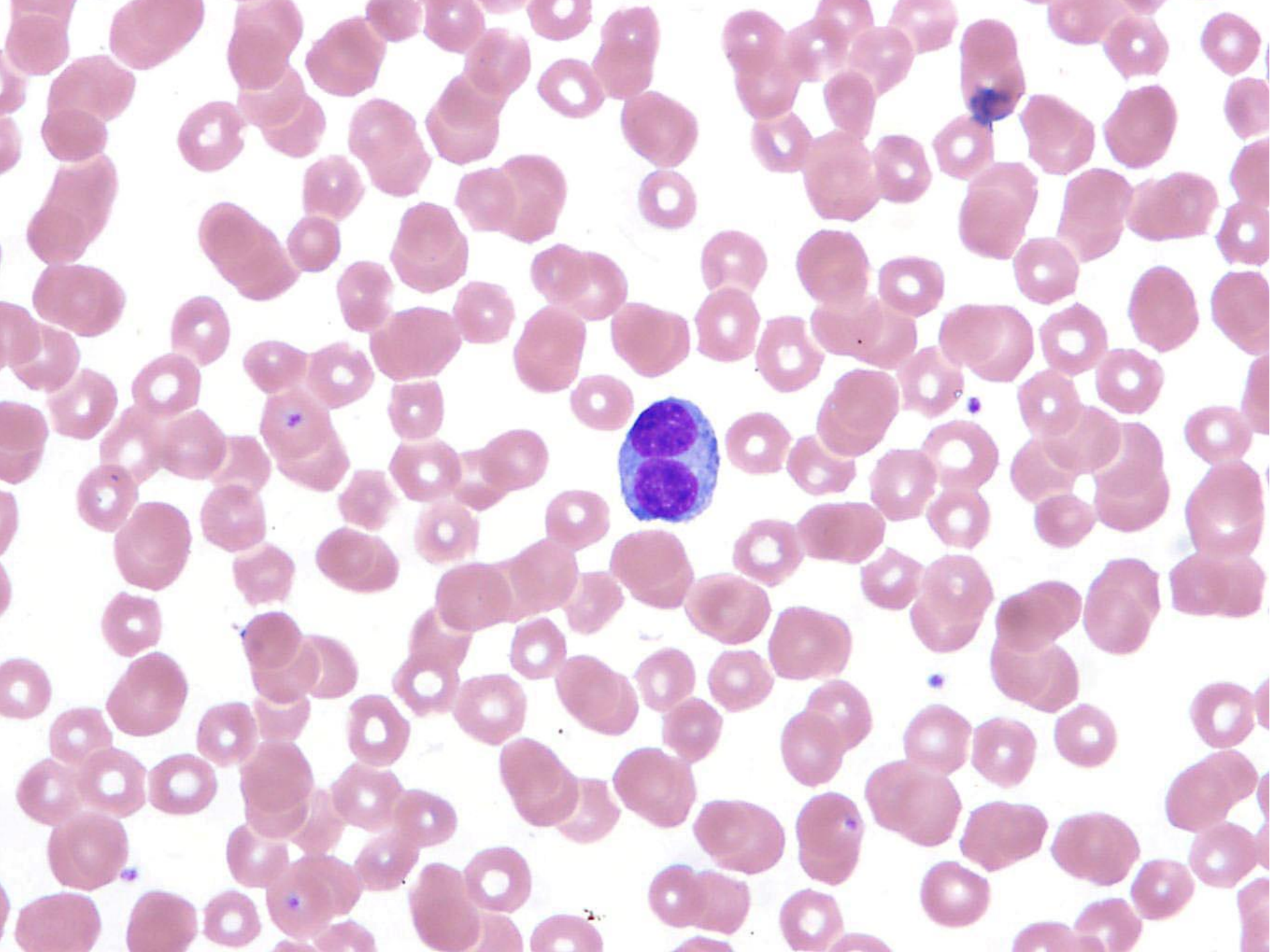
  polyclonal increase in immunoglobulins











lymphocytosis

- chronic lymphocytic leukemia
- splenic marginal zone lymphoma
- hairy cell leukemia
- follicular lymphoma
- mantle cell lymphoma
- viral infection
- *Bordetella pertussis* infection
- stress lymphocytosis
- drug reaction
- persistent polyclonal B cell lymphocytosis

persistent polyclonal B cell lymphocytosis

- persistent lymphocytosis
- binucleated lymphocytes

persistent polyclonal B cell lymphocytosis clinical features

- 82% women
- median age ~40 years
- 98% smokers
- asymptomatic or minor, nonspecific complaints
- normal physical exam except mild splenomegaly in 10%

Cornet, et al. Leukemia (2009) 23, 419-422.

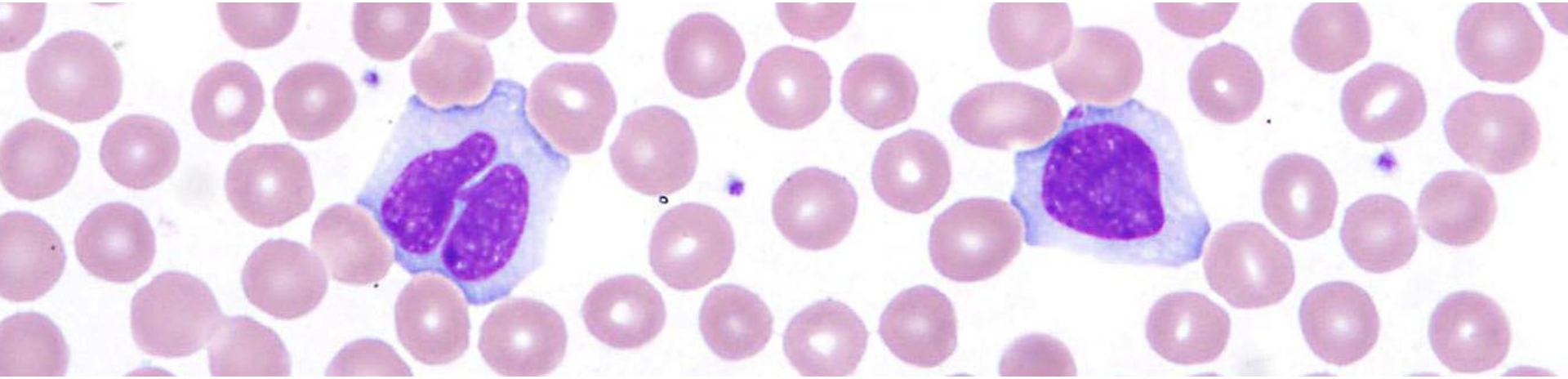
persistent polyclonal B cell lymphocytosis clinical features

- binucleated lymphocytes, whatever the lymphocyte count
- 87% mild lymphocytosis, 17% lymphocyte count < 4 k/uL
- median lymphocyte count 5.45 k/uL (range 2.45-20.52 k/Ul)
- binucleated lymphocytes median 4%, range 1-40%
- median serum IgM 6.0 g/L (normal 0.5-2.7 g/L, range 1.2-17.3 g/L)

Cornet, et al. Leukemia (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis peripheral blood morphology

- large lymphocytes
- round, indented or bilobed nucleus or binucleate
- abundant faintly basophilic cytoplasm

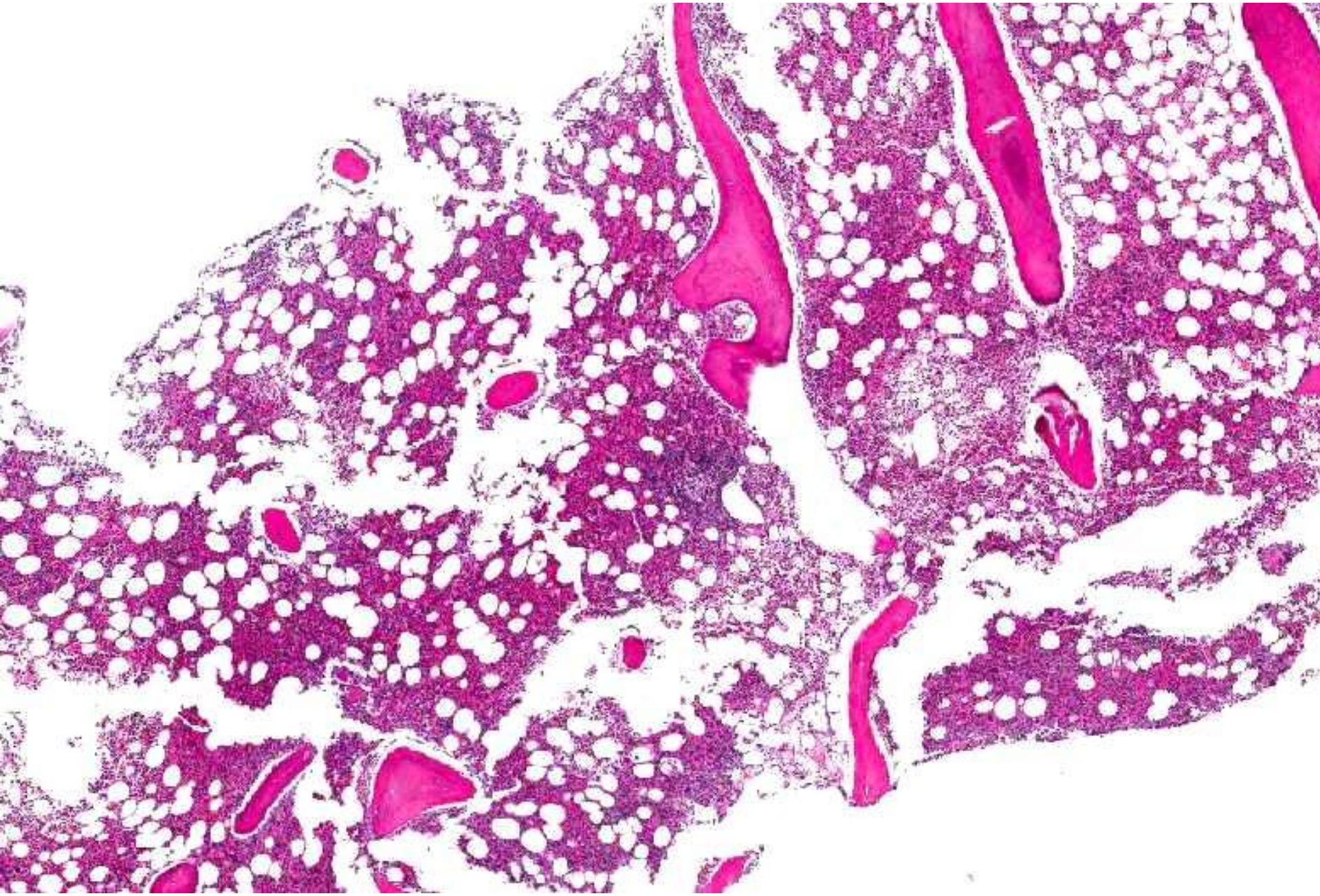


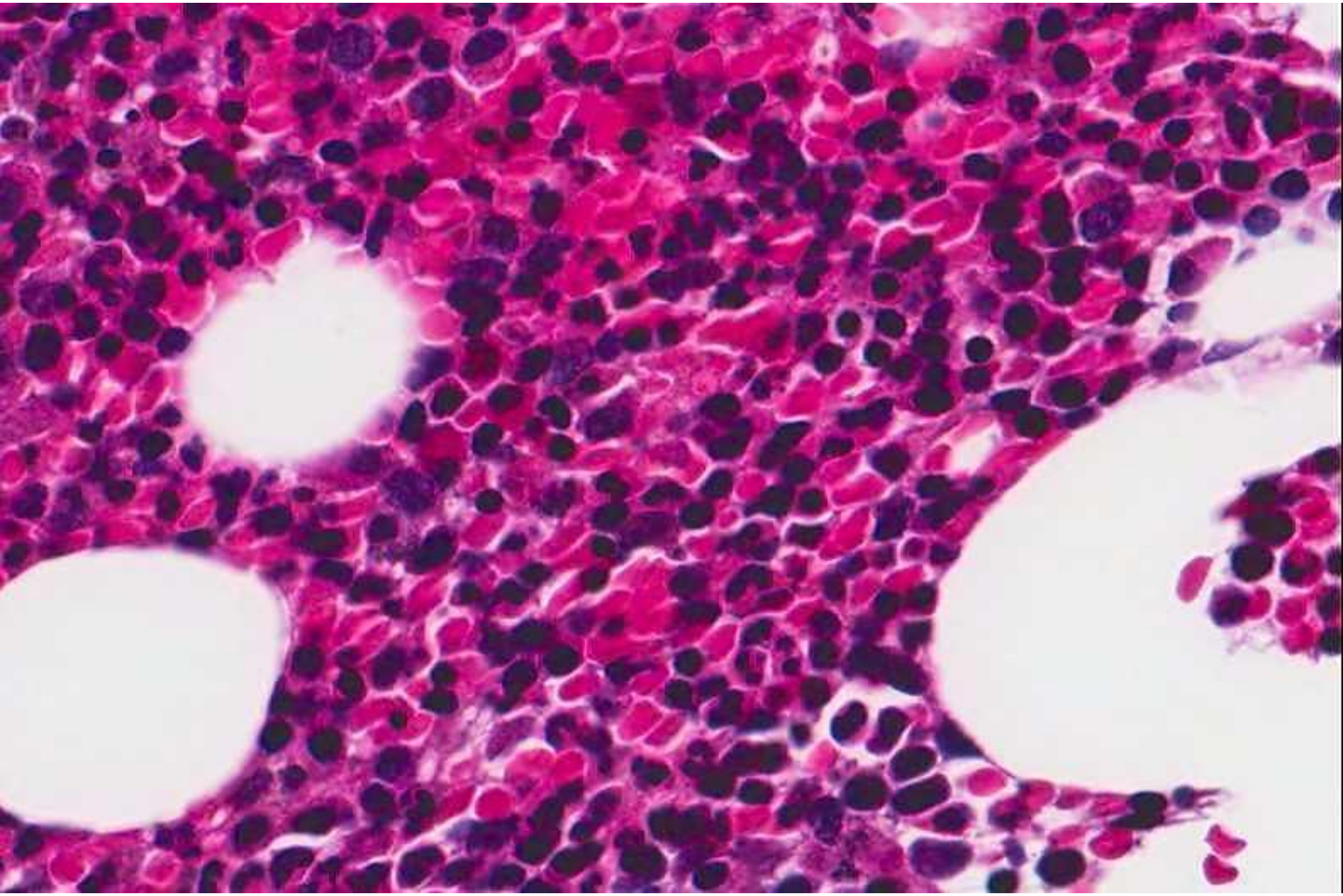
Troussard, et al. *Leuk and Lymphoma* (1996) 20, 275-279.

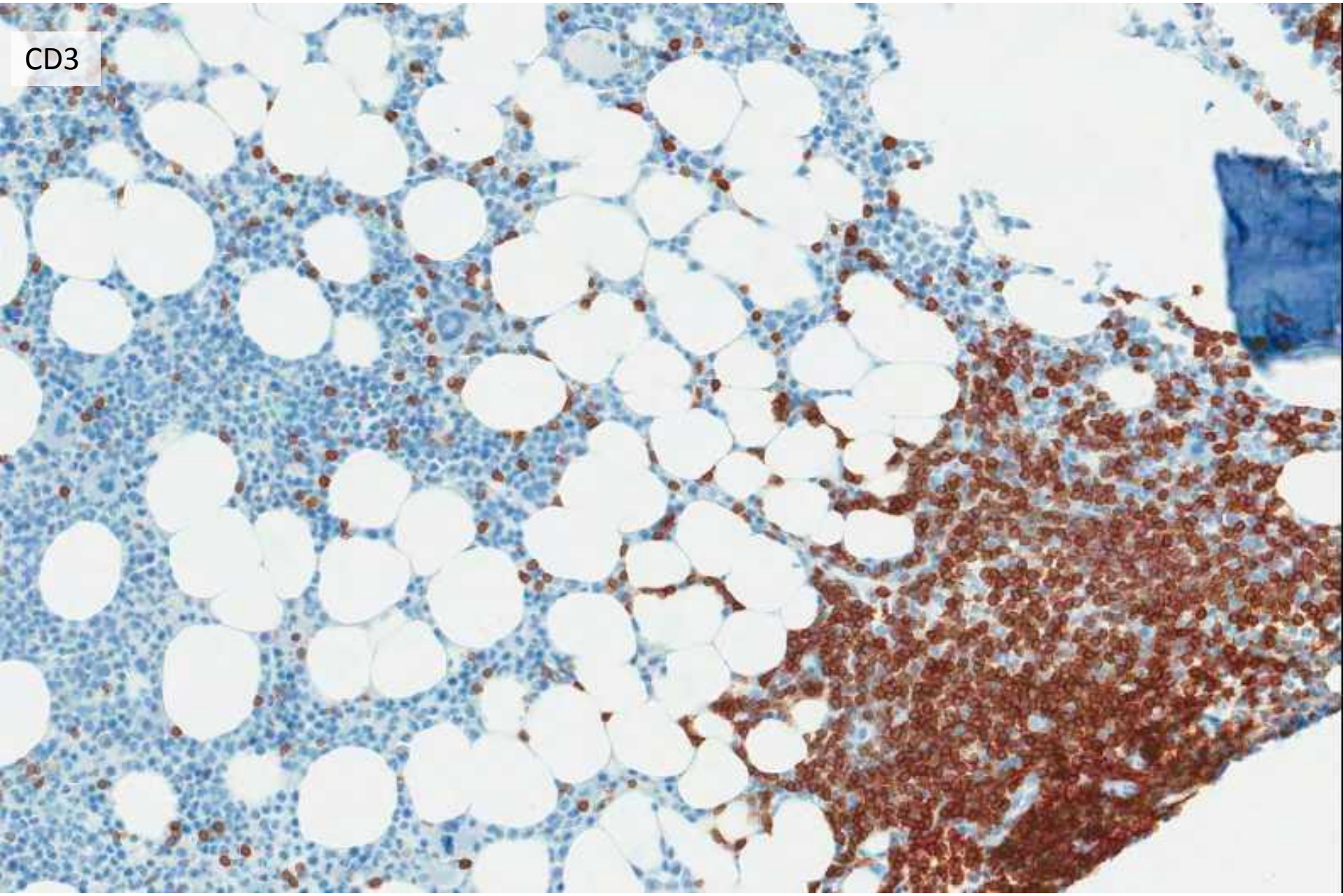
persistent polyclonal B cell lymphocytosis bone marrow

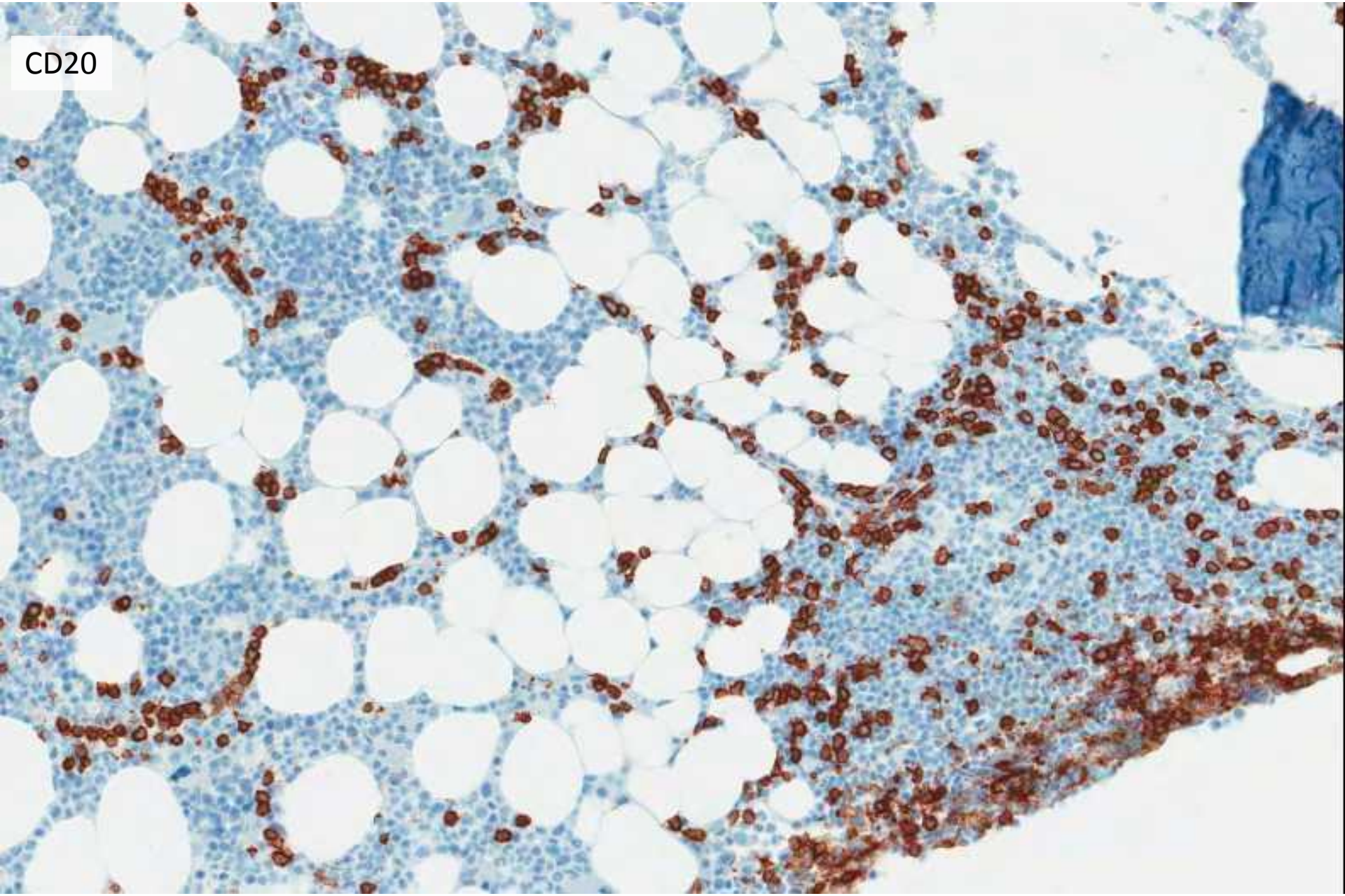
- morphology
  - normocellular (3 cases) or hypercellular (4 cases)
  - intravascular infiltrate of lymphocytes
    - lymphocytes arranged in chains in capillaries or in small clusters in slightly distended venous sinuses
  - interstitial infiltrate
    - less prominent than intravascular infiltrate
  - lymphoid aggregates (3 cases)
    - nonparatrabecular
- immunohistochemistry
  - intravascular and interstitial lymphocytes predominantly B cells
  - B cells express BCL2 (heterogeneous)
  - B cells CD5, CD23 and CD43 negative
  - lymphoid aggregates predominantly T cells

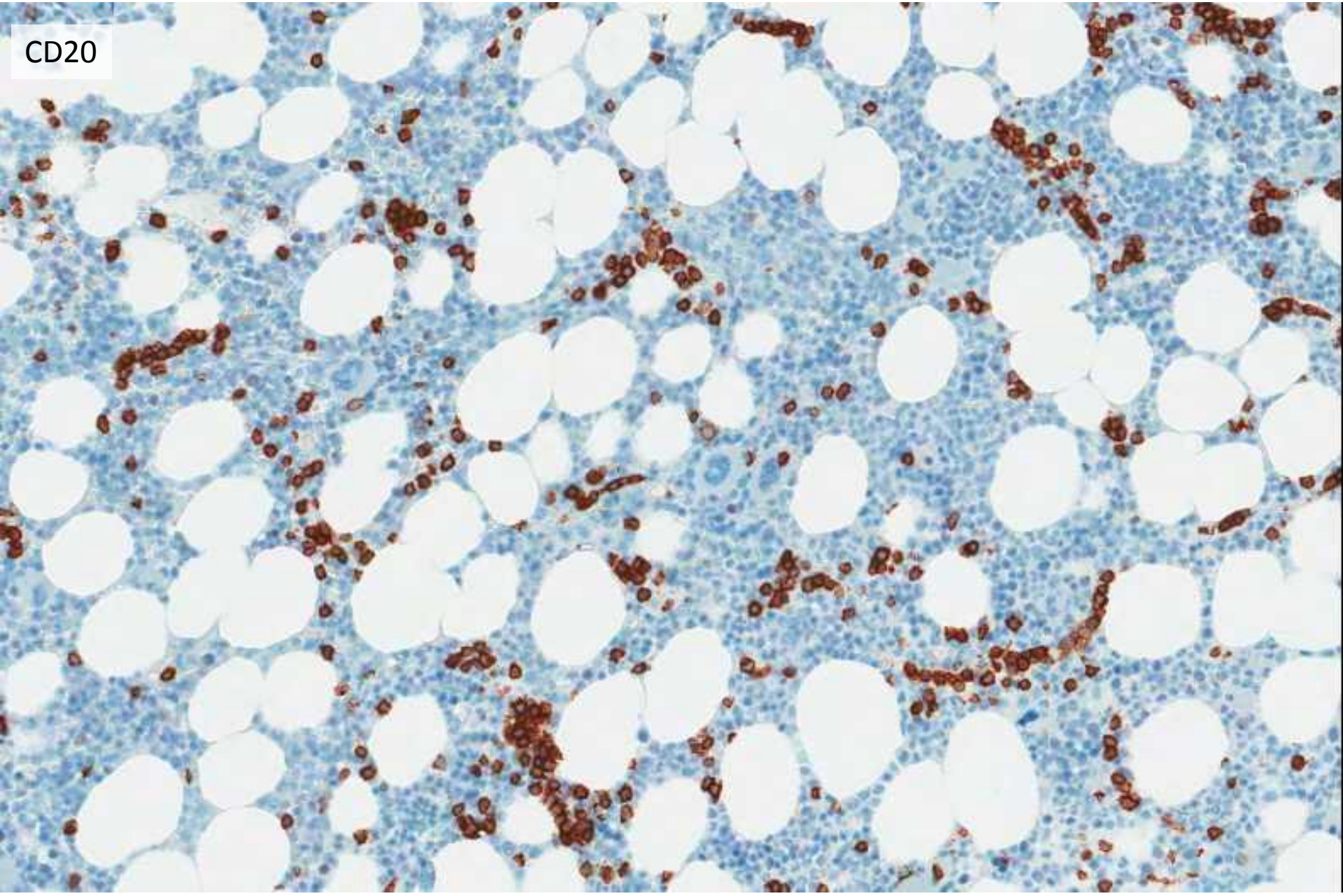
Feugier, et al. *Modern Pathology* (2004) 17, 1087-1096.






CD3


CD20


CD20

persistent polyclonal B cell lymphocytosis spleen

- 5 patients with PPBL and progressive splenomegaly, splenectomy in 3
- white pulp marginal zone expansion
- red pulp sinuses infiltrated

Del Giudice, et al. *Br J Haematology* (2009) 144, 726-731.

persistent polyclonal B cell lymphocytosis flow cytometry

- polyclonal B cell lymphocytosis in all cases
- CD19+, CD5-

Cornet, et al. Leukemia (2009) 23, 419-422.

- CD19+, CD22+, CD79+ B cells majority of lymphocytes
- residual CD3+ T cells in some patients
- B cells CD5-, CD43-, CD10-
- surface IgM+, IgD±, IgG-, IgA-
- polyclonal

Feugier, et al. *Modern Pathology* (2004) 17, 1087-1096.

persistent polyclonal B cell lymphocytosis genetics

- IgH gene rearrangement polyclonal or oligoclonal

Feugier, et al. *Modern Pathology* (2004) 17, 1087-1096.

- multpile IgH/BCL2 rearrangements in most cases
  - 11 patients 1-7 rearrangements

Delage, et al. *Leuk and Lymphoma* (1998) 31, 567-574.

  - 4 of 6 patients 1-2 rearrangements

Feugier, et al. *Modern Pathology* (2004) 17, 1087-1096.

persistent polyclonal B cell lymphocytosis cytogenetics

- performed in 98 cases
- +i(3q) 34% (33 of 98)
- premature chromosome condensation in 8% (8 of 98)
- both abnormalities 31% (30 of 98)
- neither abnormality in 28% (27 of 98)

Cornet, et al. Leukemia (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis FISH

- performed in 84 cases
- +i(3q) detected in 71% (60 of 84)

Cornet, et al. Leukemia (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis cytogenetics and FISH

- 84 cases with cytogenetics and FISH
- +i(3q) detected by FISH in 17 patients with negative cytogenetics
- +i(3q) confirmed in 43 patients with positive cytogenetics
- FISH and cytogenetics negative in 24 cases

Cornet, et al. Leukemia (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis genetic predisposition

- HLA-DR7
  - 6 of 6 cases

    Troussard, et al. *Br J Haematology* (1994) 88, 275-280.
  - 19 of 20 cases

    Mossafa, et al. *Br J Haematology* (1999) 104, 486-493.
- family clusters
  - PPBL in monozygotic twins

    Carr, et al. *Br J Haematology* (1997) 96, 272-274.
  - PPPBL in brother and sister

    Himmelmann, et al. *Leuk Lymphoma* (2001) 41, 157-160.
  - PPBL and multiple BCL2/IgH rearrangements in first degree relatives

    Delage, et al. *Br J Haematology* (2001) 114, 666-670.

persistent polyclonal B cell lymphocytosis follow up

- 111 cases
- median follow up 4.4 years (0.5-29 years)
- stable in 89% (99 of 111)
- decreased lymphocytosis and number of binucleated lymphocytes with persistent +i(3q) in 2 patients 2 years after stopping tobacco use

Cornet, et al. *Leukemia* (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis follow up - deaths

- MI
- cerebral aneurysm rupture
- lung cancer 9 years after PPBL diagnosis
- diffuse large B cell lymphoma
- unknown cause (2 patients)

Cornet, et al. *Leukemia* (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis follow up - malignancies

- lung cancer (2 cases)
- cervical cancer (12 years after PPBL diagnosis)
- diffuse large B cell lymphoma (2 cases, 3 and 9 years after PPBL diagnosis)
- splenic marginal zone lymphoma (3 years after PPBL diagnosis)

Cornet, et al. Leukemia (2009) 23, 419-422.

persistent polyclonal B cell lymphocytosis IgM monoclonal gammopathy

- 111 cases, median follow up 4.4 years (0.5-29 years)
- 2 patients had IgM MGUS at time of PPBL diagnosis
- 2 other patients developed IgM MGUS 12 and 22 years after PPBL diagnosis
- no bone marrow biopsy performed
- remained asymptomatic and stable after median follow up of 102 months (range 52-348 months)

Cornet, et al. Leukemia (2009) 23, 419-422.

summary

- women, median age 40 years
- smoking
- persistent lymphocytosis with bilobed/binucleate cells
- polyclonal B cells
- polyclonal increase in serum IgM
- +i(3q), IgH/BCL2 rearrangements
- HLA-DR7