



3^a Jornada Profesional del Laboratorio Clínico

Importancia del Laboratorio Clínico en el
Diagnóstico Precoz de la Enfermedad Oculta

“Papel del Laboratorio Clínico en la detección de
enfermedades ocultas mediante el análisis citológico
de sangre periférica y líquidos biológicos”

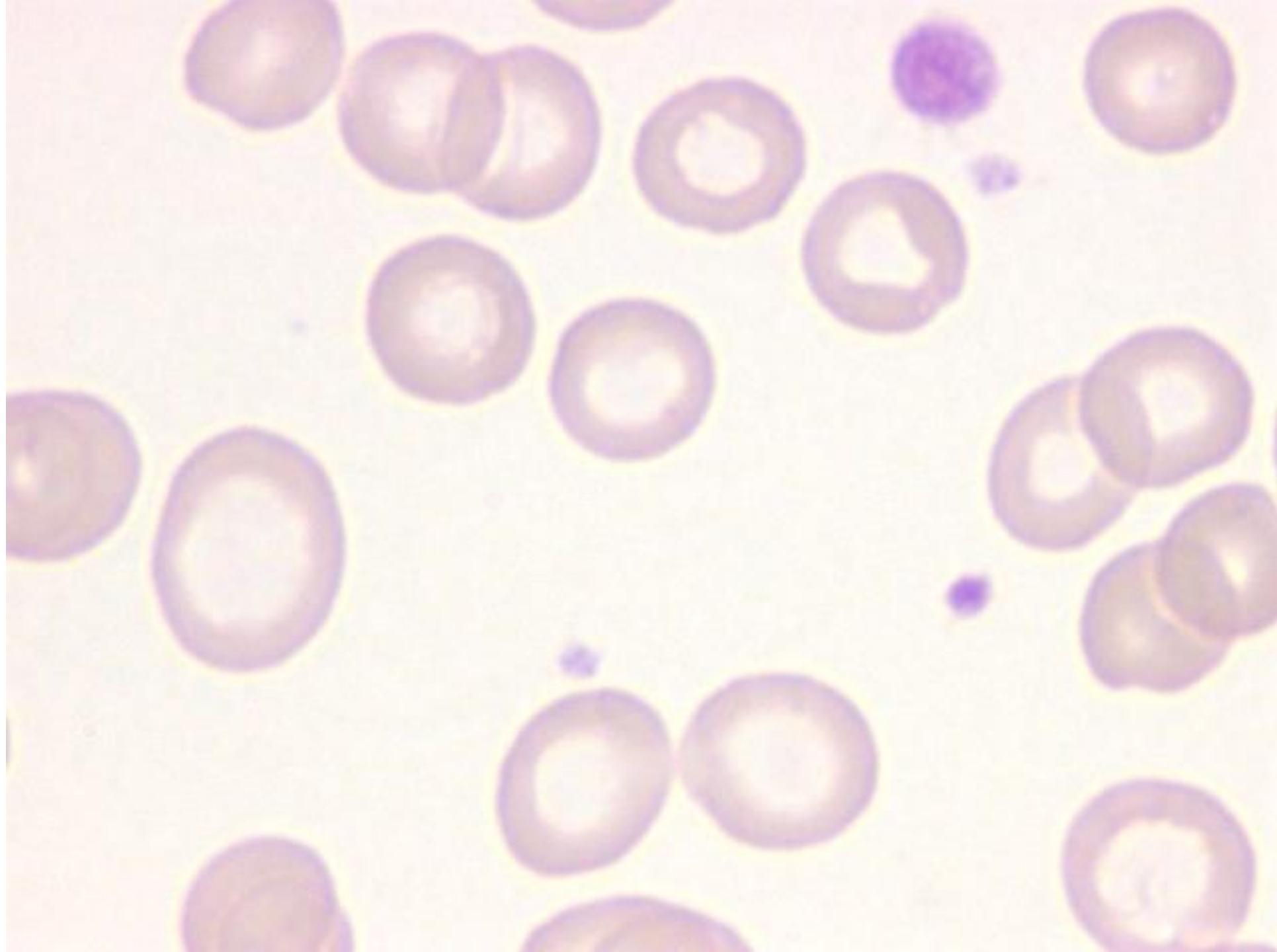
Dra. Anna Merino



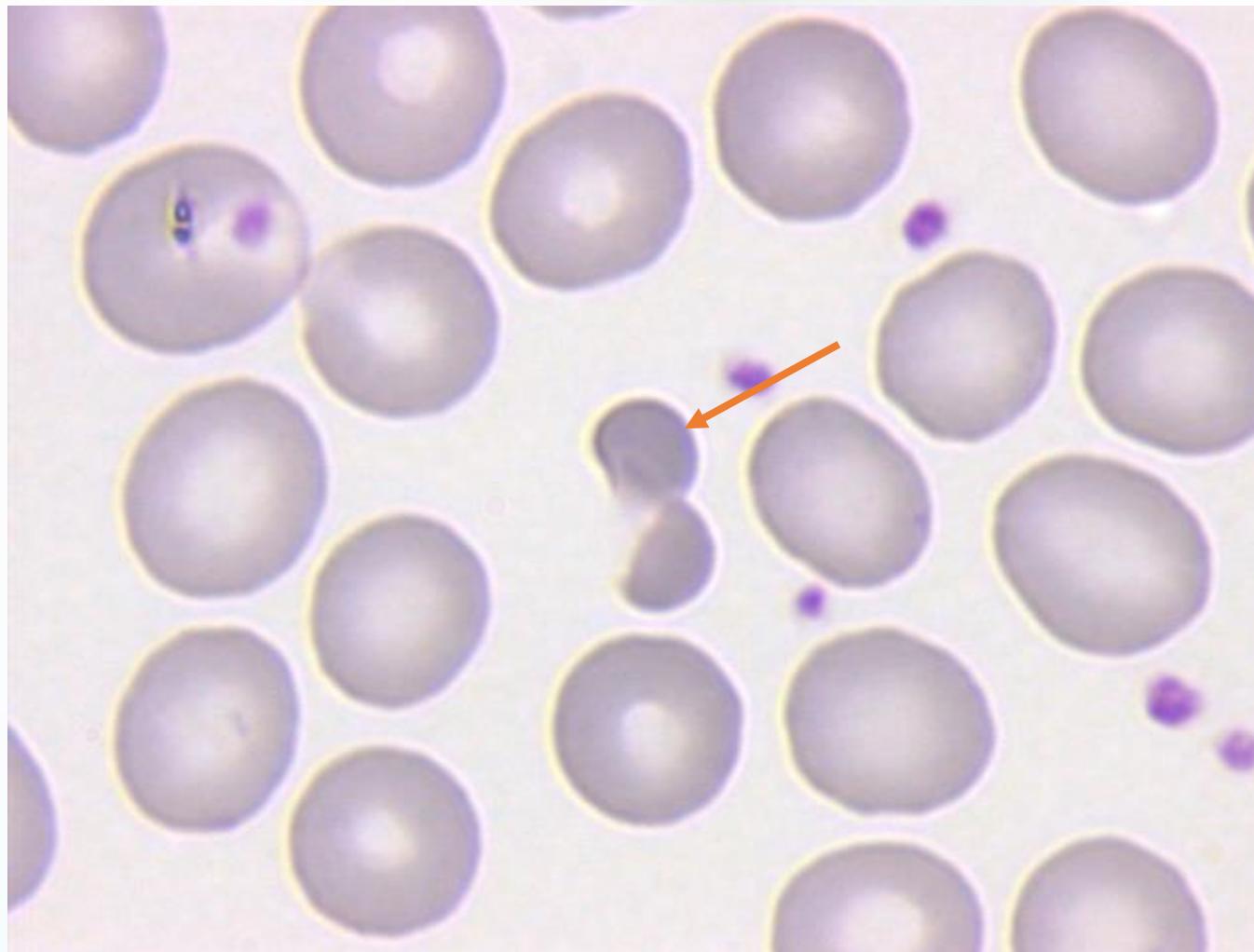
Vocalía Nacional
de Analistas Clínicos

Valor de la revisión del frotis

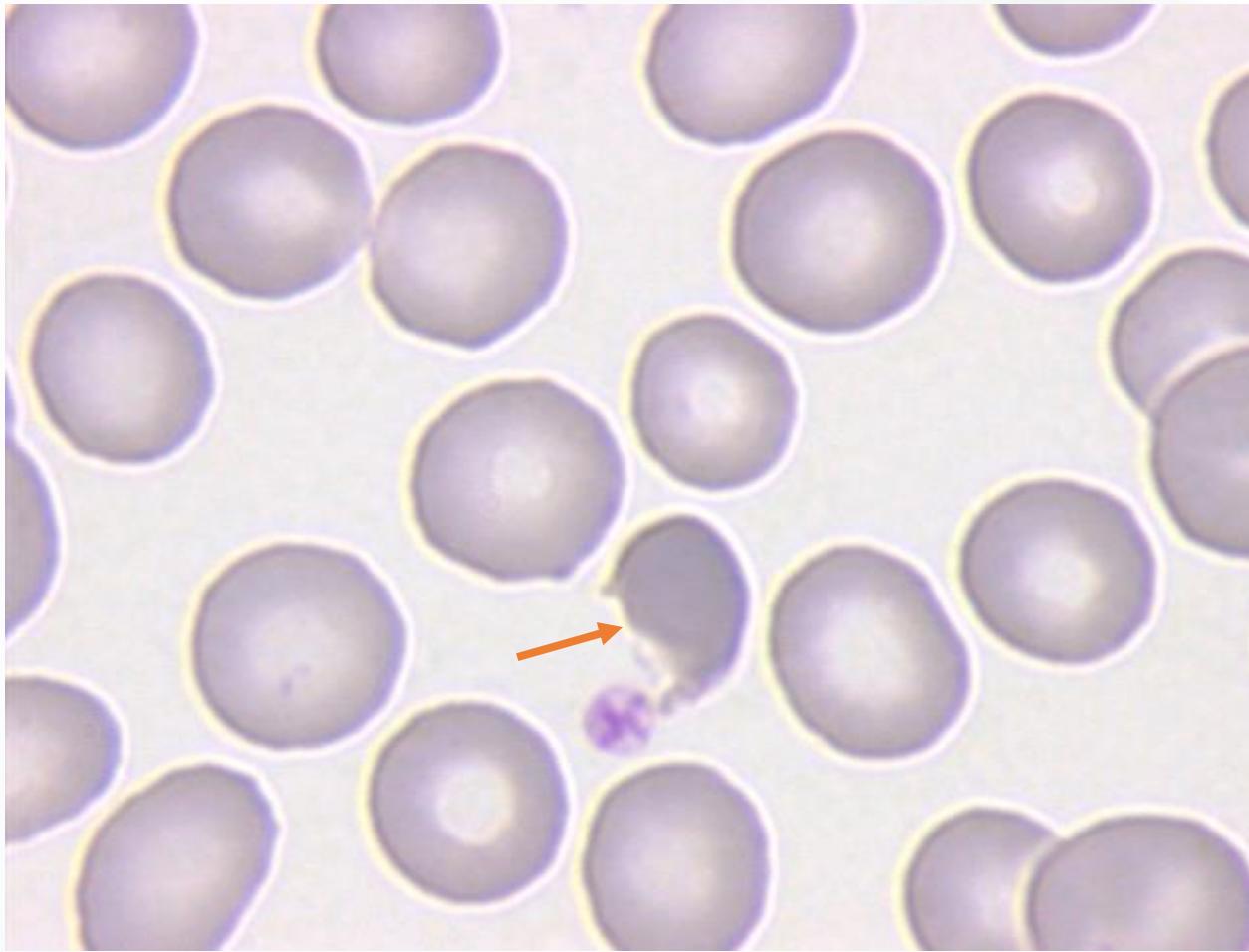
1. Complementa/valida los hallazgos proporcionados por el autoanalizador hematológico.
2. Proporciona información de anomalías hematológicas que no pueden ser detectadas por los analizadores automáticos actuales:
 - Serie roja anormal
 - Presencia de blastos o células linfoides anormales
 - Agregados plaquetarios o morfología plaquetar anómala
 - Dishematopoiesis
3. Permite obtener la primera orientación sobre lo que le pasa al paciente: contribución al diagnóstico inicial
4. Orienta hacia qué otras pruebas diagnósticas complementarias deben realizarse para llegar al diagnóstico definitivo.

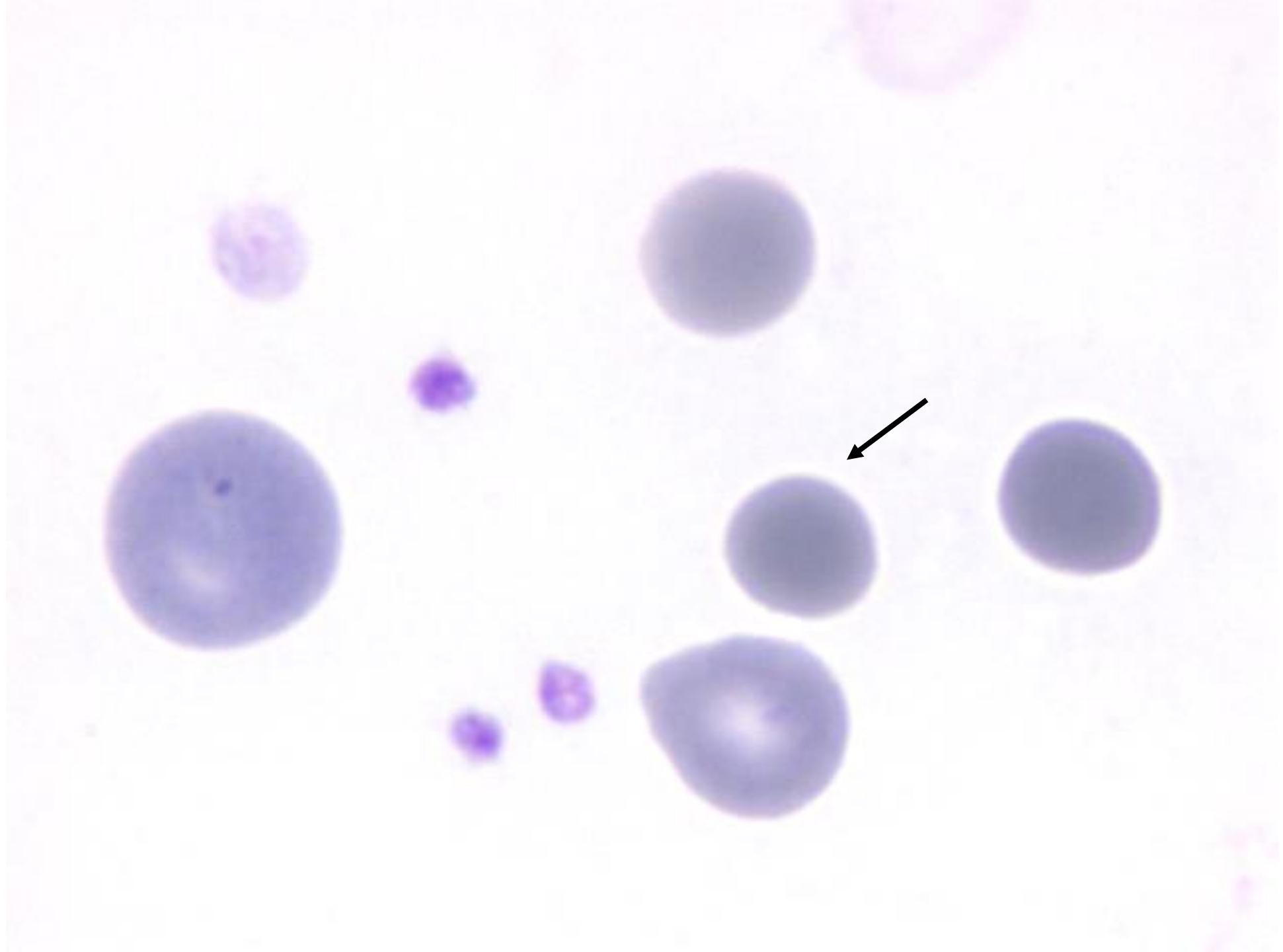


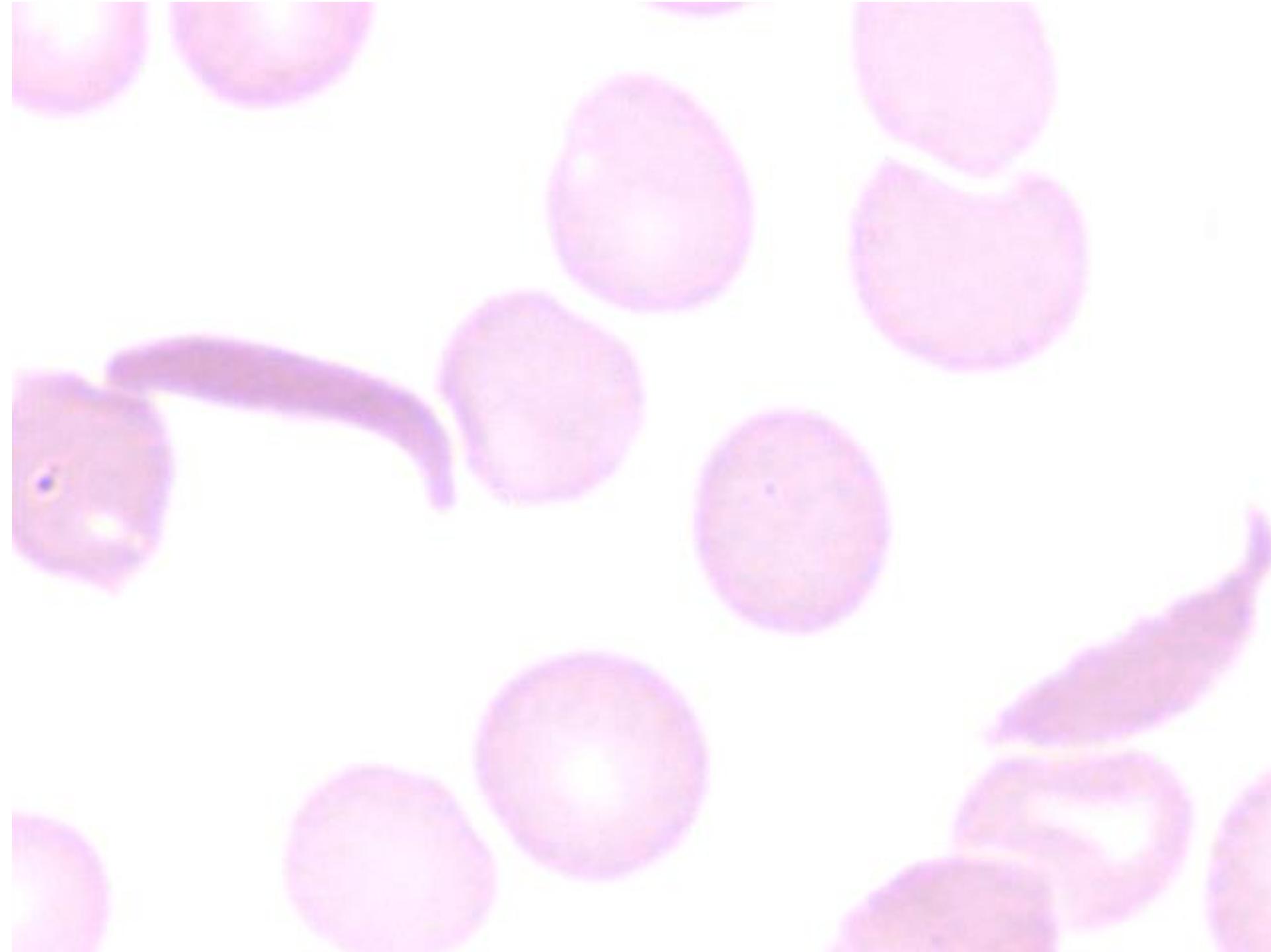
Excentrocito



Excentrocito

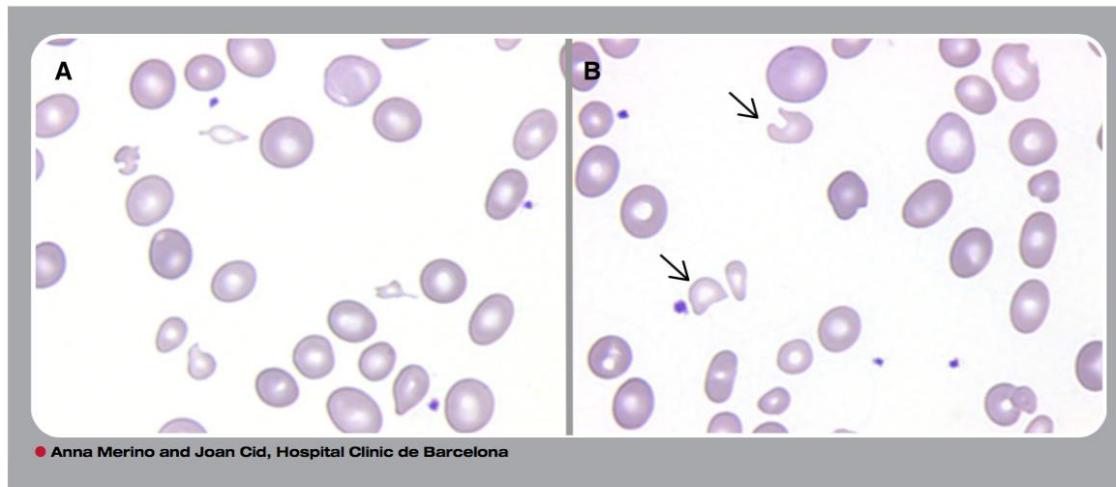






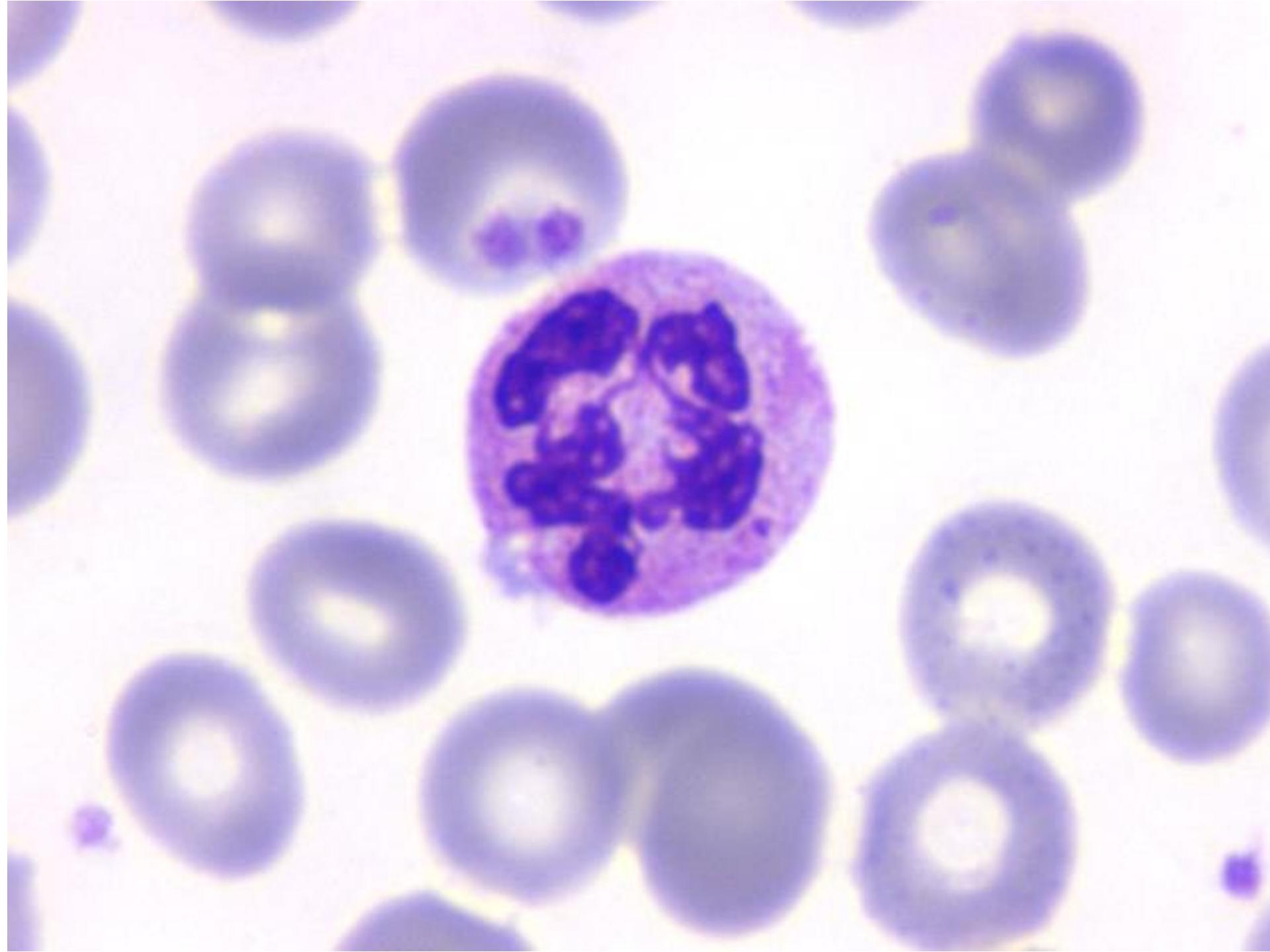


Very unusual presentation of pernicious anemia with schistocytes in peripheral blood



A 36-year-old man without any relevant past medical history presented with asthenia for 3 to 4 weeks. A physical examination showed pale conjunctivae and skin. An automatic blood cell count revealed advanced anemia (hemoglobin, 58 g/L), high mean cell volume (129 fL), low white blood cell count ($3.3 \times 10^9/L$), and normal platelet count. Reticulocyte values were $72 \times 10^9/L$. A peripheral blood (PB) film revealed anisocytosis, red blood cell fragments (panel A), some bite cells (panel B, arrows), and oval macrocytes. Serum lactate dehydrogenase levels were elevated (3100 U/L) and the bilirubin value was 1.8 mg/dL. Coagulation parameters were normal and direct antiglobulin test was negative. Microangiopathic hemolytic anemia (MAHA) was suspected. On reevaluation, his vitamin B₁₂ value was low (150 pg/mL [normal, 250-1050]) and ADAMTS13 testing was 70%. The presence of antiintrinsic factor antibodies was confirmed, and gastrointestinal endoscopy revealed atrophic gastritis.

We report a very unusual presentation of pernicious anemia (PA) with schistocytes in PB that was initially diagnosed as MAHA. Morphologic erythrocyte changes in PA may include the presence of red cell fragments, which should not be considered evidence of MAHA. The presence of bite cells and oval macrocytes, along with the schistocytes in PB, can be useful in determining the correct diagnosis.



Caso clínico

Paciente varón de 72 años que acude a Urgencias por fiebre y mal estado general

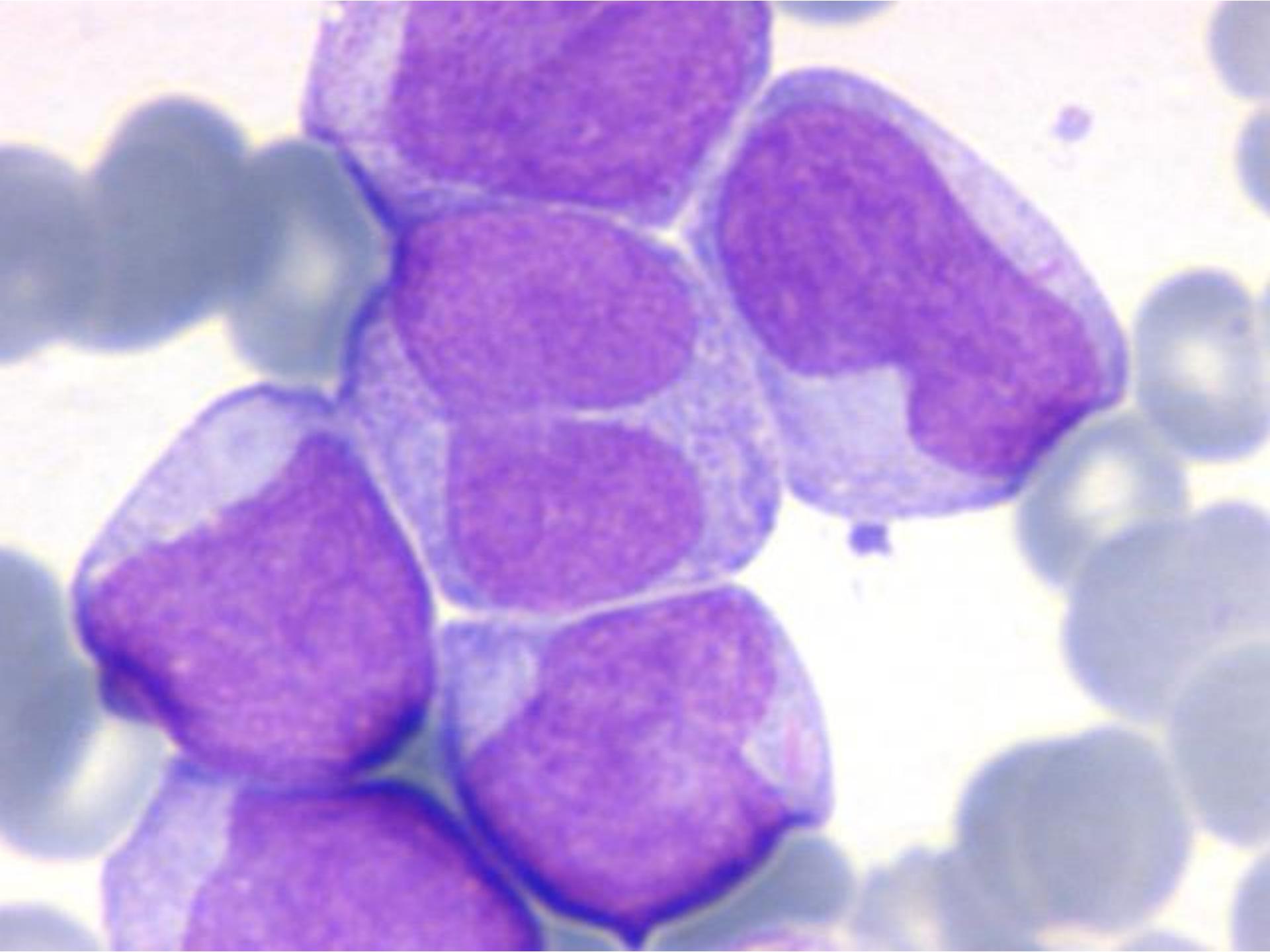
Hemograma (anemia y leucocitosis)

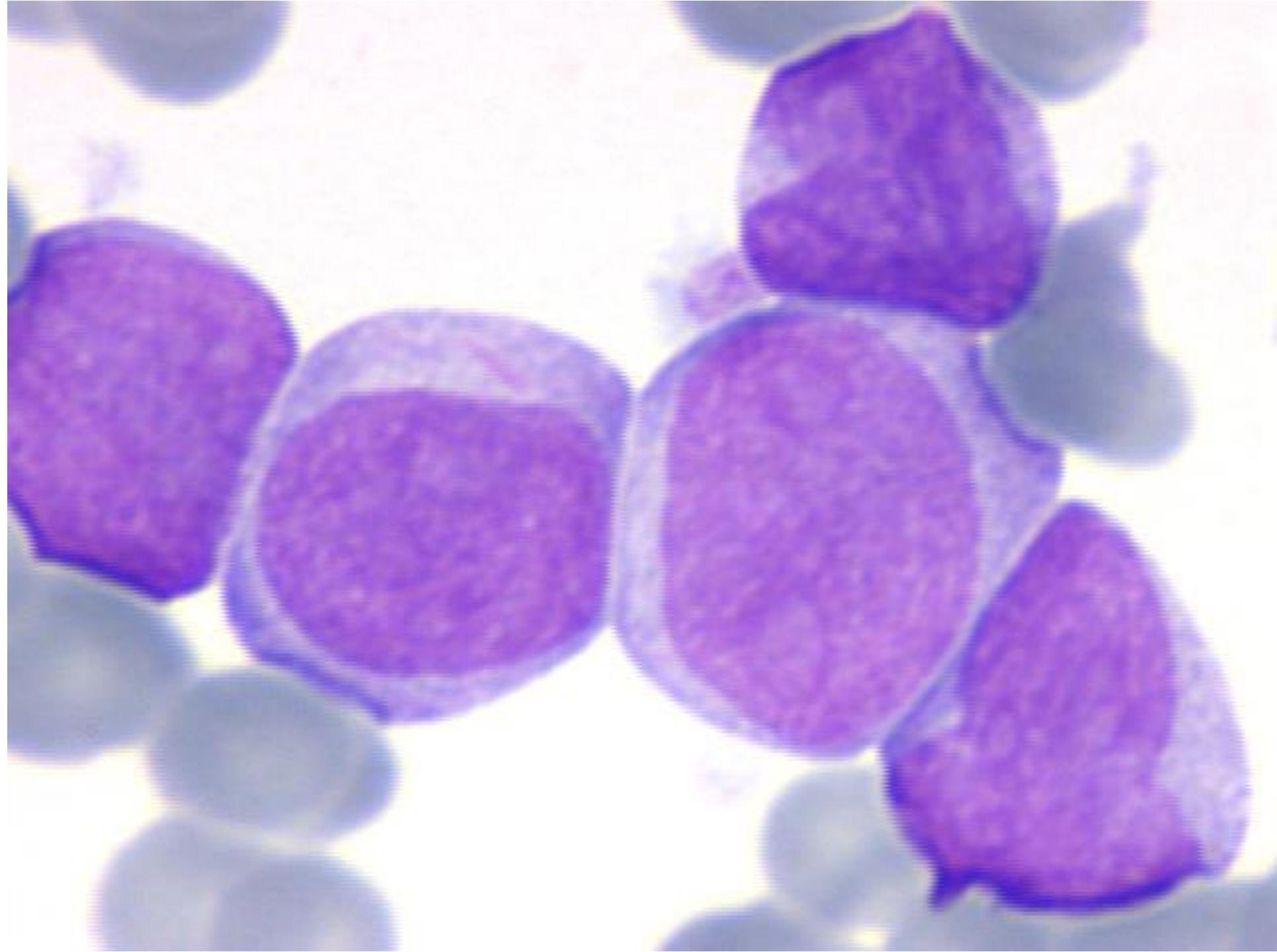
Leucocitos: $40.5 \times 10^9/L$

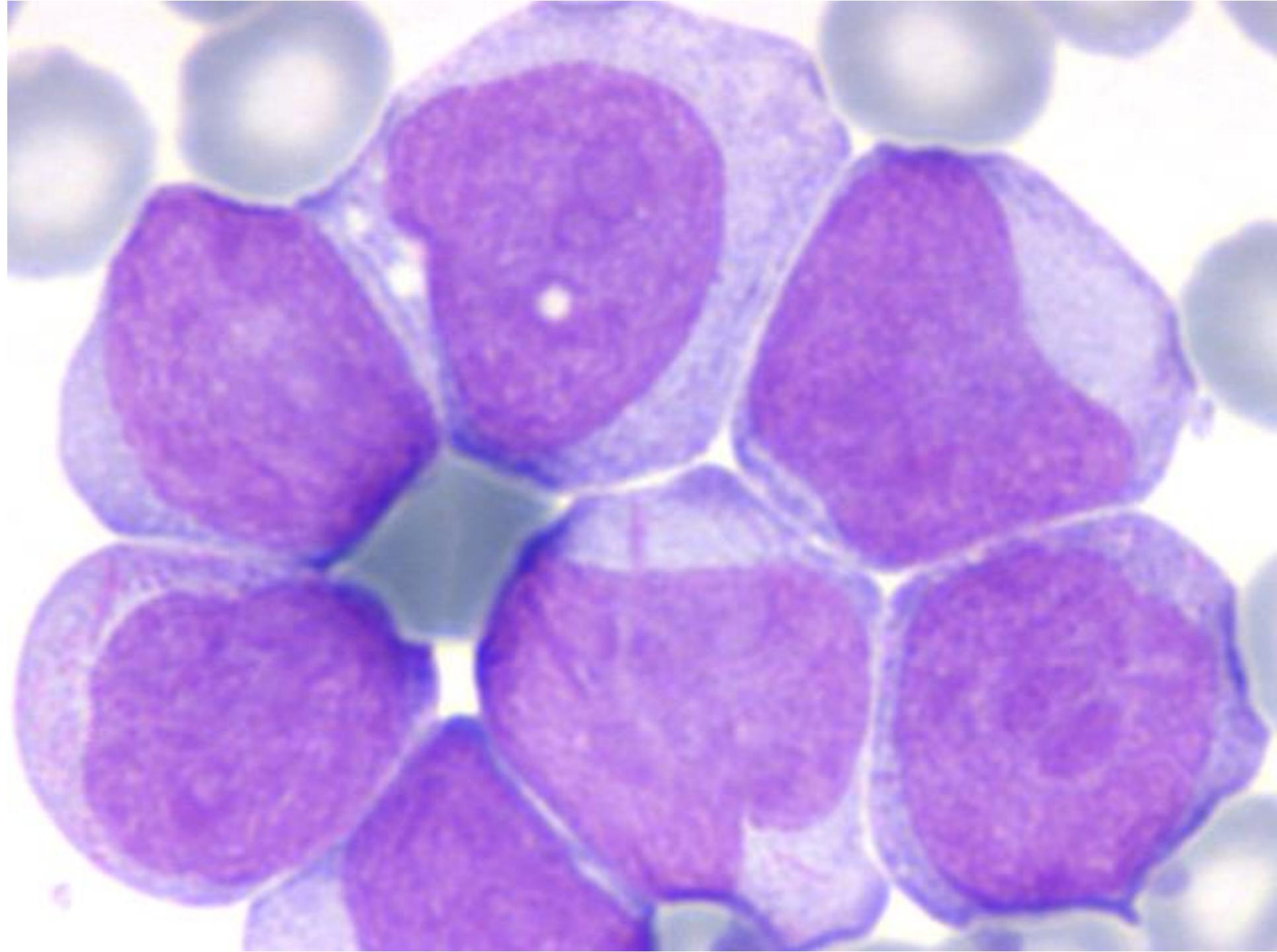
Hematocrito: 33%

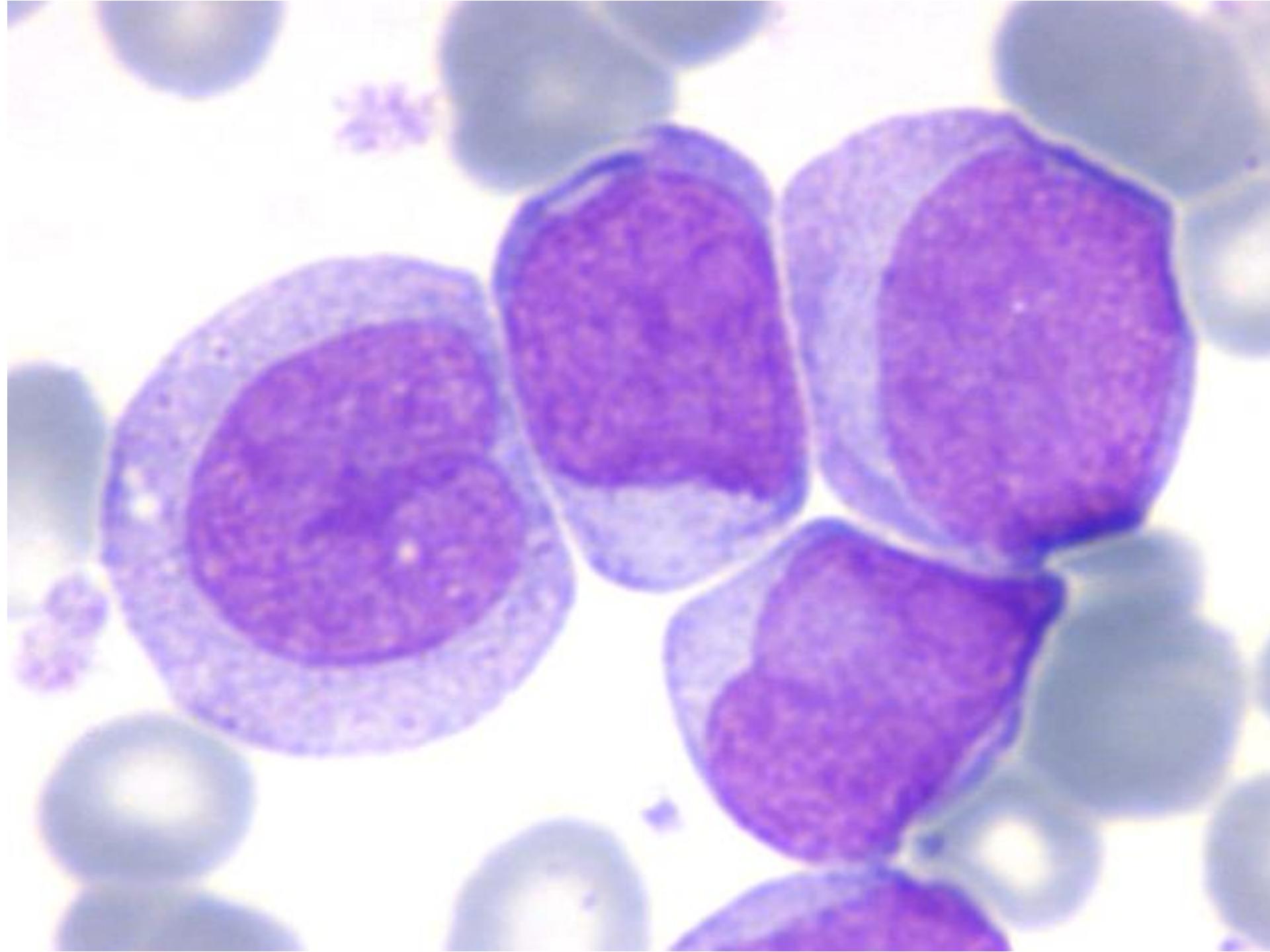
Hemoglobina: 105 g/L

Plaquetas: $273 \times 10^9/L$



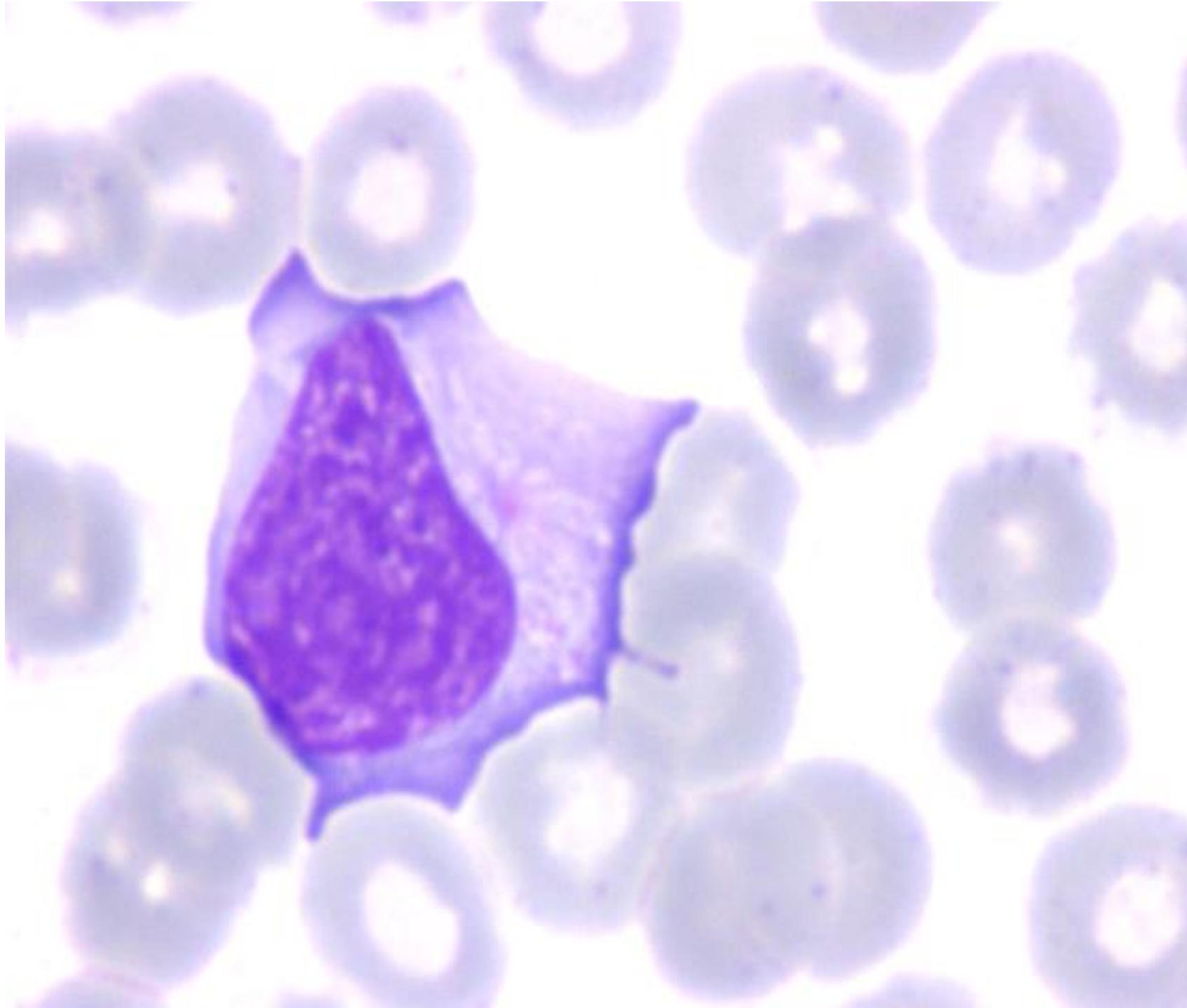


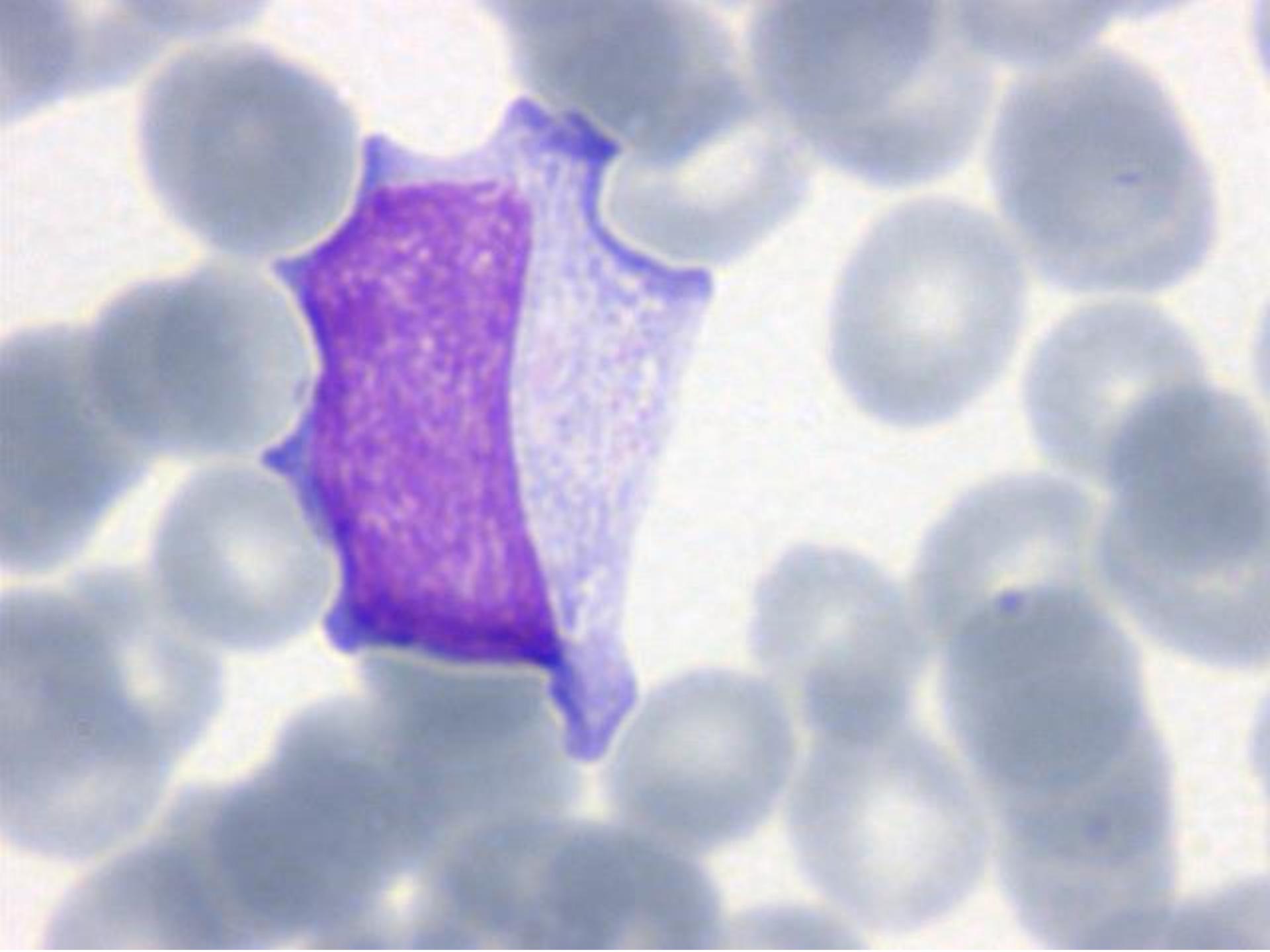


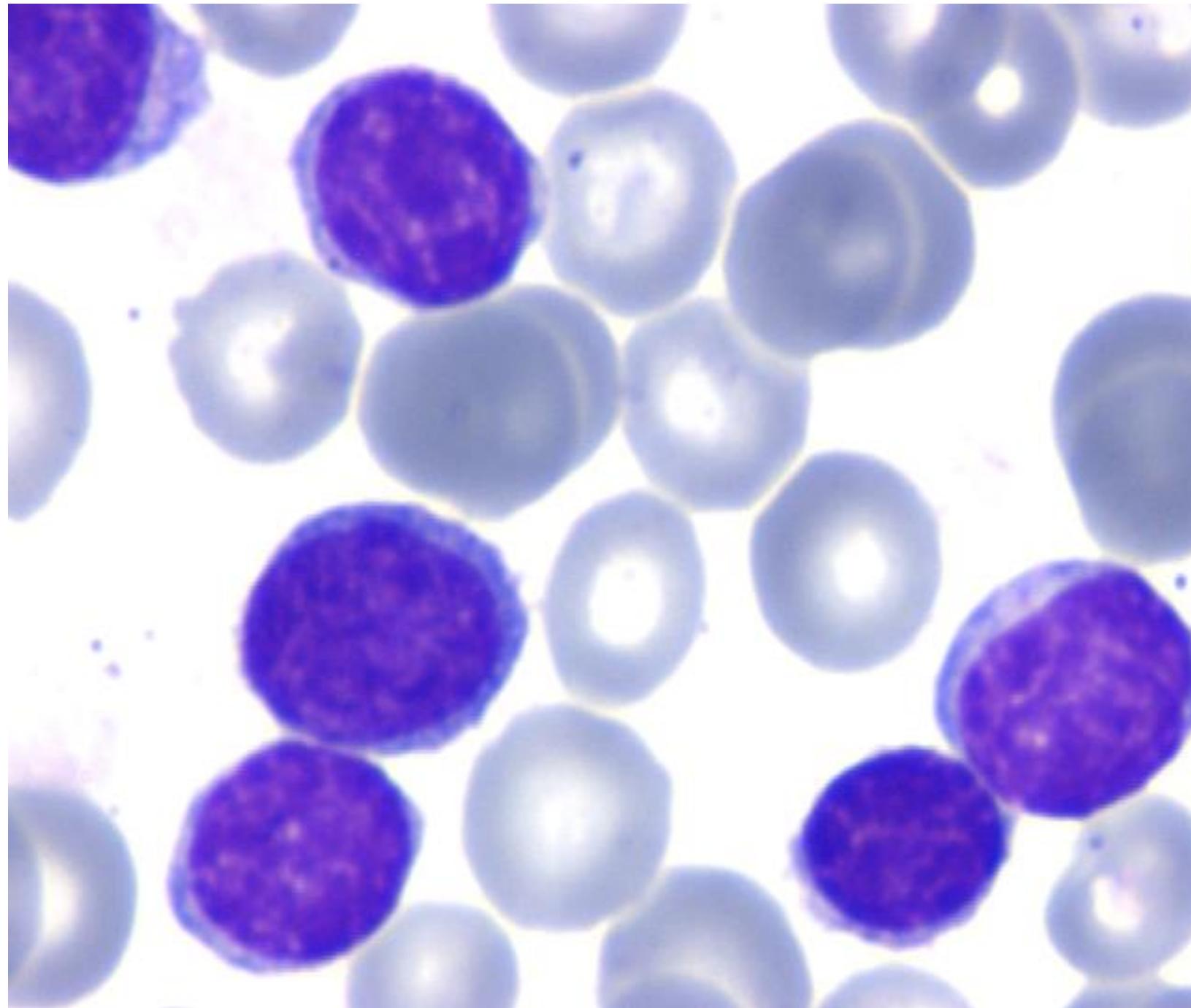


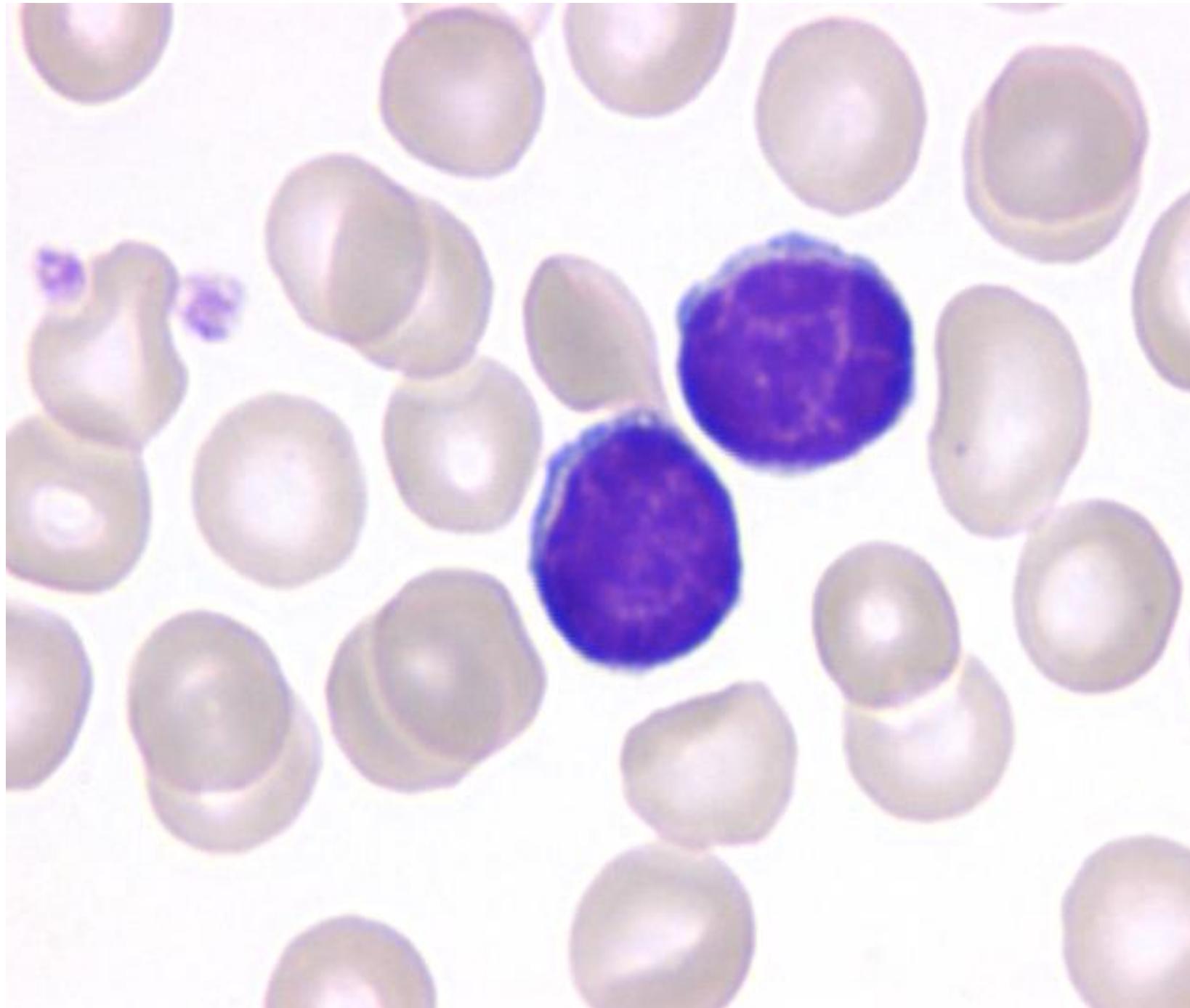
Leucemia Mielomonocítica Aguda

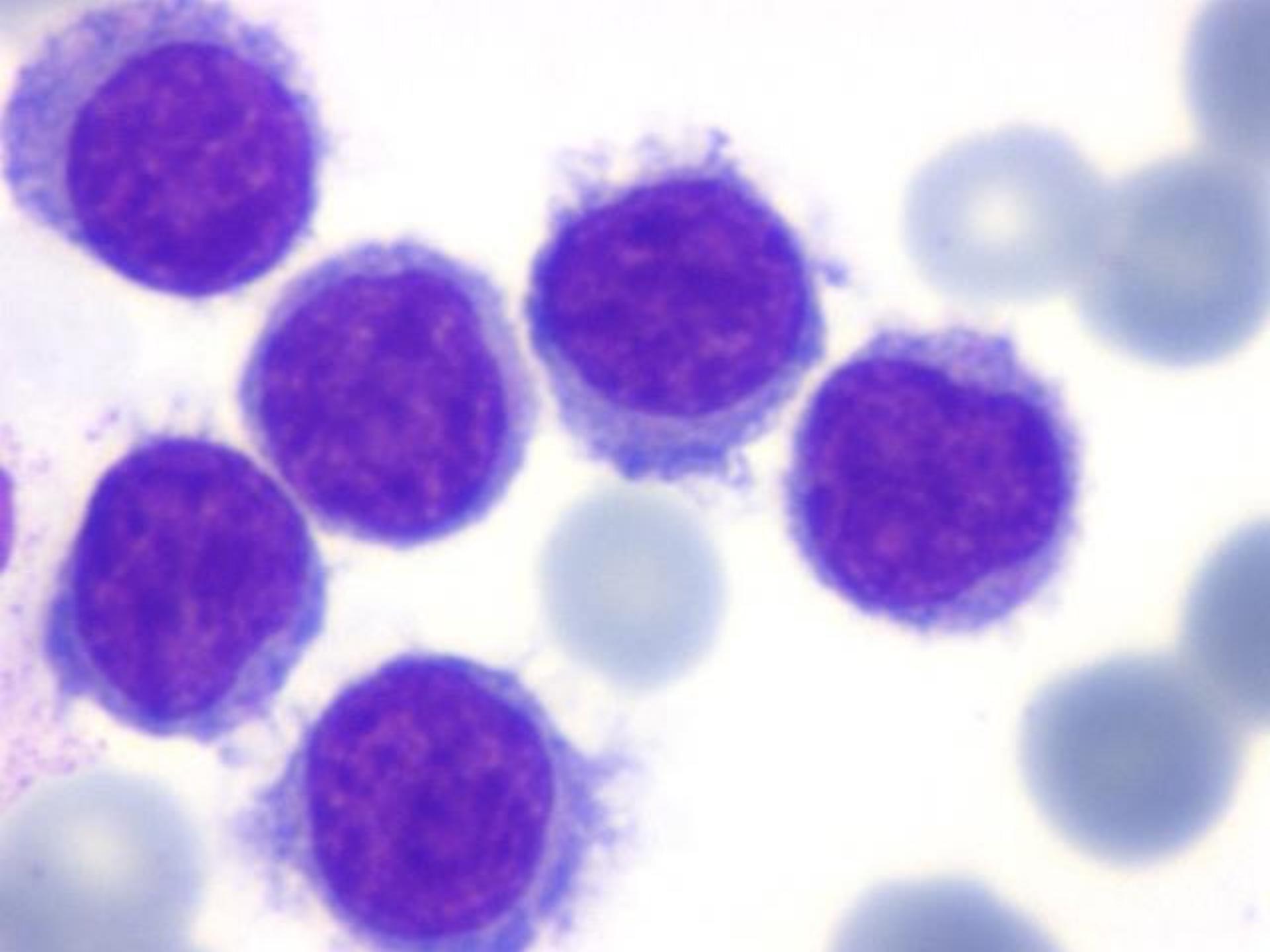
Detección de linfocitosis en una primera analítica

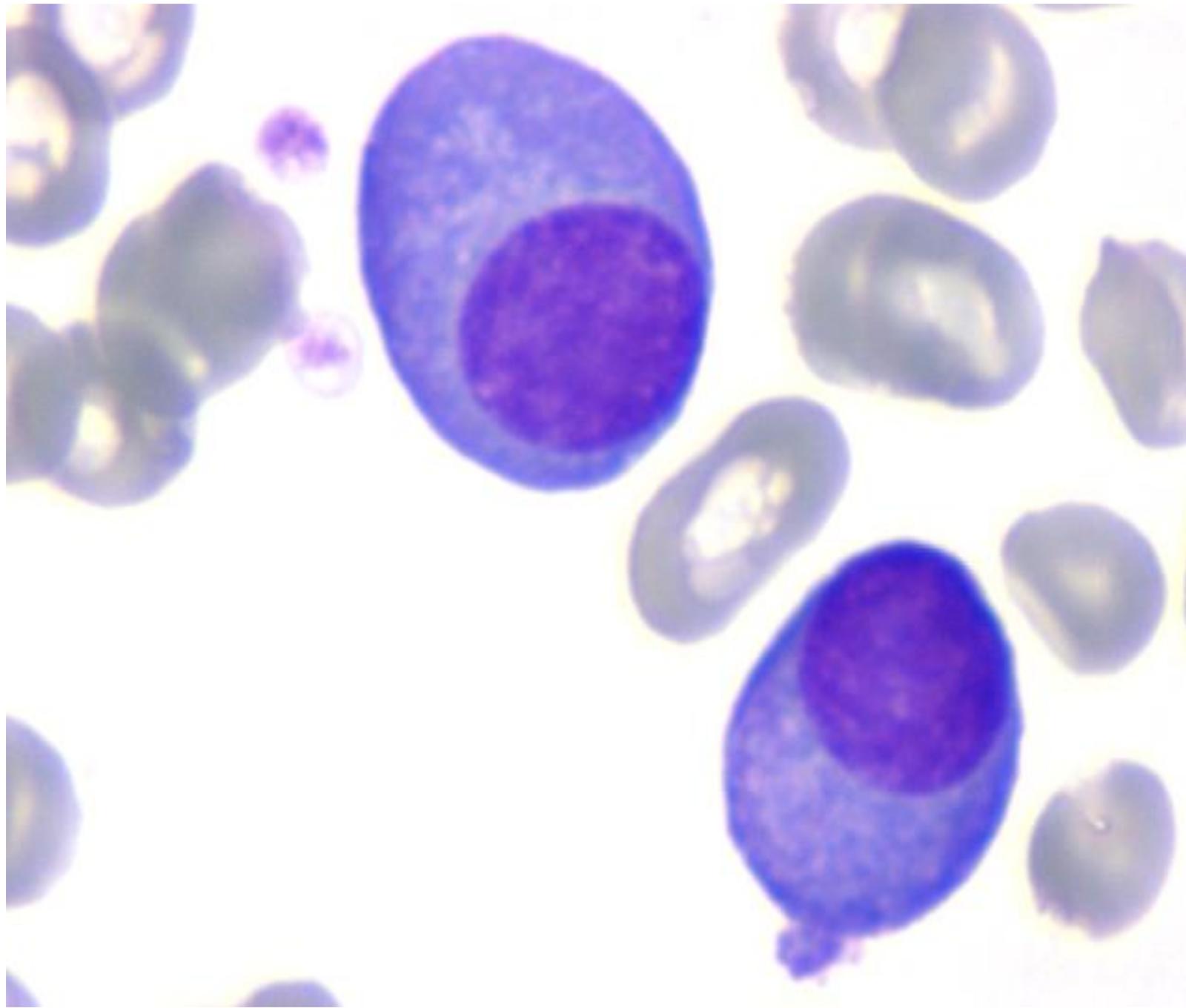


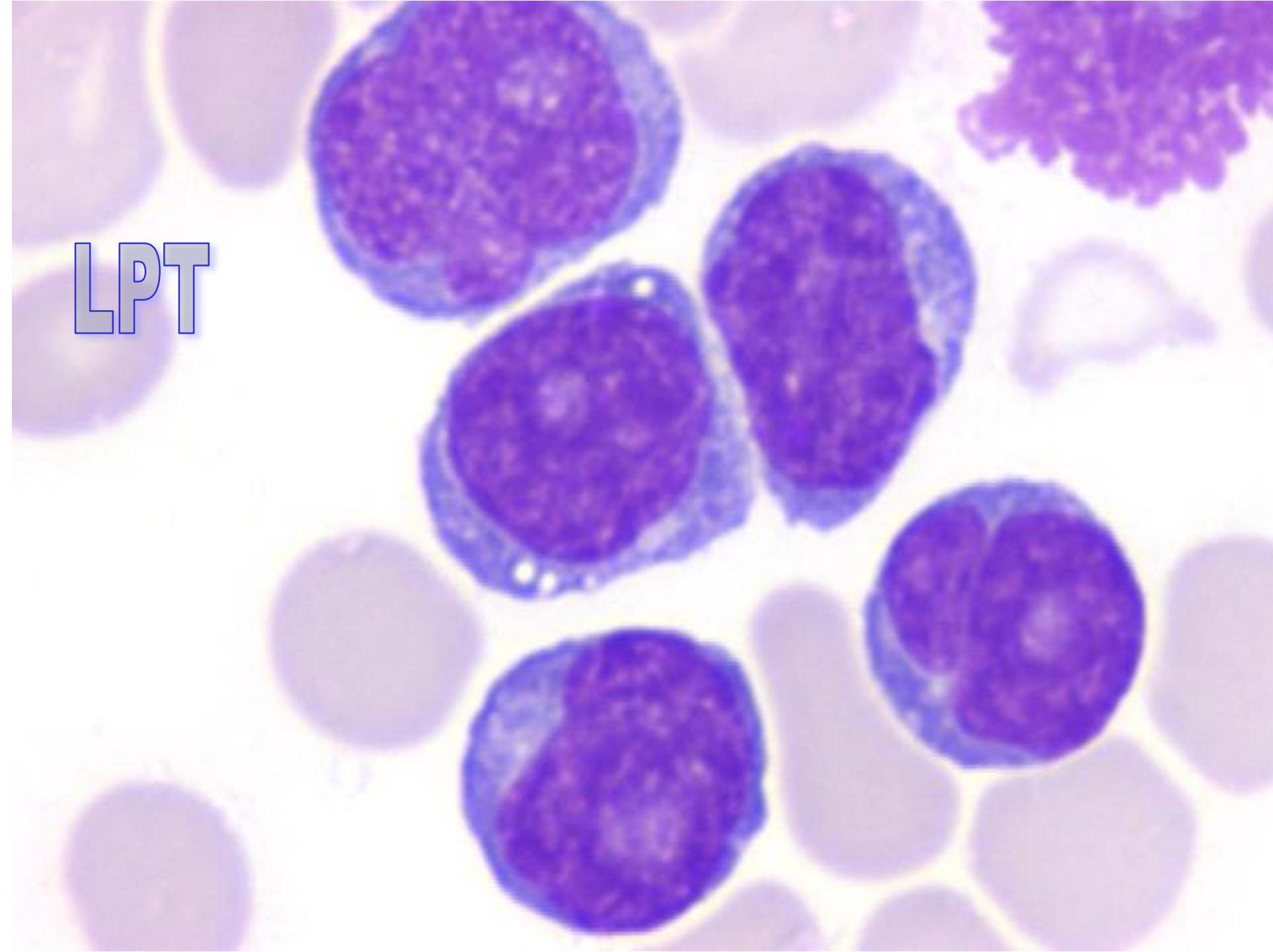


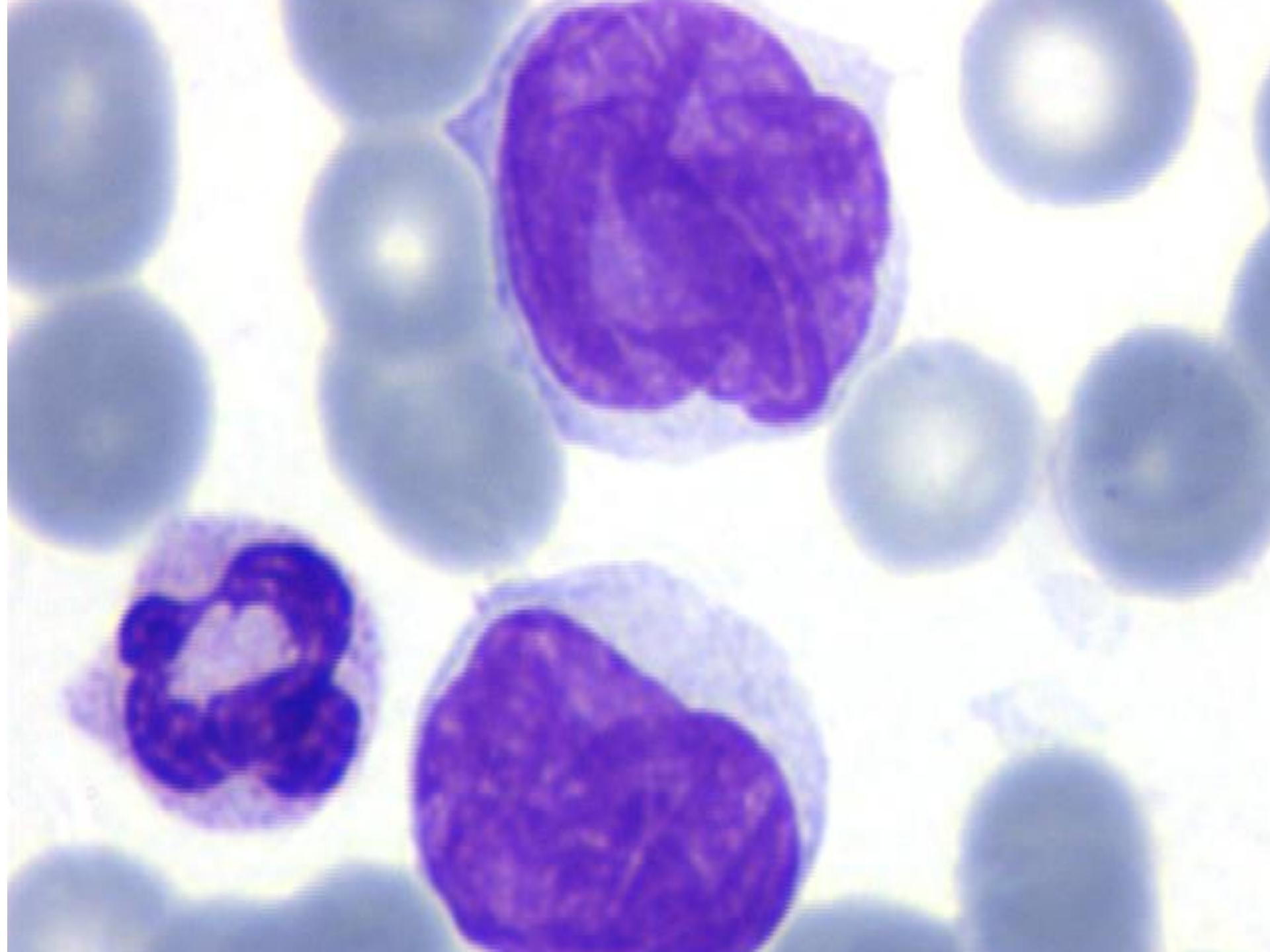














Detección de leucopenia y linfocitosis en una primera analítica

una

primera analítica

Caso clínico

Paciente varón de 28 años que acude a Urgencias en Mayo de 2003 con el informe de otro centro en el que se destaca una bicitopenia (anemia y plaquetopenia) junto a la presencia de células linfoides anormales.

Exploración física: Marcada esplenomegalia

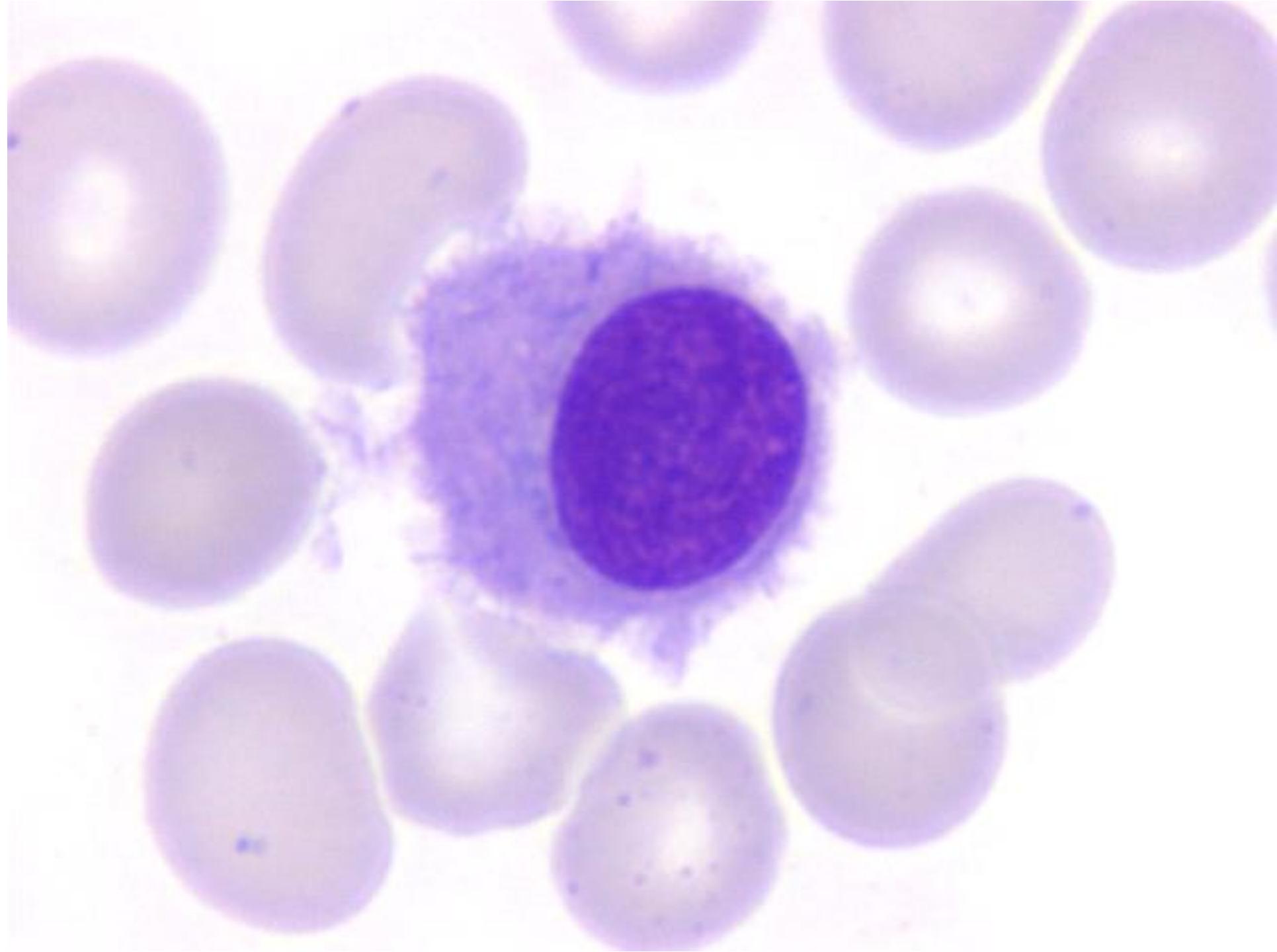
Hemograma: Leucocitos: **3,9 x 10⁹/L**

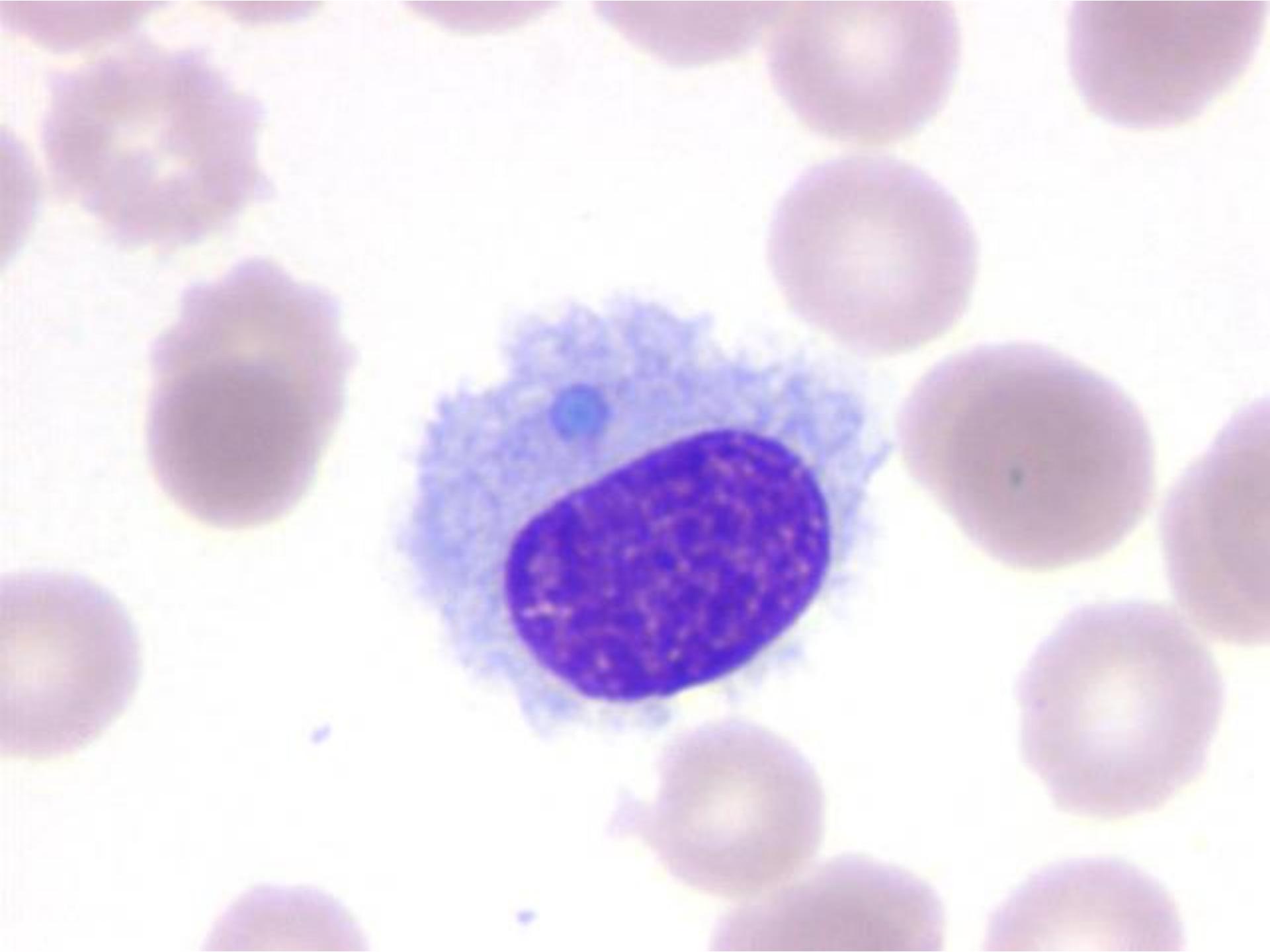
Hto: **0.32 L/L**

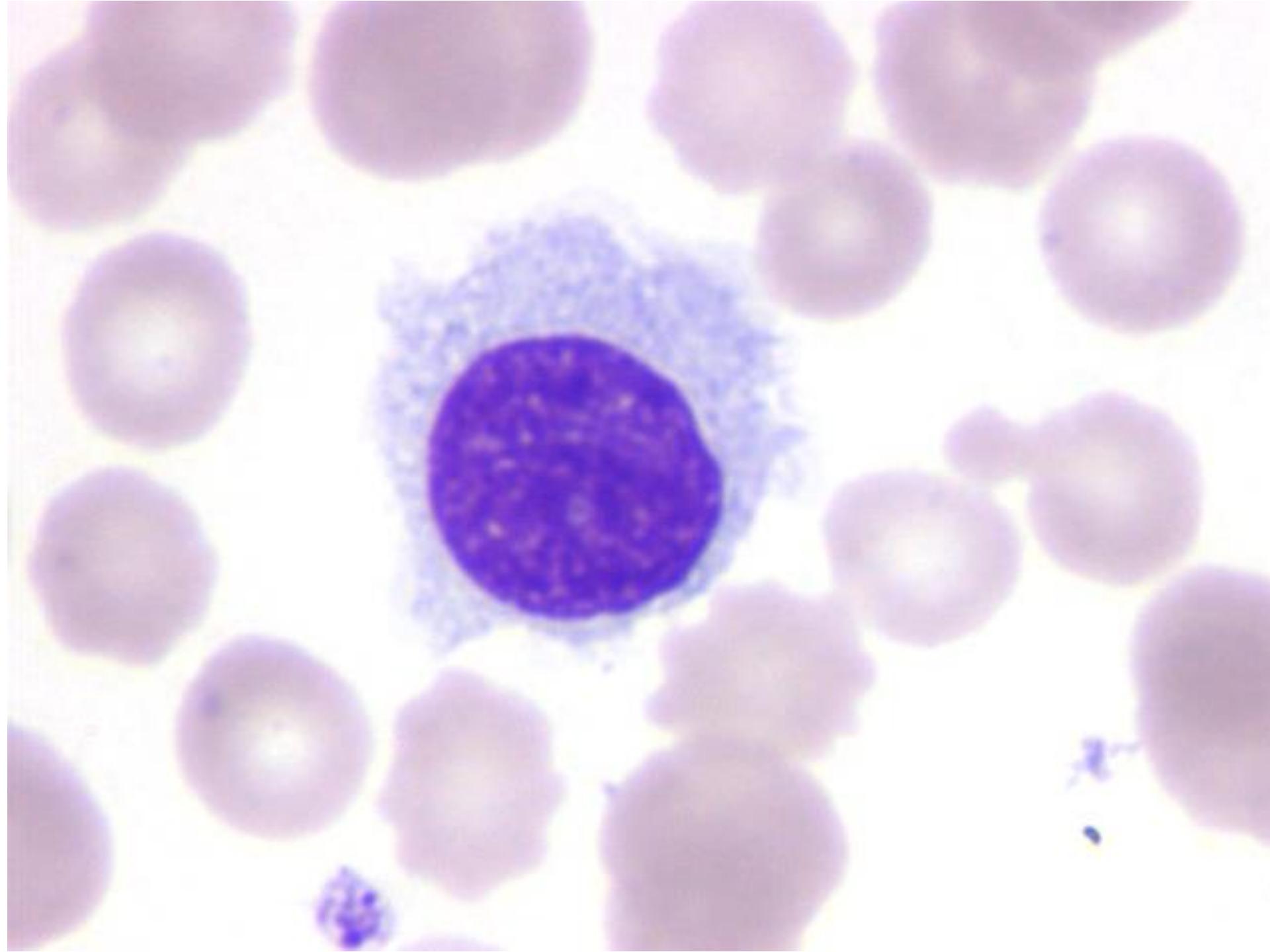
Plaquetas: **55 x 10⁹/L**

LDH: **343 UI/L (N)**

β2-microglobolina: **3 mg/L**



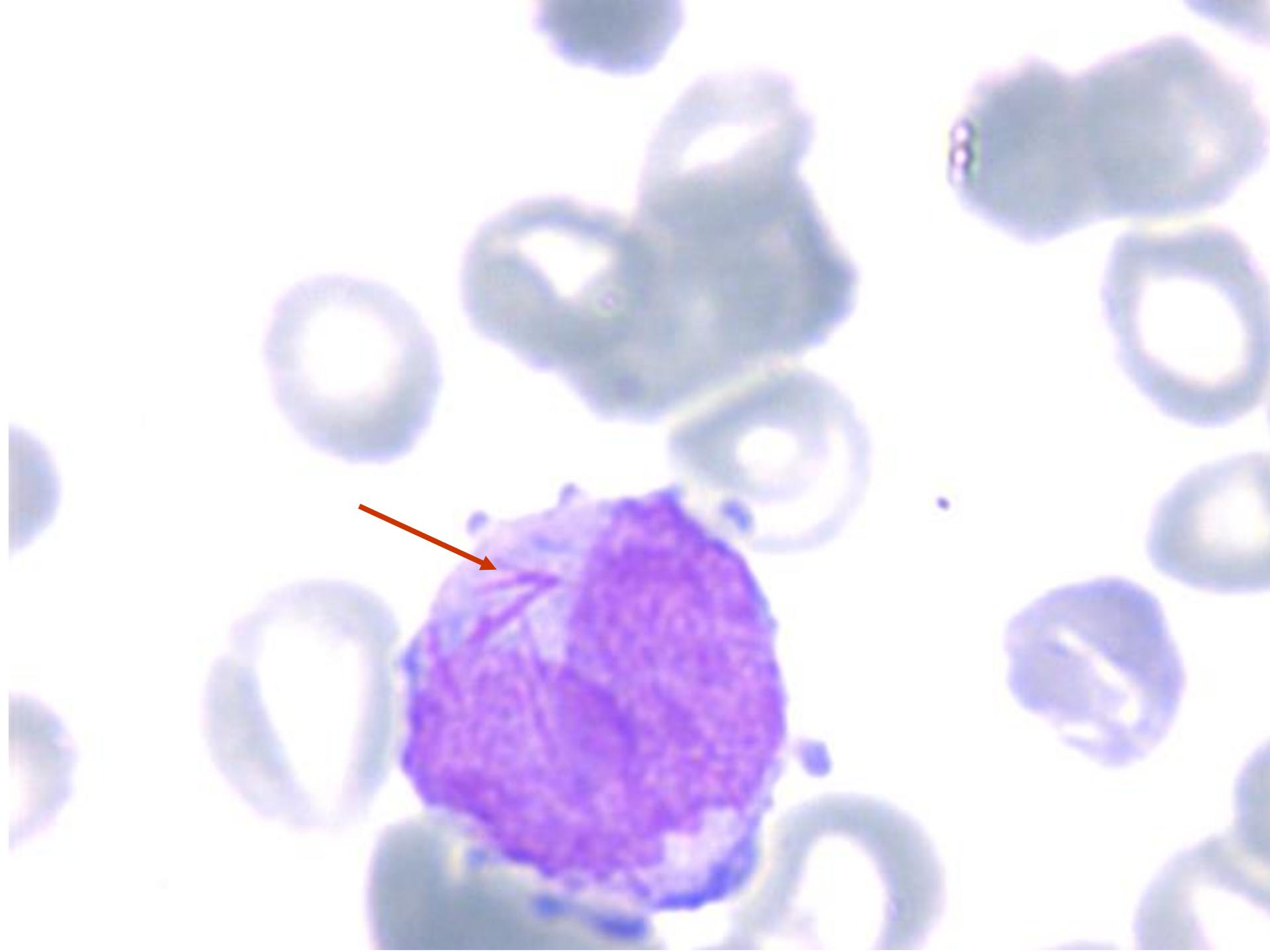




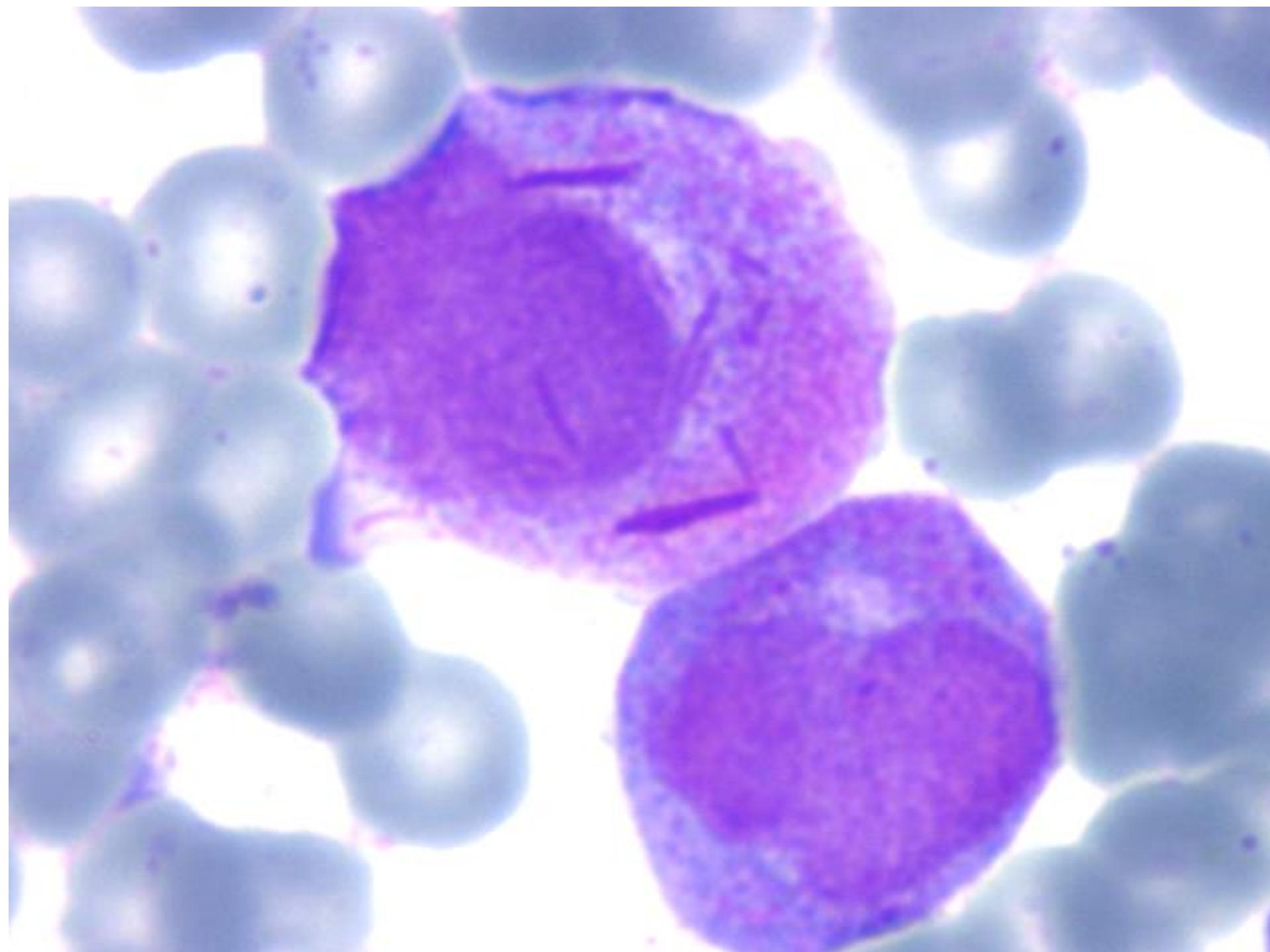
Diagnóstico

- **Neoplasia linfoide B: Tricoleucemia**

Detección de leucopenia aislada en una primera analítica







Caso clínico

Paciente varón de 53 años que consulta por la aparición de hematomas ante mínimos traumatismos desde hace 3 semanas junto a síndrome anémico progresivo con dolor torácico a mínimos esfuerzos en los últimos 4 días.
Epistaxis en las últimas 24 horas

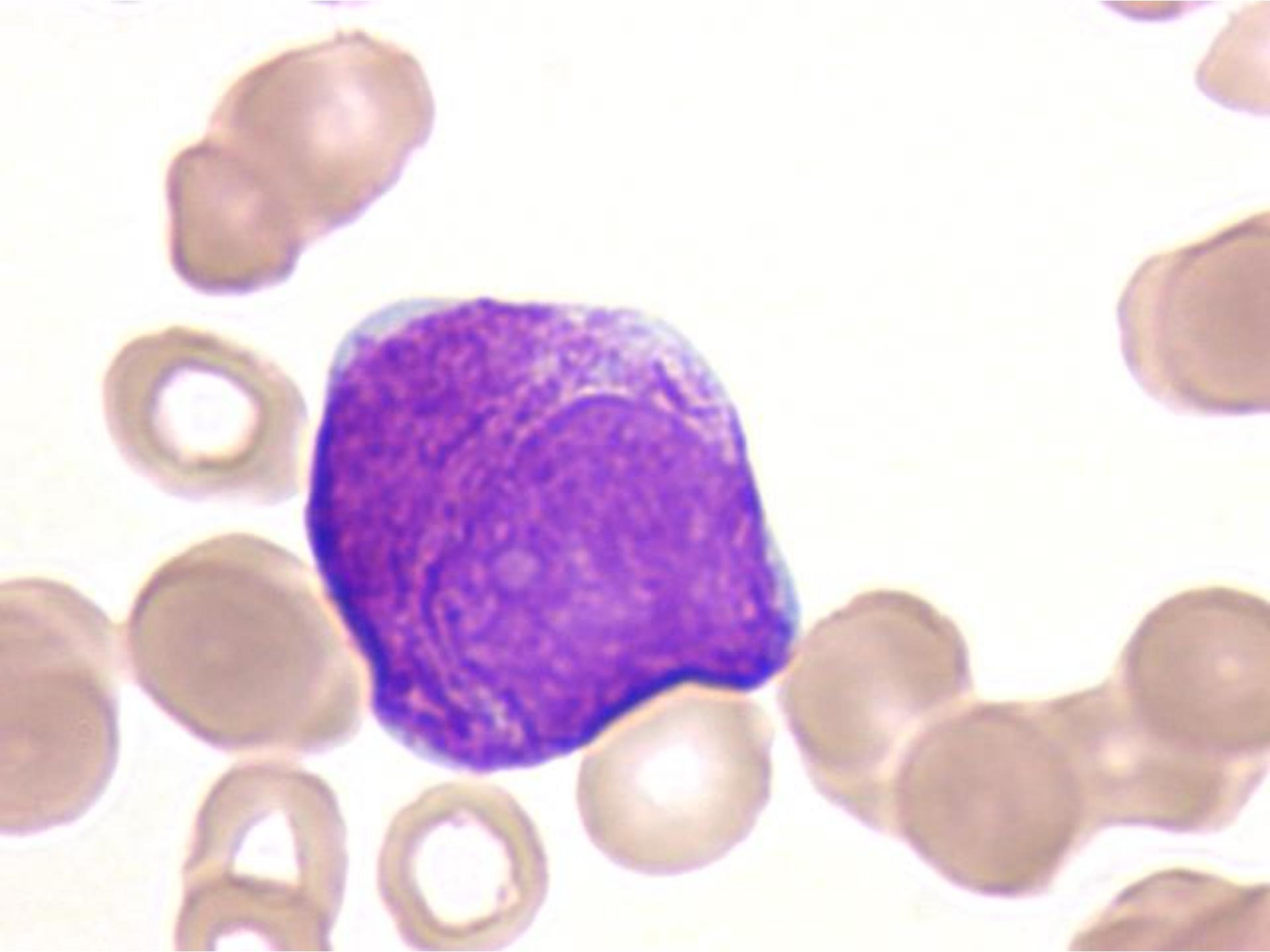
Exploración física: Afebril. Múltiples equimosis en tronco y extremidades

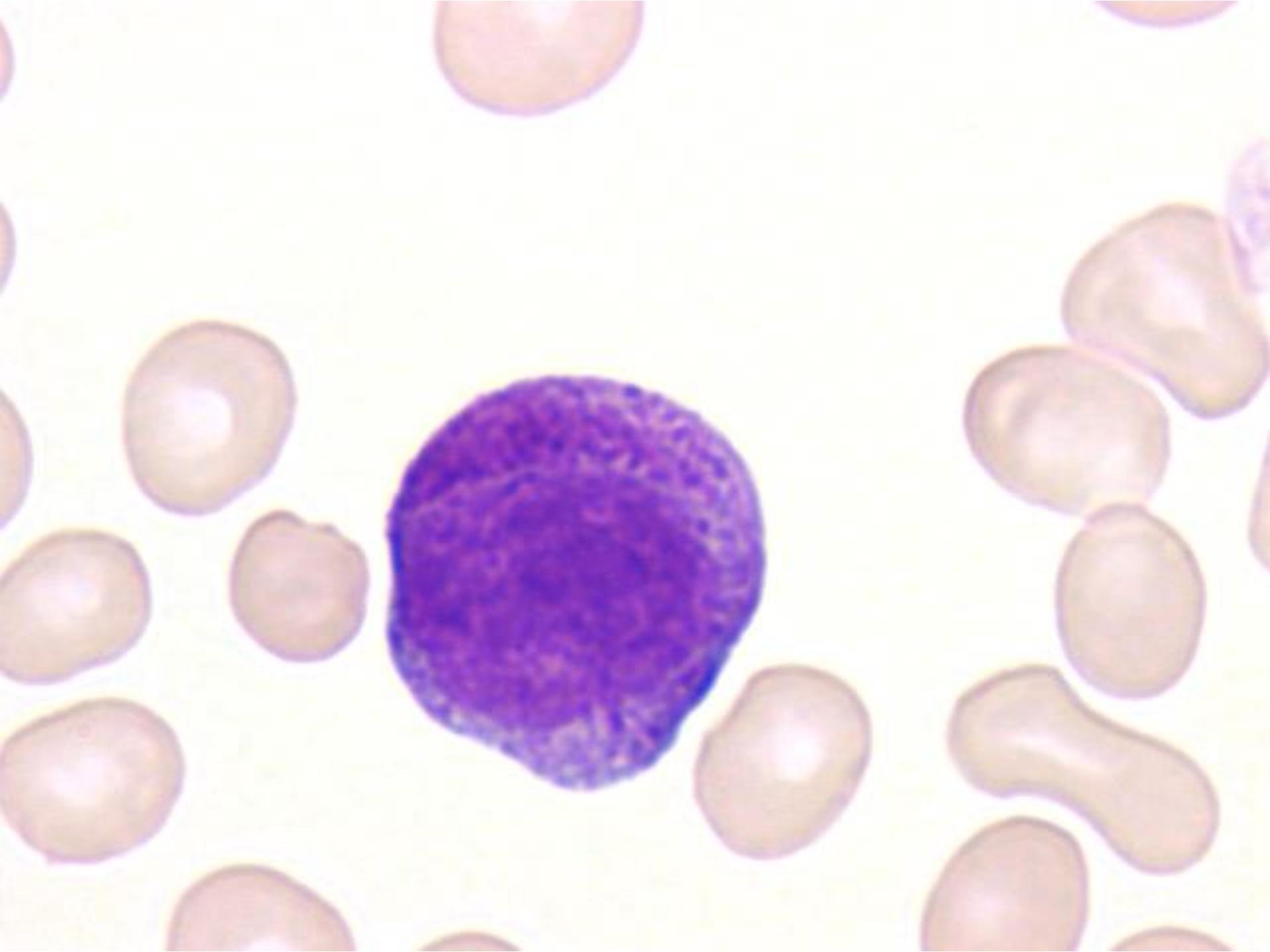
Hemograma: Leucocitos: $3,5 \times 10^9/L$

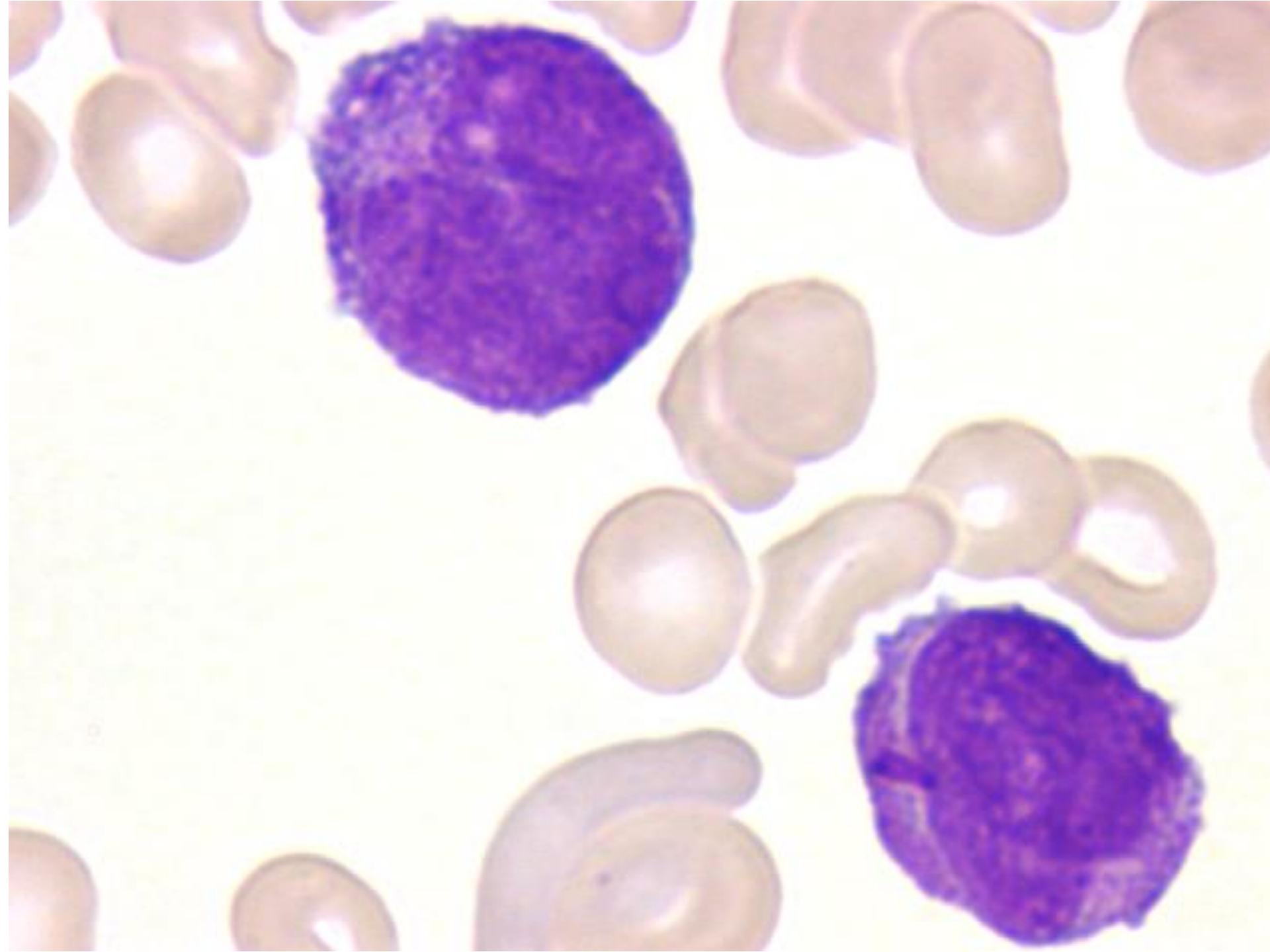
Hb: **84 g/L**

Hto: **0,24 L/L** y Plaquetas: **$17 \times 10^9/L$** . Eosinofilia marcada en RDLA (23%)

T Protrombina: 73 %



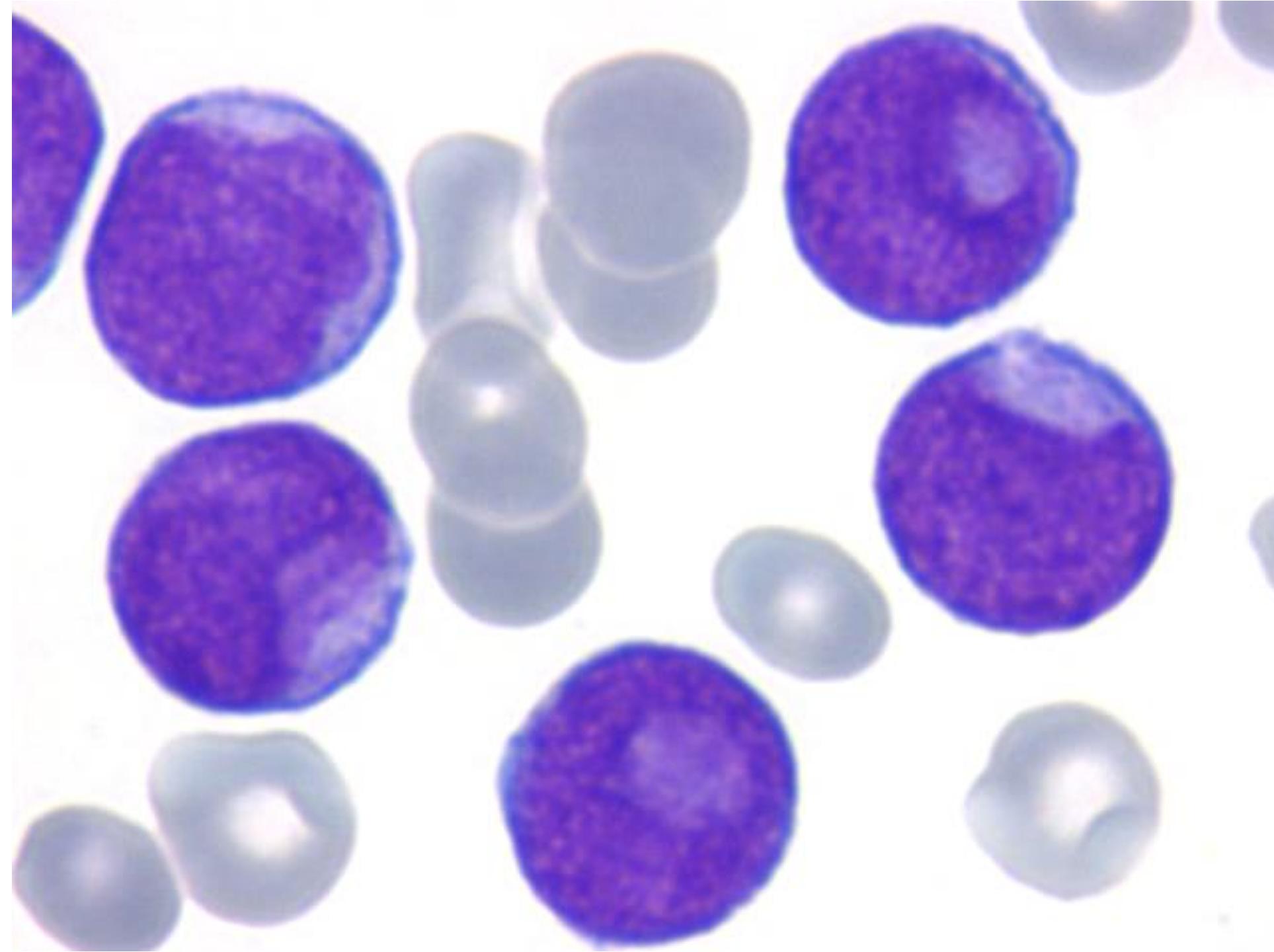


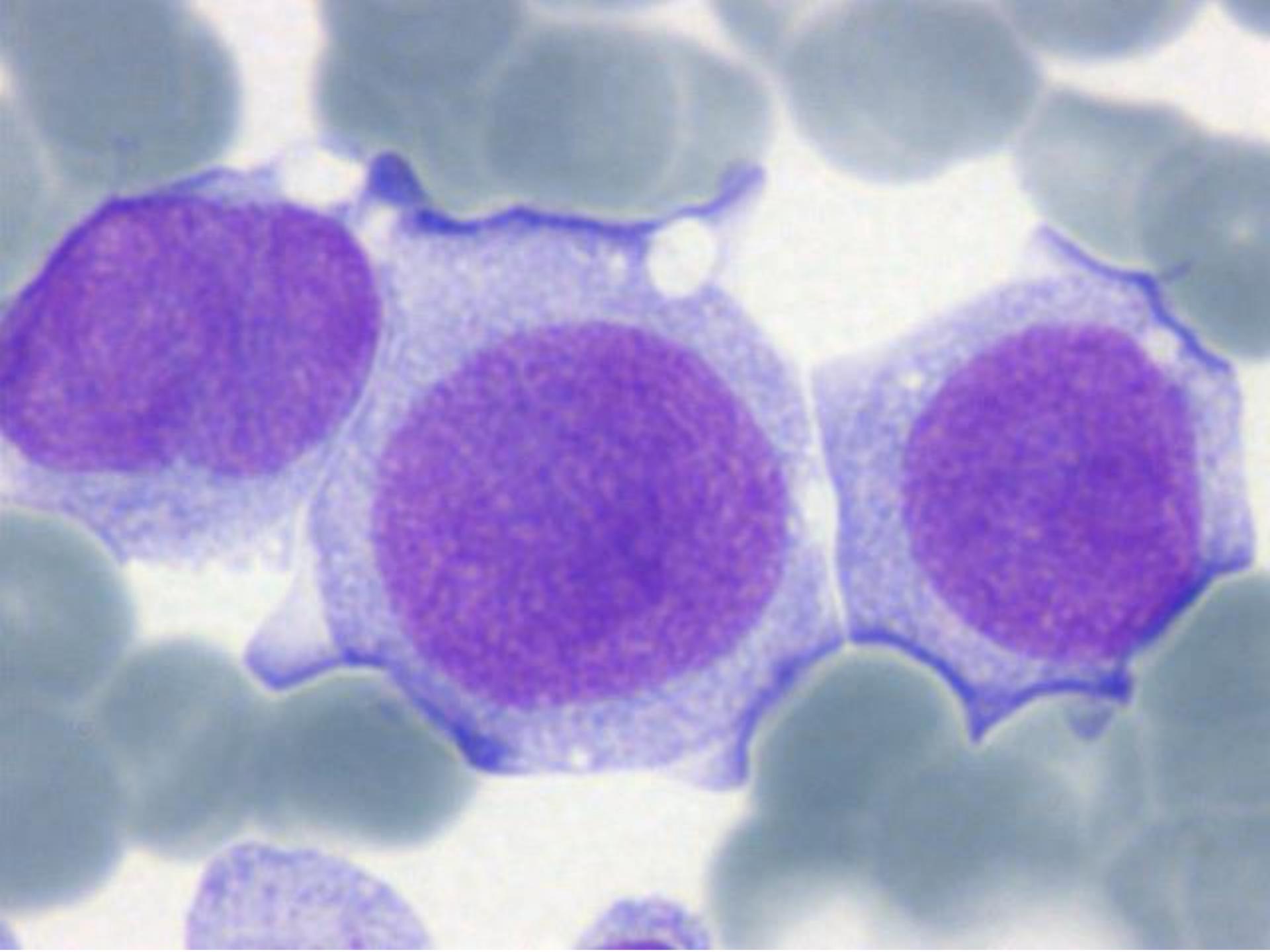


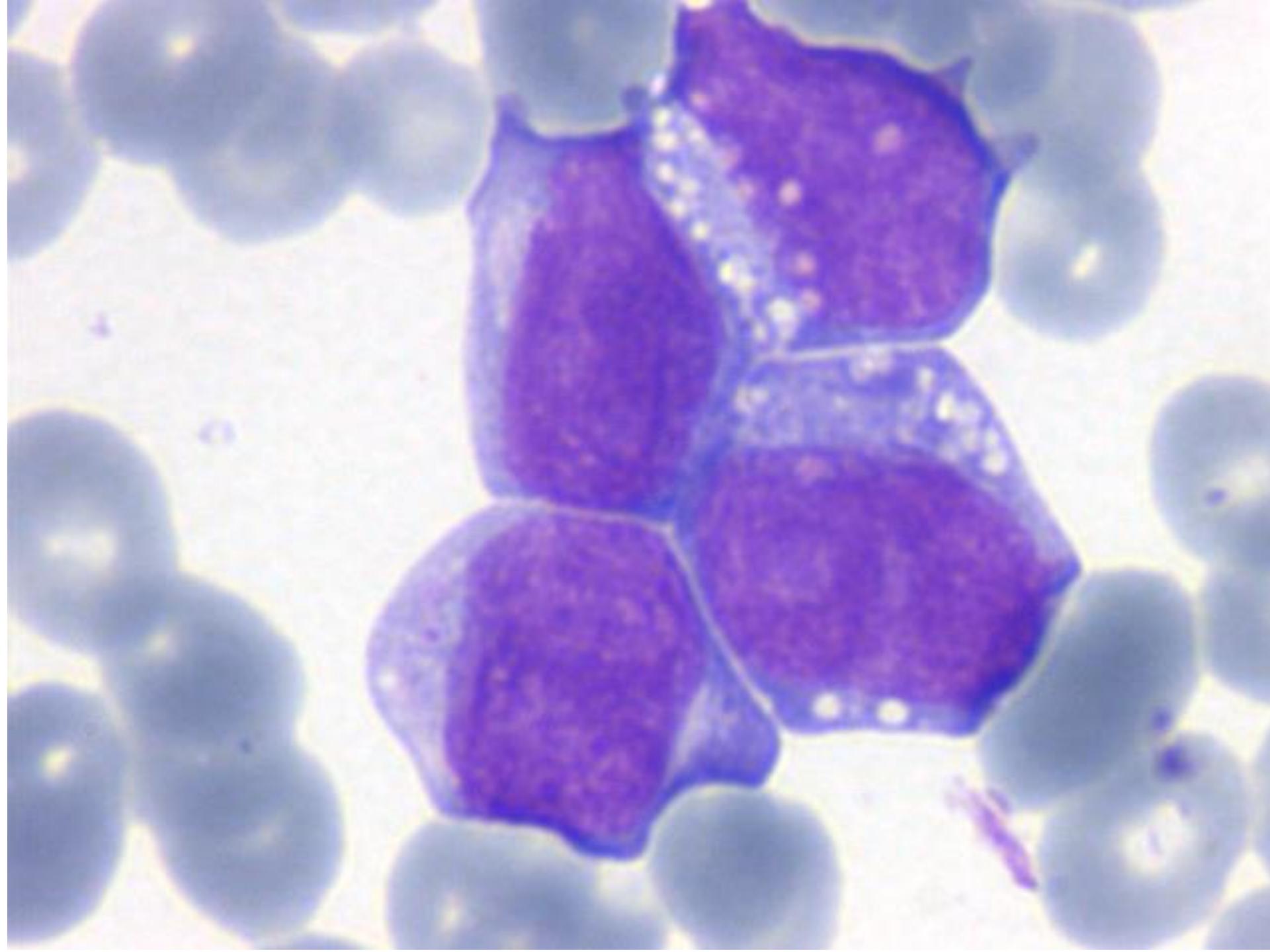
Diagnóstico

- **Leucemia Promielocítica Aguda**

Detección de plaquetopenia y anemia en una primera analítica







Caso clínico

Paciente varón de 32 años que acude a Urgencias con motivo de un accidente de moto y fractura isquiopubiana izquierda.

Hemograma (bicitopenia)

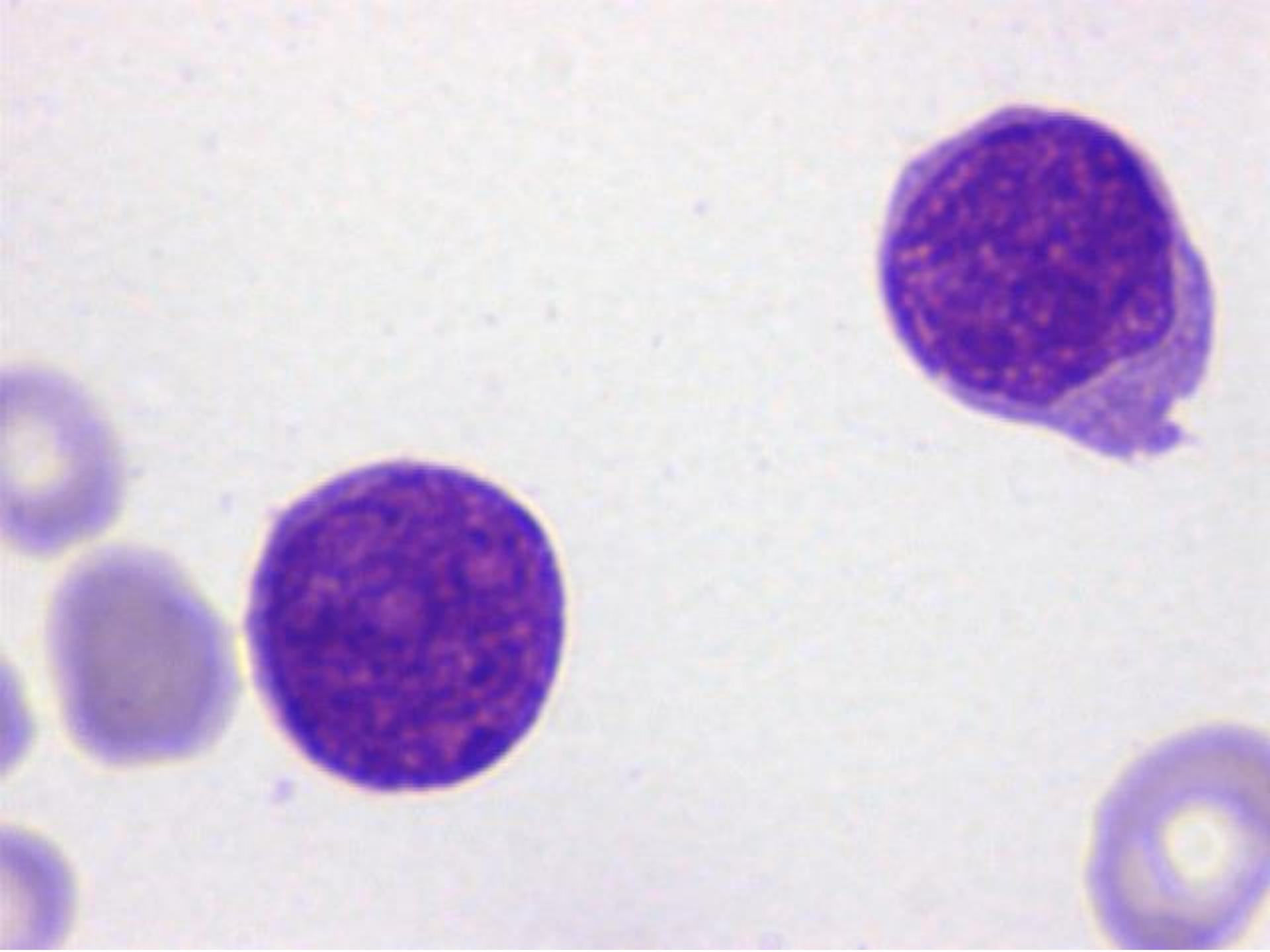
Leucocitos: $16.2 \times 10^9/L$

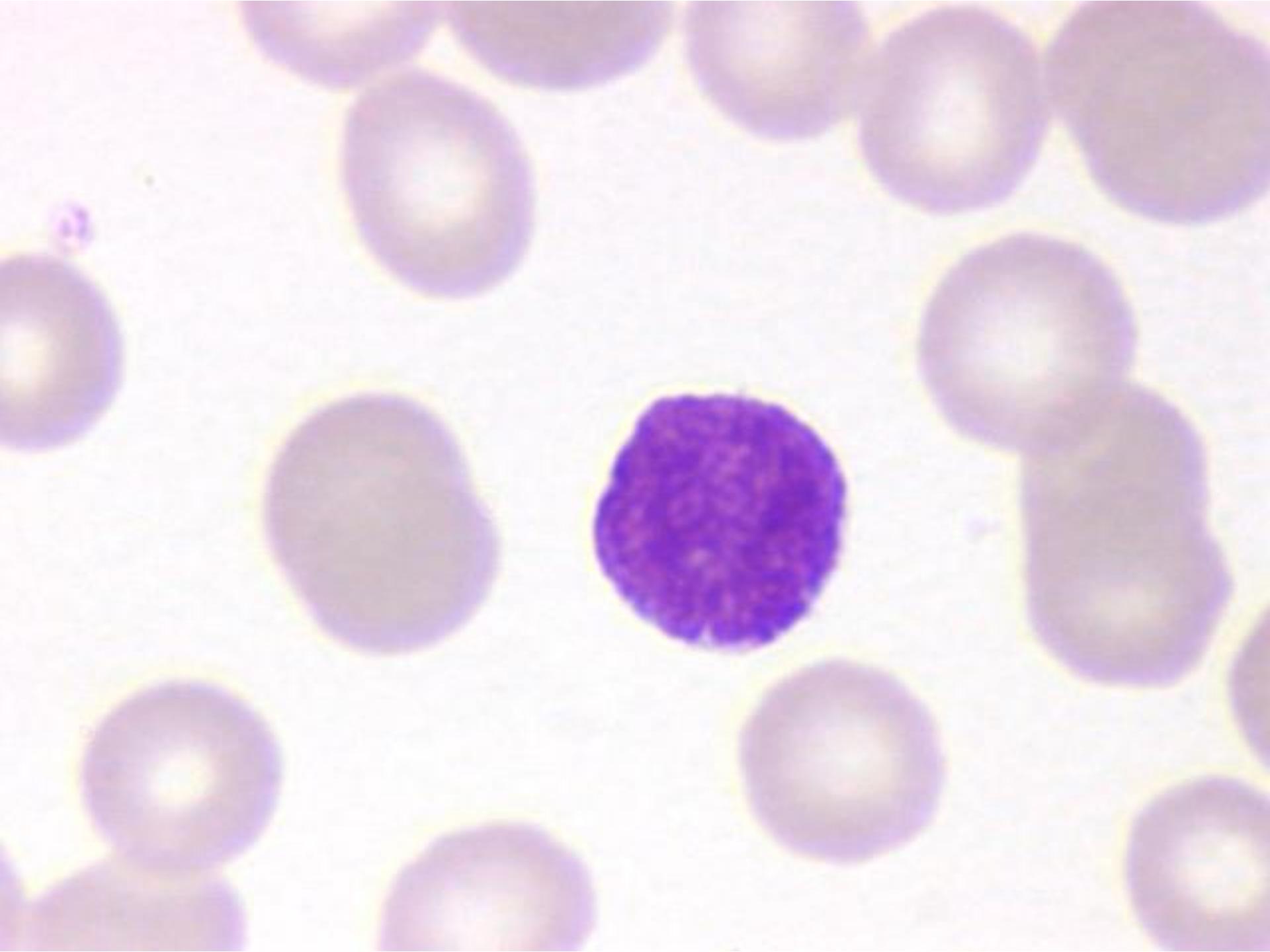
Hb: 83 g/L

Plaquetas: $81 \times 10^9/L$

LDH: 911 UI/L



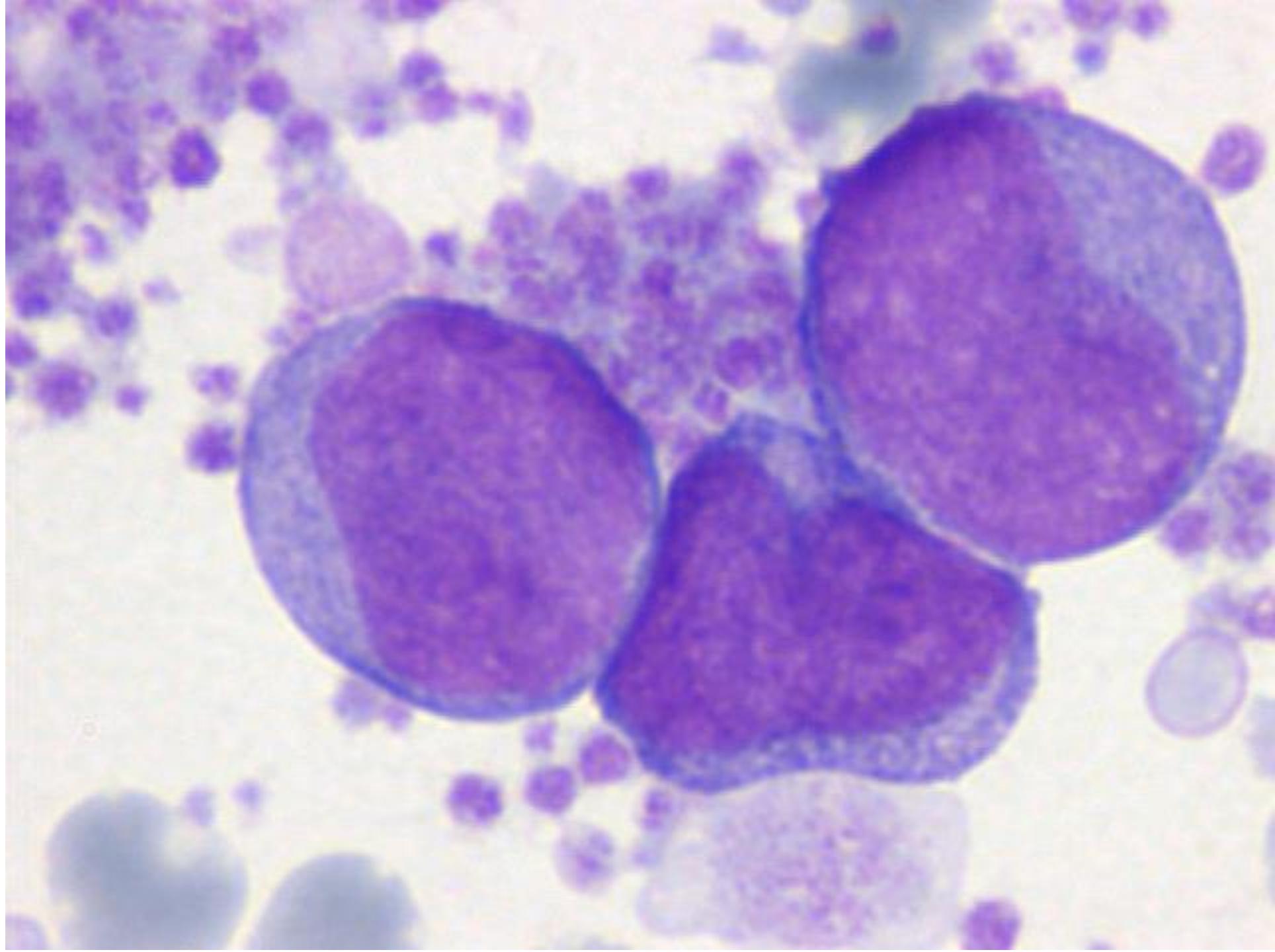


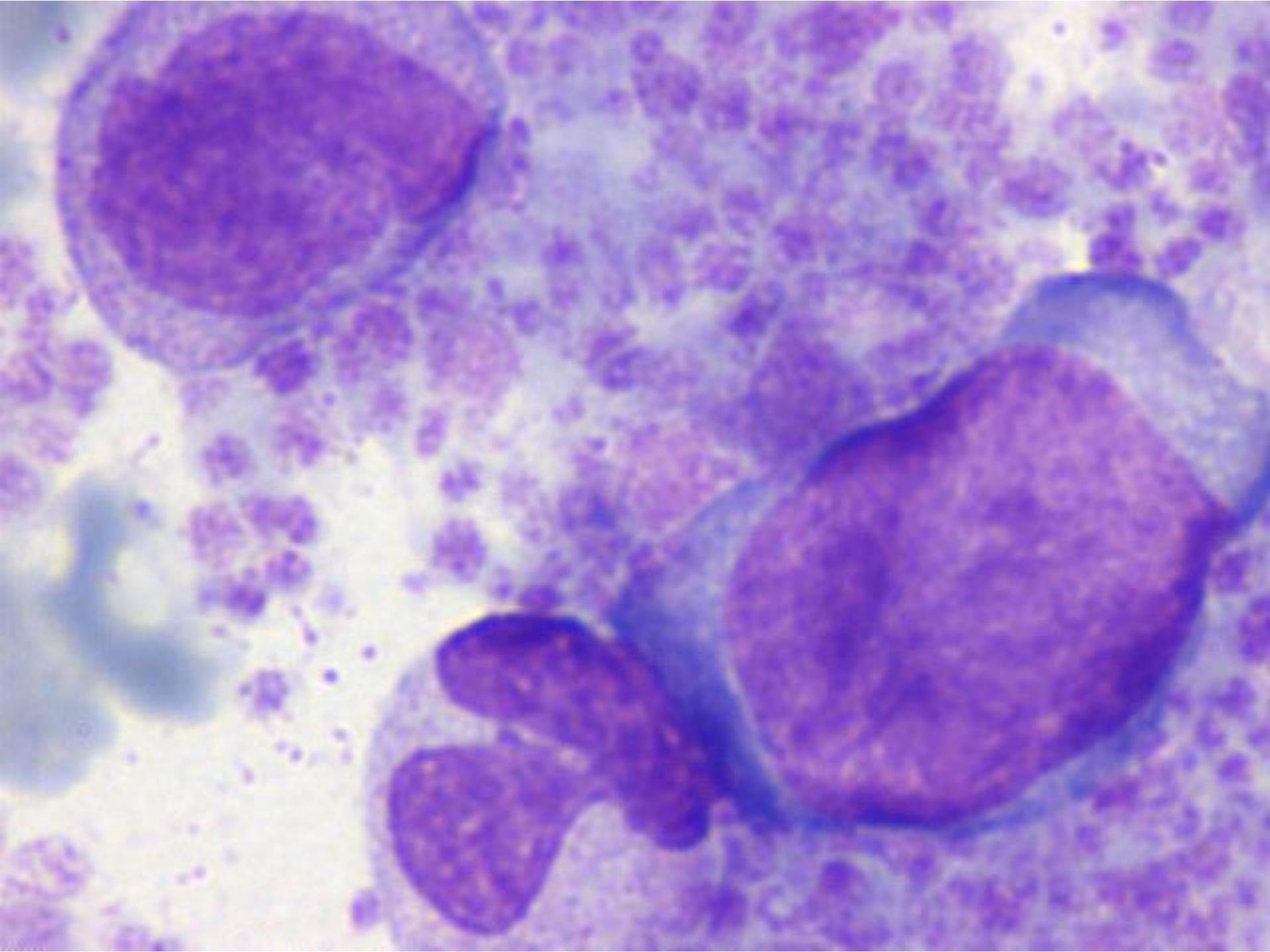


Diagnóstico

- **LAL-B común de alto riesgo por expresión de marcadores mieloides CD33 y CD13**

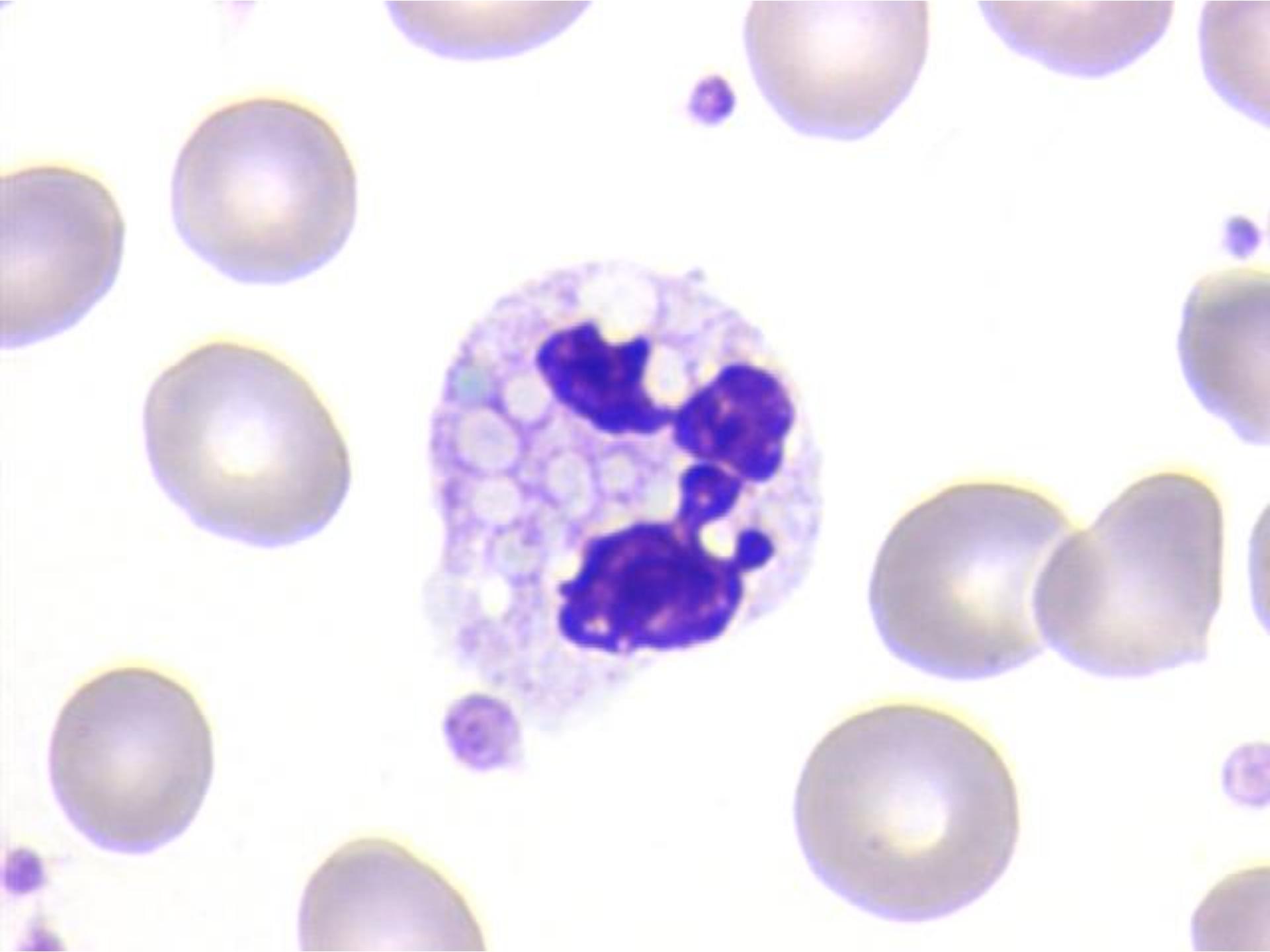
Detección de trombocitosis en una primera analítica



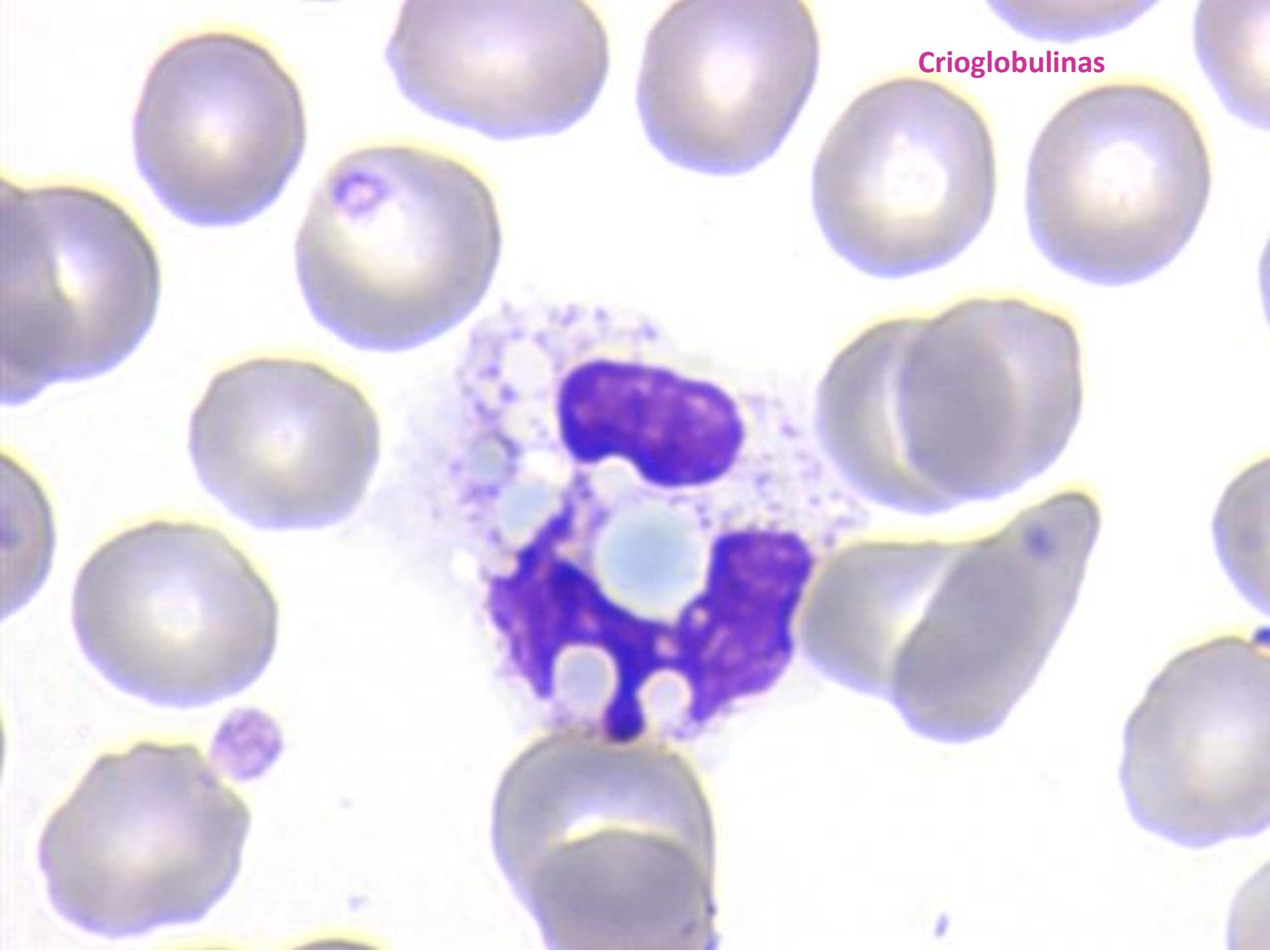


Diagnóstico

- **Leucemia mieloide crónica**



Crioglobulinas



CLINICAL PICTURE

Cytoplasmic inclusions in leukocytes associated to cryoglobulinemia and IgG-kappa monoclonal gammopathy of undetermined significance

A 74 year-old woman was admitted with a 3-year history of purpura associated to polyarthralgia, weakness and Raynaud phenomenon triggered by cold temperatures. Due to the high platelet counts in a routine peripheral blood (PB) cell analysis, the patient was in treatment with clopidogrel. With the exception of the purpuric lesions, physical examination did not show any relevant abnormality. An automatic blood cell count (Advia 2120; Siemens Healthcare Diagnosis, Deerfield, IL, USA) showed anaemia (106 g/L) and pseudothrombocytosis ($854 \times 10^9/L$) with normal white blood cell counts. Serologic test for HIV, hepatitis C and B virus were negatives. Serum protein electrophoresis showed a monoclonal immunoglobulin (M component) of 5.1 g/L of IgG-κ type by immunofixation. PB film showed abundant vacuole-like cytoplasmic inclusions with compression of the nucleus in neutrophils (Figures 1 and 2), monocytes, lymphocytes and platelets which were not present in bone marrow cells. Rheumatoid factor was negative and early complement factors were low. Erythropoietin levels were low with respect to haemoglobin values. Cryoglobulins were positive, with a cryocrit value of 3.8 %. Immunofixation of the cryoprecipitate demonstrated an IgG kappa monoclonal band. PB immunophenotyping showed normal expression of lymphoid antigens. Nevertheless, 7% of plasma cells were seen in

bone marrow aspirate that were negatives for CD19, positives for CD56 and showed low CD38 expression.

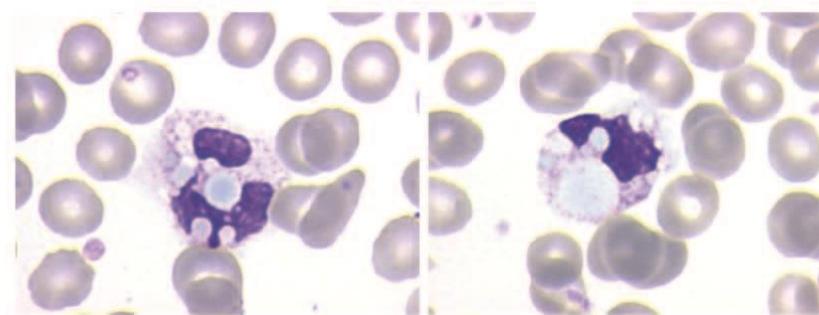
A diagnosis of type I cryoglobulinemia without visceral involvement associated to IgG-kappa monoclonal gammopathy of undetermined significance (MGUS) and a chronic anaemia with abnormal erythropoietin production was made. The patient was encouraged to avoid cold temperatures and subcutaneous erythropoietin was initiated until the resolution of anaemia.

This case illustrates the presence of characteristic blood cell cytoplasmic inclusions in a case of MGUS associated with cryoglobulins and the importance of the recognition of spurious high platelet counts associated to the cryoglobulinemia.

Anna Merino¹, Carlos Fernández de Larrea, ² Joan Bladé²

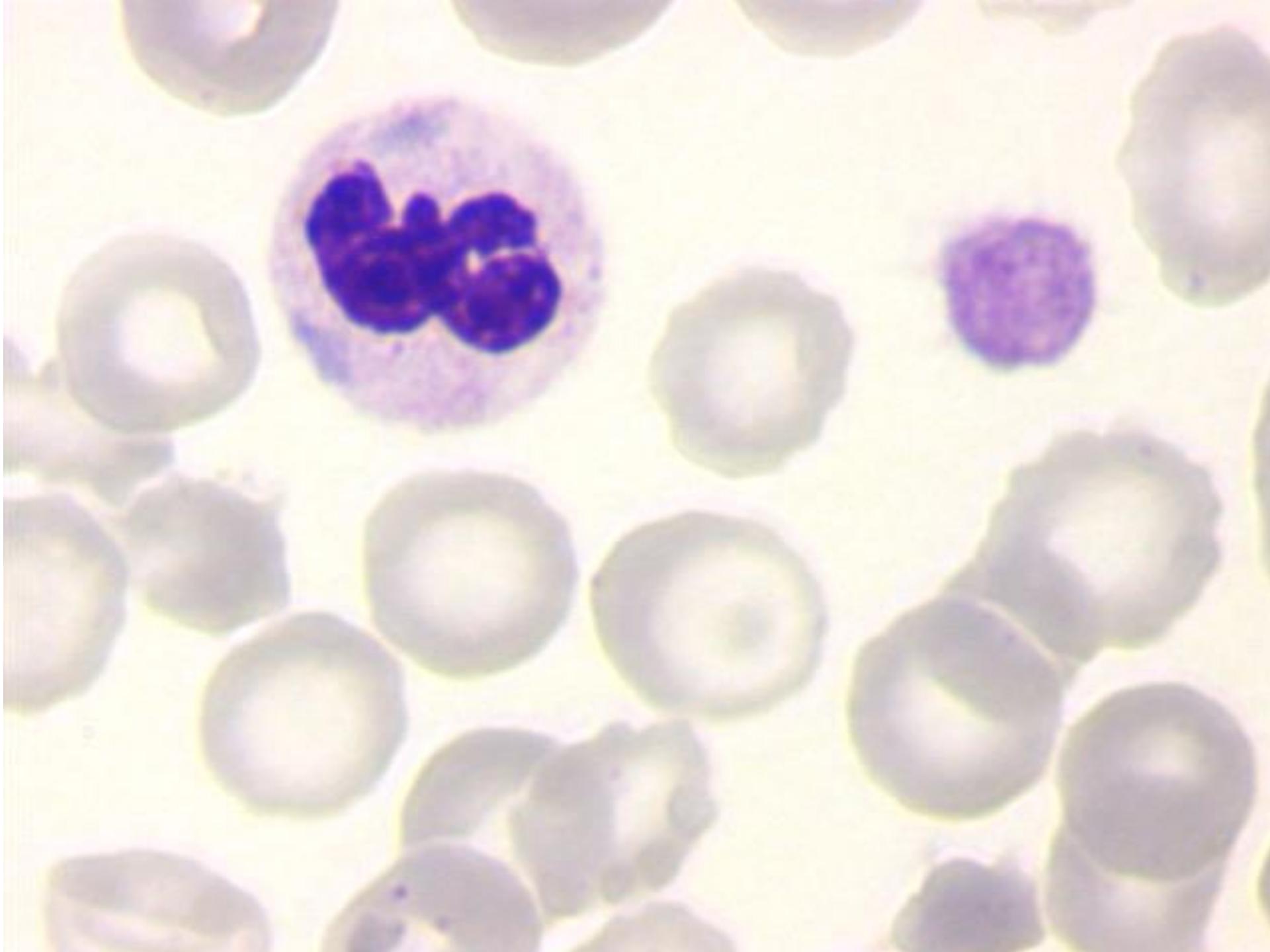
¹Servicio de Hemoterapia-Hemostasia, CDB; ²Servicio de Hematología Clínica, ICMHO, Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain

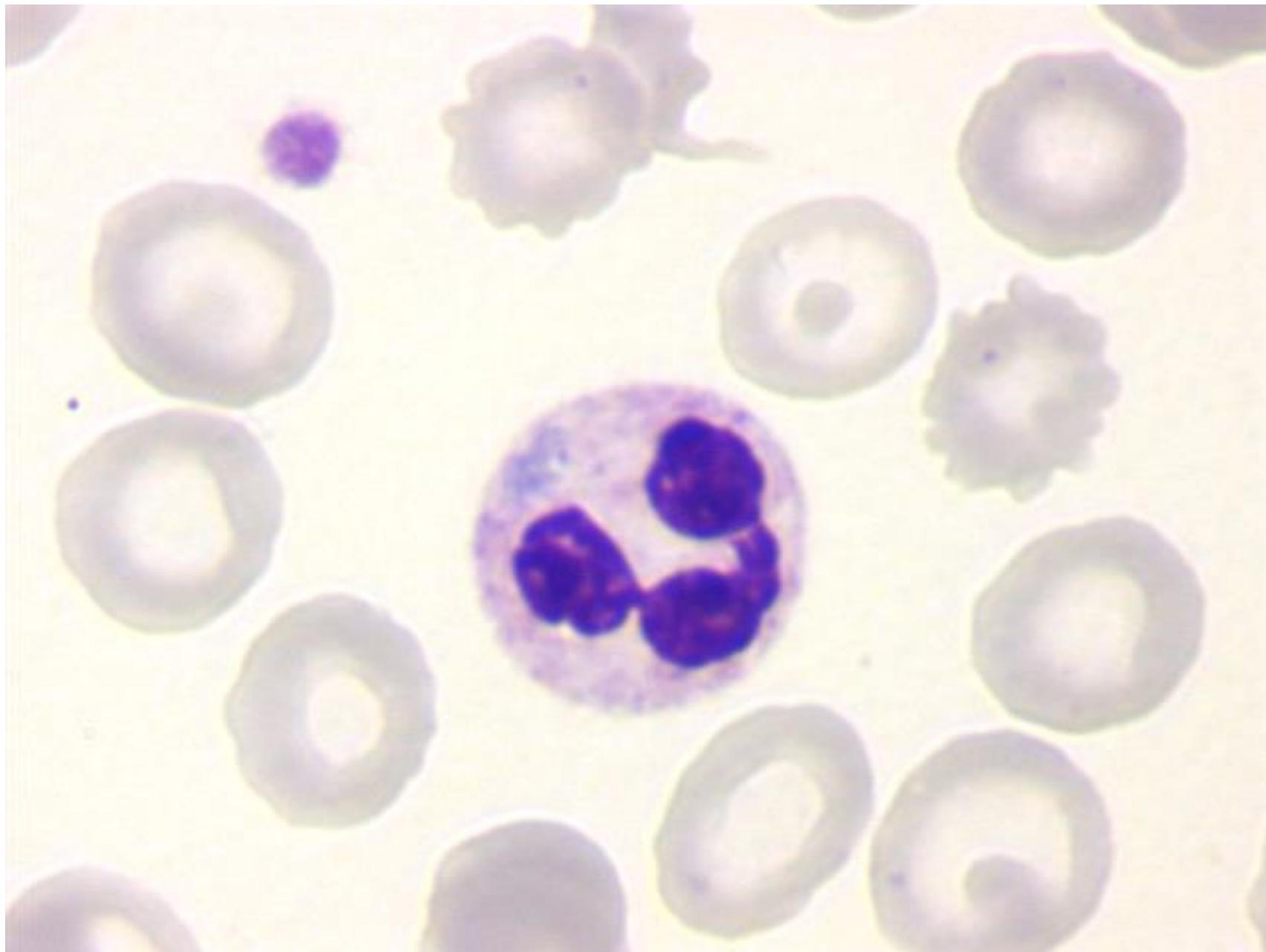
Correspondence Anna Merino, Servicio de Hemoterapia-Hemostasia, CDB.
Tel.: 3432279375;
Fax: 3432279376;
e-mail: amerino@clinic.ub.es

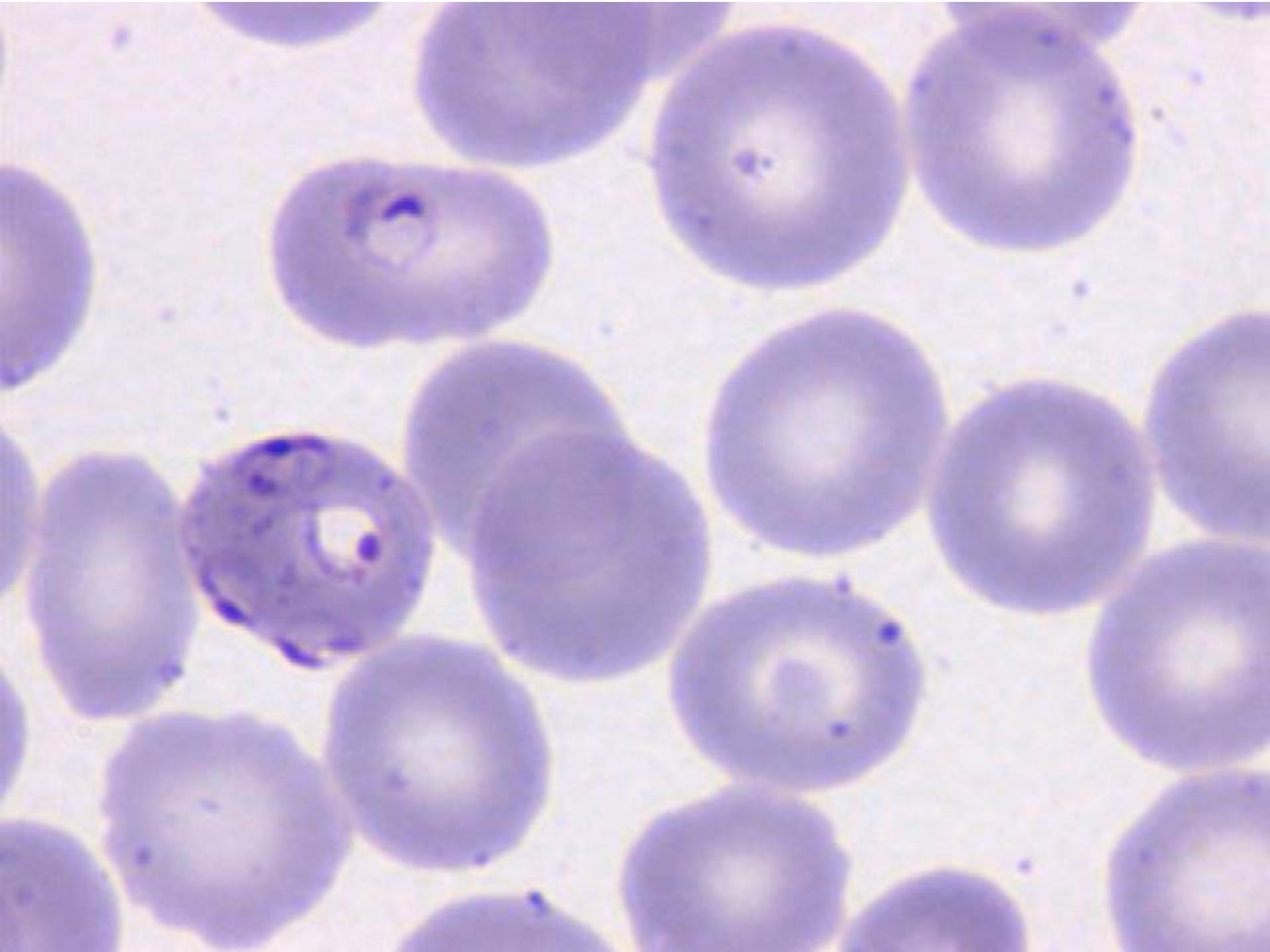


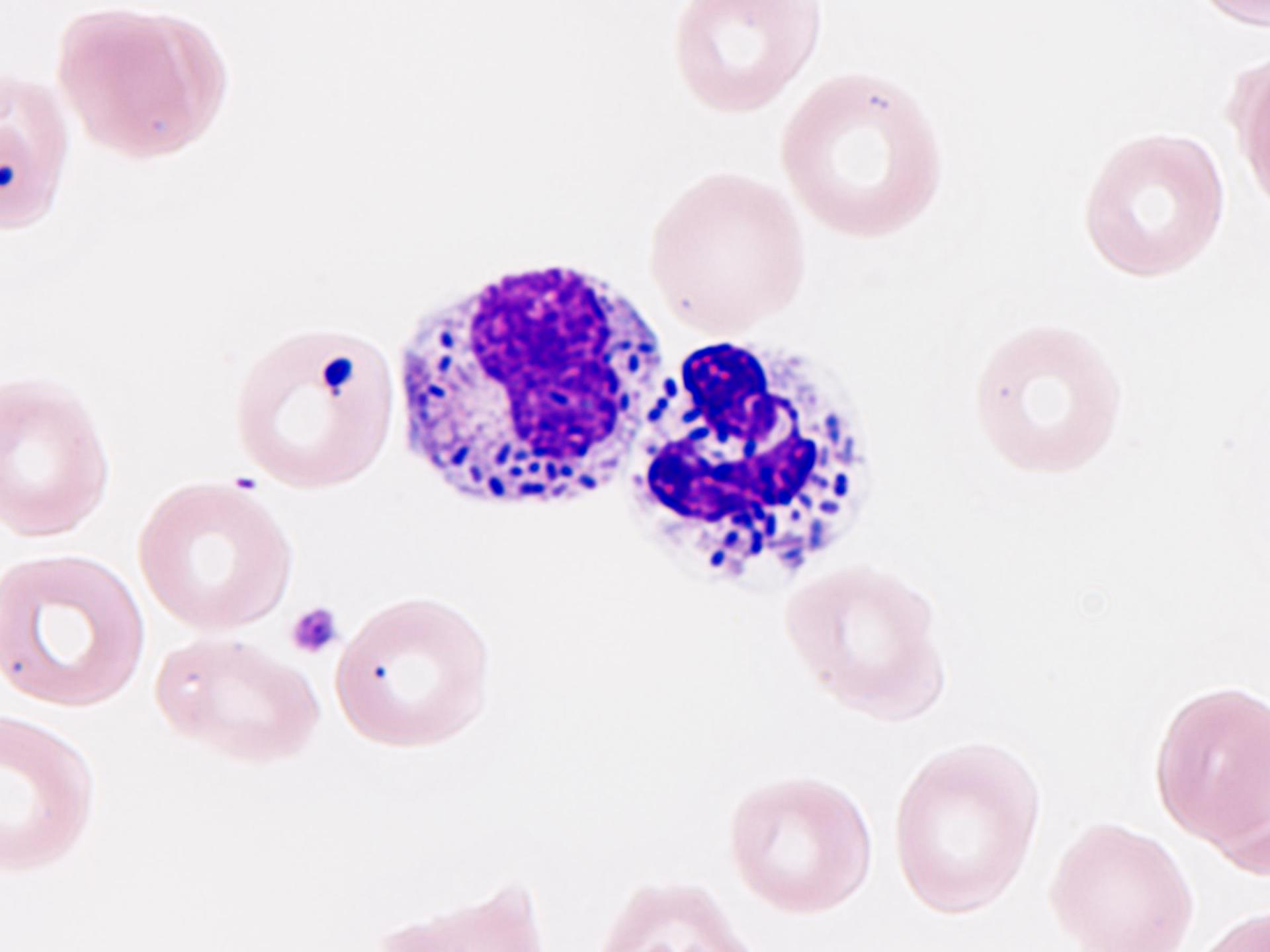
Figures 1 and 2 Cytoplasmic inclusions in neutrophils associated with cryoglobulins.

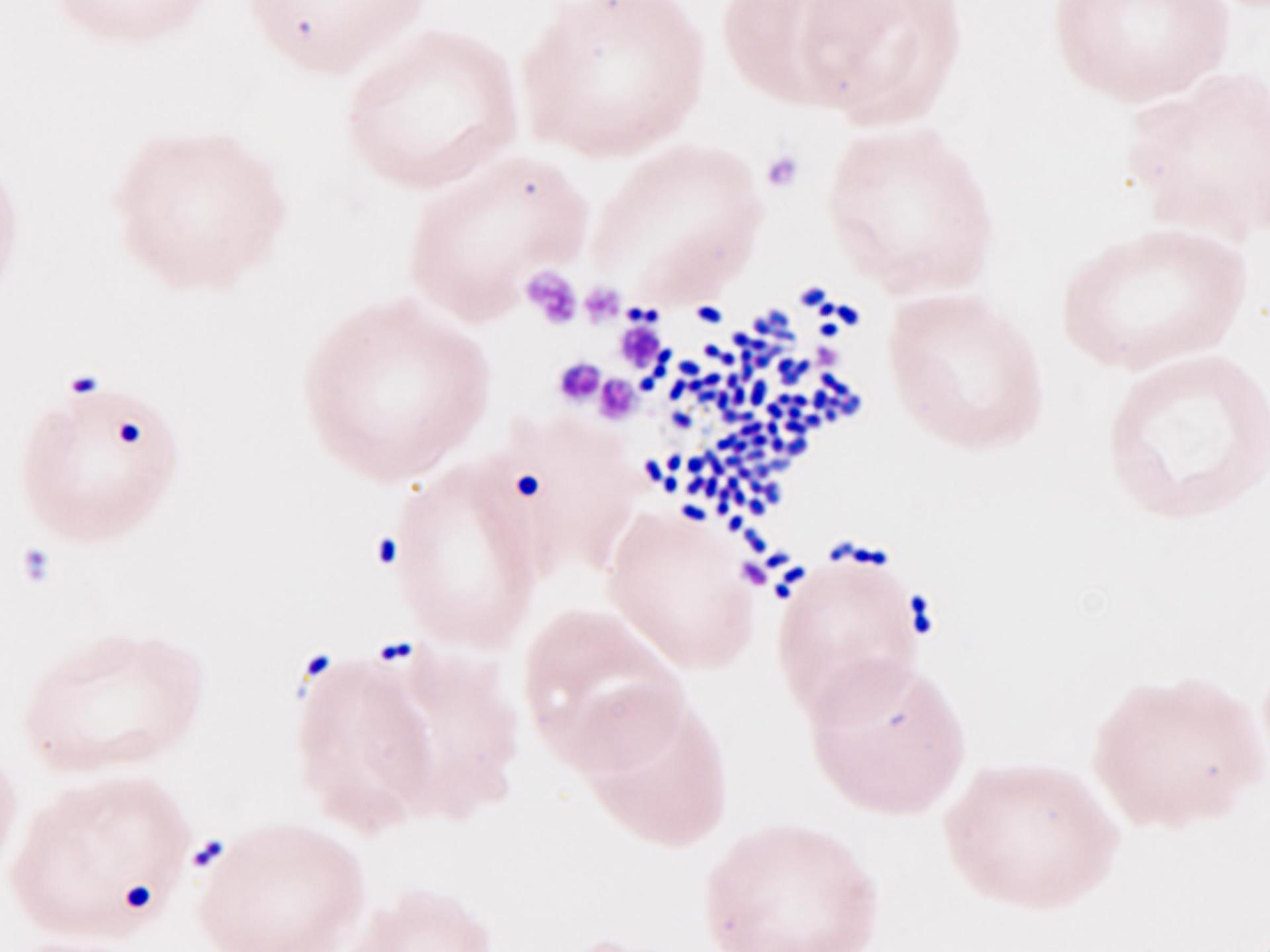
Detección de una plaquetopenia aislada en una primera analítica



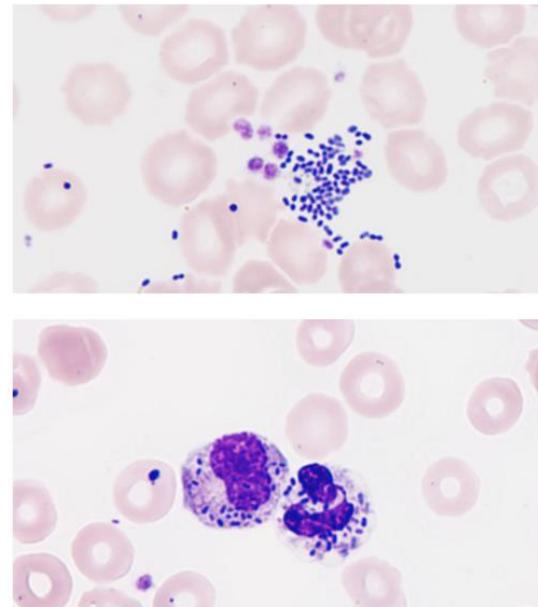








The unusual presence of *Streptococcus gallolyticus* within neutrophils in a patient with endocarditis and brain abscesses



A 70-year-old splenectomized woman with chronic natural killer cell lymphocytosis who was receiving azathioprine treatment for autoimmune hepatitis was admitted with a 6-h history of fever (39°C), progressive stupor and dysarthria. An automated full blood count showed a low white blood cell count ($2.98 \times 10^9/l$), normal red blood cell count and low platelet count ($95 \times 10^9/l$). A peripheral blood film showed the presence of cocci, both extracellularly (top) and within neutrophils. A computerized tomography scan of her brain revealed multiple nodular lesions compatible with brain abscesses. With these findings, sepsis was suspected and broad-spectrum antibiotics were administered. After a short period in hospital the patient developed haemodynamic failure. By this time there had been a further fall in the leucocyte count ($1.49 \times 10^9/l$), platelet count ($29 \times 10^9/l$) and haemoglobin concentration (58 g/l). Coagulation tests

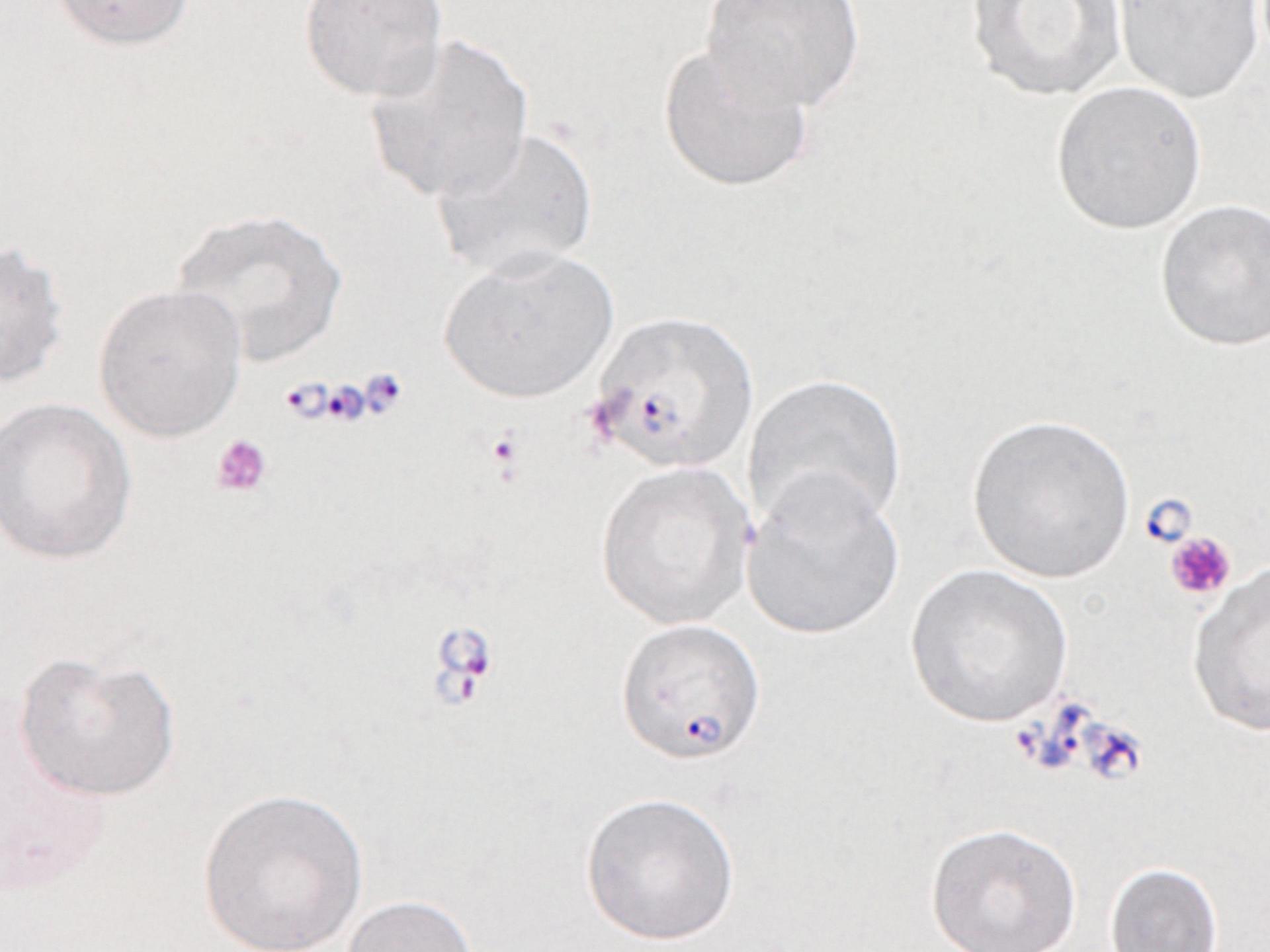
indicated disseminated intravascular coagulation. The blood film now showed large numbers of cocci within neutrophils (bottom). With these findings, the diagnosis of infective endocarditis was suspected. Echocardiography revealed mitral valve rupture. The patient died within a few hours. Blood cultures were subsequently found to be positive for *Streptococcus gallolyticus* (*Streptococcus bovis* biotype I), which has long been associated with endocarditis and with underlying gastrointestinal malignancy or liver disease. The presence of numerous micro-organisms in the blood film of this patient on immunosuppressive therapy for autoimmune hepatitis is noteworthy.

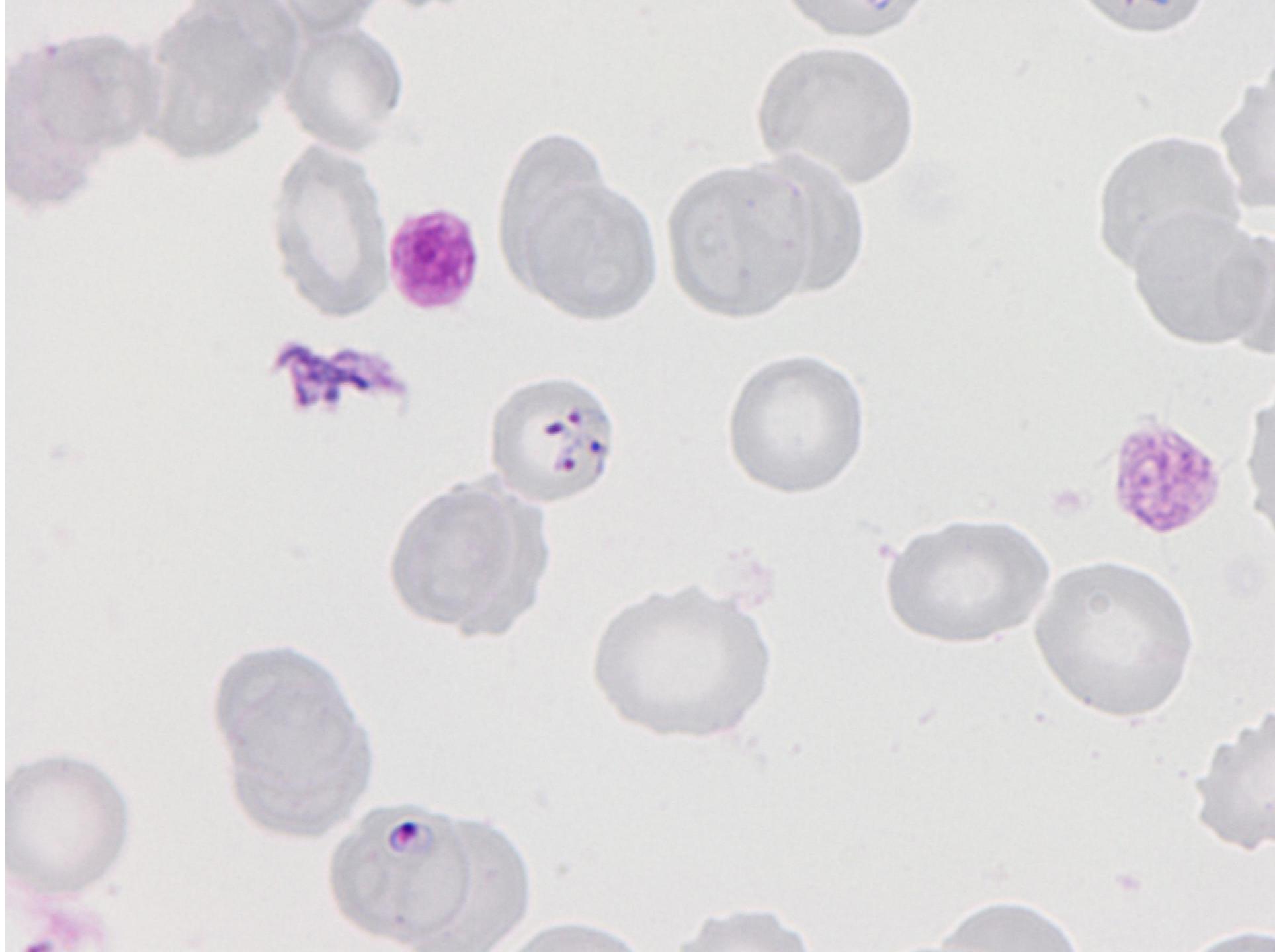
Laura Bigorra and Anna Merino

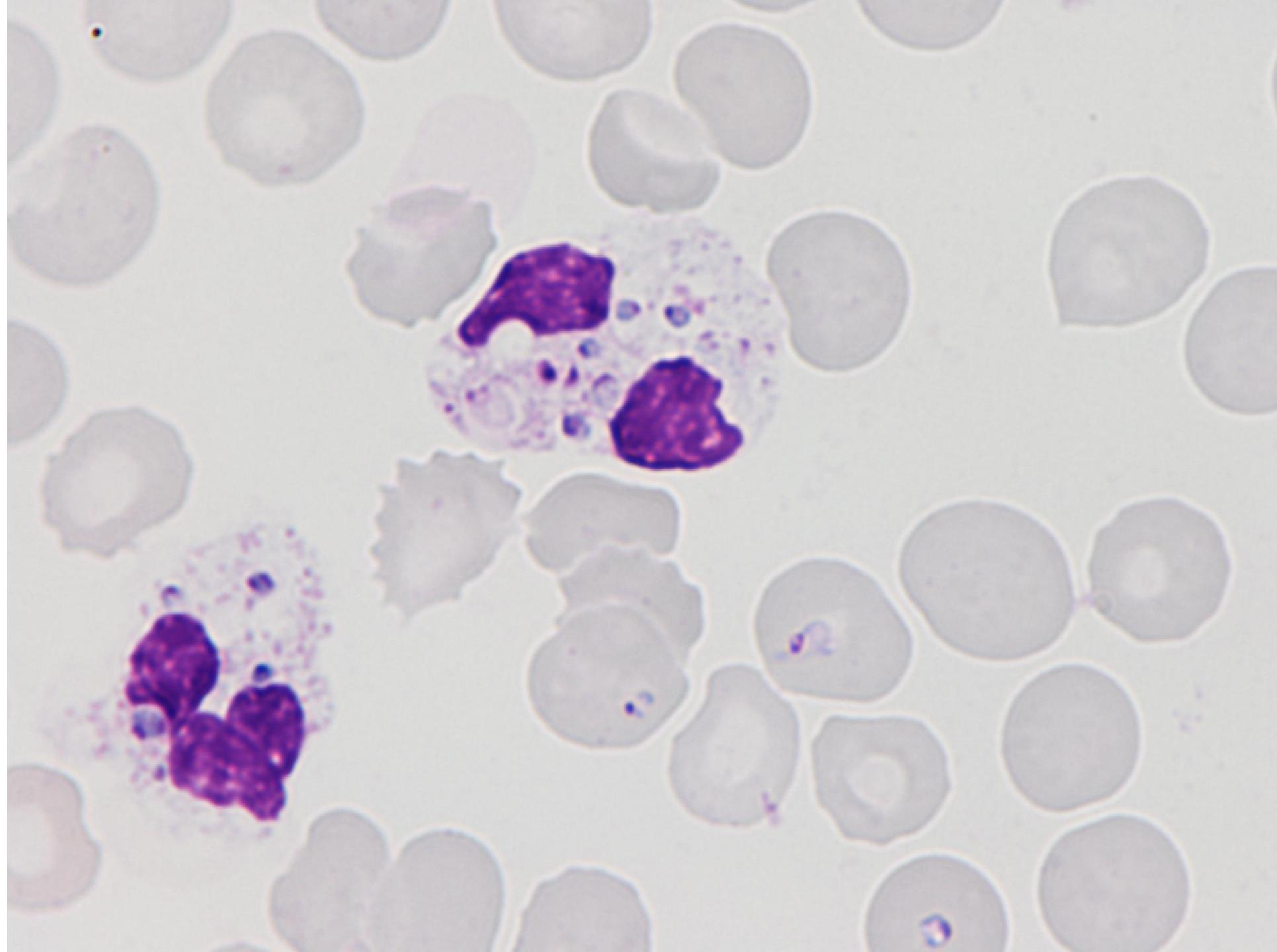
Haemotherapy-Haemostasis Service, CDB, Hospital Clínic of Barcelona, Barcelona, Spain. E-mail: amerino@clinic.ub.es

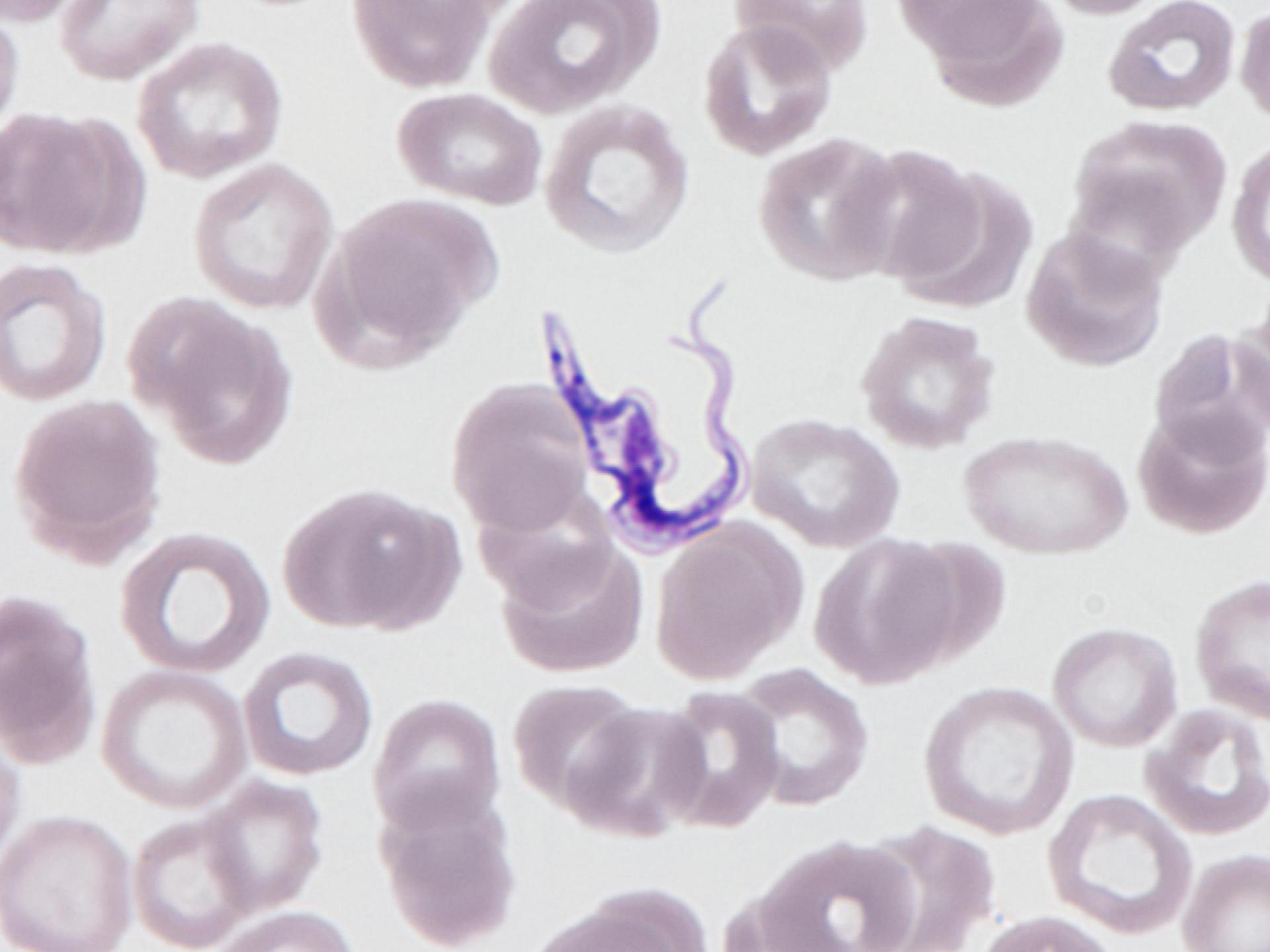
First published online 18 March 2015
doi: 10.1111/bjh.13337

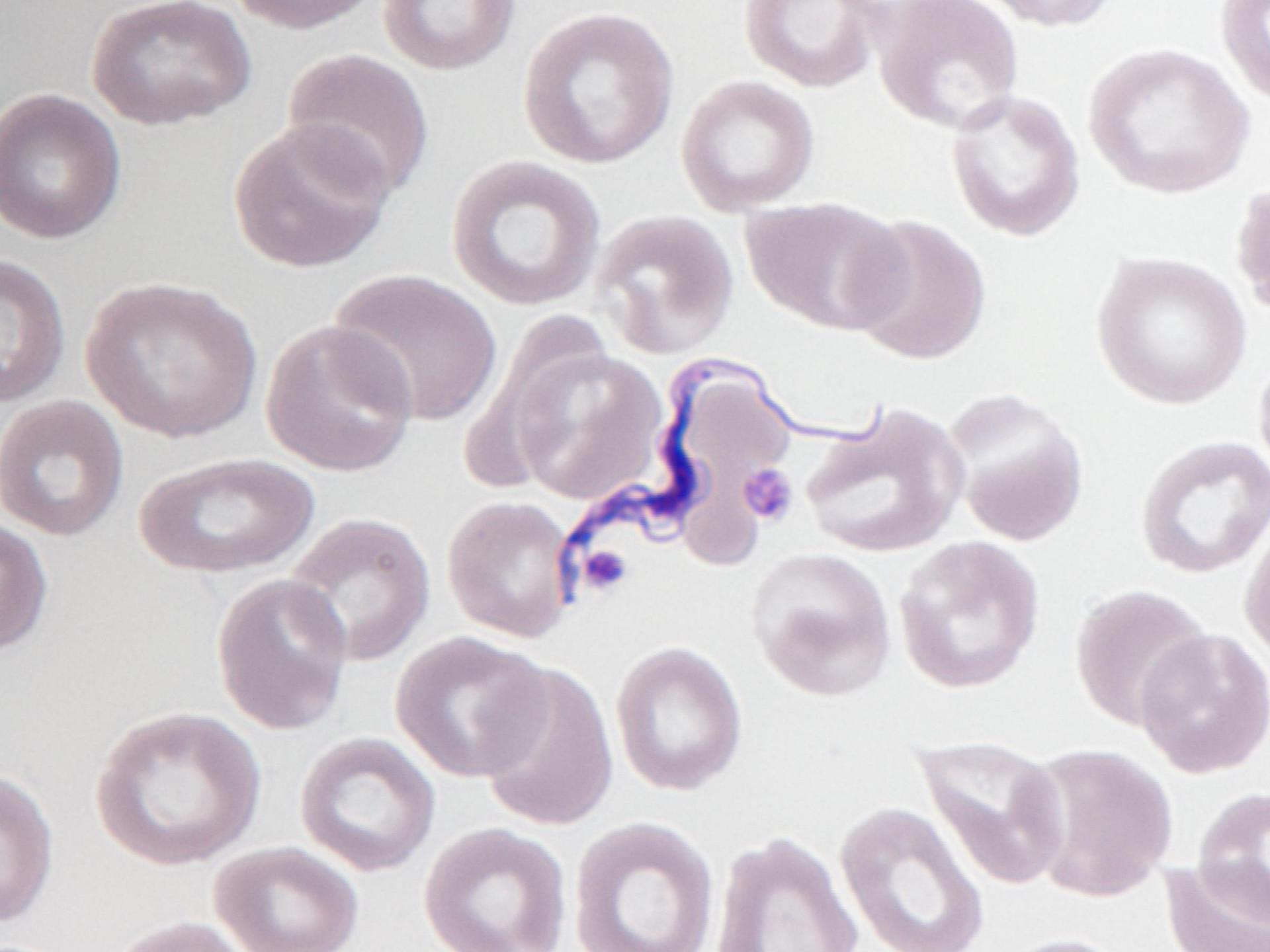
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British Journal of Haematology, 2015, 169, 308







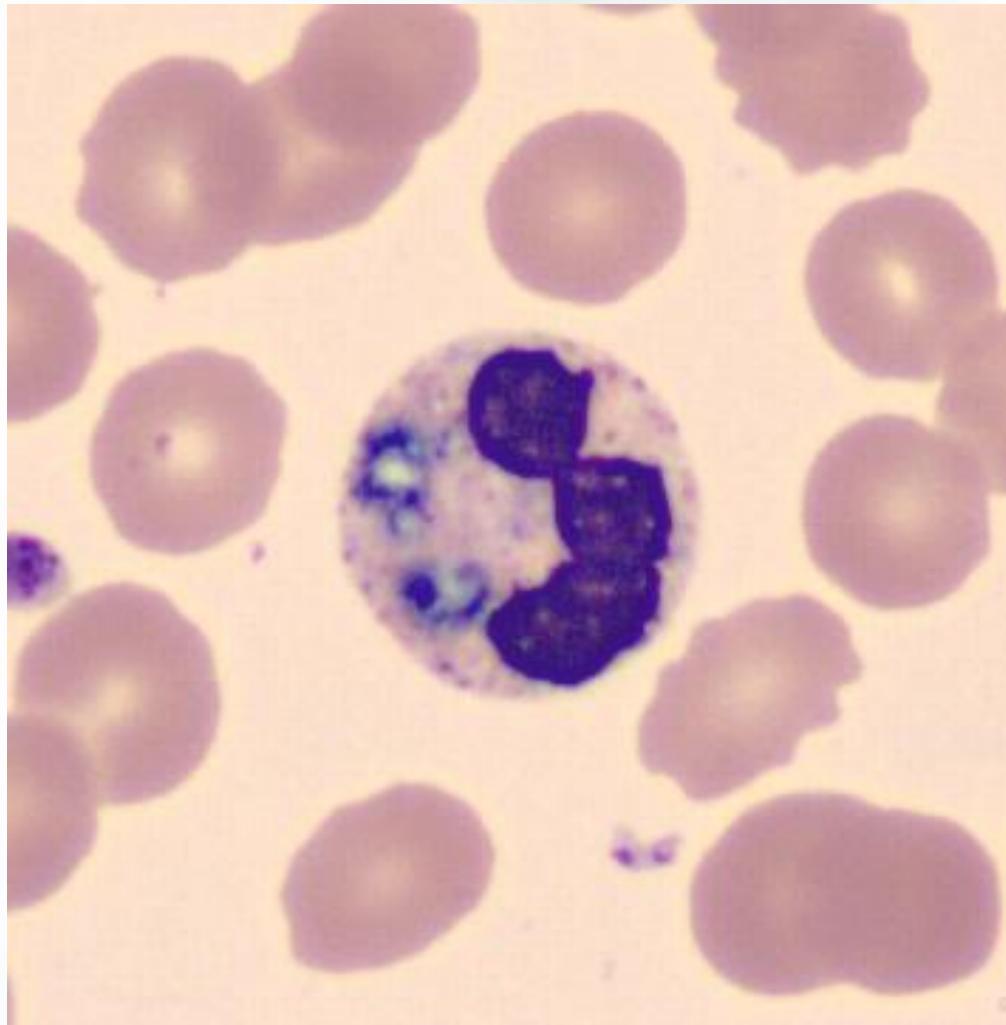




Revisión facultativa del frotis en una primera analítica

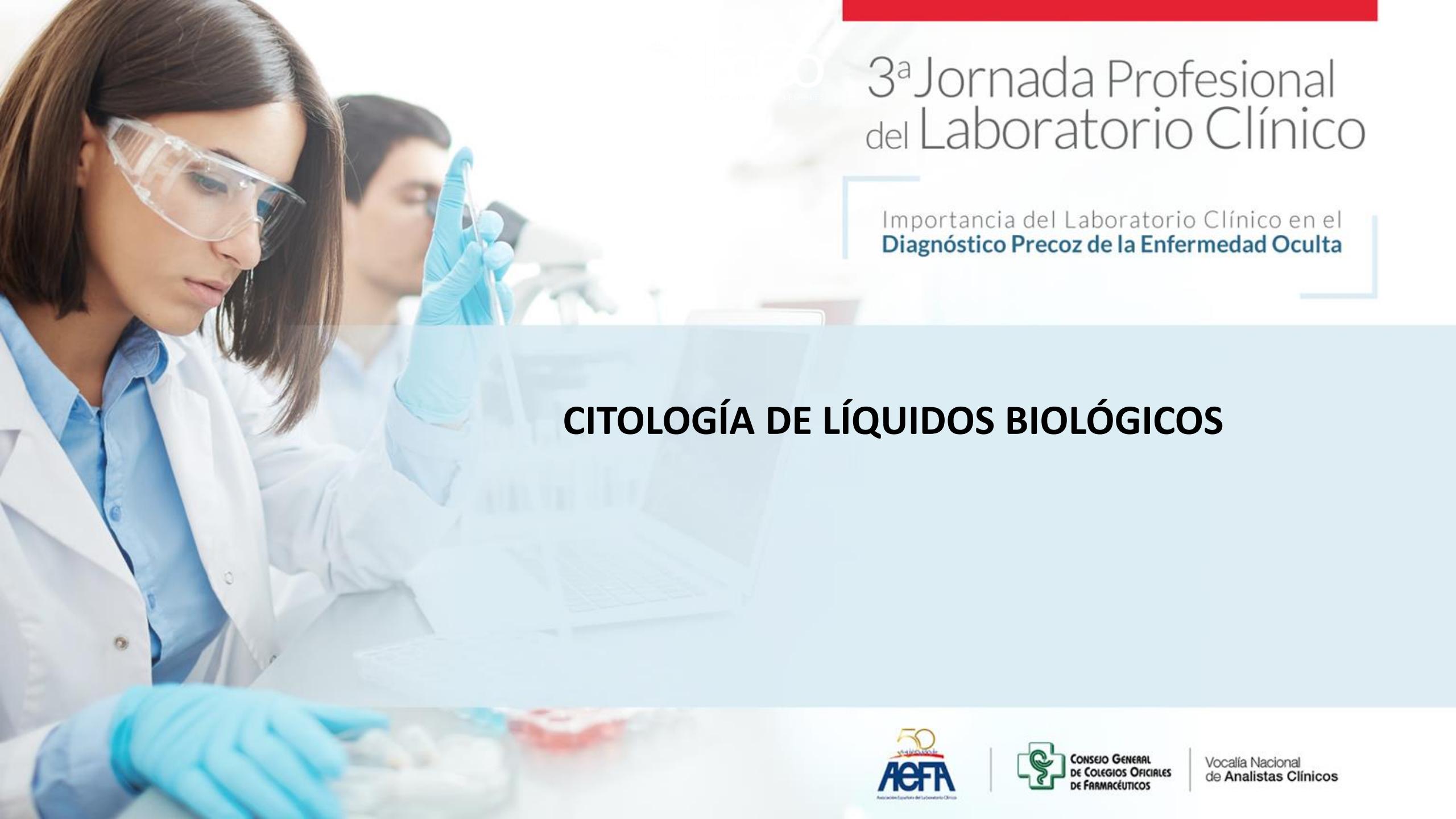
- **Pancitopenia/bicitopenia***
- **Hb < 90 g/L sin evidencia de sangrado**
- **Leucocitos < $3 \times 10^9/L$**
- **Plaquetas < $50 \times 10^9/L$**
- **Linfocitosis > $4,5 \times 10^9/L$**
- **Plaquetas > $1000 \times 10^9/L$**
- **Blastos/Linfocitos anormales/Promielocitos anormales/inclusiones, gérmenes o cristales.**

Cristales verdes “de la muerte”



Cristales verdes “de la muerte”





3^a Jornada Profesional del Laboratorio Clínico

Importancia del Laboratorio Clínico en el
Diagnóstico Precoz de la Enfermedad Oculta

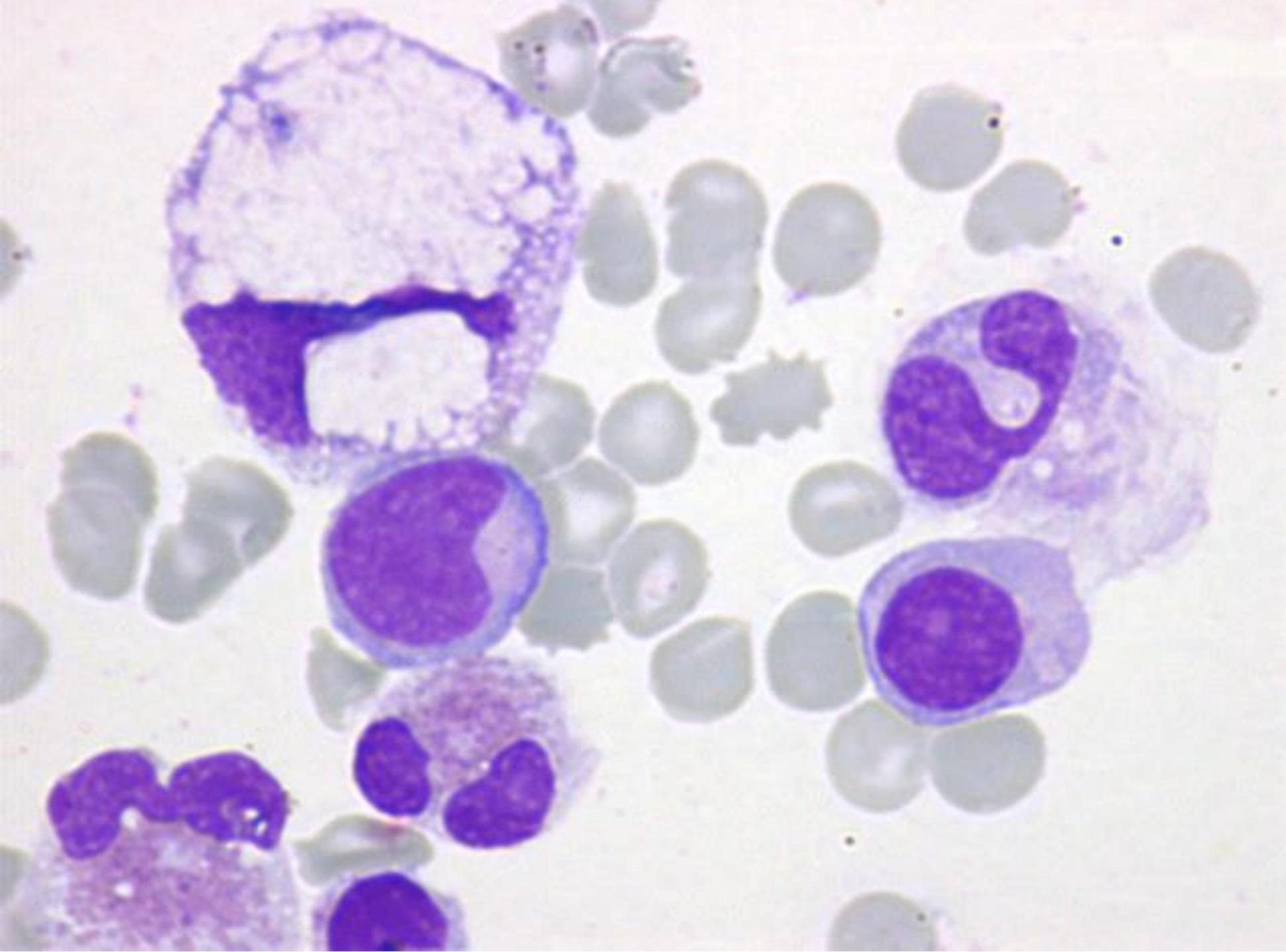
CITOLOGÍA DE LÍQUIDOS BIOLÓGICOS

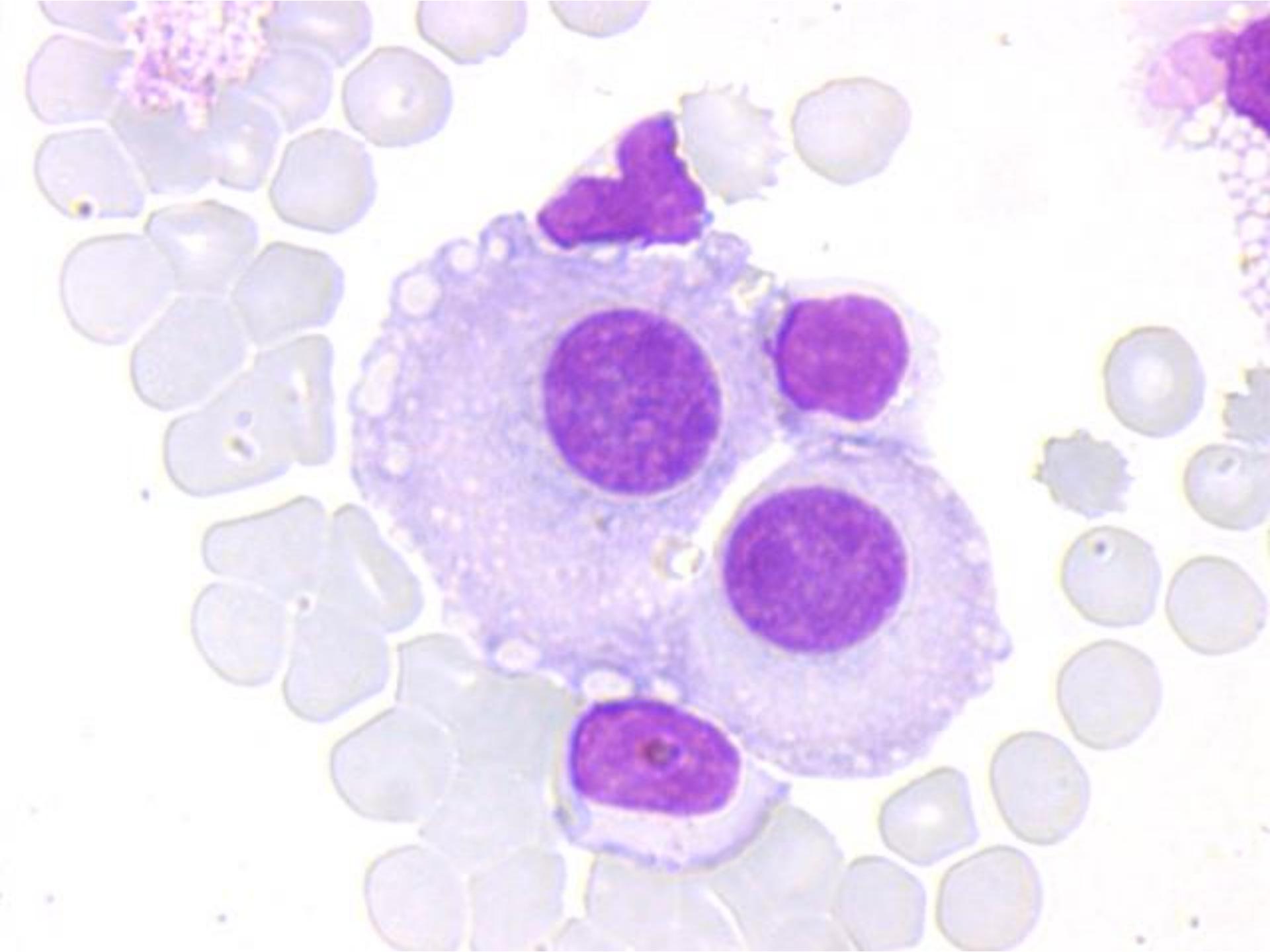


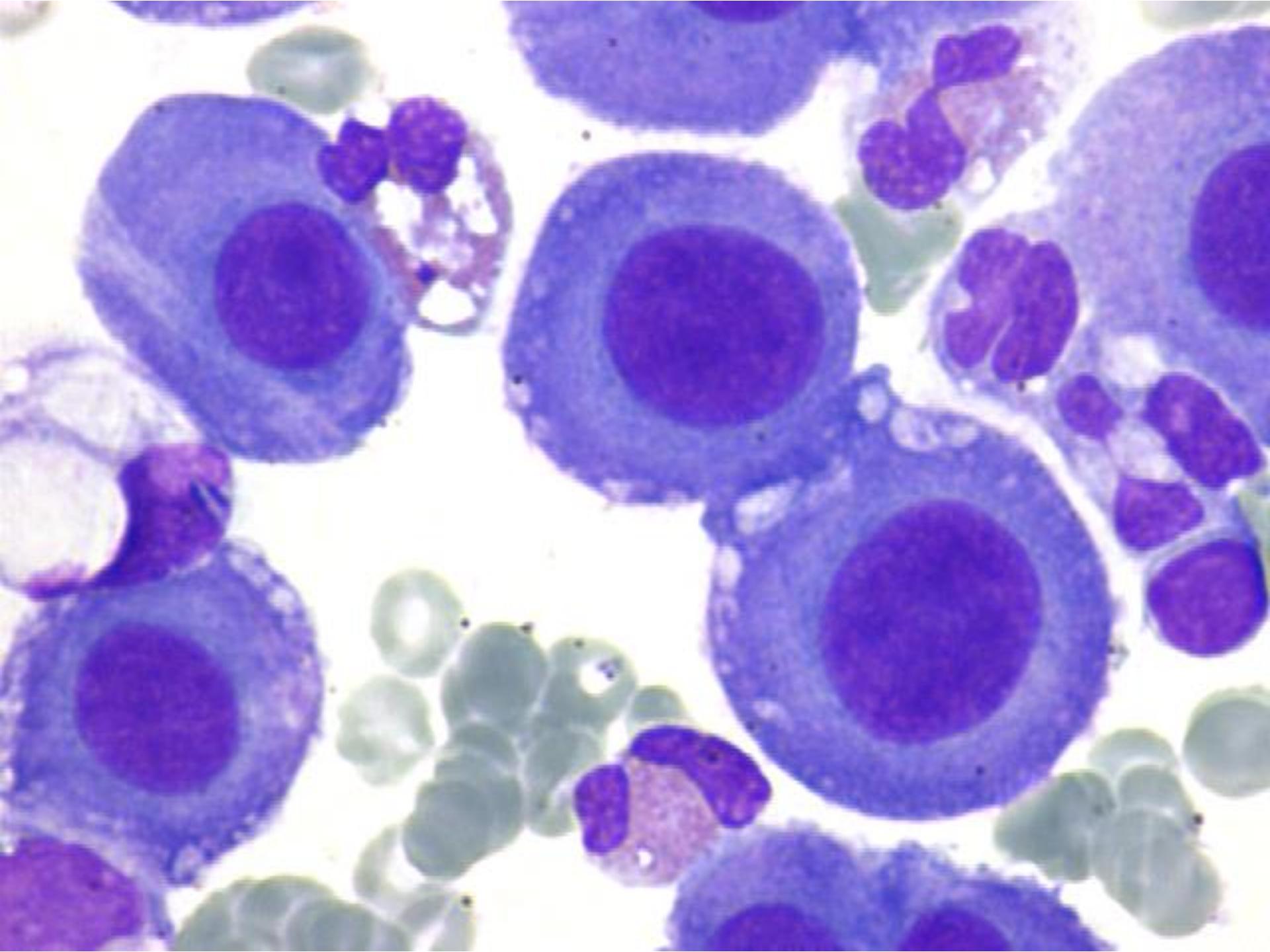
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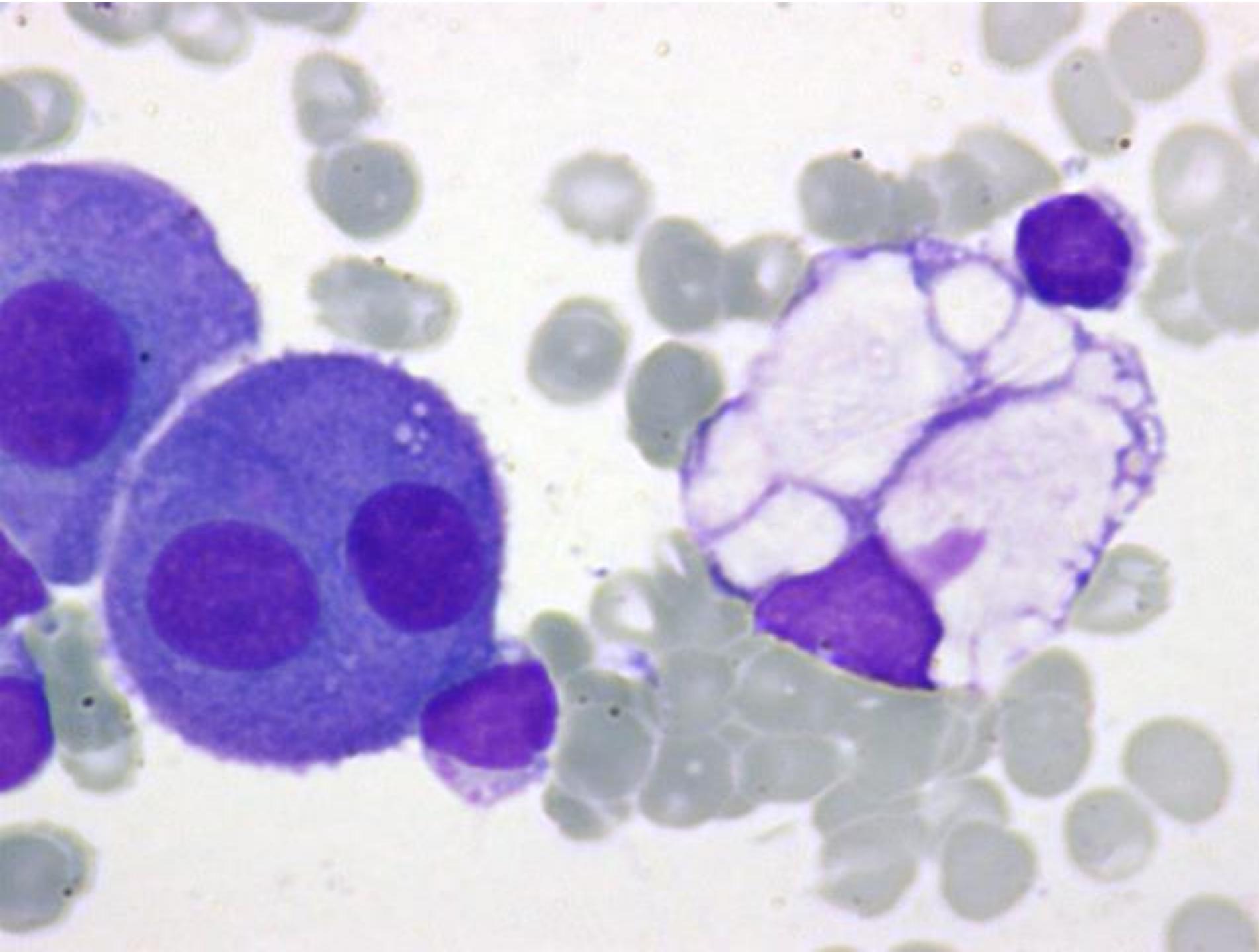
Celularidad en líquidos biológicos

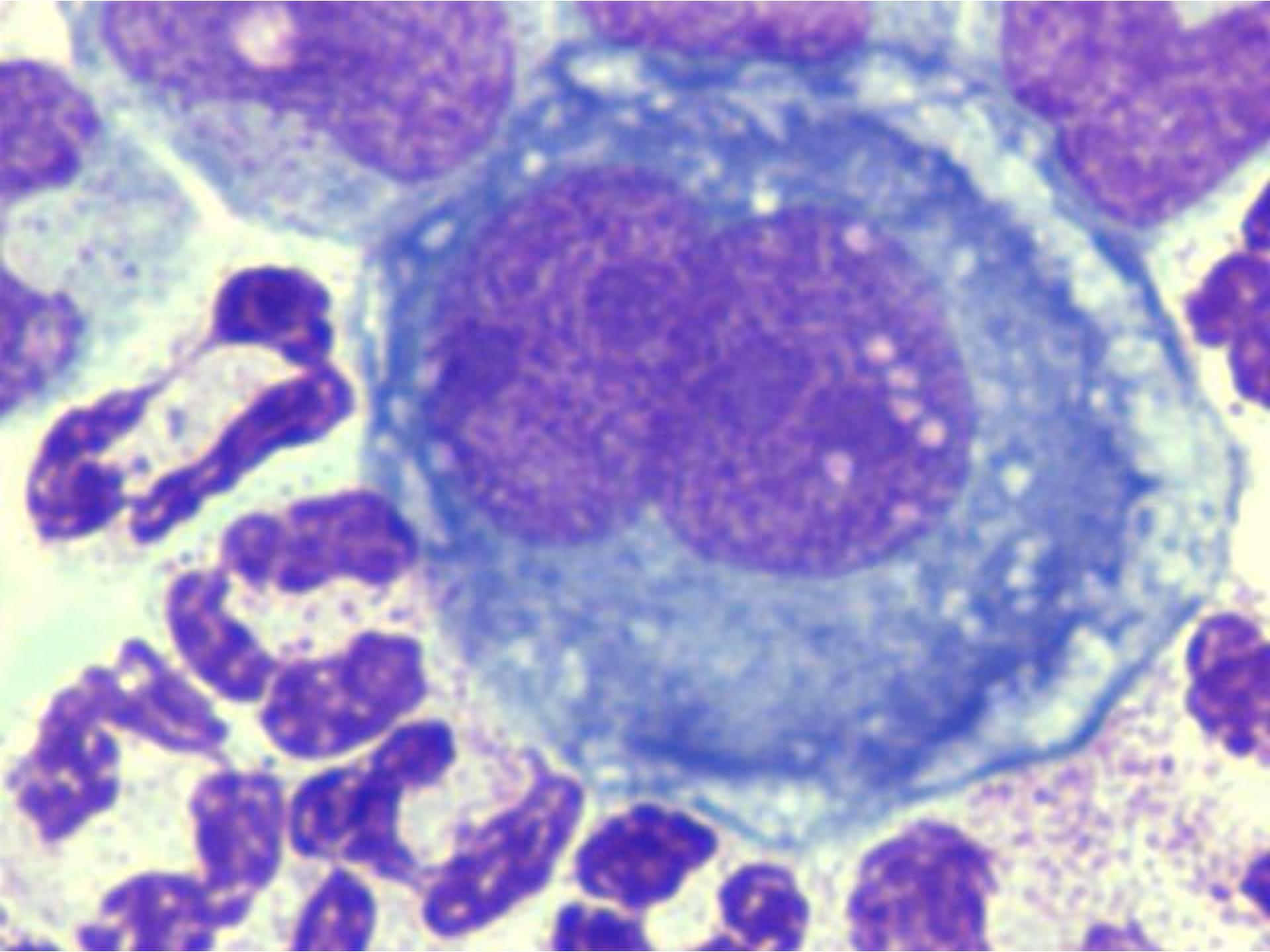
- **Sanguíneas**
- **Macrófagos**
- **Mesoteliales**
- **Neoplásicas**

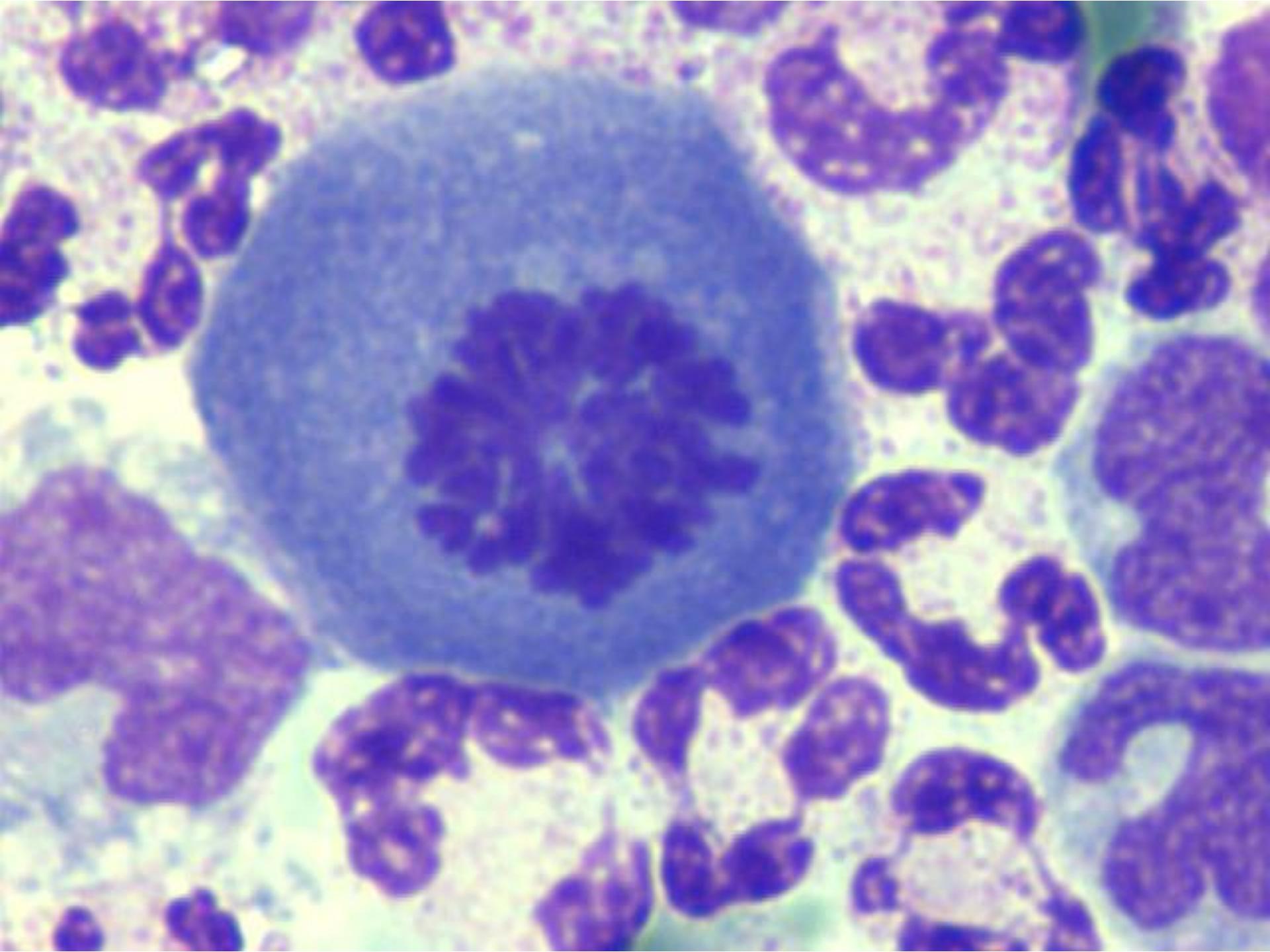












Células neoplásicas I

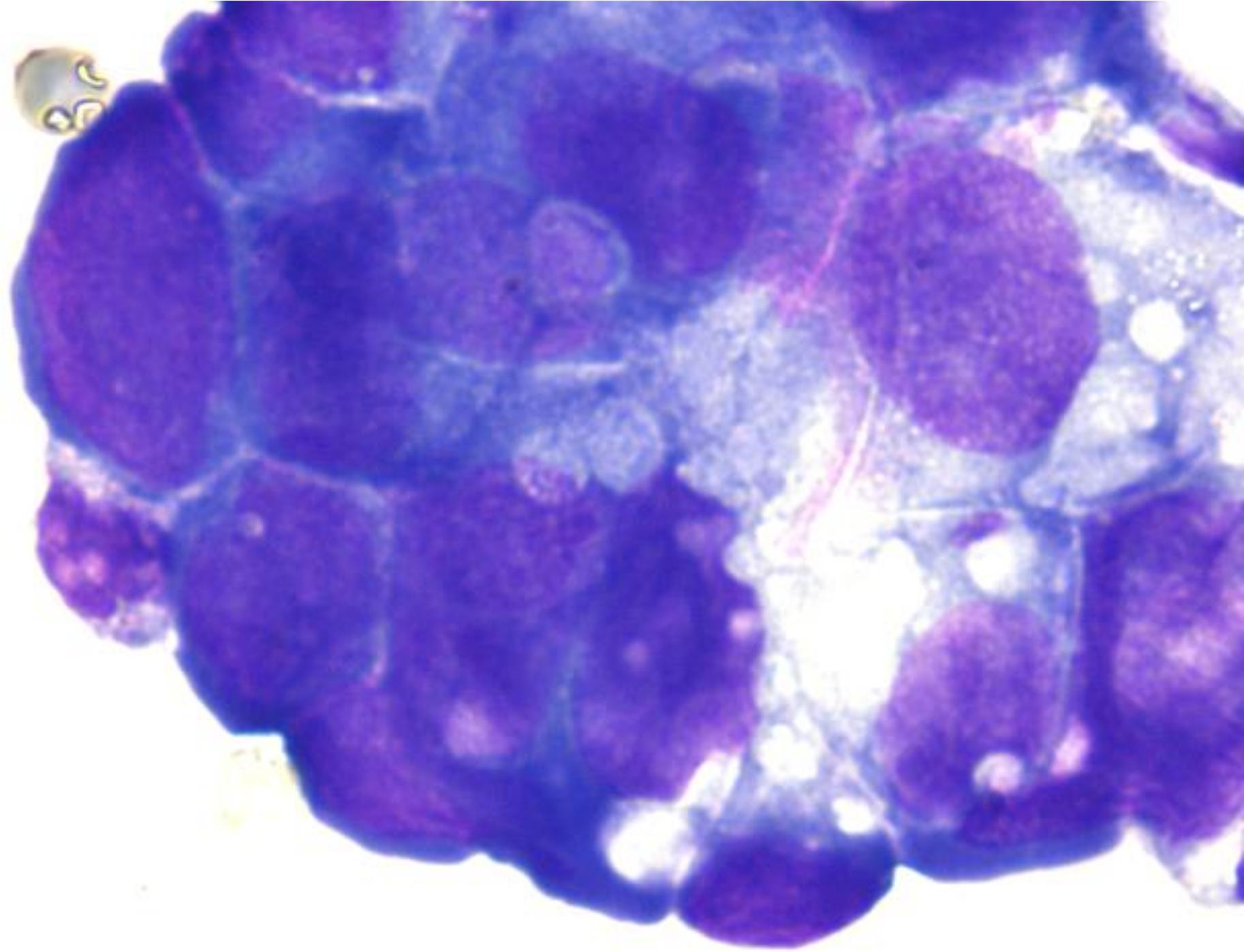
- Tendencia a agruparse y formar “nidos” celulares.
- El citoplasma de las células tumorales muestra tendencia a confluir y formar “sincitio”.
- Pleomorfismo celular con predominio de las de gran tamaño.
- Relación N/C aumentada.
- Núcleo de cromatina laxa e inmadura con presencia de nucleolos marcadamente visibles.
- Intensa basofilia citoplasmática.

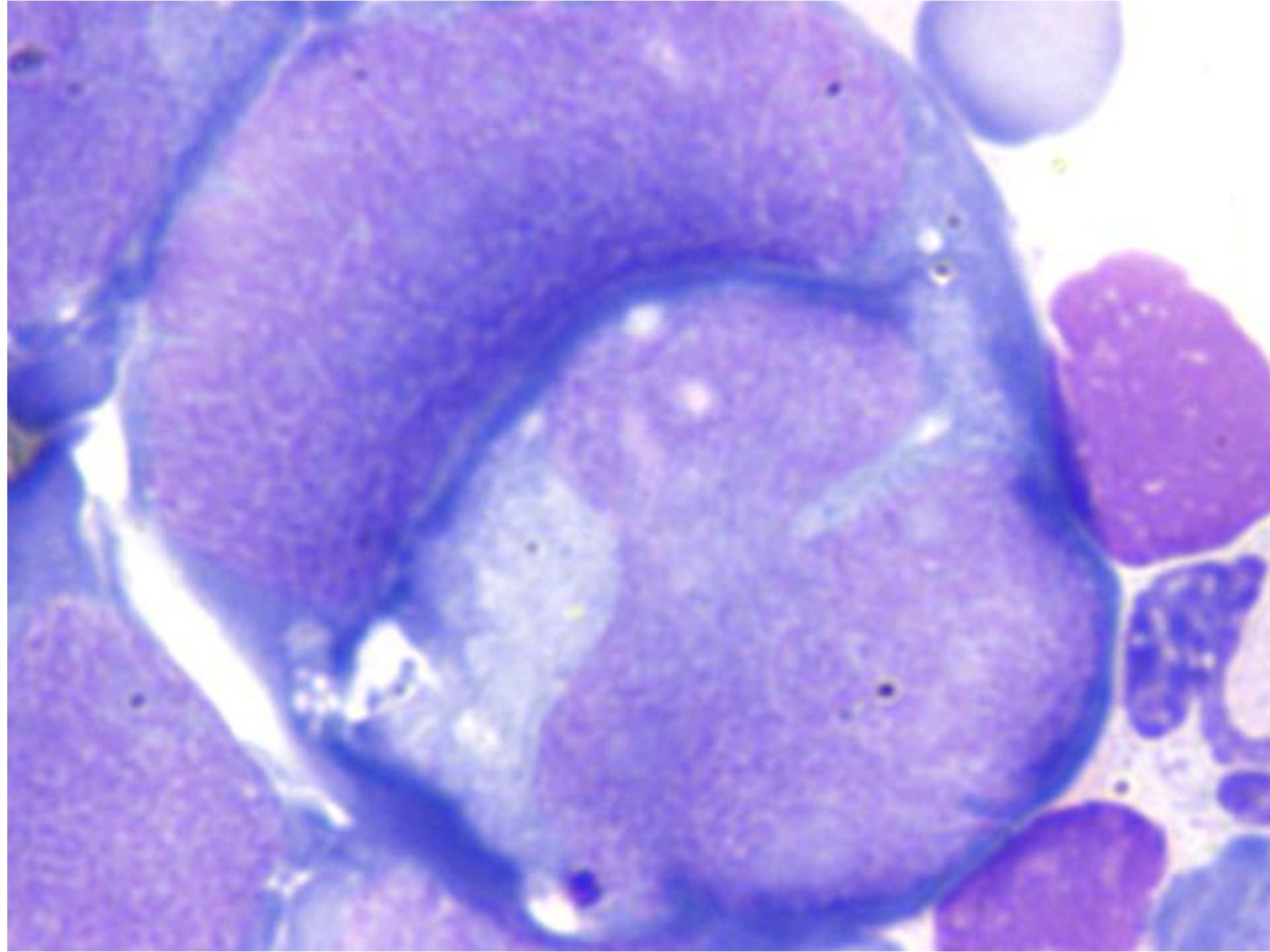
Células neoplásicas II

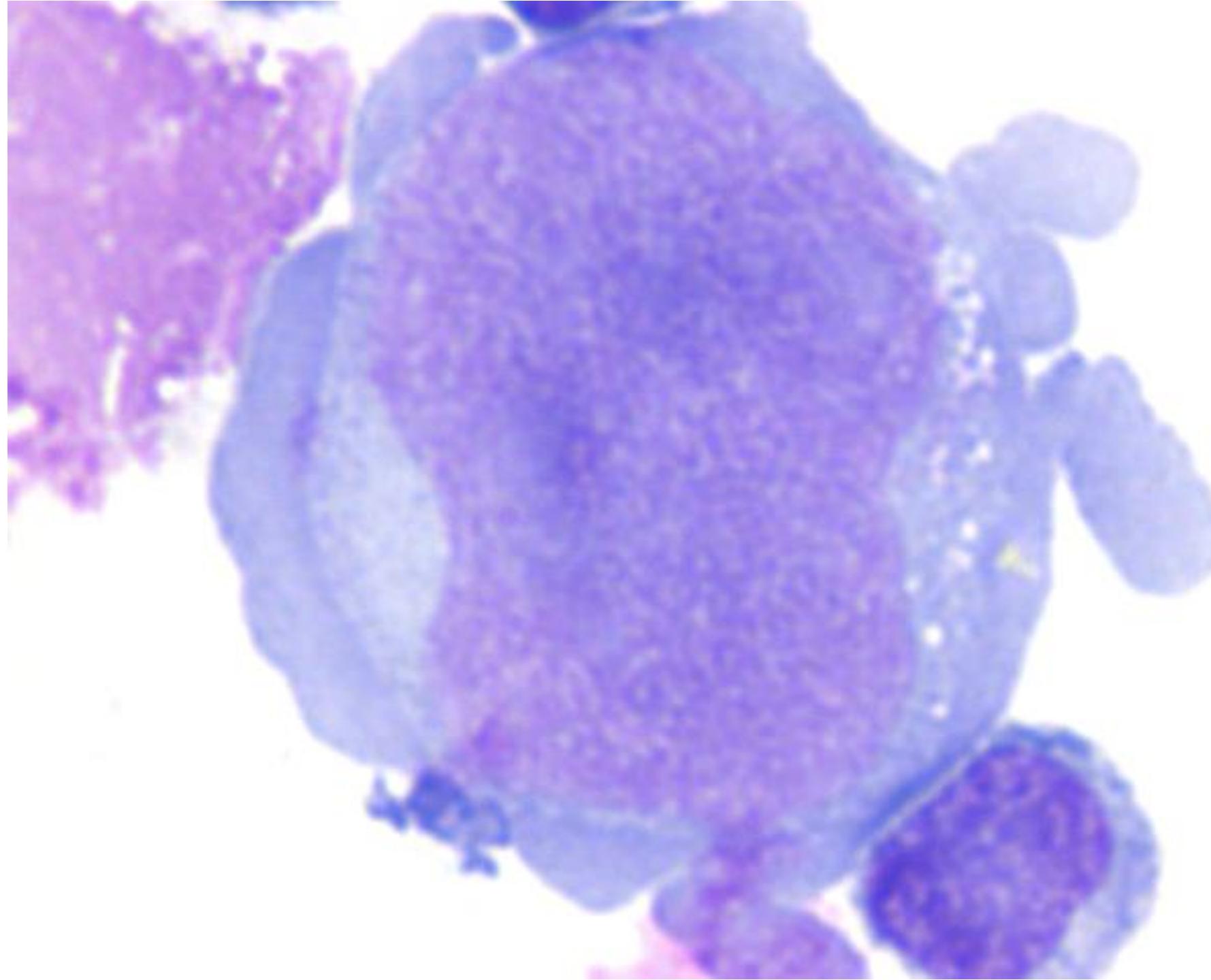
- Pueden mostrar vacuolas en uno de los polos de la célula: Neoplasia secretora.
- Presencia de mitosis anómalas.
- Facilidad de las células neoplásicas para fagocitar a otras células: *Canibalismo*.

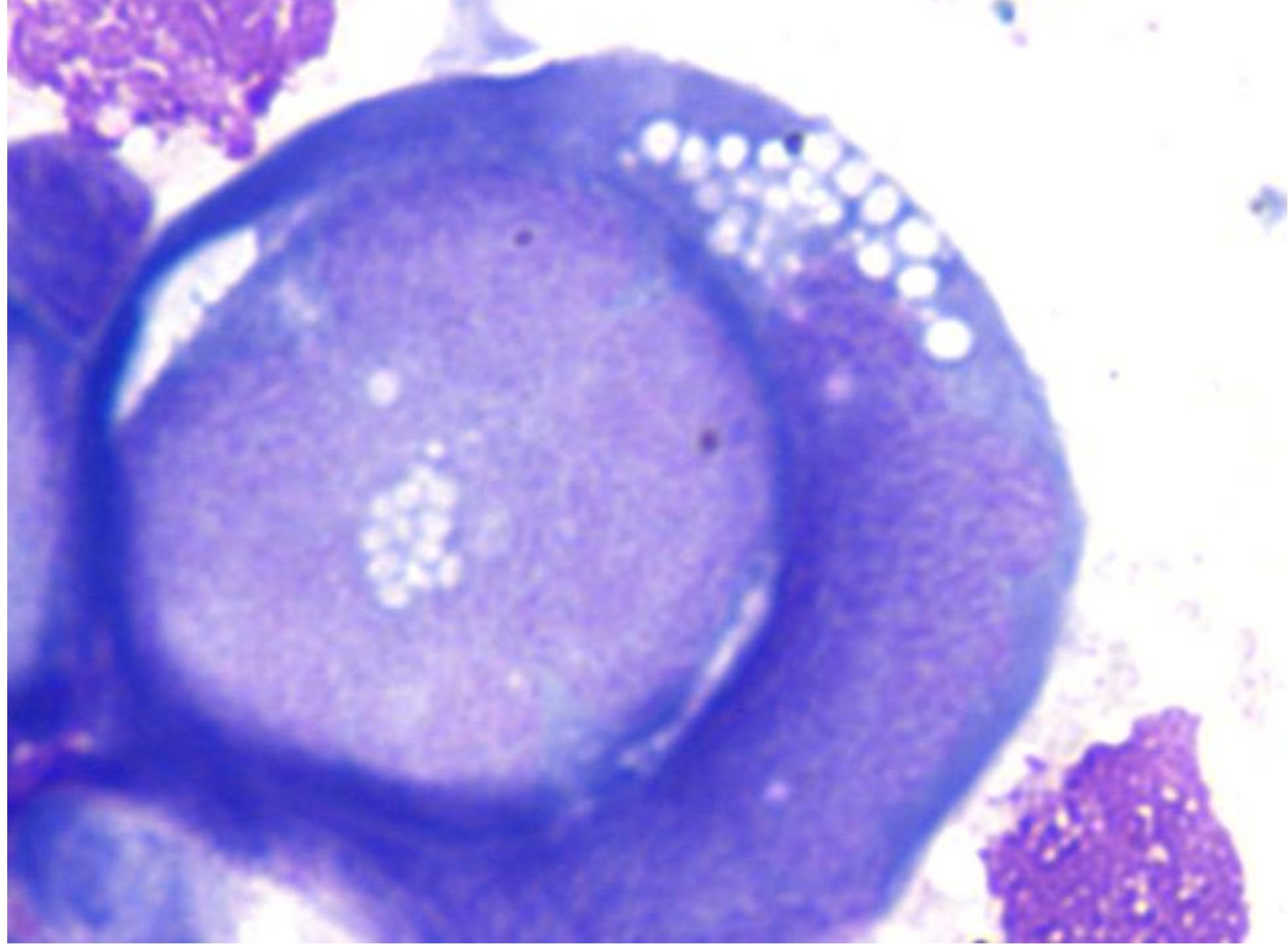
Células neoplásicas III

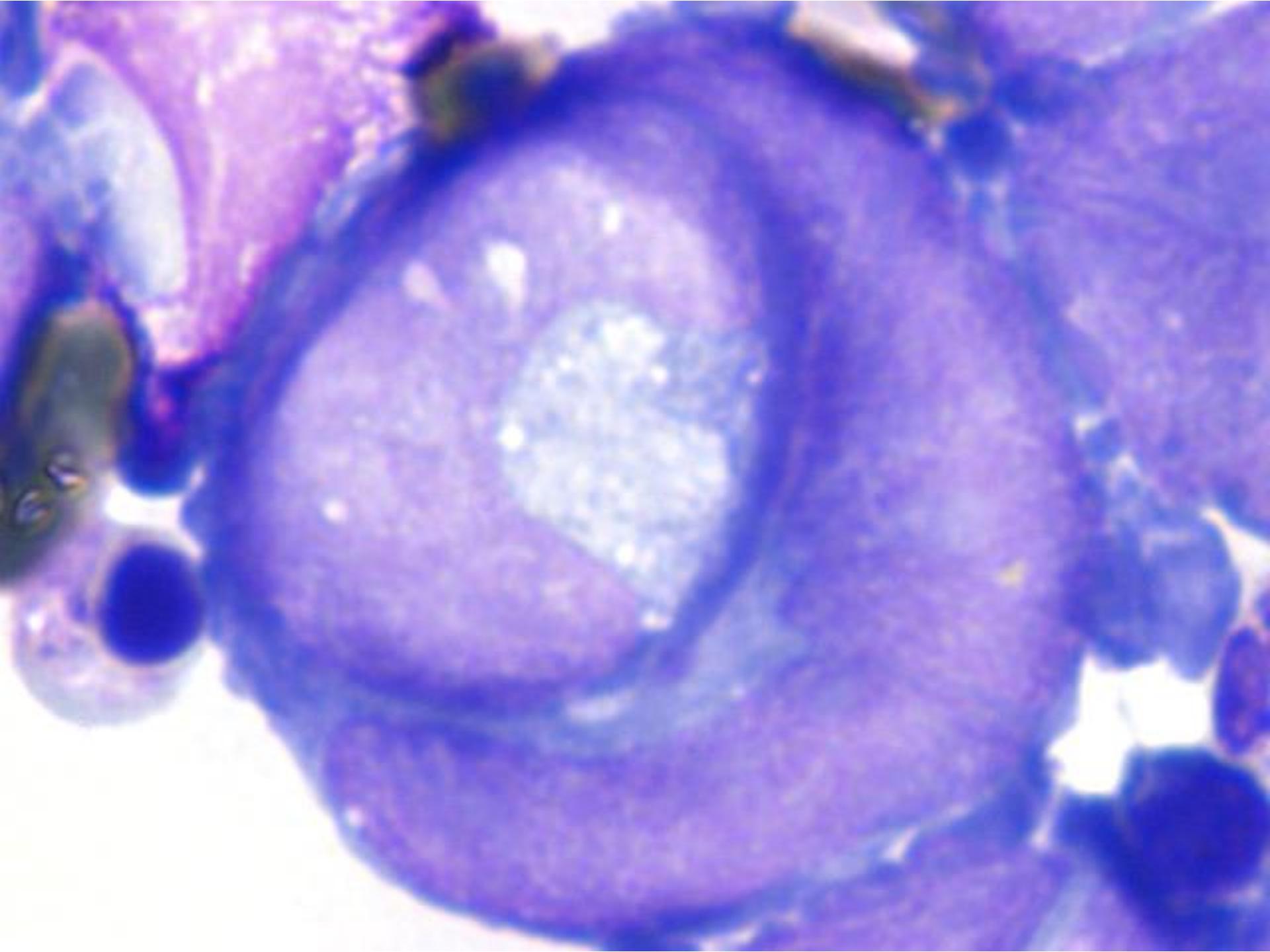
- En los derrames peritoneales las células neoplásicas que pueden observarse más frecuentemente son las del tracto gastrointestinal y ovario.
- En los derrames pleurales las células neoplásicas más frecuentes que pueden observarse son las de pulmón y mama.

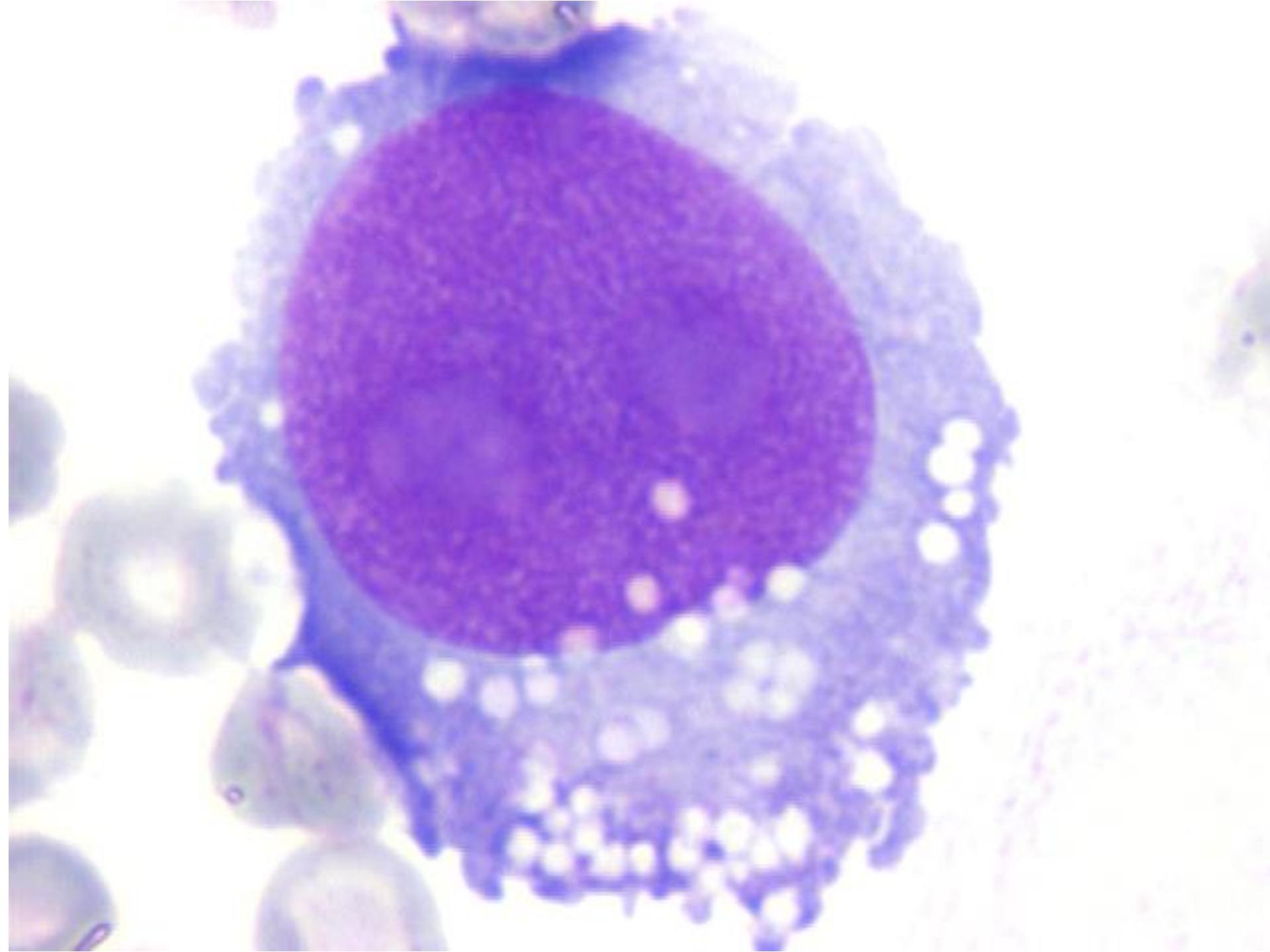


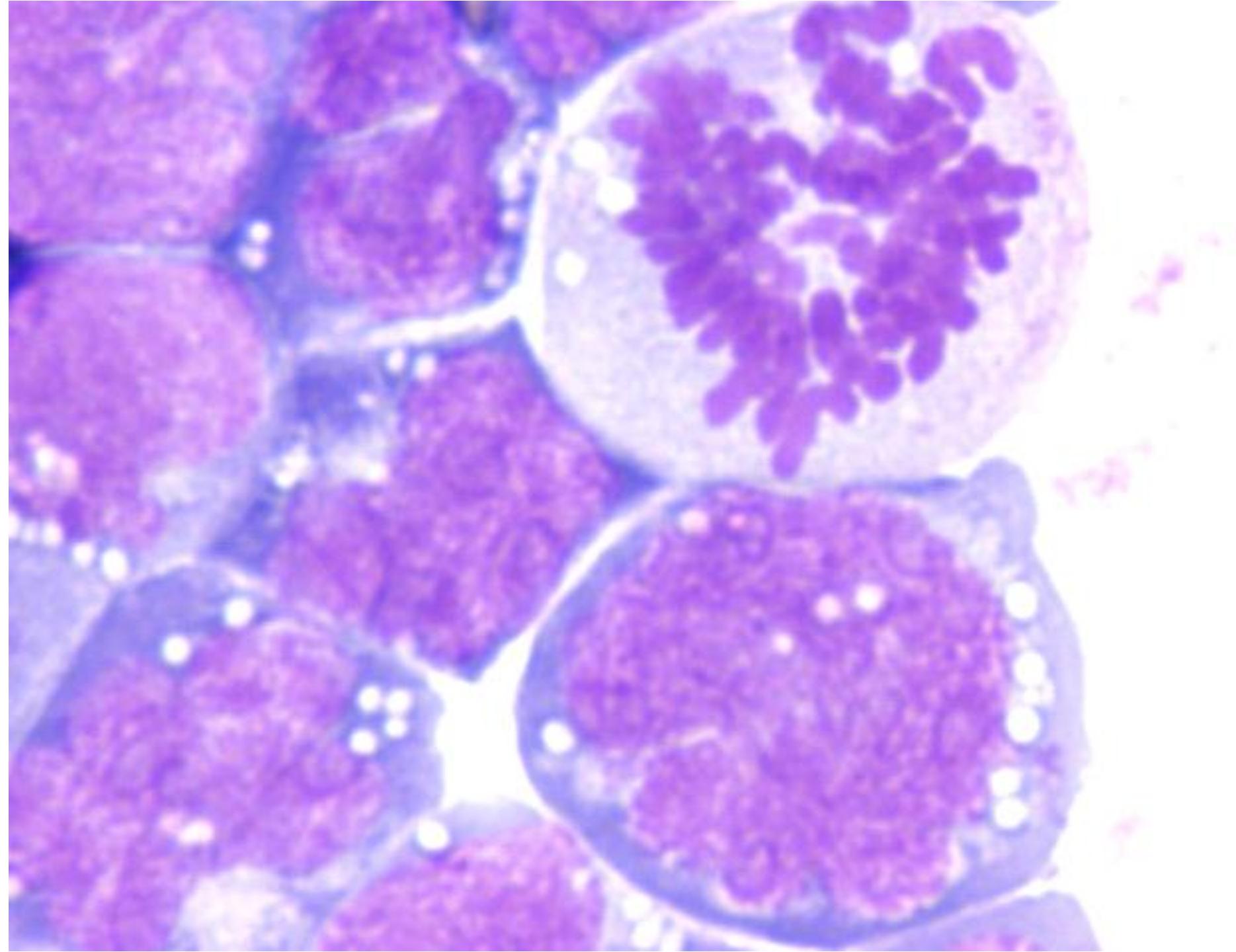


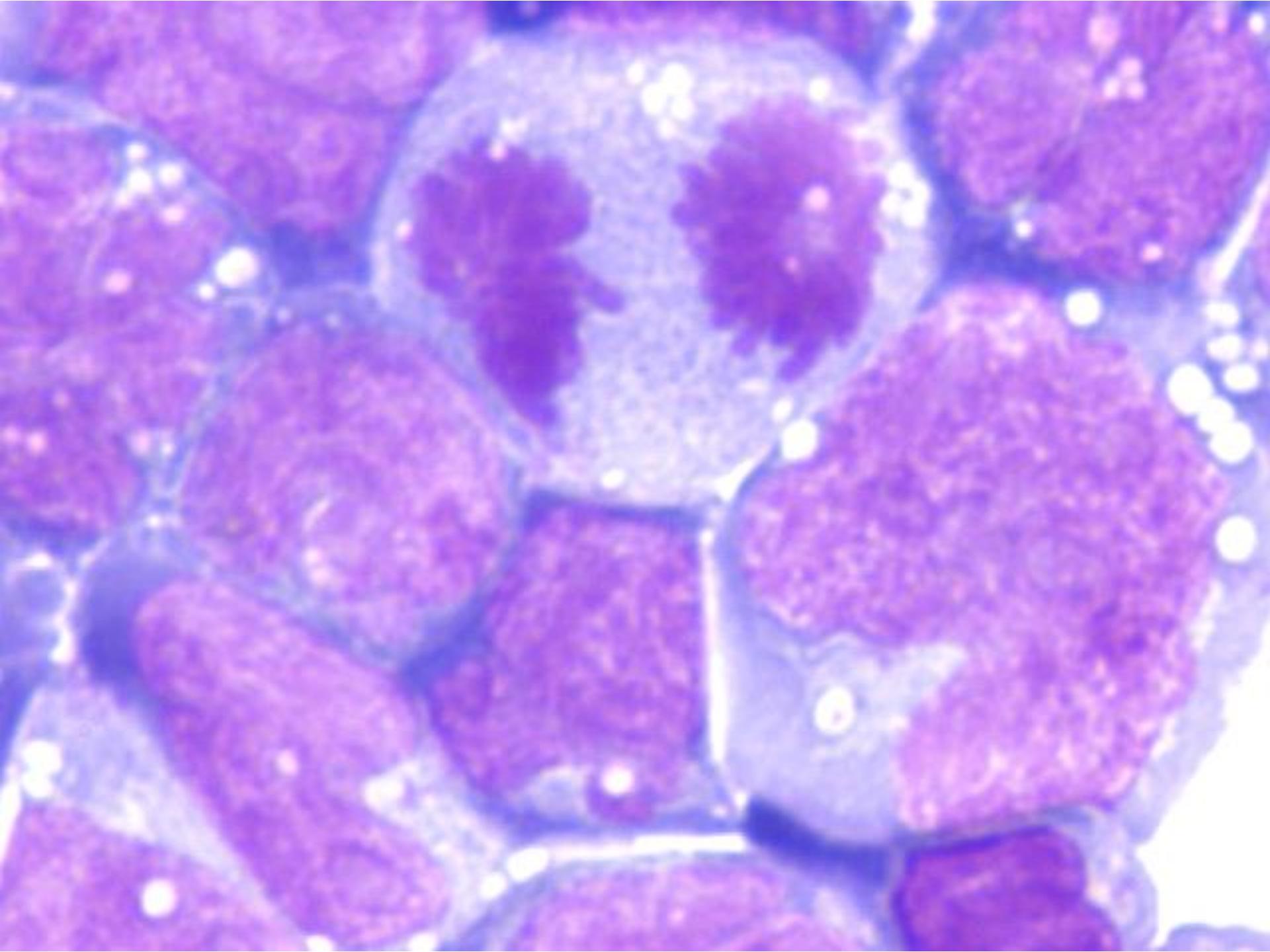


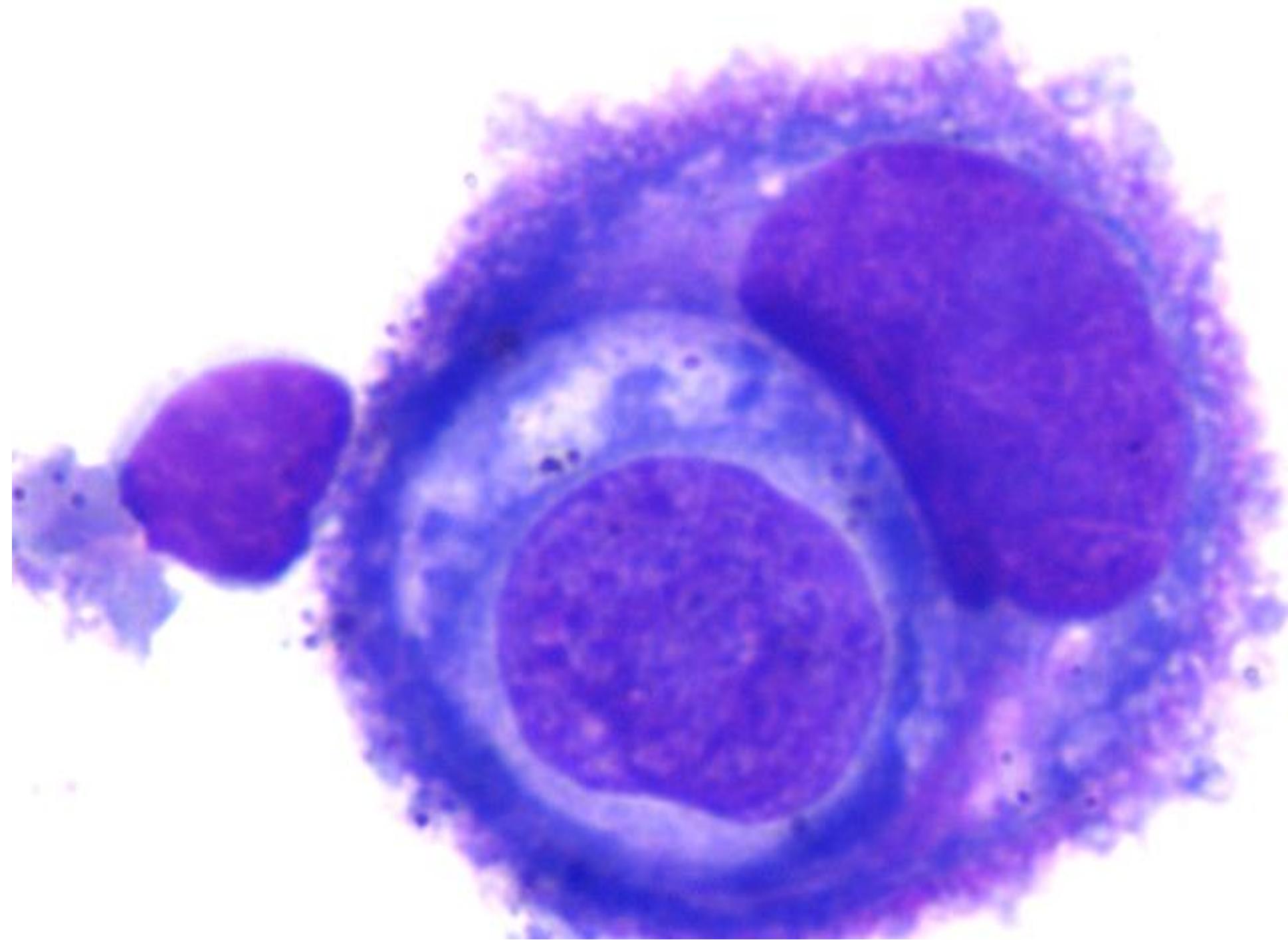


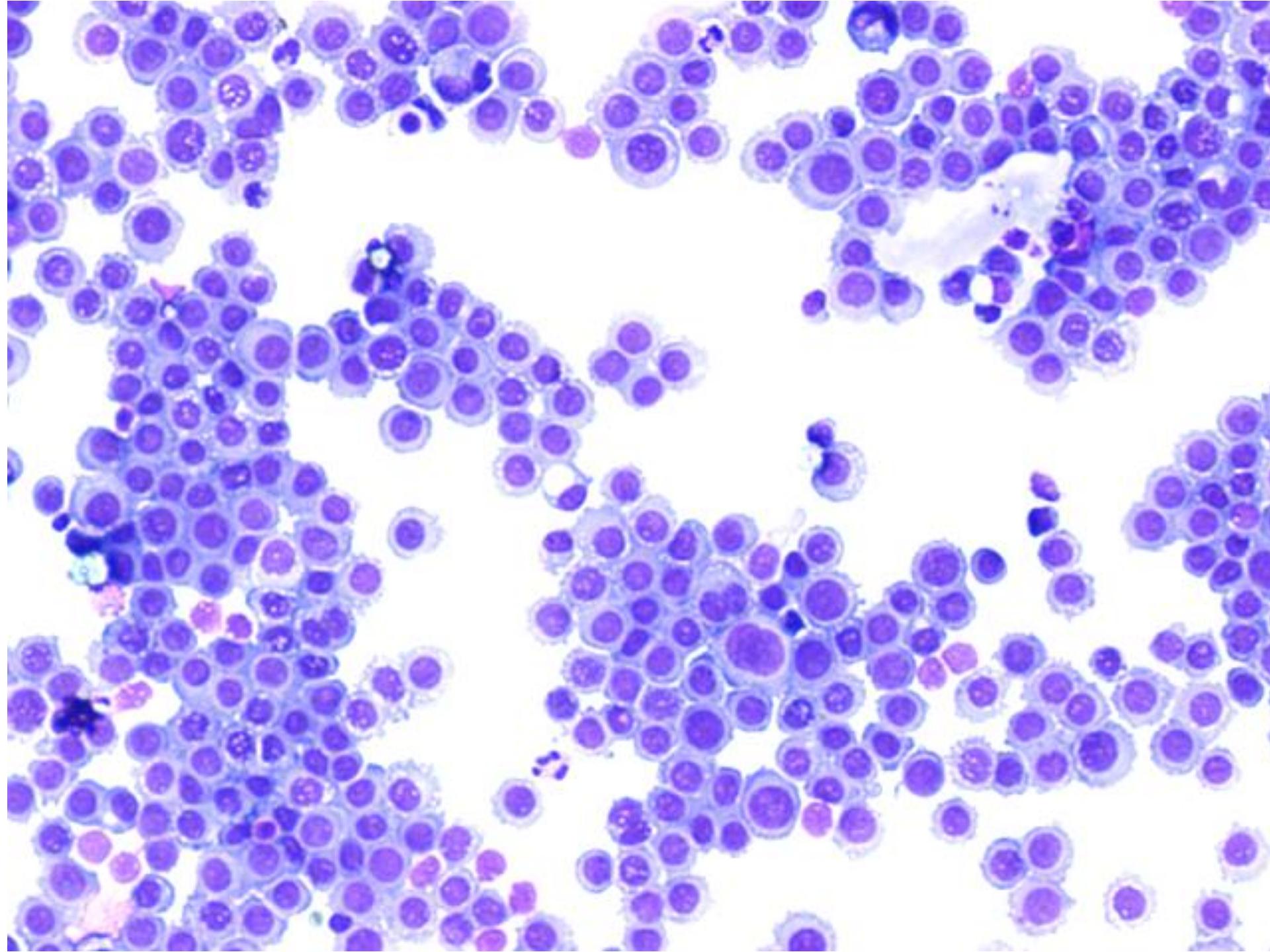


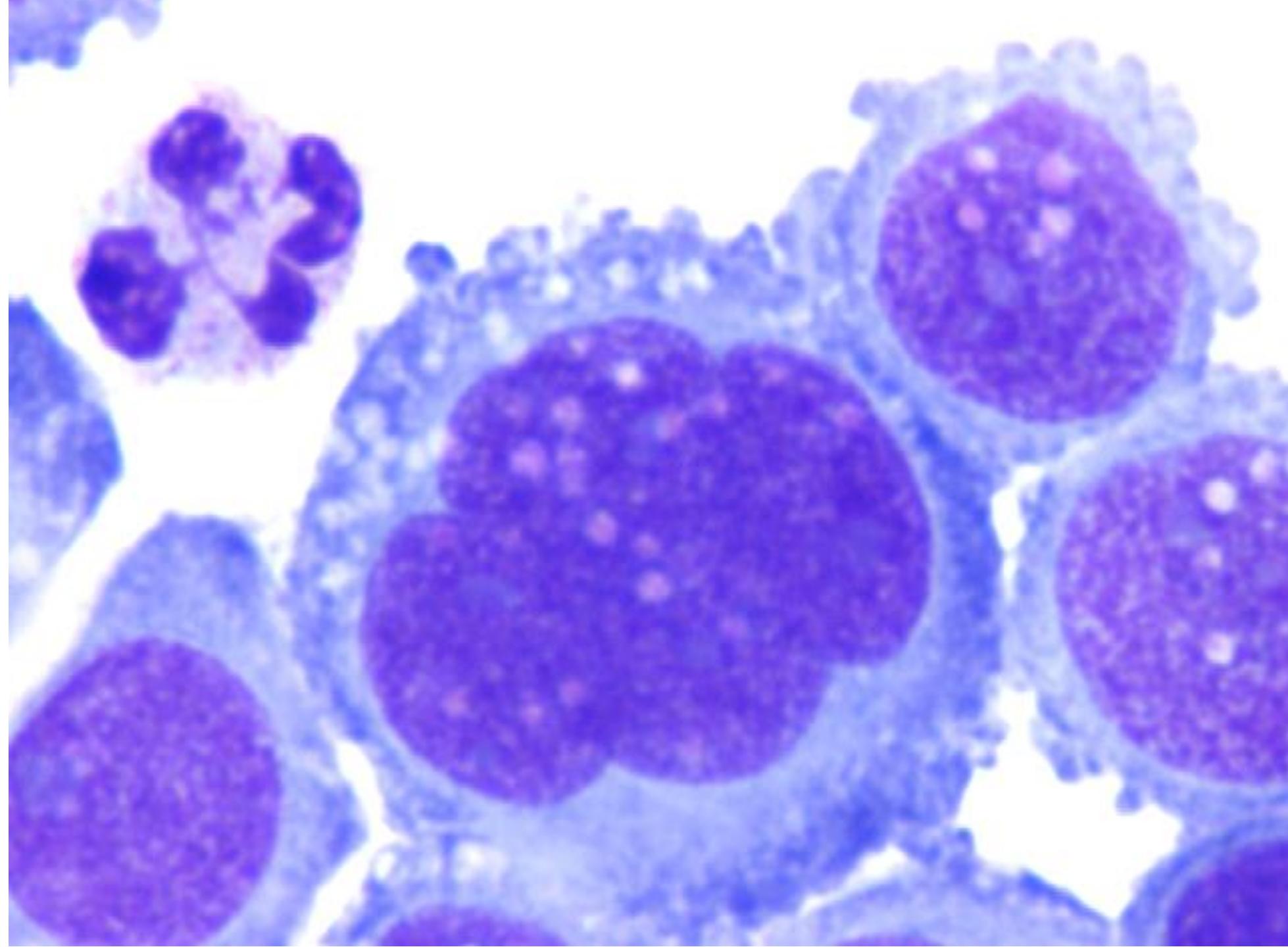


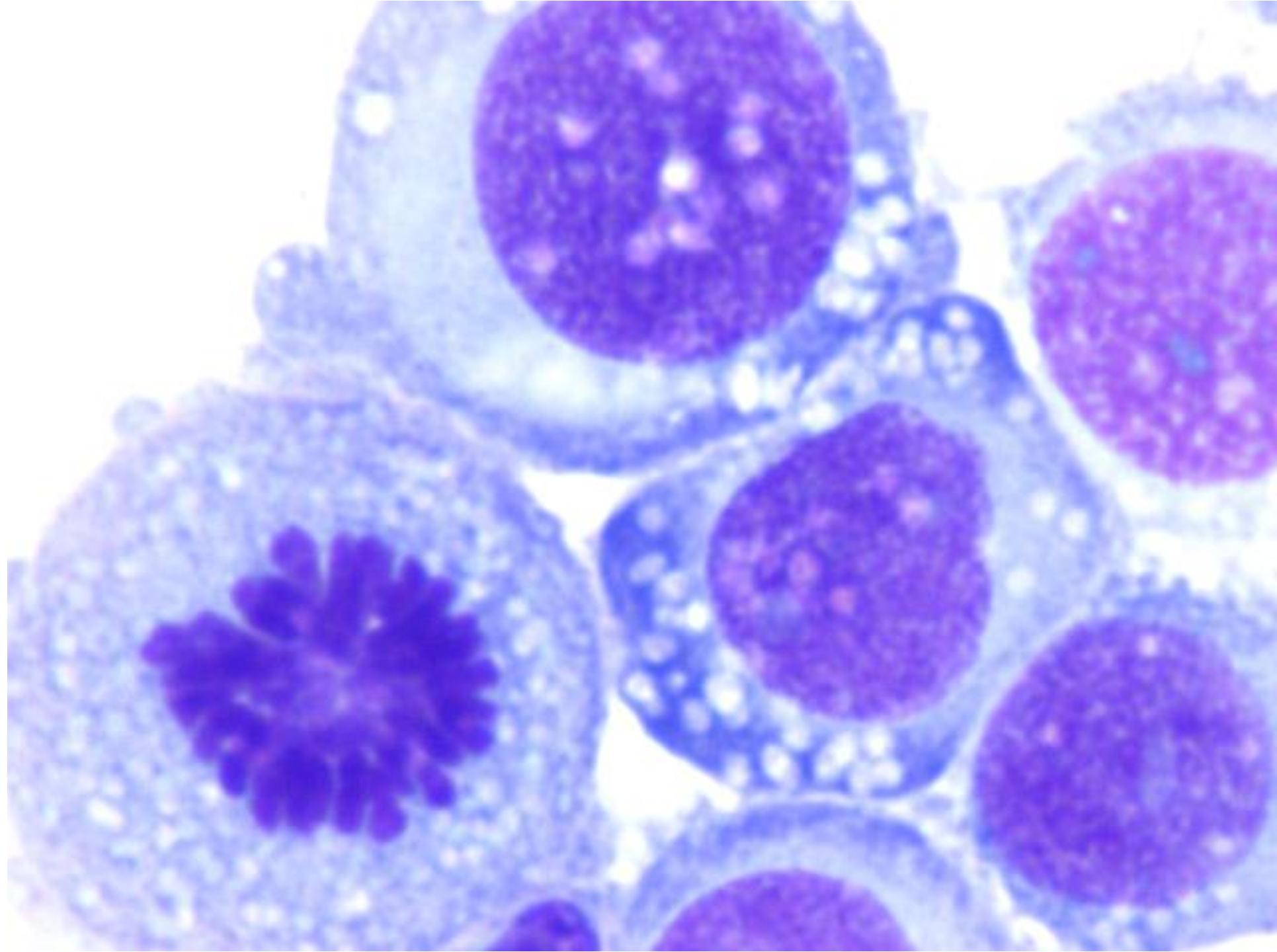


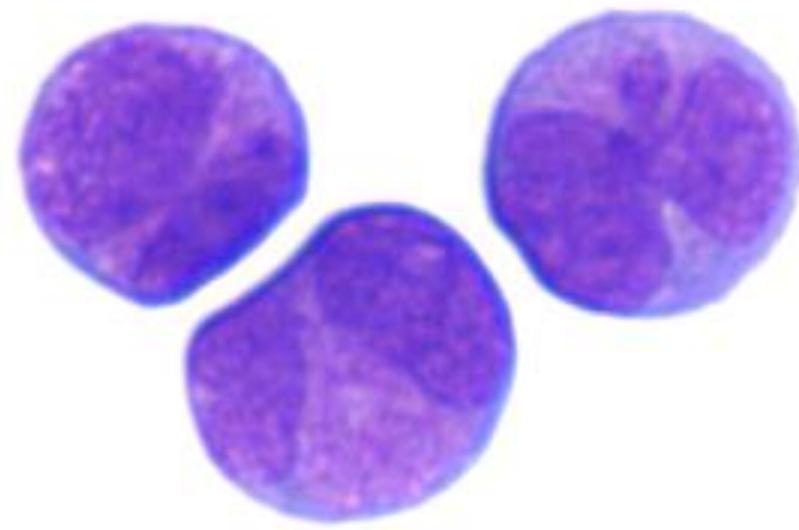


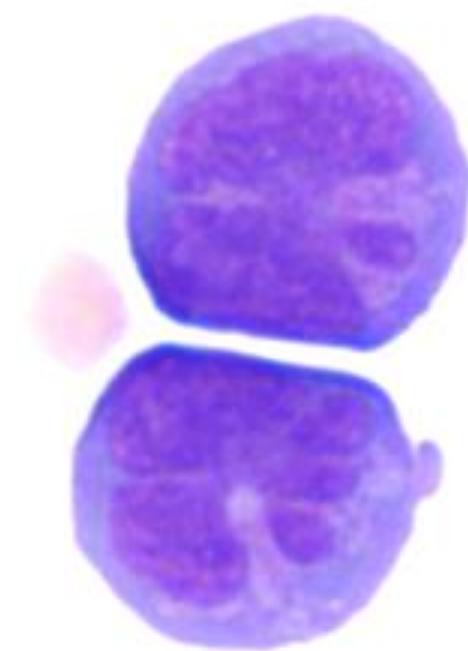
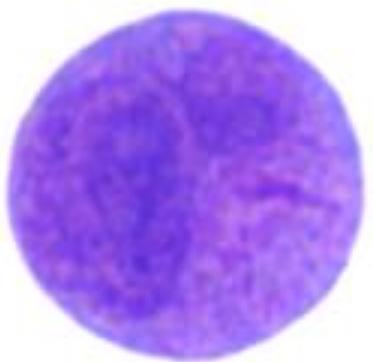
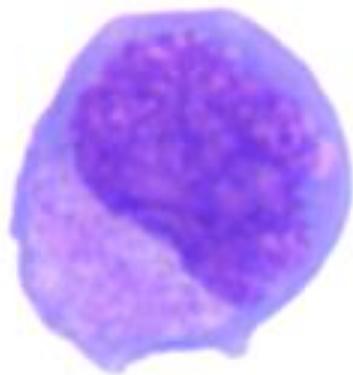












Conclusiones

- A pesar de los avances que han experimentado los equipos automatizados de recuento celular, el examen citológico del frotis de sangre periférica sigue siendo fundamental en el diagnóstico de las enfermedades no solo hematológicas, sino también no hematológicas ocultas en los pacientes que se realizan una primera analítica en nuestro hospital.

Conclusiones

- La observación de la sangre periférica por el facultativo, en la primera analítica de un paciente con signos de alarma en el hemograma, puede contribuir a una mayor rapidez en el diagnóstico del paciente, así como a determinar y seleccionar otras pruebas diagnósticas complementarias de utilidad en el diagnóstico diferencial.

Conclusiones

- La citología de líquidos biológicos es una herramienta diagnóstica fundamental del laboratorio clínico para la detección de neoplasias ocultas, especialmente en los pacientes que acuden a Urgencias.



3^a Jornada Profesional del Laboratorio Clínico

Importancia del Laboratorio Clínico en el
Diagnóstico Precoz de la Enfermedad Oculta

Gracias por
su atención



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