PANCITOPENIA

Dra. Lilian Pilleux
Unidad de Hematologia
Hospital de Valdivia

Citopenia

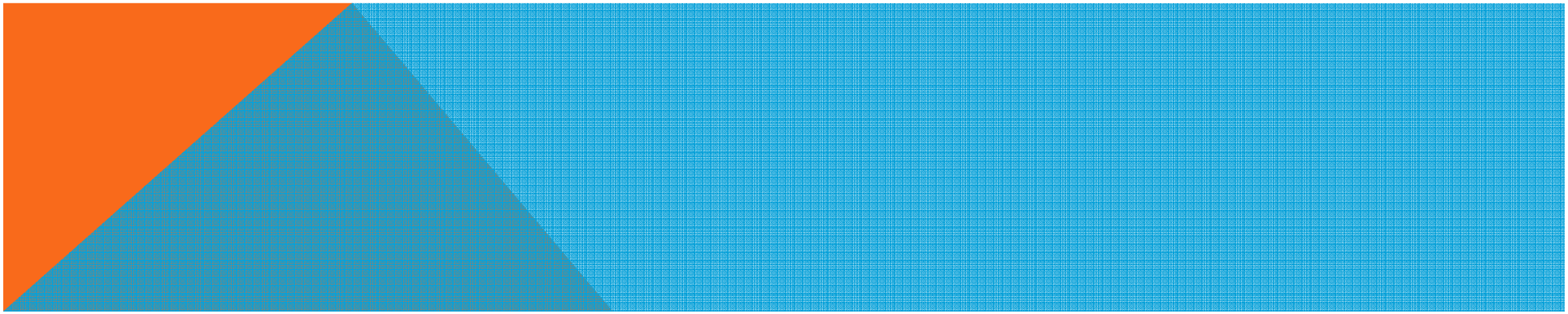
- Definición: Condición en que uno o más líneas celulares sanguíneas están disminuídas.

Pancitopenia

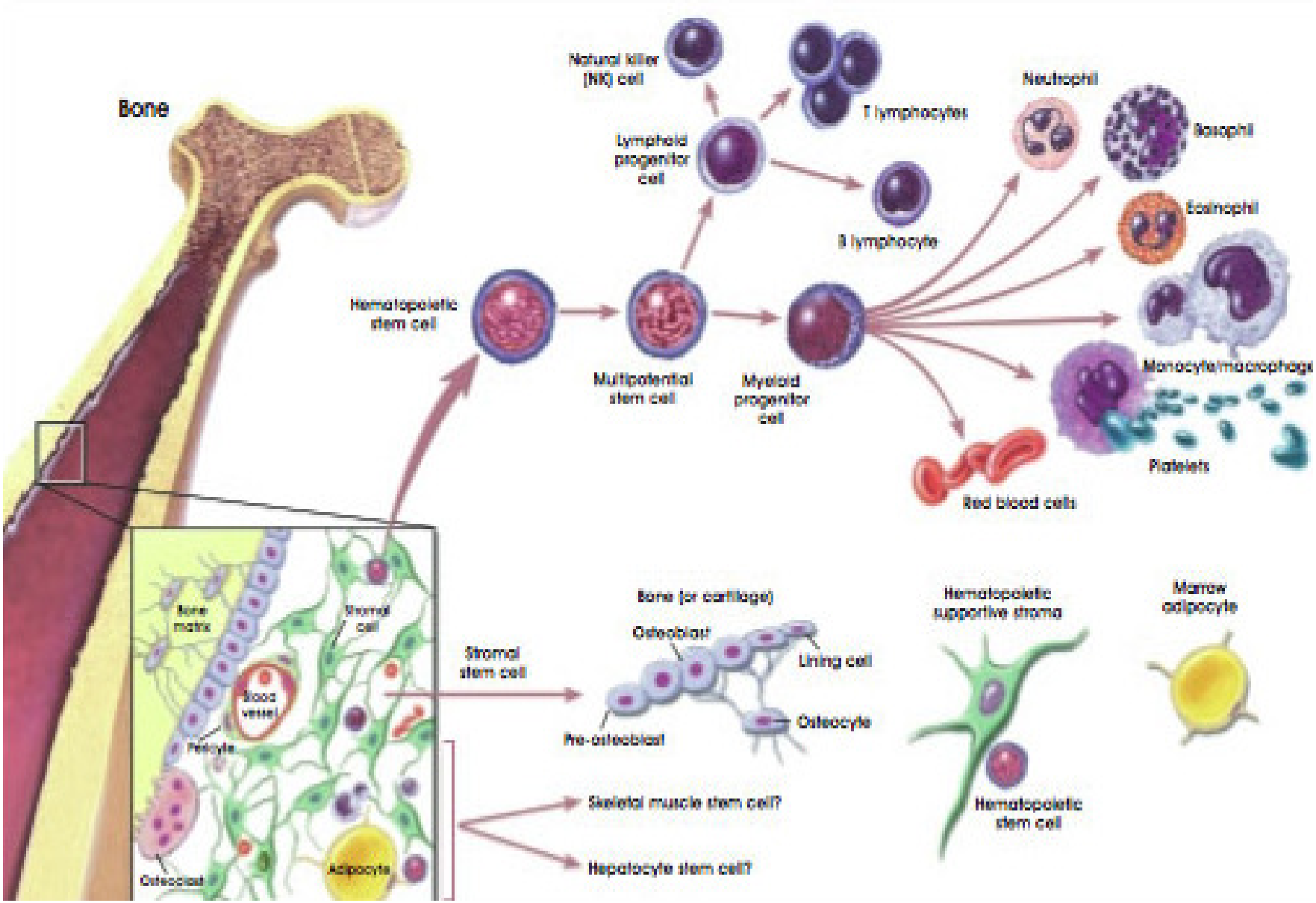
- Presencia simultánea de anemia, leucopenia y trombocitopenia.
- No es una enfermedad en sí, sino el signo de una que necesita ser diagnosticada.

Recuentos Hematológicos Normales y Definición Citopenias (WHO)

	Hb (g/dL)	RAN (x uL)	Plaq (x uL)
Normal	≥ 12(f) ≥ 13(m)	≥ 1800	≥ 150.000
Citopenia	< 12 (f) < 13(m)	< 1800	< 150.000



Hematopoyesis Normal



Regulación de la Hematopoyesis

Factores de Crecimiento

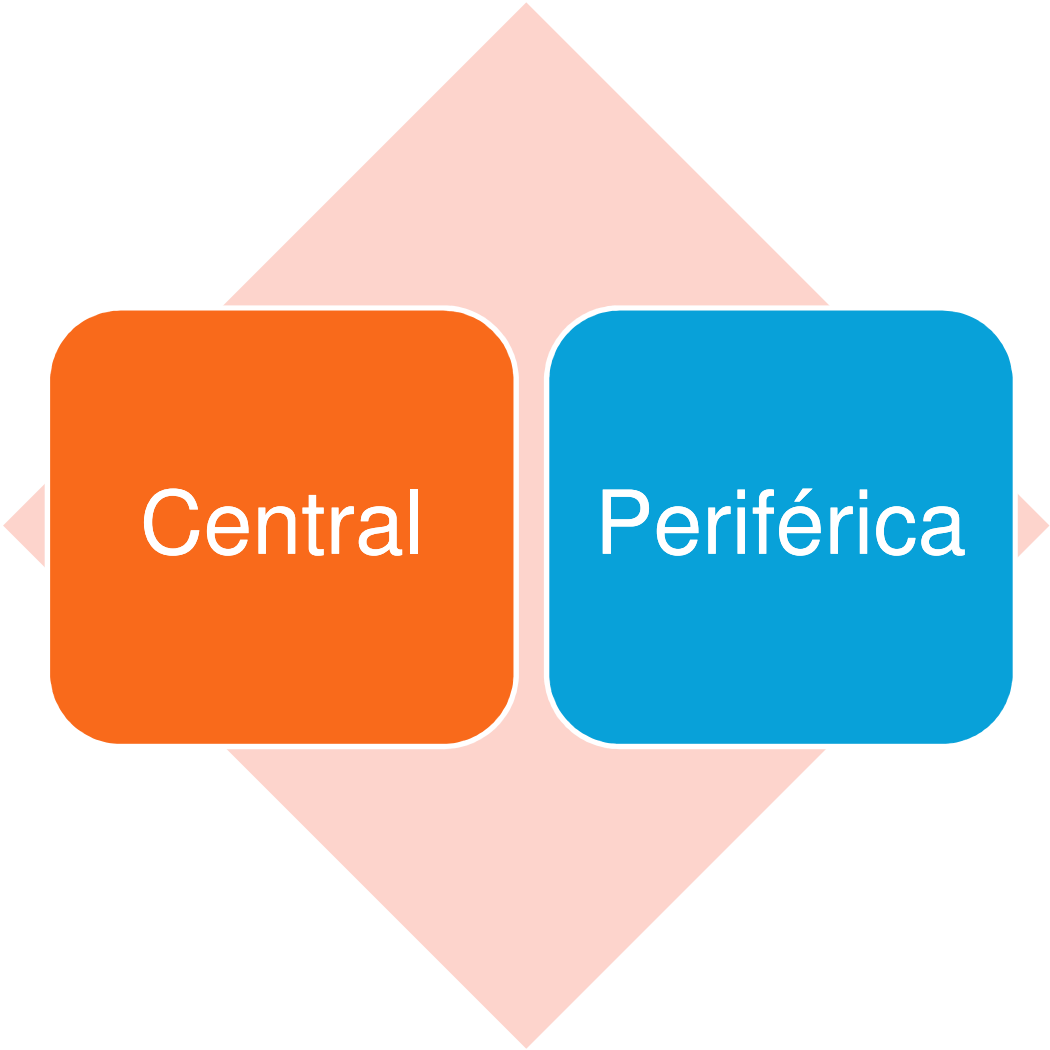
Citoquinas

Microambiente Medular

Factores Genéticos, Epigenéticos y Metabólicos

Mecanismos de Regulación Negativos y Clearance

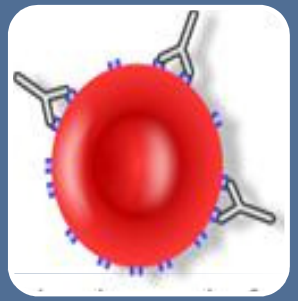
Pancitopenia



Causas de Falla Medular Adquirida

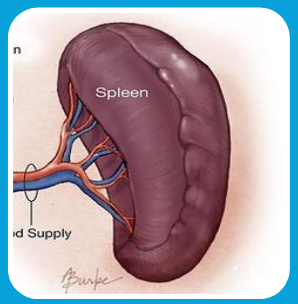
- **Aplasia Medular**
- **Síndromes Mielodisplásticos**
- **Leucemias Agudas**
- **Mieloptisis**
- **Fibrosis Medular**
- **Anemia Megaloblástica Severa**
- **Infección Severa HIV**
- **Síndrome Hemofagocítico**
- **Leucemia Linfocitos Granulares Grandes**
- **Degeneración Gelatinosa M.O.**
  (Anorexia nerviosa)

Causas de Pancitopenia de Origen Periférico



Destrucción Inmune

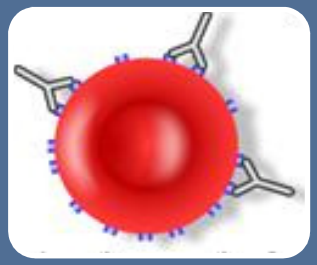
- Pancitopenias Autonmunes



Secuestro

- Hiperesplenismo

Causas de Pancitopenia de Origen Periférico

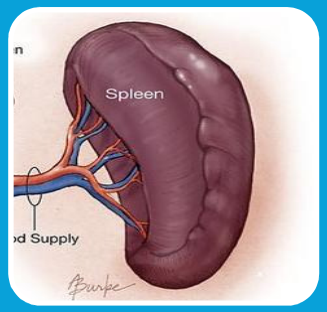


Destrucción Inmune

- Síndrome de Evans
- LES
- Otras enfermedades autoinmunes
- Síndrome Hemofagocítico

Causas de Pancitopenia de Origen Periférico

Secuestro



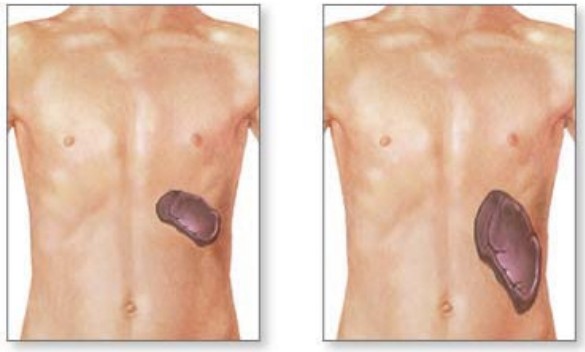
- Congestión (síndrome de Banti)
  - Cirrosis hepática
  - Trombosis vena porta
  - Síndrome Budd-Chiari
  - Insuficiencia Cardíaca Congestiva
- Enfermedades Infiltrativas
  - Neoplásias
  - Enfermedades de depósito
- Anemias Hemolíticas Hereditarias
- Infecciones
- Tumores
- Quistes

Hiperesplenismo

- **Aumento de las funciones normales del bazo.**

  (Control de calidad)

- **El hiperesplenismo habitualmente se asocia a esplenomegalia.**



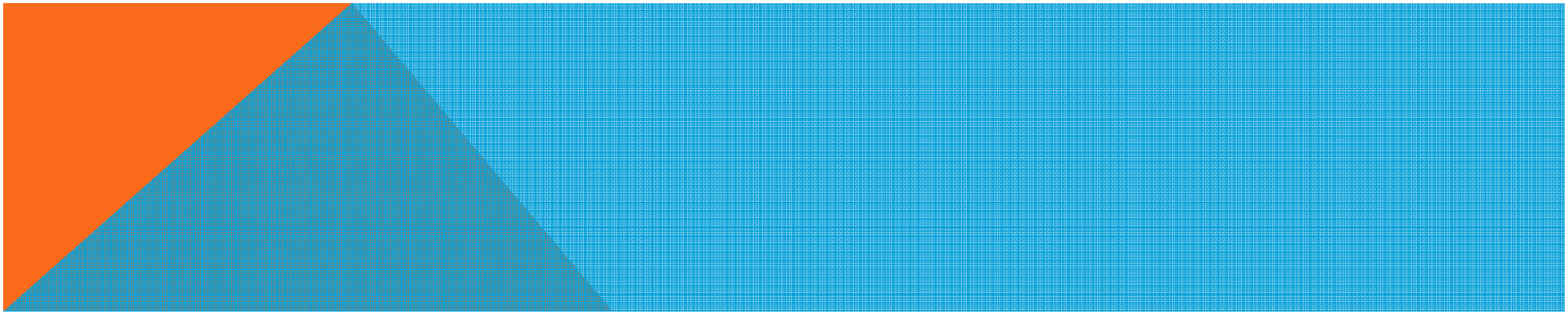
Hiperesplenismo

- Plaquetas son más susceptibles de ser secuestradas.

- Los leucocitos secuestrados, así como las plaquetas, pueden tener una sobrevida normal en el bazo encontrándose disponibles, aunque en forma lenta en caso de necesidad.

- Los glóbulos rojos son menos autosuficientes metabólicamente pudiendo ser destruidos en forma prematura en la pulpa roja.

- Las citopenias producen un aumento de la producción medular.



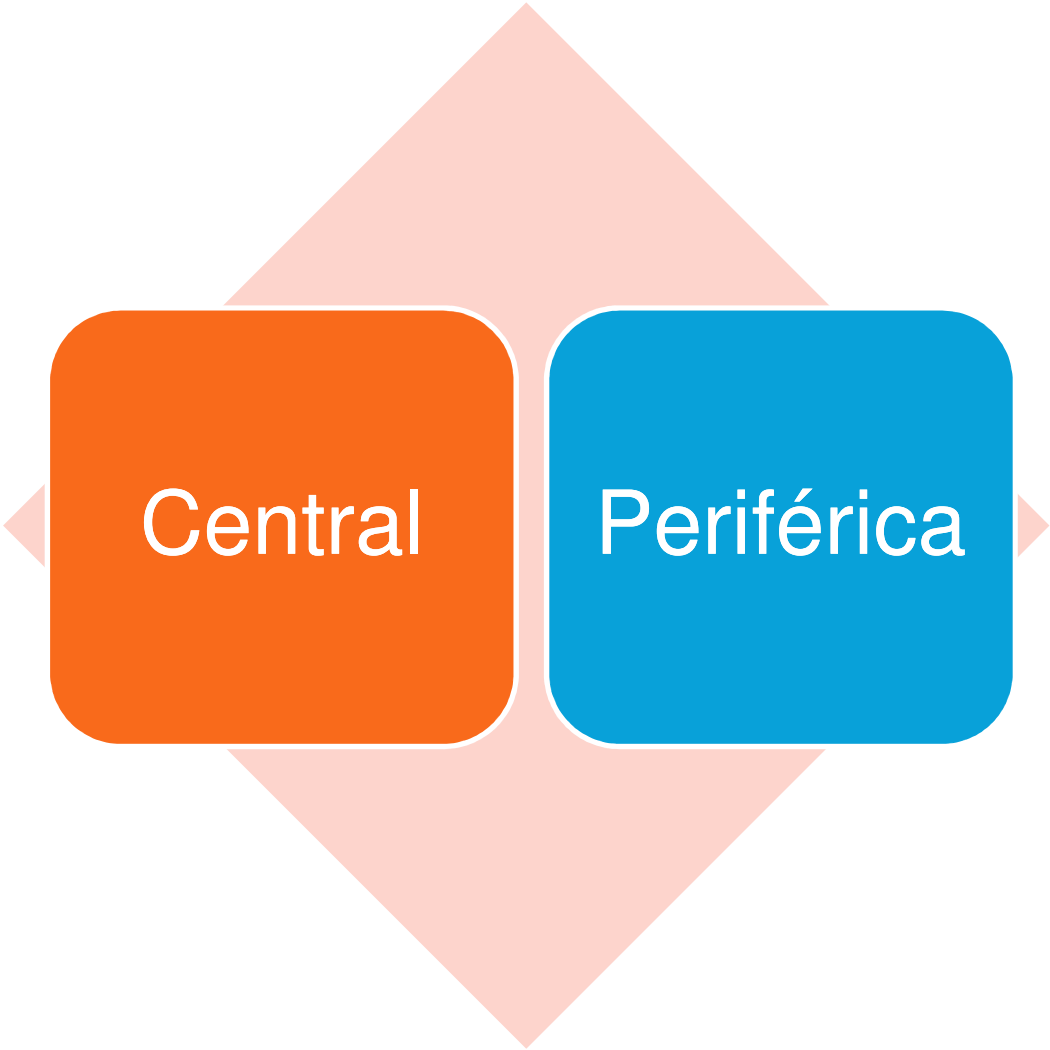
Triada del Hiperesplenismo

Citopenias

Esplenomegalia

Hiperplasia M.O.

Pancitopenia



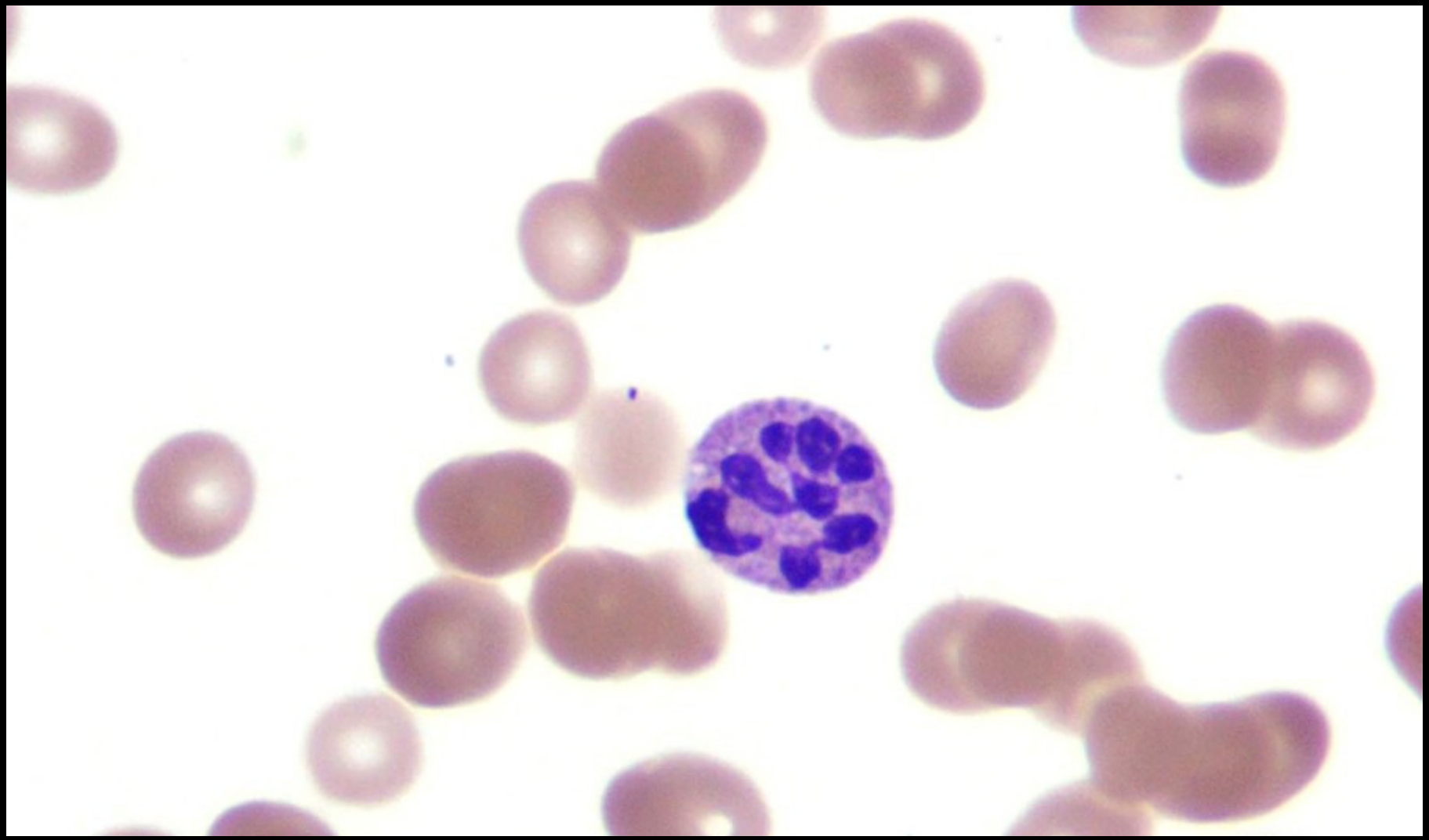
Estudio Paciente con Pancitopenia

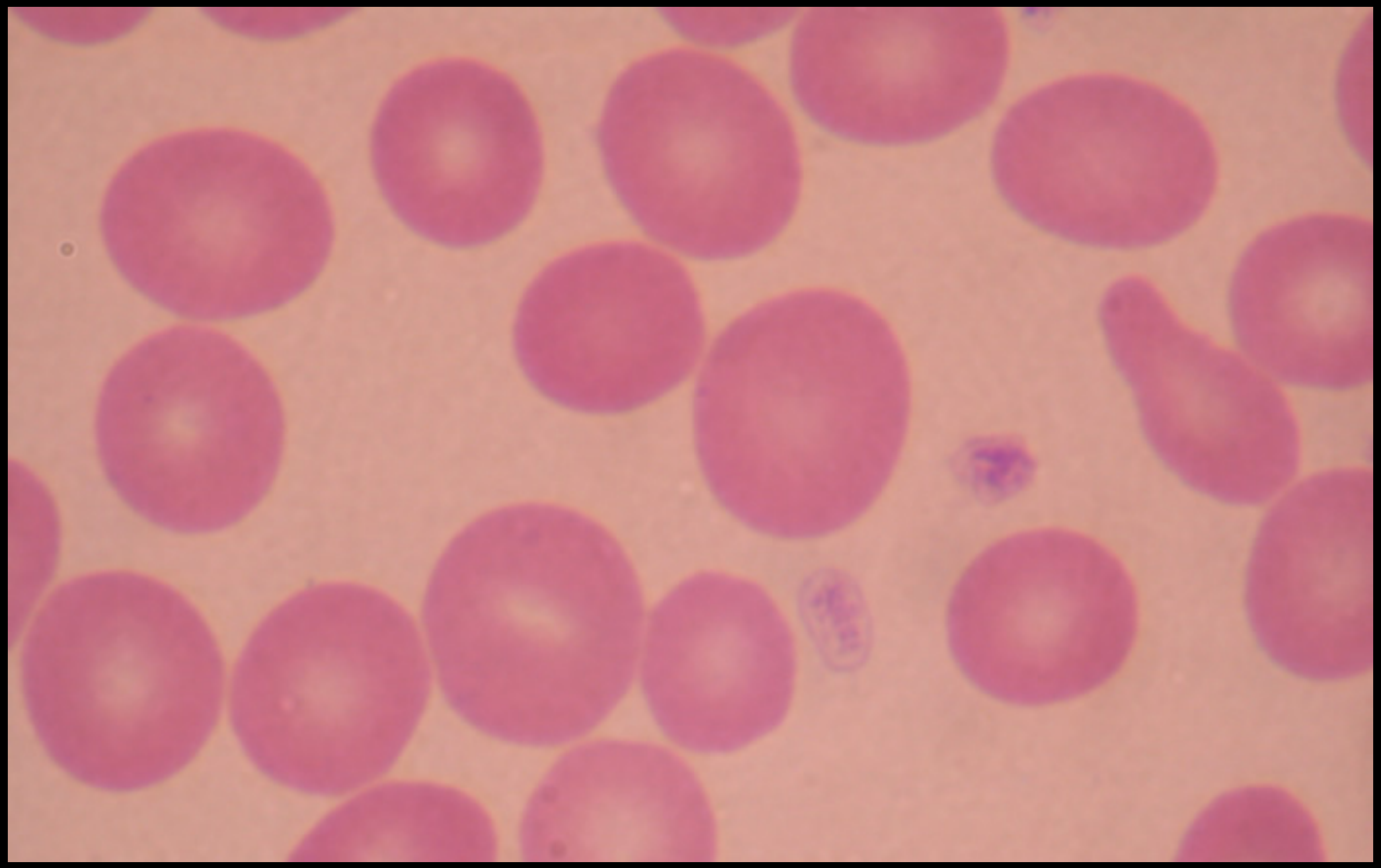
- **Anamnesis y Examen Físico**
- **Exámenes**:
  - Hemograma
  - Perfil Bioquímico
  - PCR
  - Ferritina
  - Fibrinógeno
  - Ig G-A-M
  - Imagenología
    - Ecografía
    - TC Abdomen

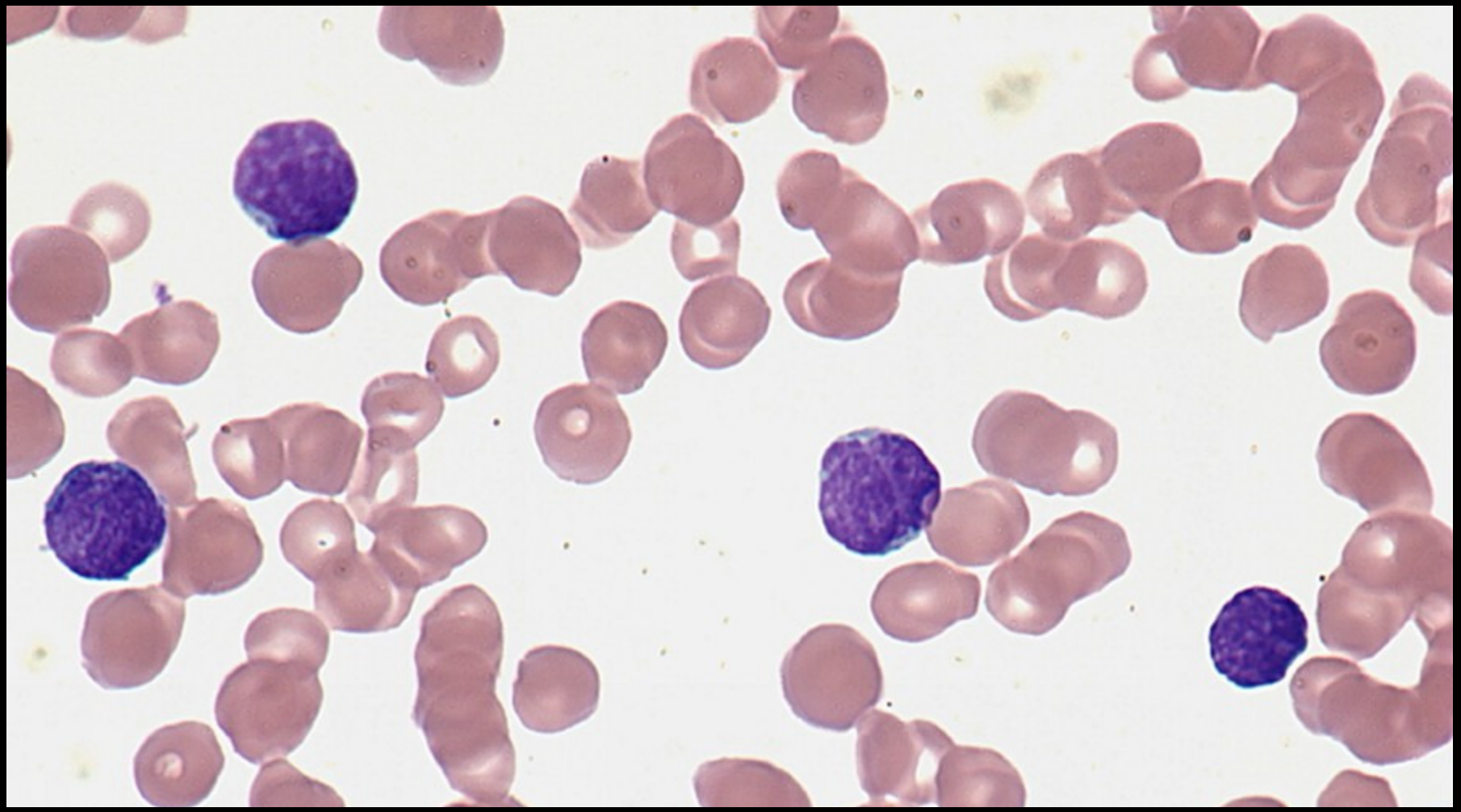
Hemograma

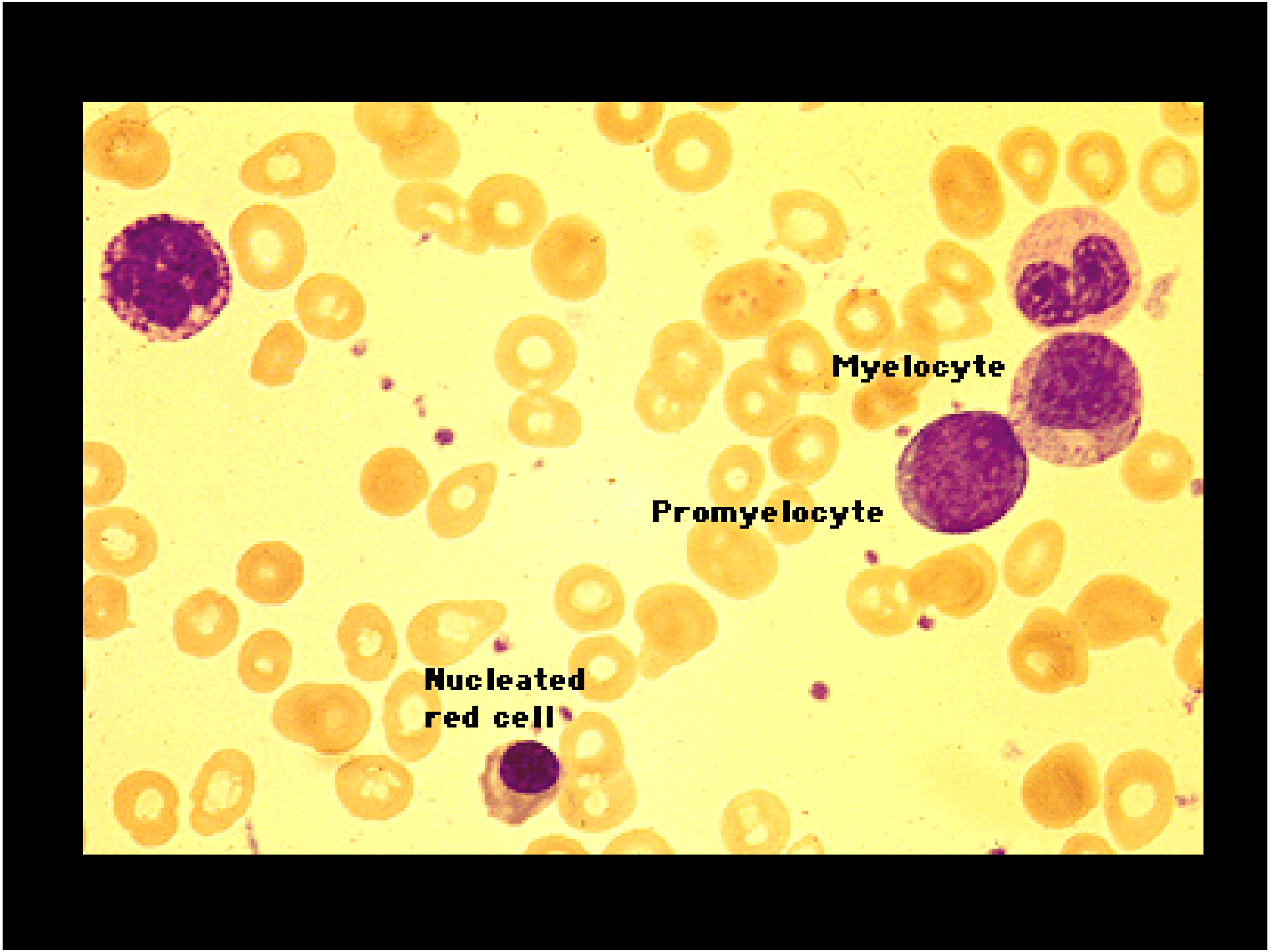
Incluye: - Análisis de frotis sanguíneo

- Recuento reticulocitos.

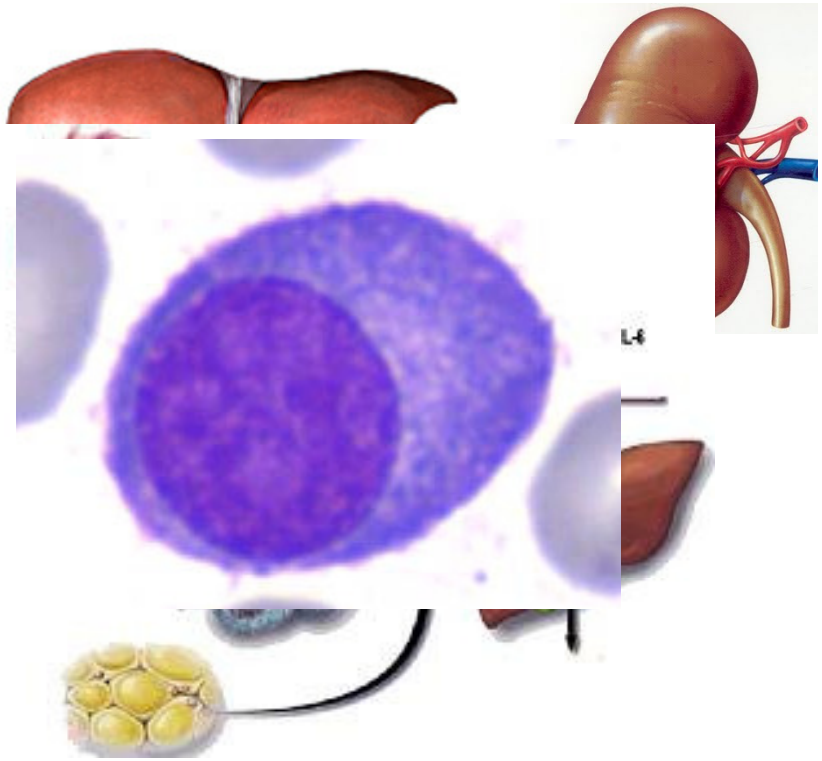




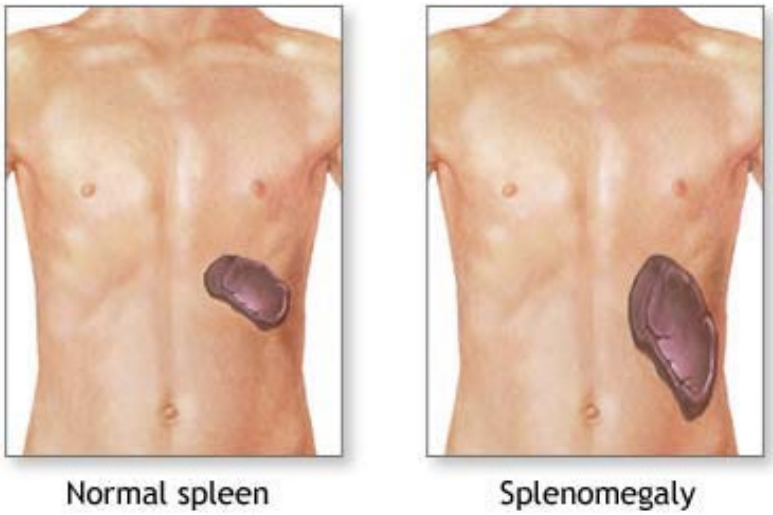


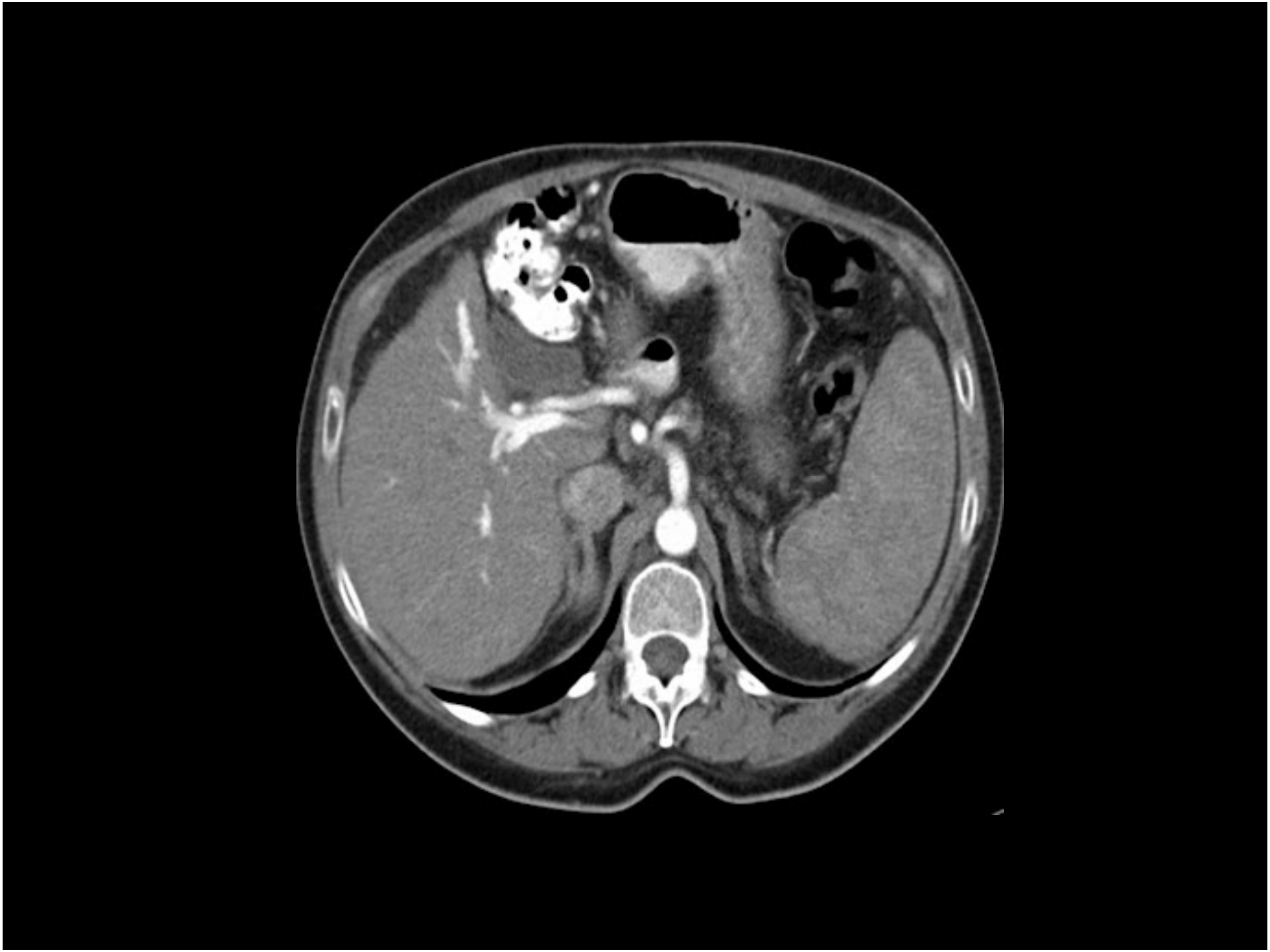

Myelocyte
Promyelocyte
Nucleated
red cell

- Perfil Bioquímico
- PCR
- Ferritina
- Fibrinógeno
- Ig G-A-M
- Niveles Vitamina B12

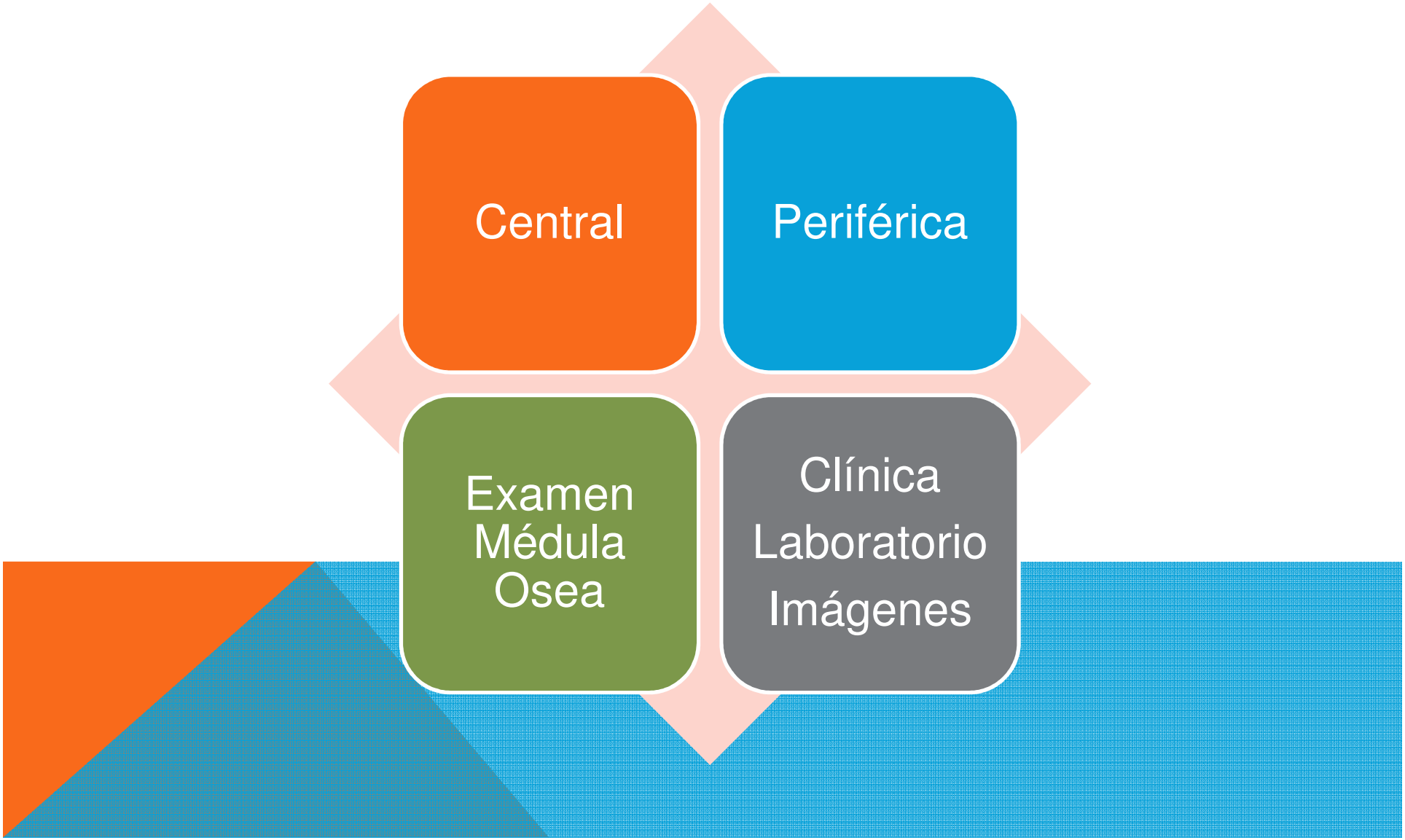


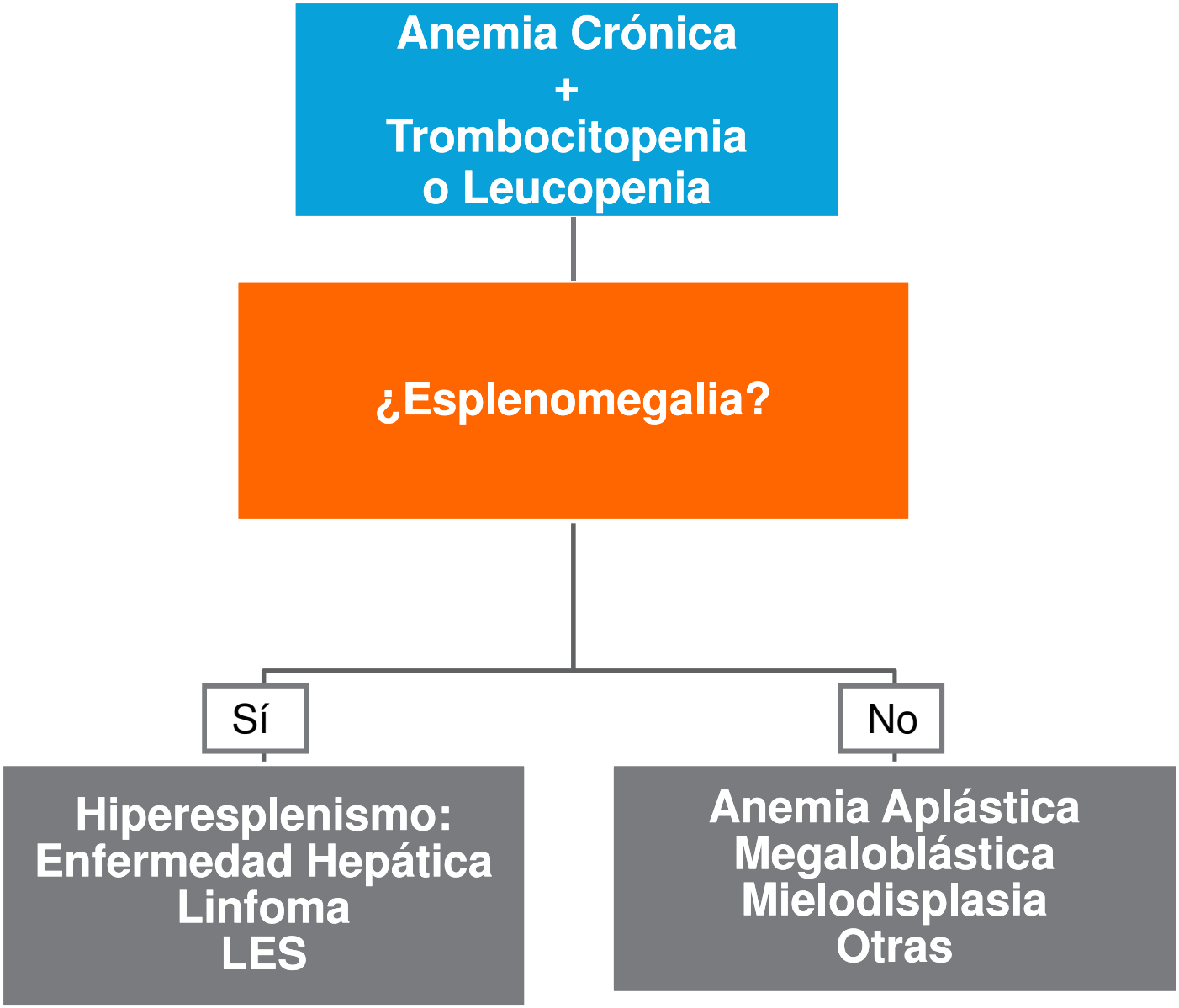
- Imagenología
  - Ecografía
  - Tomografía computada
  - Rx Torax ?





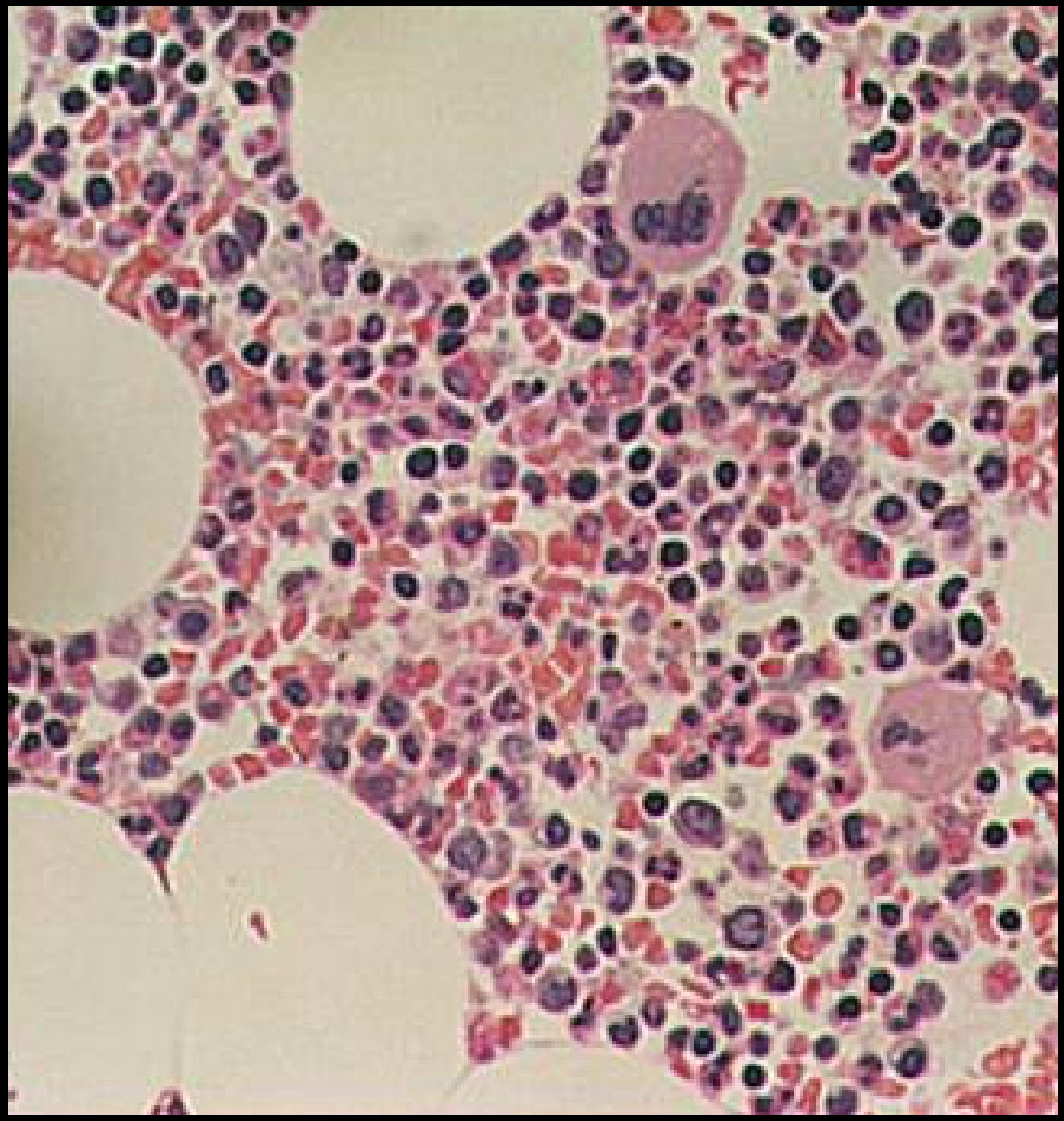
Pancitopenia

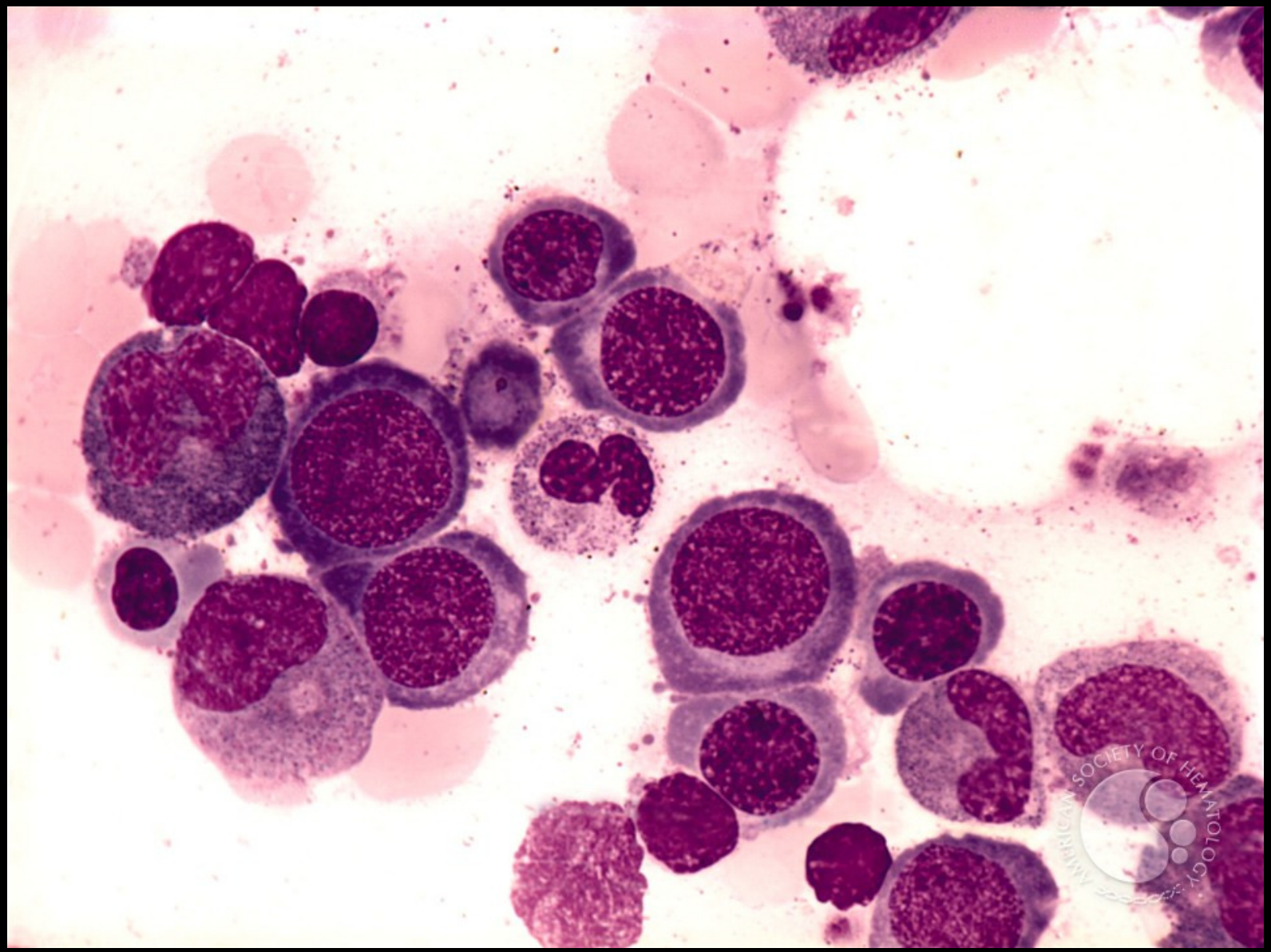


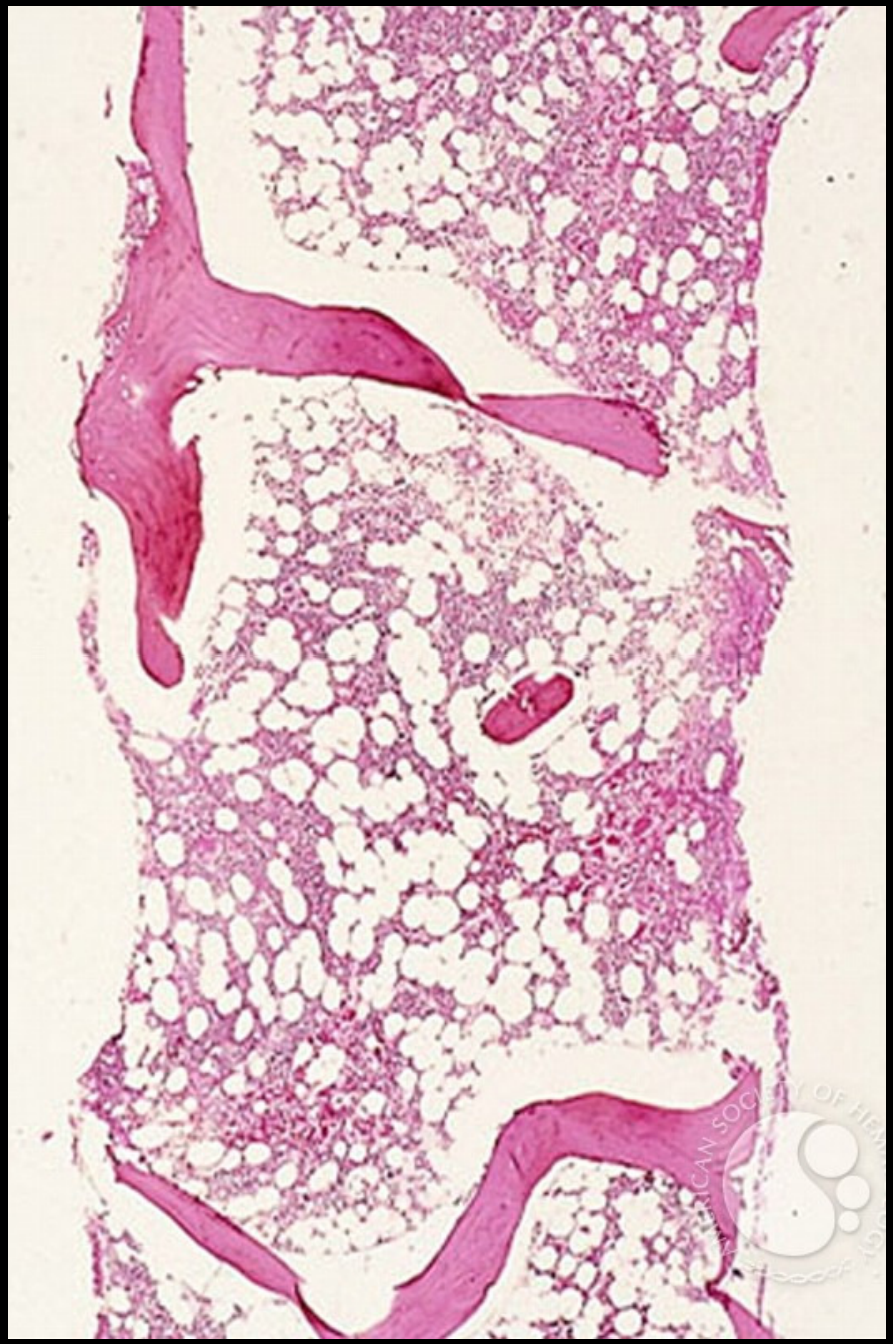

Anemia Crónica
+
Trombocitopenia
o Leucopenia
¿Esplenomegalia?
Sí
No
Hiperesplenismo:
Enfermedad Hepática
Linfoma
LES
Anemia Aplástica
Megaloblástica
Mielodisplasia
Otras

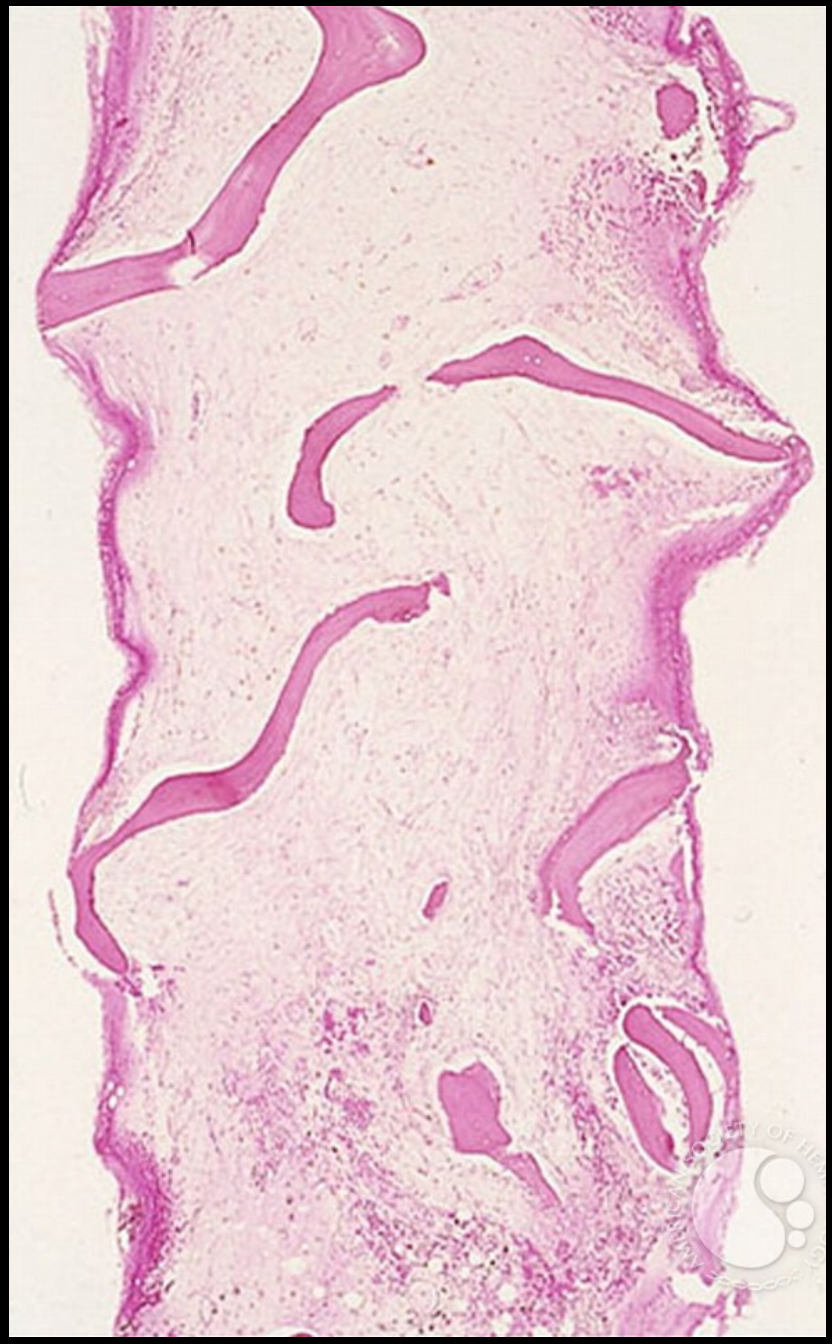
Estudio Paciente con Pancitopenia

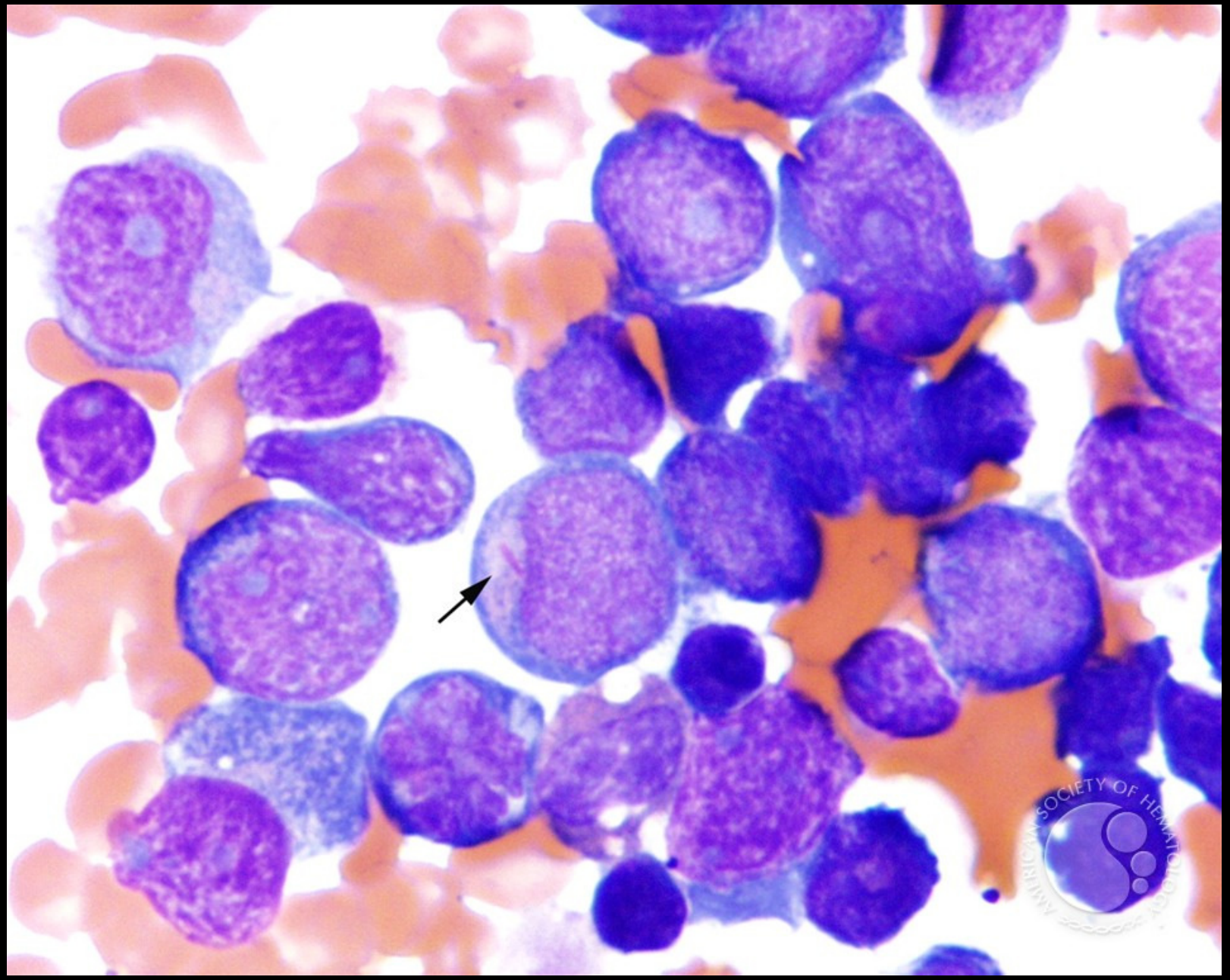
- **Anamnesis y Examen Físico**
- **Exámenes**:
  - Hemograma
  - Perfil Bioquímico
  - Niveles Vitamina B12
  - Imagenología
    - Ecografía
    - TC Abdomen
  - Mielograma
  - Biopsia Médula Osea
  - Citometría de flujo
  - Estudio Citogenético

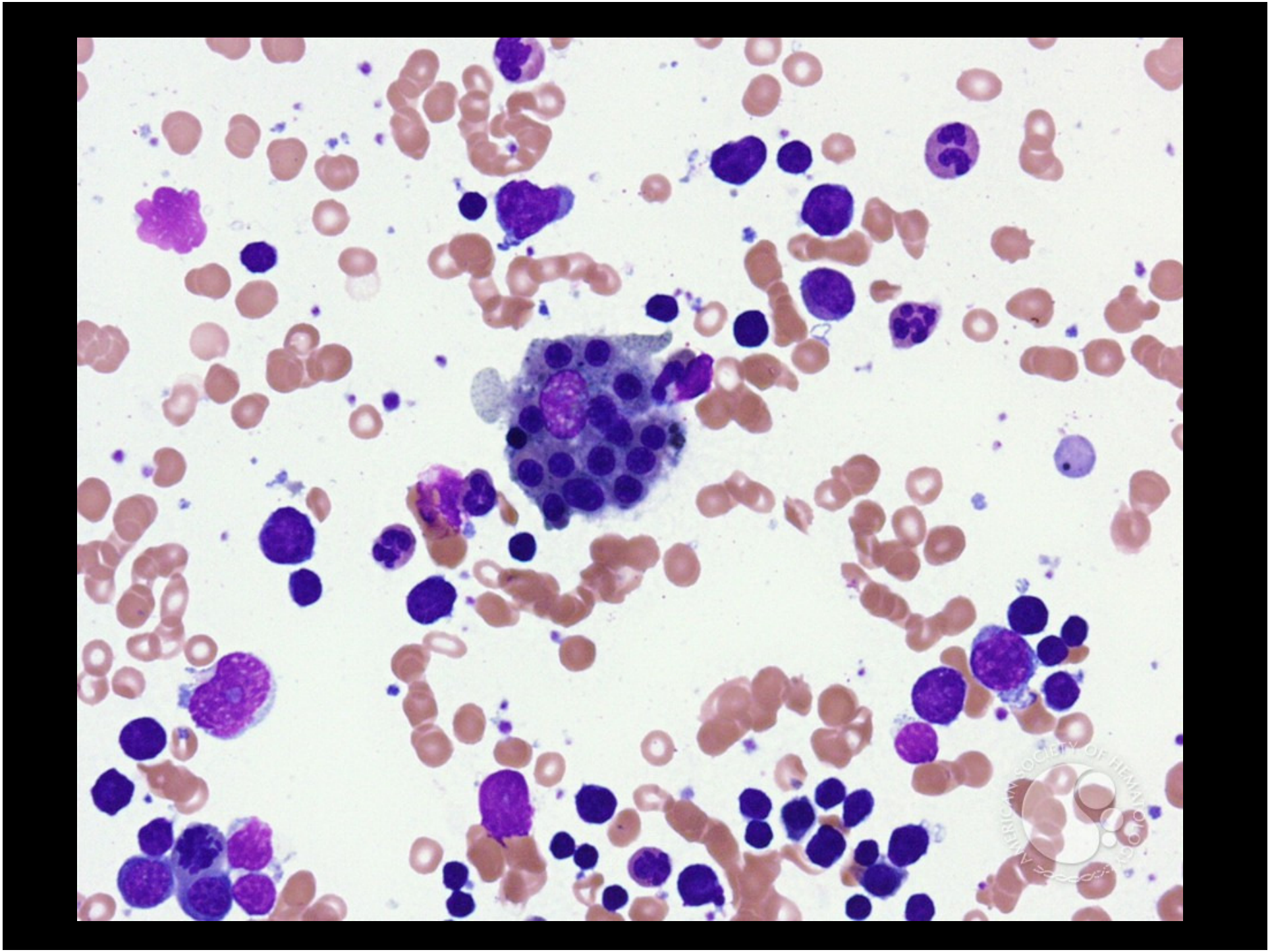


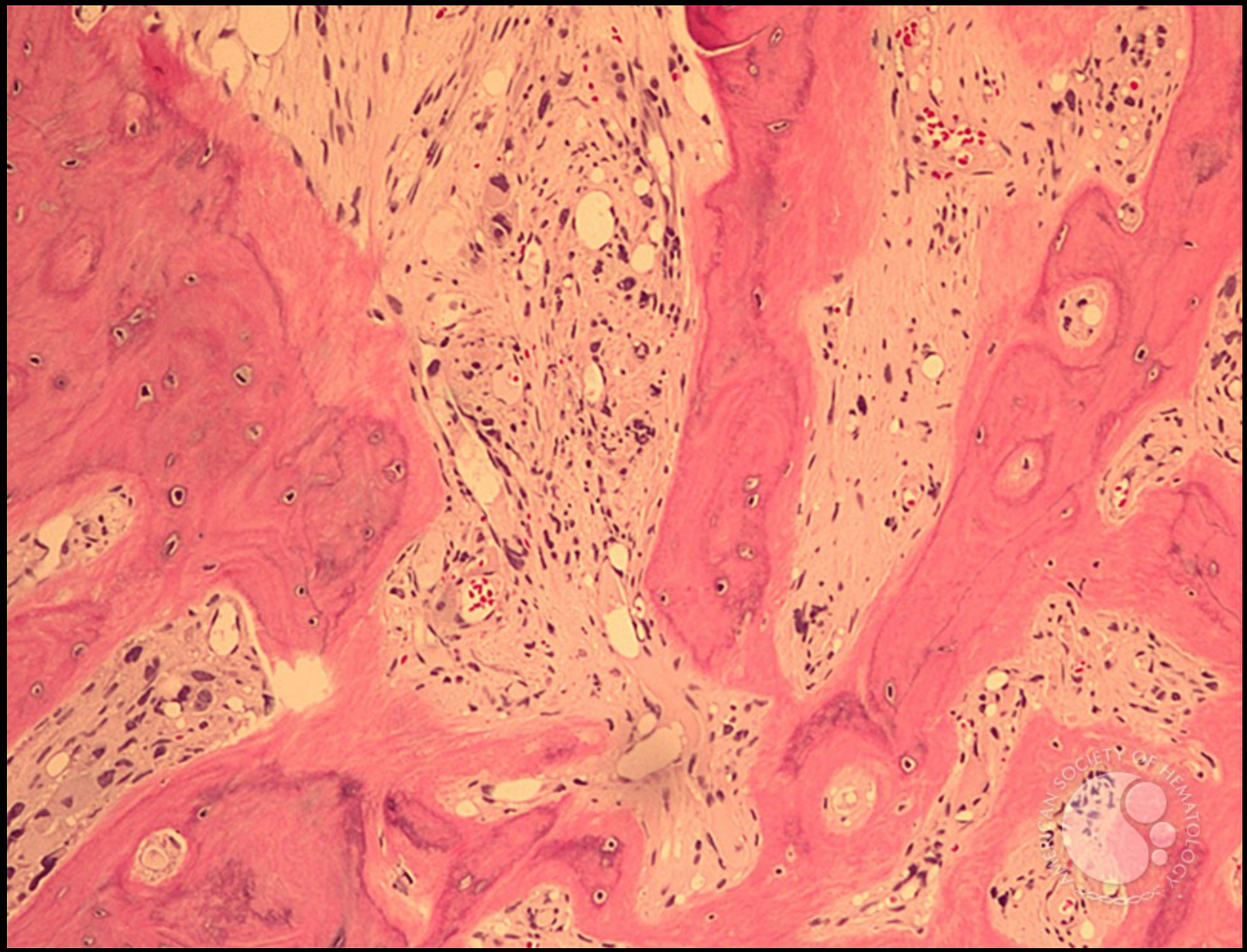

AMERICAN SOCIETY OF HEMATOLOGY

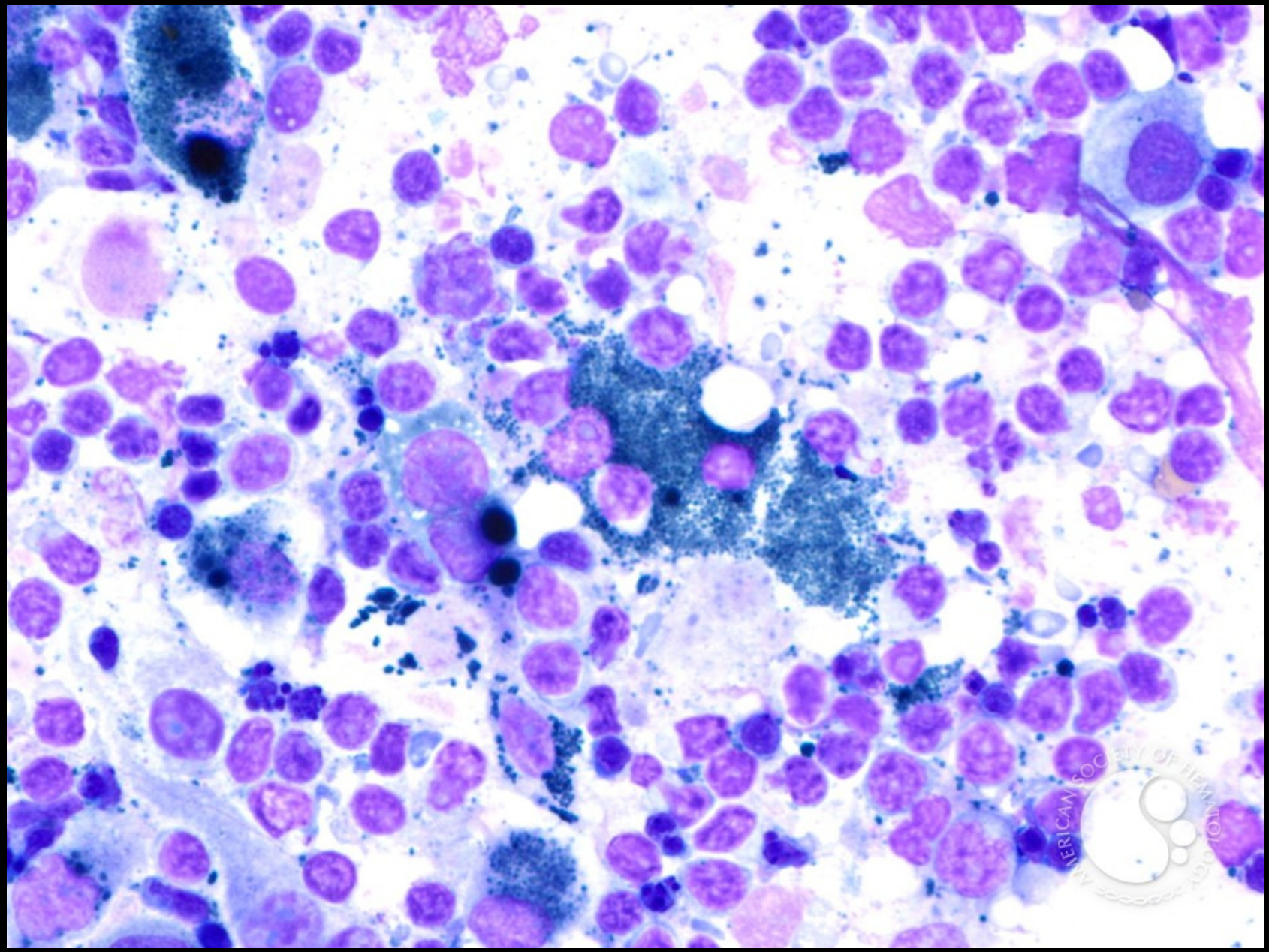


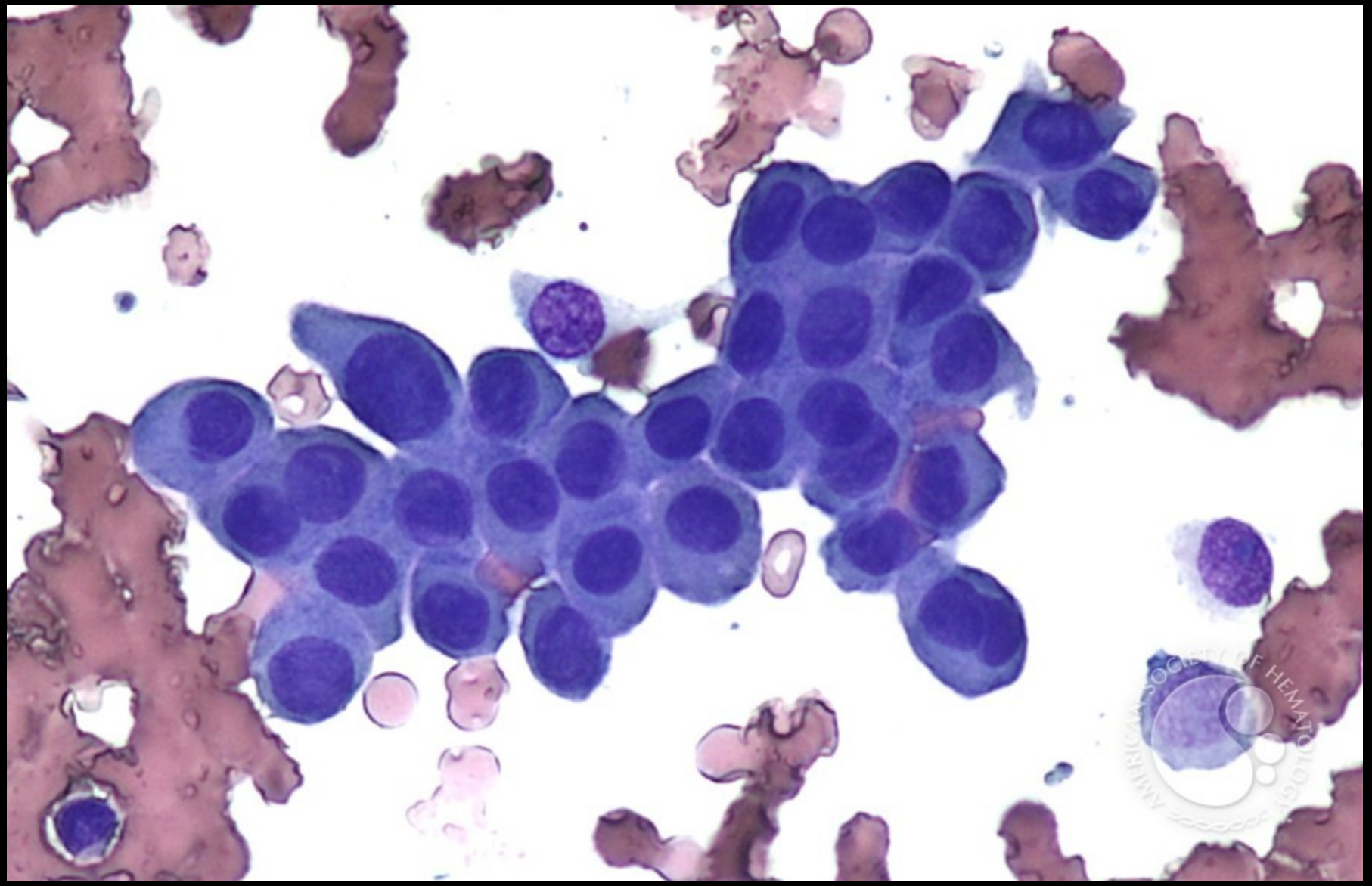


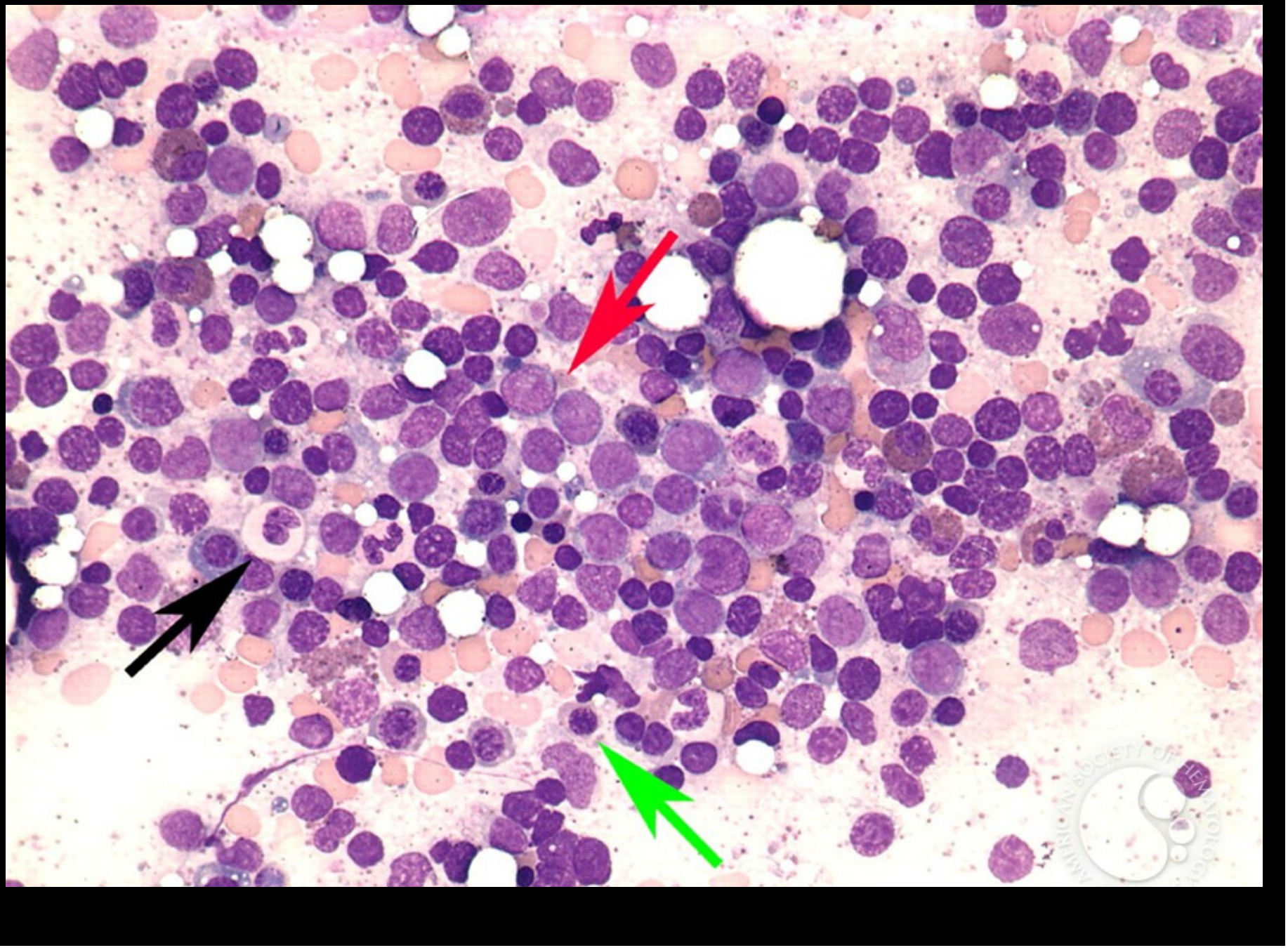





EUROPEAN SOCIETY OF HEMATOLOGY







Pancitopenia

Major Causes of Chronic Mild Cytopenia

Germline conditions (inherited)
- Inherited cytopenia syndromes (rare)*
- Ethnic background*

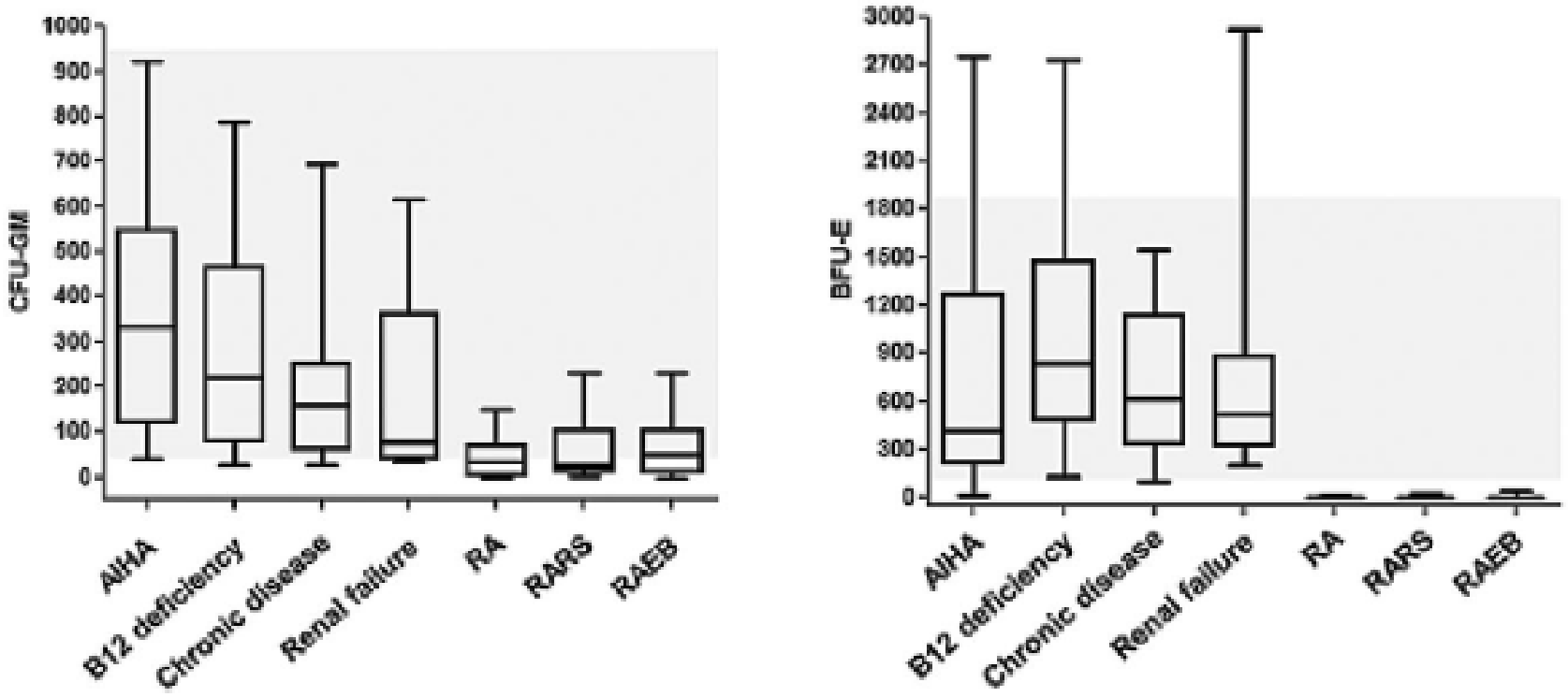
BM failure syndromes
- Low-risk MDS
- Cachexia/anorexia-associated BM failure (gelatinous transformation)
- Nonsevere aplastic anemia
- Infiltration of the BM by an indolent hematologic neoplasm (eg, indolent NHL and indolent mastocytosis)†
- BM fibrosis (early stage)
- Toxic damage involving the BM

Idiopathic states
- ICUS
- IDUS
- Idiopathic cytopenia not fulfilling criteria of ICUS or IDUS
- Idiopathic splenomegaly with mild thrombocytopenia
- Idiopathic hemolysis with mild anemia
- Idiopathic hepatopathy with neutropenia and/or thrombocytopenia
- Chronic idiopathic inflammation with mild anemia

Reactive conditions
- Chronic hepatic disorders with neutropenia and/or thrombocytopenia
- Chronic infectious (viral) diseases
- Chronic inflammatory noninfectious diseases
- Autoimmune-mediated cytopenias (eg, AIHA)

Nutritional deficiency syndromes (examples) and EPO deficiency
- Vitamin B12 deficiency
- Folate deficiency
- Copper deficiency
- Iron deficiency
- Chronic renal anemia
- AOE with low endogenous EPO production

Número de Células Progenitoras CFU en Pacientes con SMD y Controles



CFU-GM **BFU-E**

Numbers of circulating CFU-GM cells (left panel) and BFU-E cells (right panel) were determined in a methylcellulose assay. Peripheral blood mononuclear cells were plated on day 0 and cultured for 14 days in the presence of cytokines (IL-3, GM-CSF, and EPO). Colonies were counted under an inverted microscope. Results show the numbers of CFUs/BFUs/μL blood and represent the ranges (bars), 50 percentile values (boxes), and median values (horizontal lines within boxes) in each group of patients (10-15 patients per group). The grey area indicates the normal range of CFU-GM and BFU-E cells. All investigations were performed within (as part of) the routine examination of cytopenic patients at the Medical University of Vienna. AIHA indicates autoimmune hemolytic anemia; RA, refractory anemia; RARS, RA with ring sideroblasts; and RAEB, RA with excess blasts.

Table 1. Normal blood counts and definition of cytopenias

	Hb, g/dL	ANC × 10^9/L	PLT × 10^9/L
Definitions			
Normal (WHO)	≥12 (f), ≥13 (m)	≥1.8¶	≥150
Cytopenic (WHO)	<12 (f), <13 (m)	<1.8¶	<150
Diagnostic cytopenias*			
ICUS (consensus proposal[9])†	<11	<1.5	<100
MDS (WHO)‡	<10	<1.8	<100
MDS and ICUS (IWGM-MDS[34,35])§	<10	<1.8	<100
MDS (IPSS[47])	<10	<1.5	<100
MDS (IPSS-R[48])	<10	<0.8	<100

Hb indicates hemoglobin; ANC, absolute neutrophil count; PLT, platelet count; IPSS, International Prognostic Scoring System; and IPSS-R, revised IPSS.

*Diagnostic cytopenias refer to threshold levels used as criteria for various BM failure syndromes. In this table, thresholds used as criteria to diagnose MDS and ICUS are shown. It is important to note that apart from these lower blood count levels, other criteria have to be fulfilled as well to establish the diagnosis MDS or ICUS and the cytopenia must be persistent (> 6 months) to count as a criterion.

†The definition and criteria of ICUS were published by a consensus group in 2007.[9]

‡Based on the WHO classification, a MDS may also be diagnosed in patients with less severe cytopenia if morphologic and cytogenetic evidence clearly argue for MDS.

§The proposal of the IWGM-MDS group was presented at several MDS meetings.

¶In the white population, ANC values are higher than in people of African descent, in whom ANC levels are often < 1800/μL of blood in healthy controls.

ICUS
Idiopathic Cytopenias of Undetermined Significance

- **Describe una entidad en que existe:**
  - Citopenia leve persistente
  - No cumple los criterios diagnósticos de síndrome mielodisplástico (displasia <10% en S.P. o M.O.)
  - Exige estudio de médula ósea y descarte de otras etiologías.
  - Puede afectar una o más series.
  - Debe durar al menos 6 meses.

IDUS
Idiopathic Dysplasia of Unknown Significance

Describe una entidad en que:

- Existe una displasia de la M.O. representada por células clonales.
- No existe citopenia.

Para que una IDUS se manifieste como SMD existen diversos mecanismos:

- Transformación maligna
- Comorbilidad renal o hepática
- Baja producción de EPO.