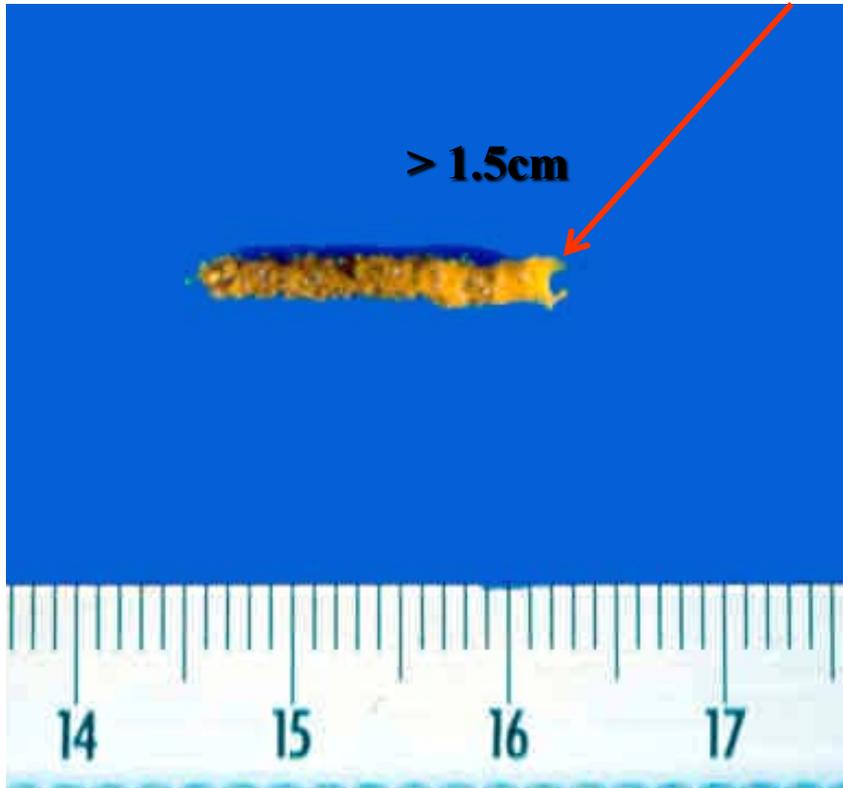


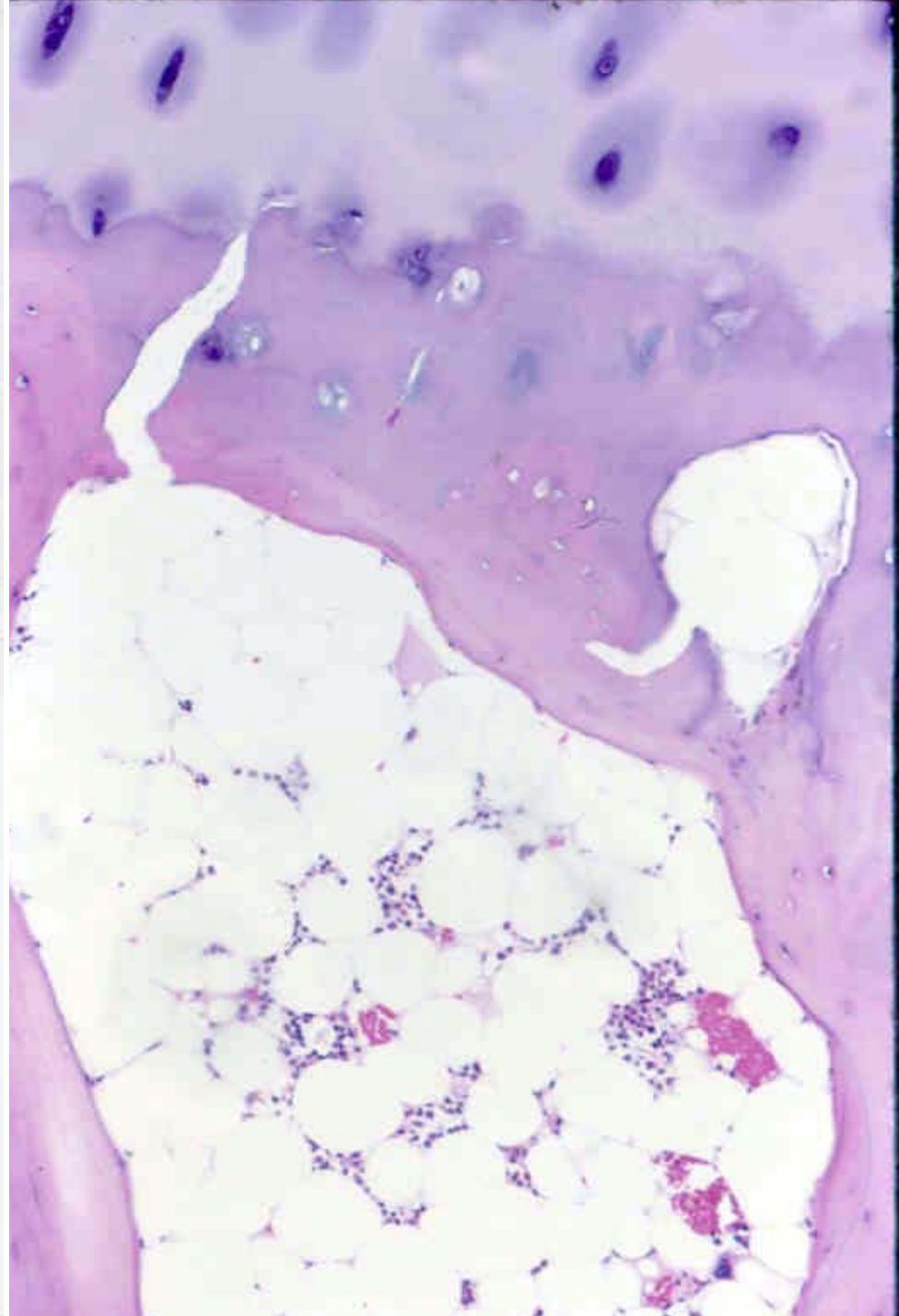
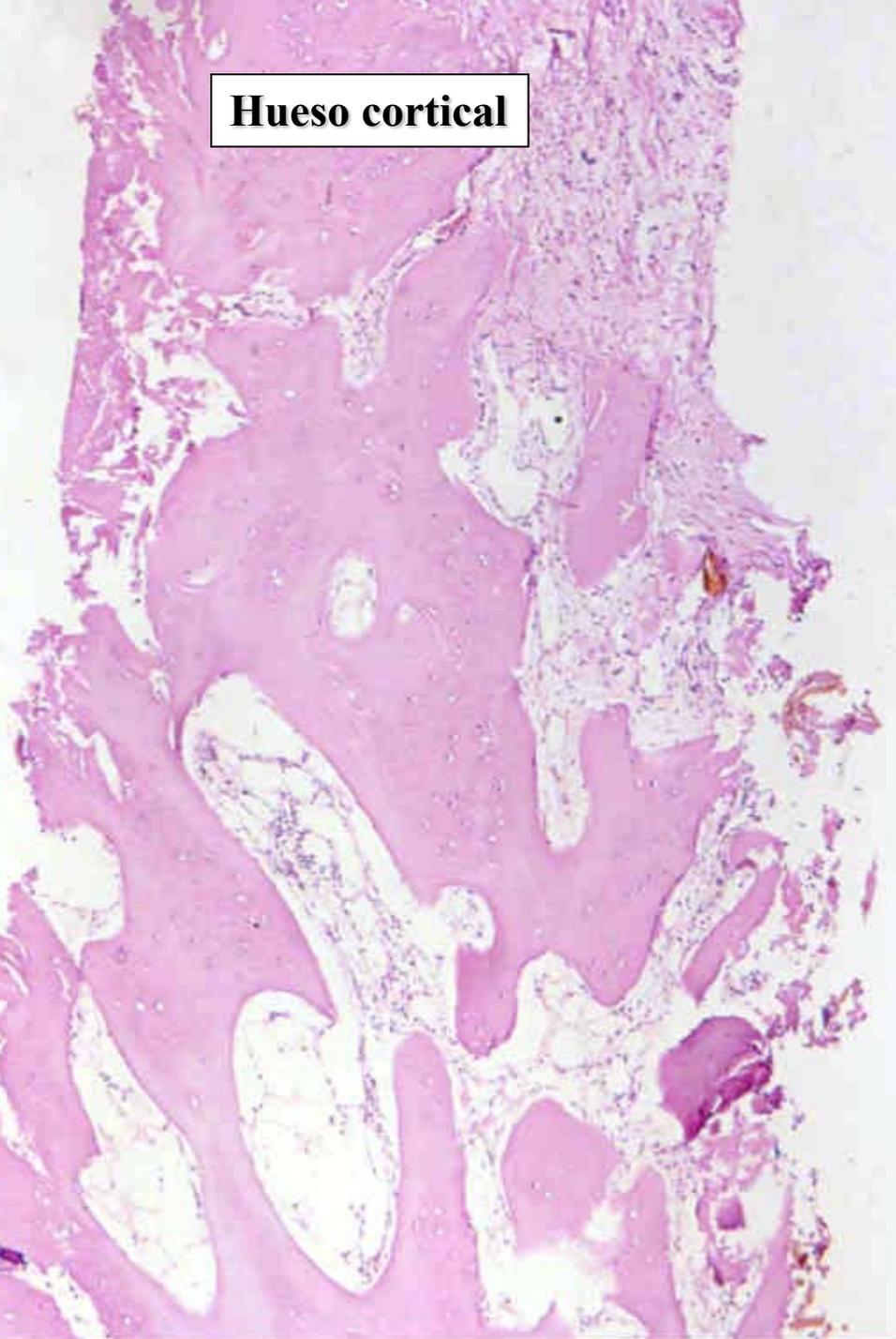
Biopsia de Médula Ósea

Cresta iliaca posterior y superior

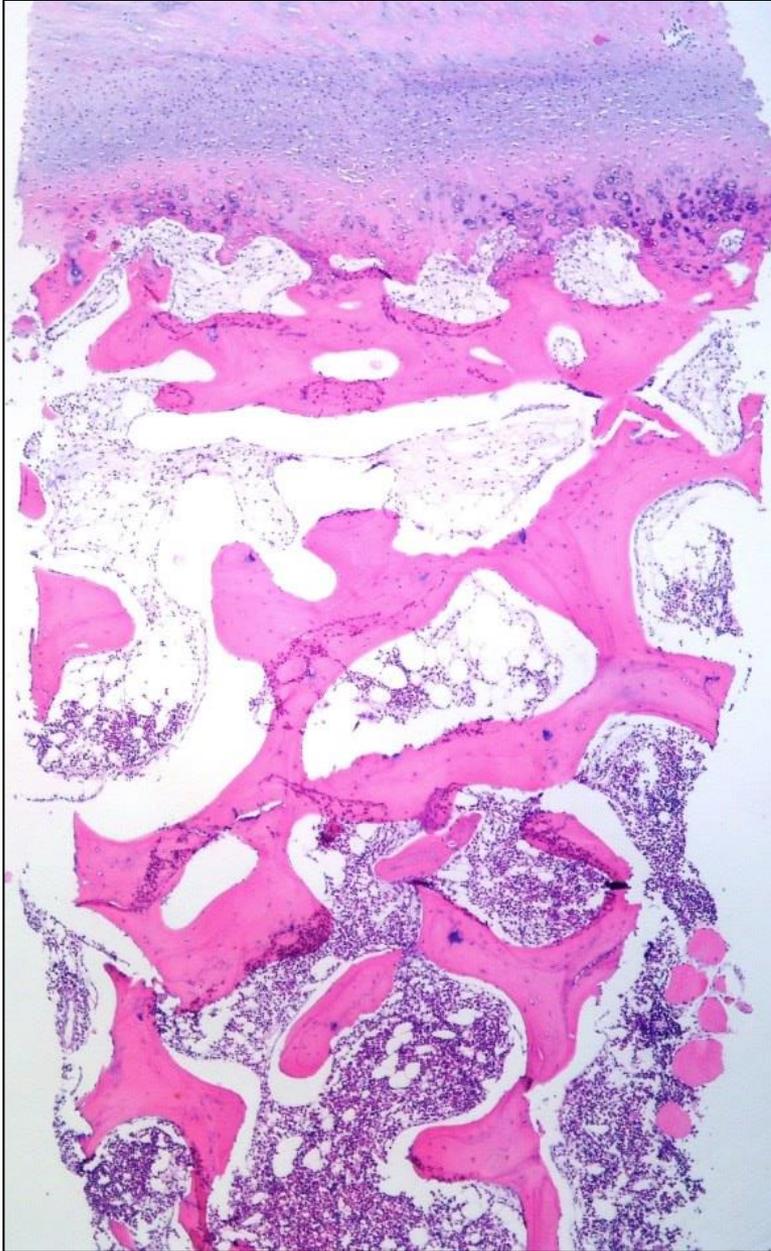
Hueso cortical



Hueso cortical



Normal

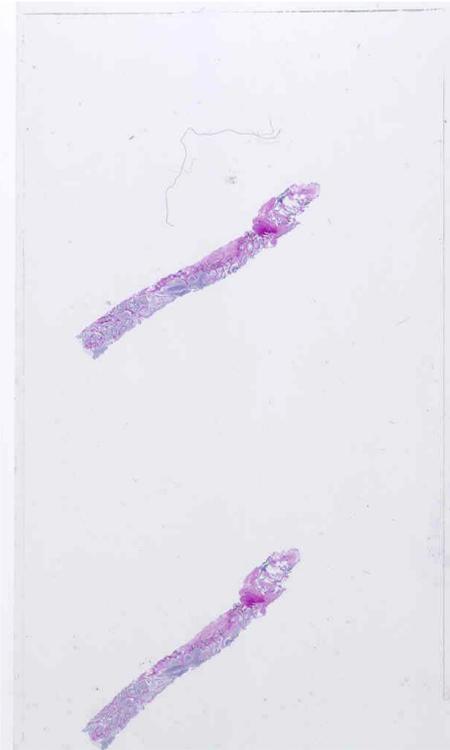


Neoplasia Mieloproliferativa



Biopsia de médula ósea

PAS



PERLS



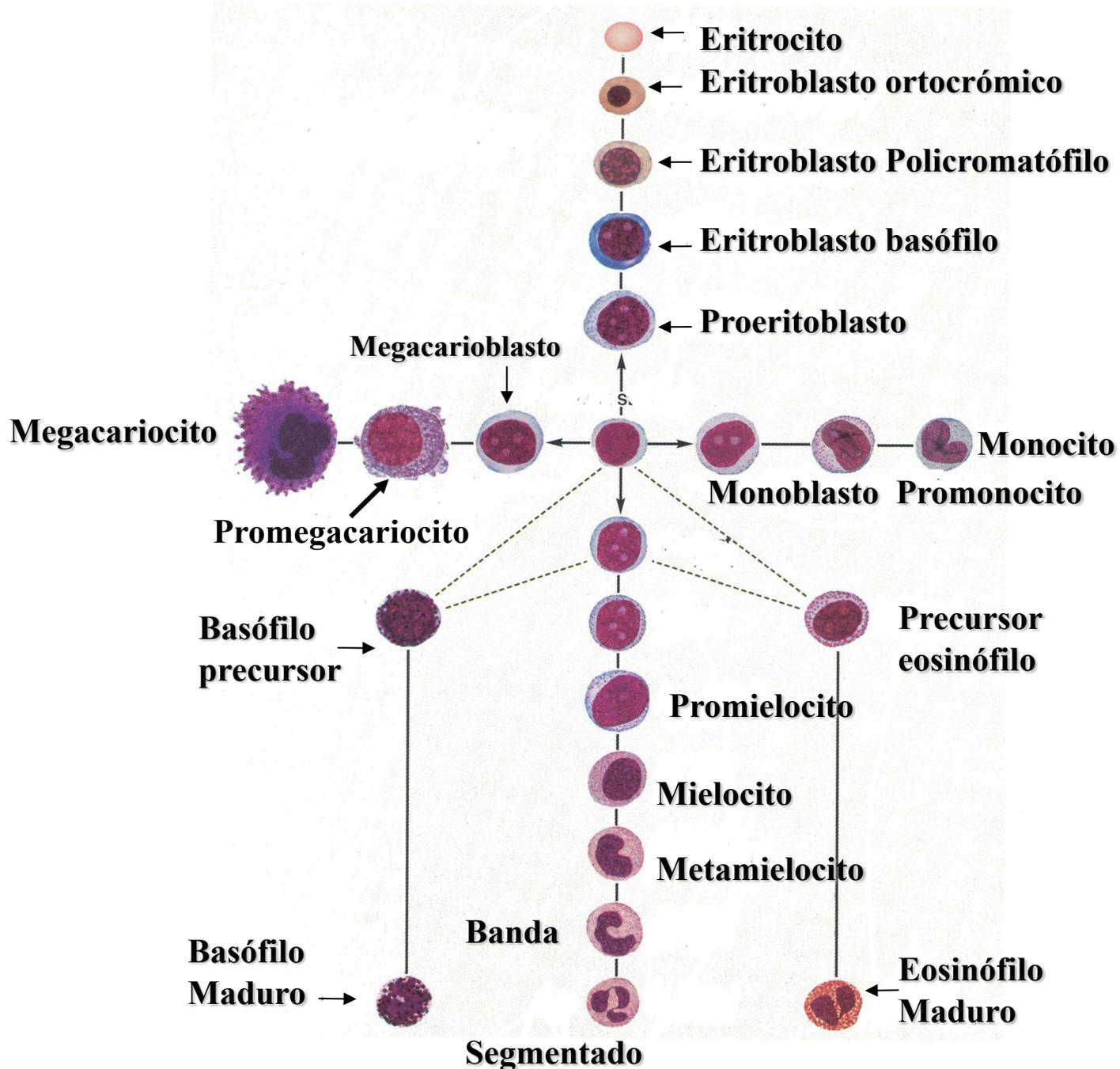
RETICULO



Para Fibras Reticulares
Colágena Tipo III

- Gordon-Sweet
- Wilder
- Gömöri

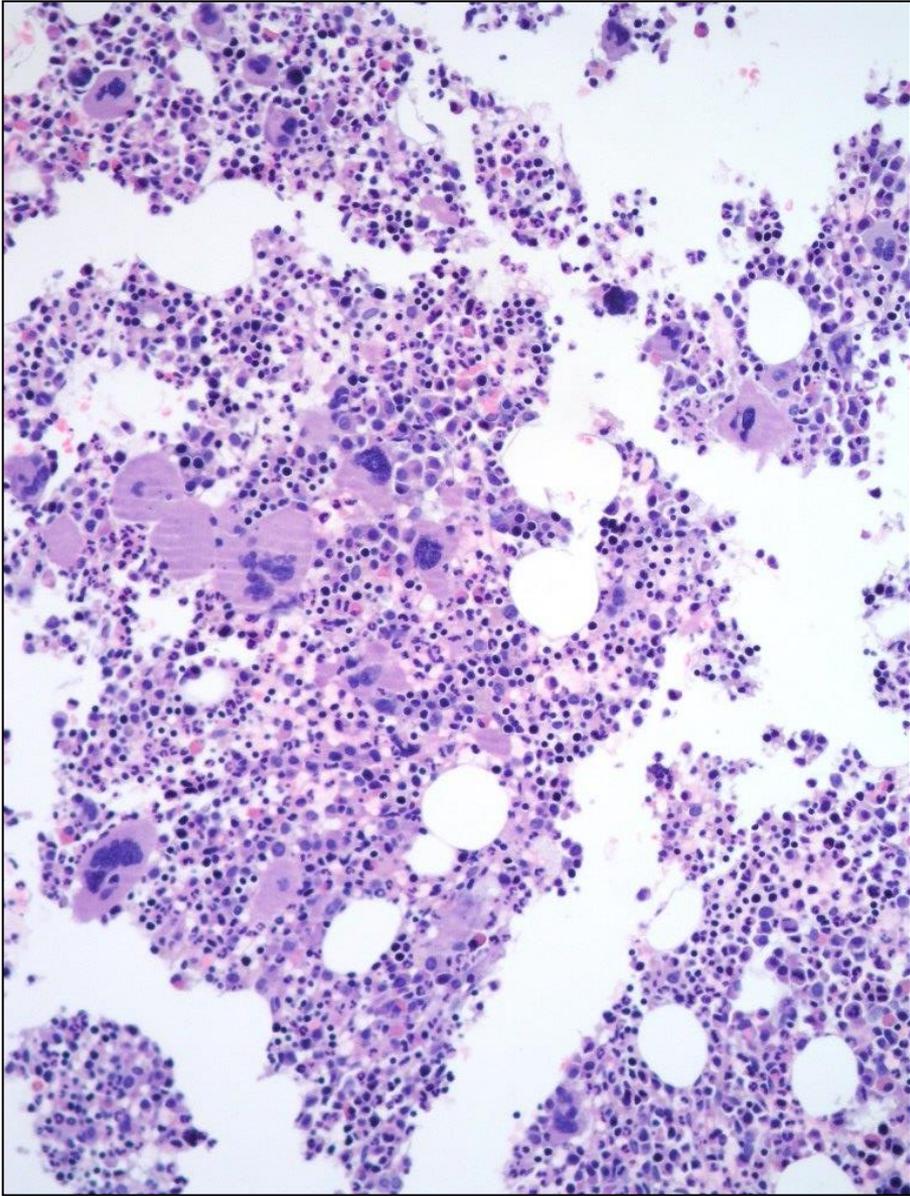
• Masson
Para colágena Tipo I



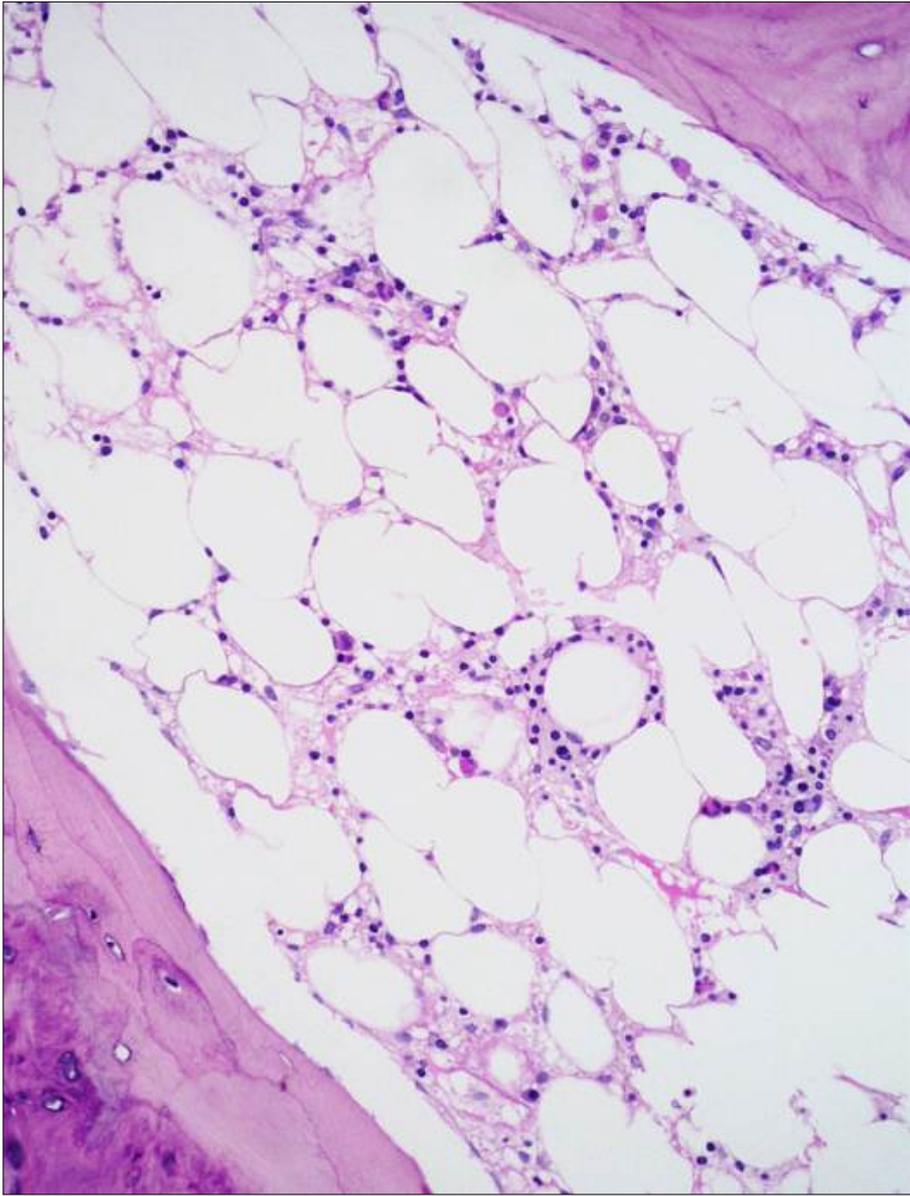
Informe de Médula ósea

- **Celularidad**
- **Relación M:E**
- **Serie Eritroide**
- **Serie Granulocítica**
- **Megacariocitos**
- **Fibrosis**
- **Hemosiderina**
- **Otros**

70%



10%

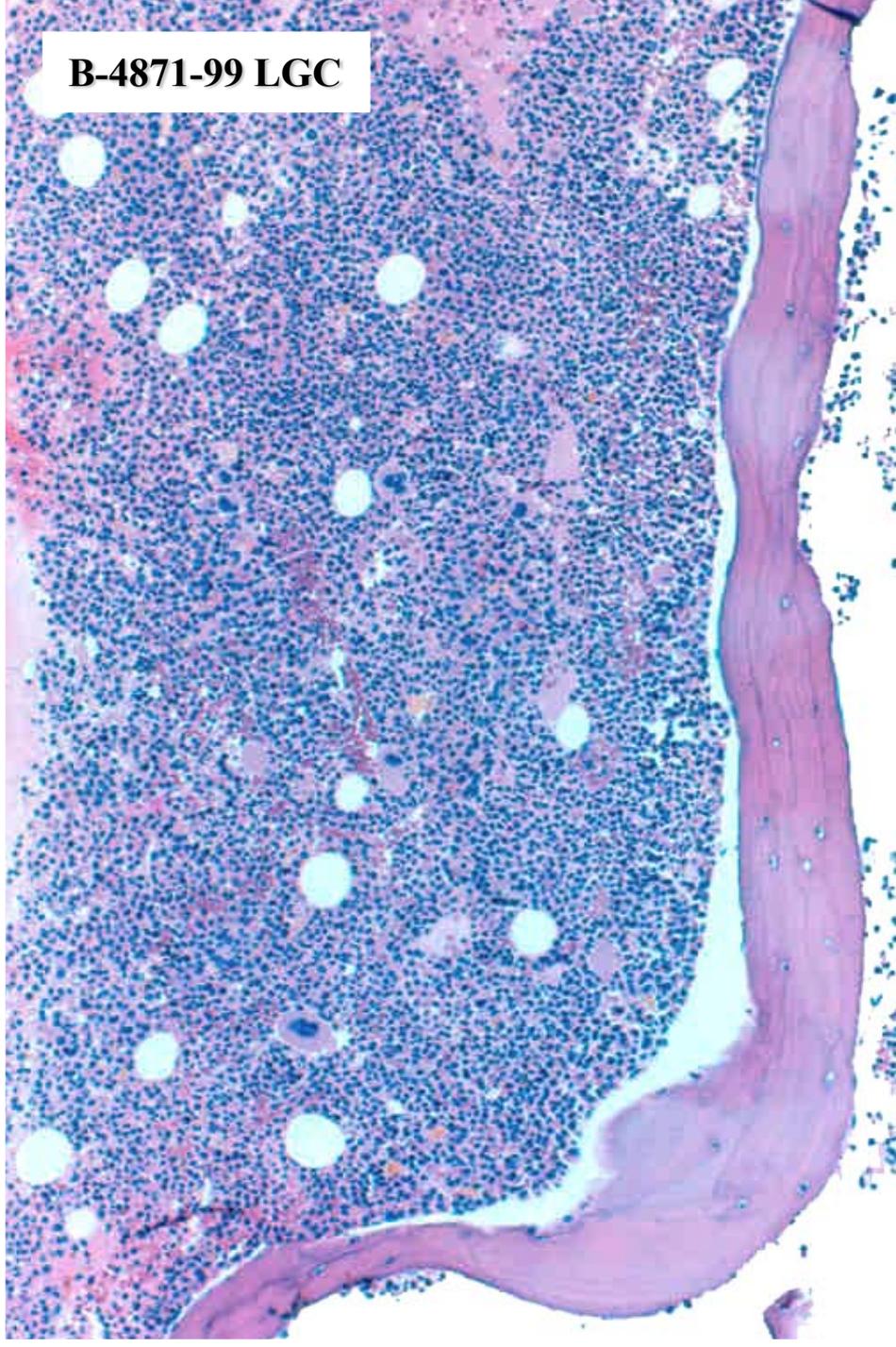


Celularidad de Médula Ósea

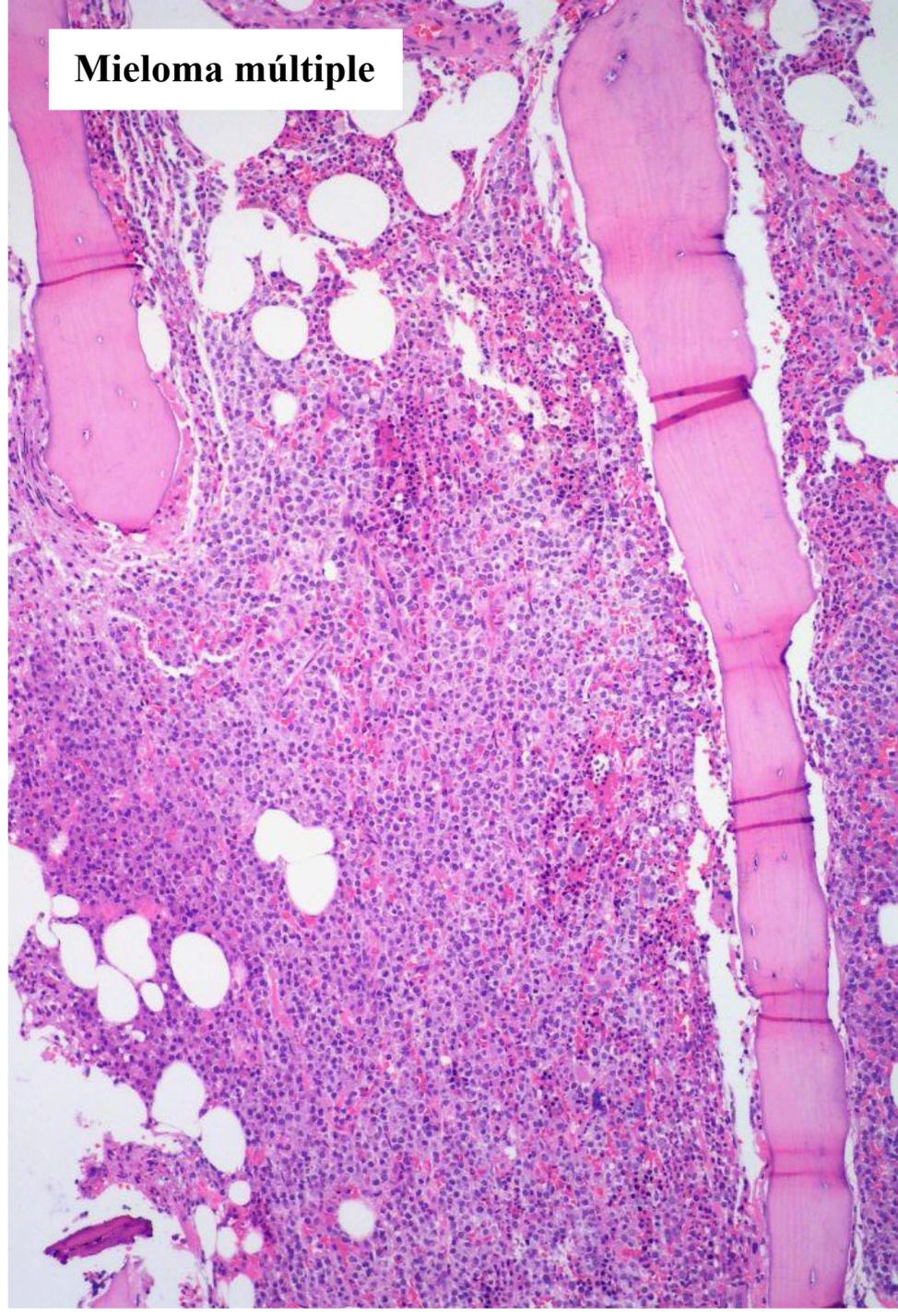
Harstock R.J. Am J Clin Pathol 1965;4:26

Edad	Celularidad promedio (%)	Intervalo de variación (%)
Recién Nacido	100	80-100
10 años	80	60-95
20 años	65	50-90
30 años	60	30-85
40 años	55	30-80
50 años	50	20-80
60 años	50	25-75
70 años	40	20-65
80 años	30	15-45

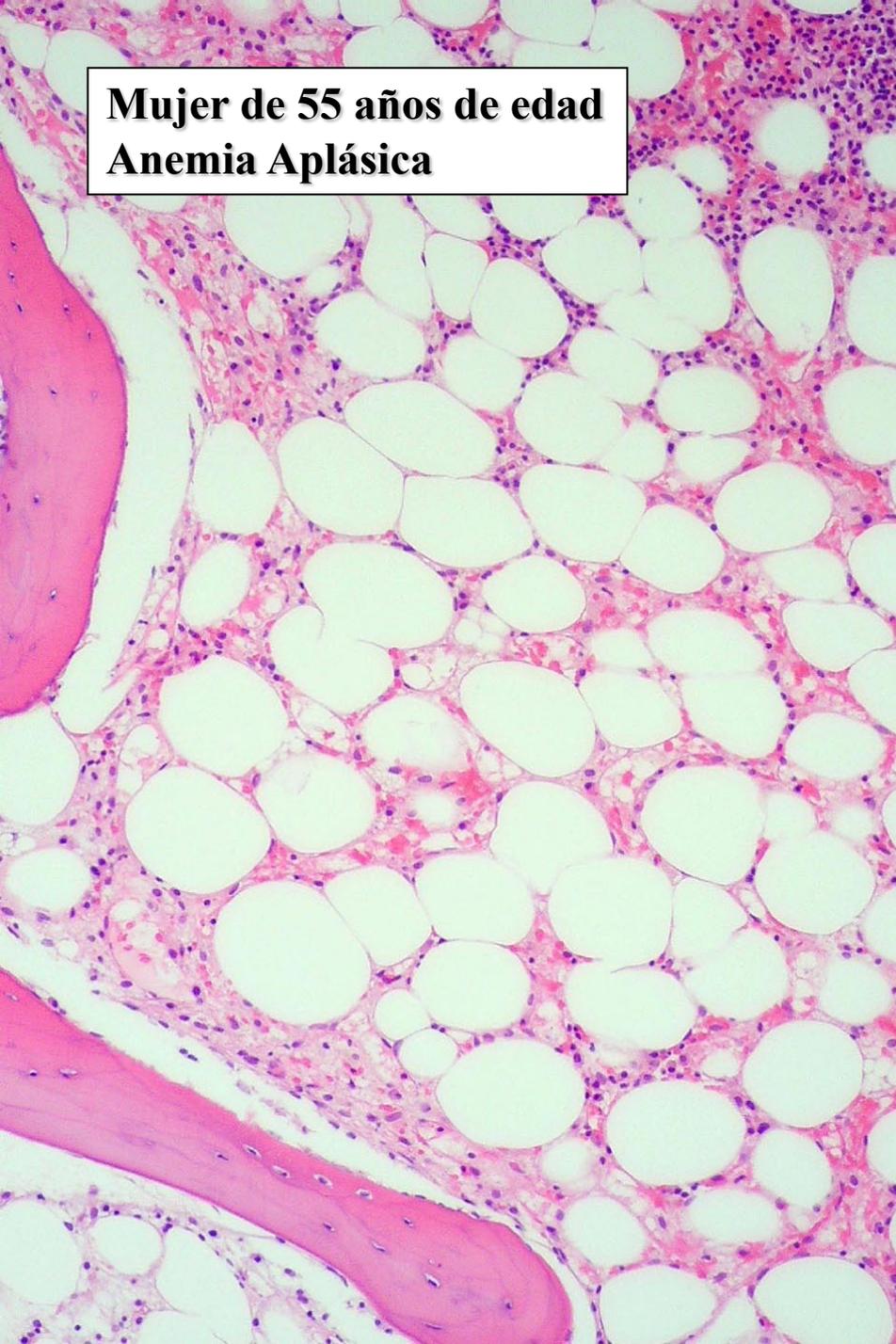
B-4871-99 LGC



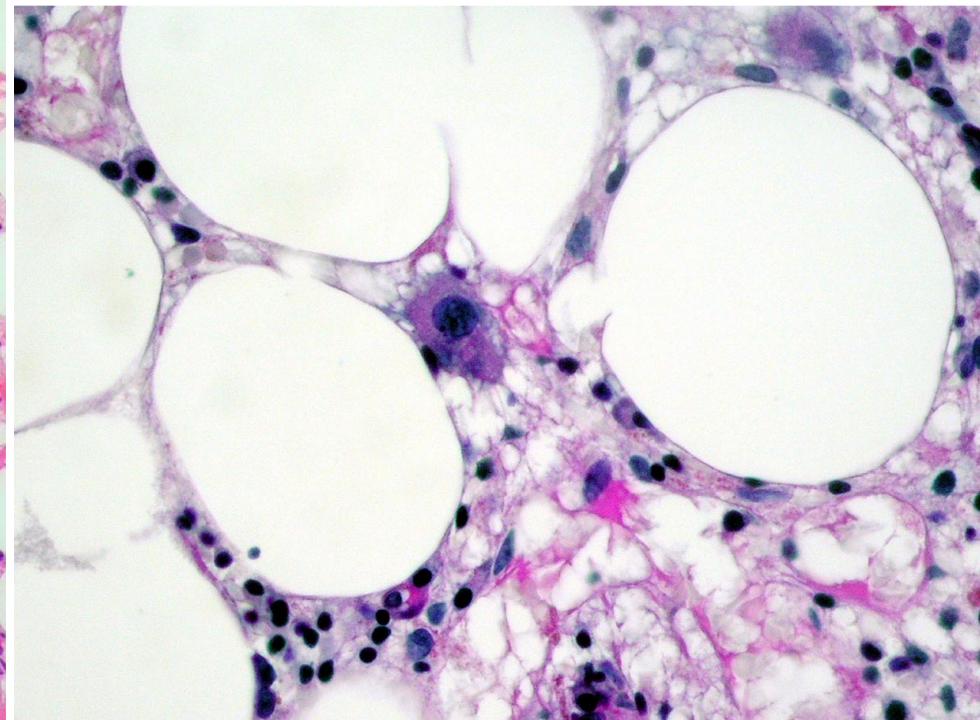
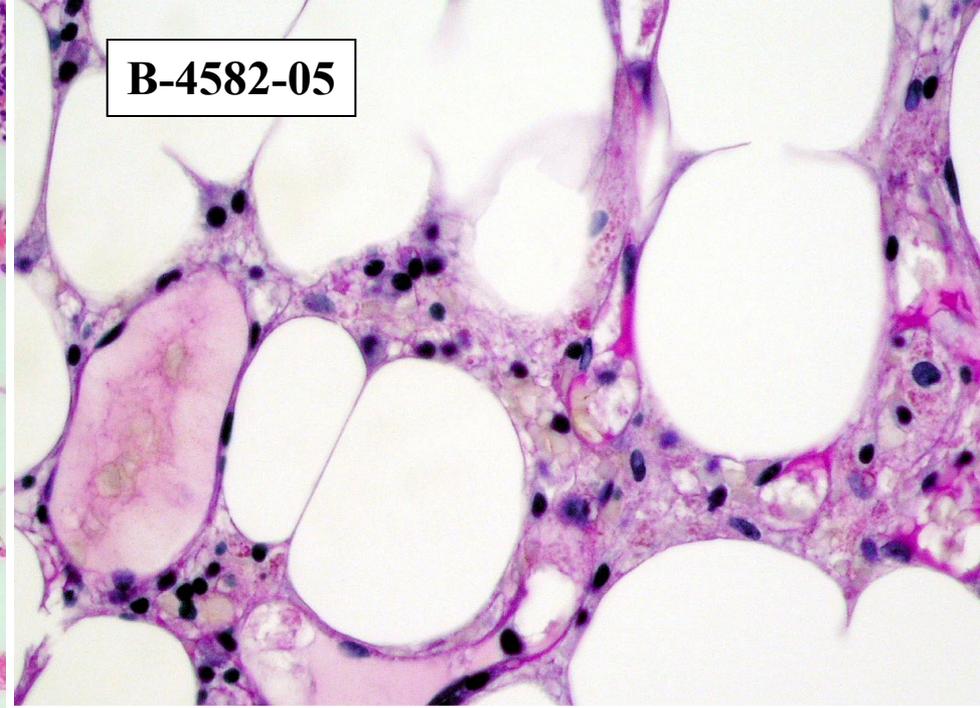
Mieloma múltiple

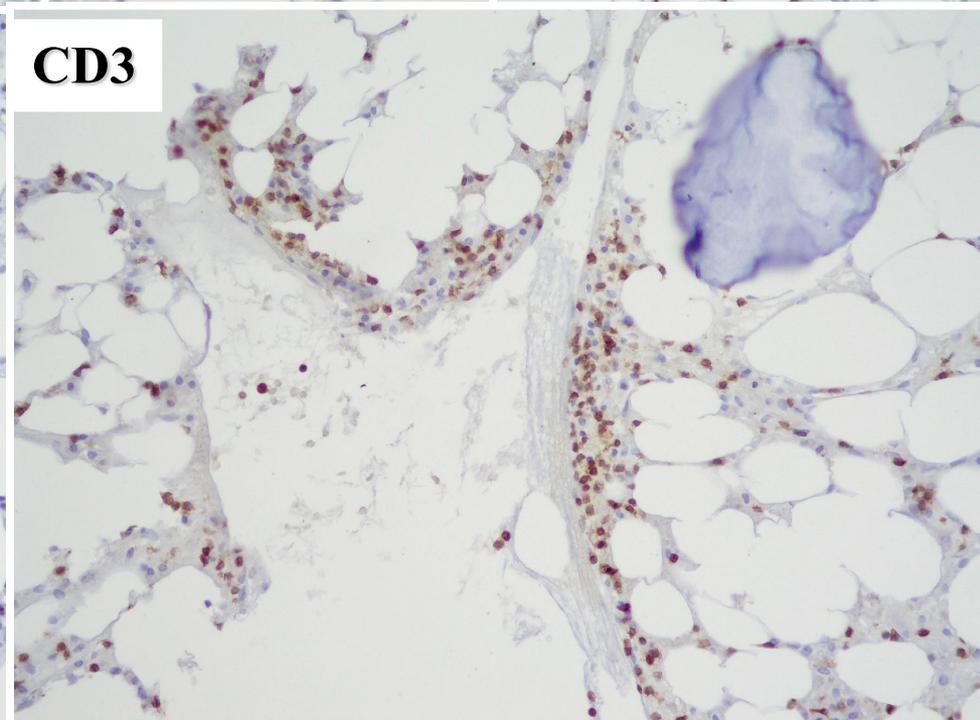
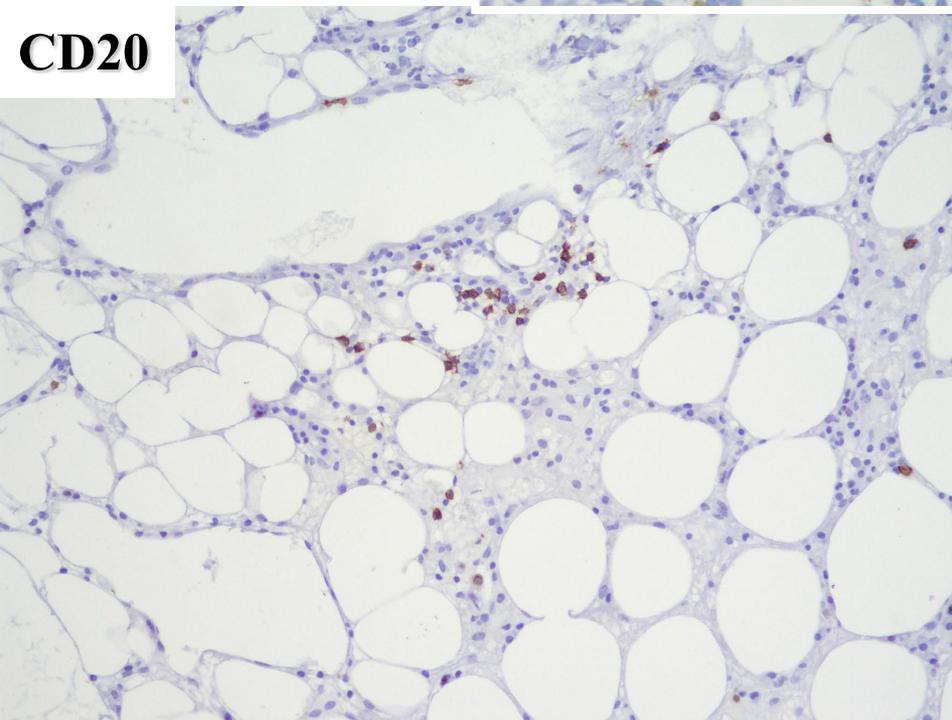
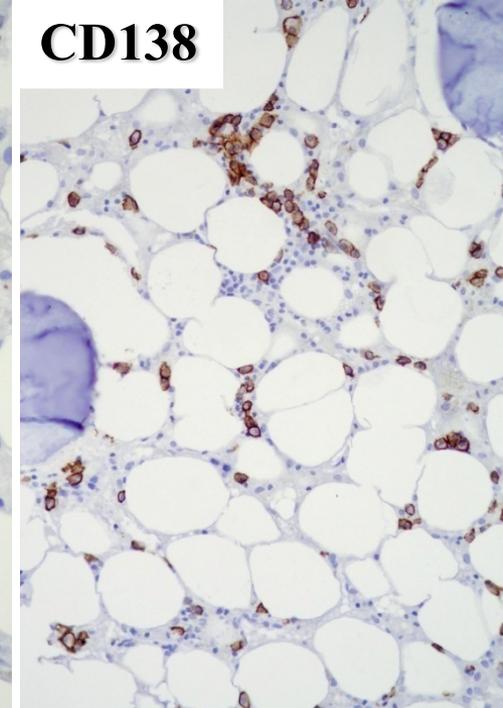
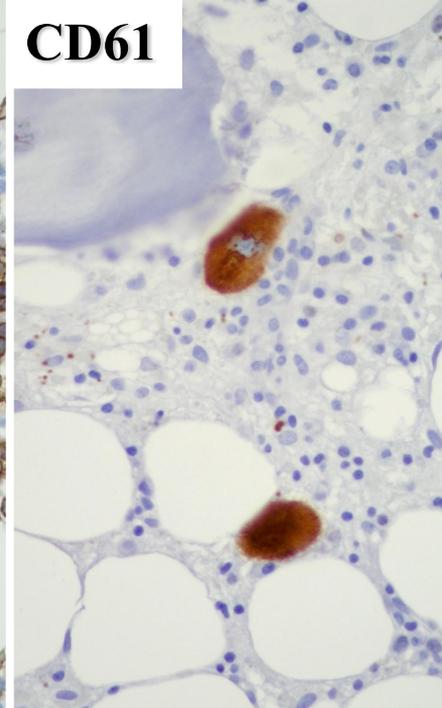
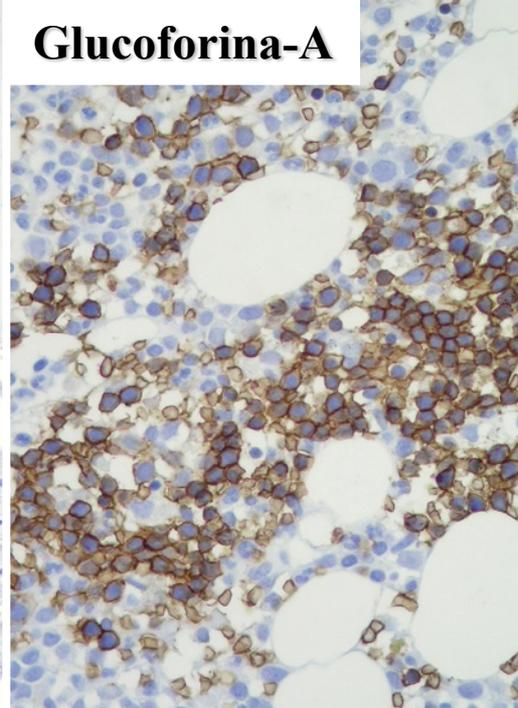
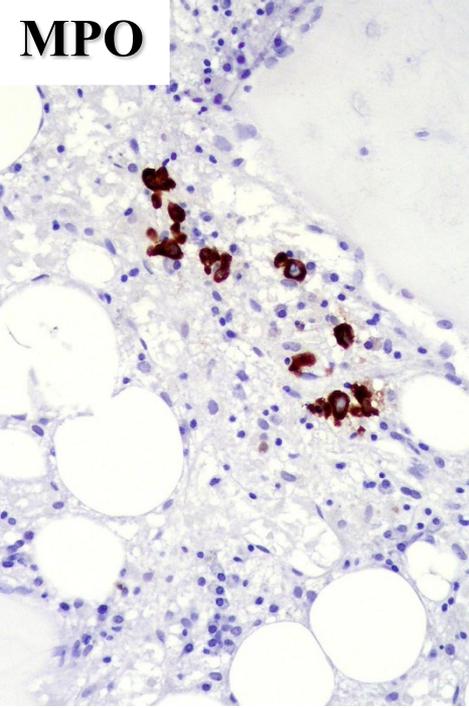


Mujer de 55 años de edad
Anemia Aplásica

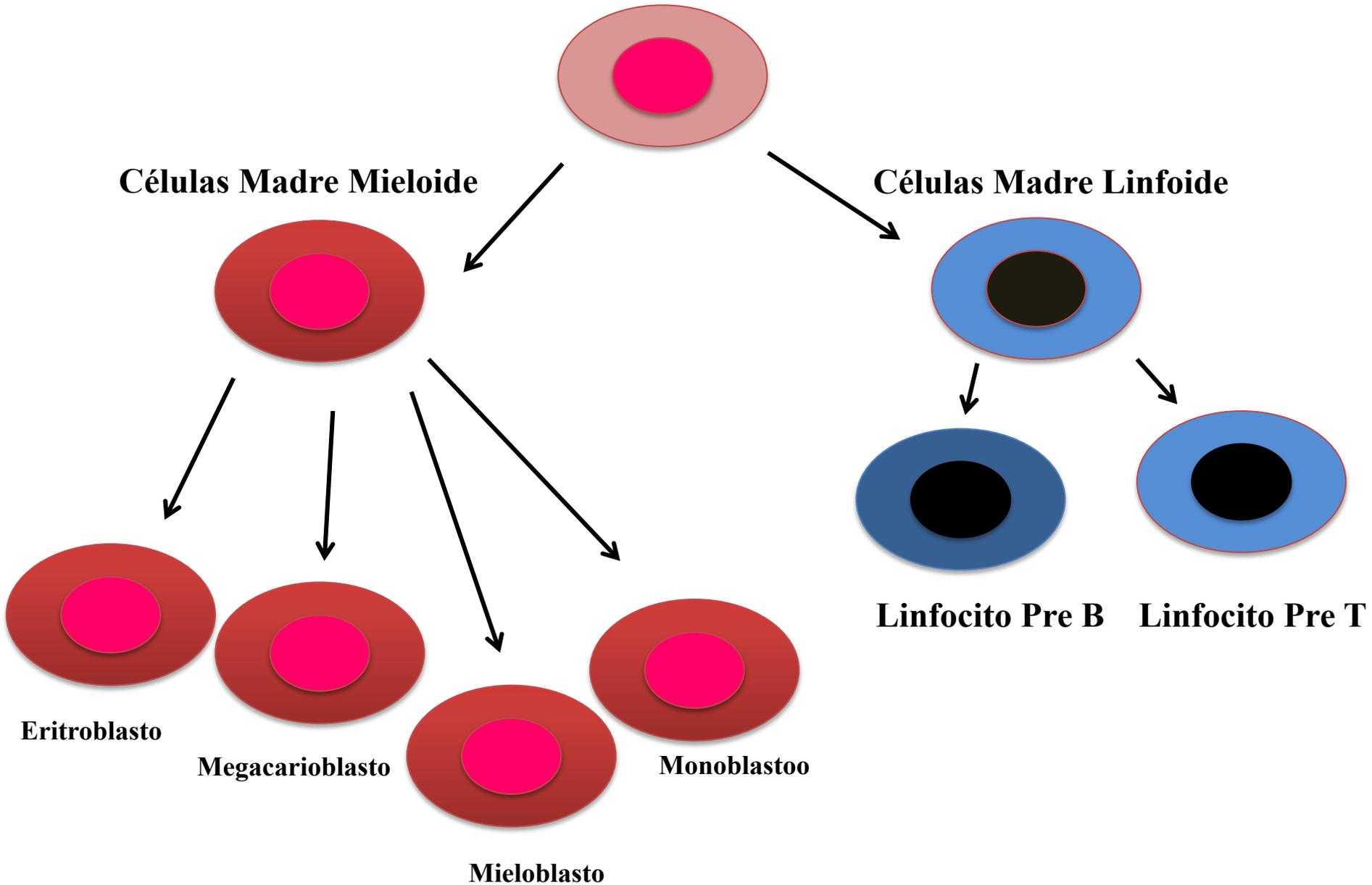


B-4582-05





Célula Madre Hematopoyética



RELACION MIELOIDE: ERITROIDE

- **“Relación granulocítica : eritroide”**
- **Primera semana de vida 70% son células de serie eritroide.**
 - **La relación es de 1: 2-3.**
- **Relación se estabiliza de 2.5:1 a 4:1**

Célula Madre Hematopoyética

(5-8 días)

C.M. Mieloide

Proeritroblasto (RER) ← **Eritropoyetina**

Eritroblasto basófilo (RER/HB)

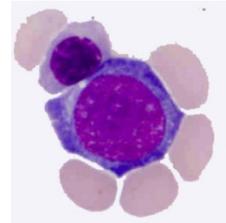
Eritroblasto policromatófilo

Eritroblasto ortocromático

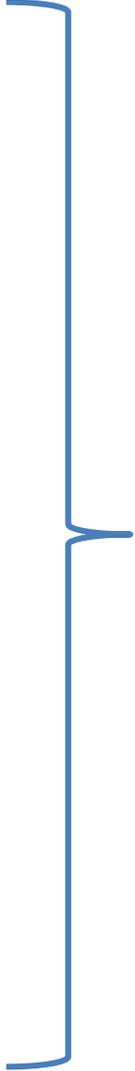
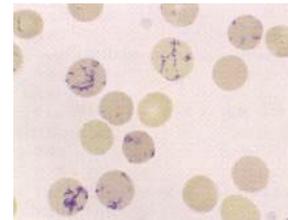
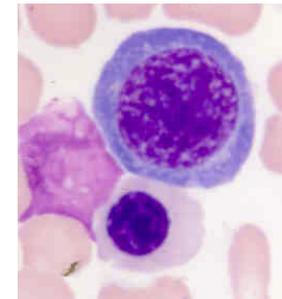
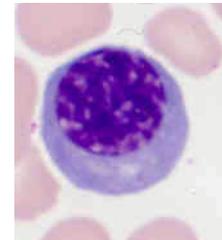
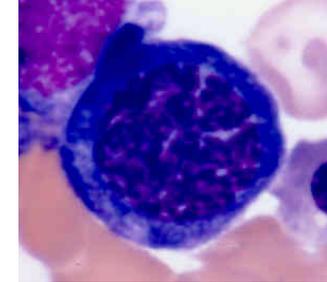
Reticulocito

Sinusoide

Eritrocito

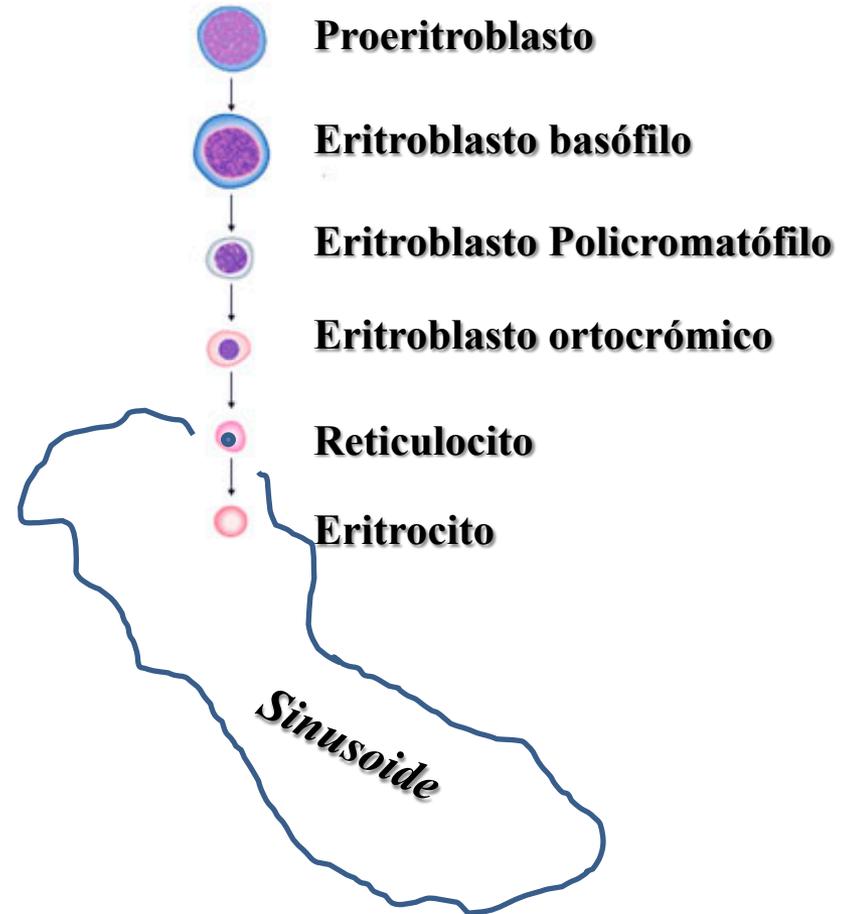
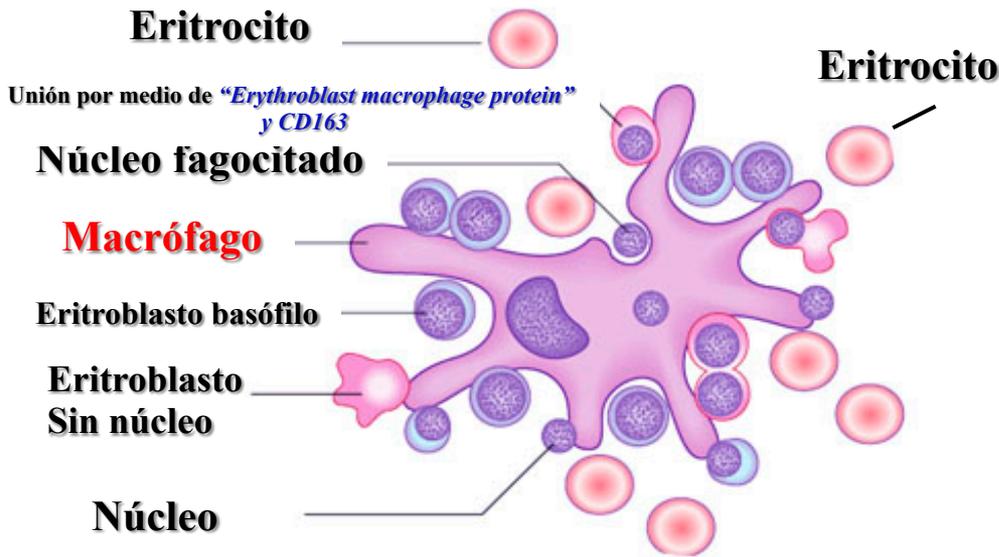


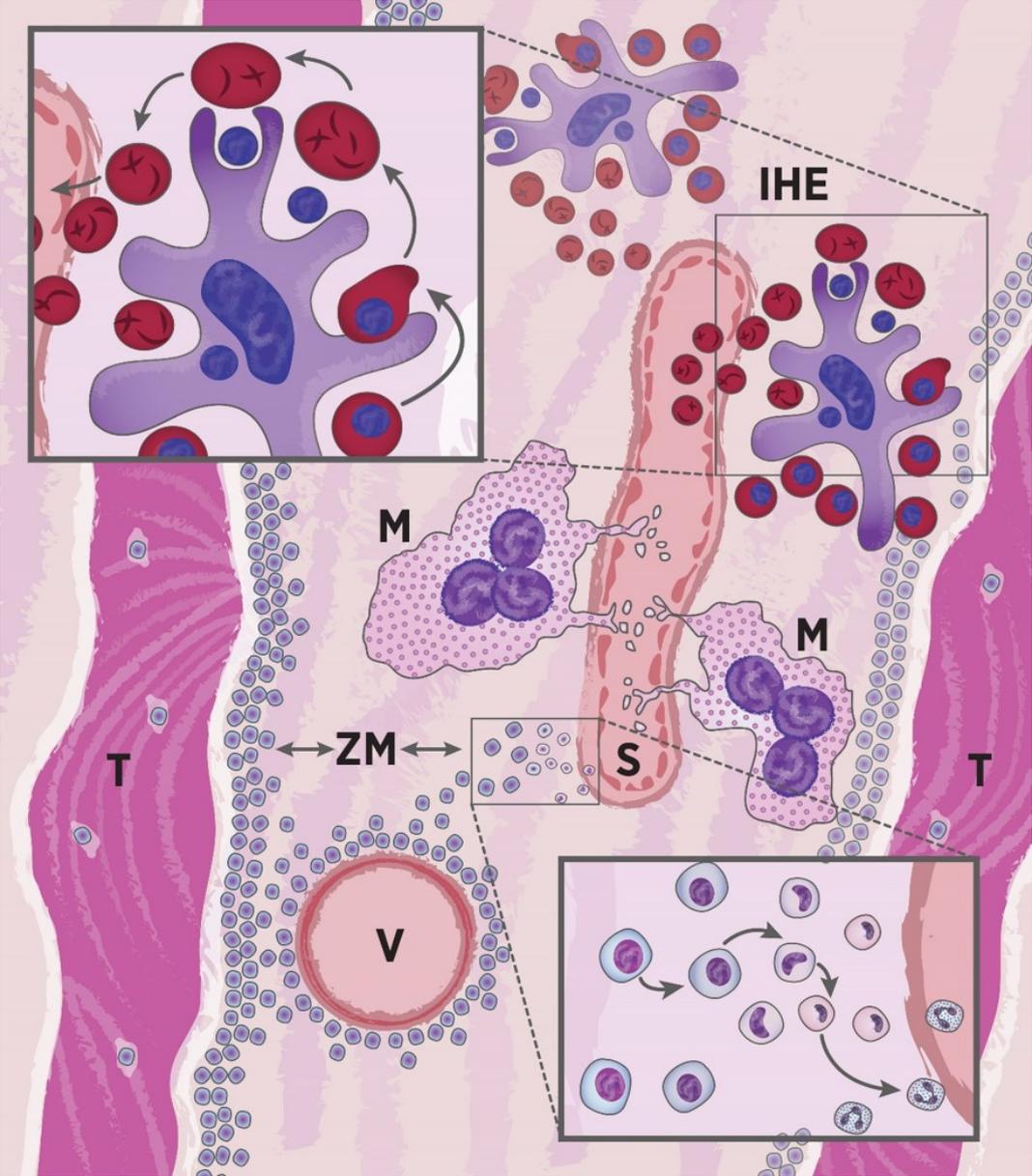
Cortesía Dr. Carillo Farga



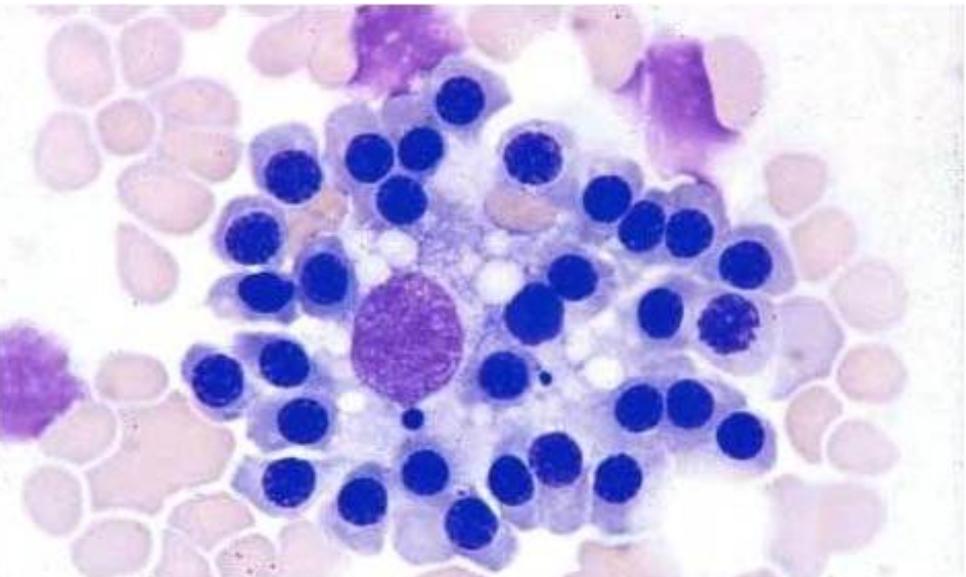
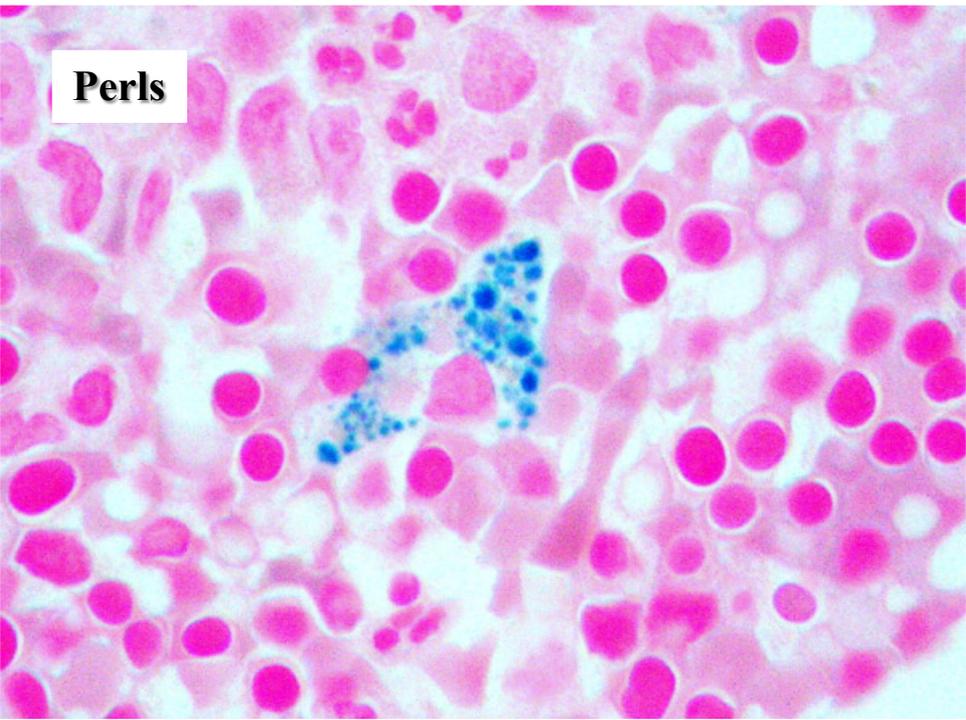
ISLA HEMATOPOYÉTICA

5-30 eritroblastos por macrófago

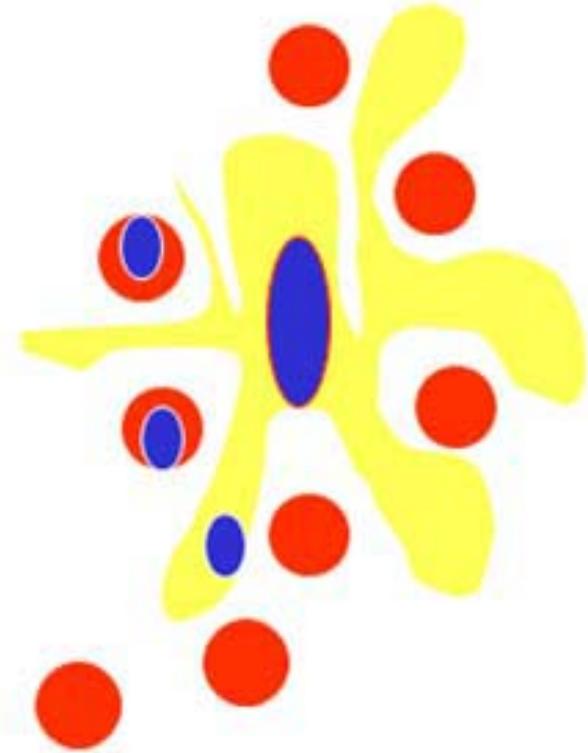




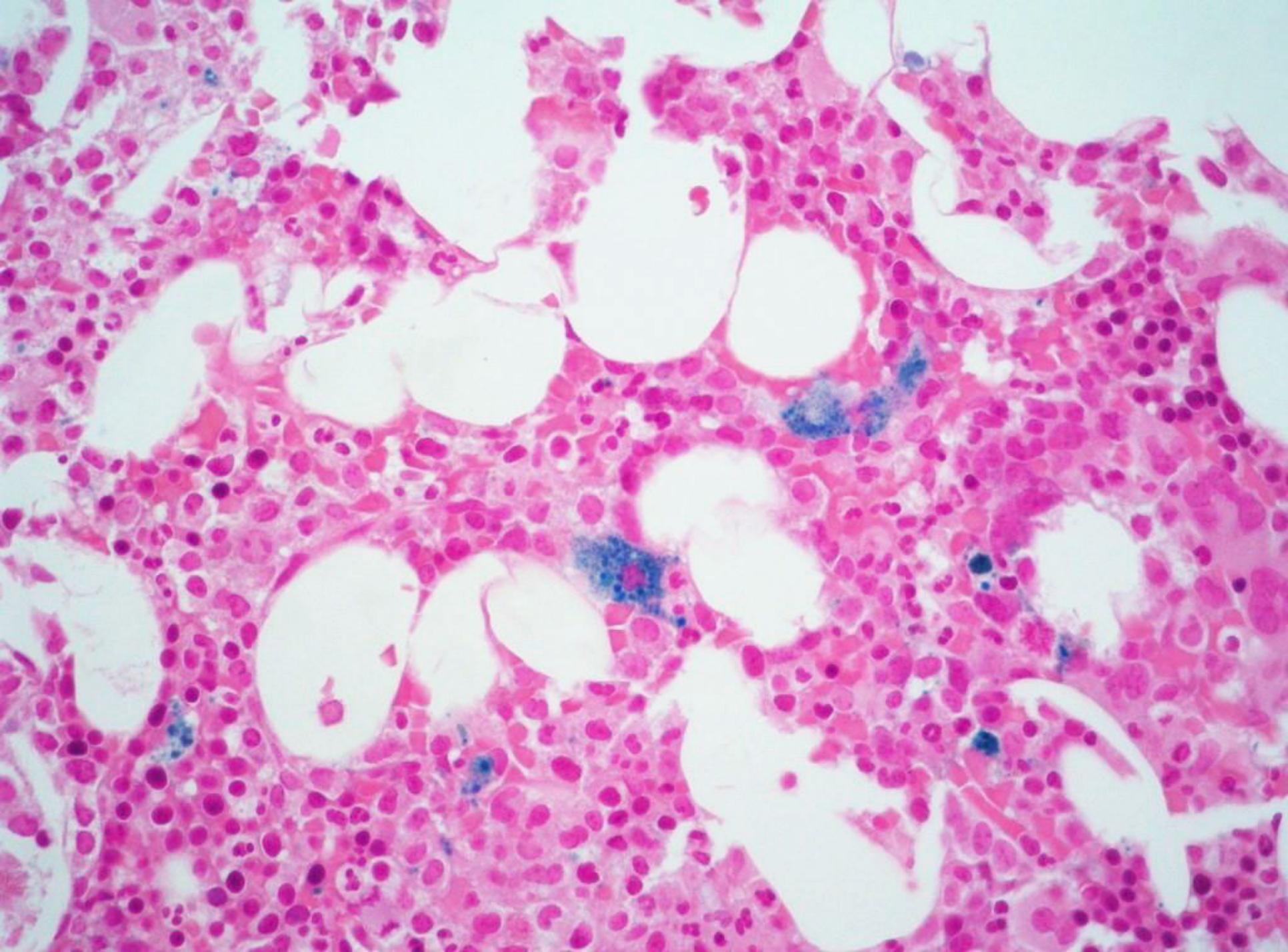
Perls



Arquitectura normal

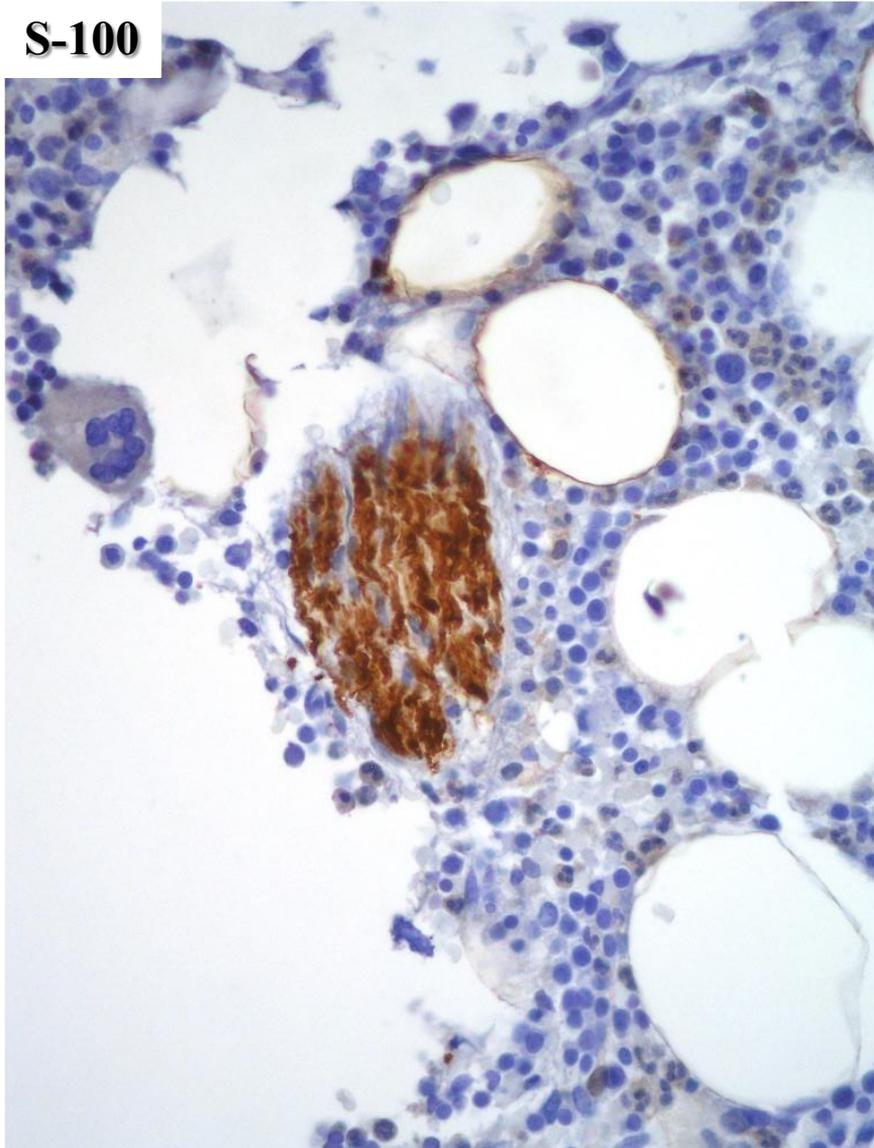


Isla hematopoyética



Células de Schwann en regulación Hematopoyética

S-100



Yamazaki S et al.

Cytokine signals modulated via lipid raftsmimic niche signals and induce hibernation in hematopoietic stem cells.

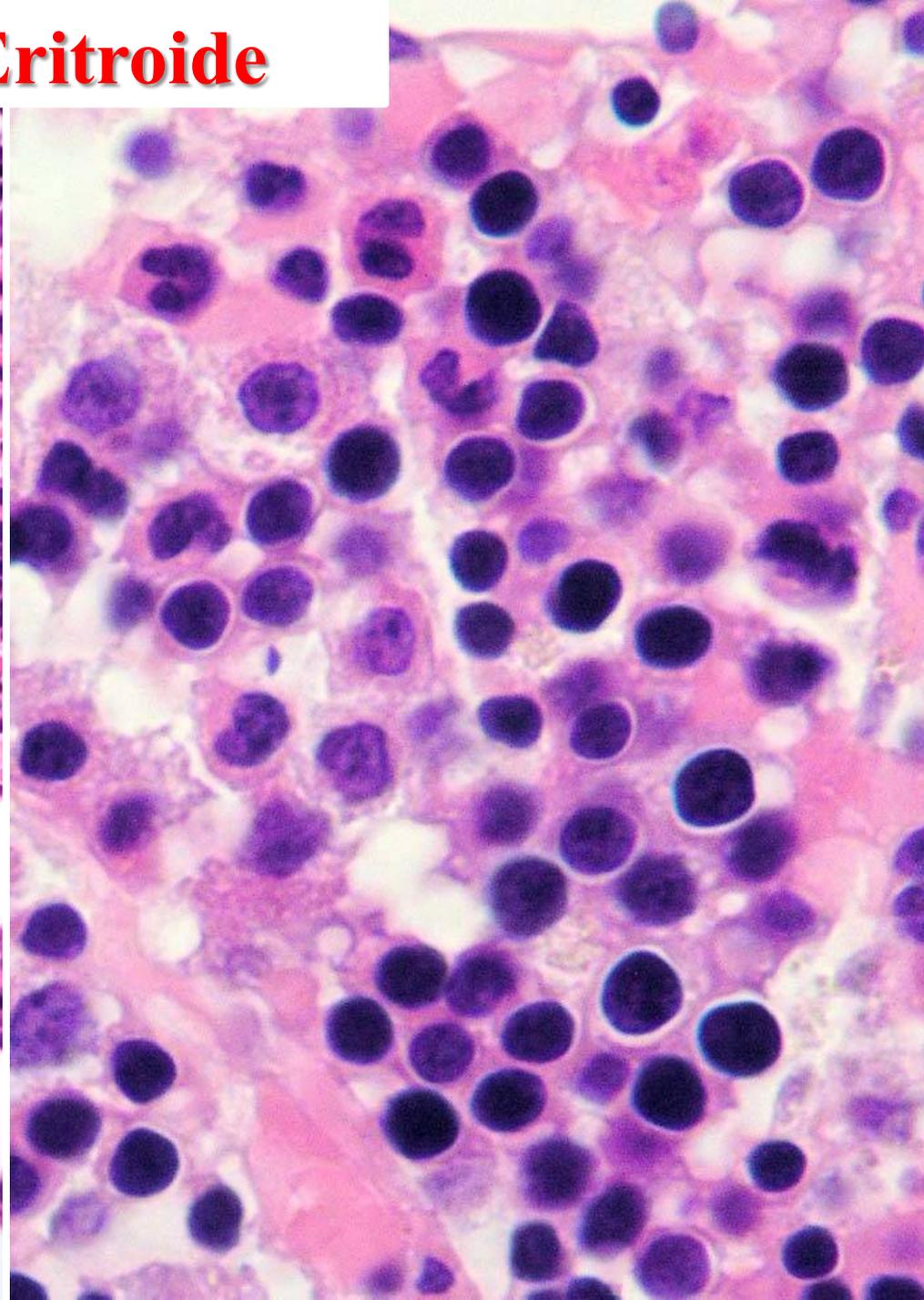
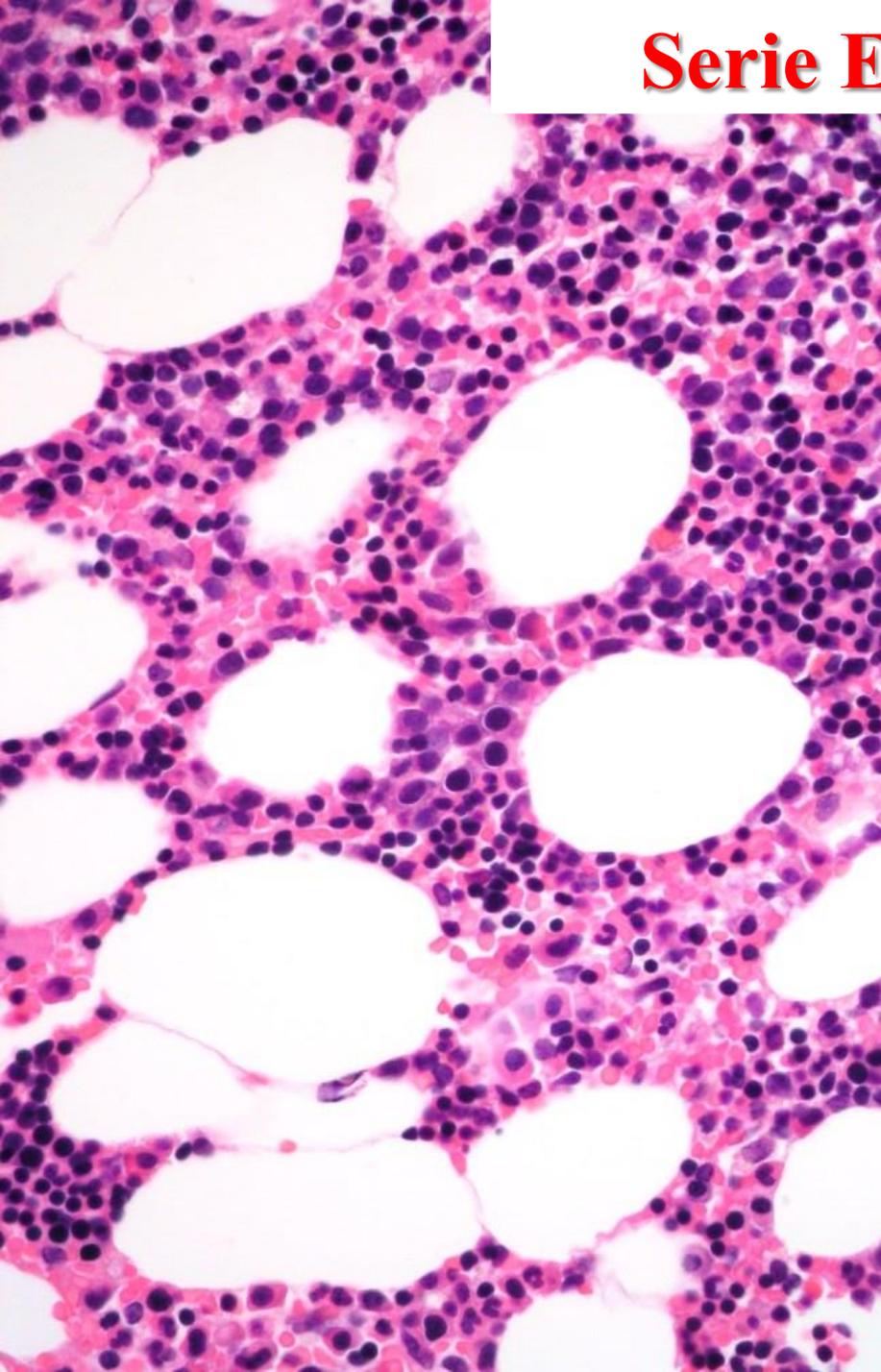
EMBO J 2006;25:3515–23.

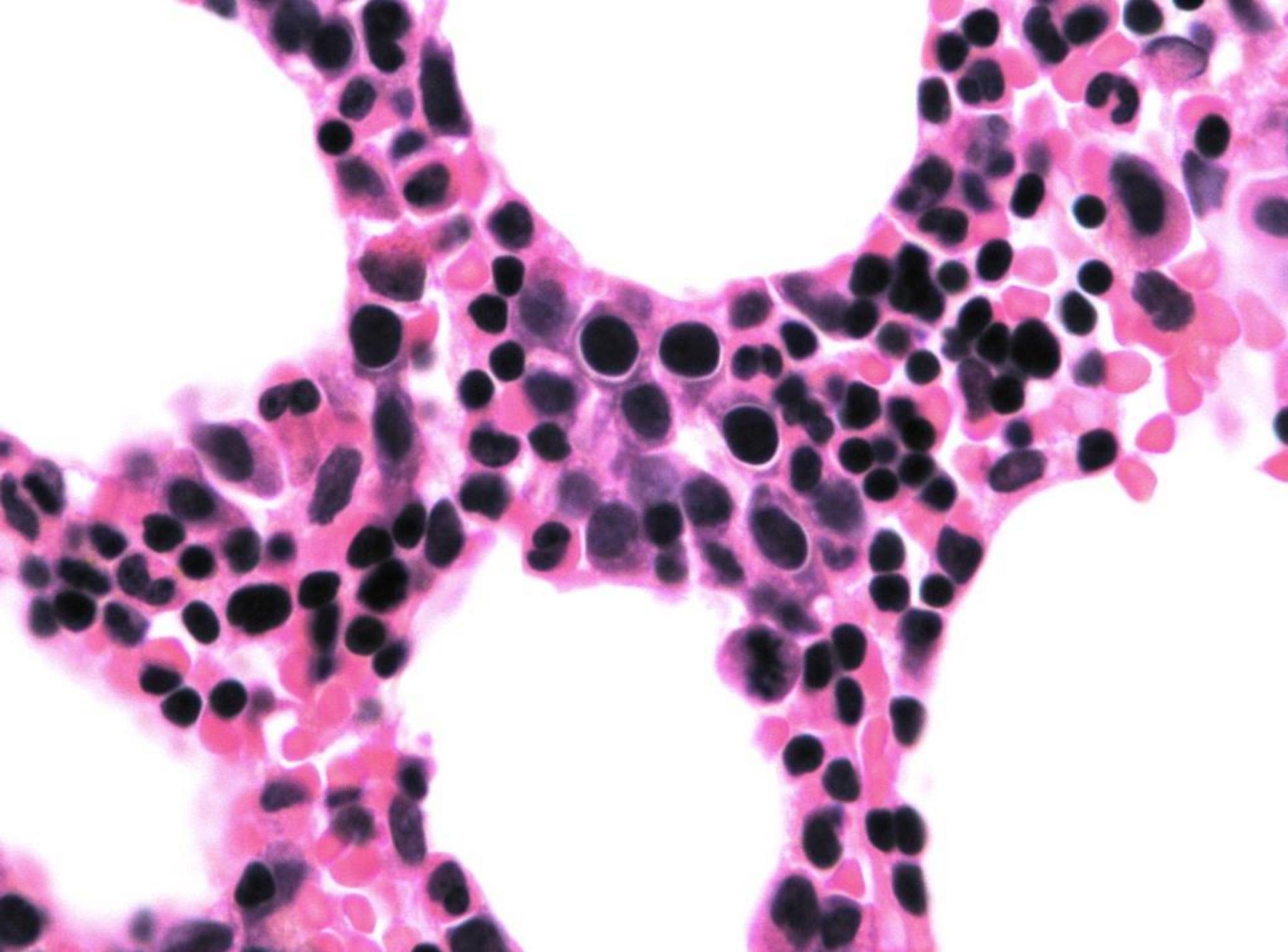
Yamazaki S, et al.

TGF-beta as a candidate bone marrow niche signal to induce hematopoietic stem cell hibernation.

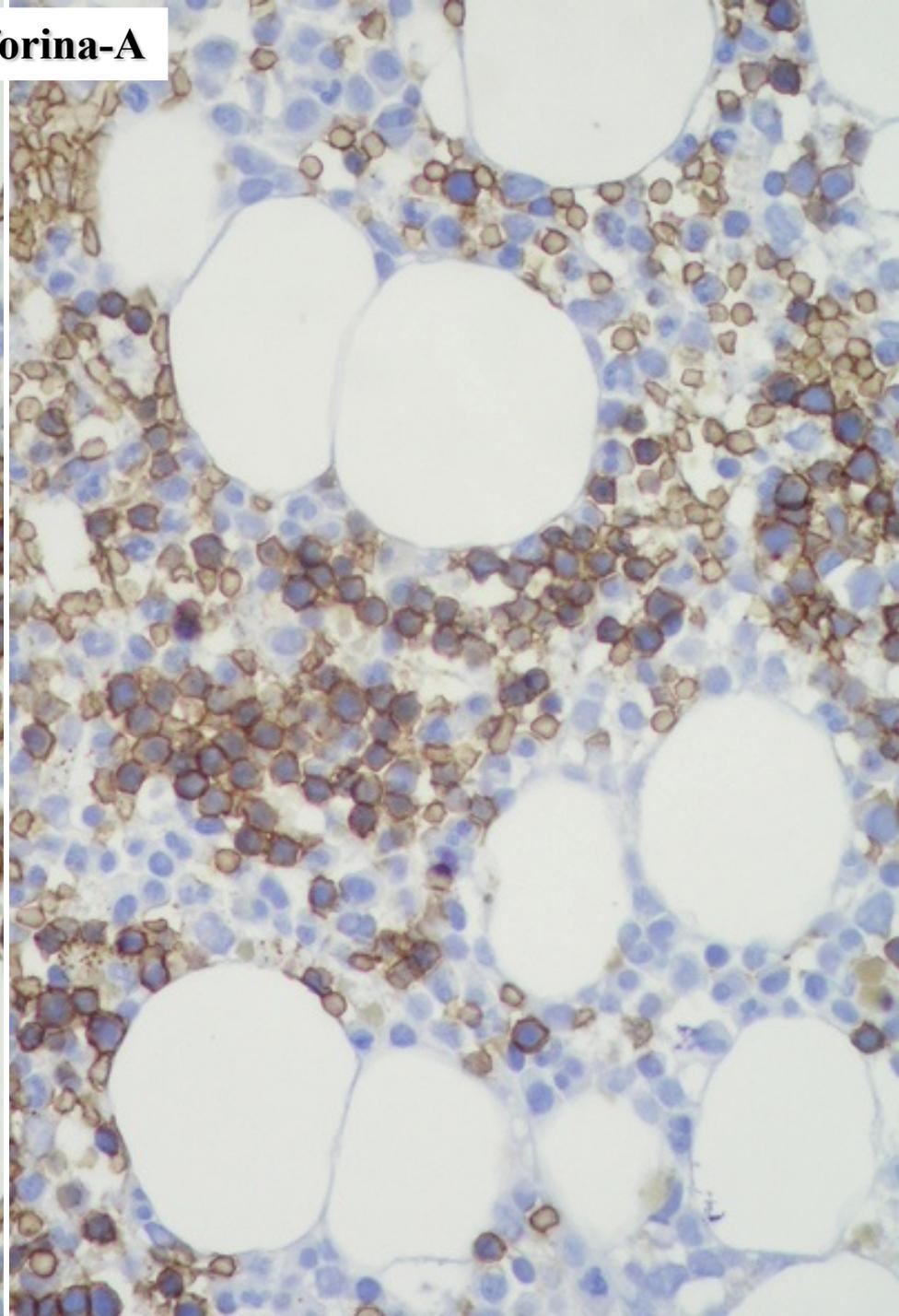
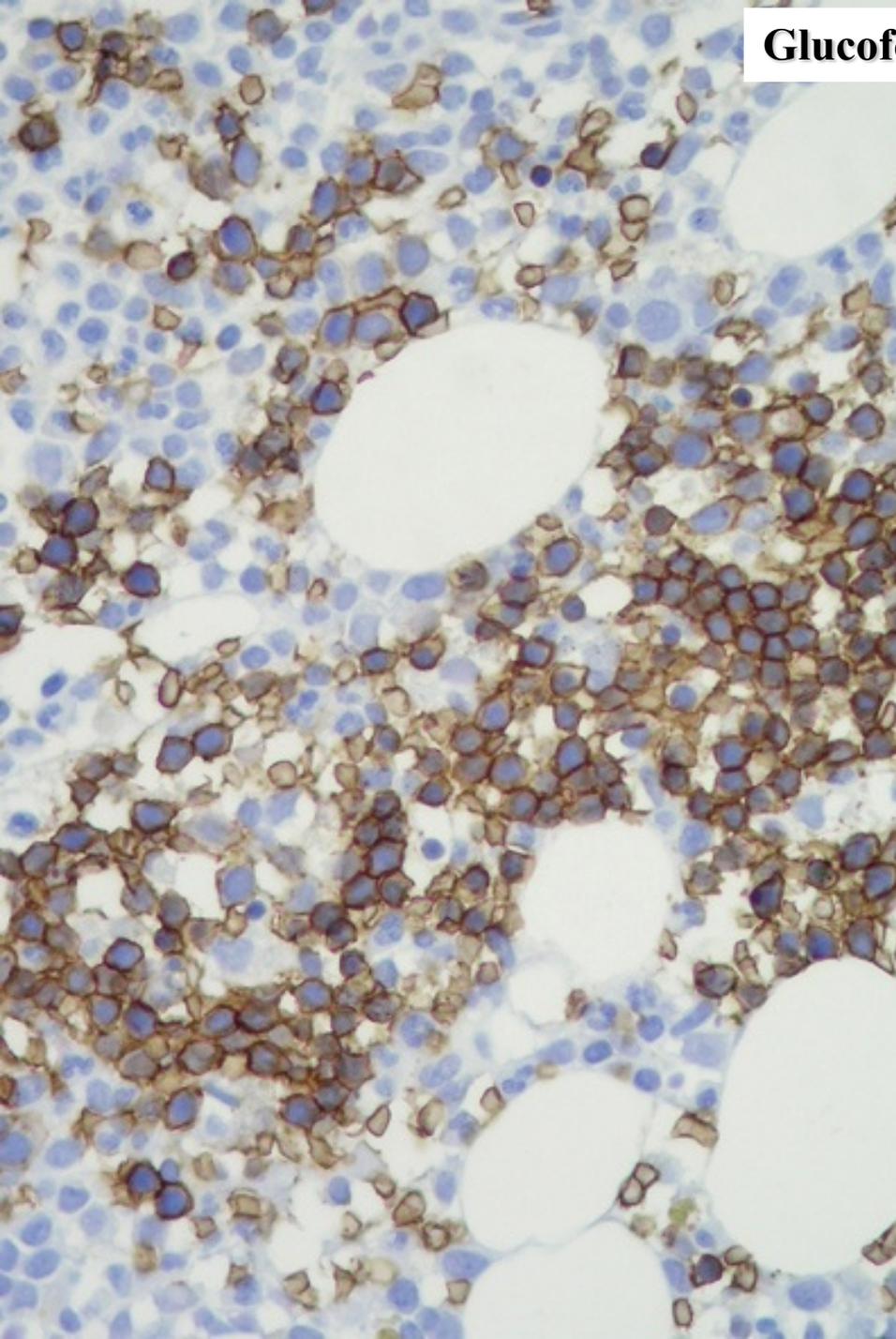
Blood 2009;113:1250–6.

Serie Eritroide

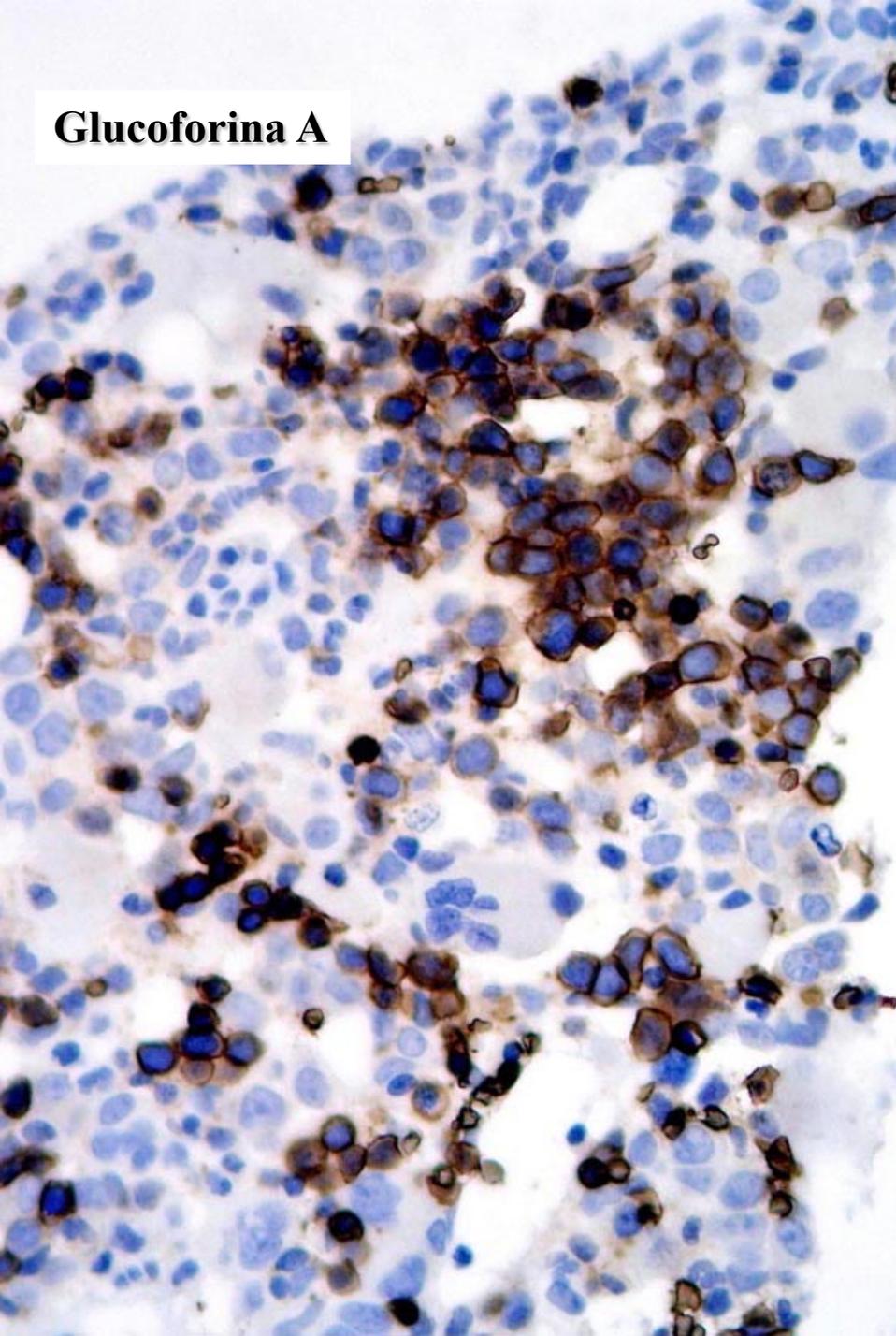




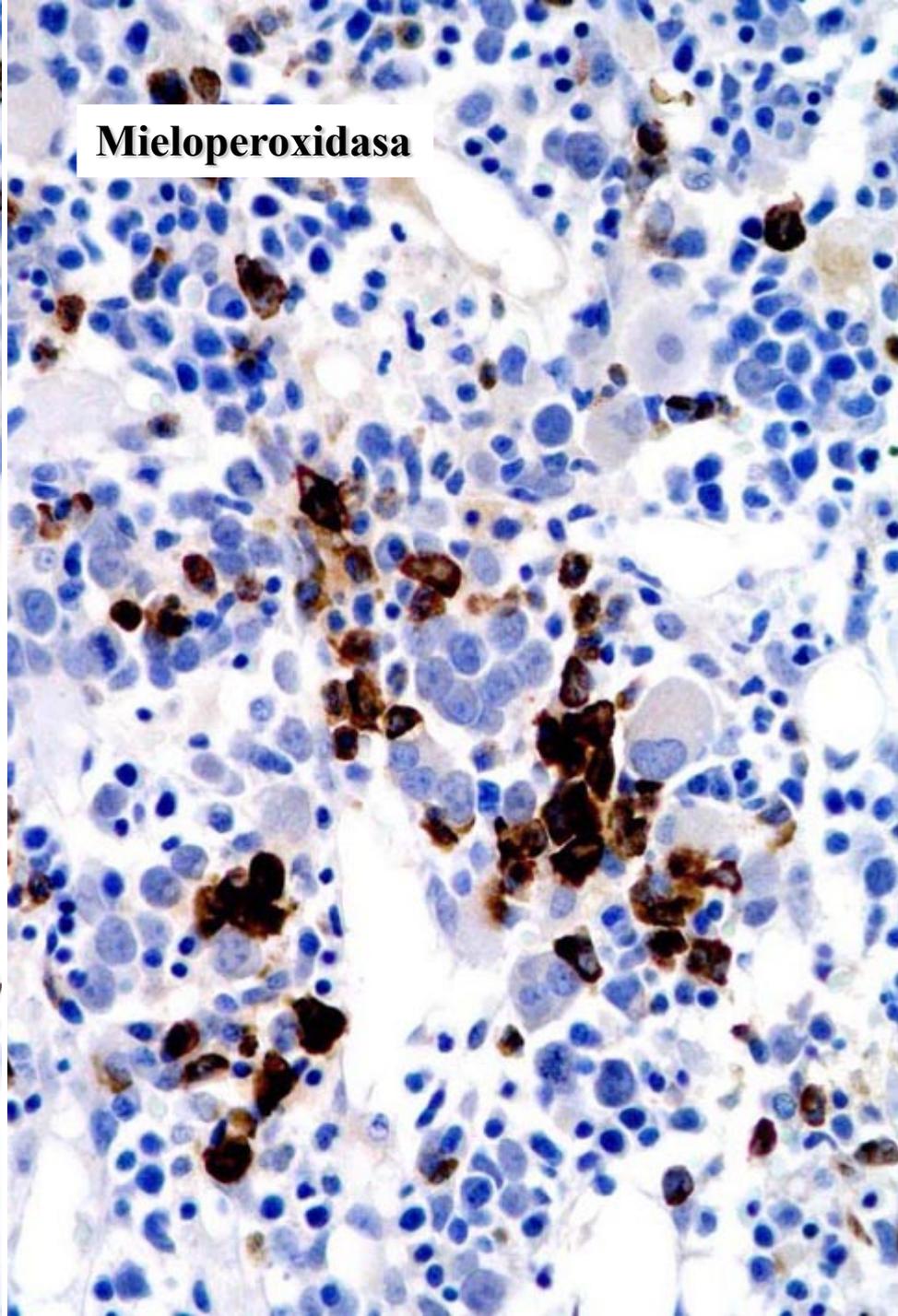
Glucoforina-A

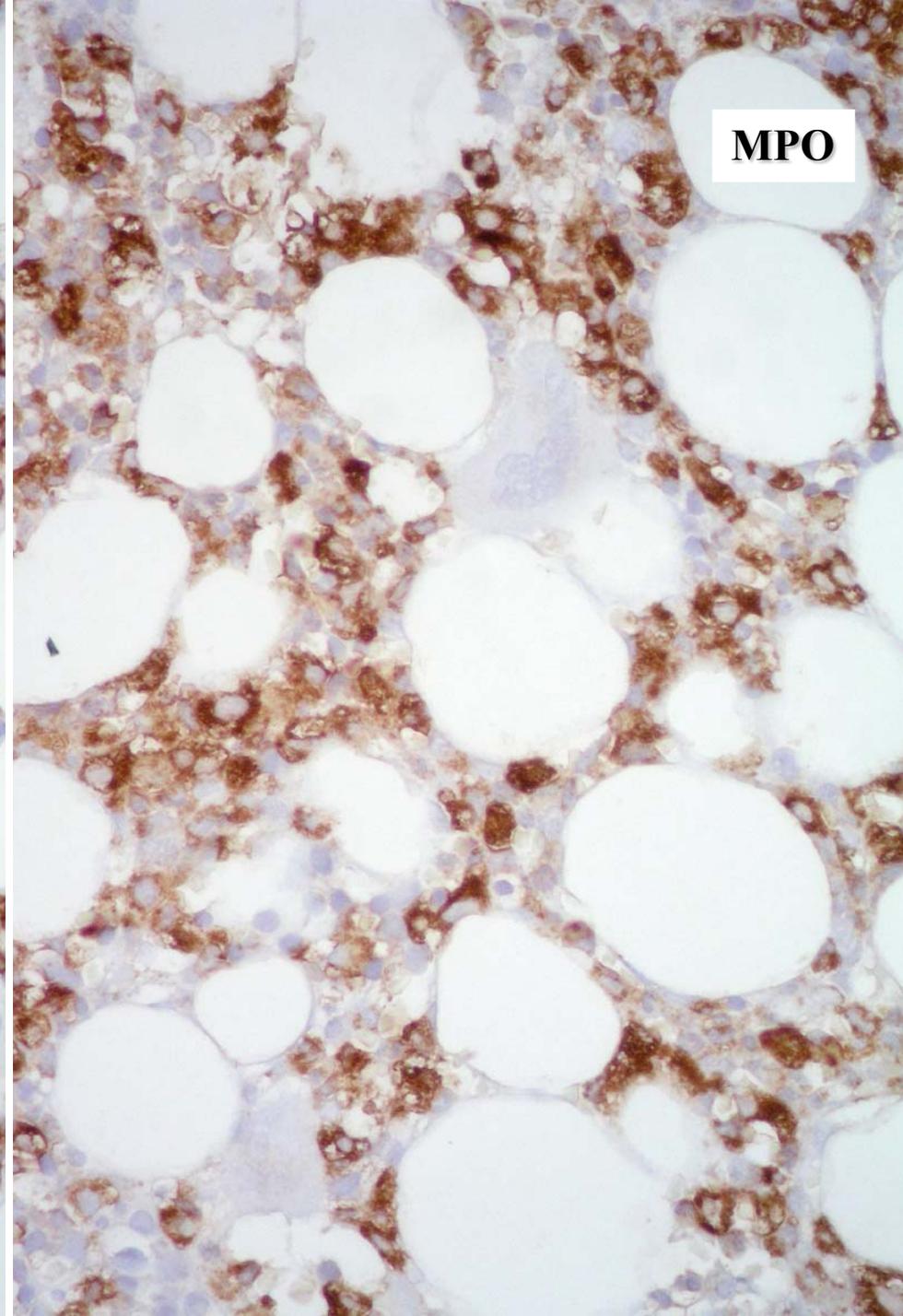
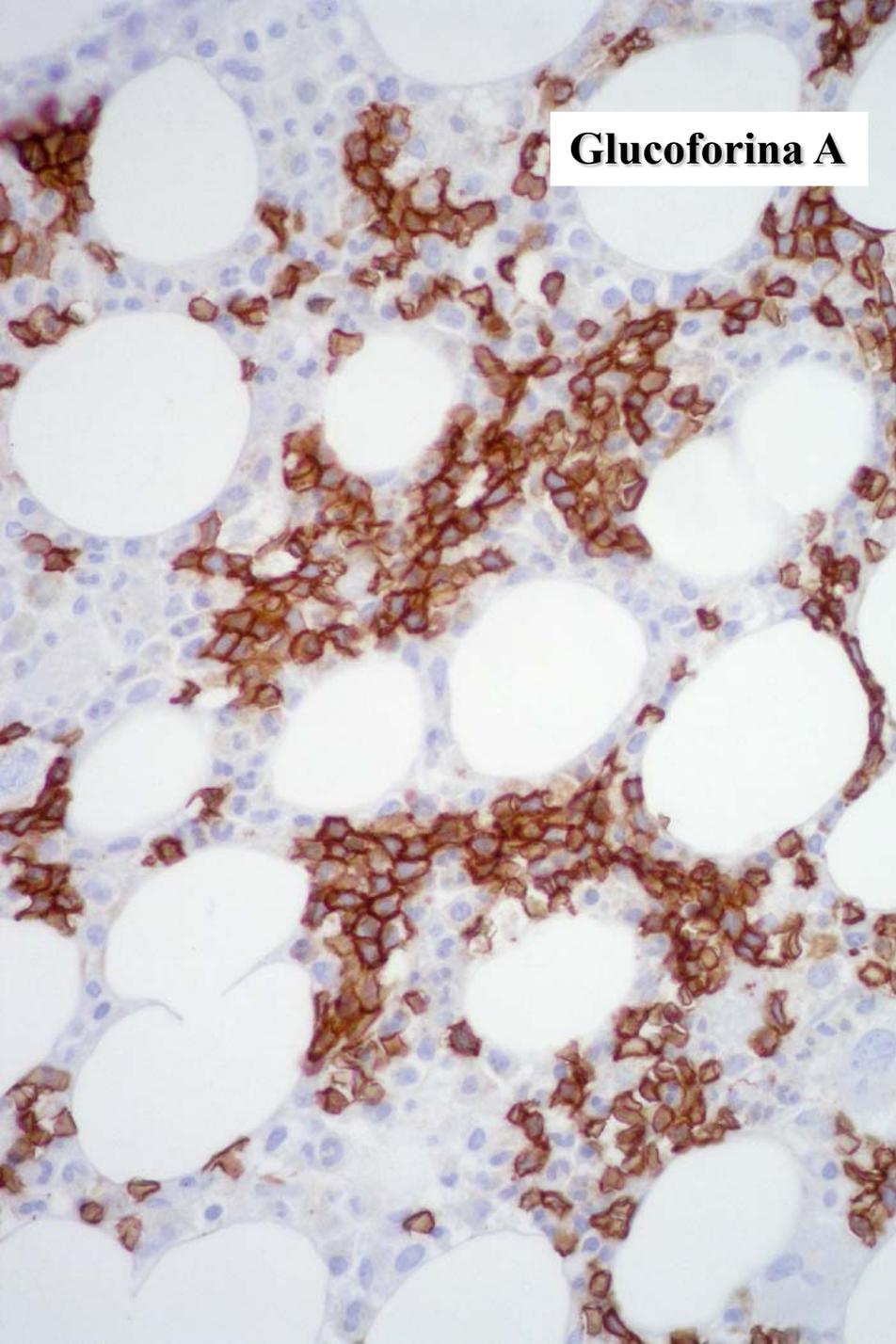


Glucoforina A

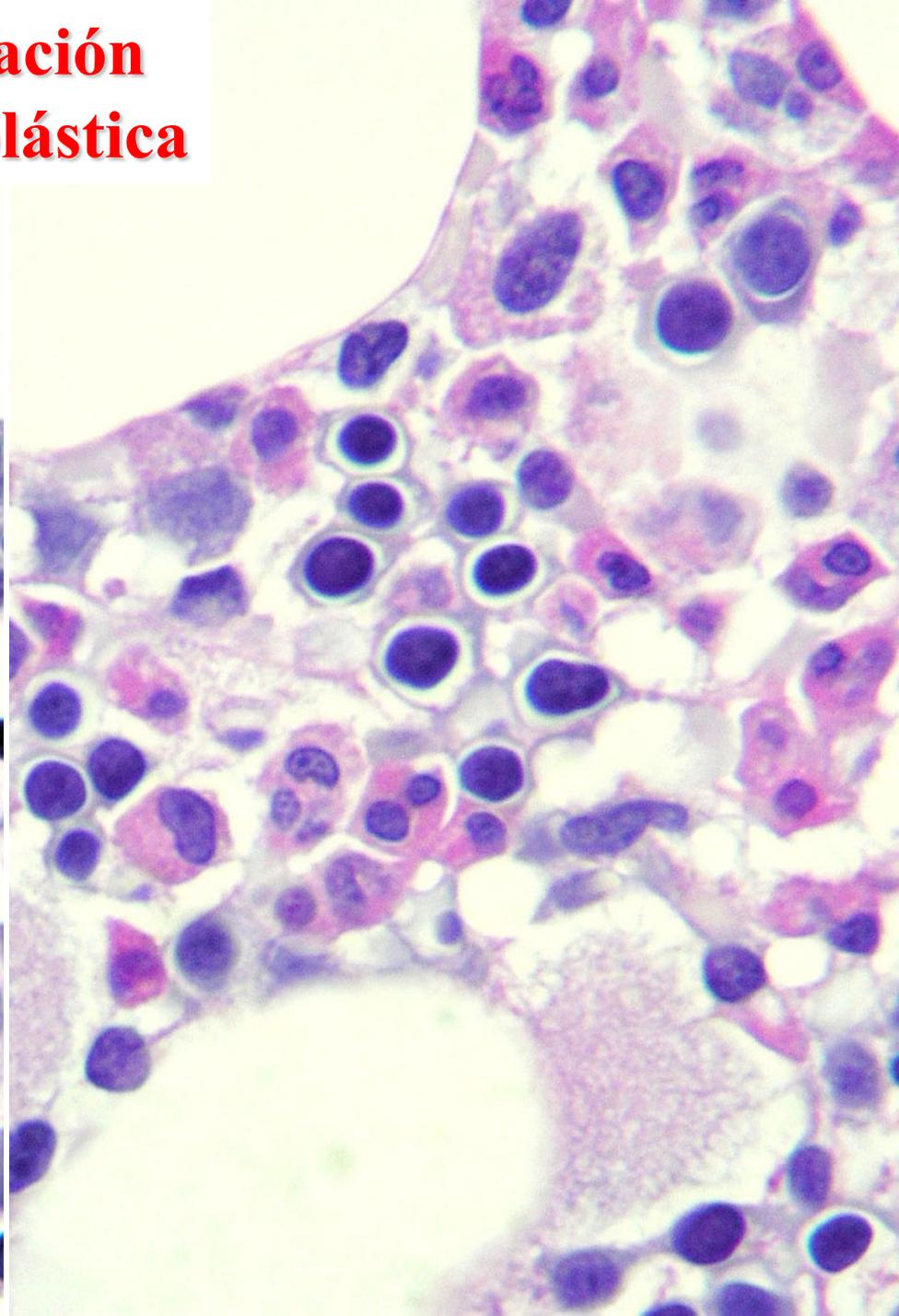
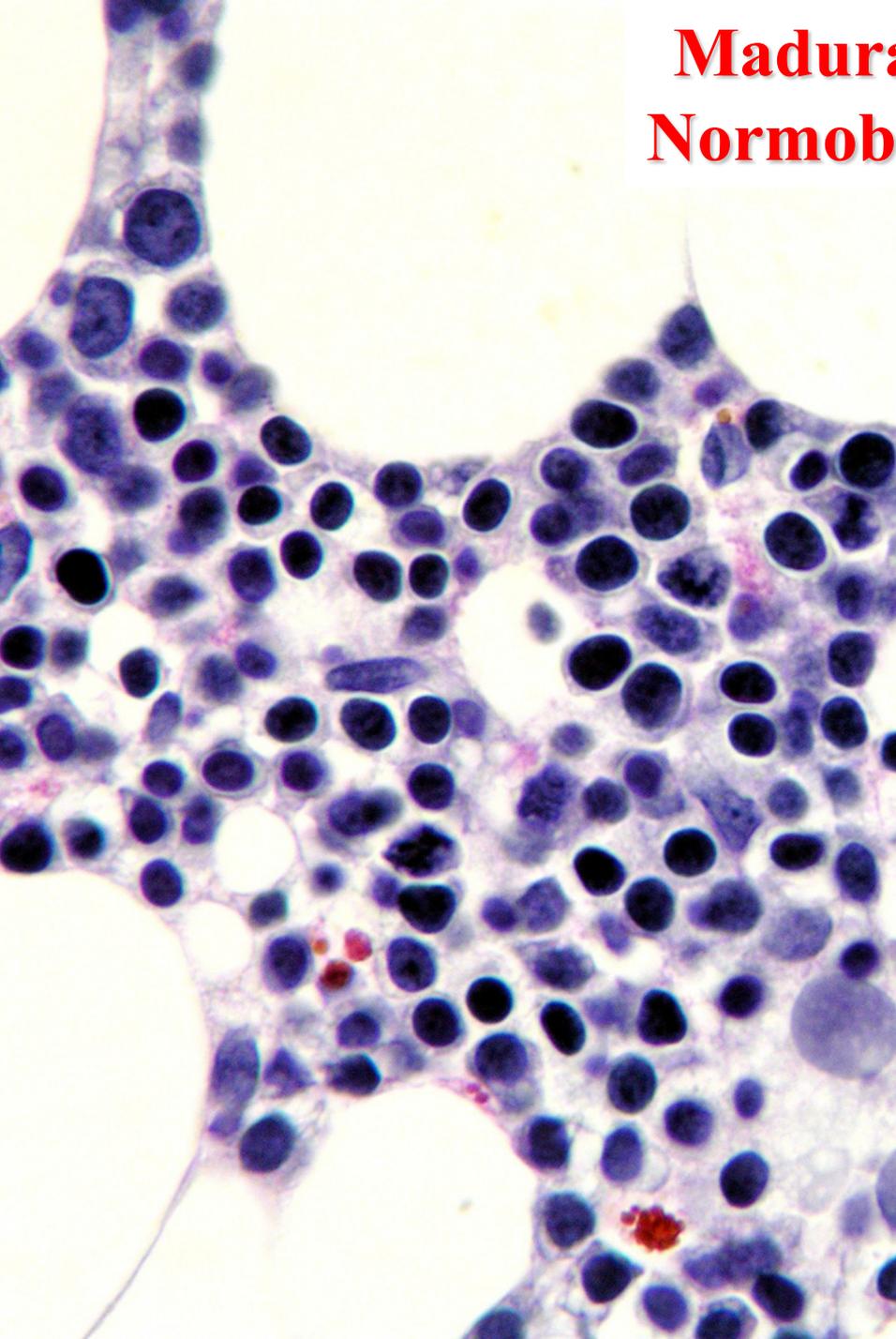


Mieloperoxidasa

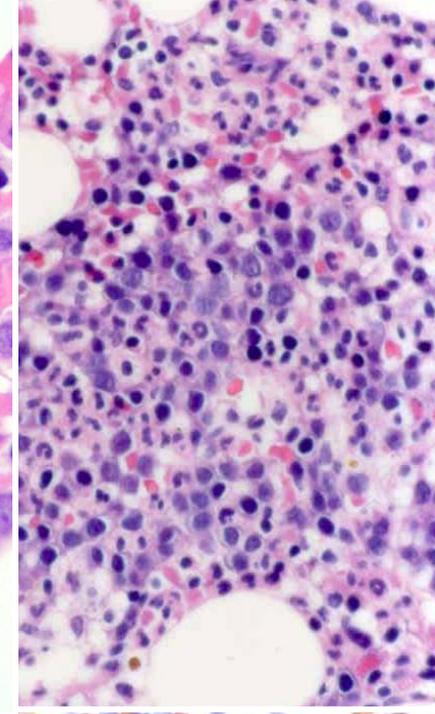
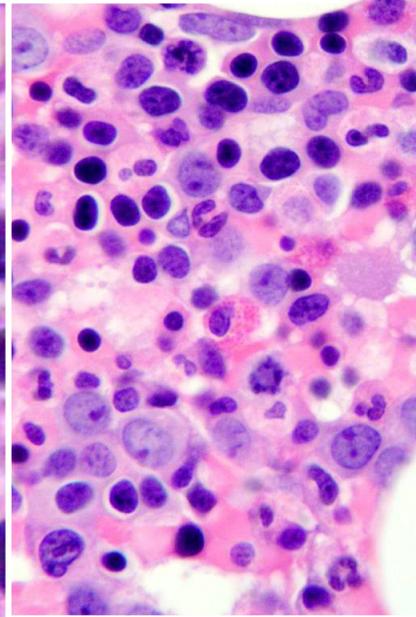
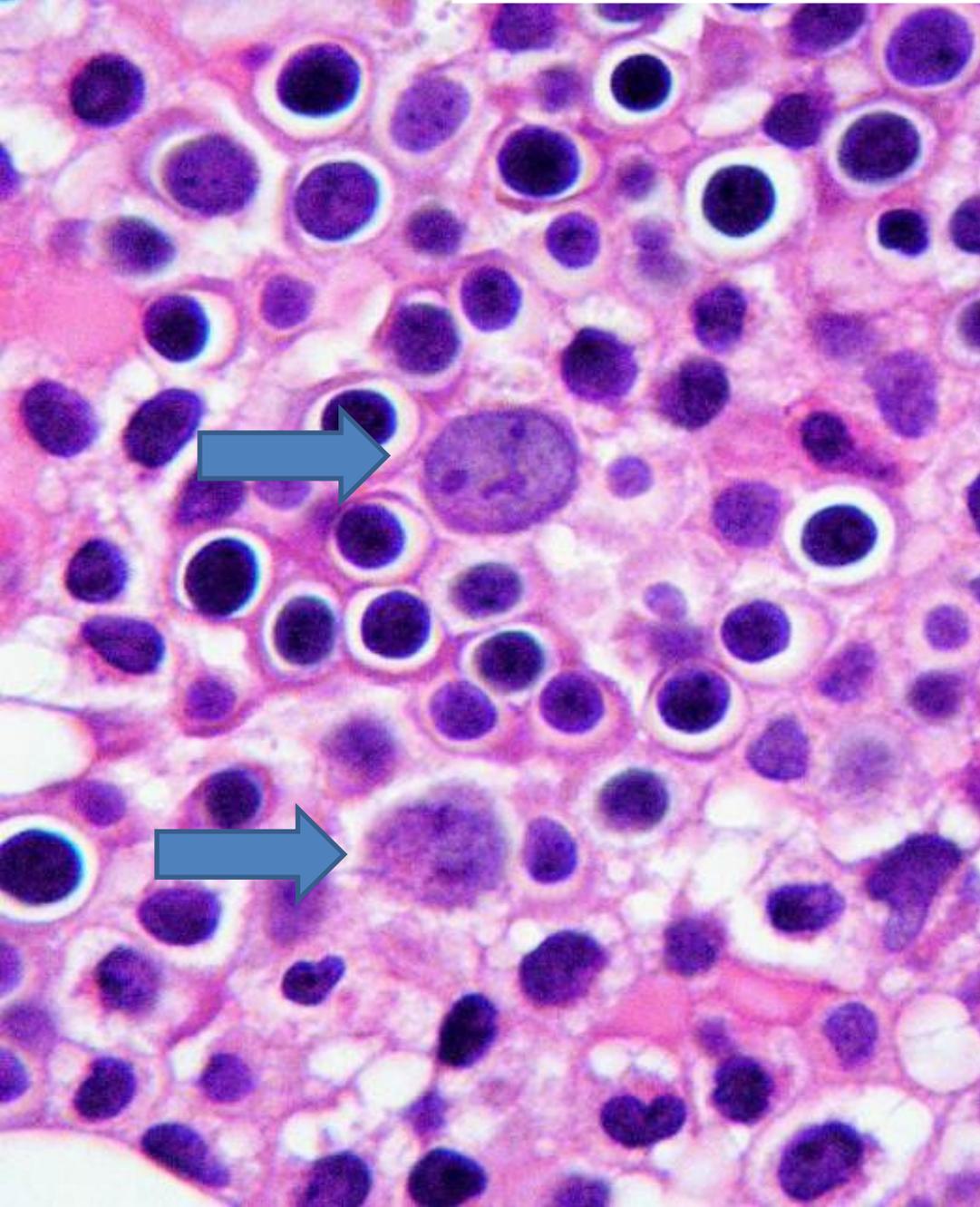




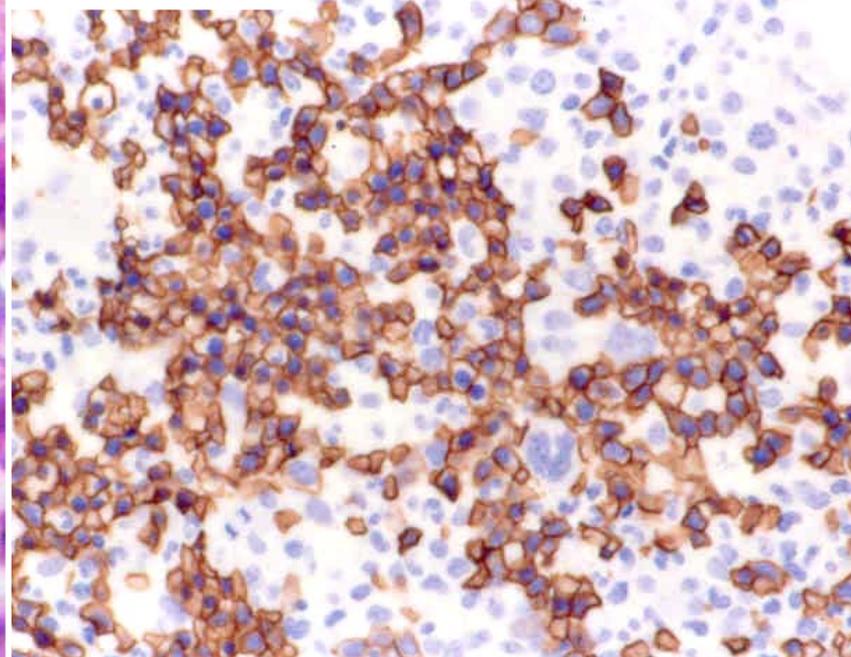
Maduración Normoblástica

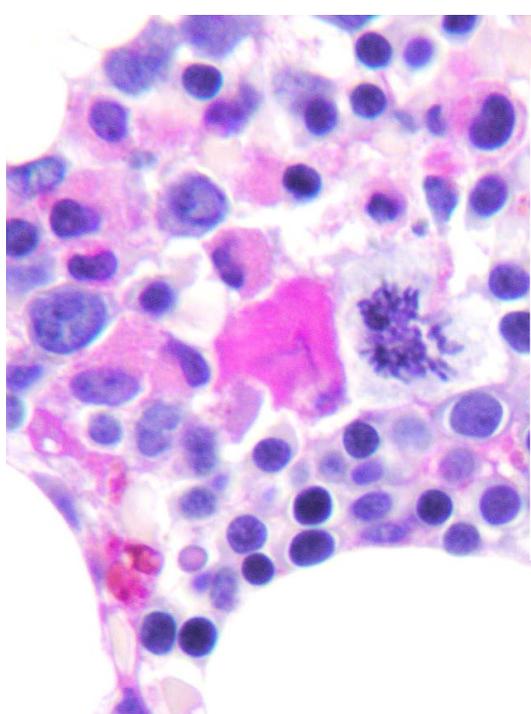
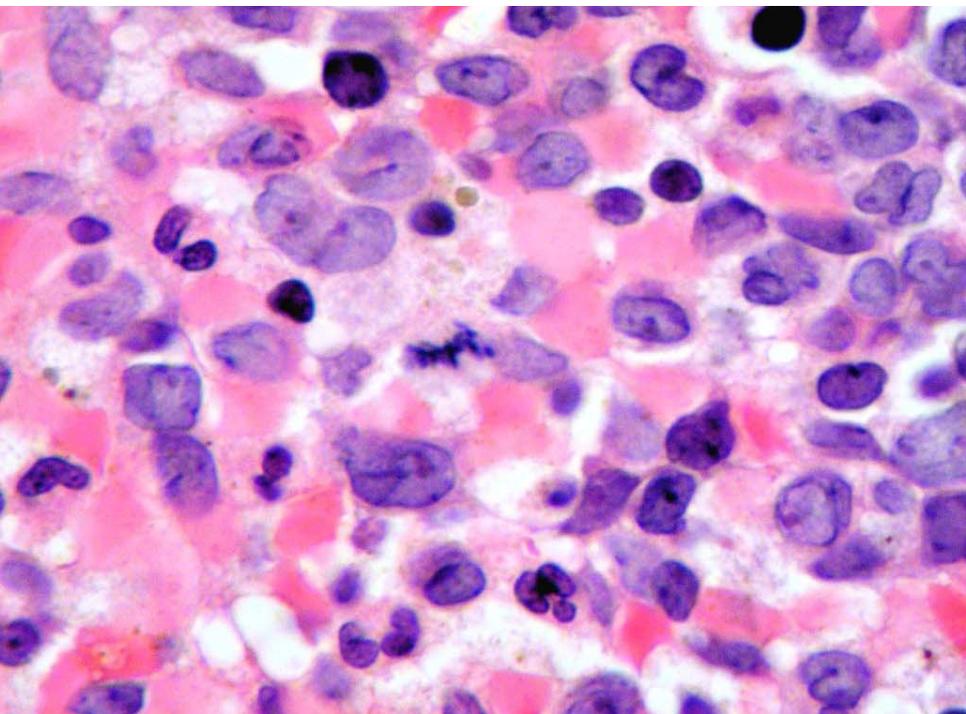
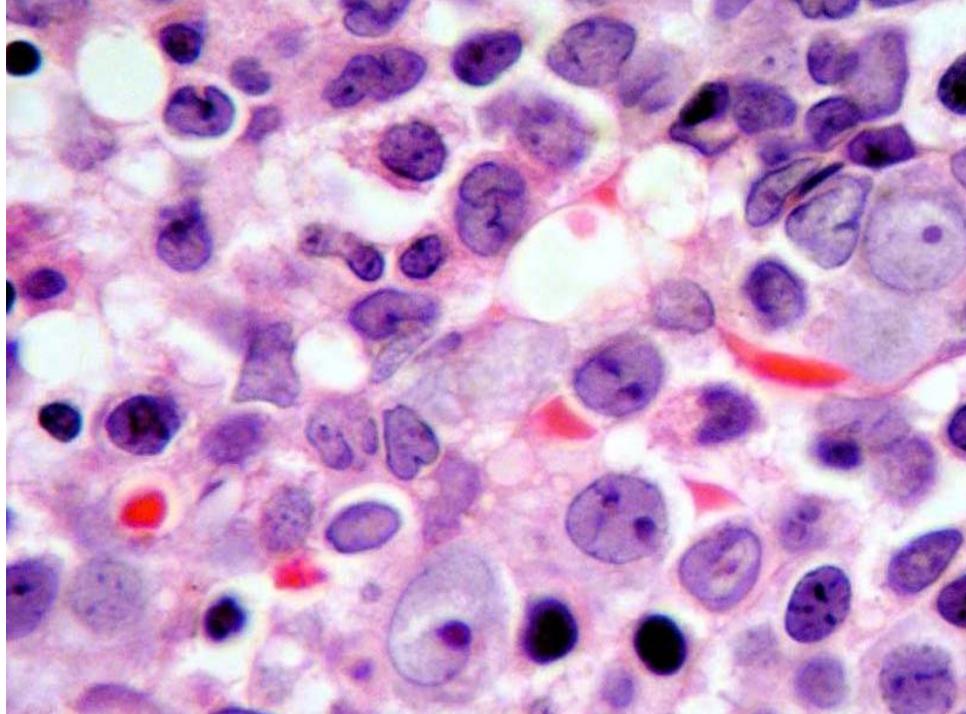
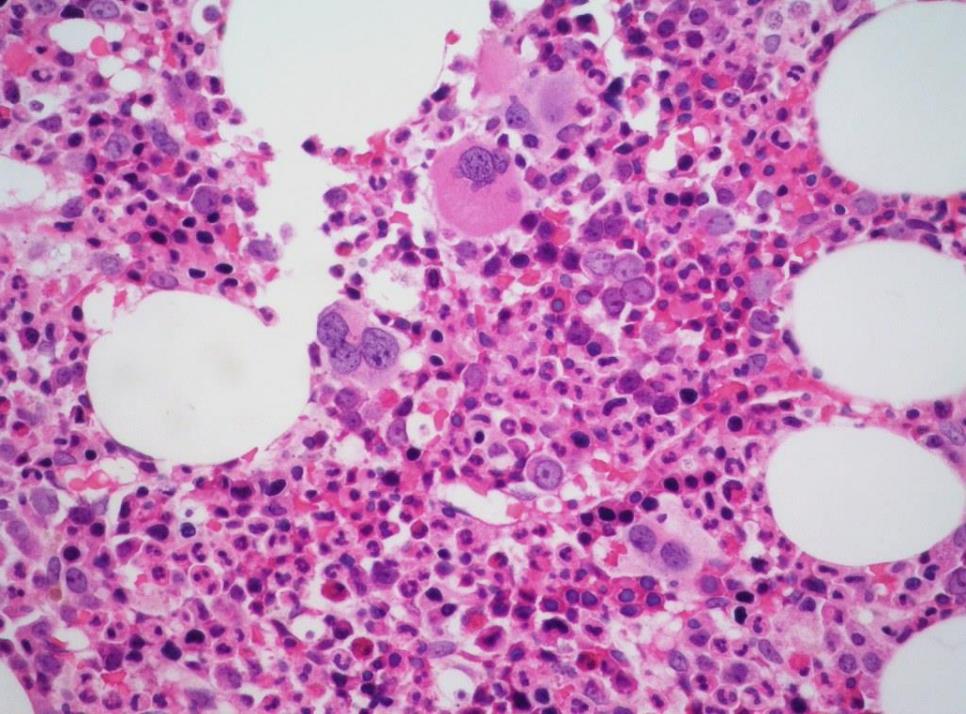


Cambios Megaloblasticos /oides

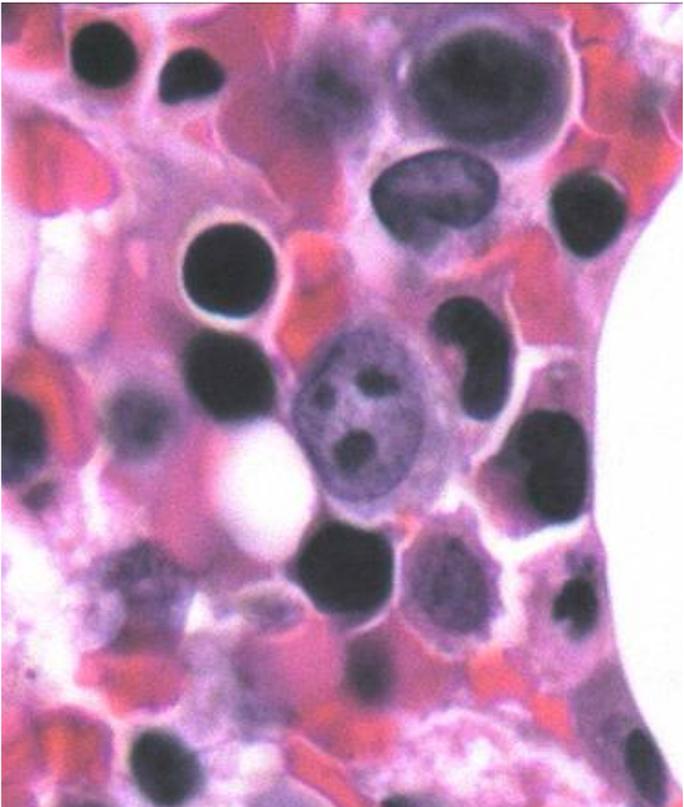
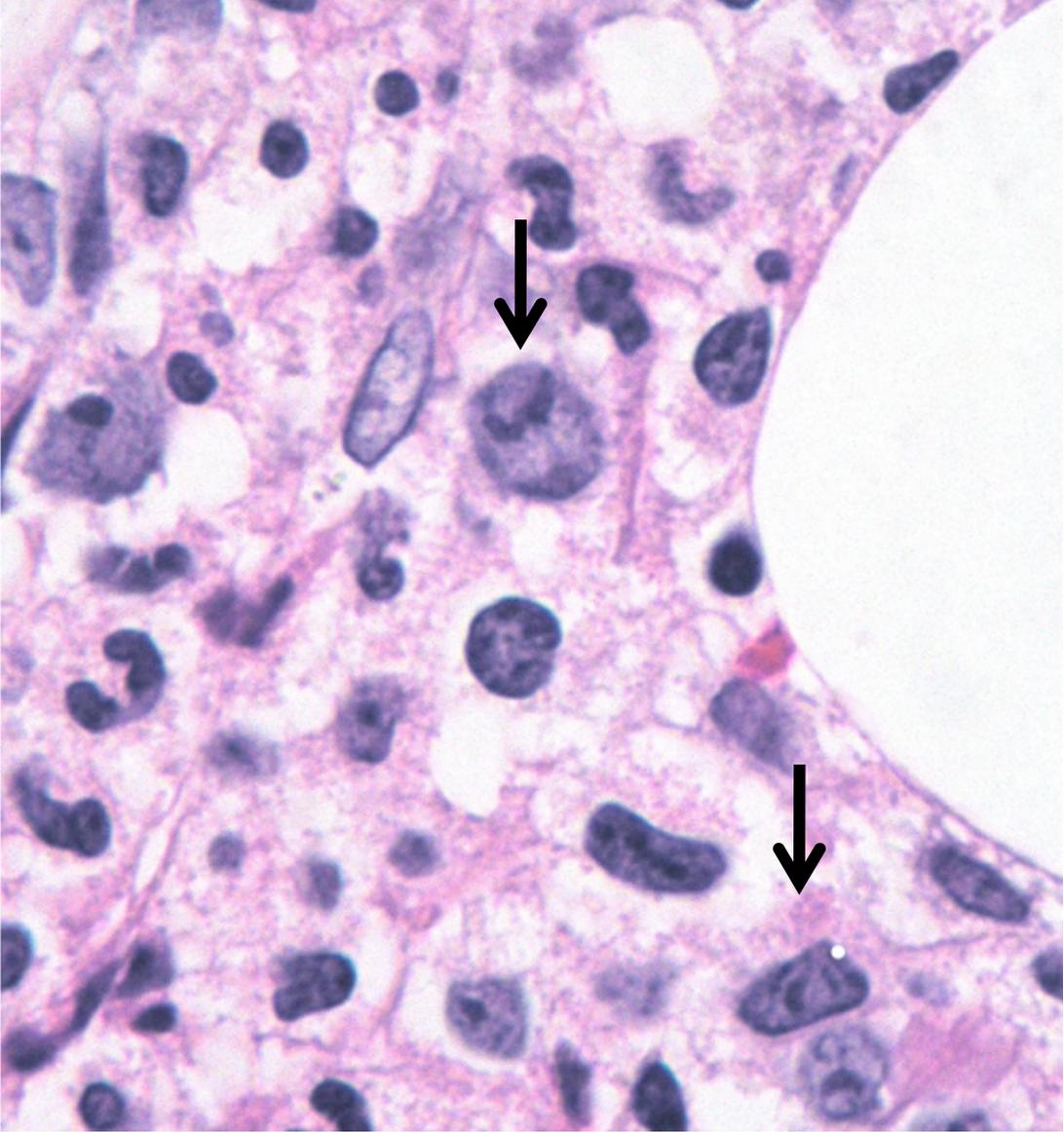
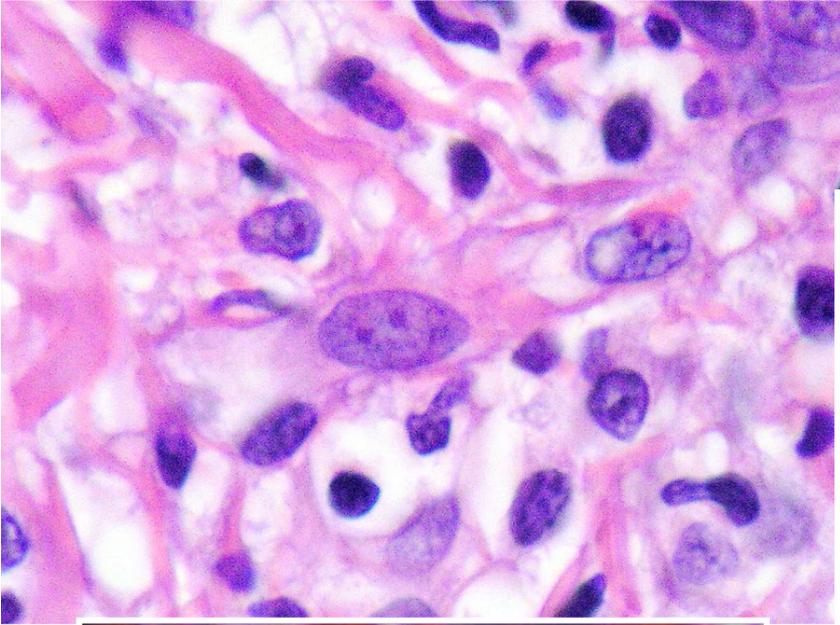


Glucoforina A

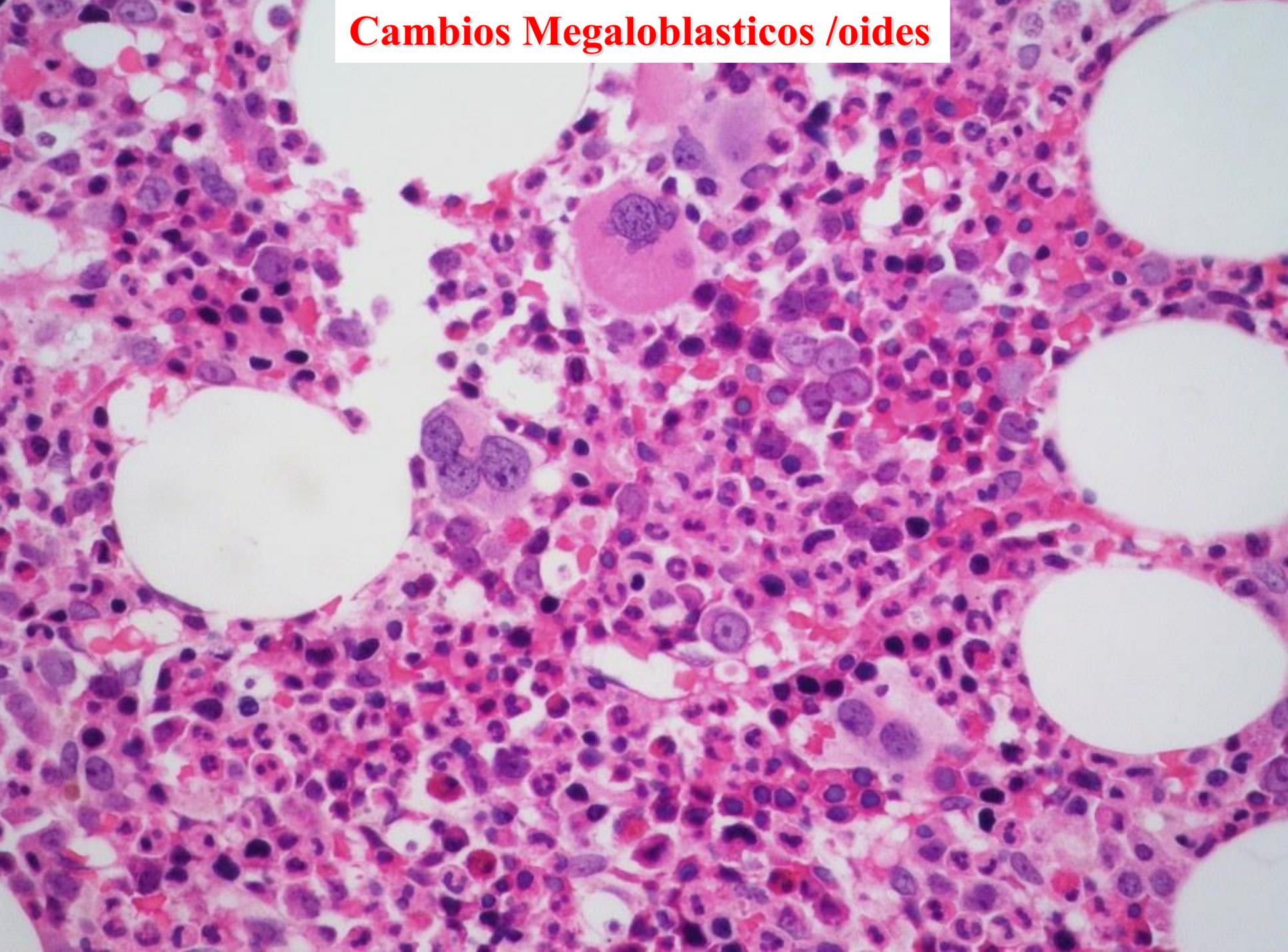




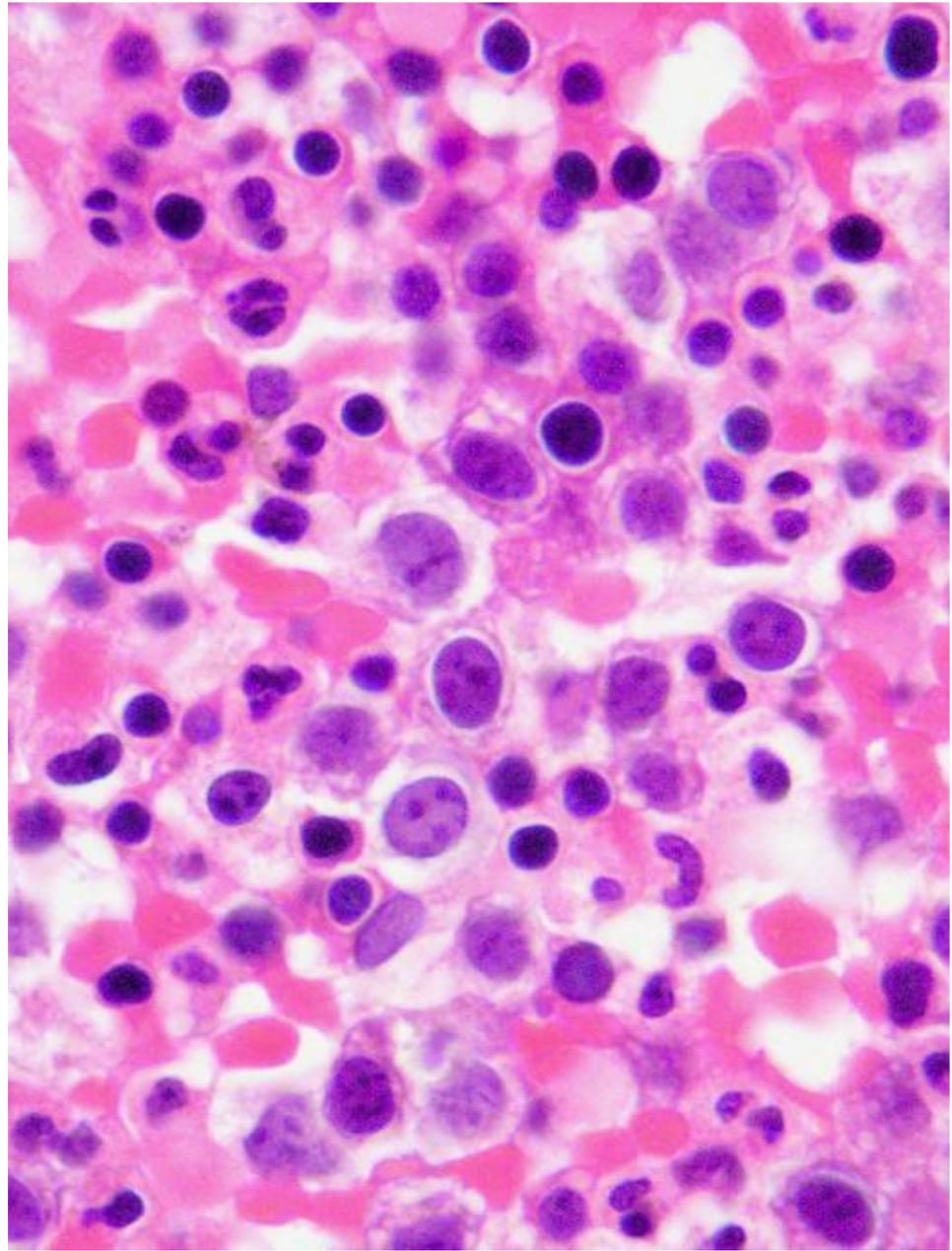
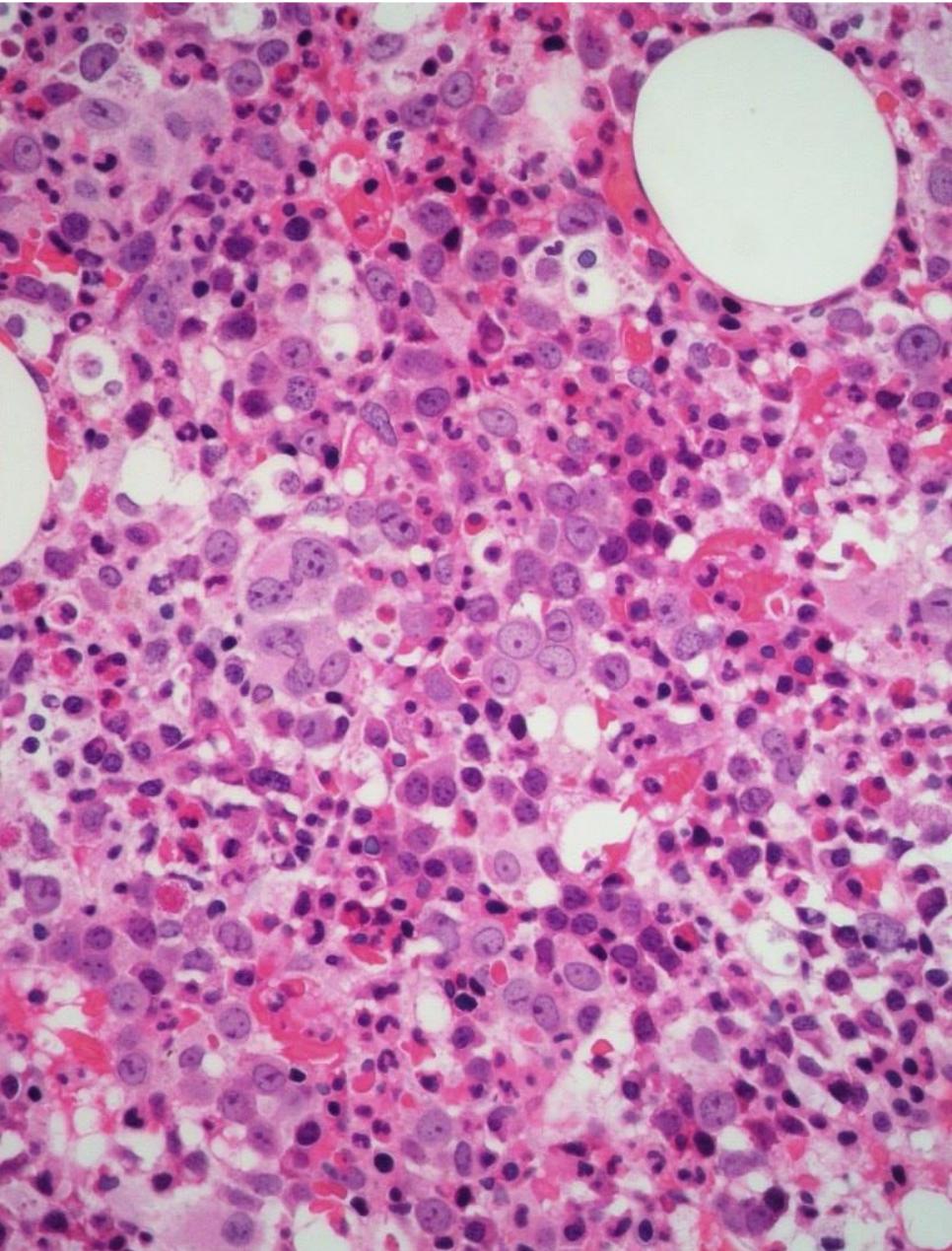
Cambios Megaloblastoide

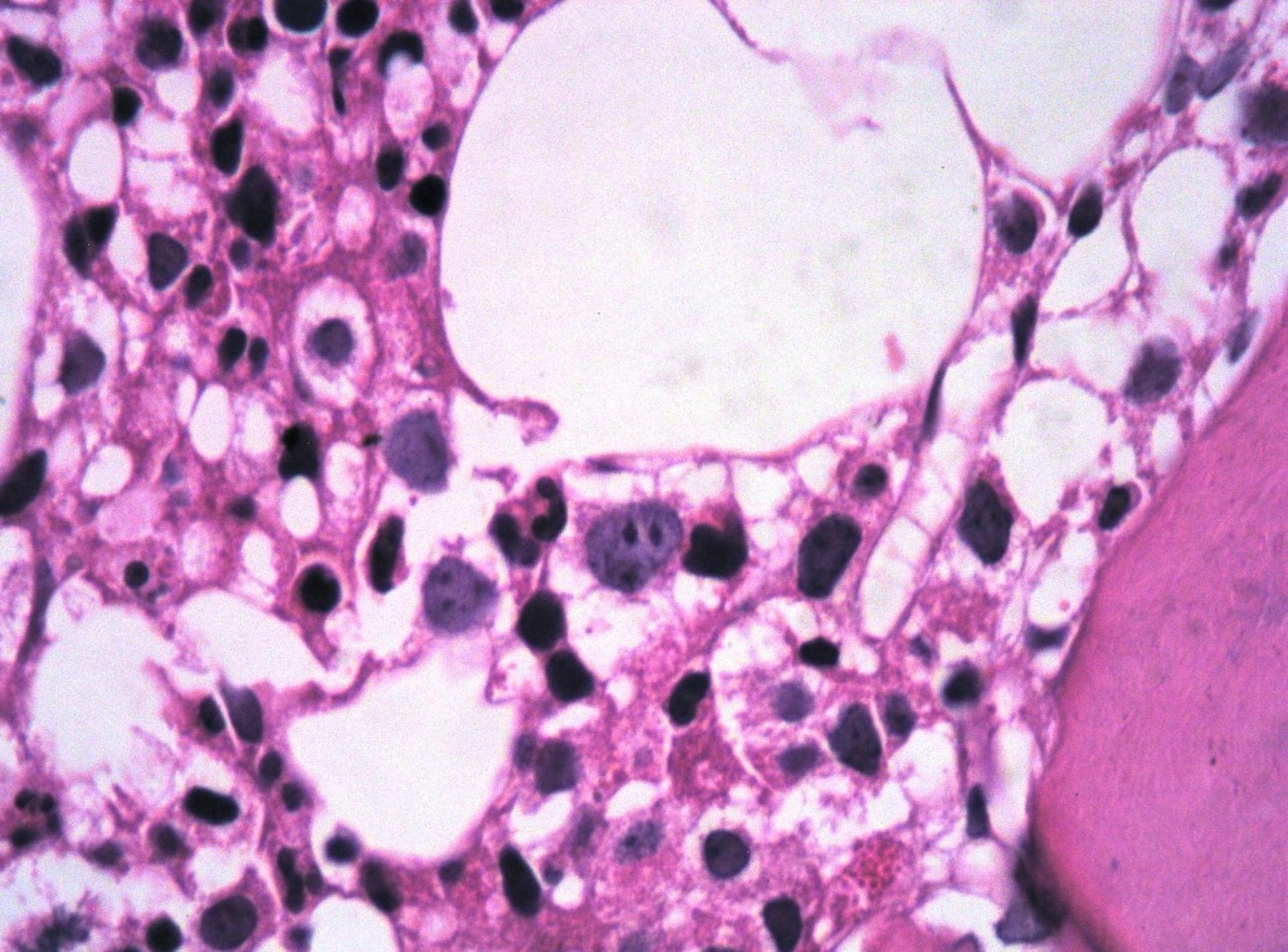


Cambios Megaloblasticos /oides

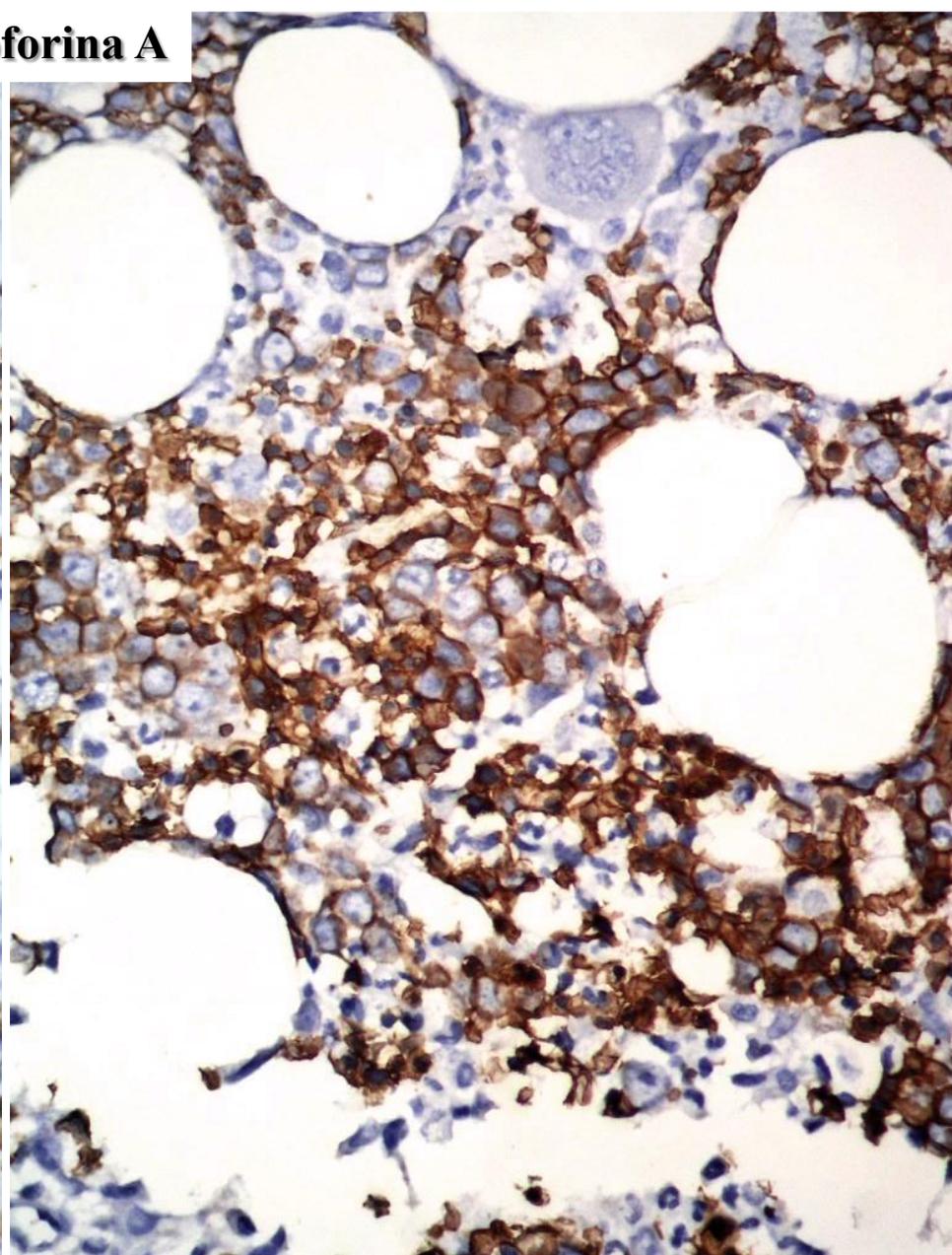
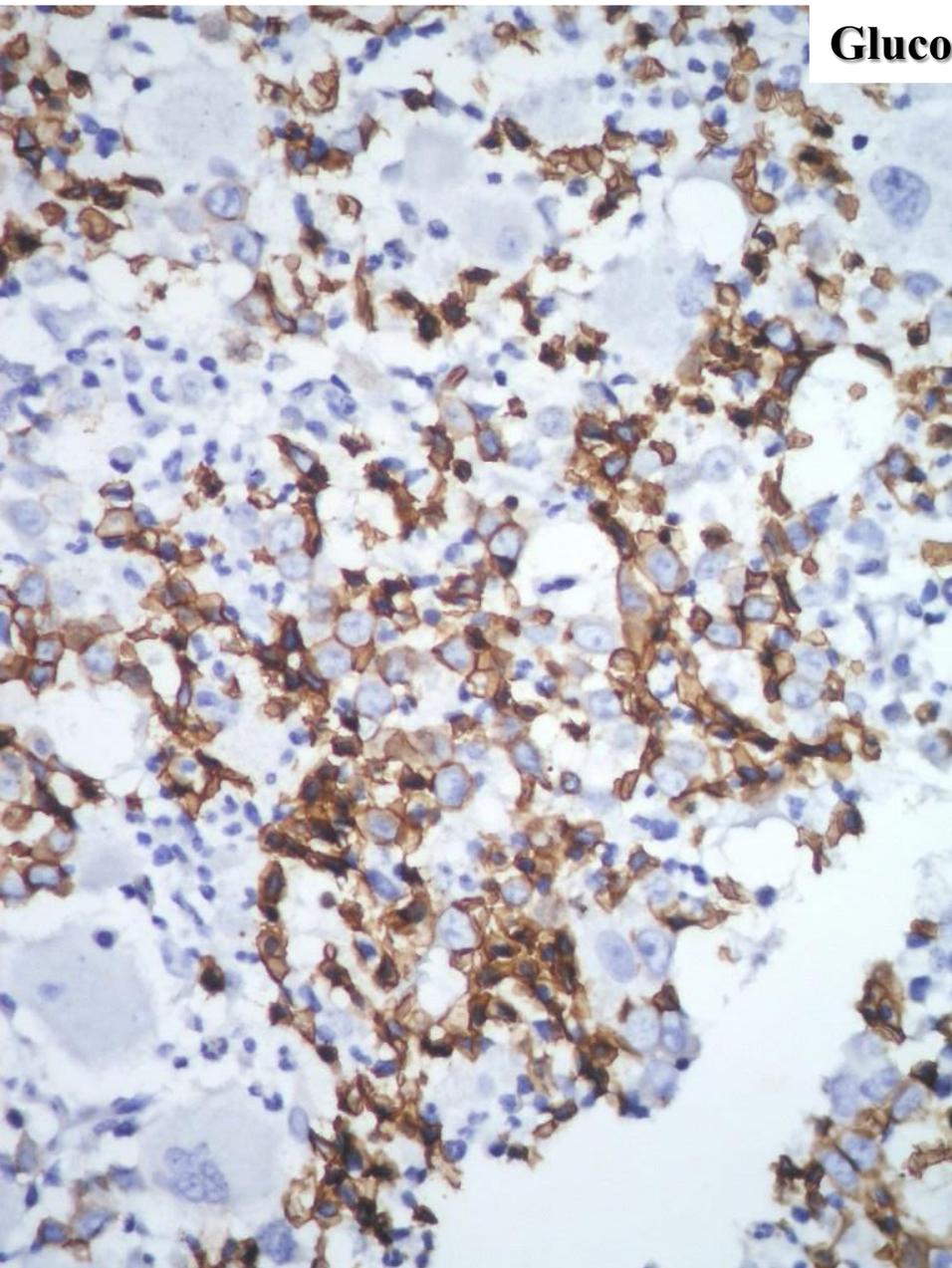


Cambios Megaloblasticos /oides





Glucoforina A



Cambios Megaloblásticos

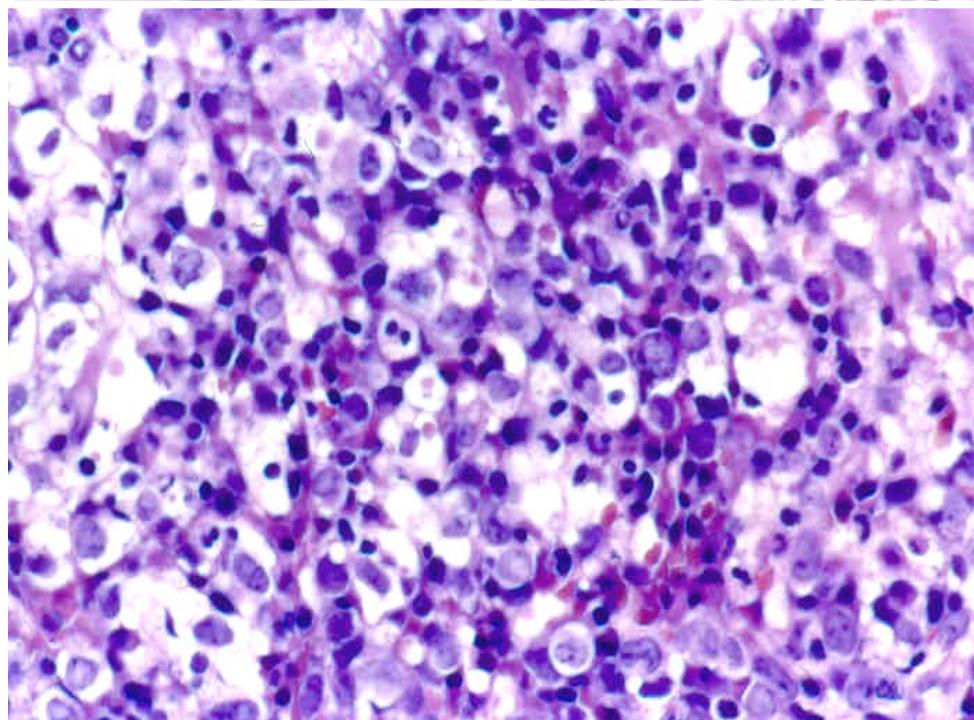
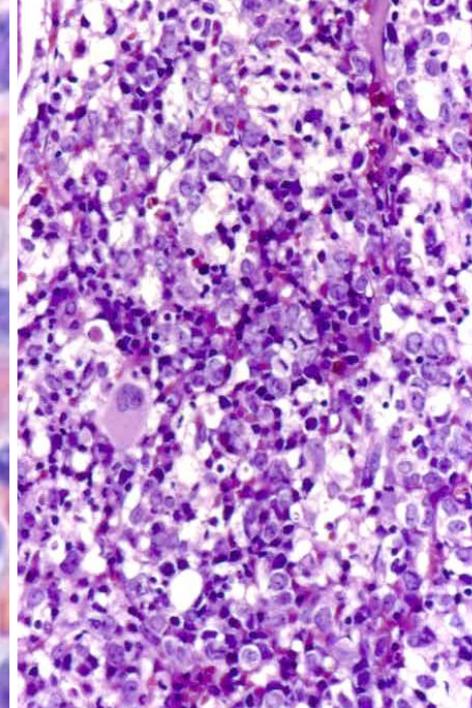
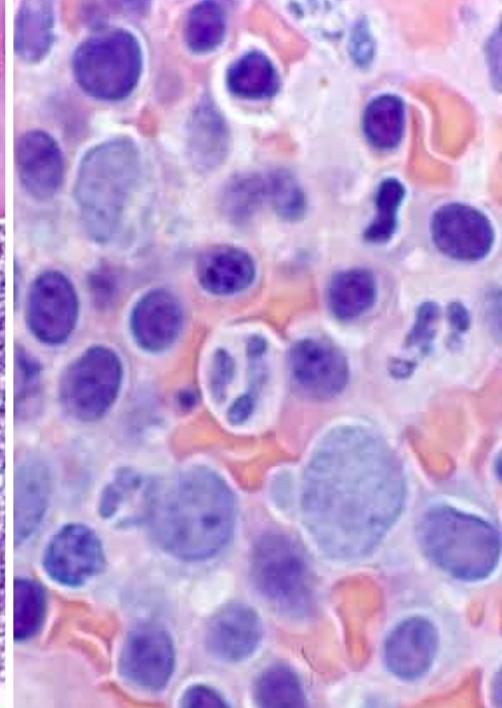
- **Dieta: (Folatos / Cobalamina)**
- **Infecciones virales (HIV)**
- **Medicamentos**
Anti folatos (MTX/ Aminopterina)
Análogos de Purinas: (6-MP/ Acyclovir

Análogos de pirimidinas:
5F-U /Zidovudine
Anticonvulsivantes:
Fenobarbital / Fenitoina
Anticonceptivos orales

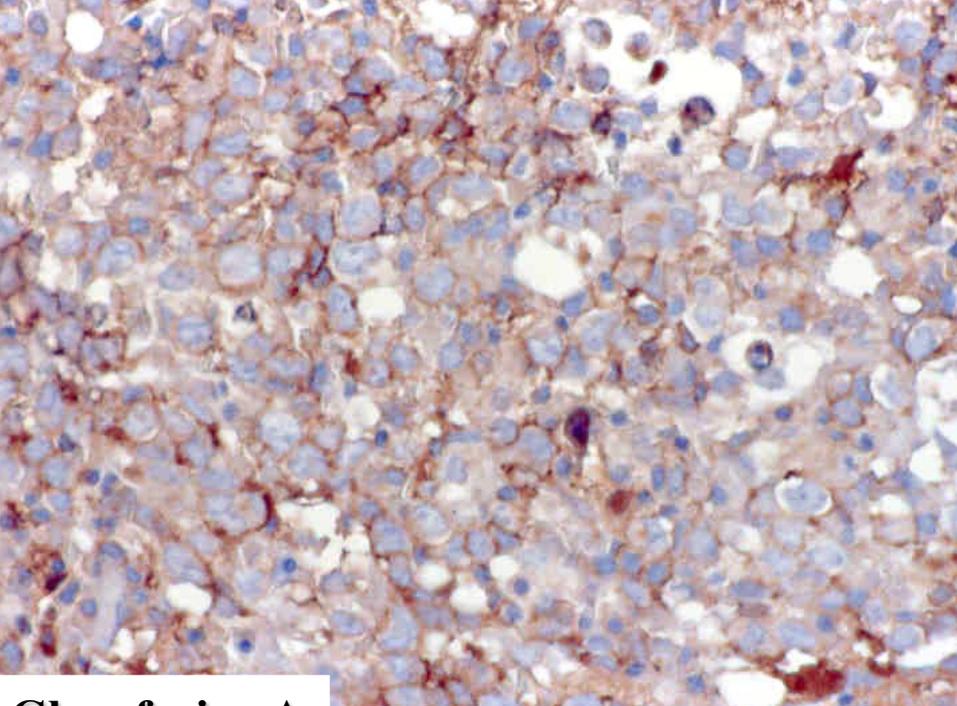
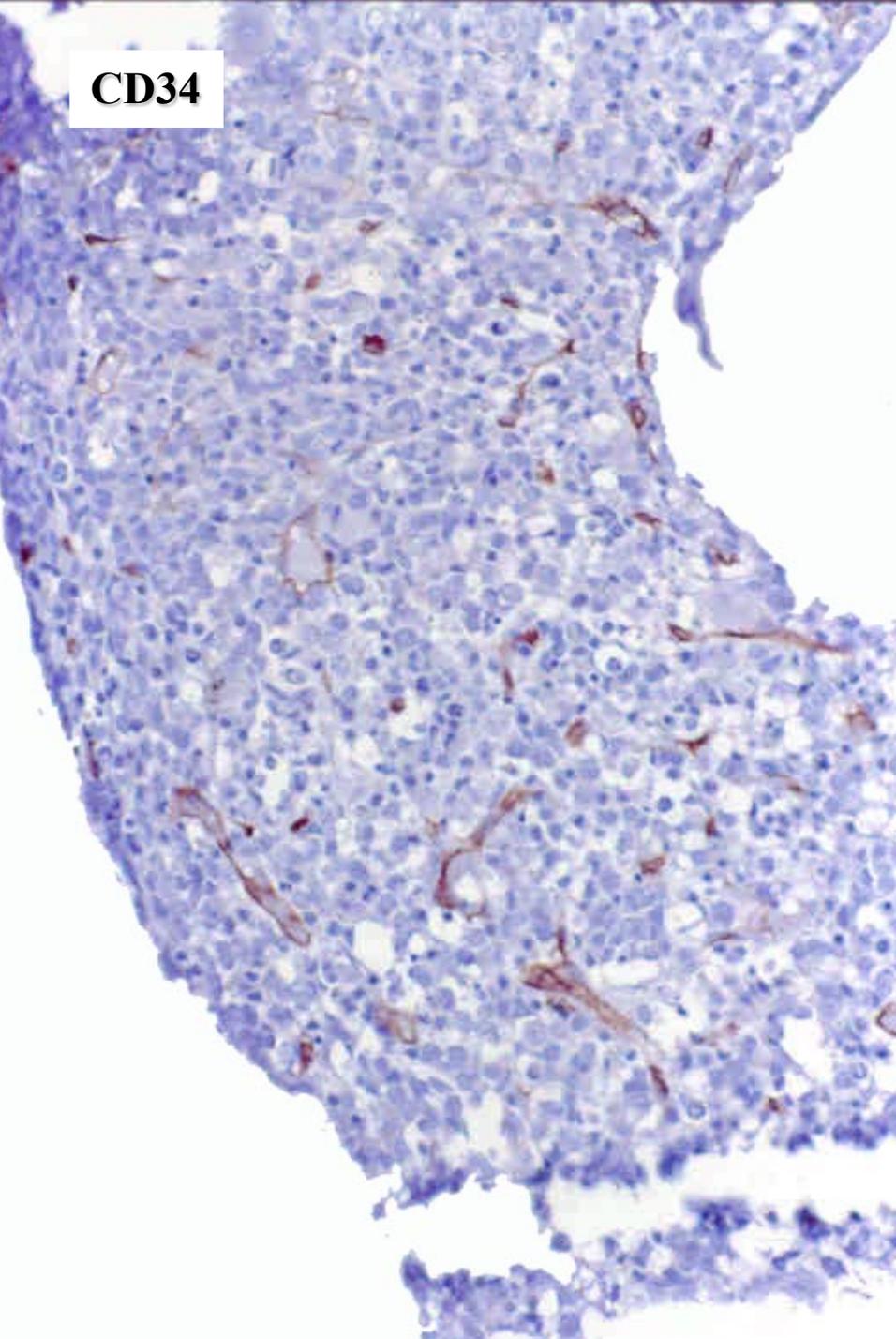
- **Sx. Mieloproliferativos / Mielodisplasia**
(Megaloblastoides)

I-3932-05

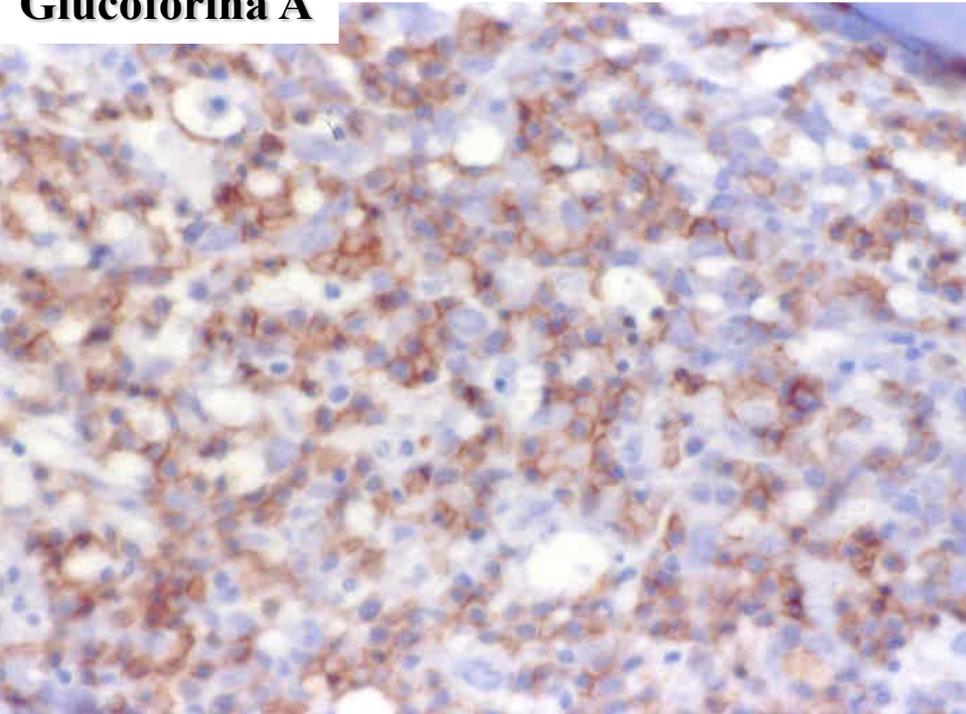
**Síndrome
de Down**



CD34

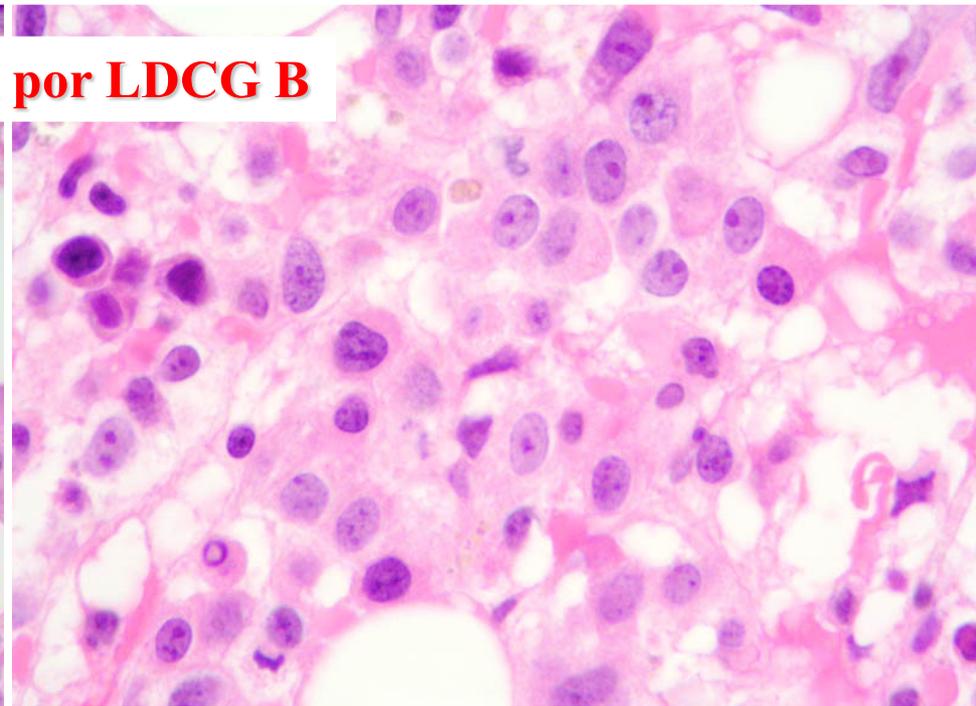
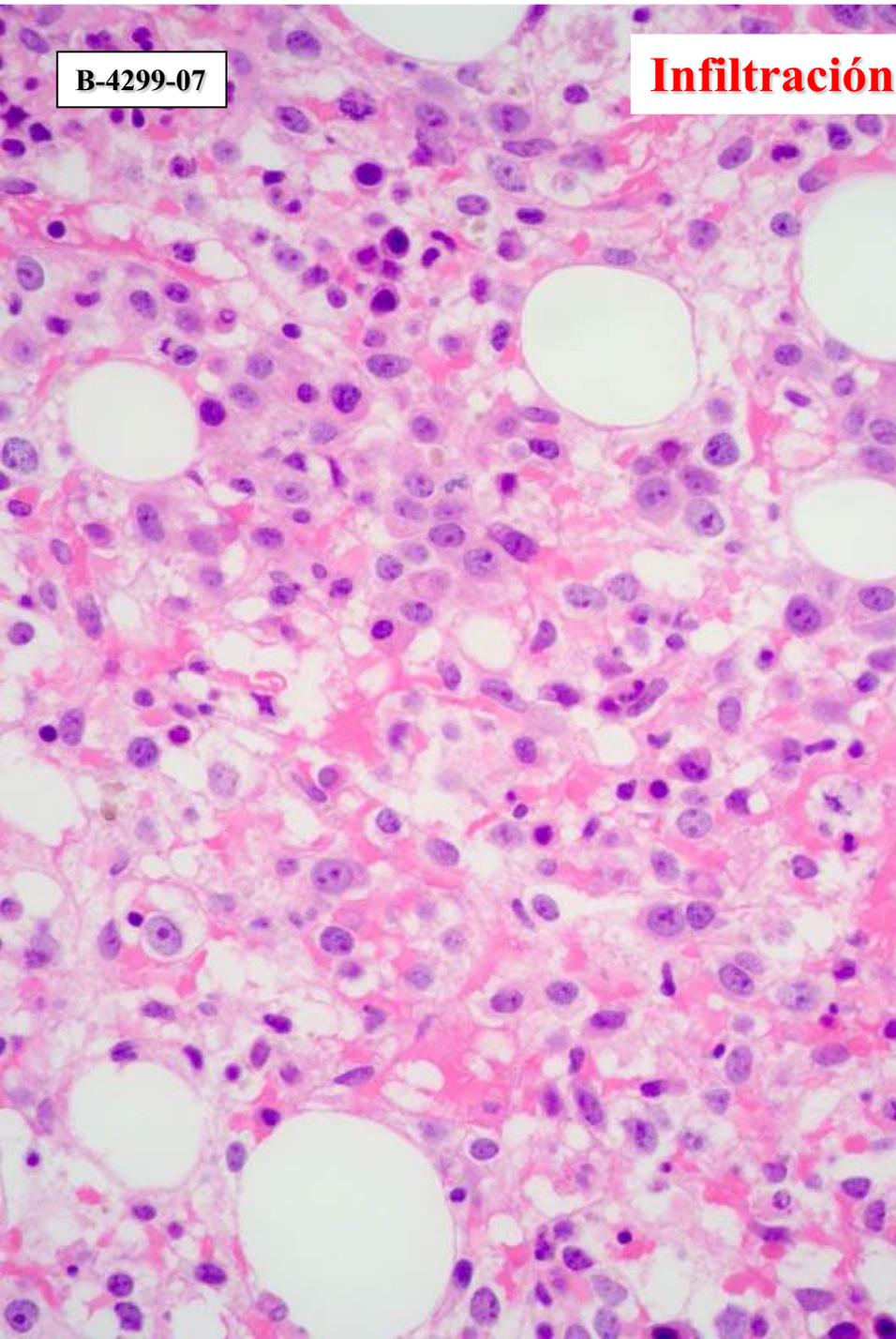


Glucoforina A

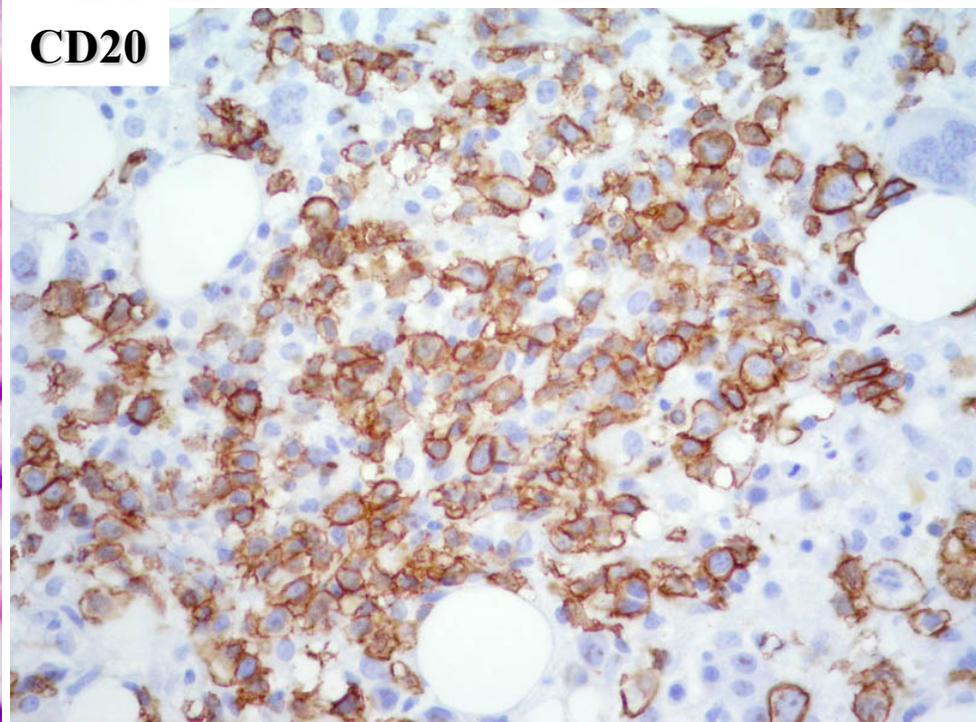


B-4299-07

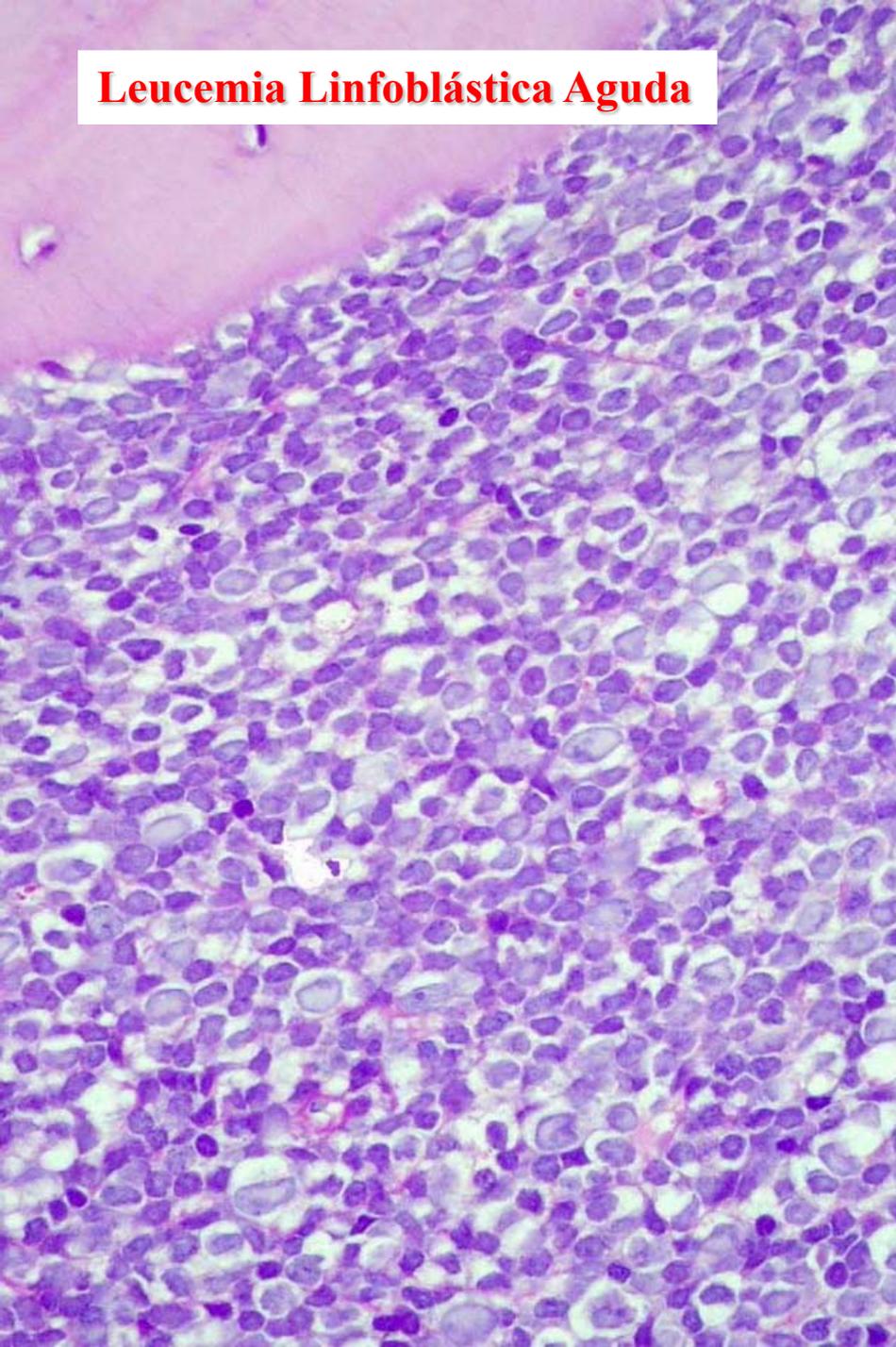
Infiltración por LDCG B



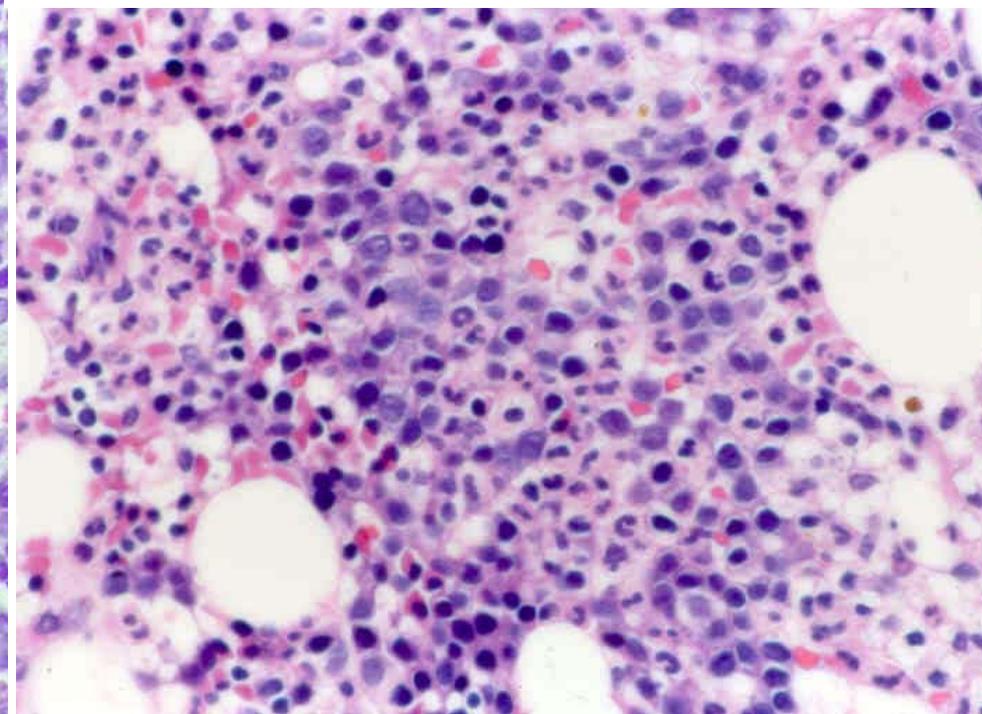
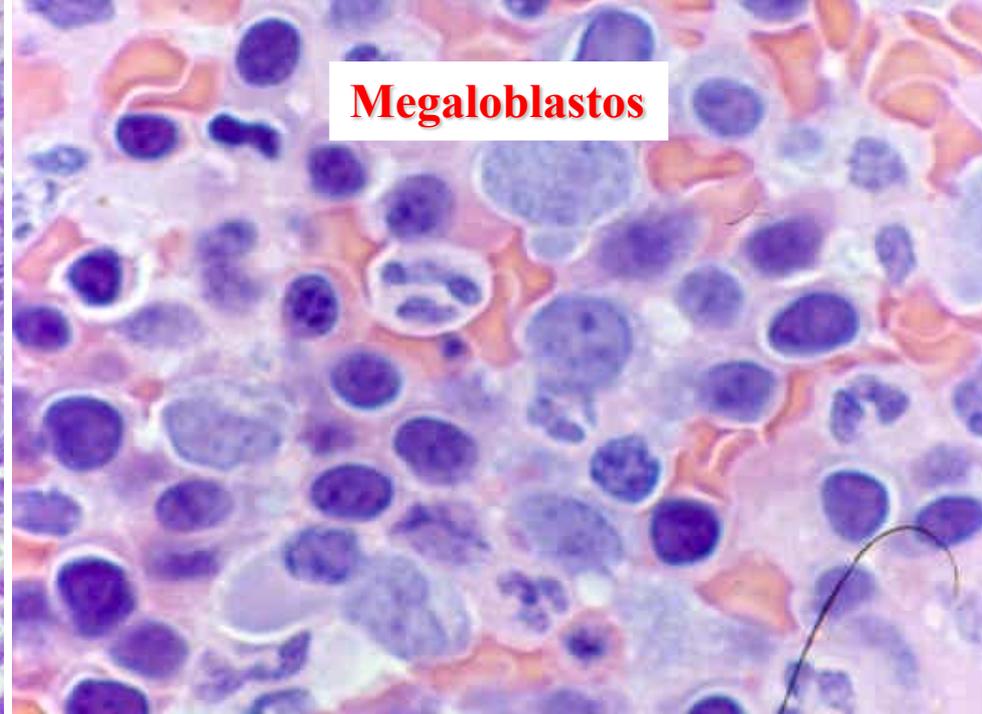
CD20



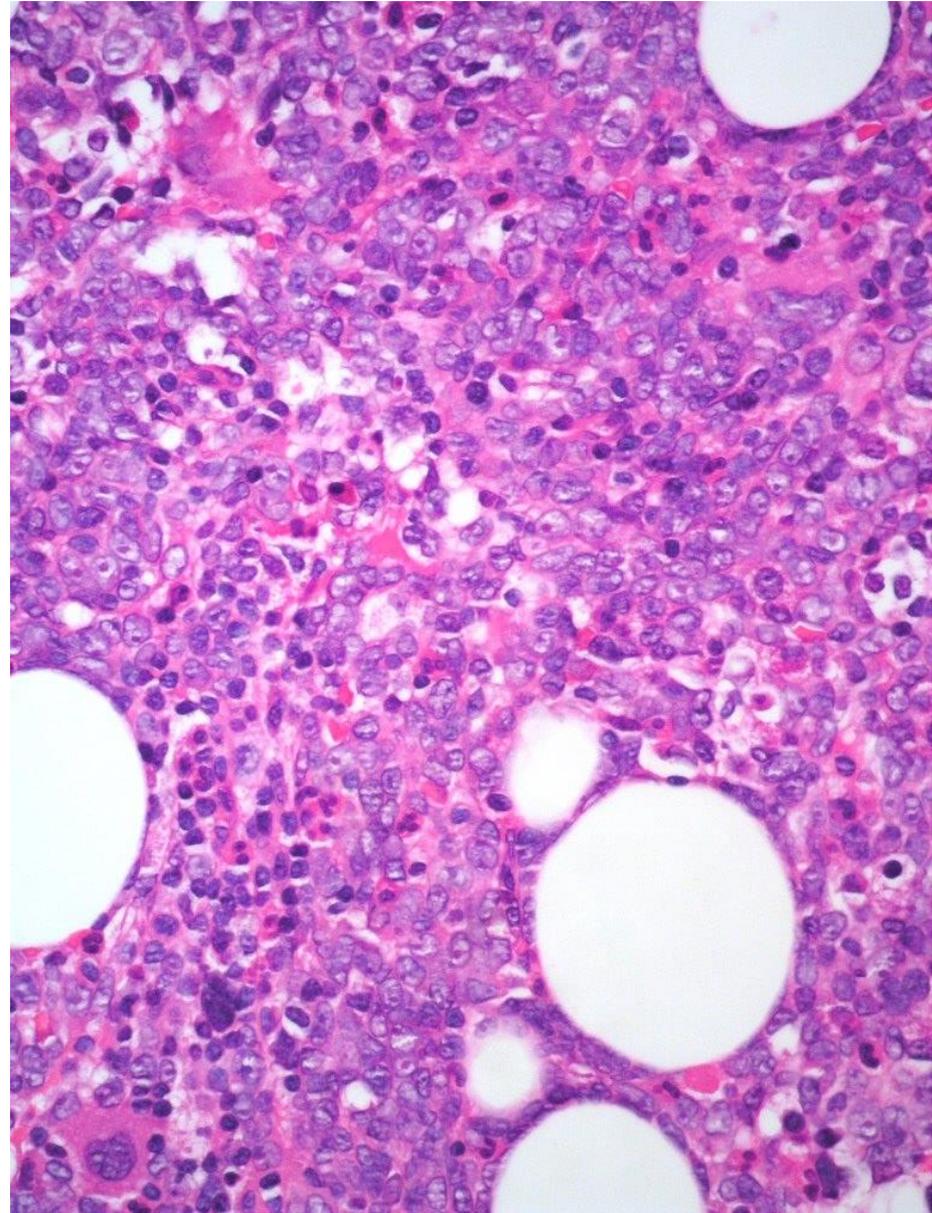
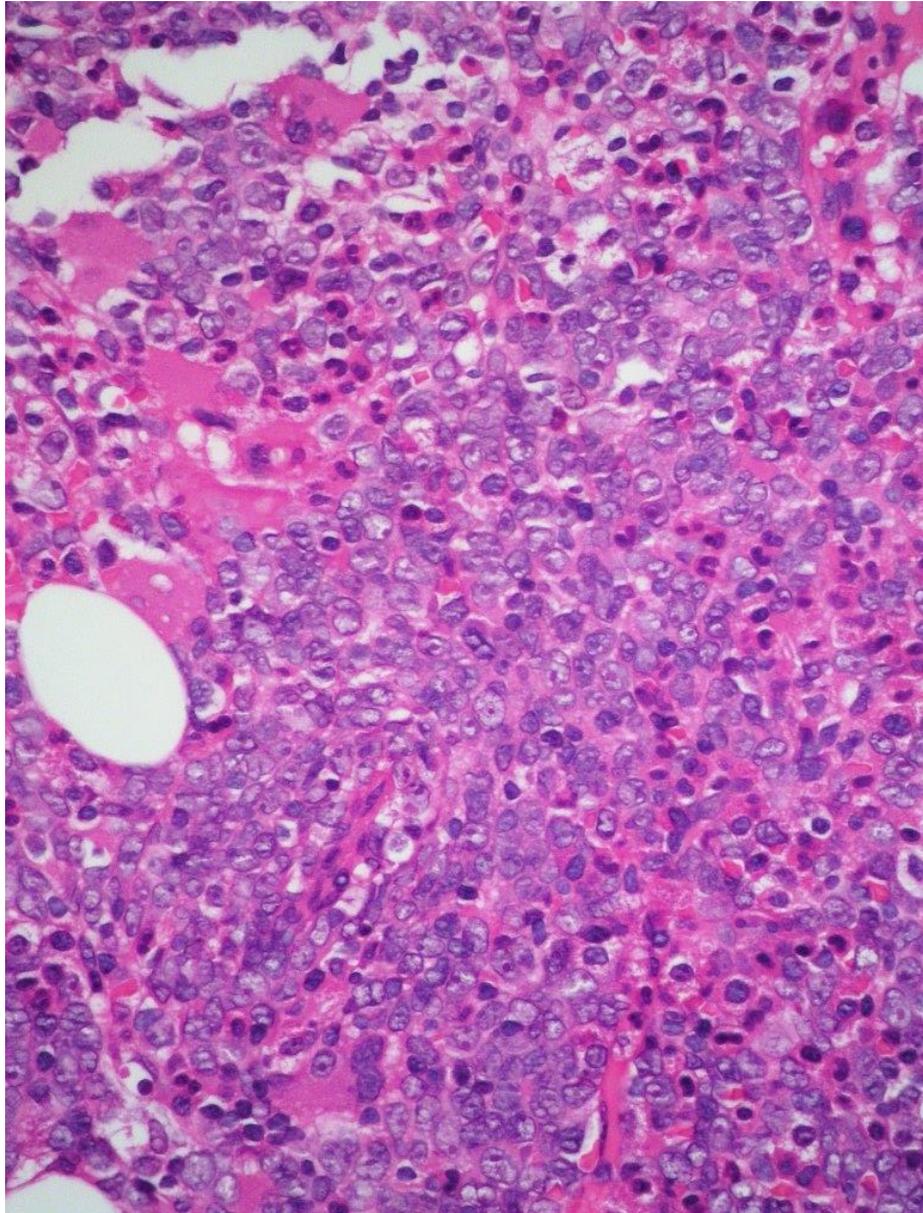
Leucemia Linfoblástica Aguda



Megaloblastos

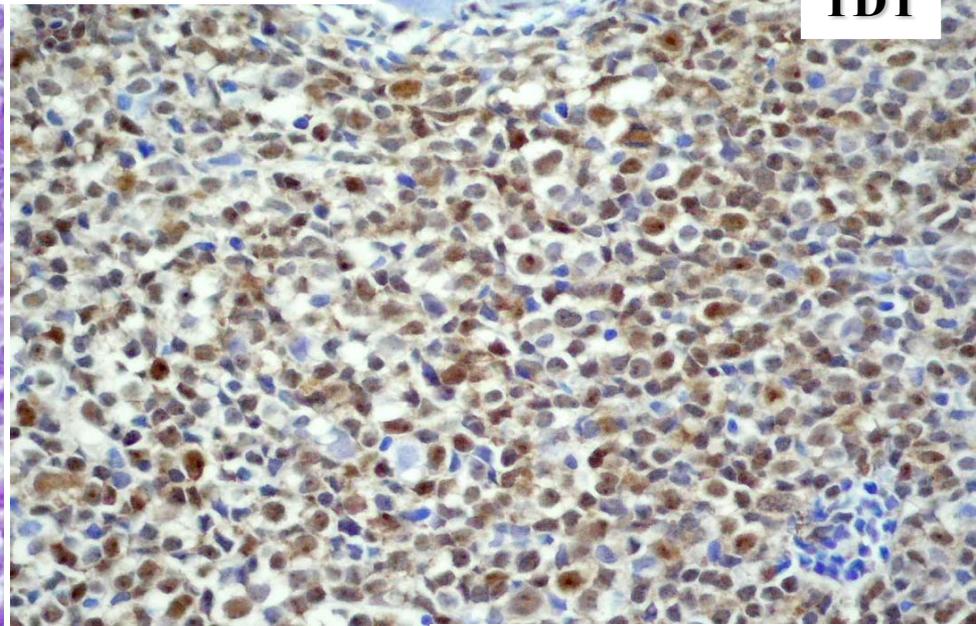
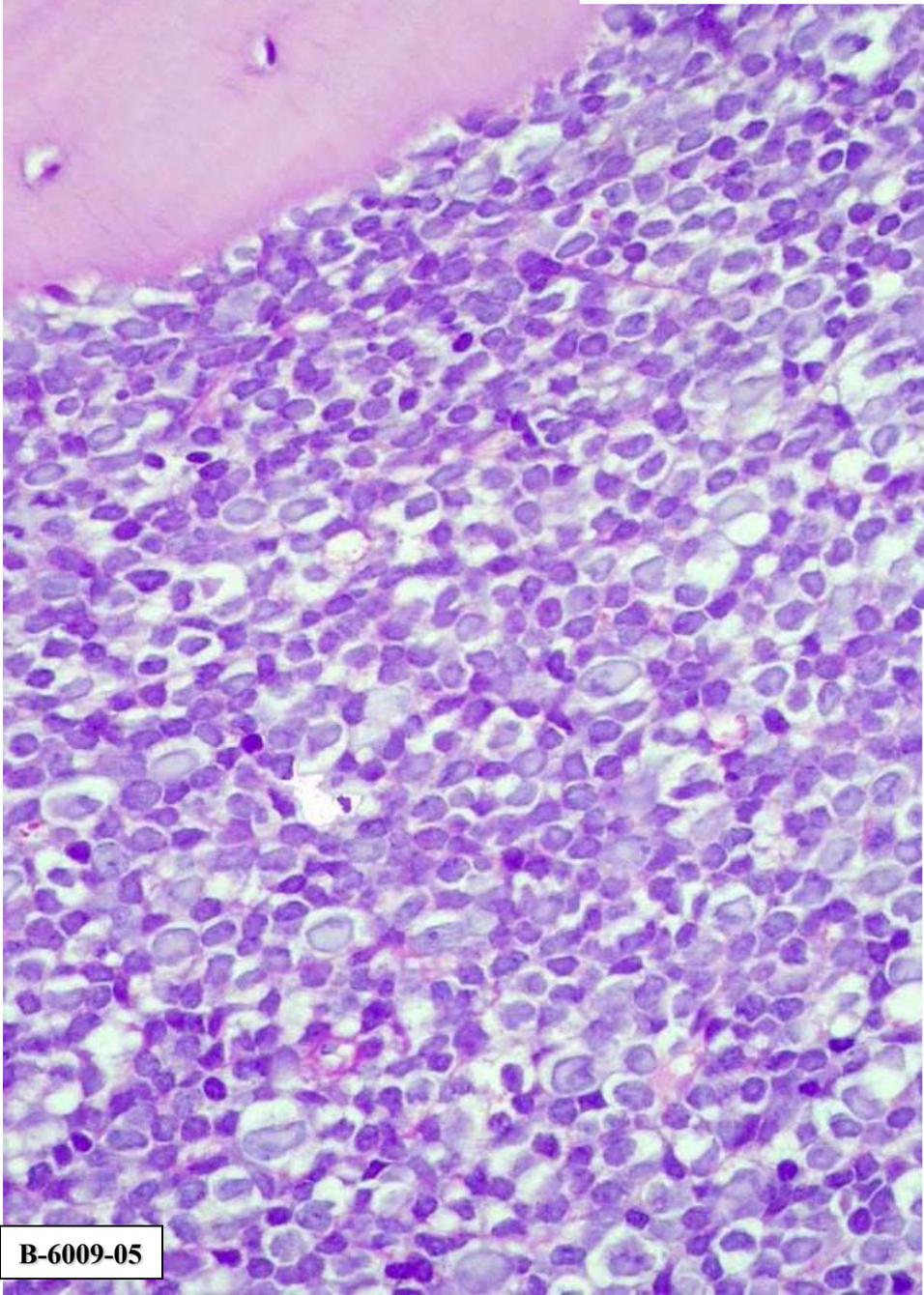


Leucemia Linfoblástica Pre-B

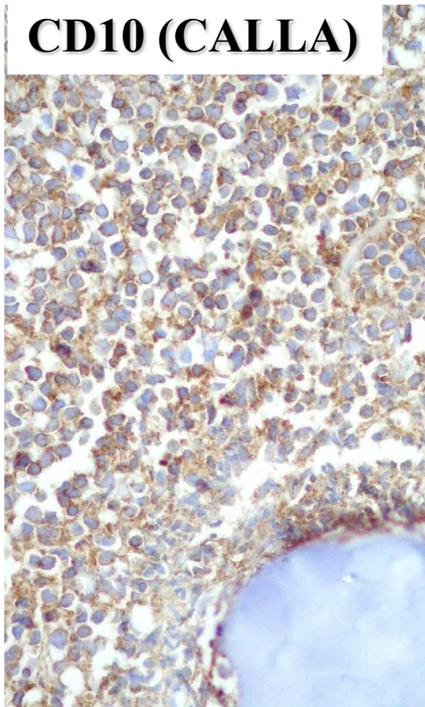


Leucemia Linfoblástica Pre-B

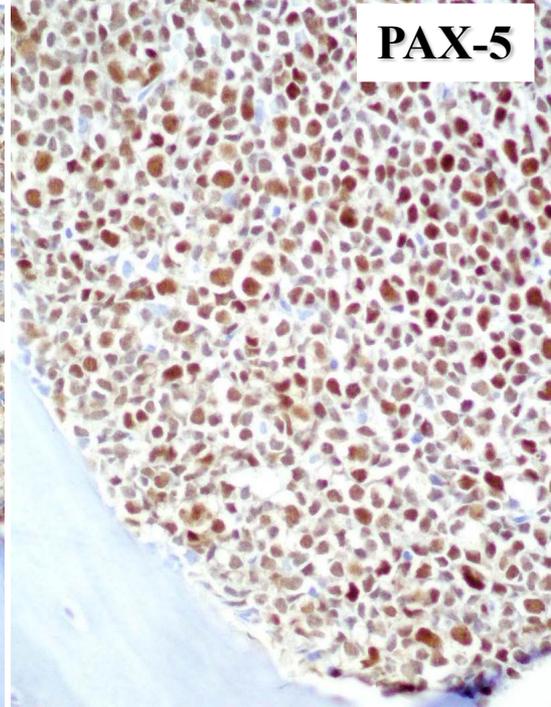
TDT



CD10 (CALLA)



PAX-5

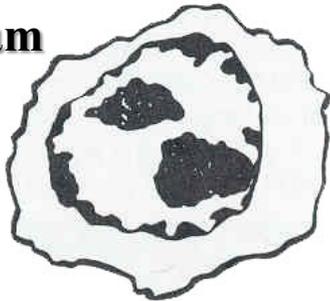


B-6009-05

Desarrollo de Granulocitos

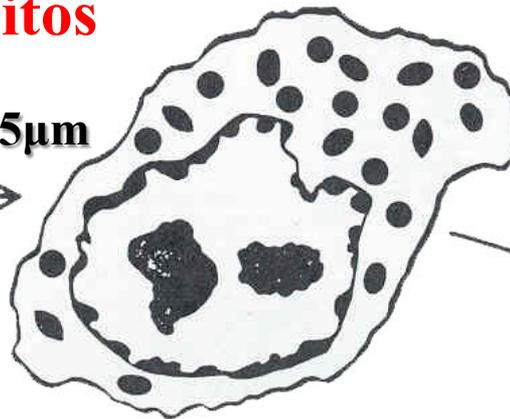
(14 días)

15-20 μ m

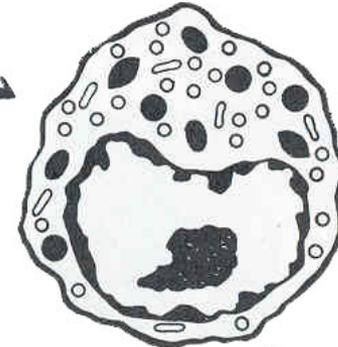


Mieloblasto
Nucléolos, **sin gránulos**

15-25 μ m

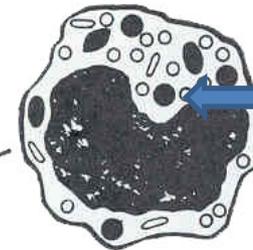


Promielocito
(Nucleolos y gránulos primarios **(Azurófilos)**)

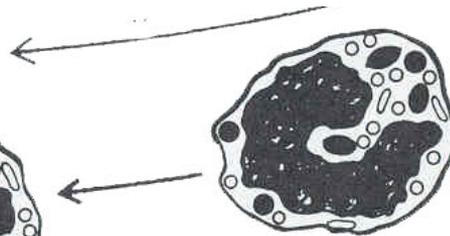


Mielocito
Gránulos 1 y 2darios **(Específicos)**

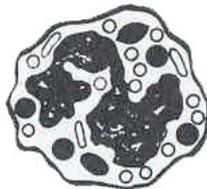
Ap Golgi



Metamielocito



Banda



Segmentado
Gránulos terciarios (Gelatinasa +)

SANGRE

Tejido (Función 1-2 días)

Maduración Mieloide

- Paratrabecular
- Periarterioles

MADURACION

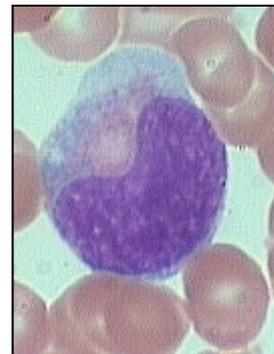
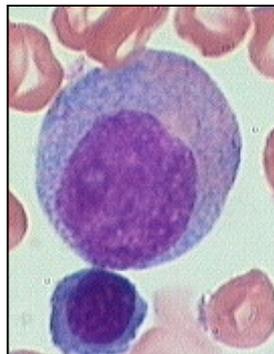
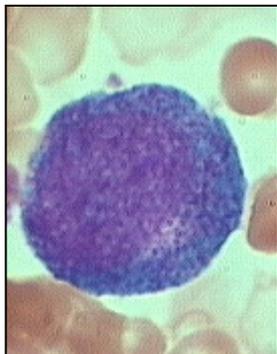
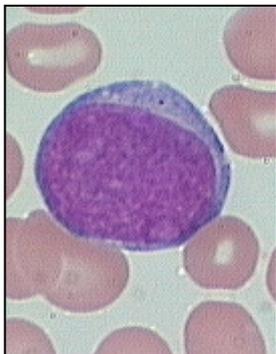
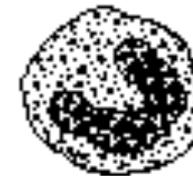
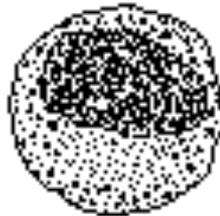
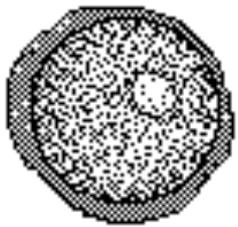
mieloblasto promielocito

mielocito

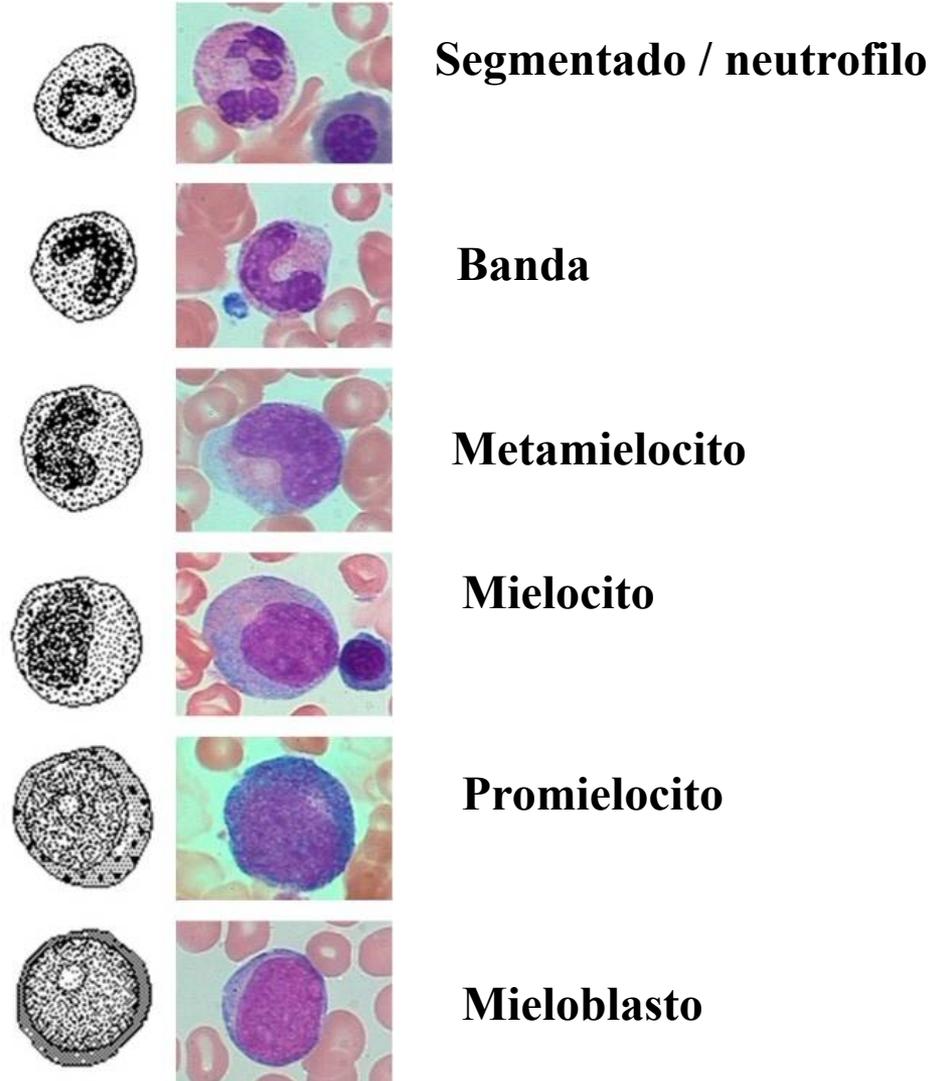
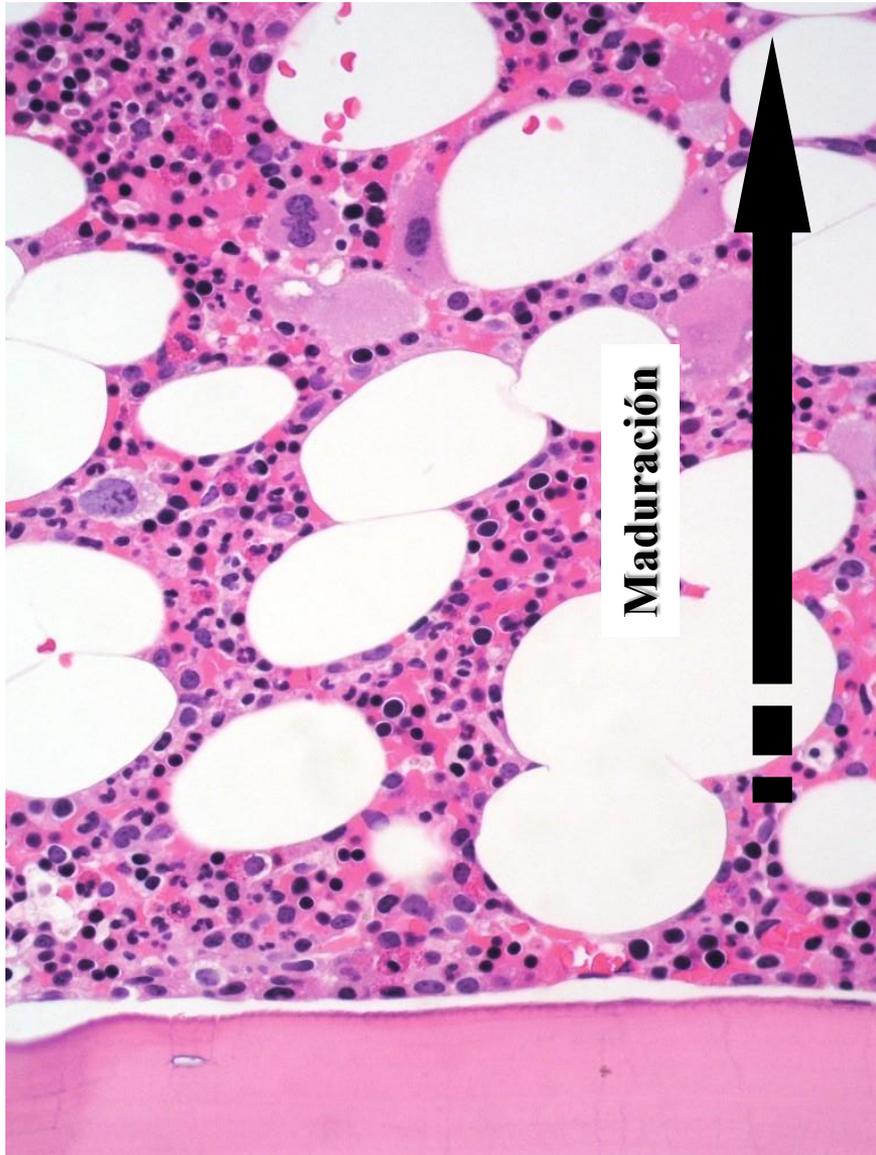
metamielocito

banda

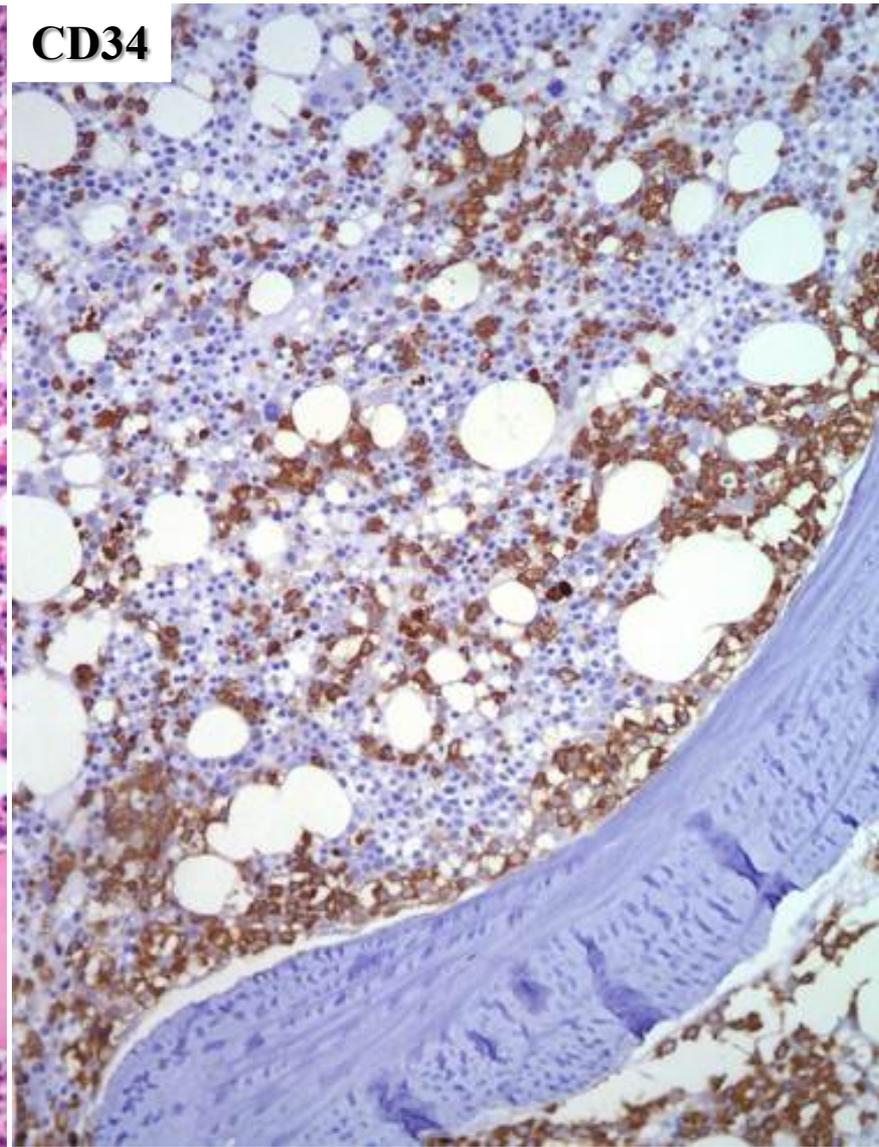
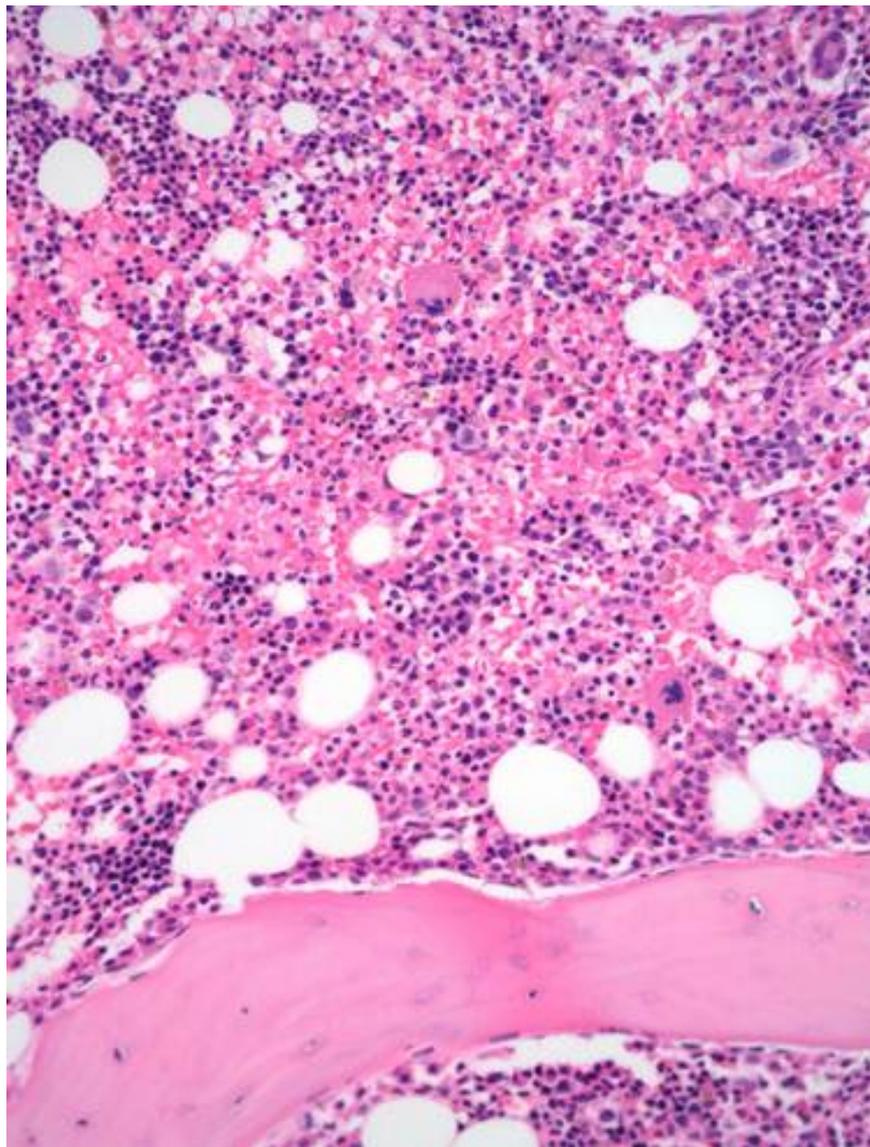
neutrofilo



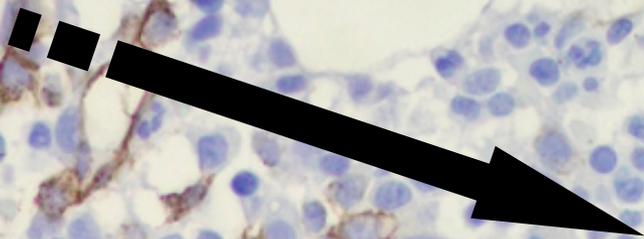
Maduración de Serie Granulocítica



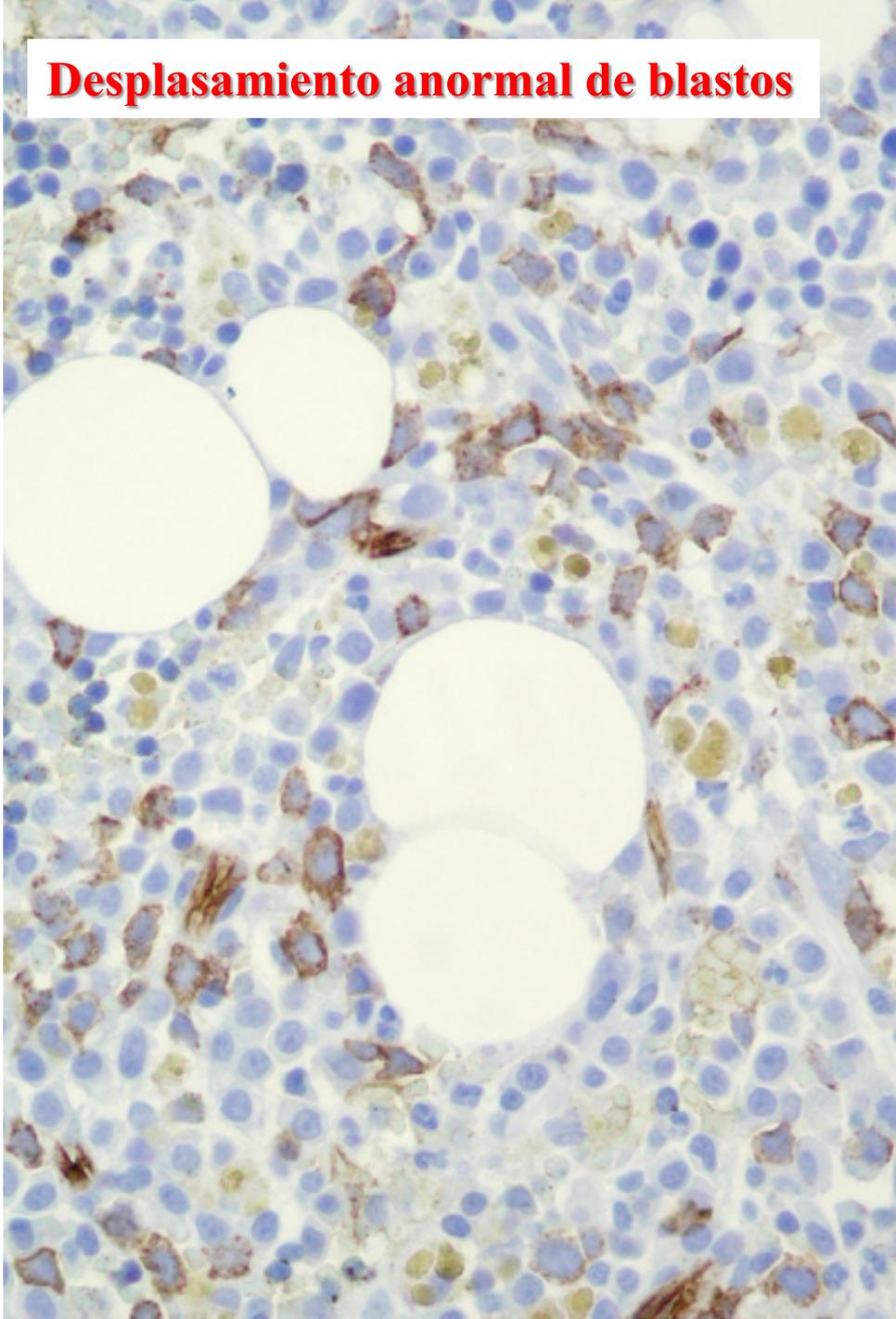
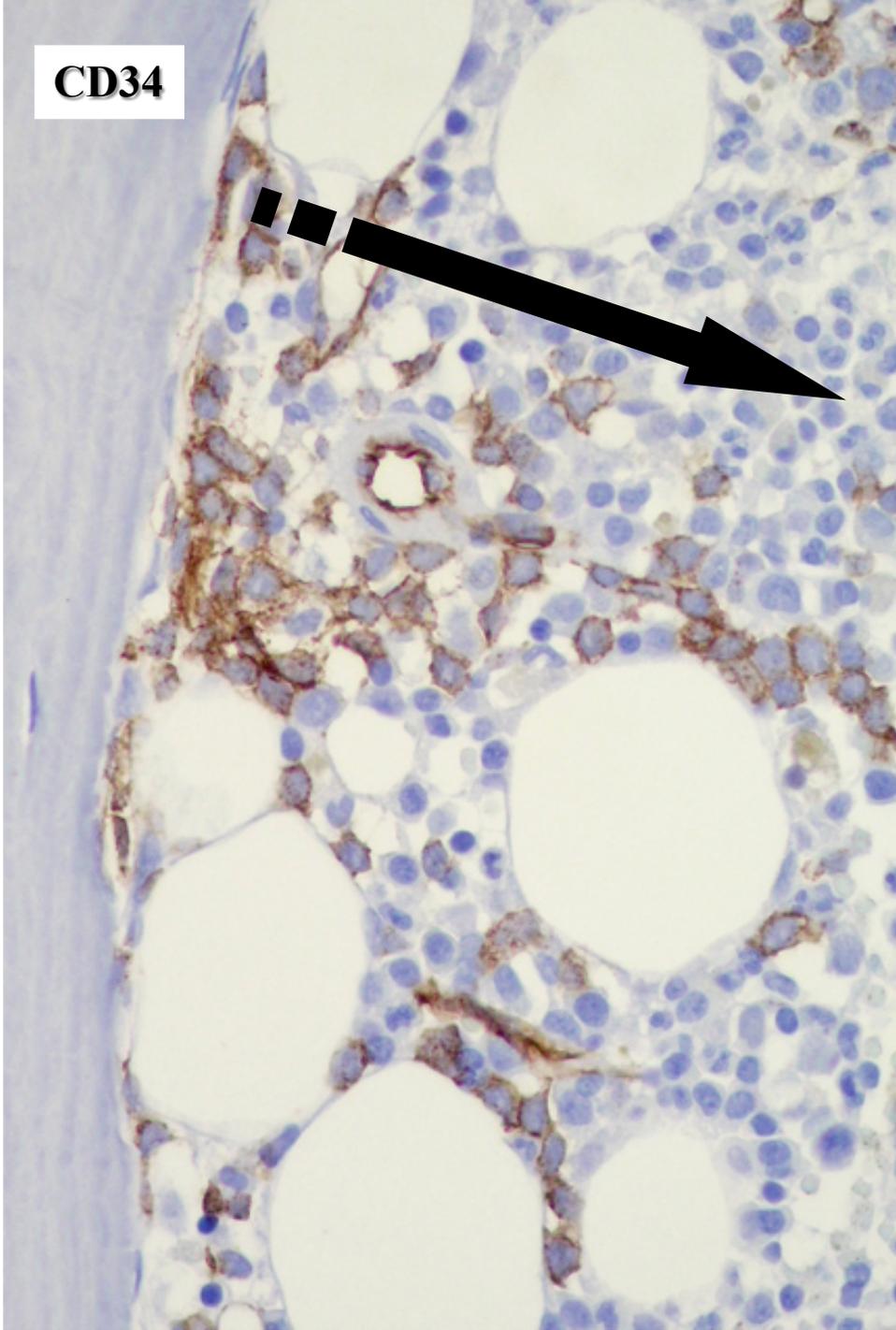
Localización Anormal de Blastos

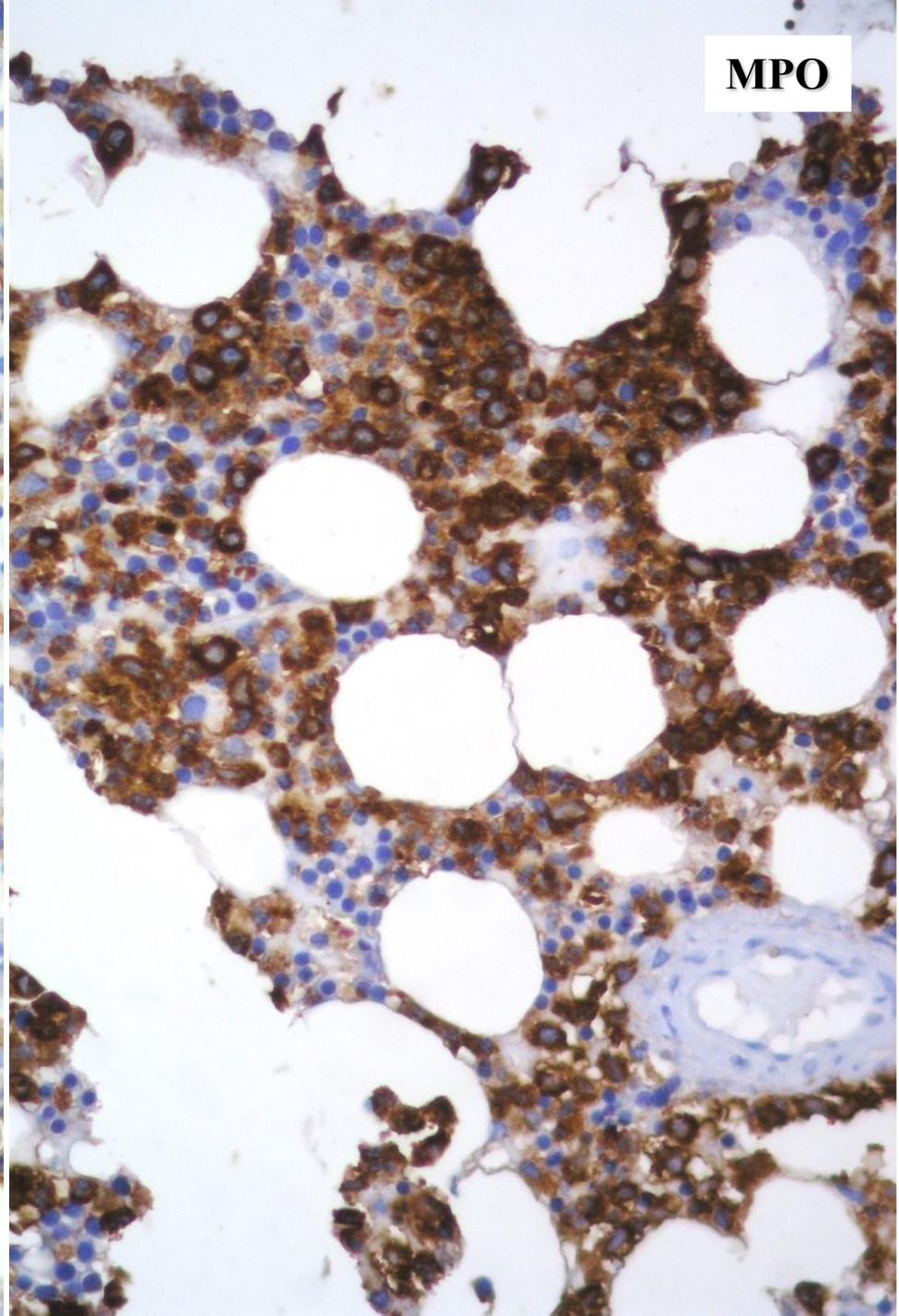
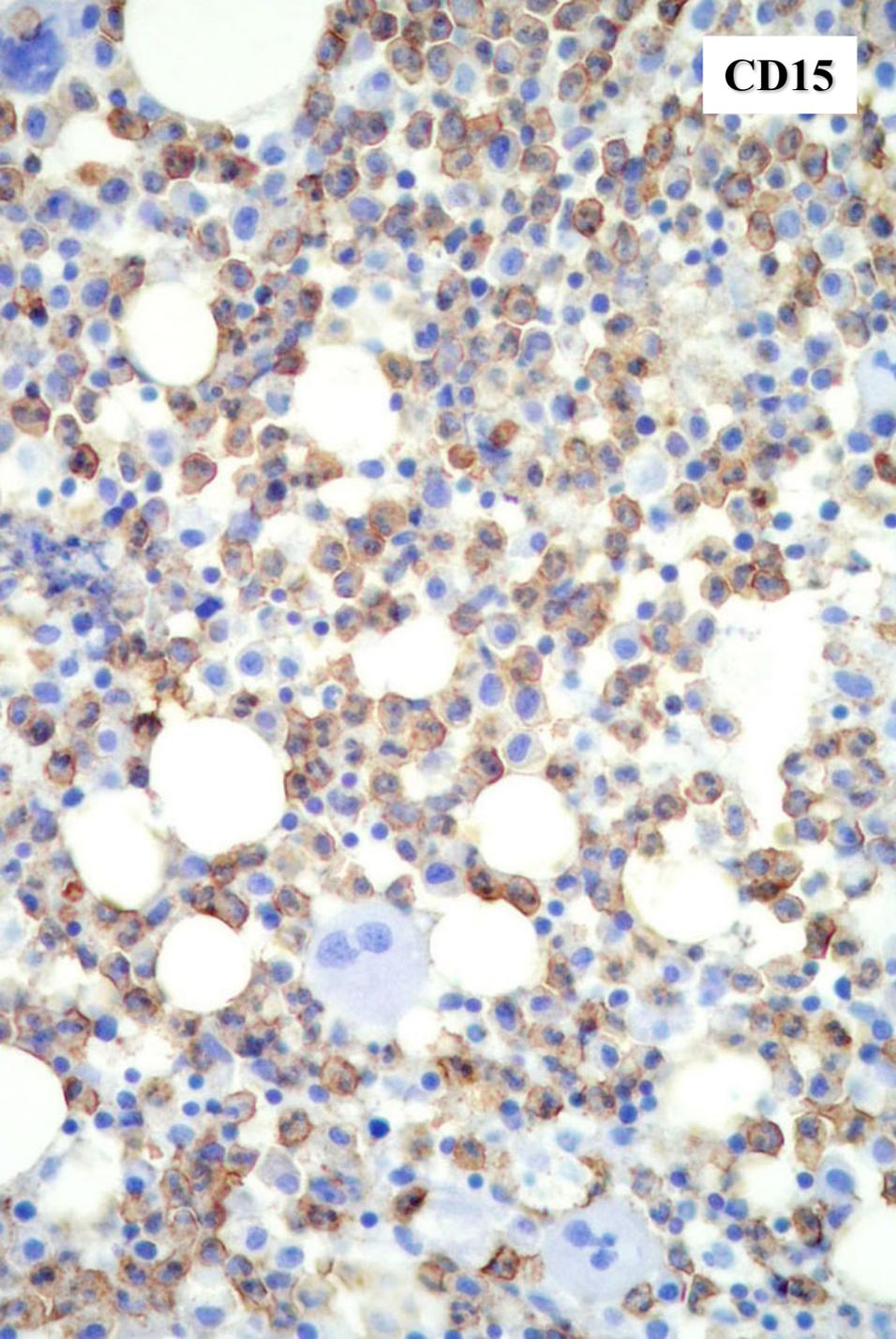


CD34



Desplazamiento anormal de blastos





Diagnóstico Diferencial

Hiperplasia Granulocítica (Reacción leucemoide)

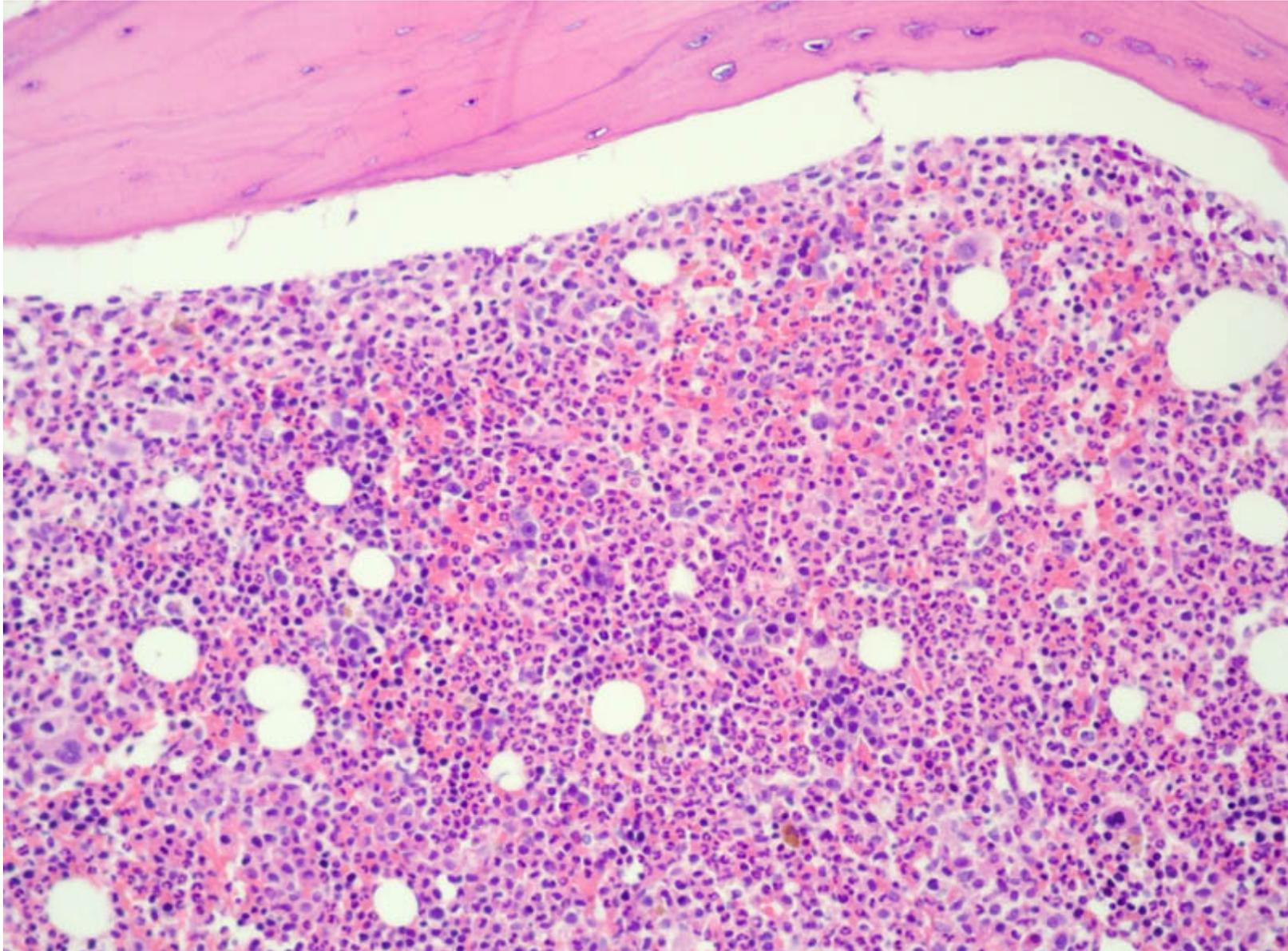
- **Celularidad: 70-80%**
- **Fibrosis: 0 / leve**
- **Megacariocitos: normales**
- **Granulaciones tóxicas**
- **Cuerpos de Döhle**
- ***BCR-ABL1* negativo**

LMC

- **90-100%**
- **Moderada /Acentuada ?**
- **Displásicos**
- **“*Myelocyte bulge*”**
- **Basofilia absoluta**
- **Positivo (90-95%)**

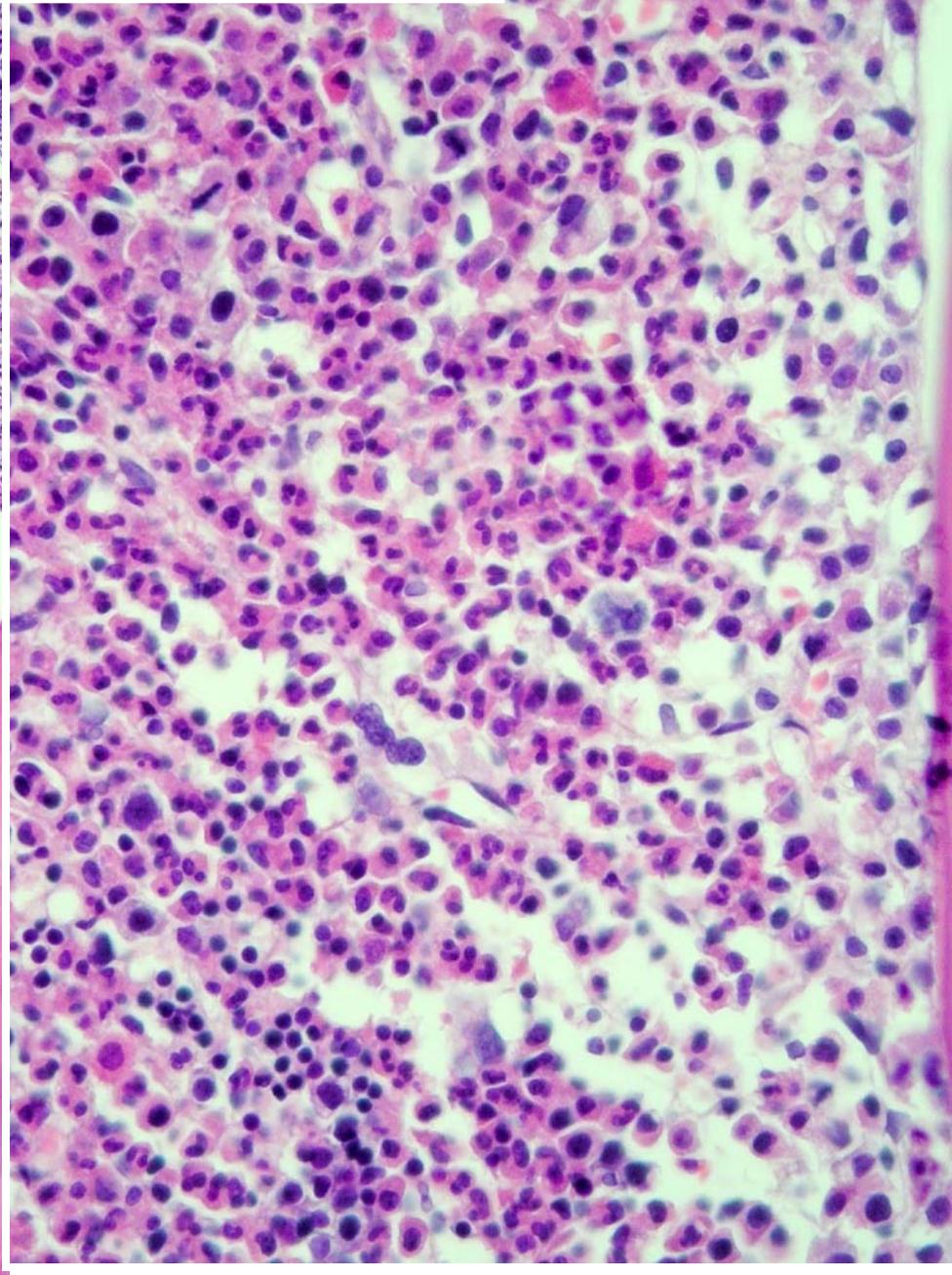
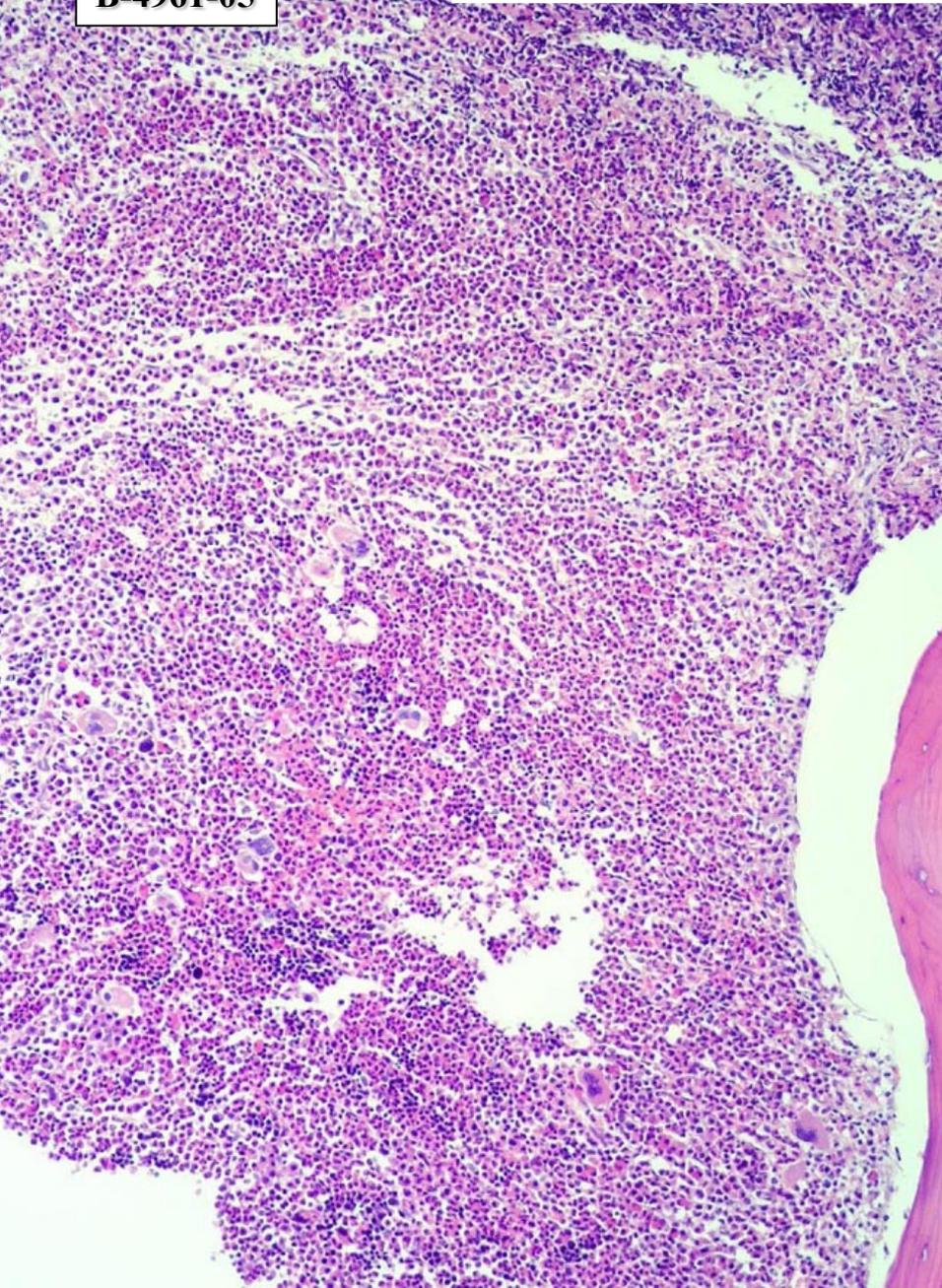
Nota: Correlacionar con aspirado y estudios genéticos.

Neupogen® (Filgrastin)

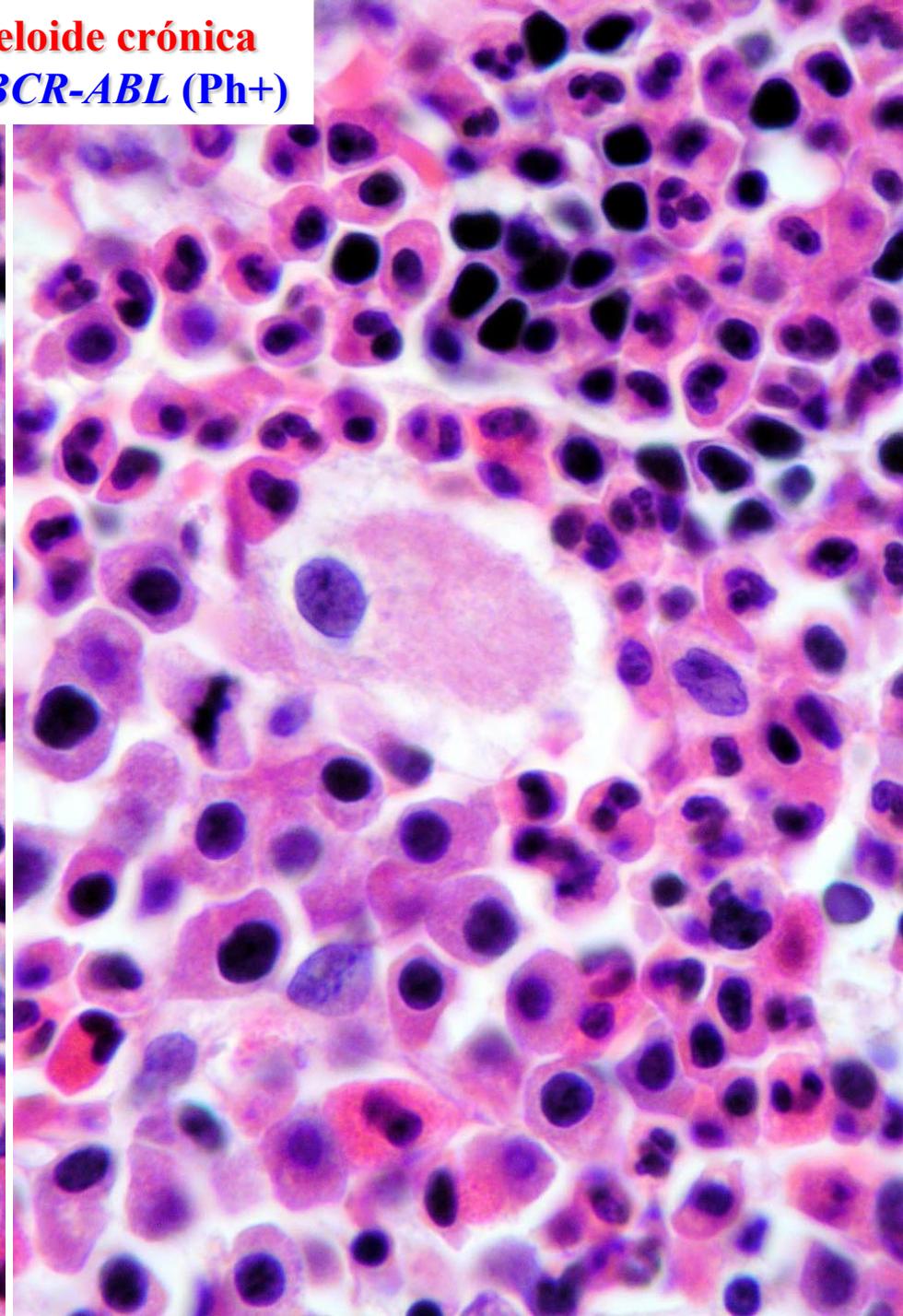
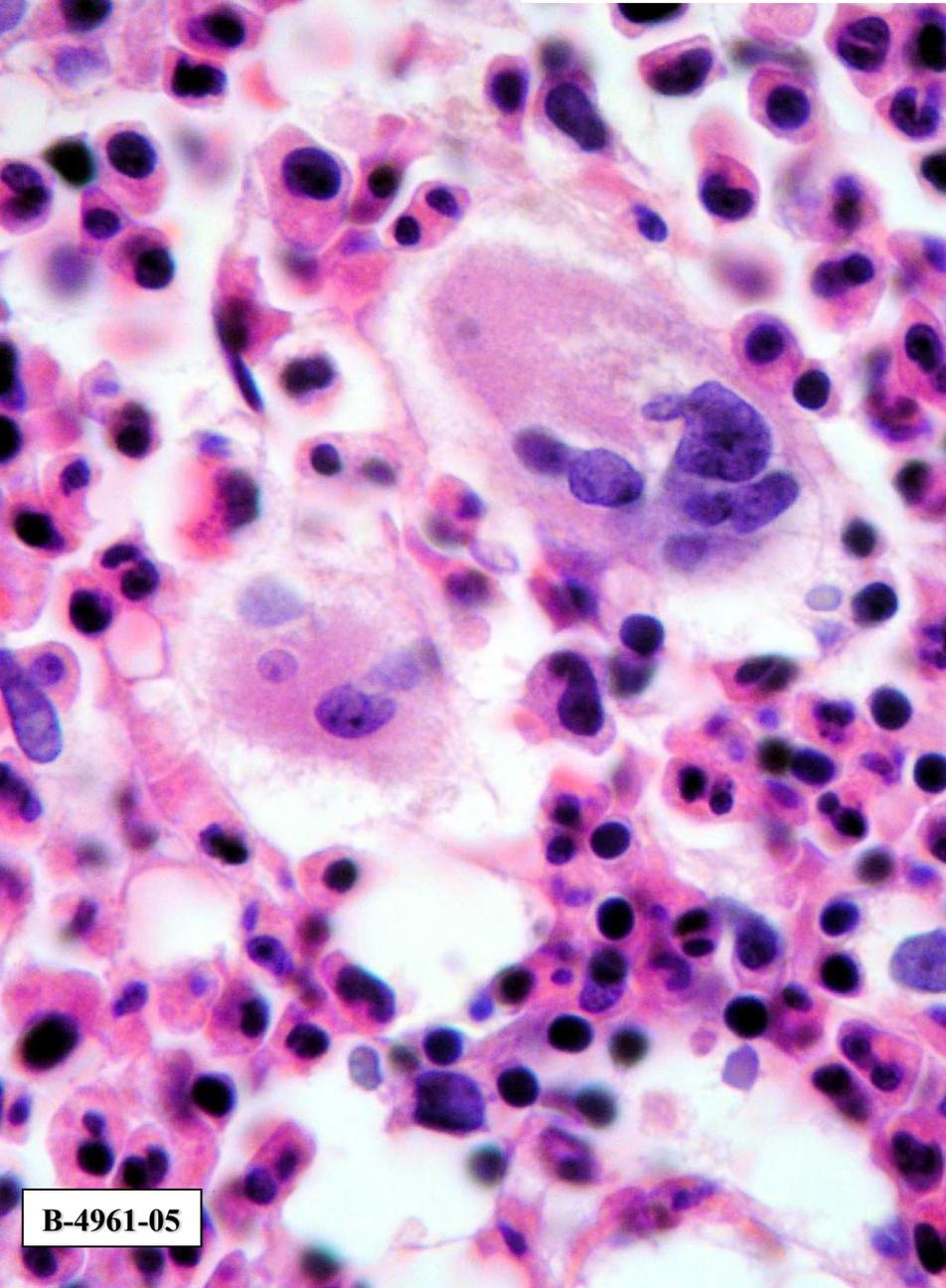


74 años Hombre, Neoplasia Mieloproliferativa
Posible Leucemia Mieloide Crónica

B-4961-05



Dx: Leucemia Mieloide crónica
Citogenética *BCR-ABL* (Ph+)

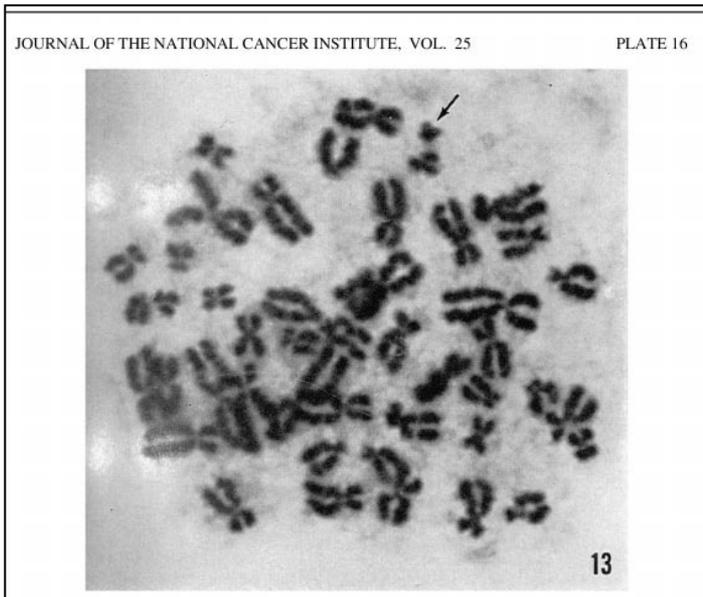


B-4961-05

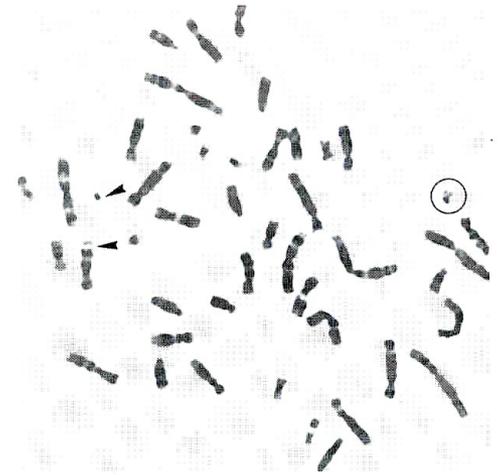
Cromosoma Filadelfia

Nowell P, Hungerford D. A minute chromosome in human chronic granulocytic leukemia. Science 1960;132:1497

Nowell P, Hungerford D. Chromosomes of normal and leukemic human leukocytes. J Natl Cancer Inst 1960;.



Peter Nowell David Hungerford



Science 1960:132:1497-

A Minute Chromosome in Human Chronic Granulocytic Leukemia

In seven cases thus far investigated (five males, two females), a minute chromosome has been observed replacing one of the four smallest autosomes in the chromosome complement of cells of chronic granulocytic leukemia cultured from peripheral blood. No abnormality was observed in the cells of four cases of acute granulocytic leukemia in adults or of six cases of acute leukemia in children. There have been several recent reports of chromosome abnormalities in a number of cases of human leukemia [including two of the seven cases reported here; Nowell and Hungerford, *J. Natl. Cancer Inst.* 25, 85 (1960)], but no series has appeared in which there was a consistent change typical of a particular type of leukemia.

Cells of the five new cases were obtained from peripheral blood (and bone marrow in one instance), grown in culture for 24–72 hours, and processed for cytological examination by a recently developed air-drying technique (Moorhead *et al.*, *Exptl. Cell Research*, in press). The patients varied from asymptomatic untreated cases to extensively treated cases of several years' duration in terminal myeloblastic crisis. All seven individuals showed a similar minute chromosome, and none showed any other frequent or regular chromosome change. In most of the cases, cells with normal chromosomes were also observed. Thus, the minute chromosome is not a part of the normal chromosome constitution of such individuals. The findings suggest a causal relationship between the chromosome abnormality observed and chronic granulocytic leukemia.

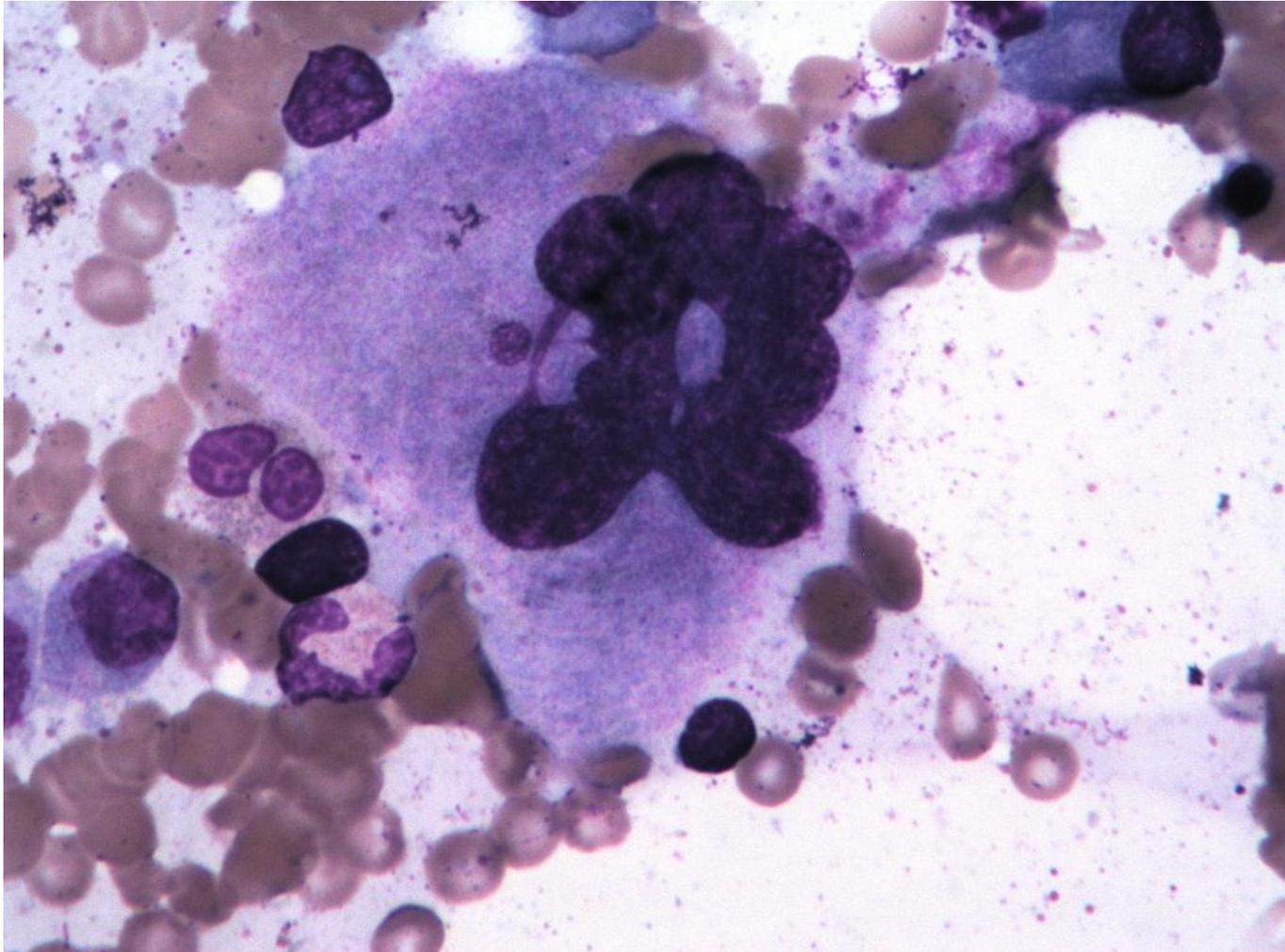
PETER C. NOWELL
School of Medicine,
University of Pennsylvania

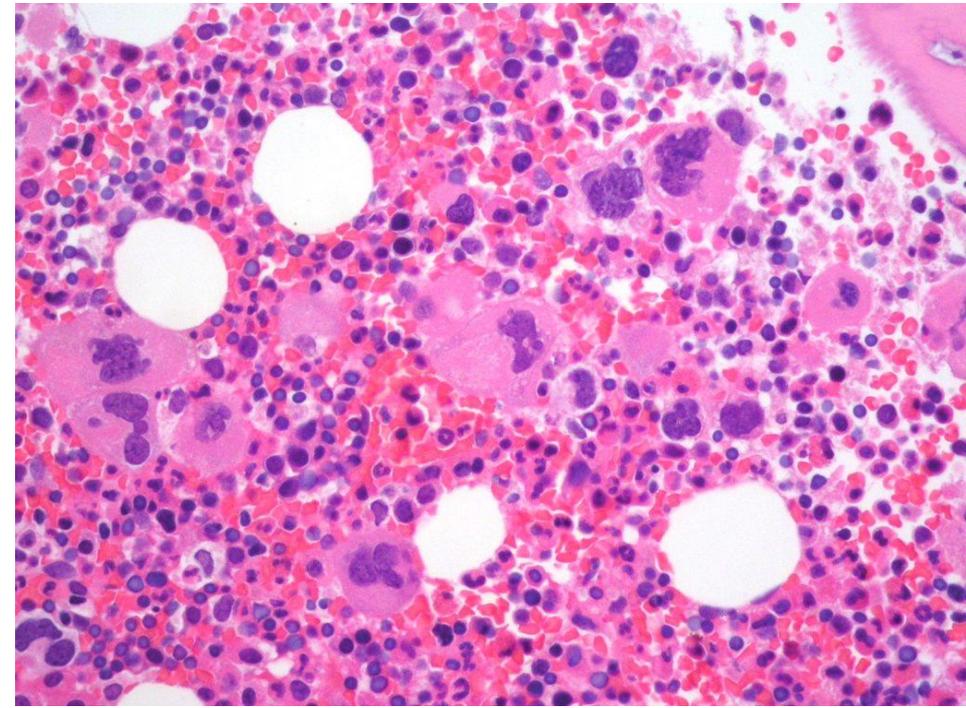
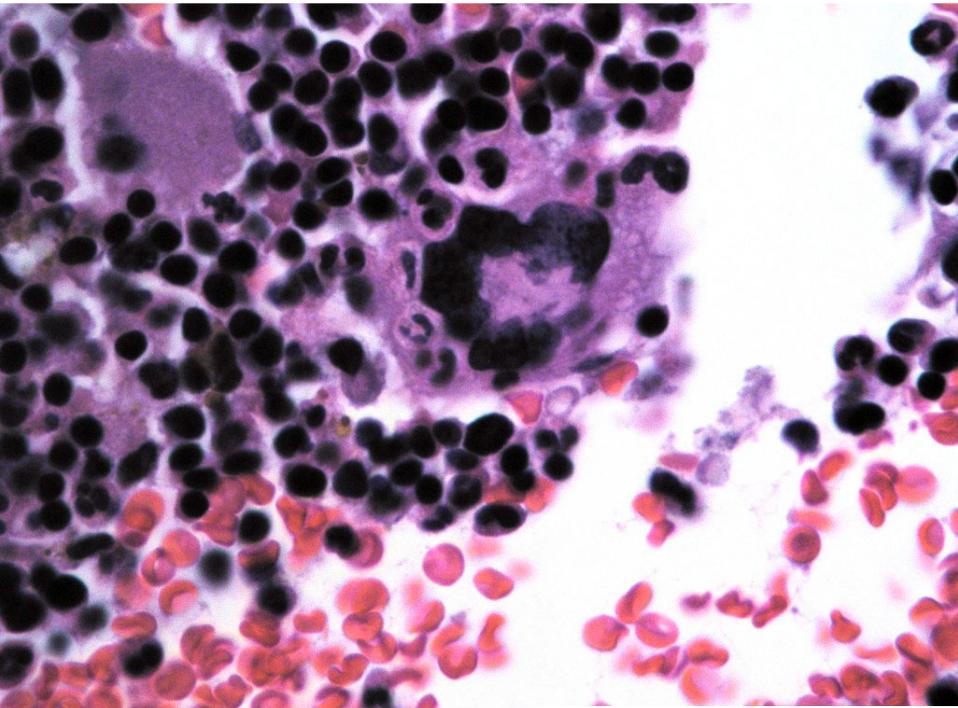
DAVID A. HUNGERFORD
Institute for Cancer Research

MEGACARIOCITO: 100 μ m

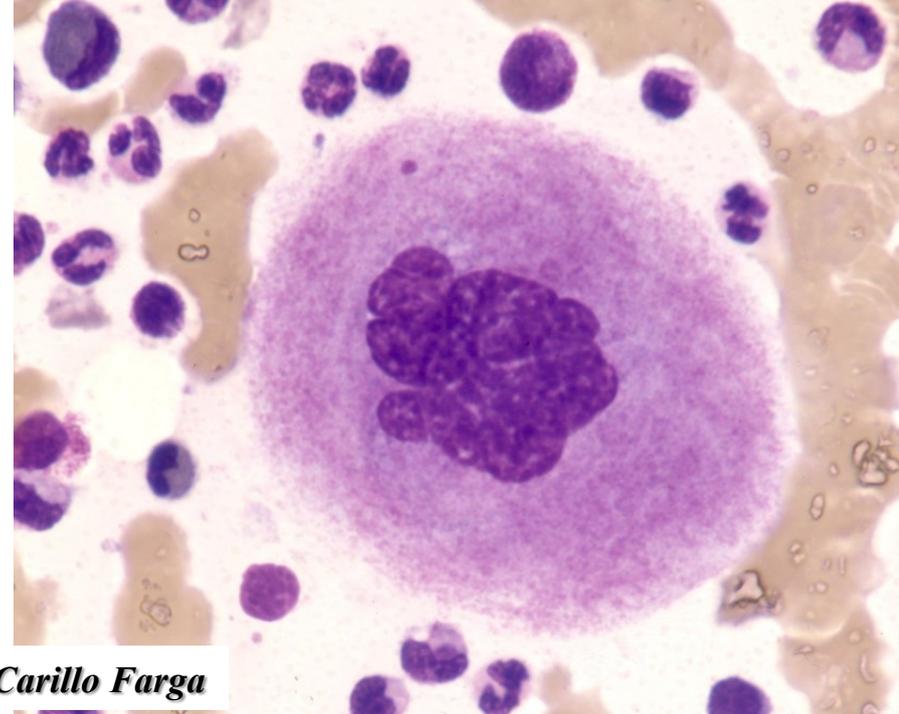
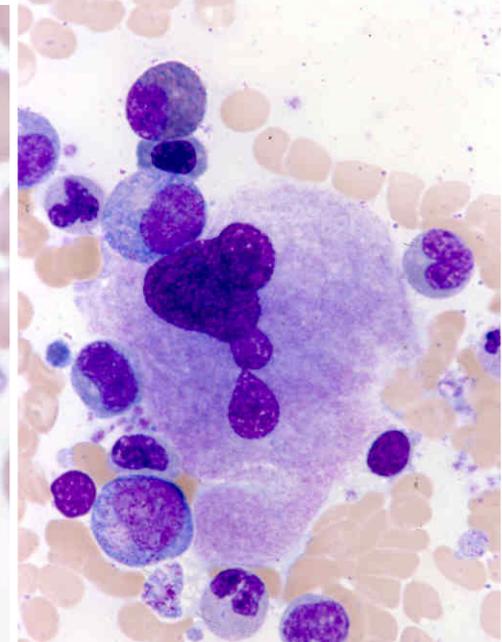
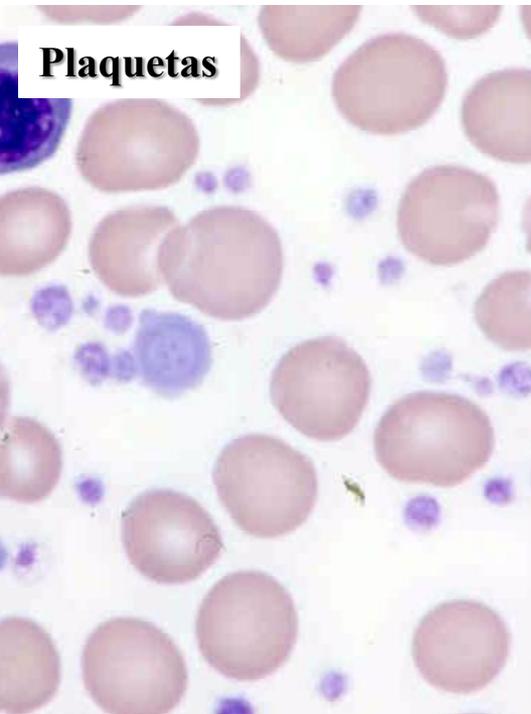
Endomitosis (replicación cromosómica sin división nuclear ni citoplásmica)

Núcleo multilobulado





Plaquetas

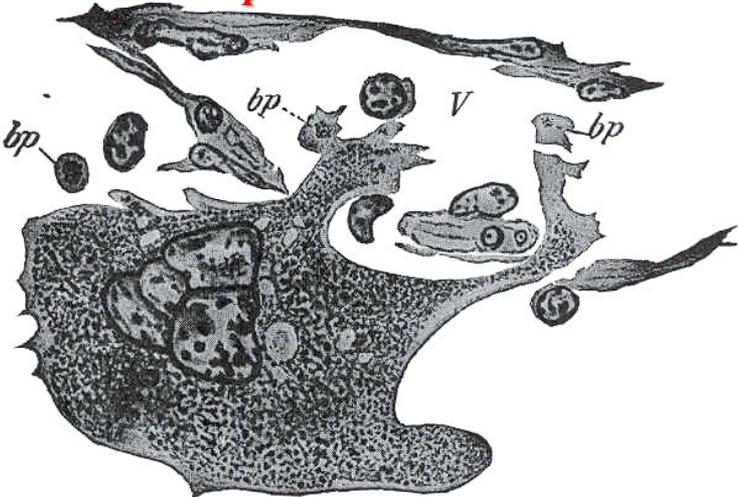


Cortesía Dr Carillo Farga

James Homer-Wright (1869-1928)



J Morphol 1910 21:263



James Homer-Wright (1869-1928)

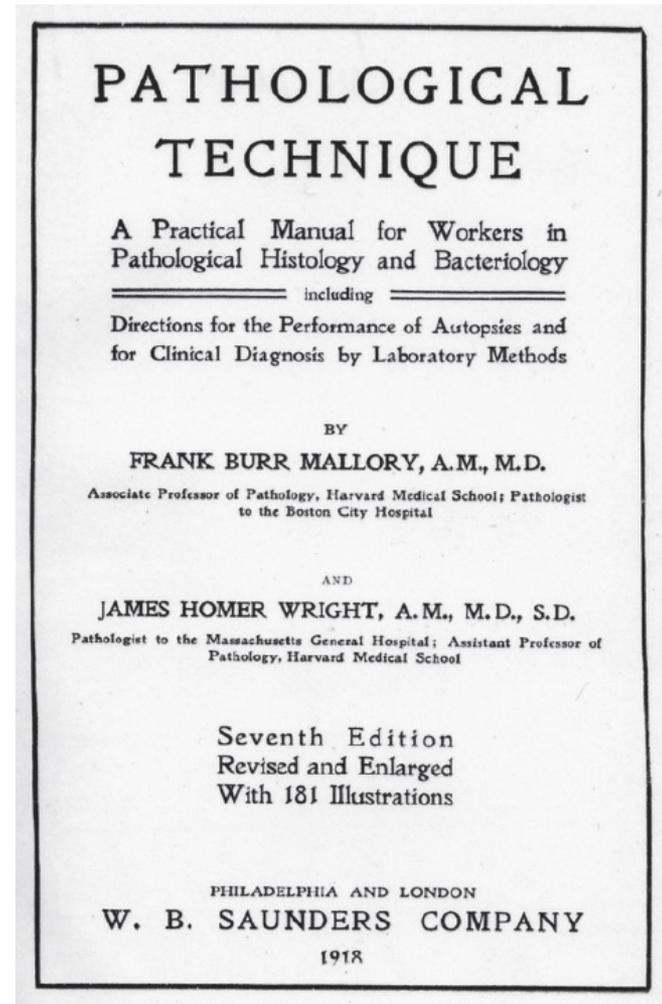
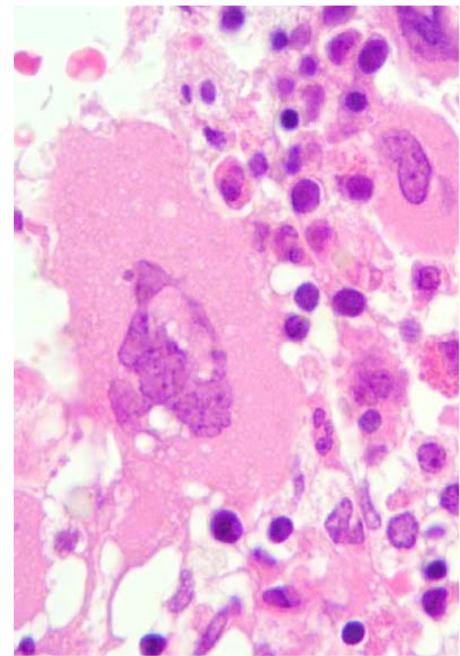
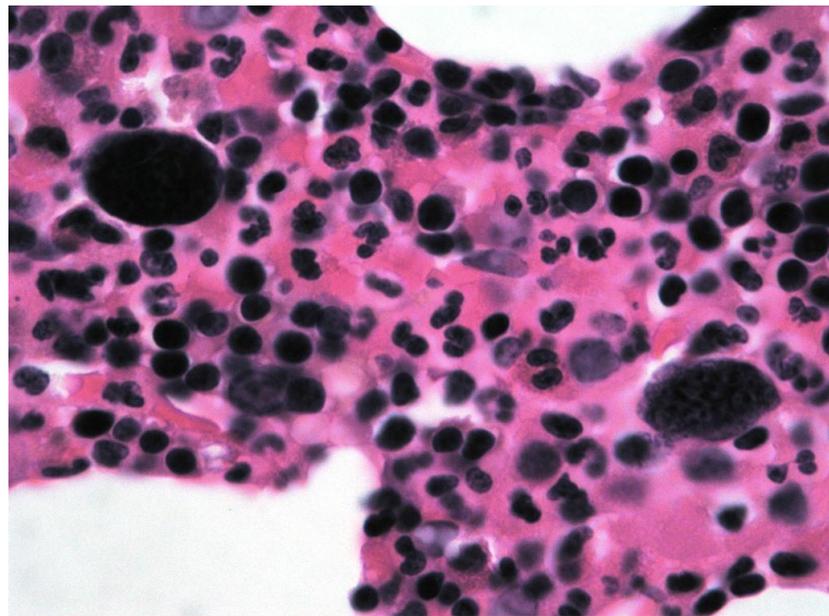
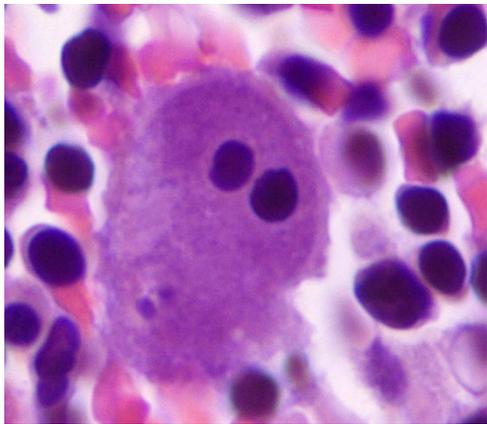
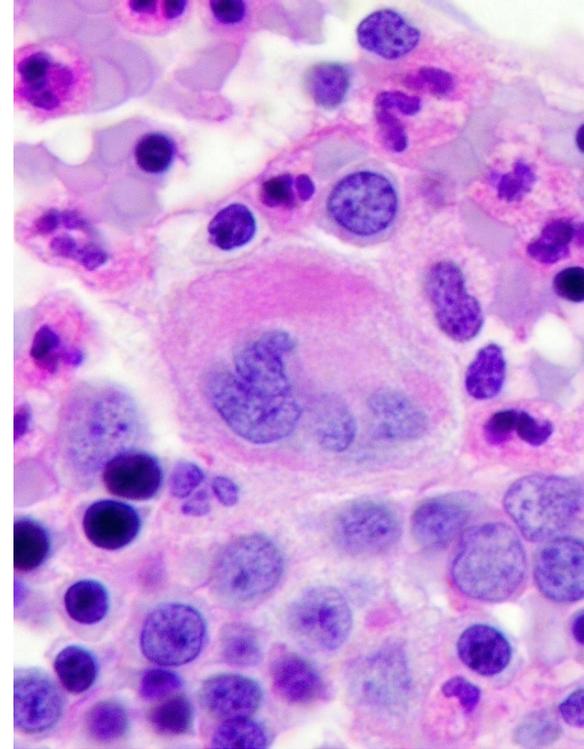
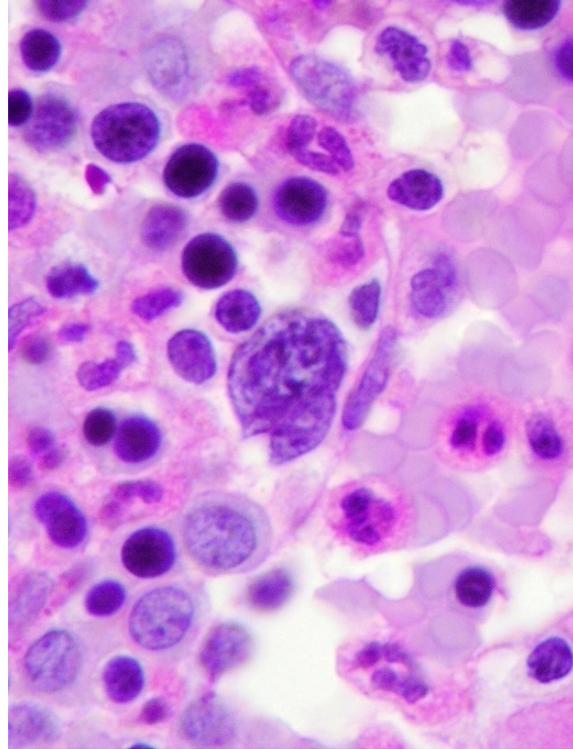
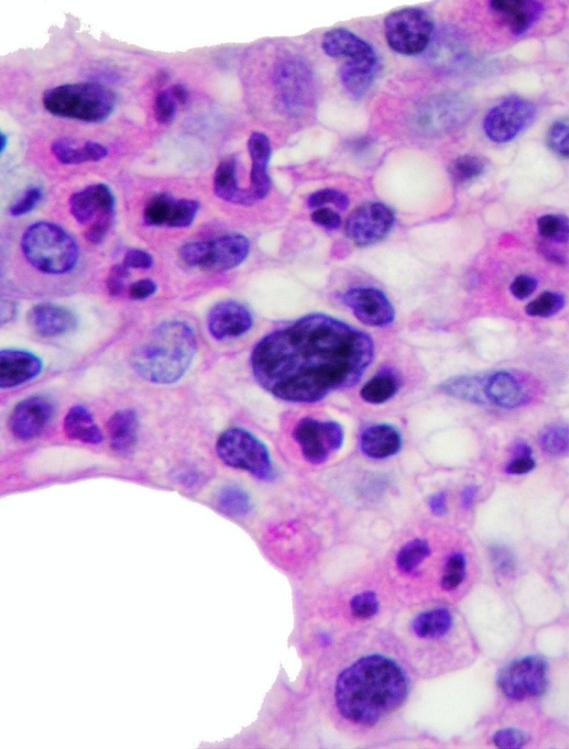
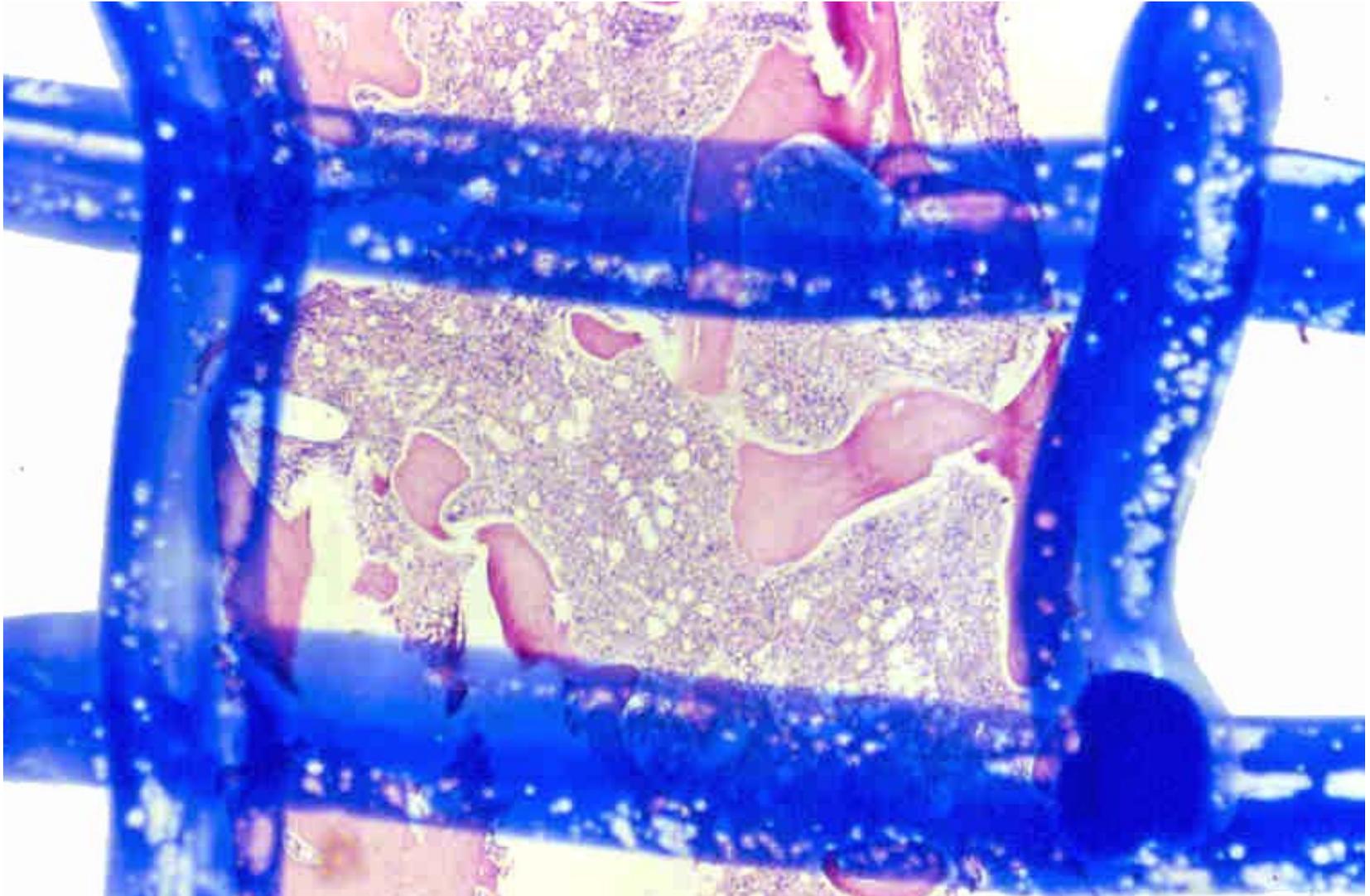


Figure 4.3 Title page of the 7th edition of

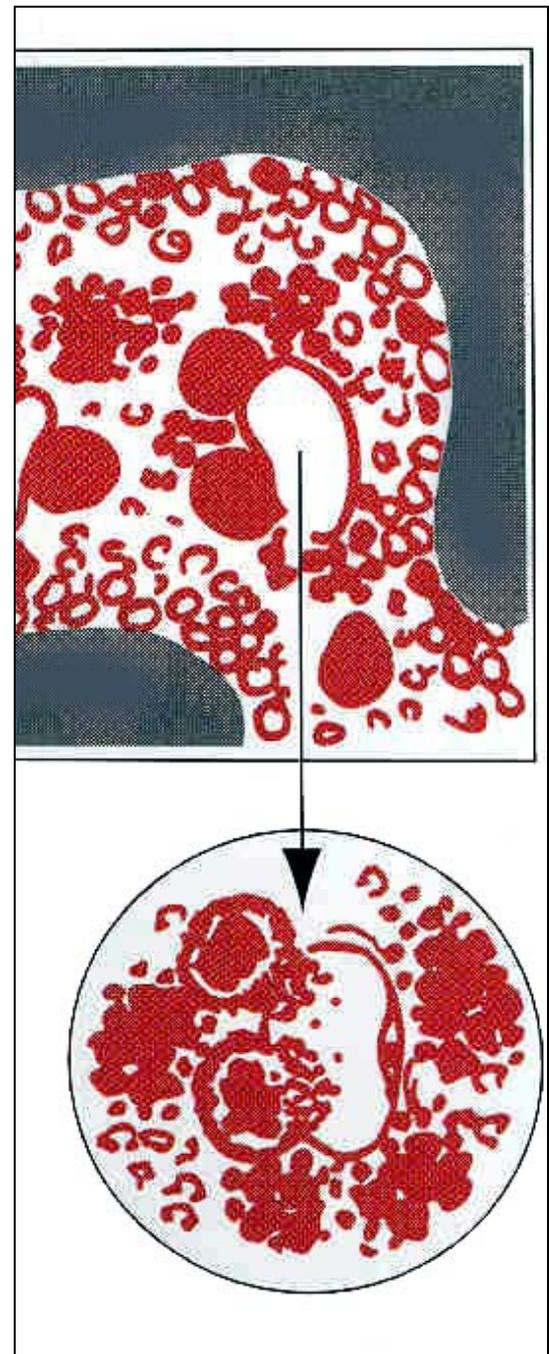
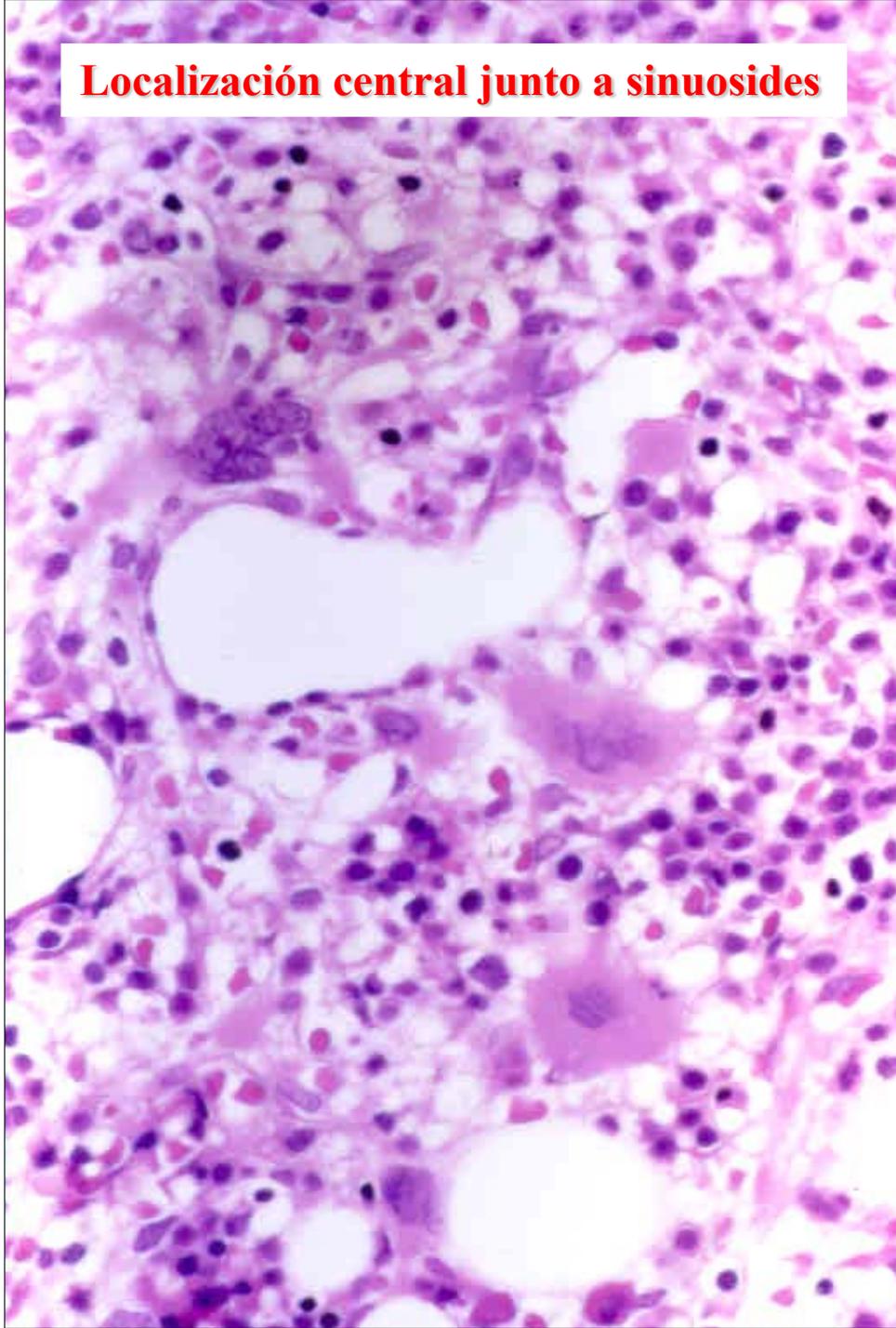


Normal: en 1 mm² = de 7 a 15 megacariocitos

Hiperplasia: > 35 x mm²



Localización central junto a sinusoides



Células perivascular

**Requerimiento de plaquetas
IV VEGF-A PLGF-1**

SINUSOIDE

Plaquetas

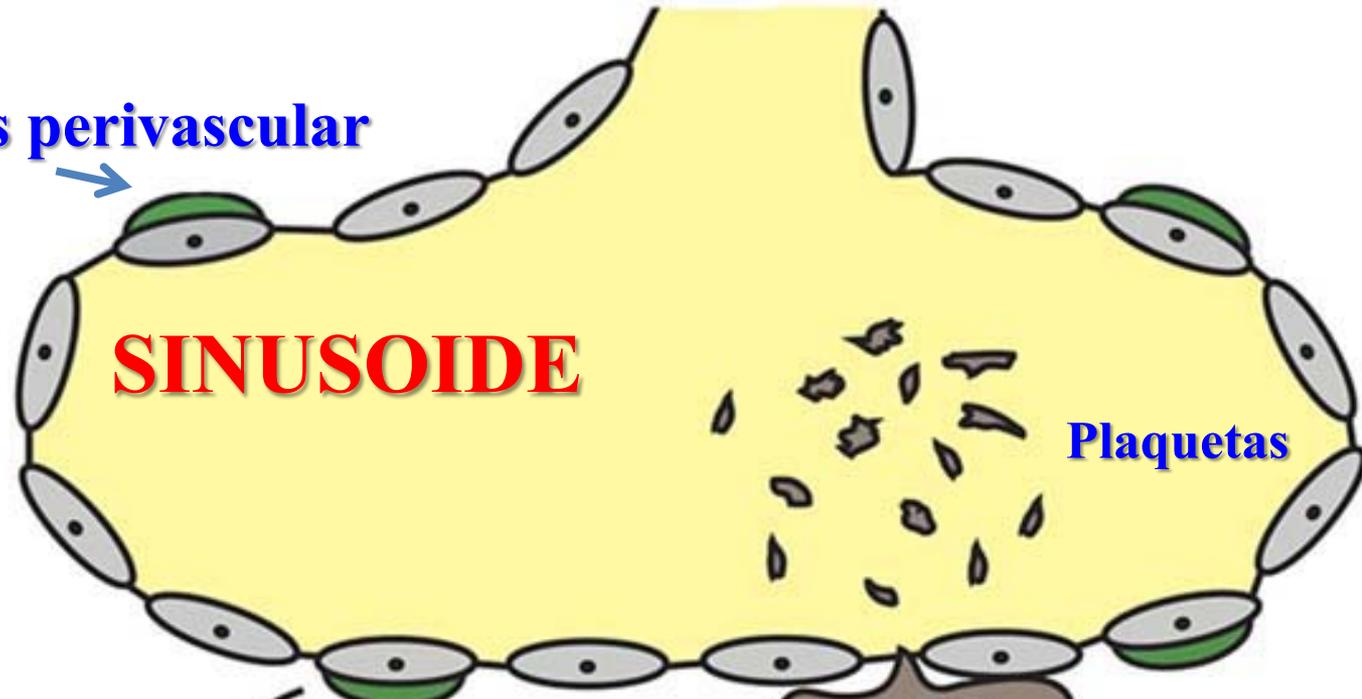
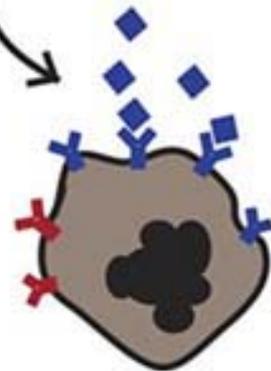
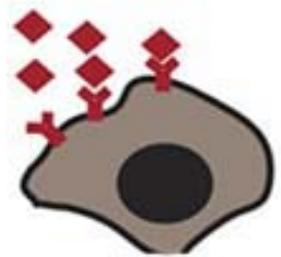
CXCL12 (SDF-1)

**Migración
Producción de plaquetas**

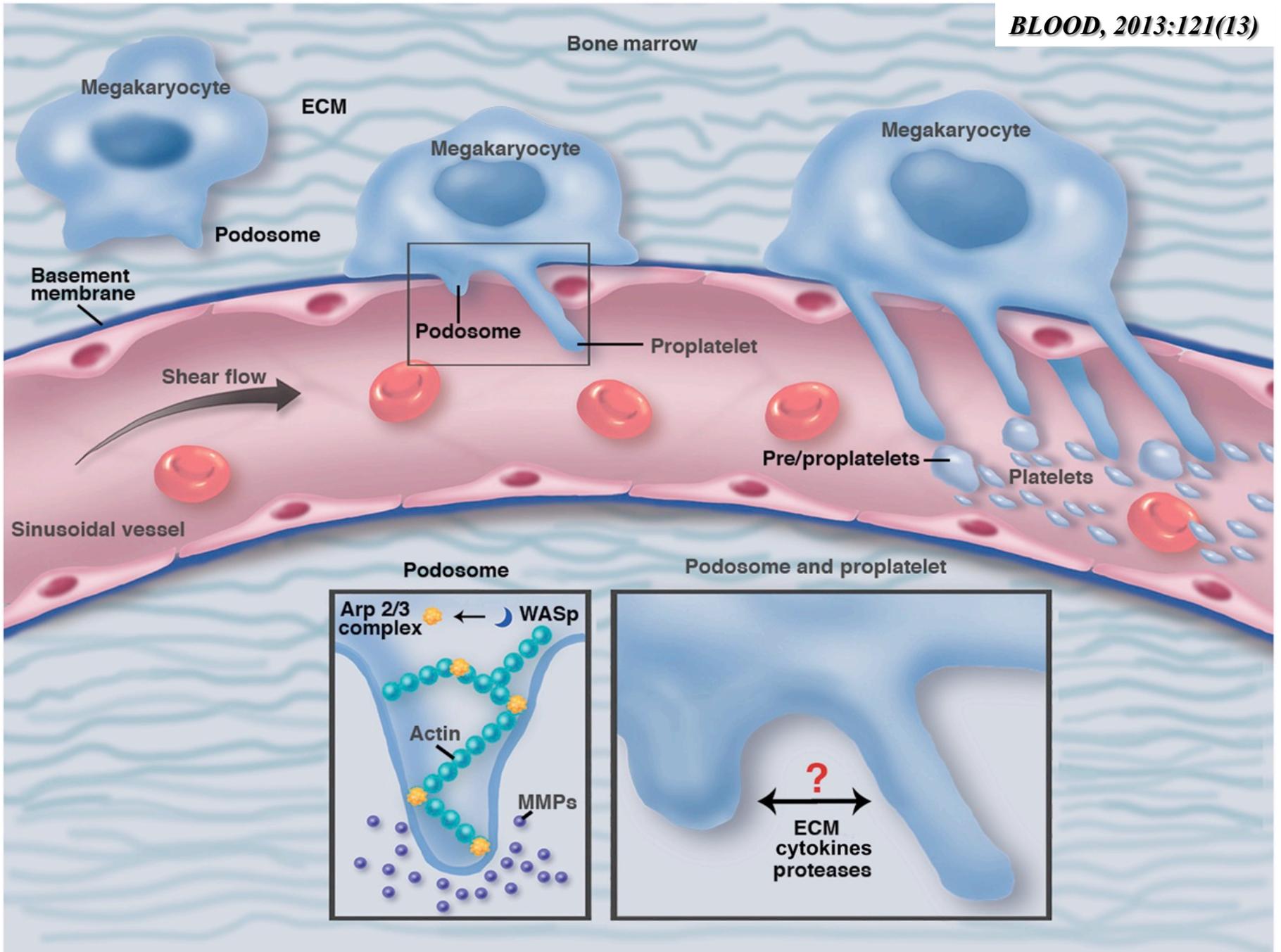
CXCR4

Endomitosis

**CXCR4
VEGF-A**



Megacariocito



Trombomodulina

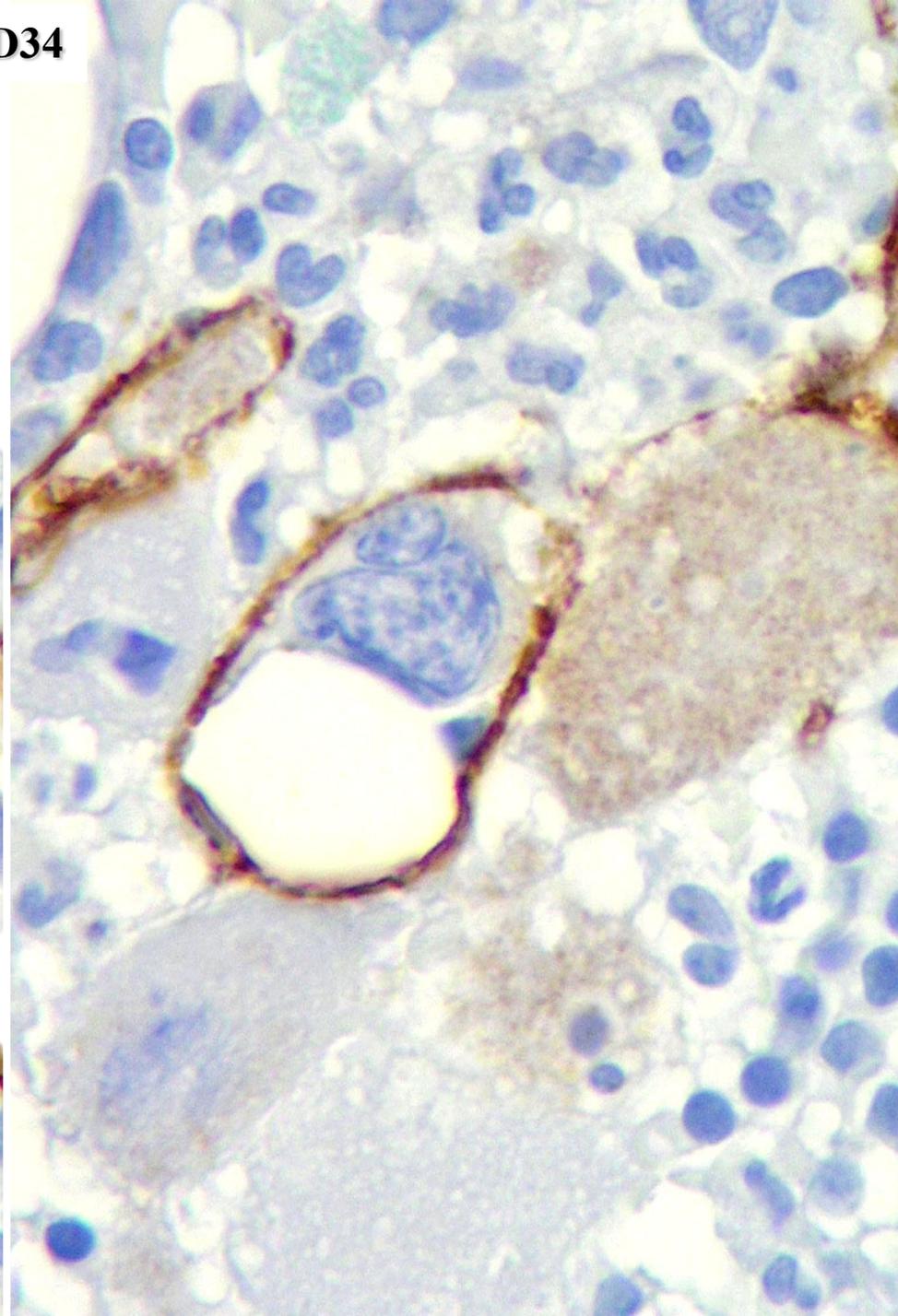
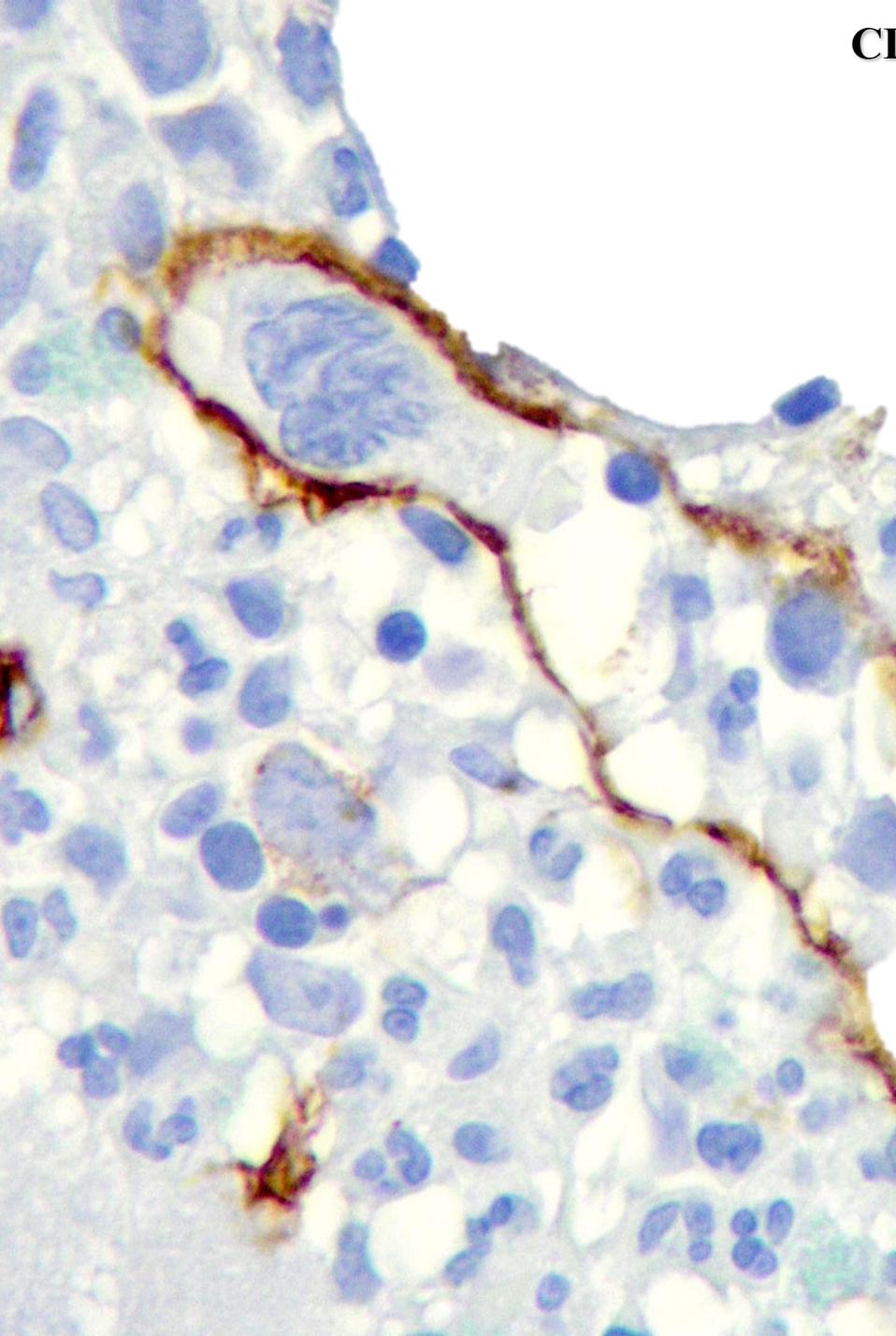
sinusoide



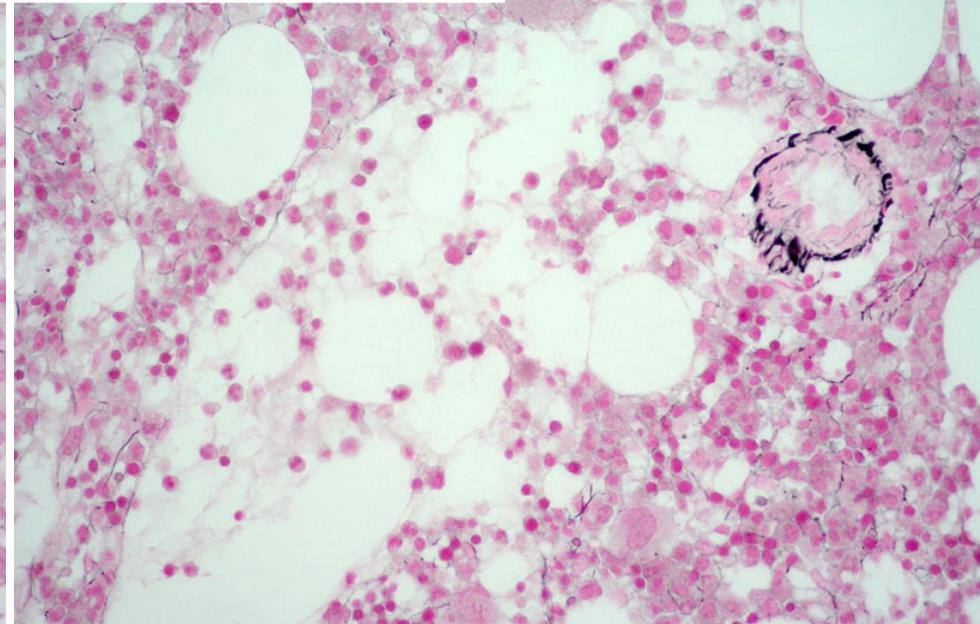
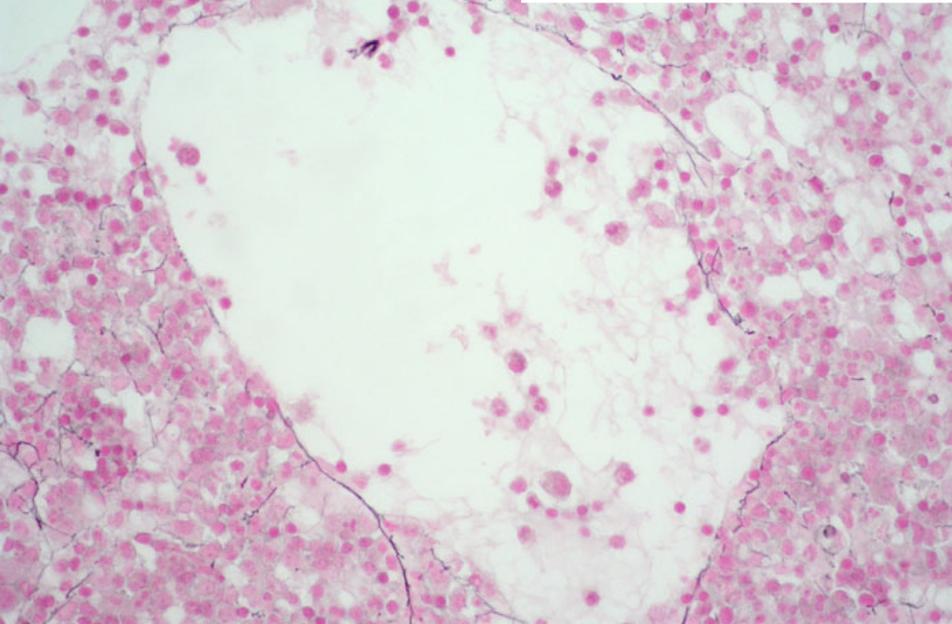
CD61



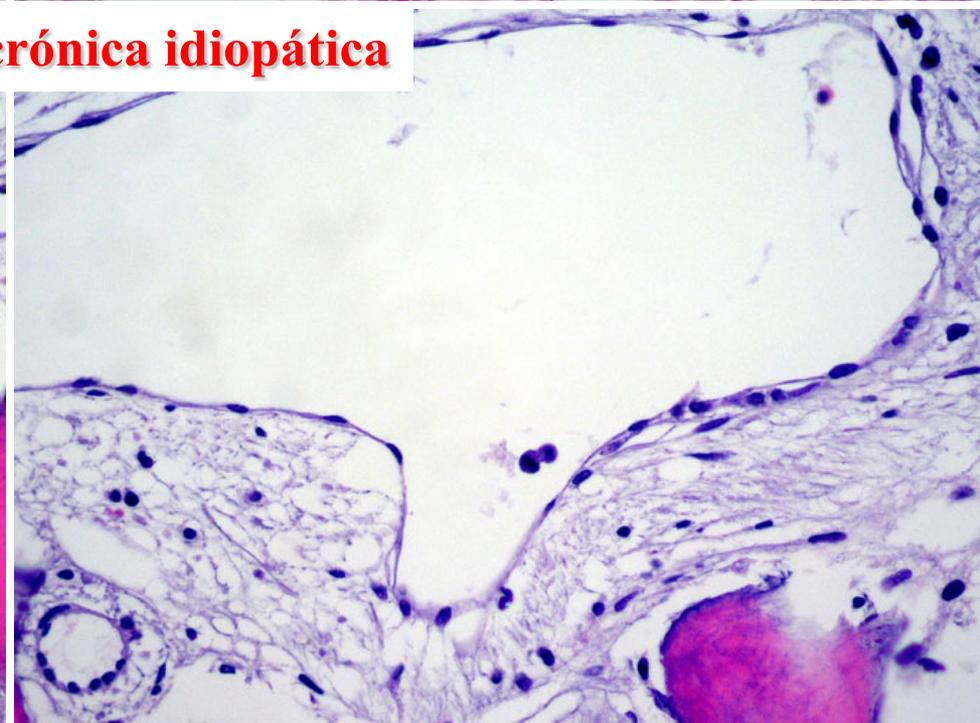
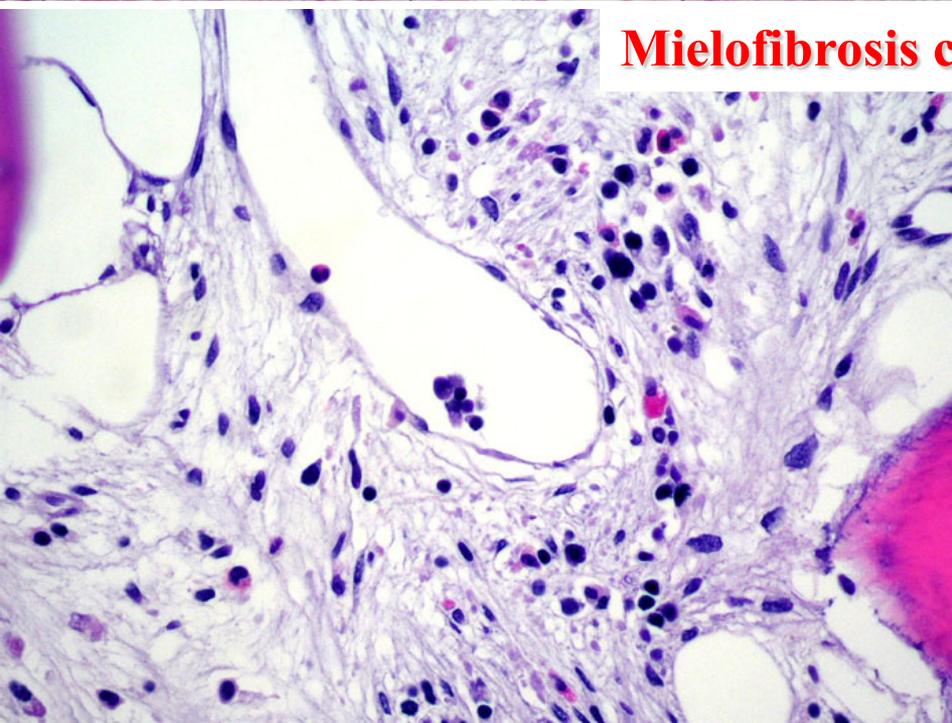
CD34



Dilatación sinusoidal Policitemia Vera



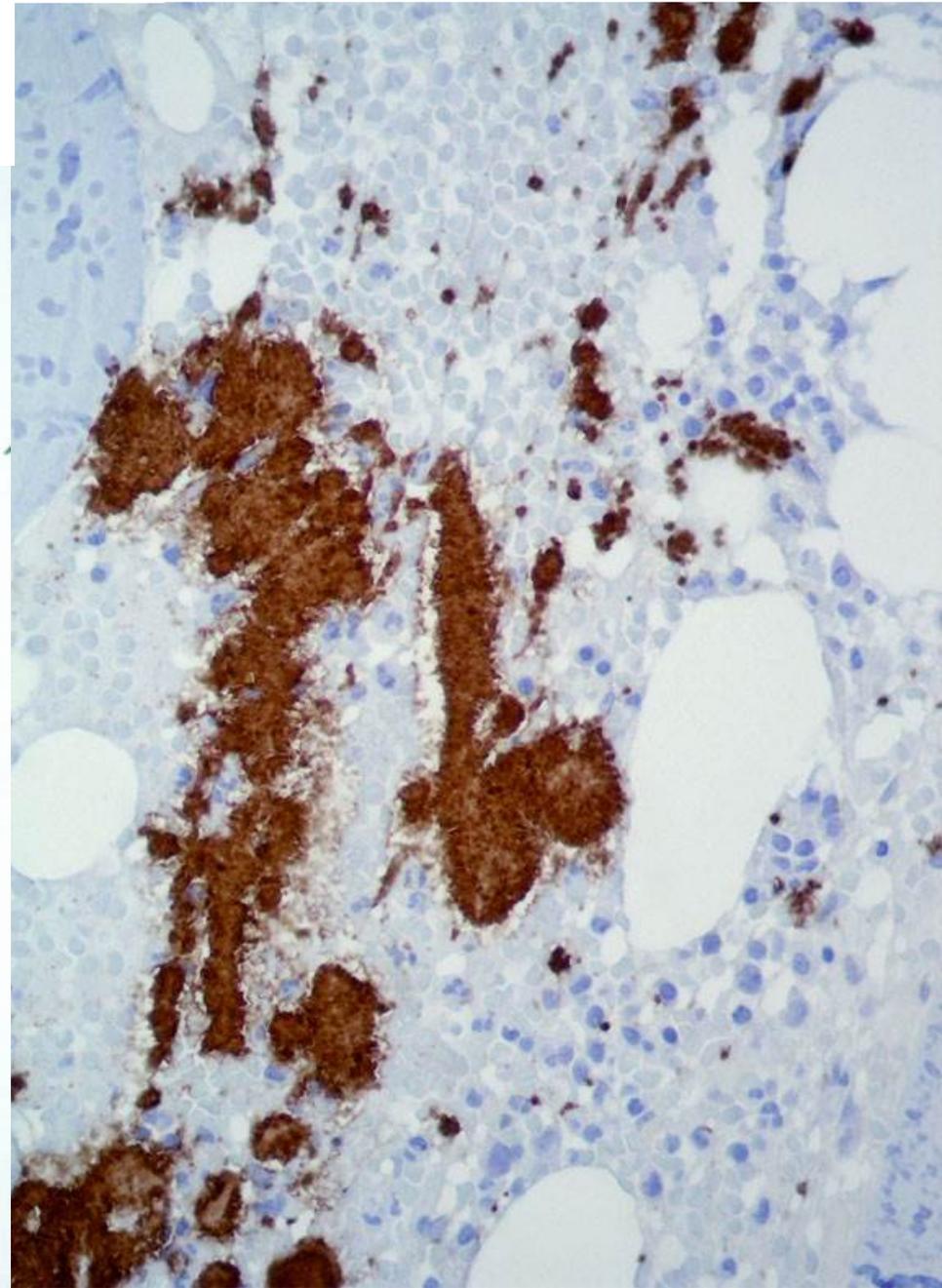
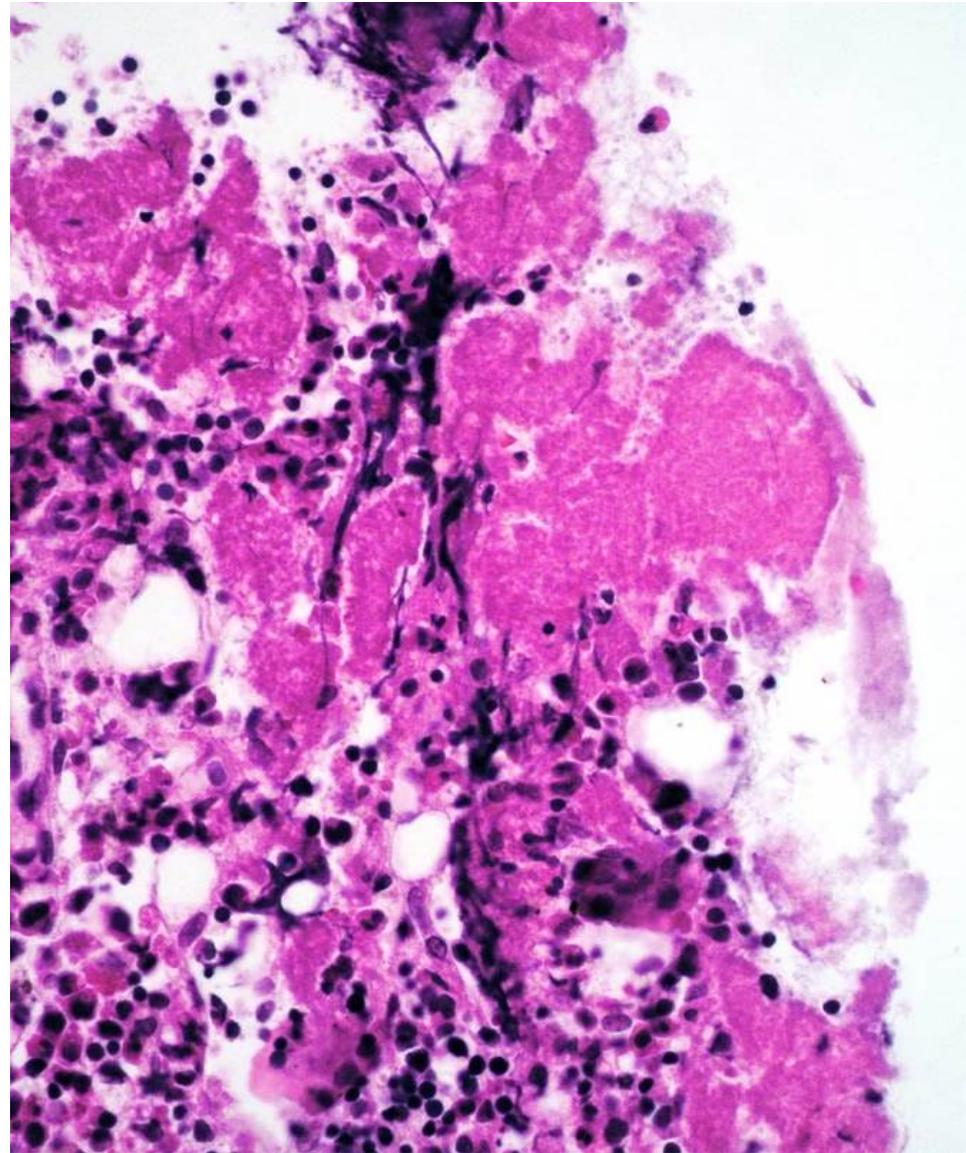
Mielofibrosis crónica idiopática

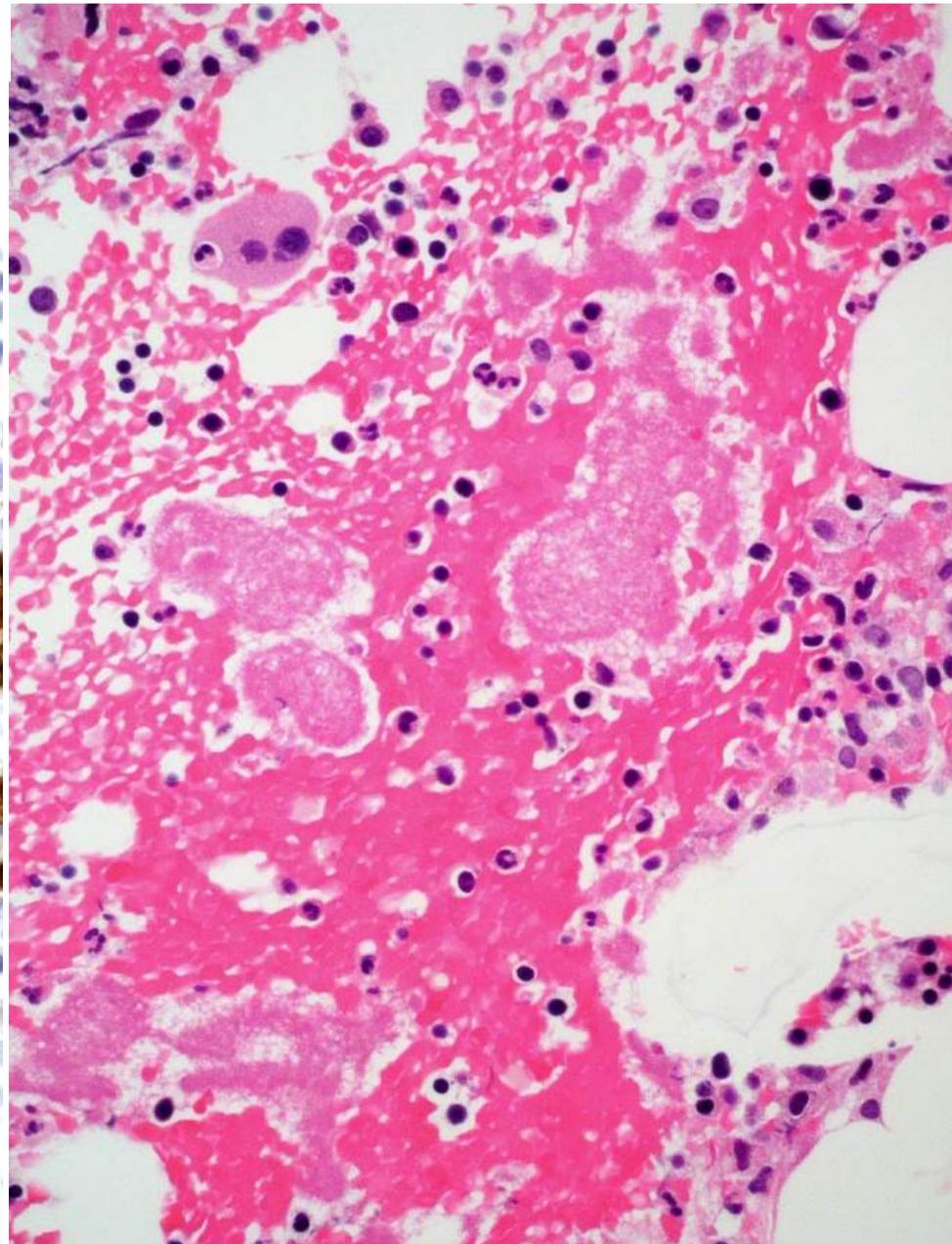
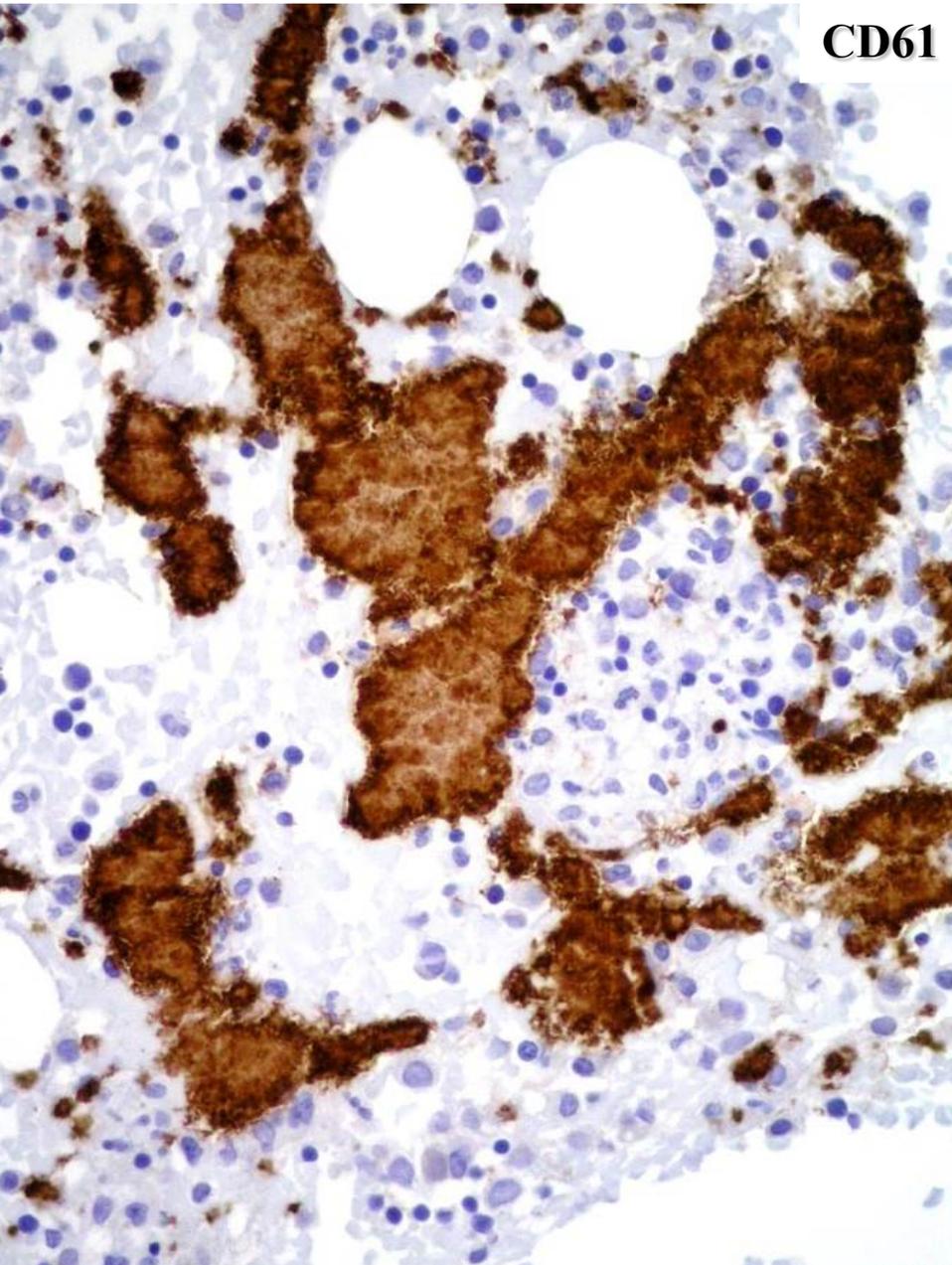


Purpura trombocitopénica

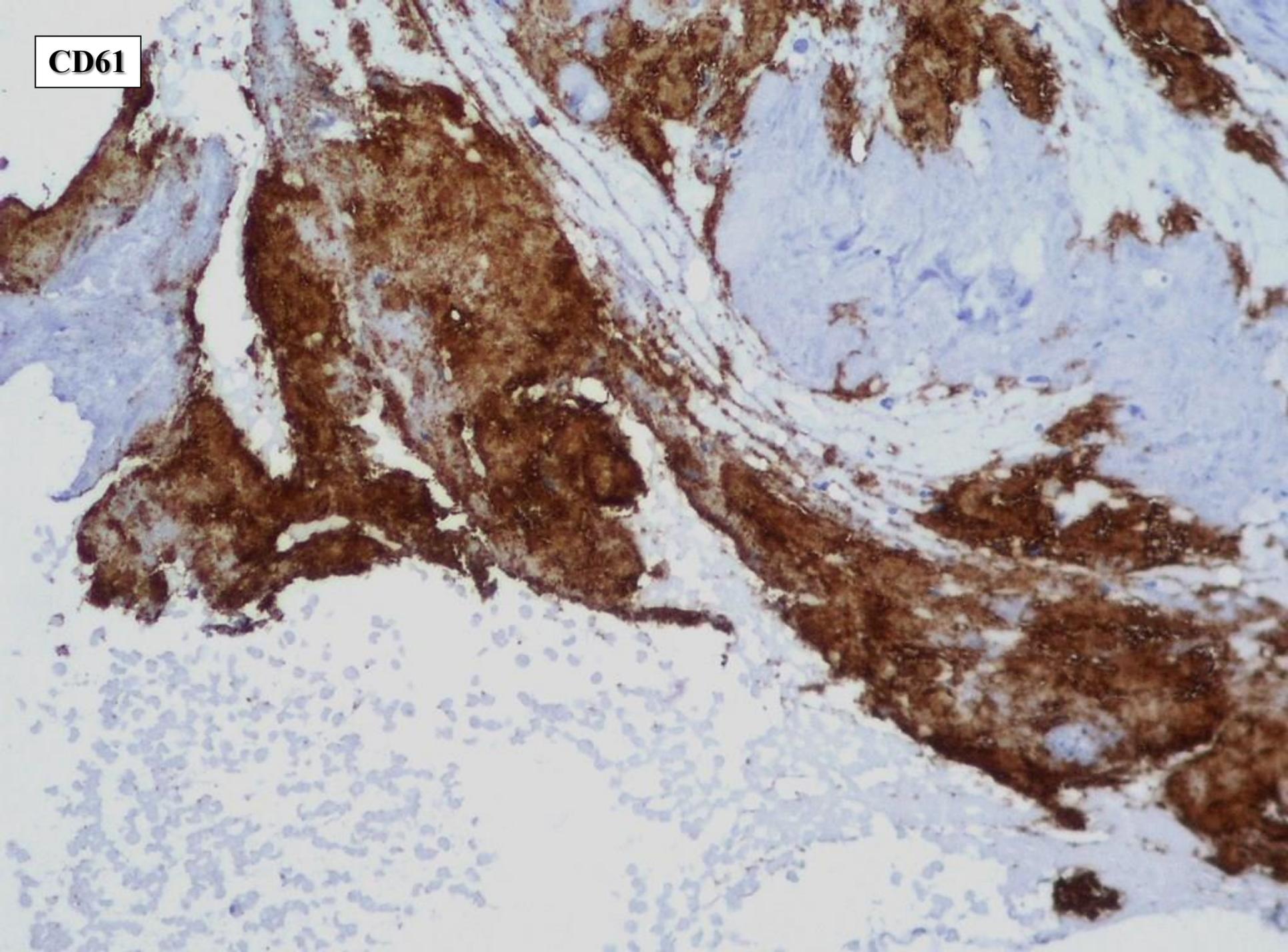
Plaquetas intra sinusoidales. Estimuladas por esteroides

CD61

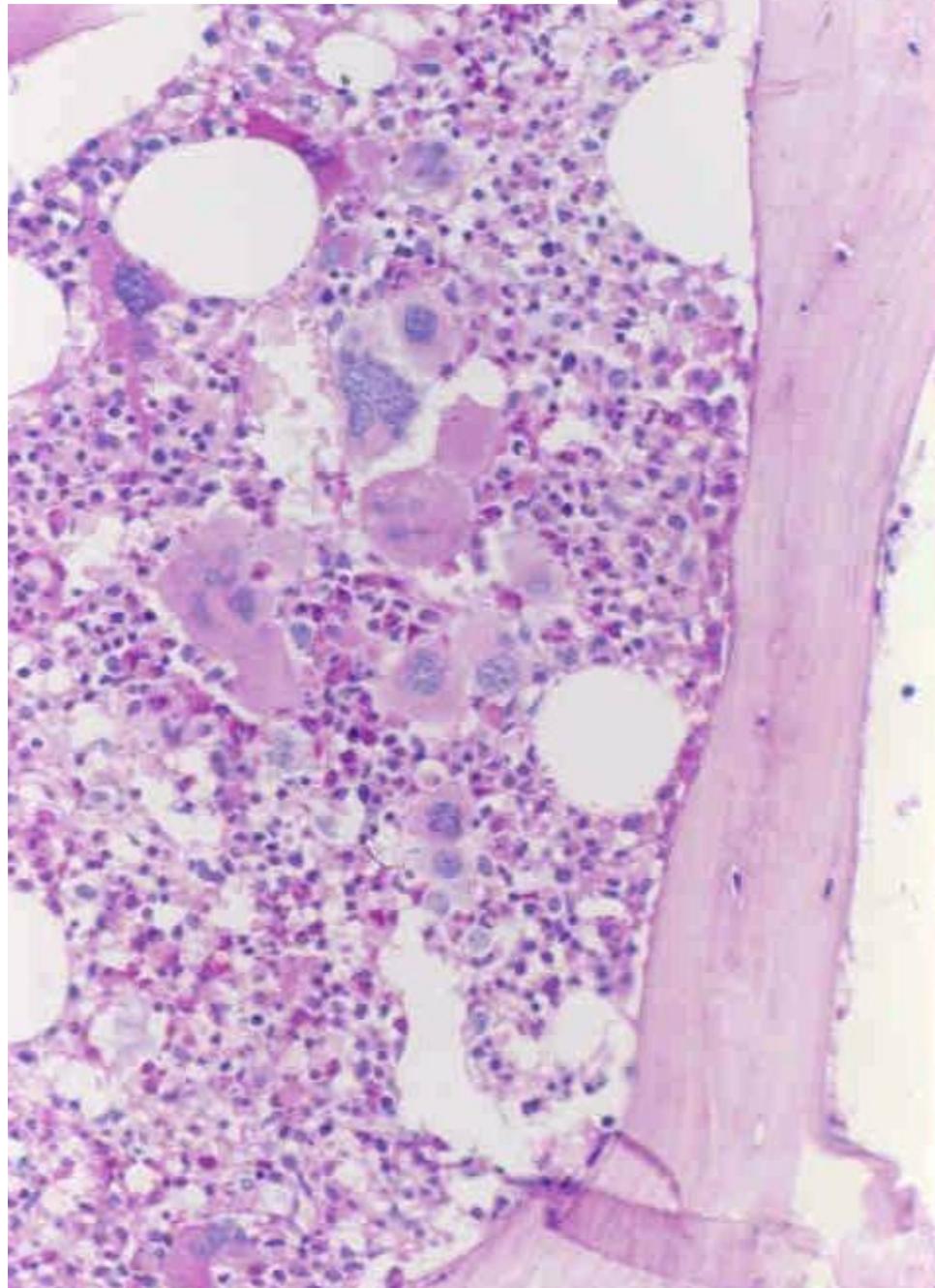
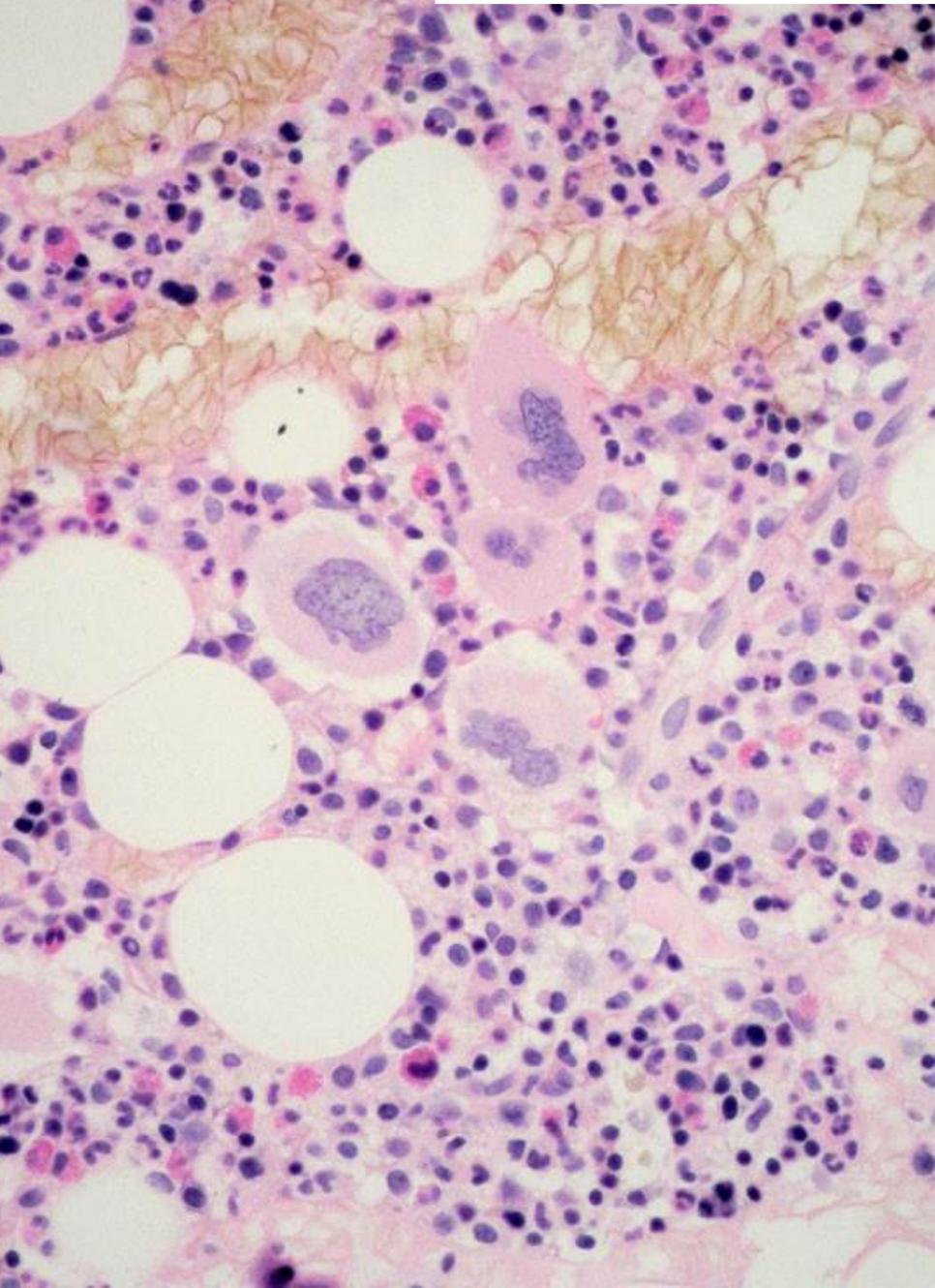




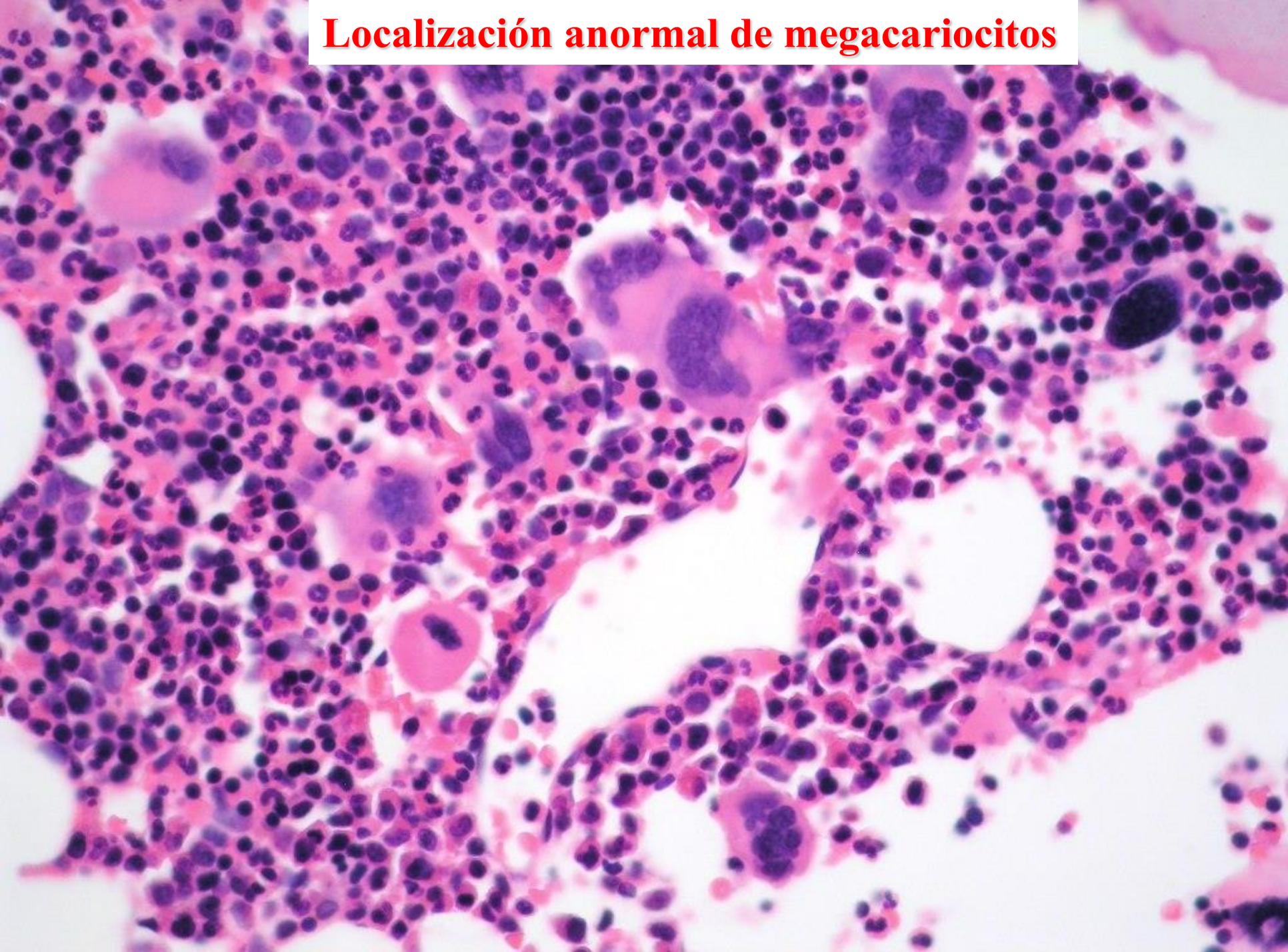
CD61



Localización anormal de megacariocitos



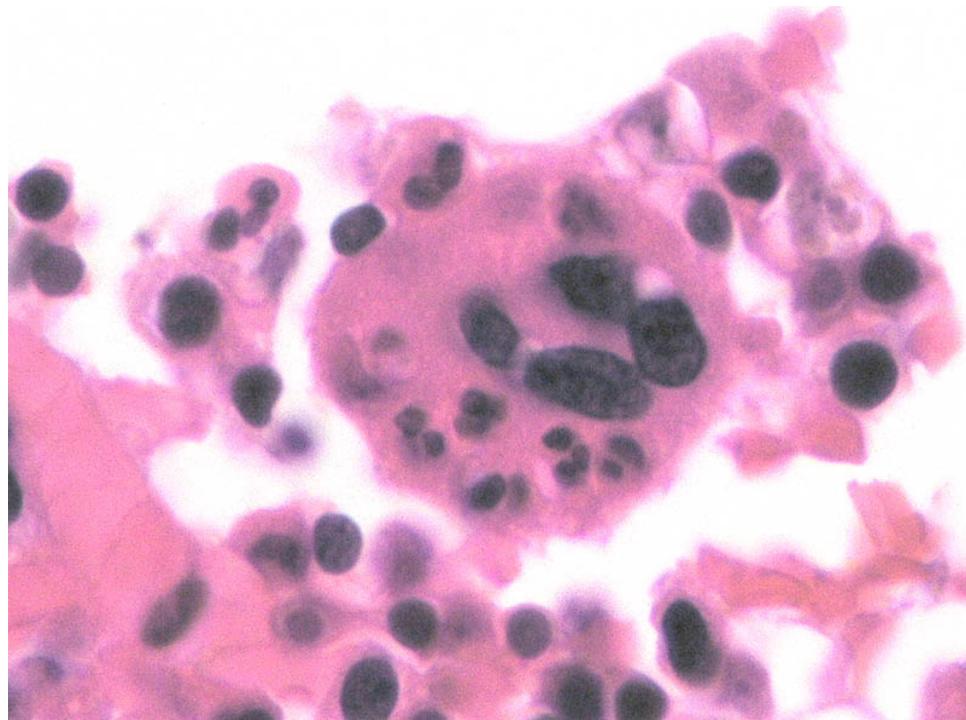
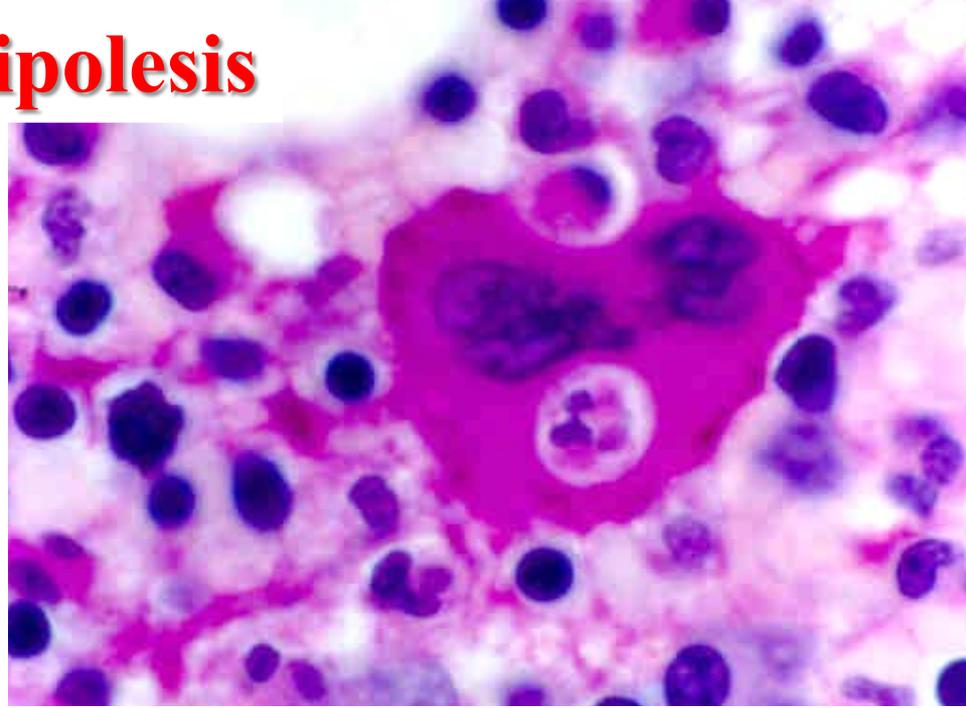
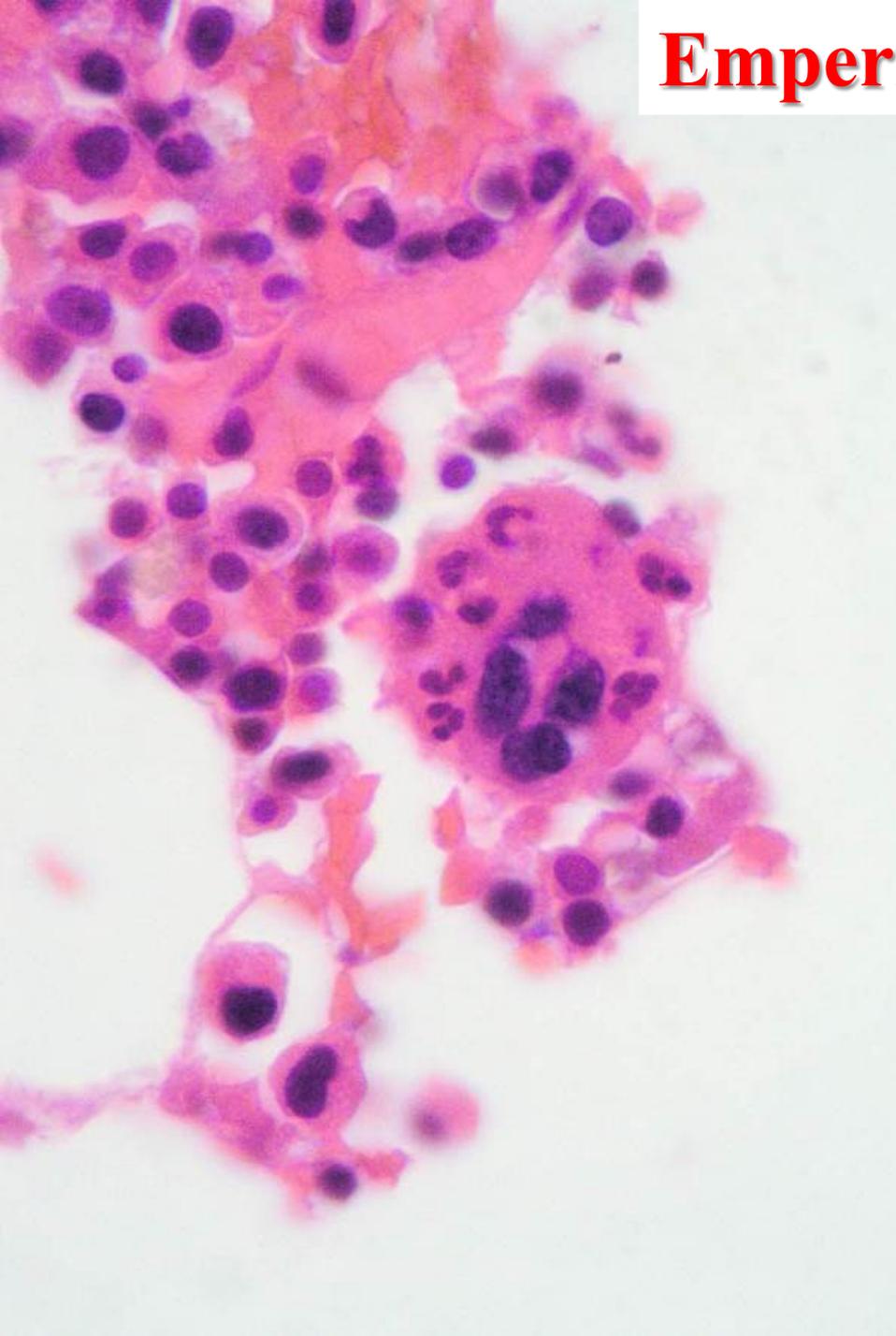
Localización anormal de megacariocitos



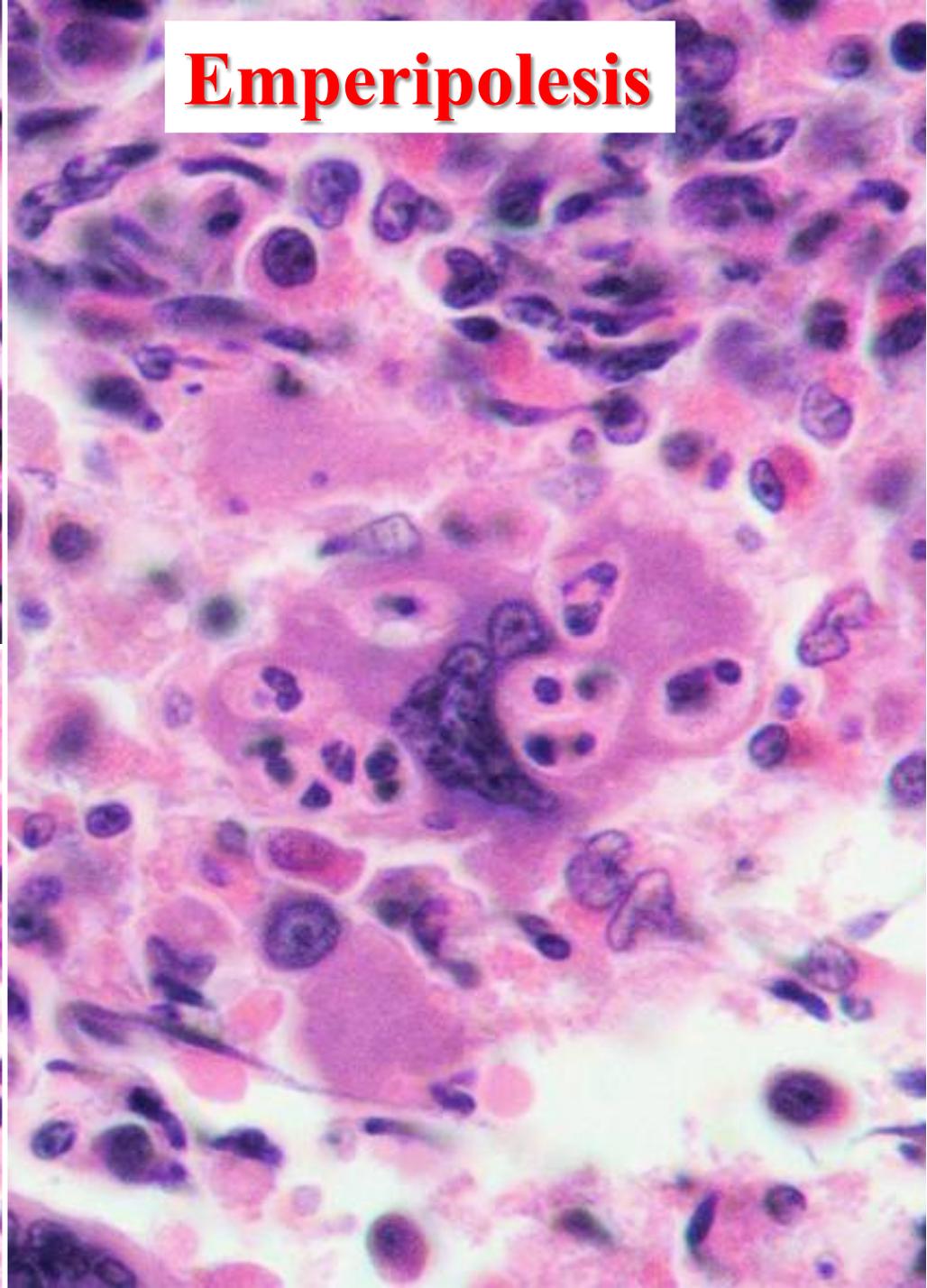
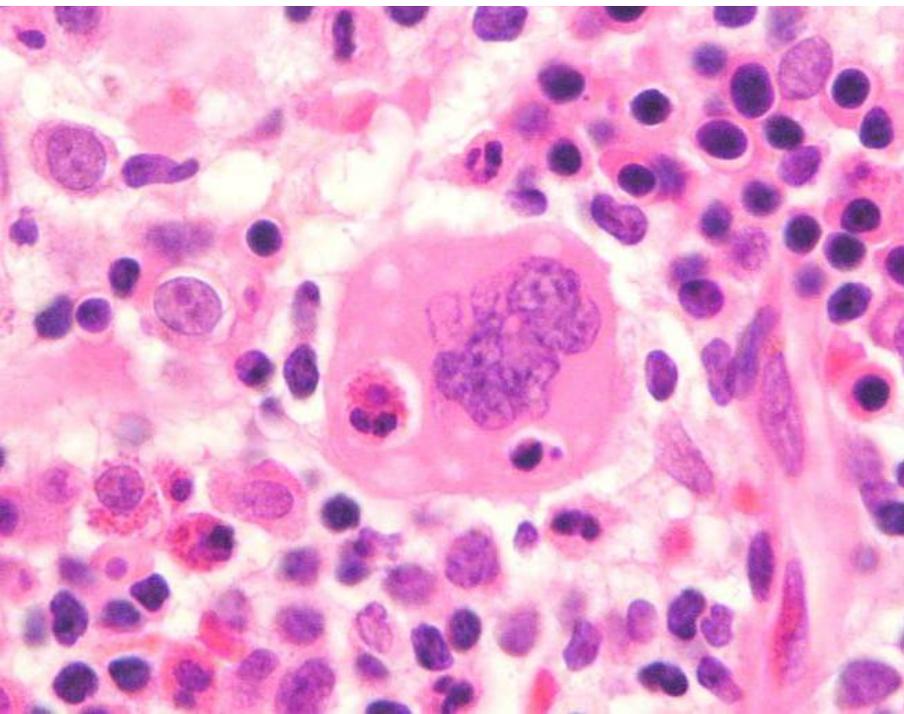
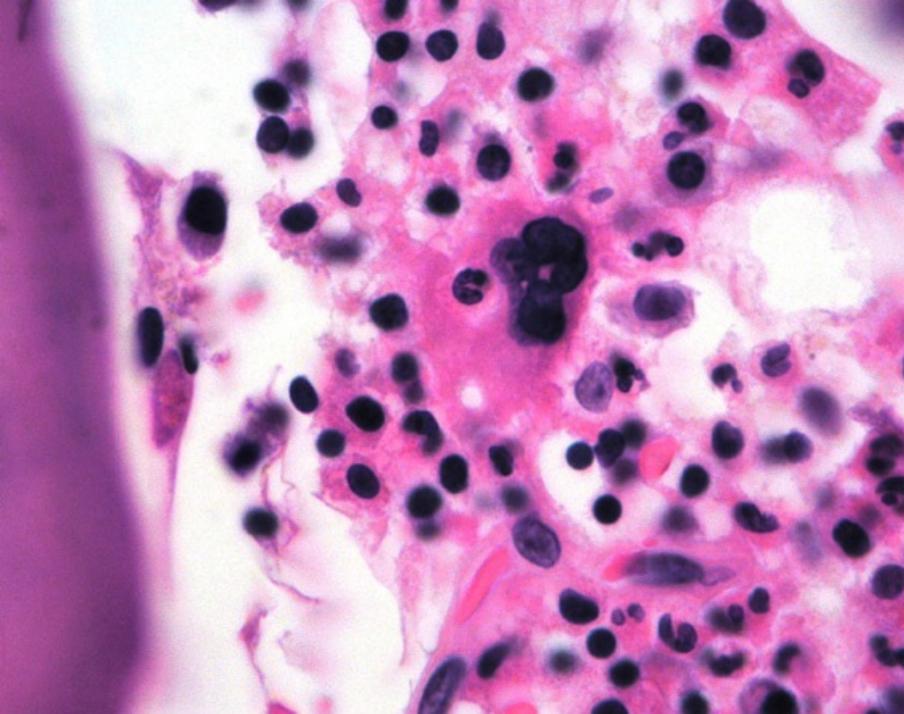
Localización anormal de megacariocitos
Mielofibrosis primaria



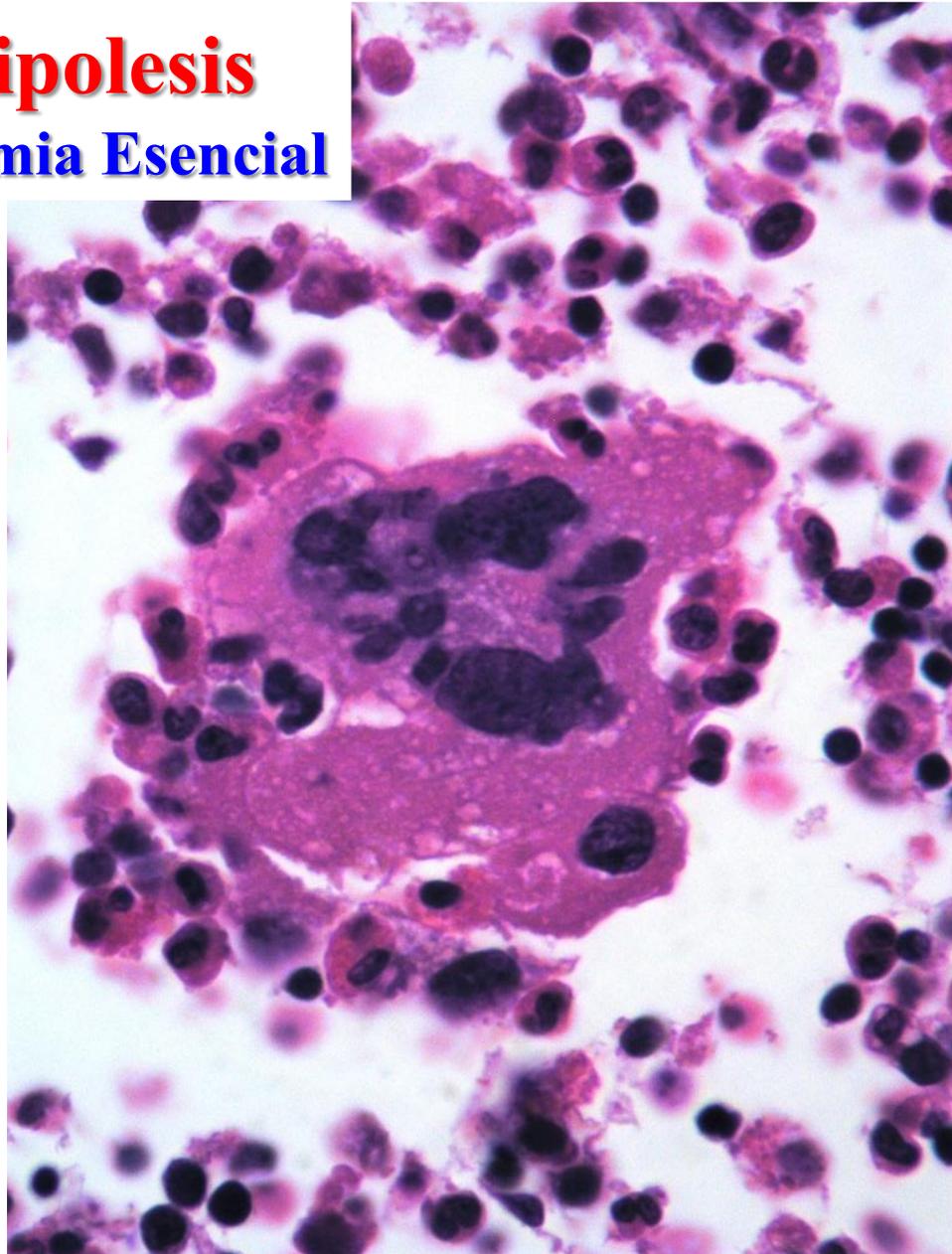
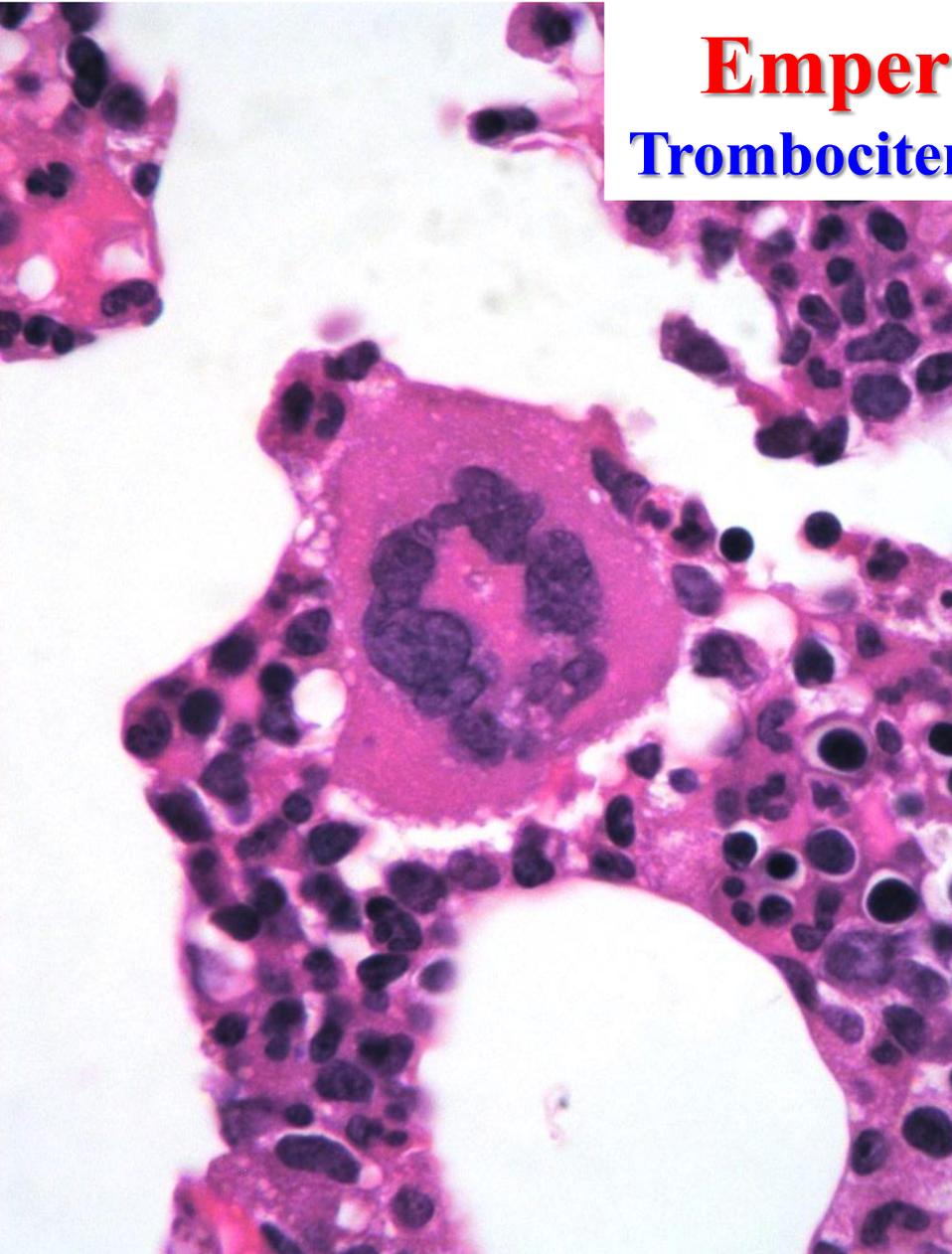
Emperipolesis



Emperipolesis

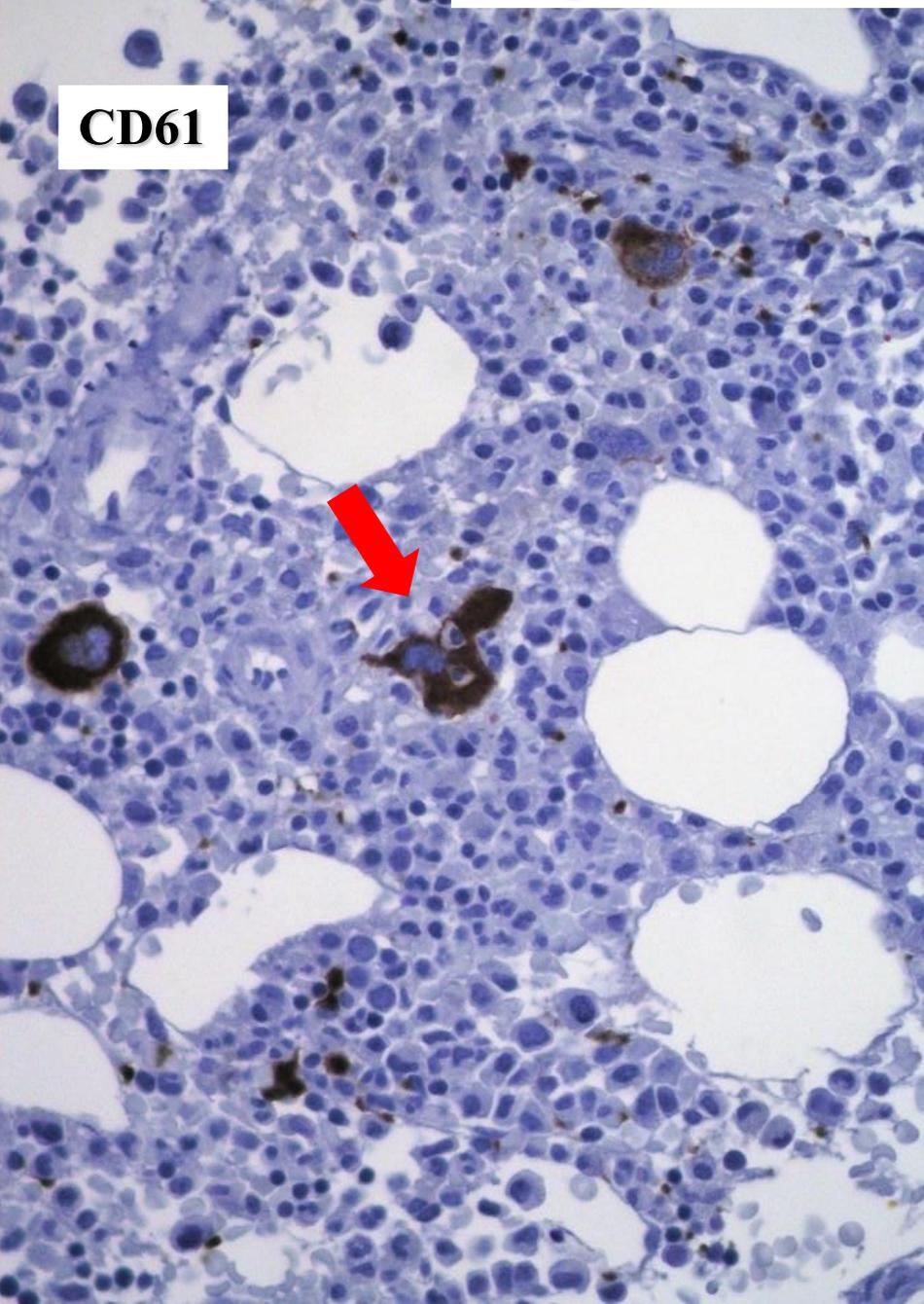


Emperipolesis
Trombocitemia Esencial

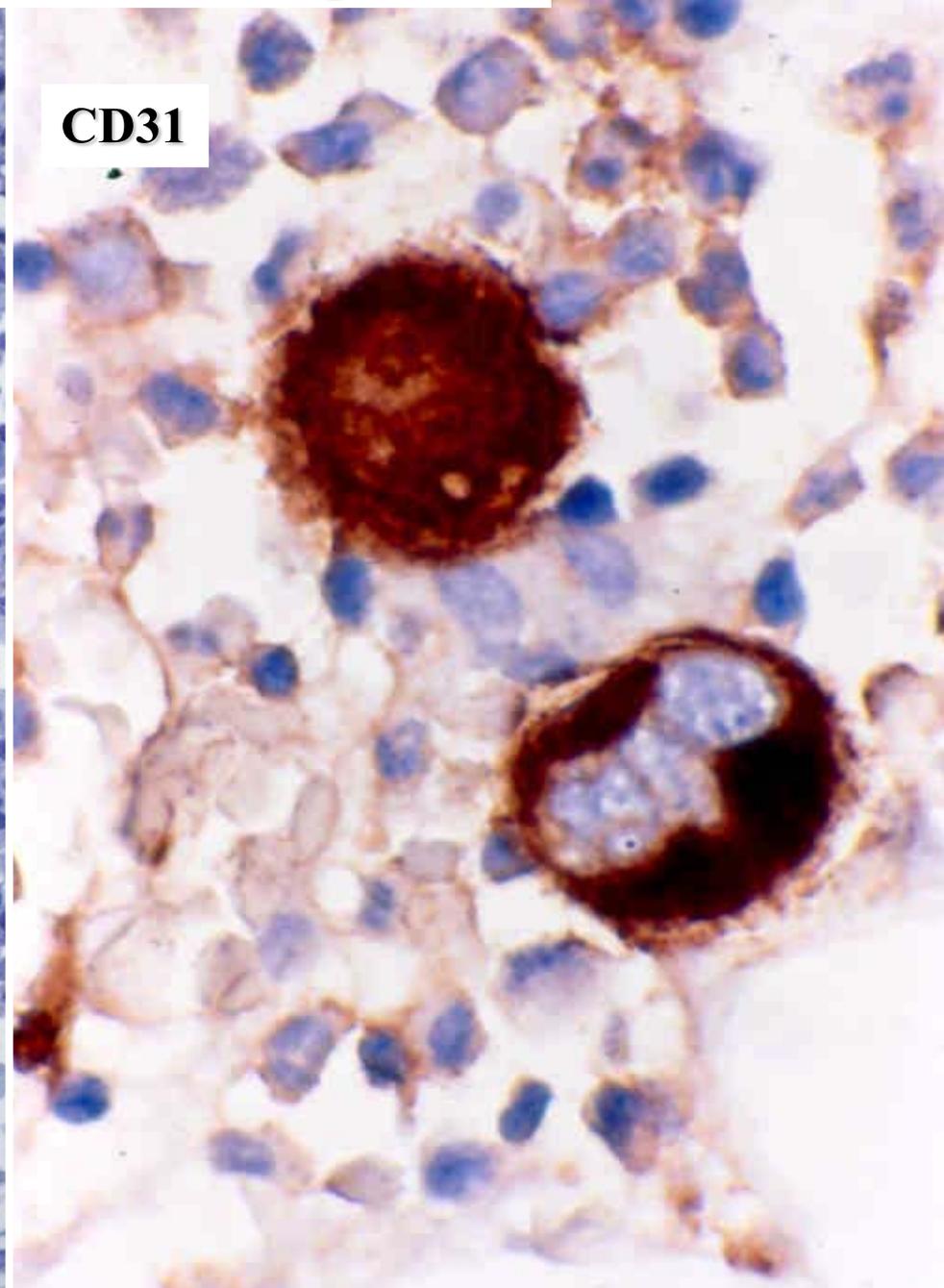


Megacariocitos Inmunohistoquímica

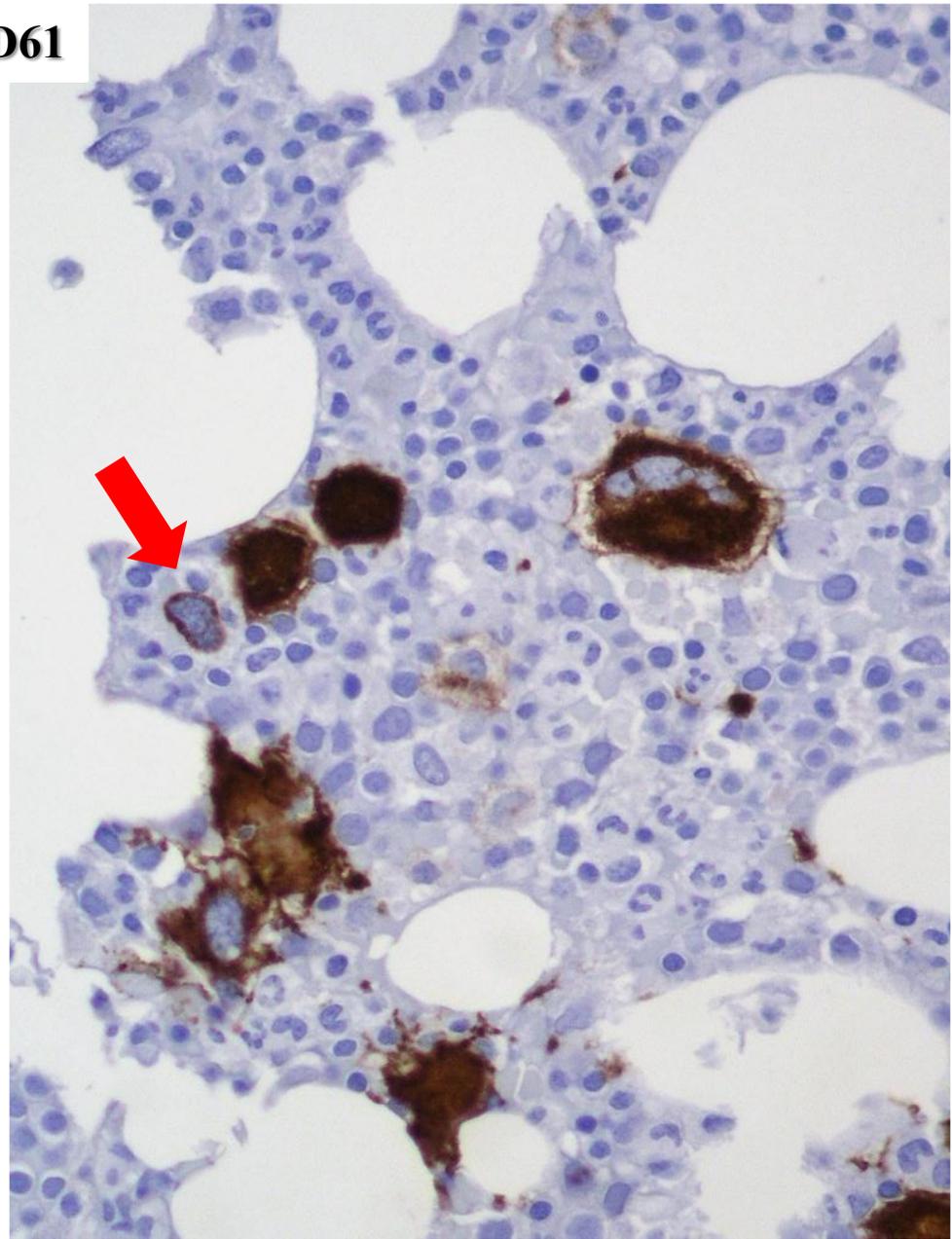
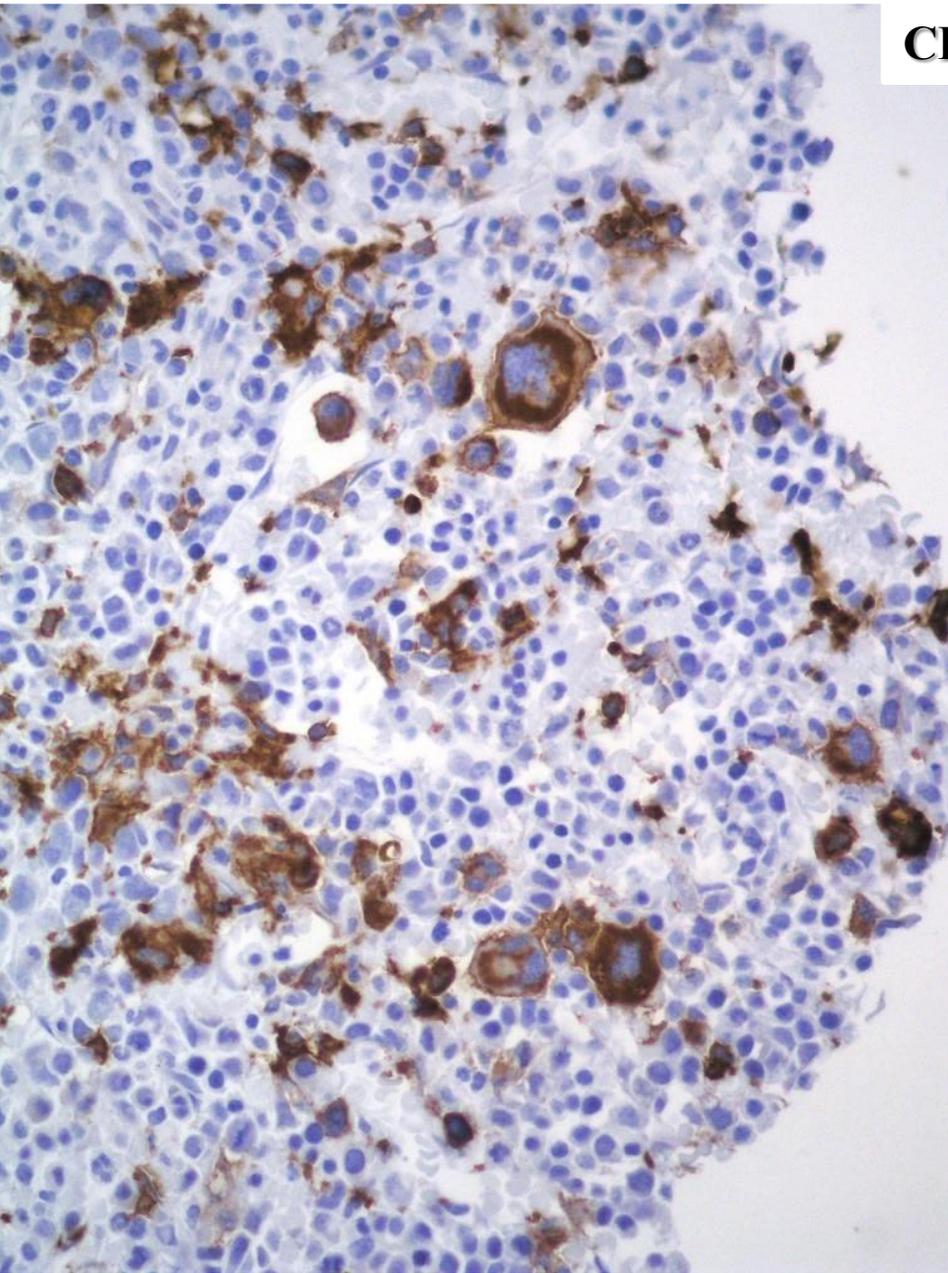
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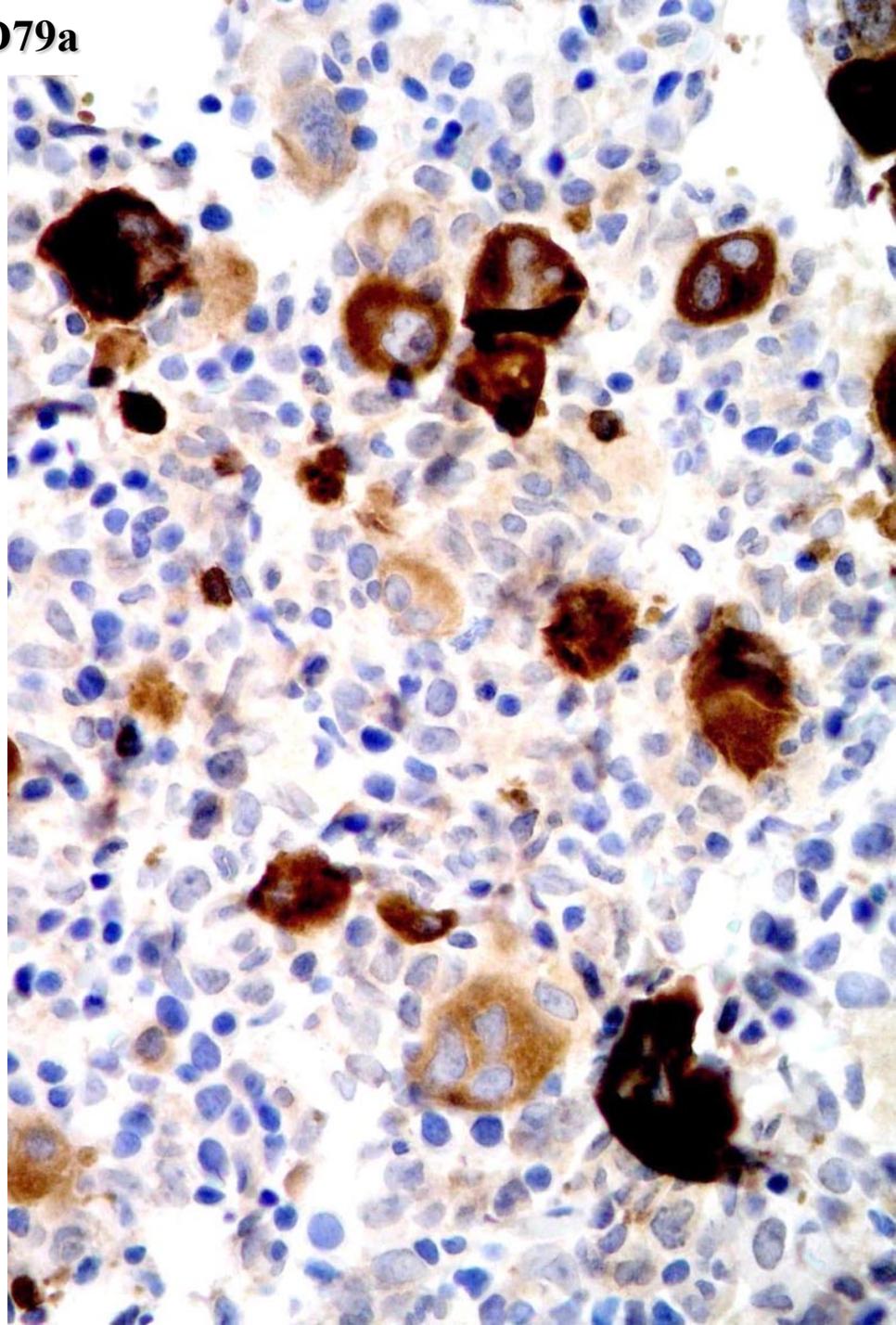
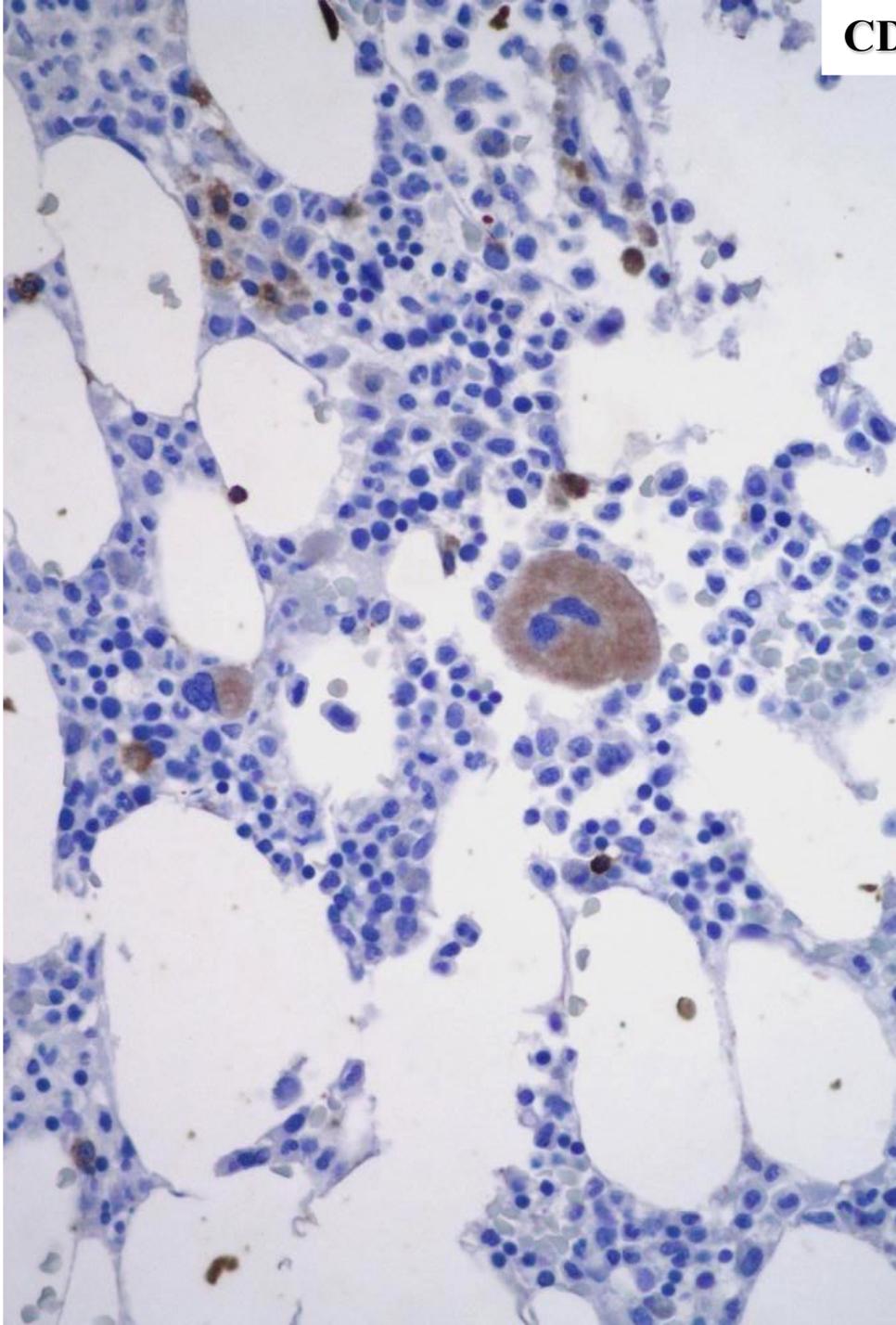
CD31



CD61

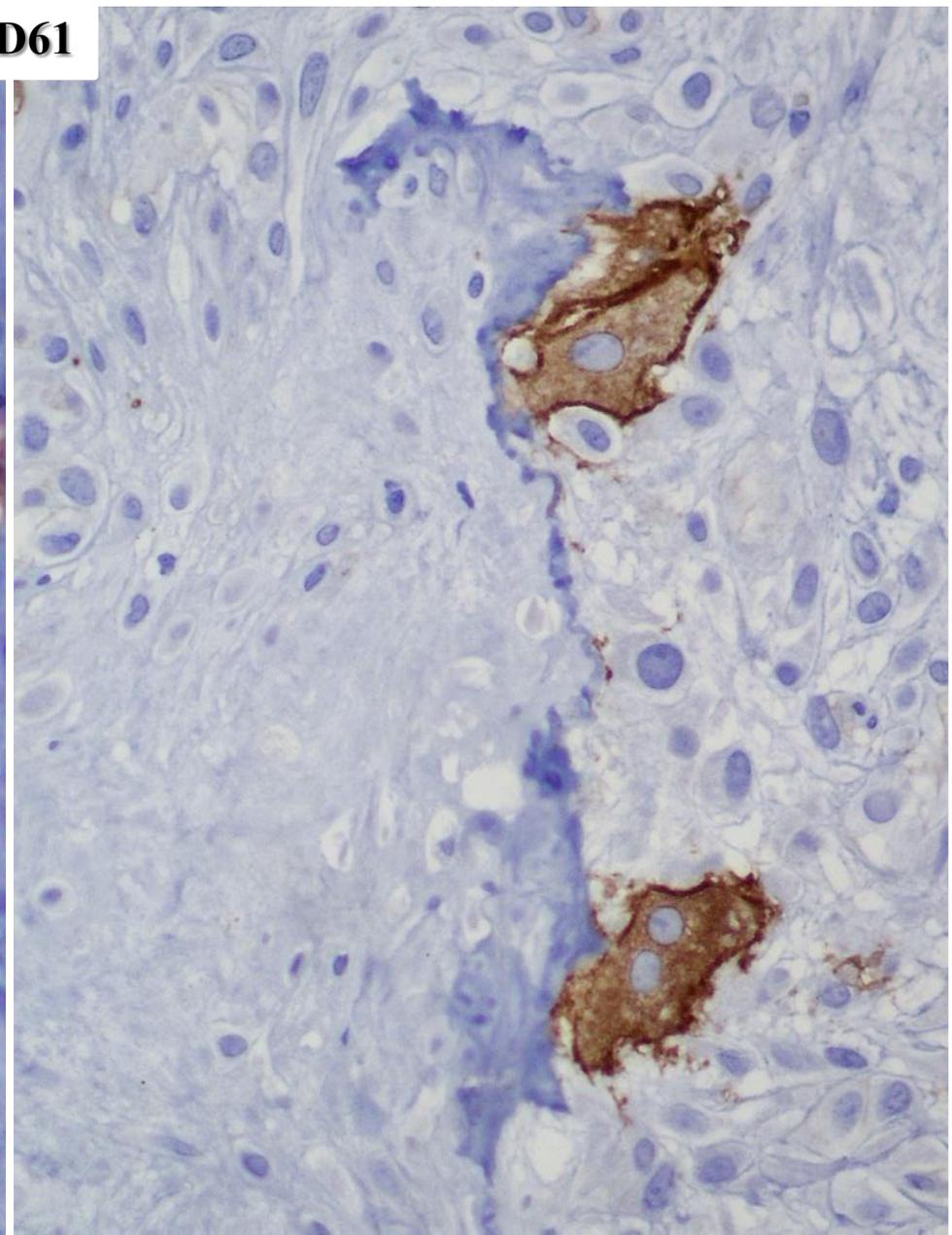
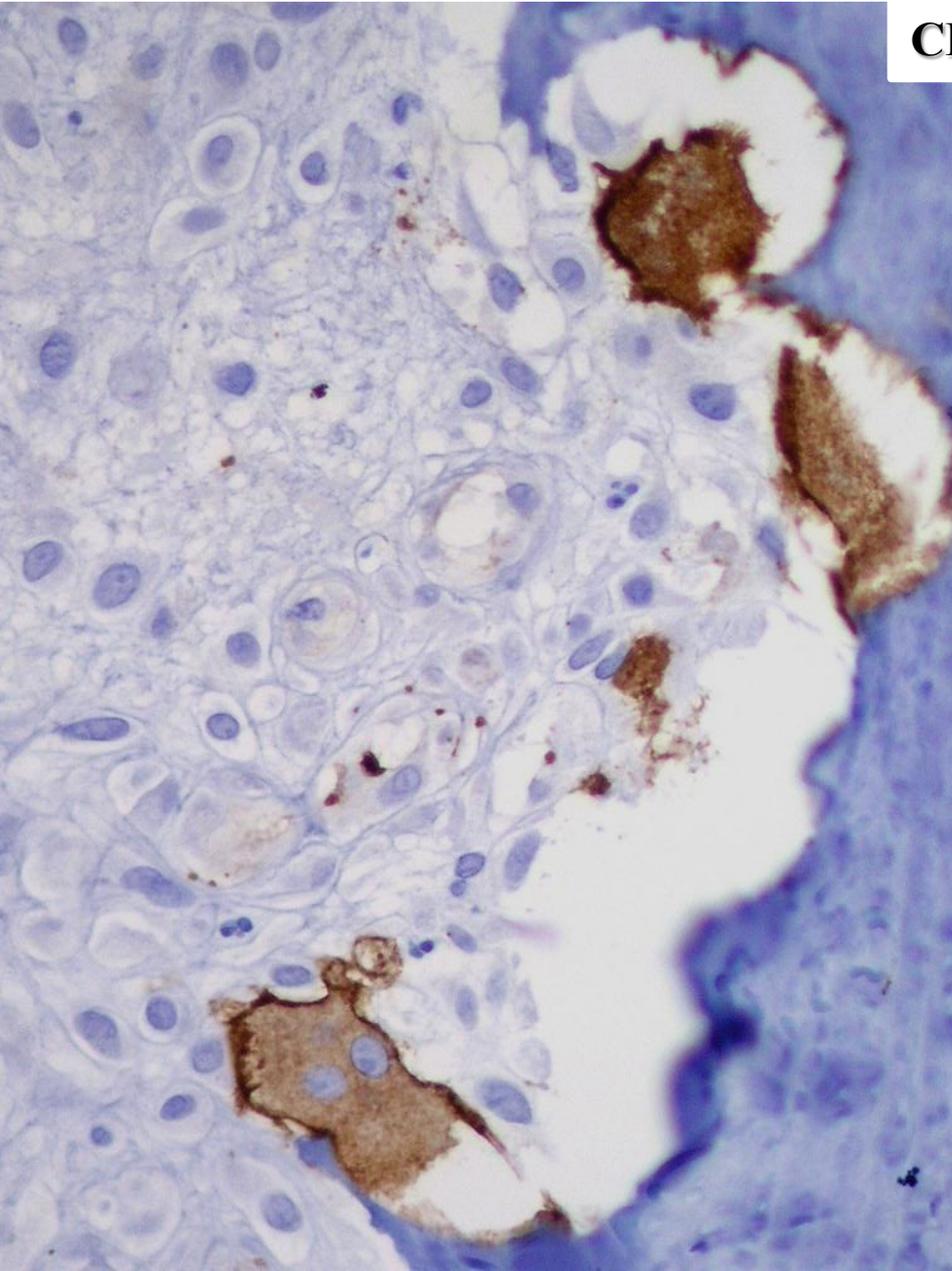


CD79a



Osteoclastos

CD61



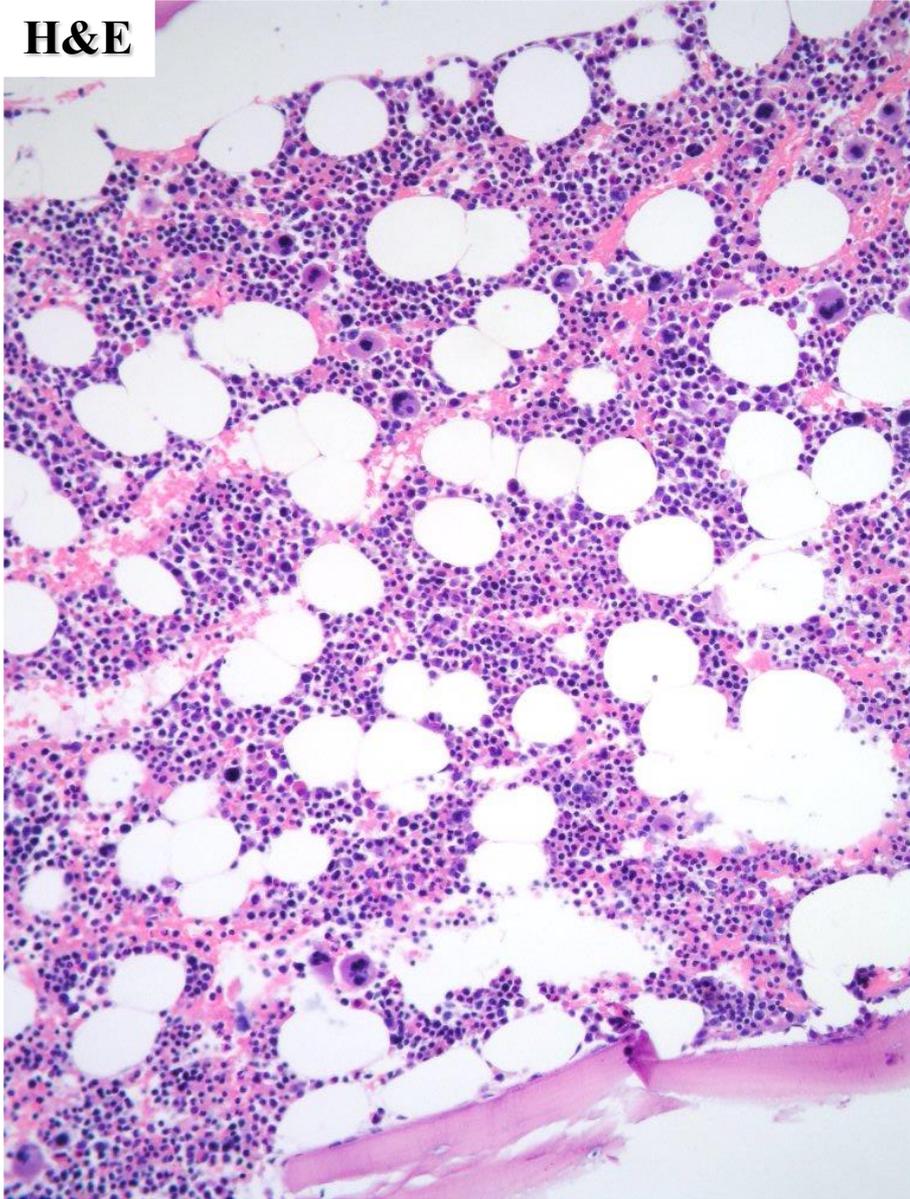
Inmunohistoquímica

Megacariocitos.

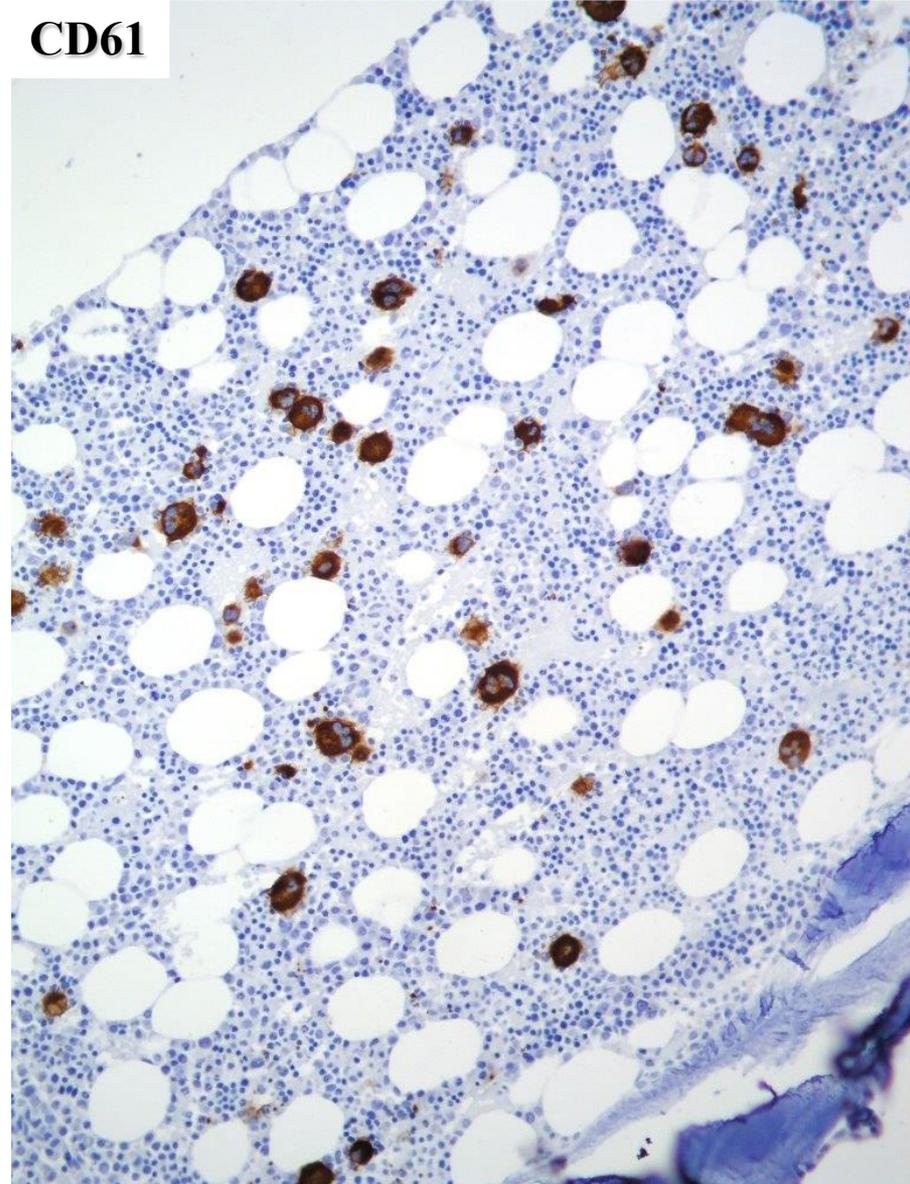
- **CD61**
- **CD42a**
- **CD41**
- **CD31**
- **Ant. Rel. Fac. VIII**
- **CD79a**

¿Contar megacariocitos con H&E o IHQ ?

H&E

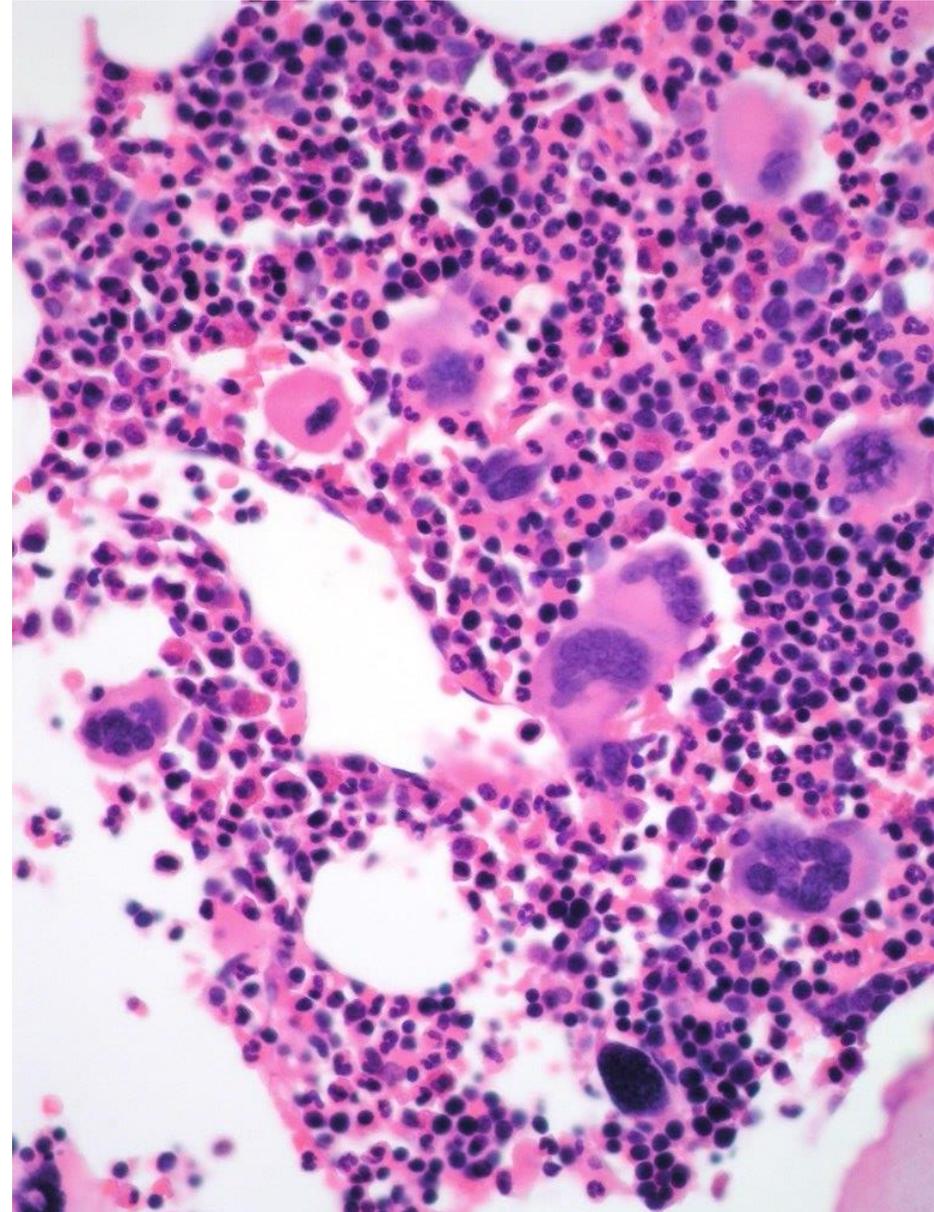


CD61



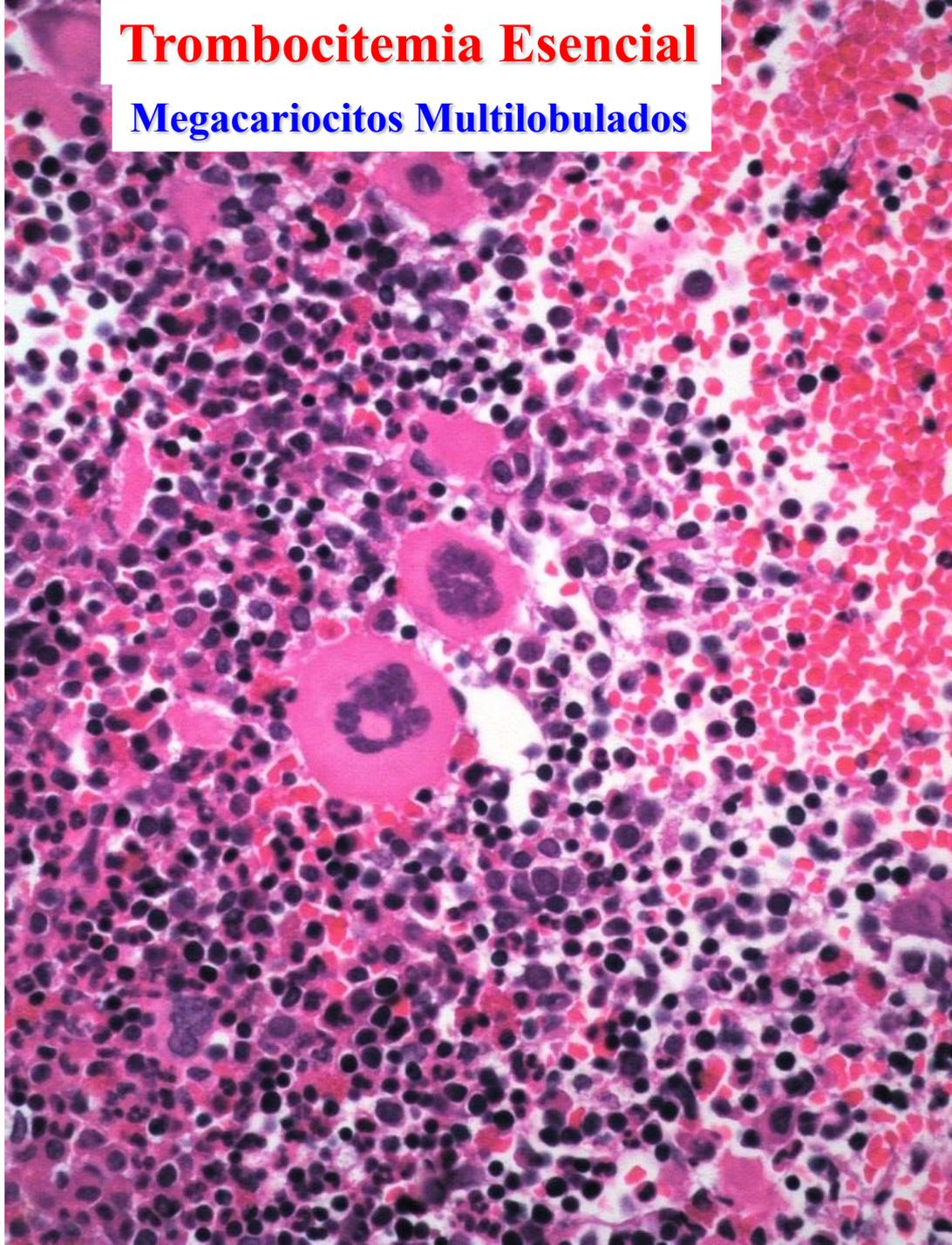
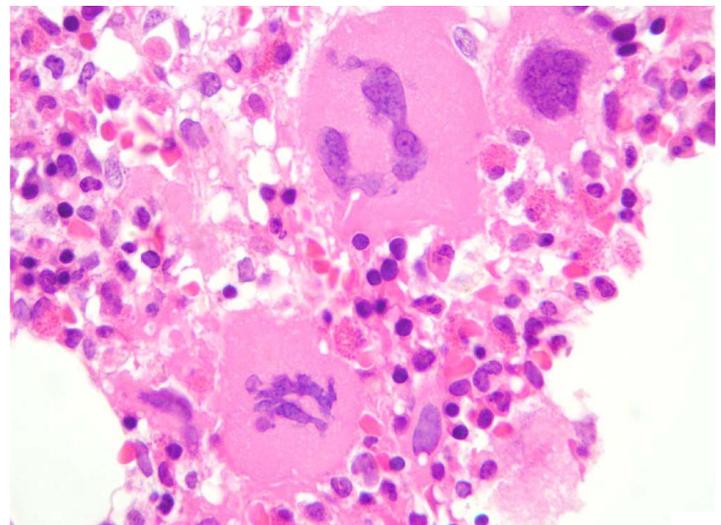
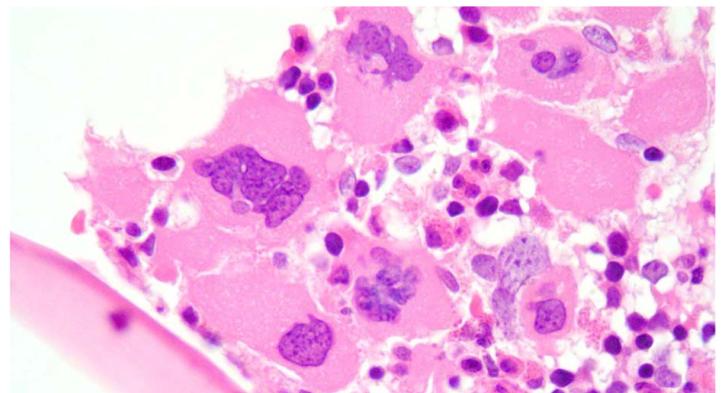
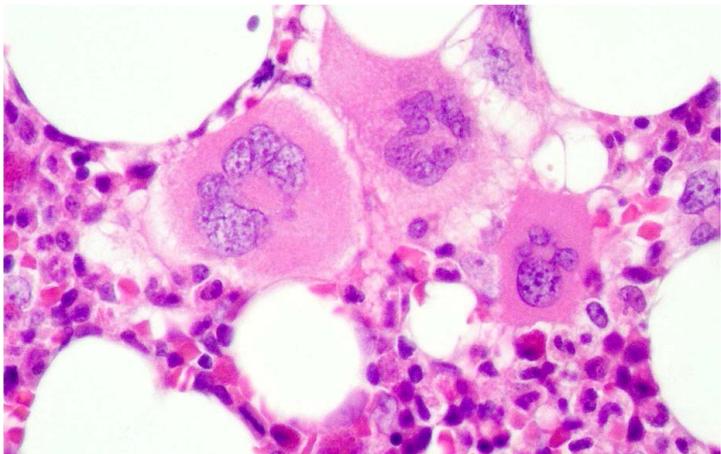
Hiperplasia de Megacariocitos

- **Neoplasias Mieloproliferativas**
- **Neoplasias Linfoproliferativas (Linfoma de Hodgkin)**
- **Sx. Mielodisplásicos**
- **Hemólisis / Metástasis**
- **Trombocitopenias diversas**
- **Hemorragias / Traumatismos**
- **Infecciones (SIDA)**



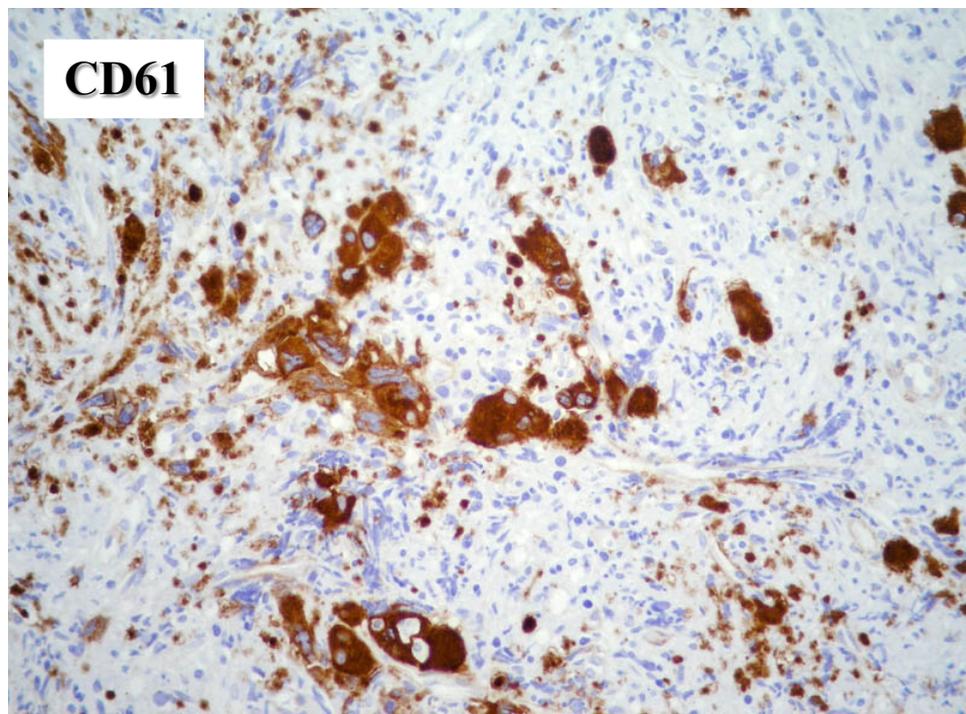
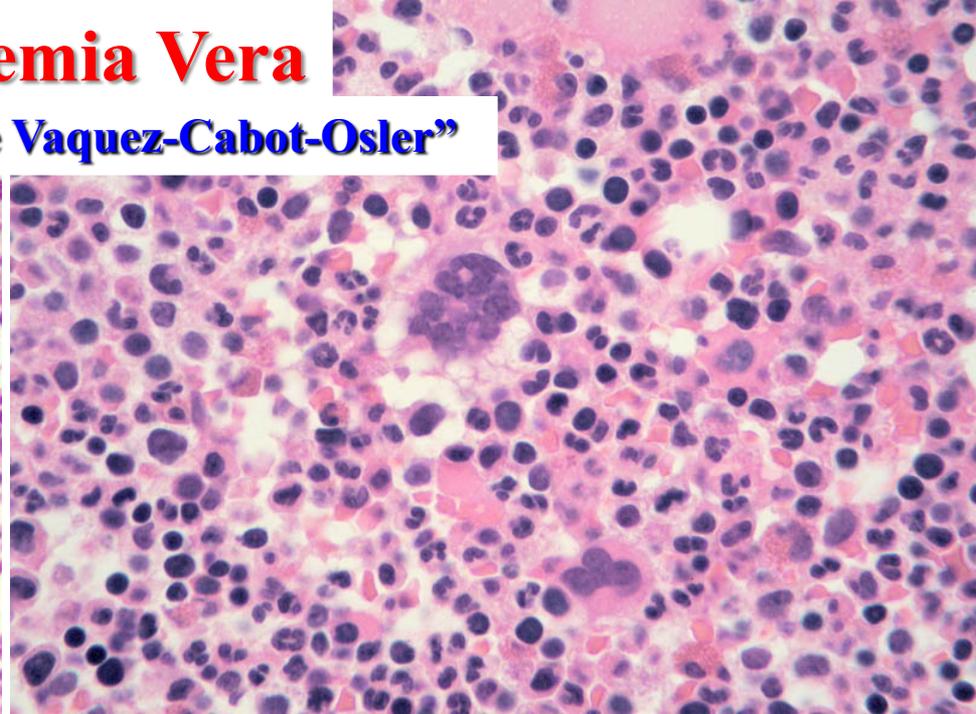
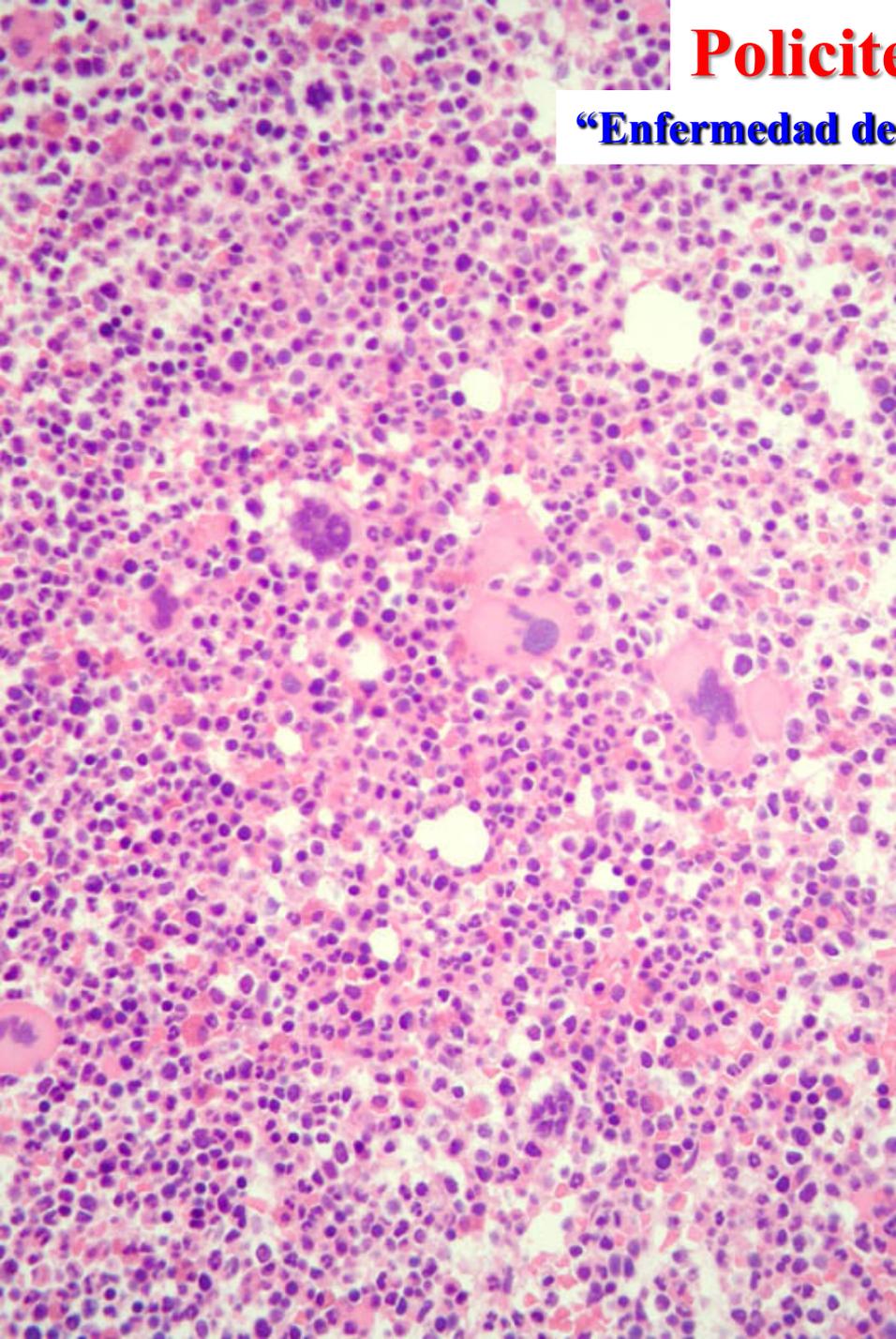
Trombocitemia Esencial

Megacariocitos Multilobulados



Policitemia Vera

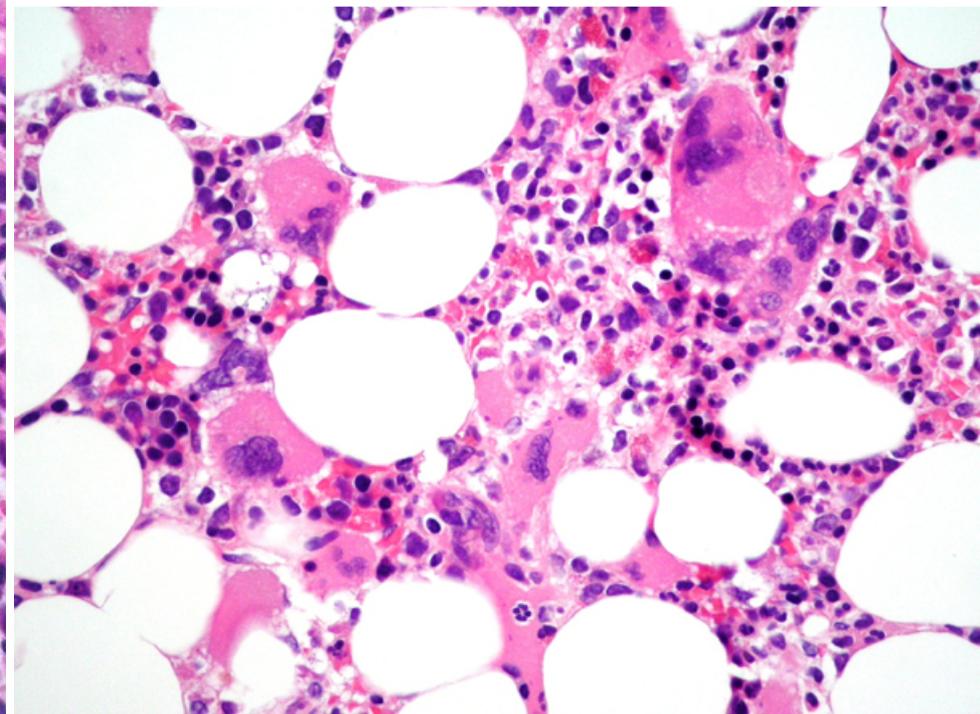
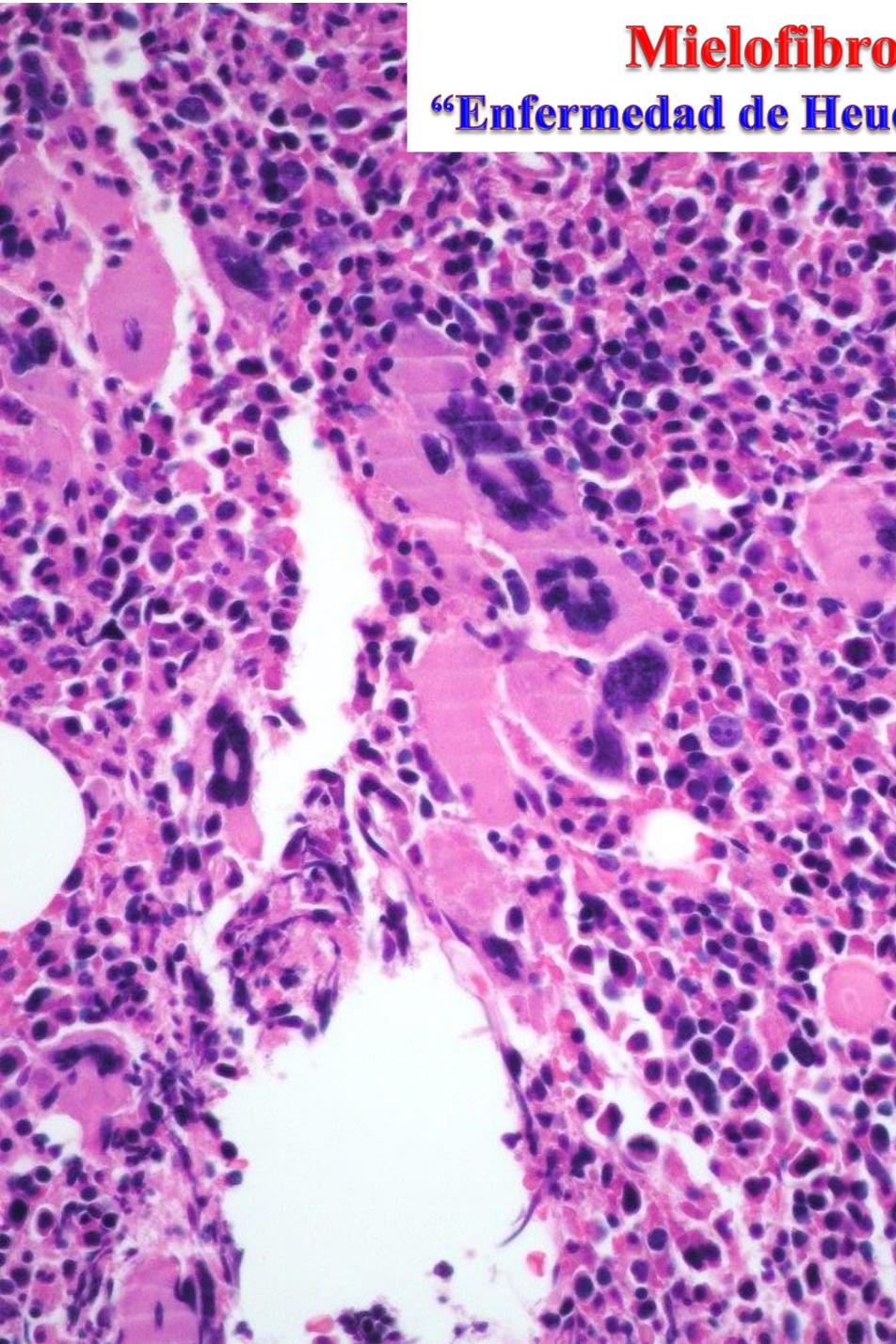
“Enfermedad de Vaquez-Cabot-Osler”



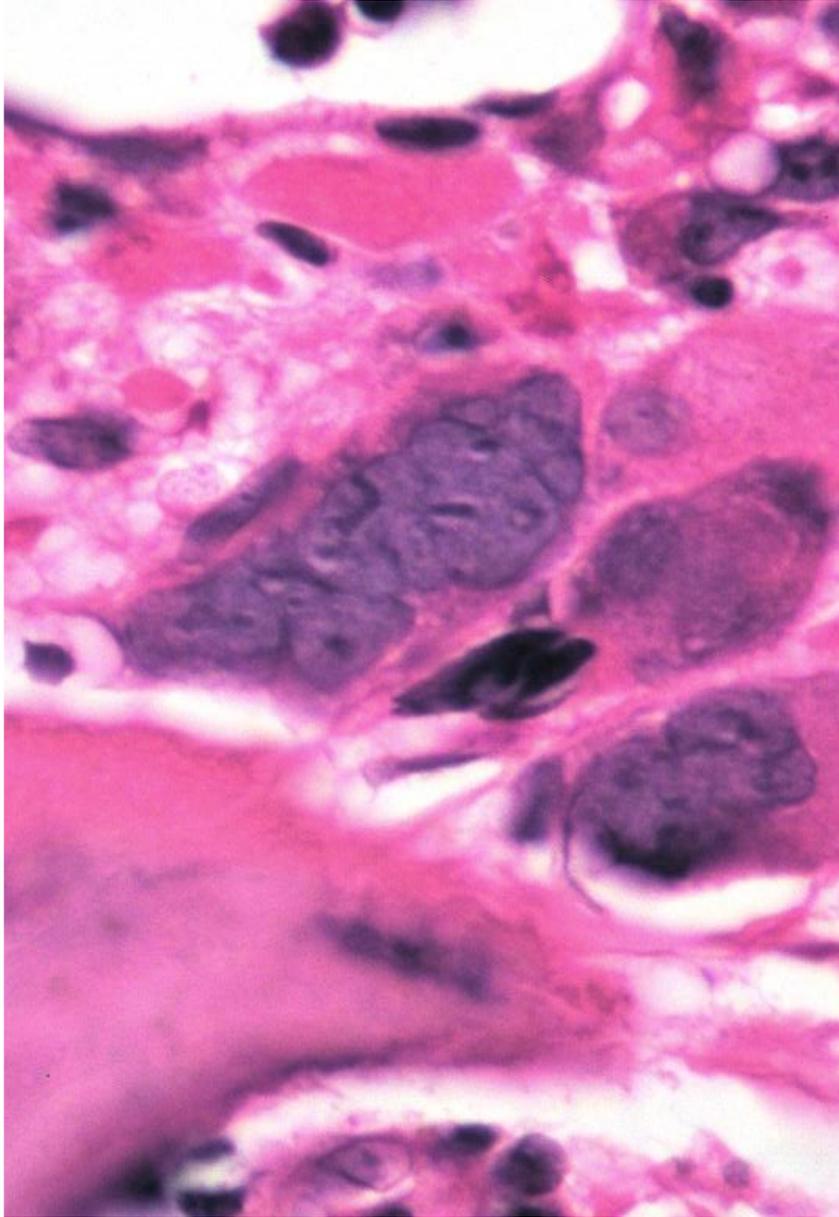
CD61

Mielofibrosis Primaria

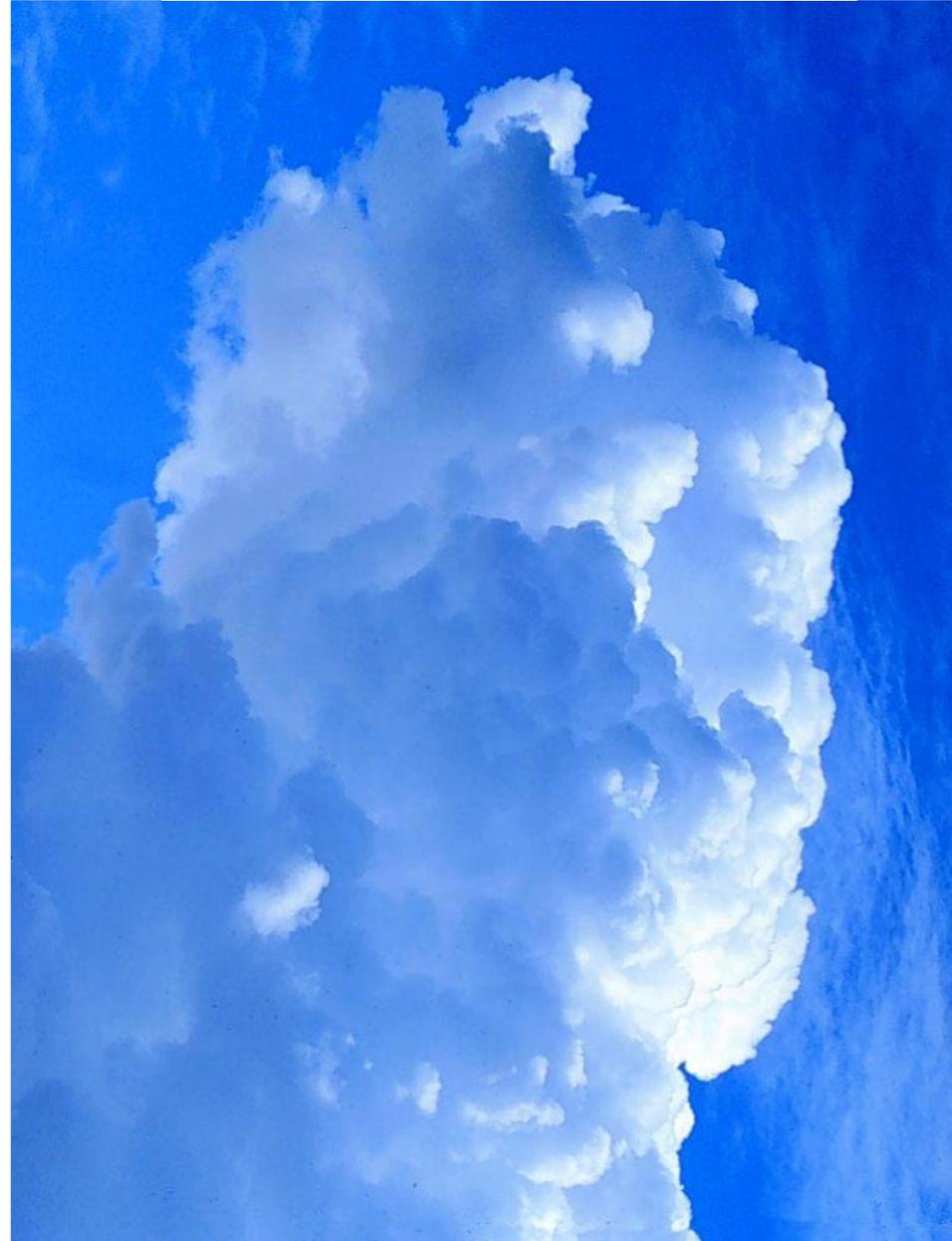
“Enfermedad de Heuck-Askanazy-Assmann”

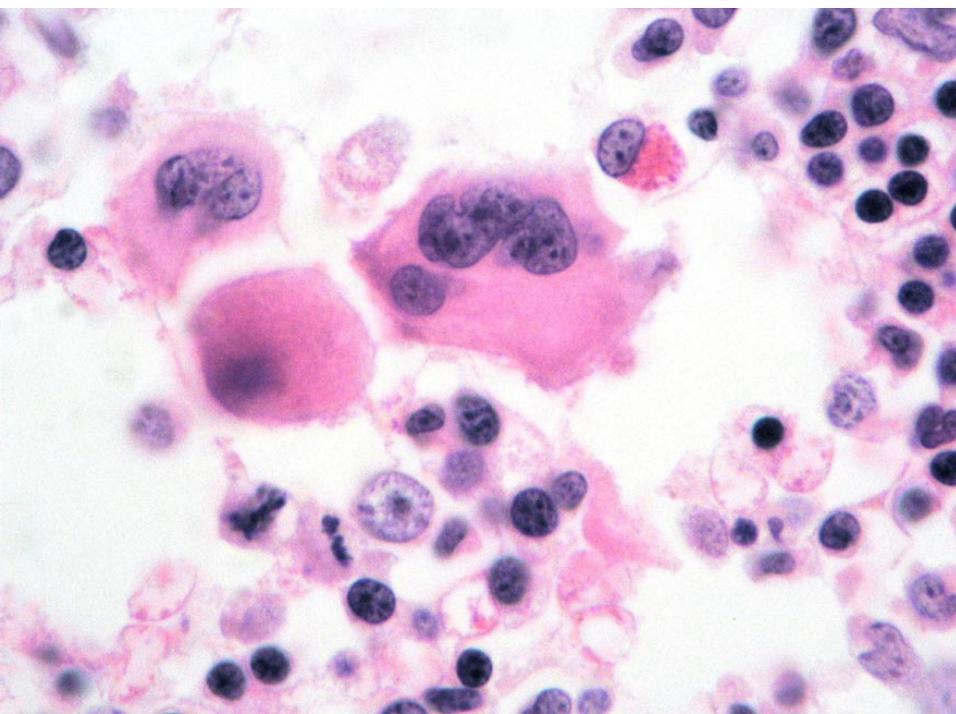
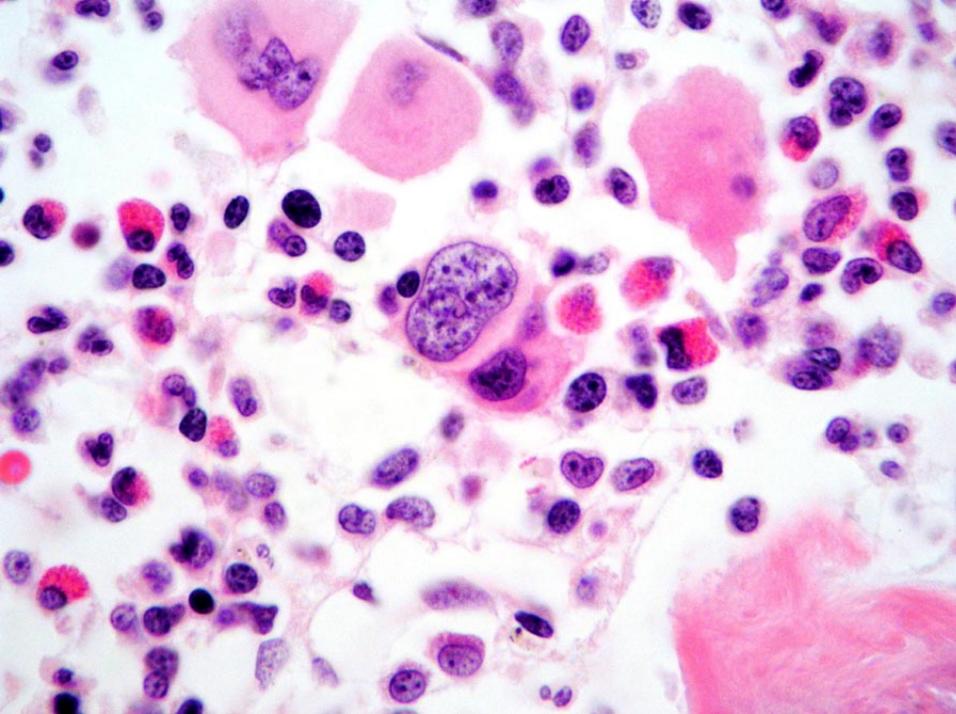


Mielofibrosis Primaria



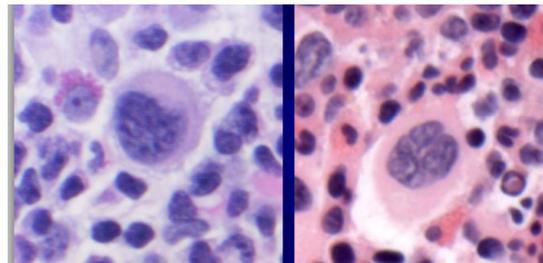
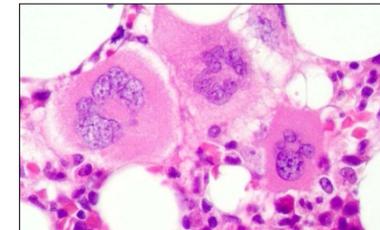
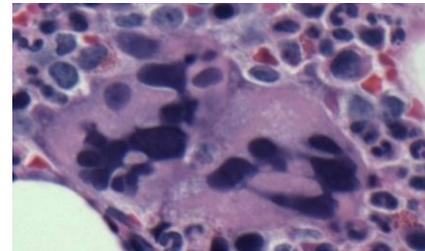
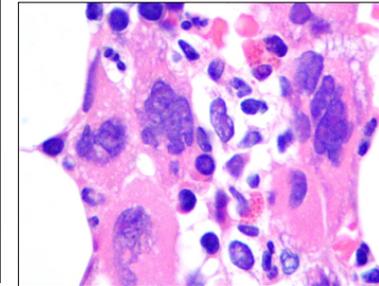
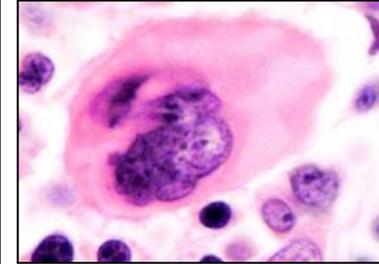
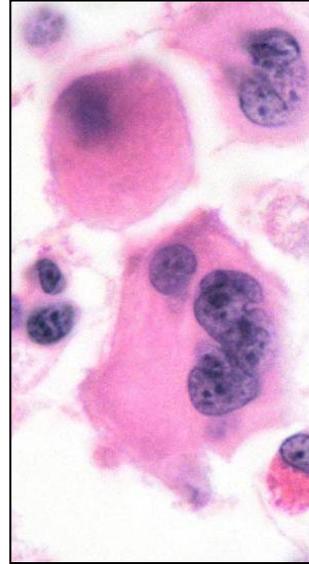
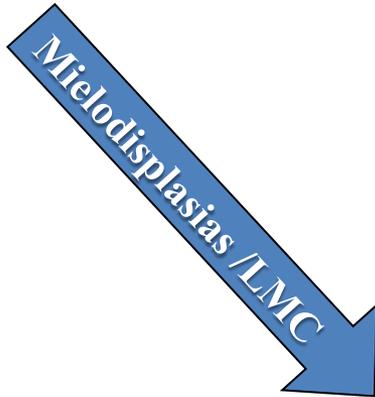
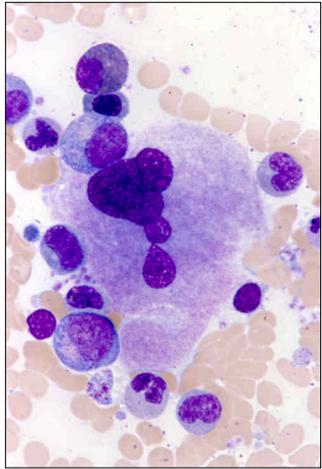
Megacariocitos en nube





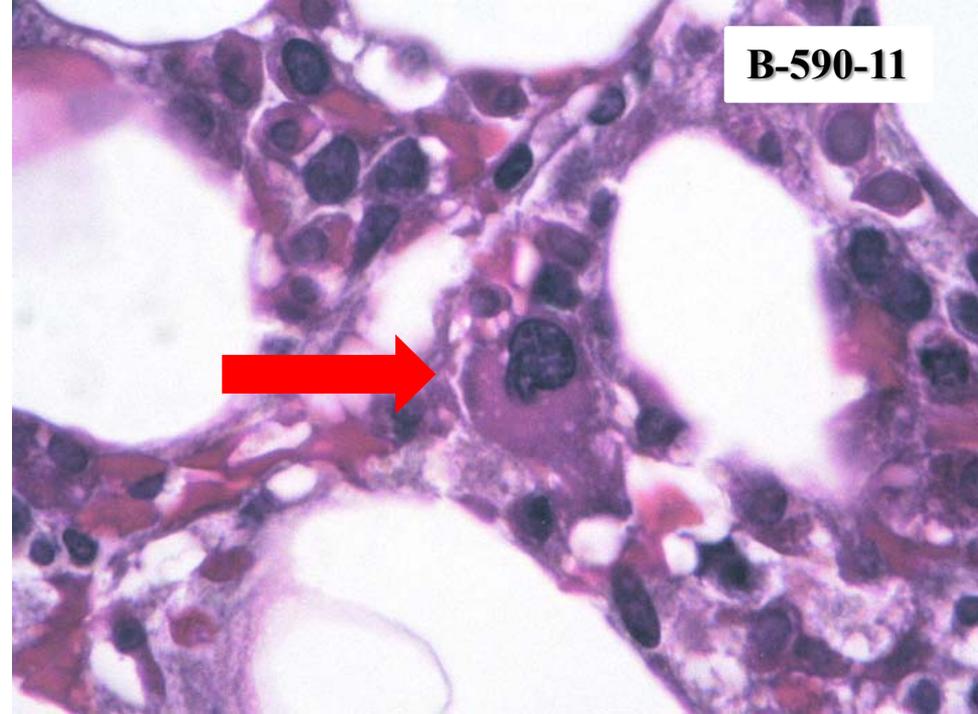
Morfología del Megacariocito en Neoplasias mieloproliferativas

Megacariocito Normal

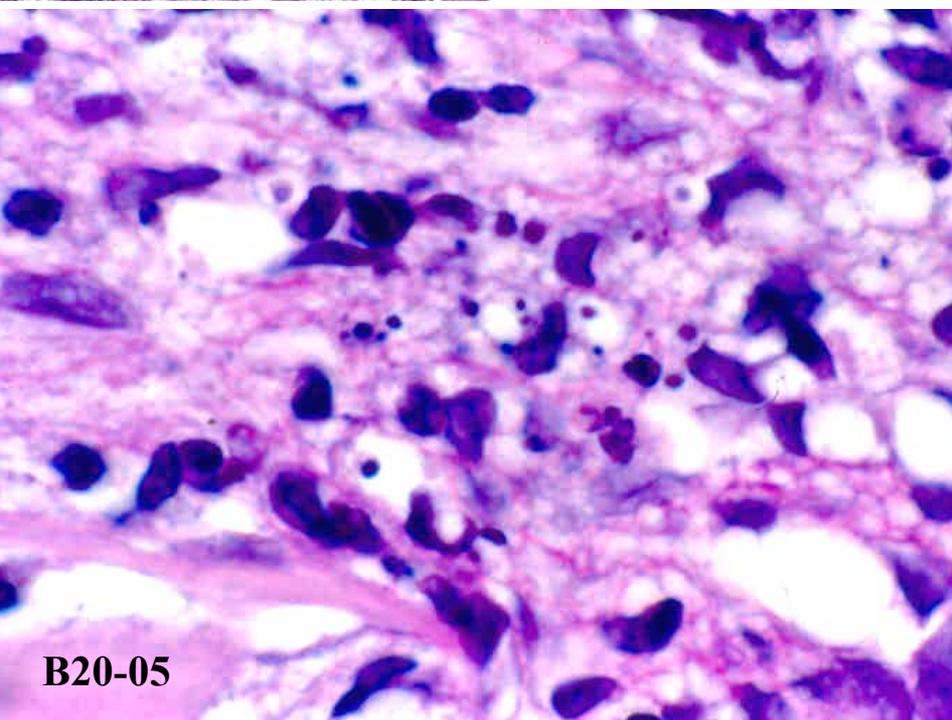
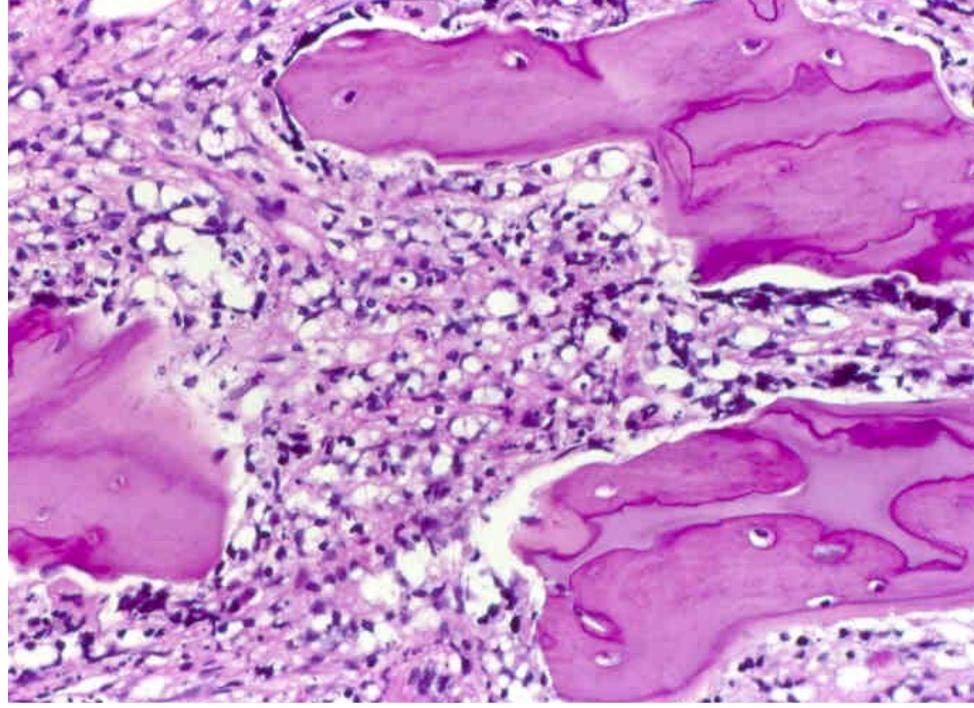
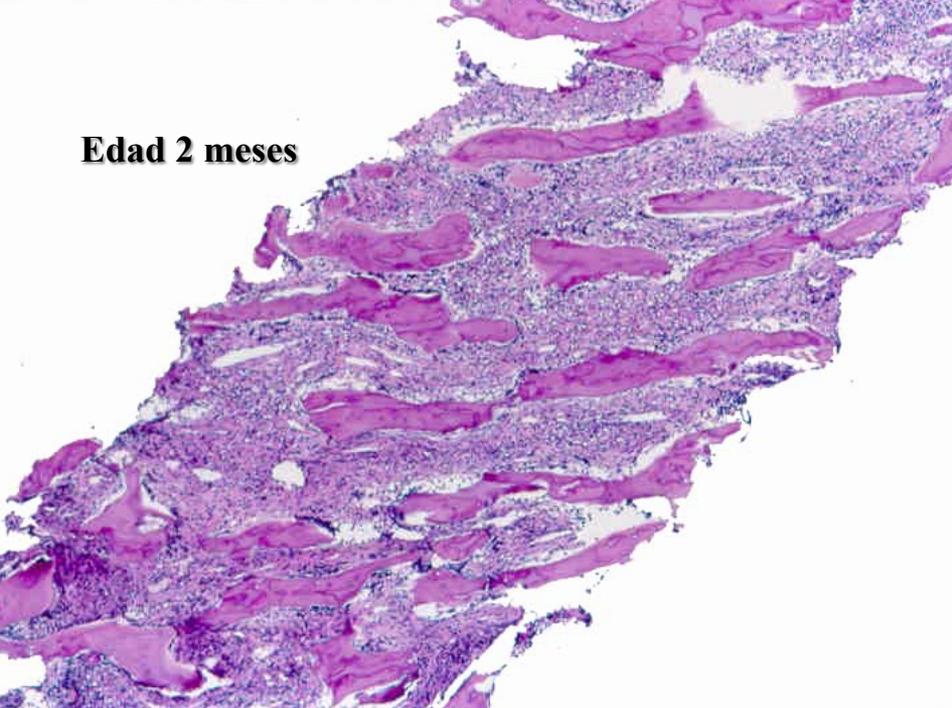


Mielodisplasia q5 del
Sx van den Berghe

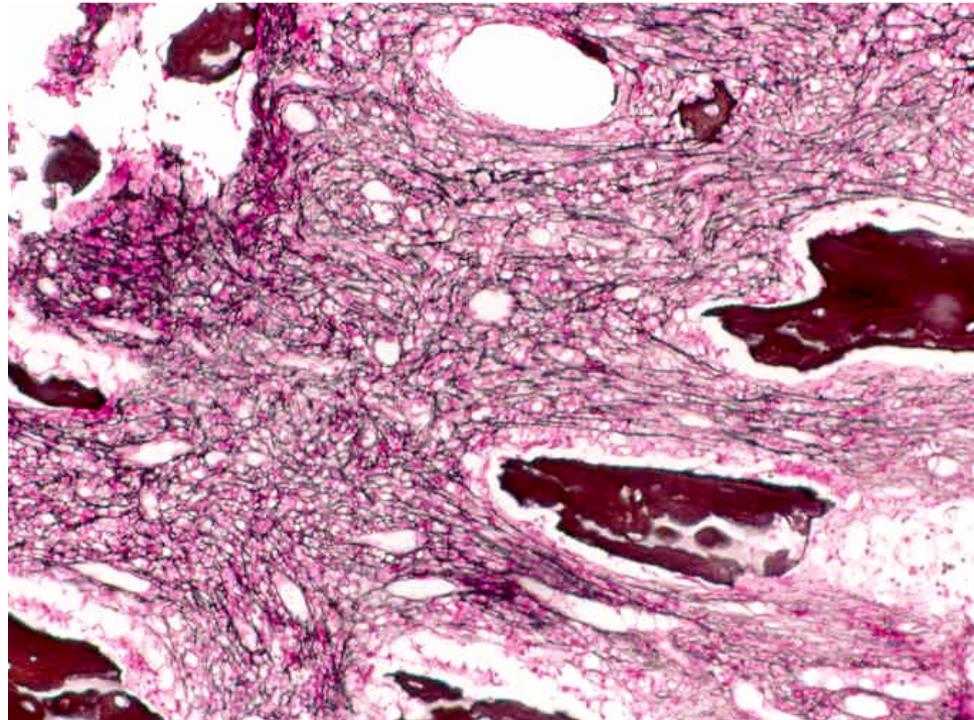
B-590-11



Edad 2 meses



B20-05

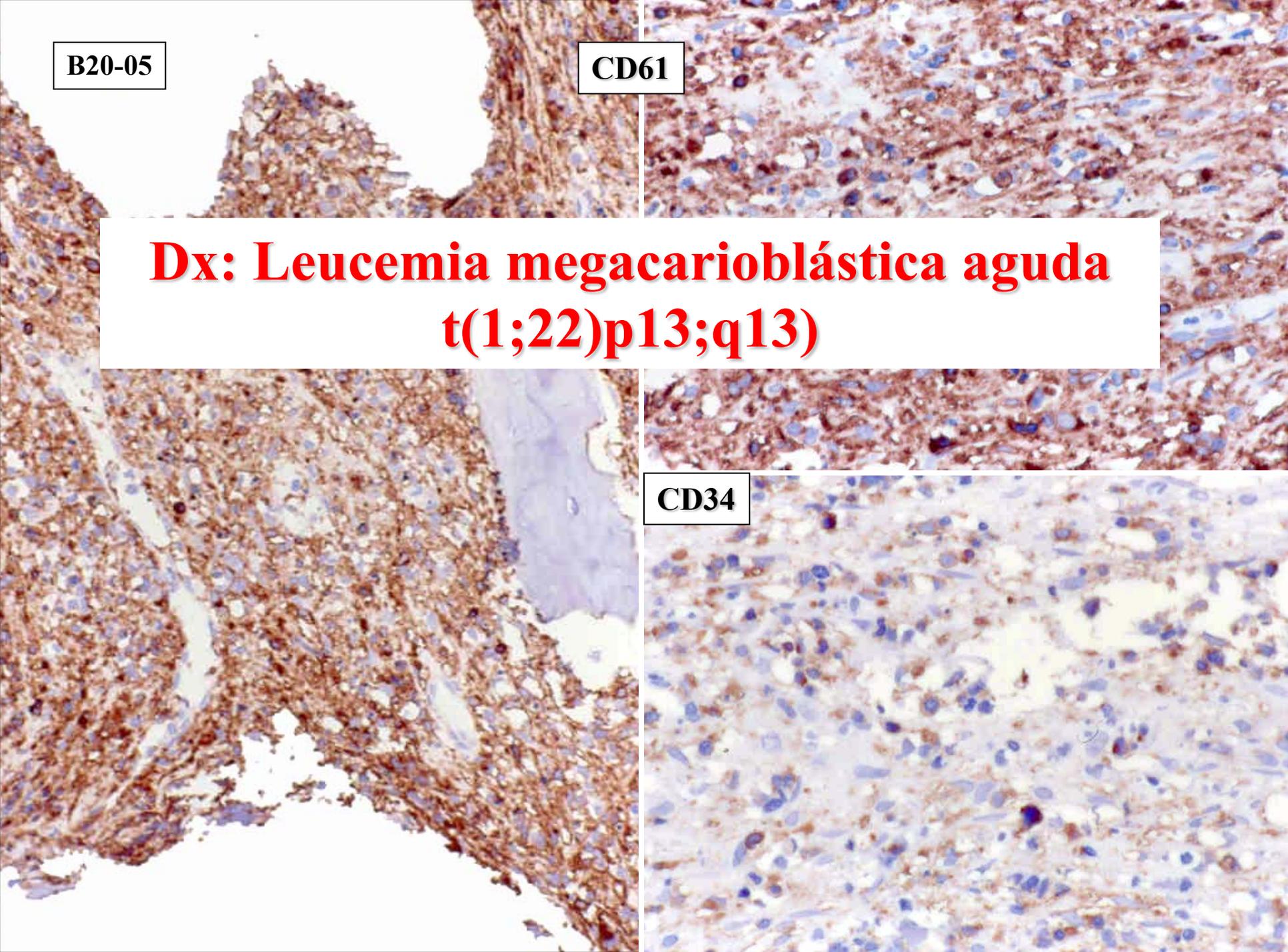


B20-05

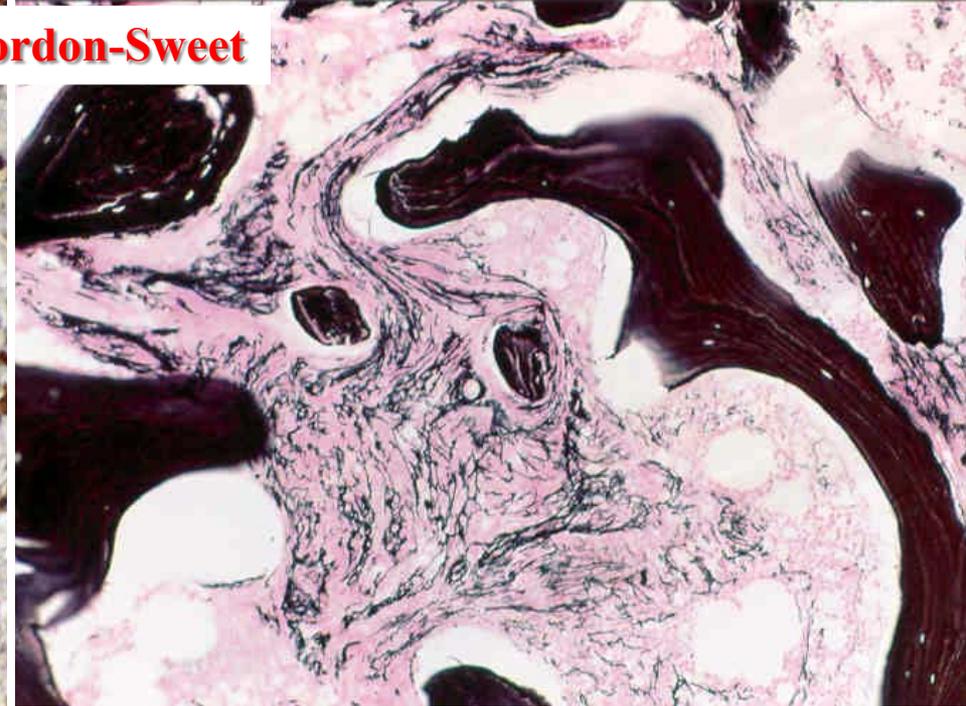
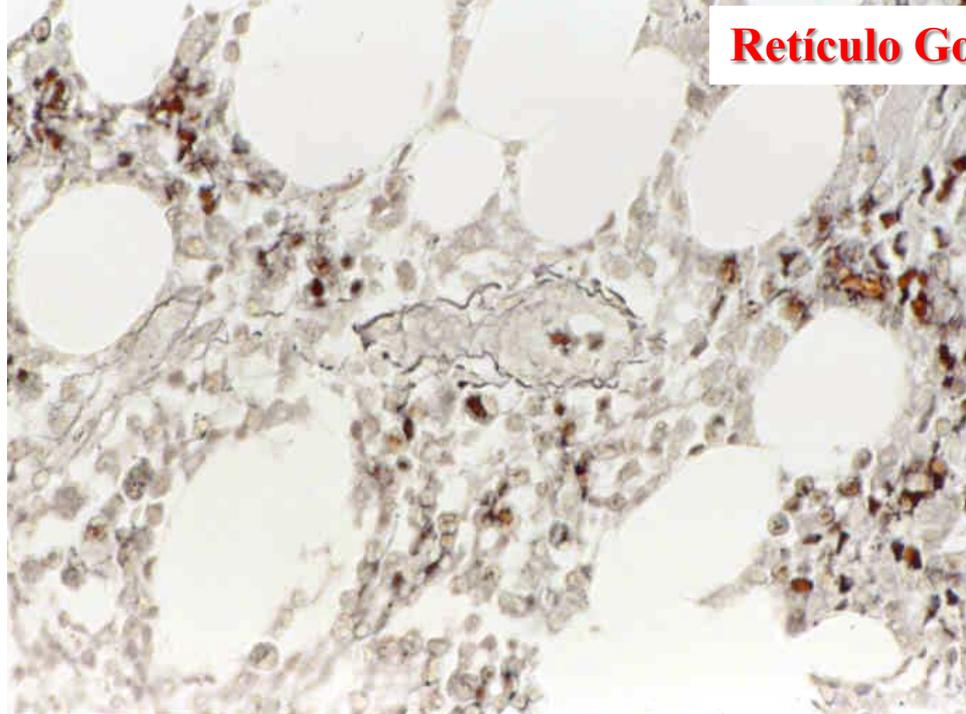
CD61

**Dx: Leucemia megacarioblástica aguda
t(1;22)p13;q13)**

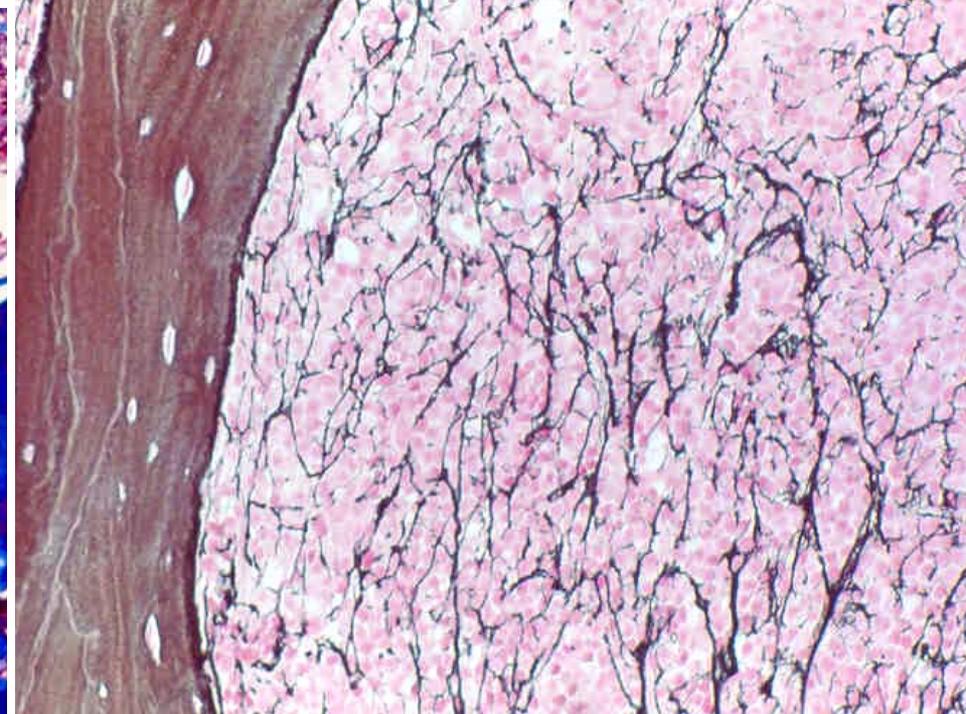
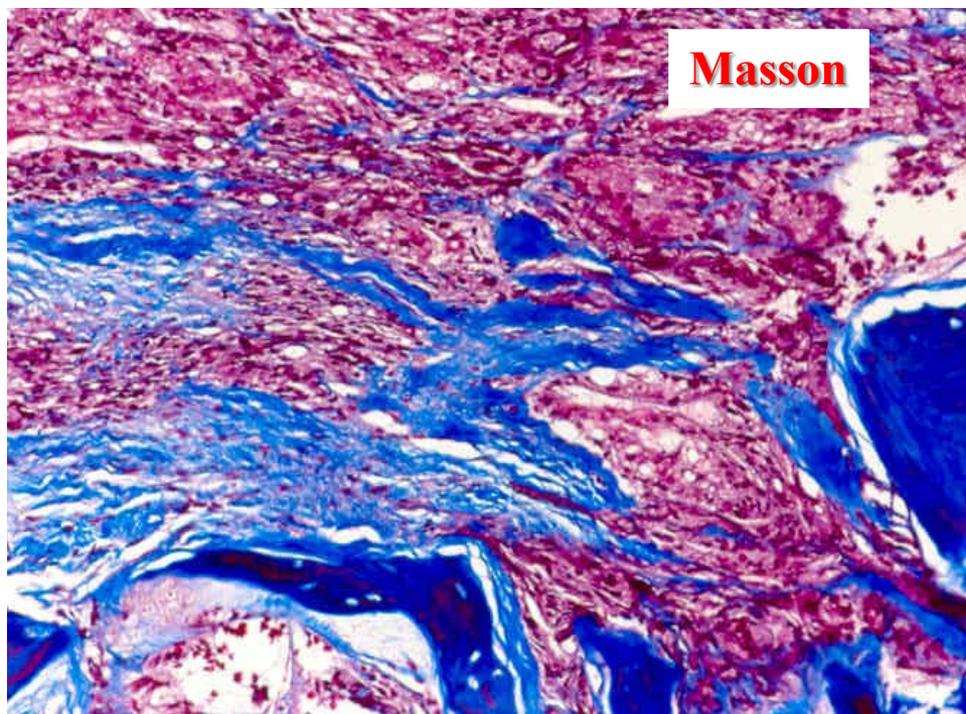
CD34



Reticulo Gordon-Sweet



Masson



Fibrosis de Médula Ósea

Alt. Hematológicas

- **Sx. MP**
- **Sx Mielodisplásicos**
- **Leucemias**
- **Alt Cél. Plasmáticas**
- **Linfomas**

Metástasis

- **Mama / Próstata**
- **Pulmón**

Reactivas /otras

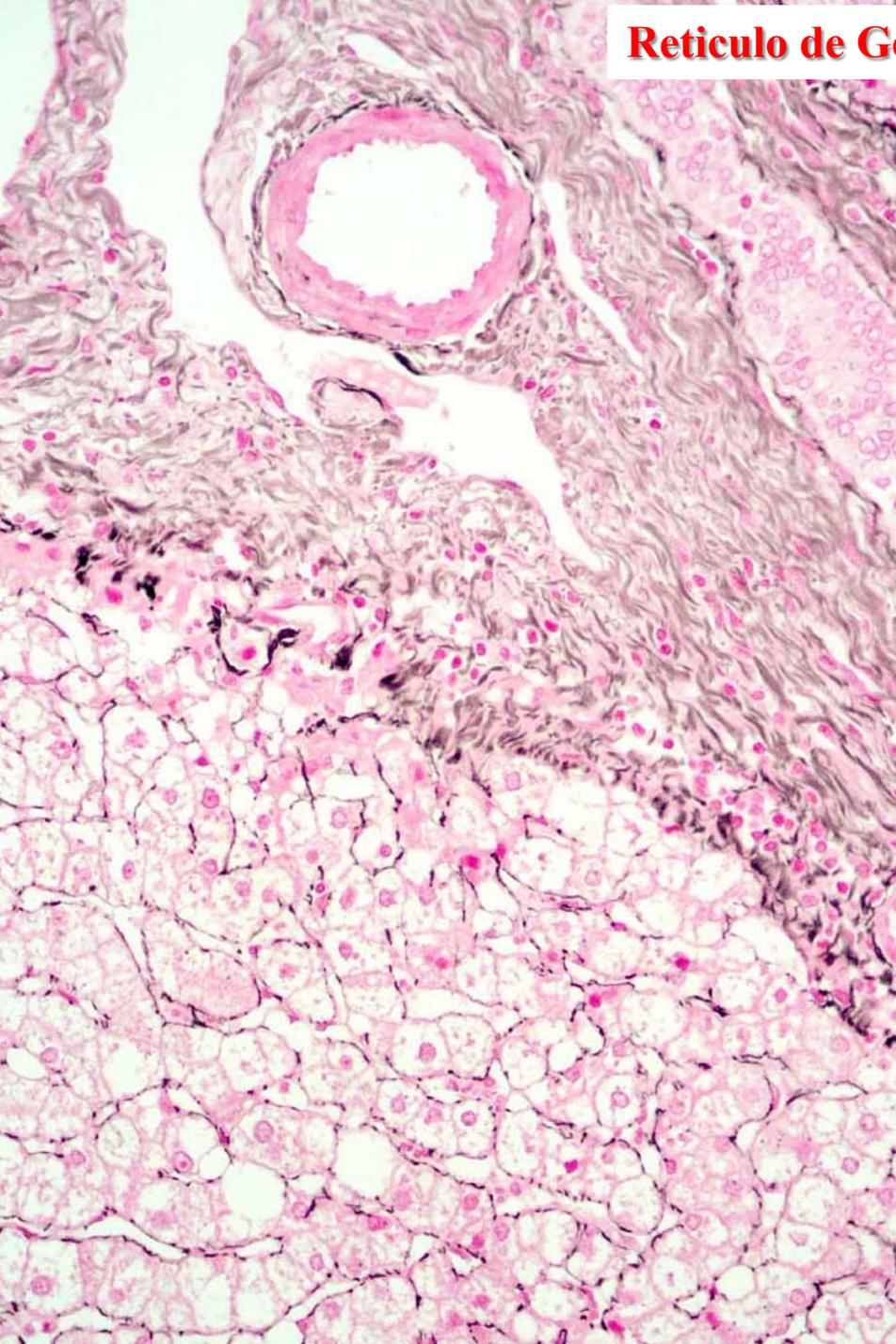
- **Toxicas**
- **Infeciosas**
- **Osteopatías**
- **Enf. Paget**
- **Hiperparatiroidismo**

Colágena / Fibras Reticulares

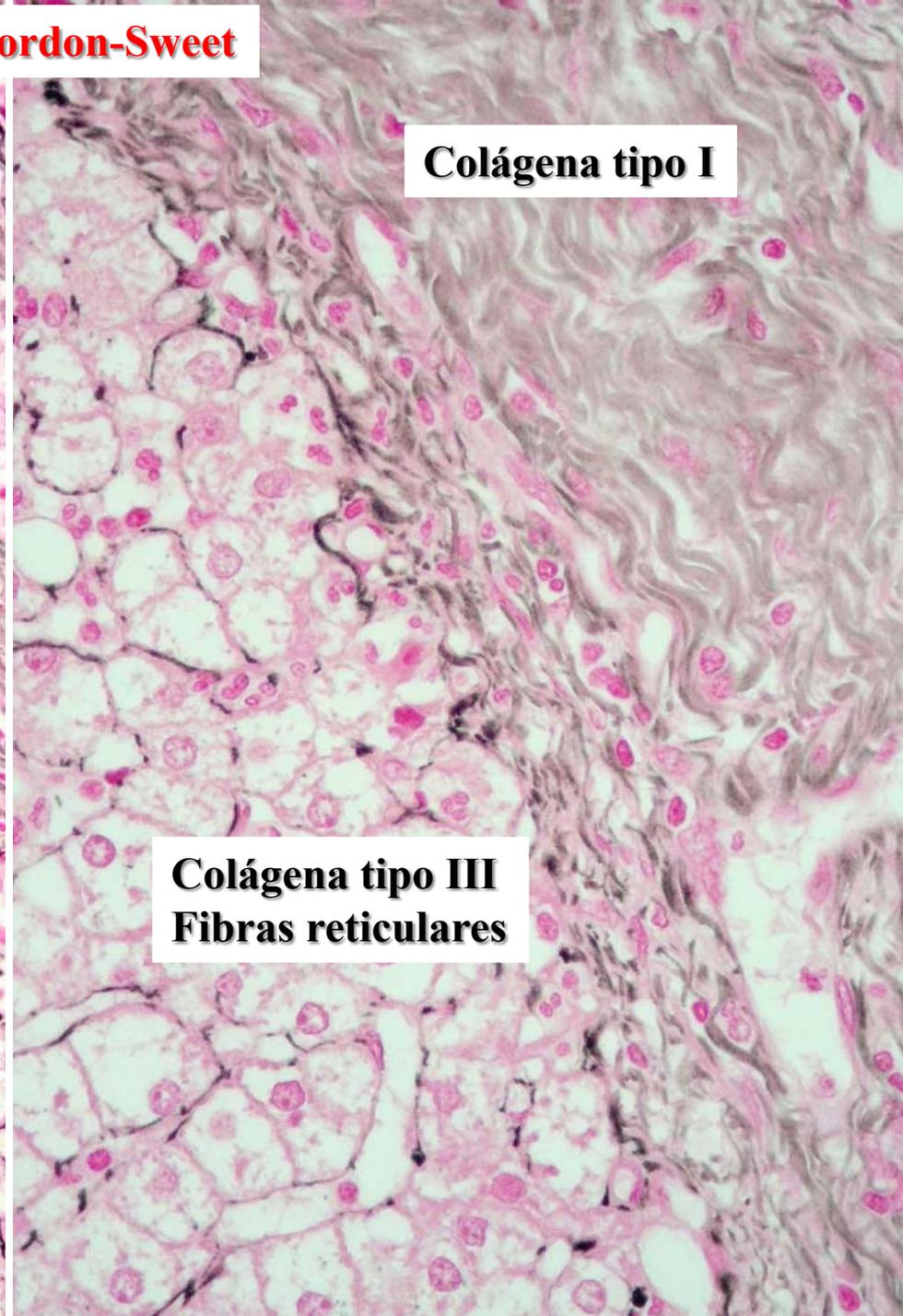
Colágena Tipo I \longrightarrow (2) α 1 y (1) α 2 1% carbohidratos
(Colágena Madura) (Masson positivos)

Colágena Tipo III (Fibras reticulares) \longrightarrow (3) α 1 10% carbohidratos
Hexosas: Impedimento estérico

Reticulo de Gordon-Sweet



Colágena tipo I

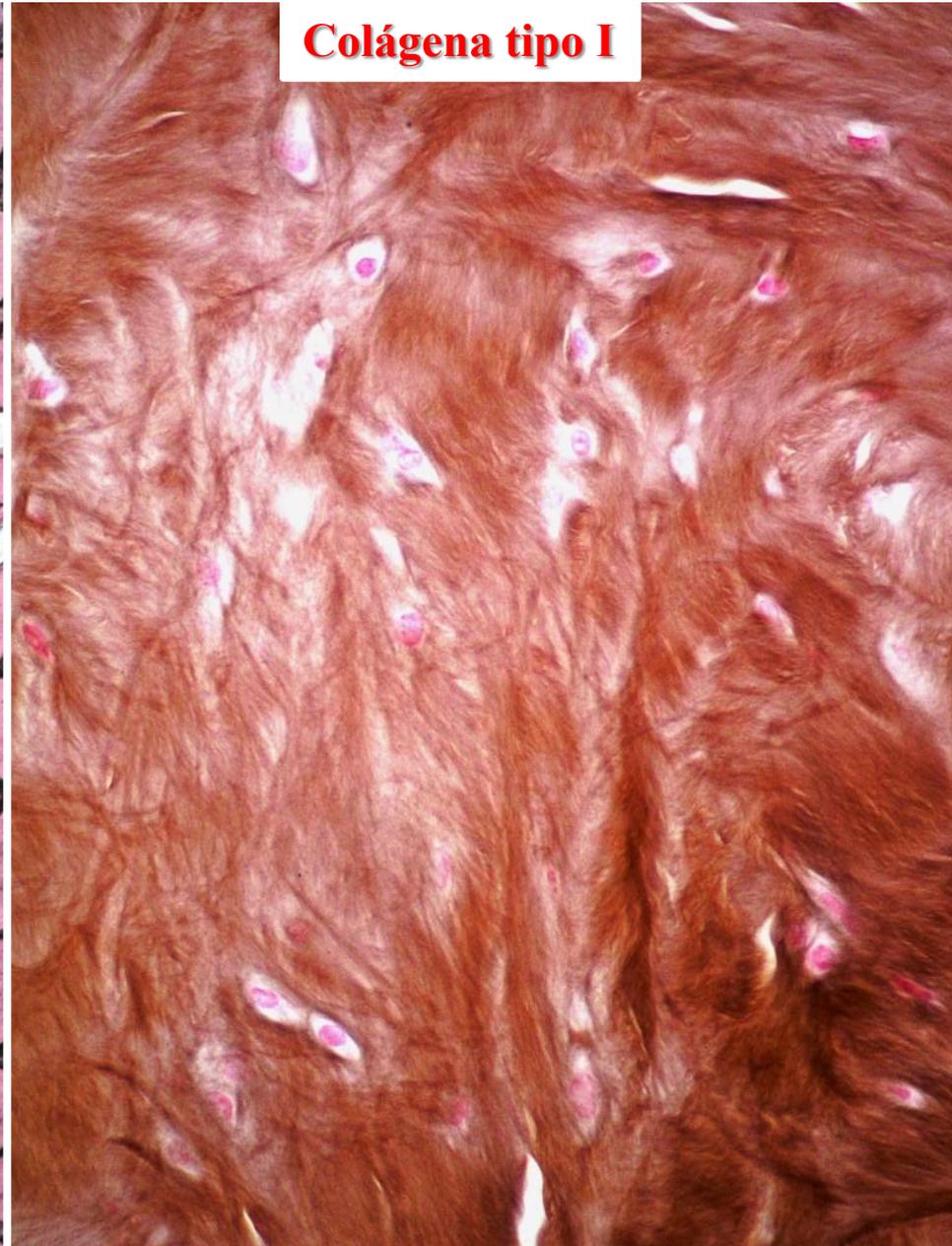


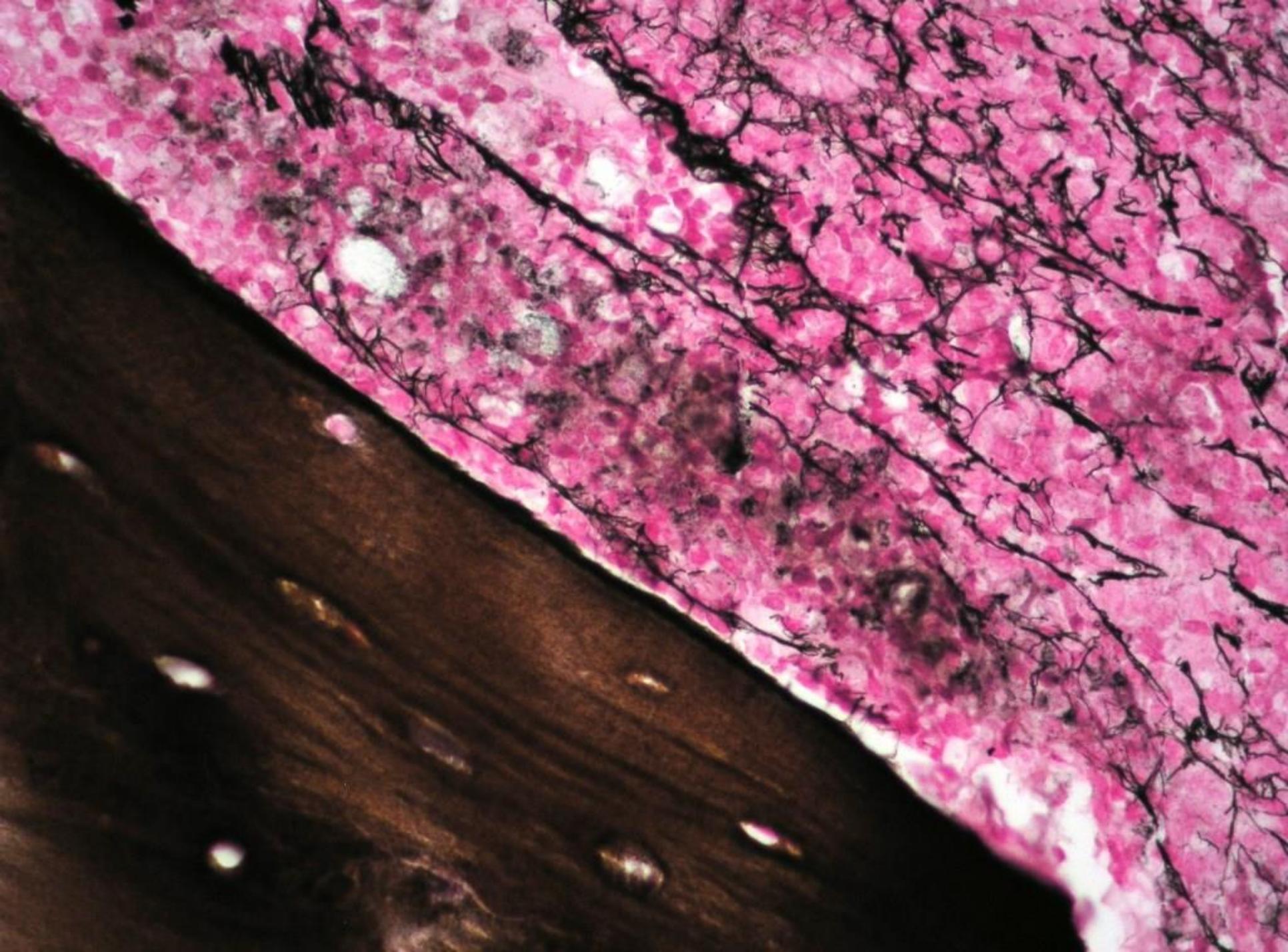
**Colágena tipo III
Fibras reticulares**

Colágena tipo III
Fibras reticulares

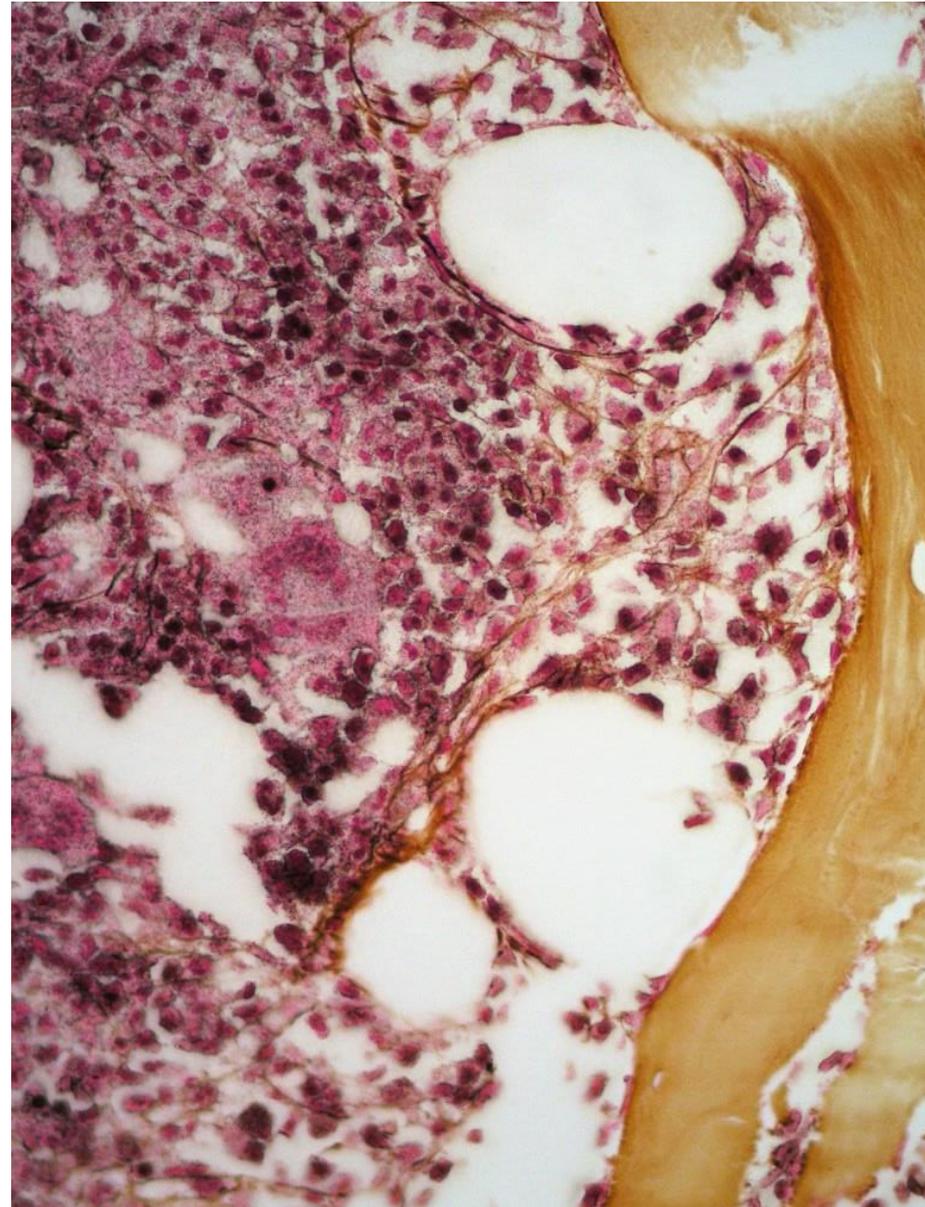


Colágena tipo I



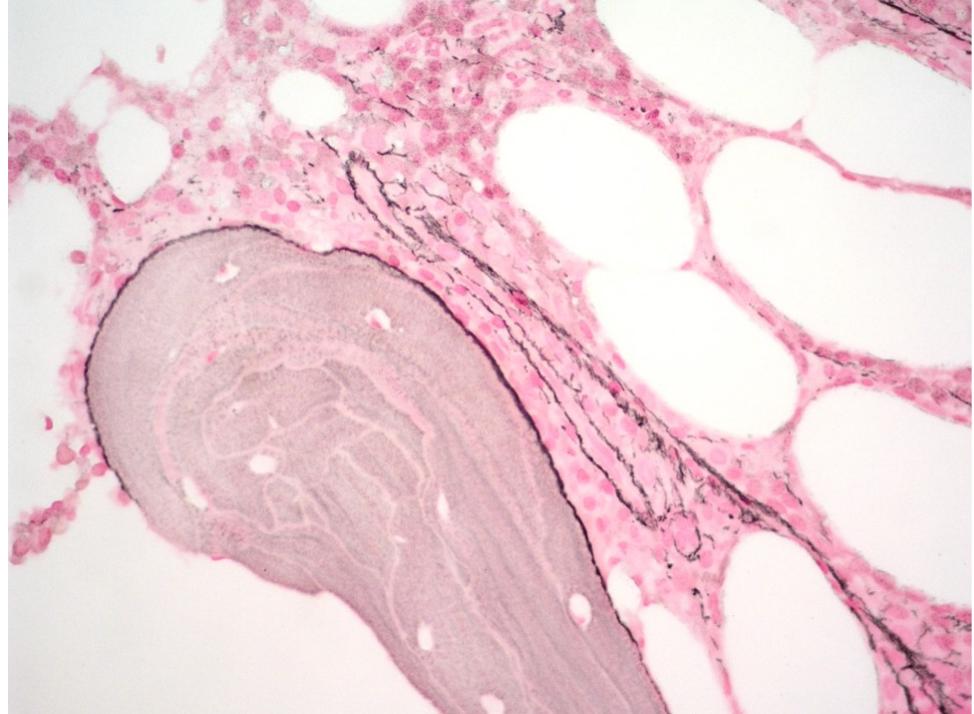
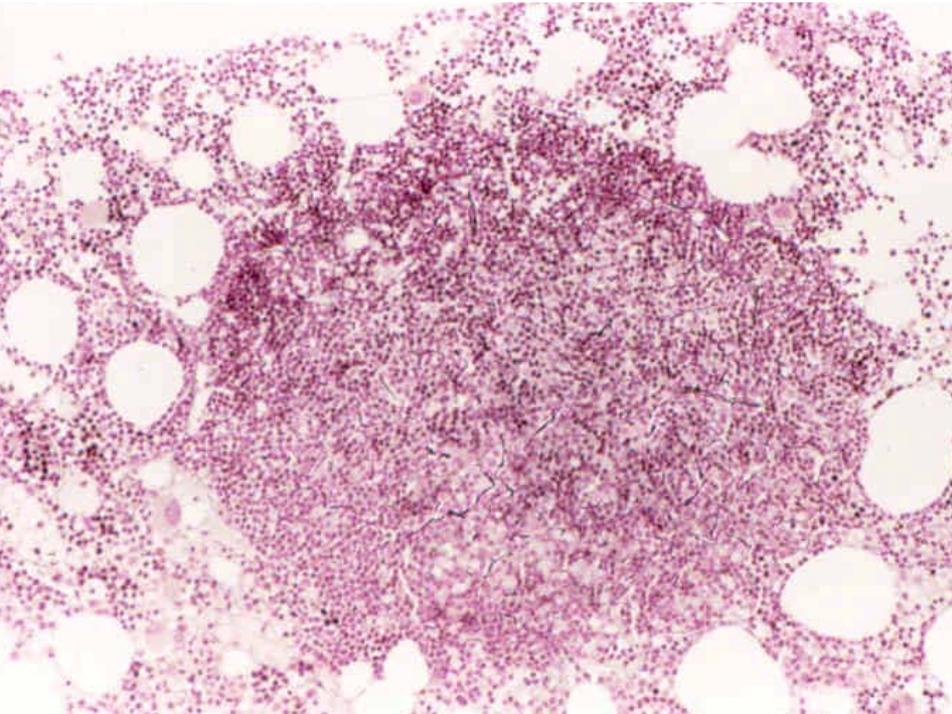
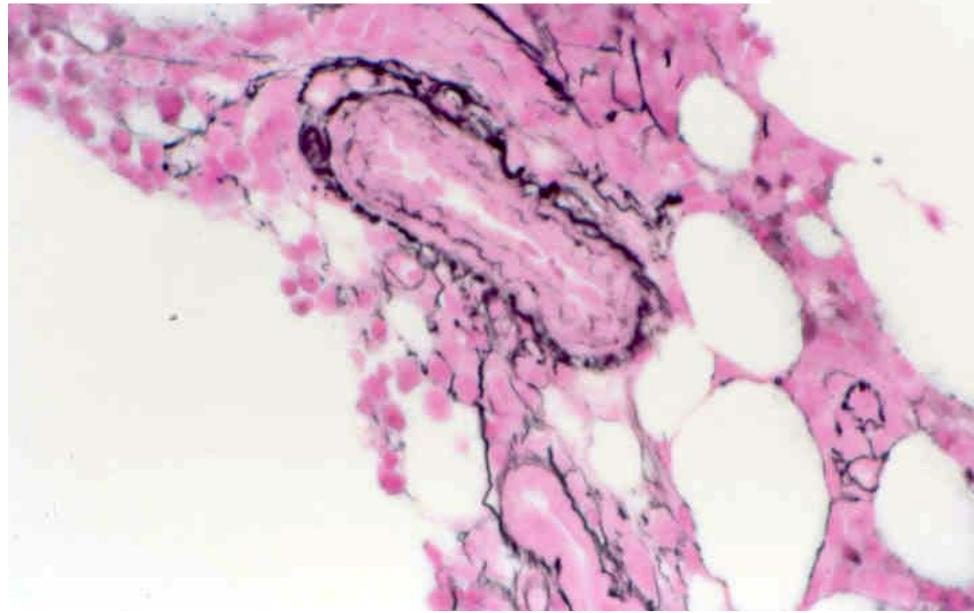
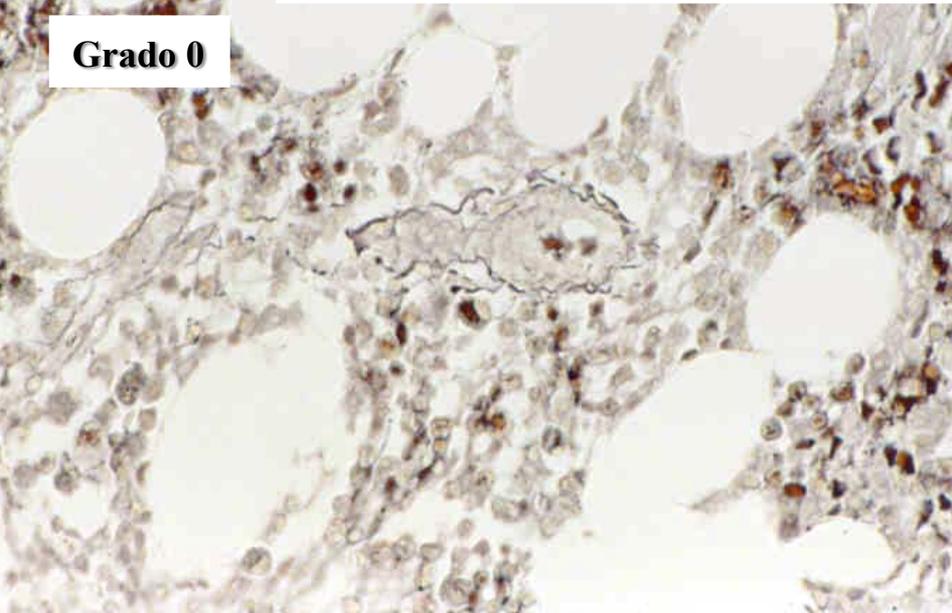


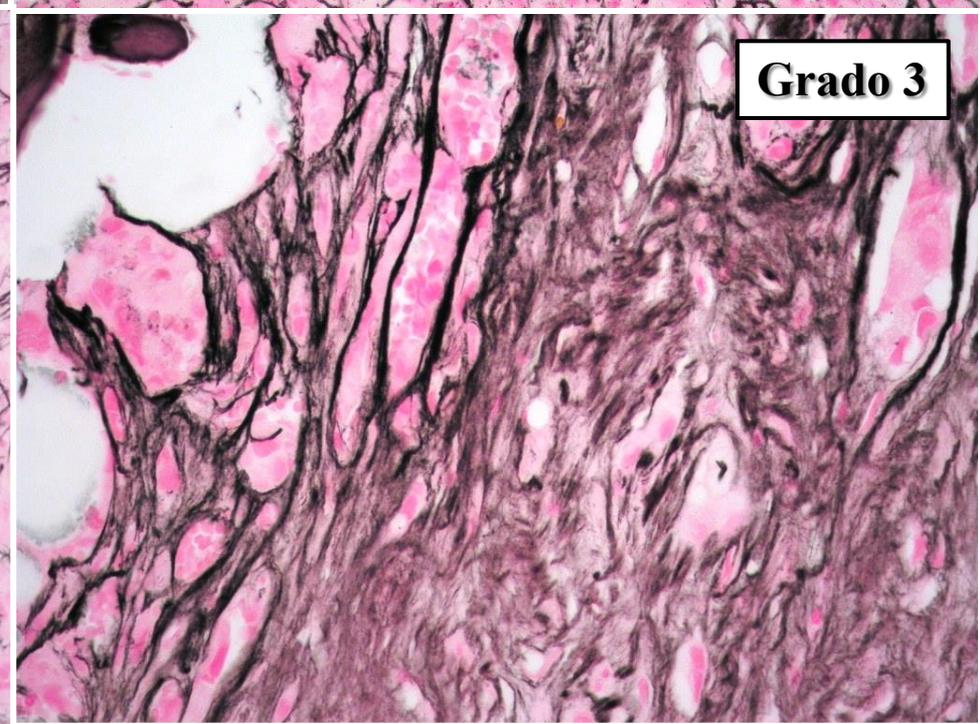
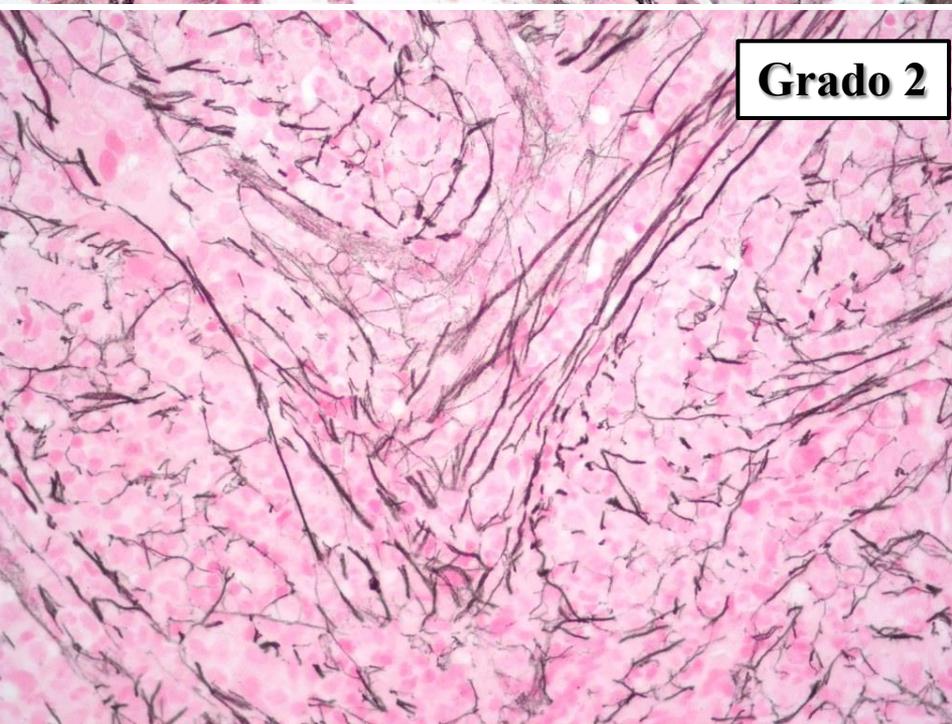
Gömöri

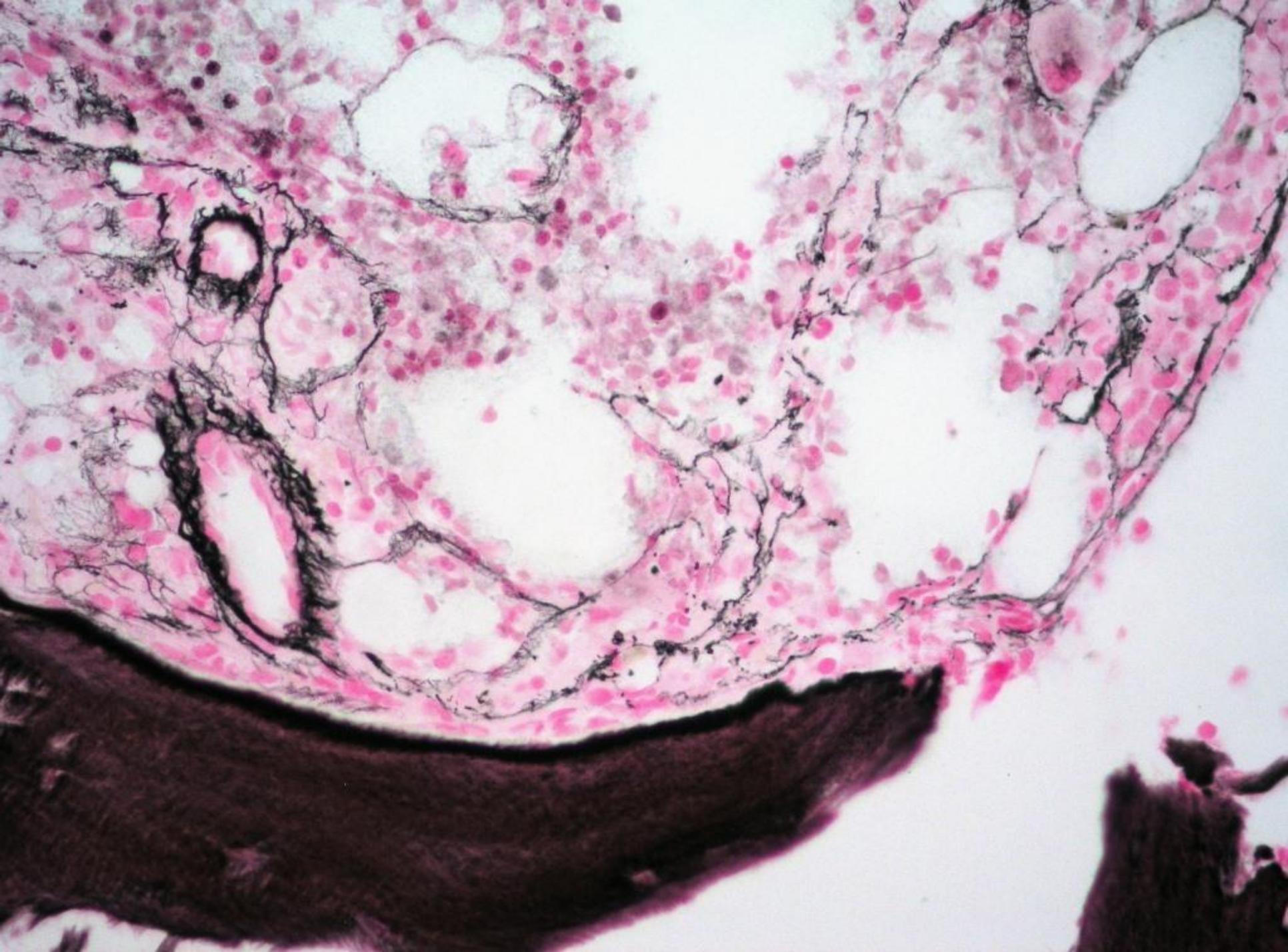


Sitios normales (perivascular, paratrabecular y nódulos linfoides)

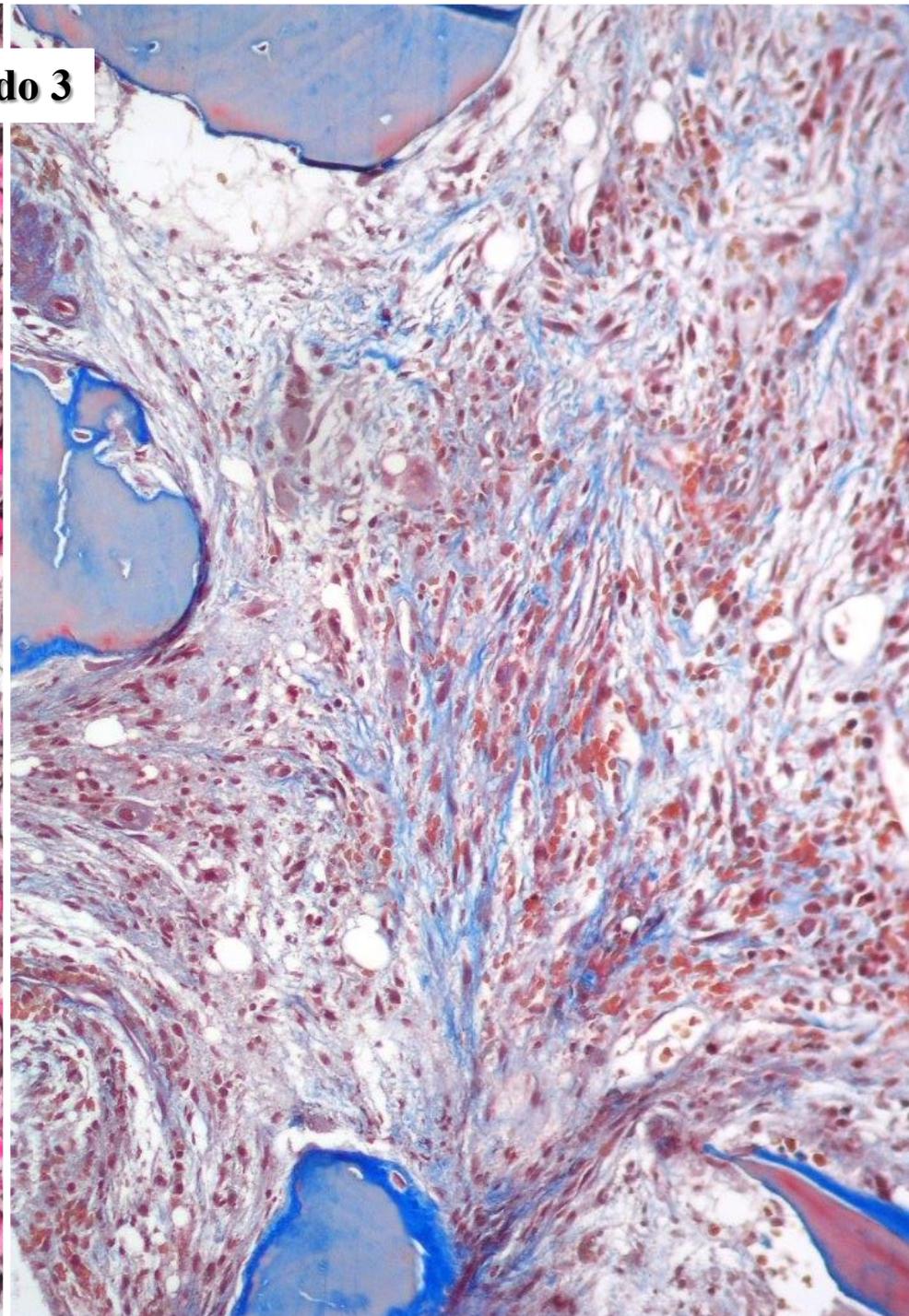
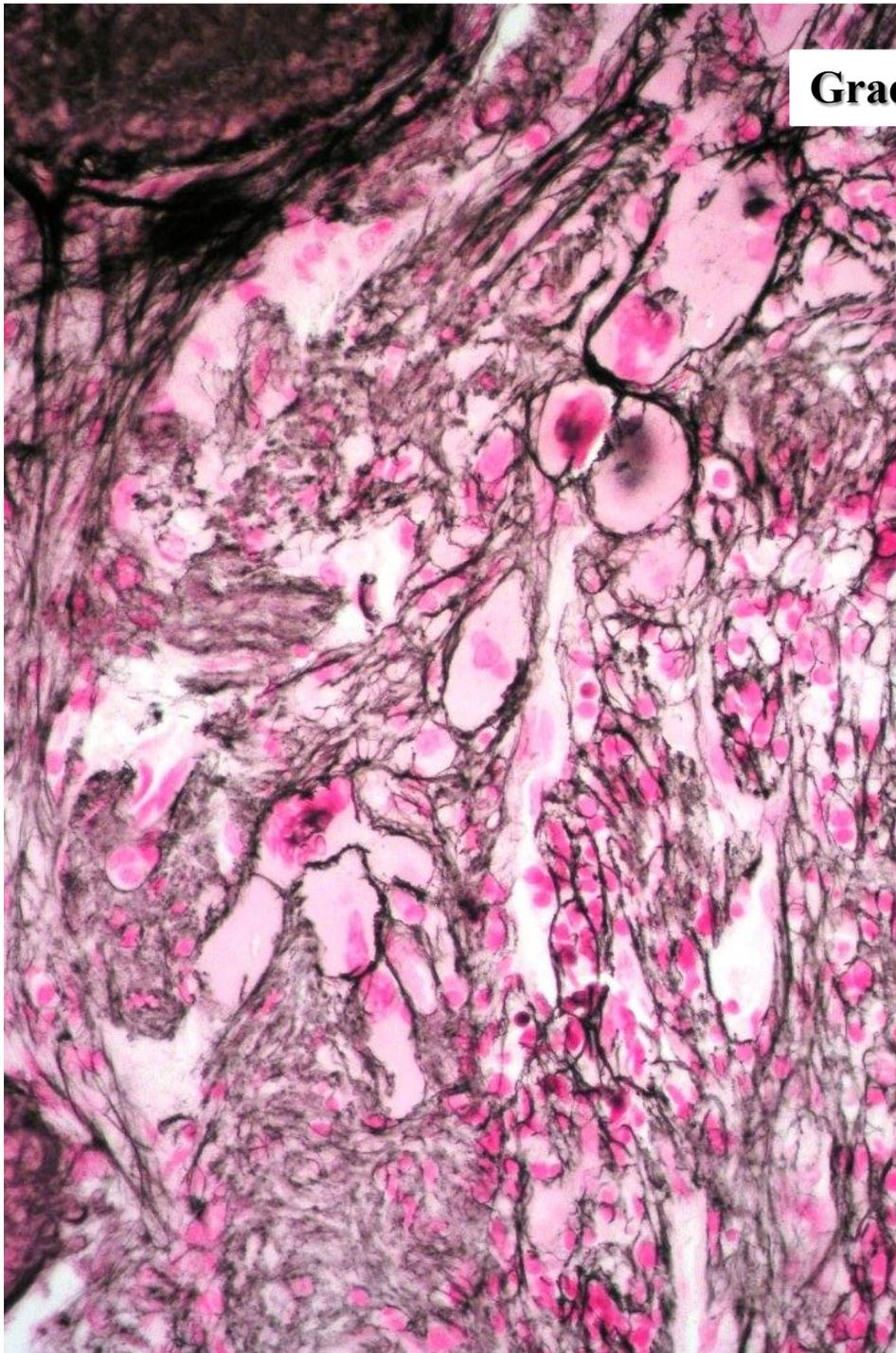
Grado 0





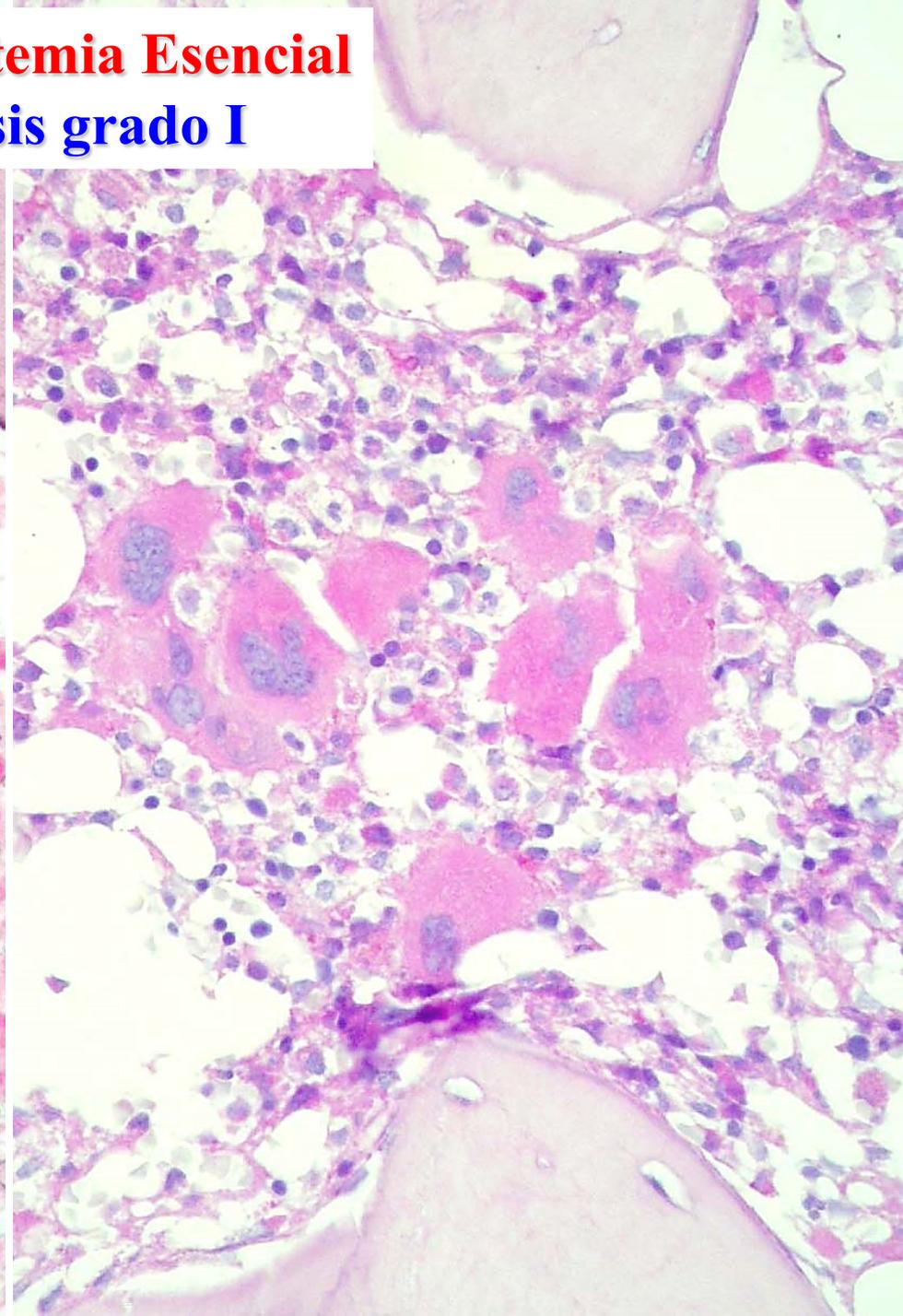


Grado 3

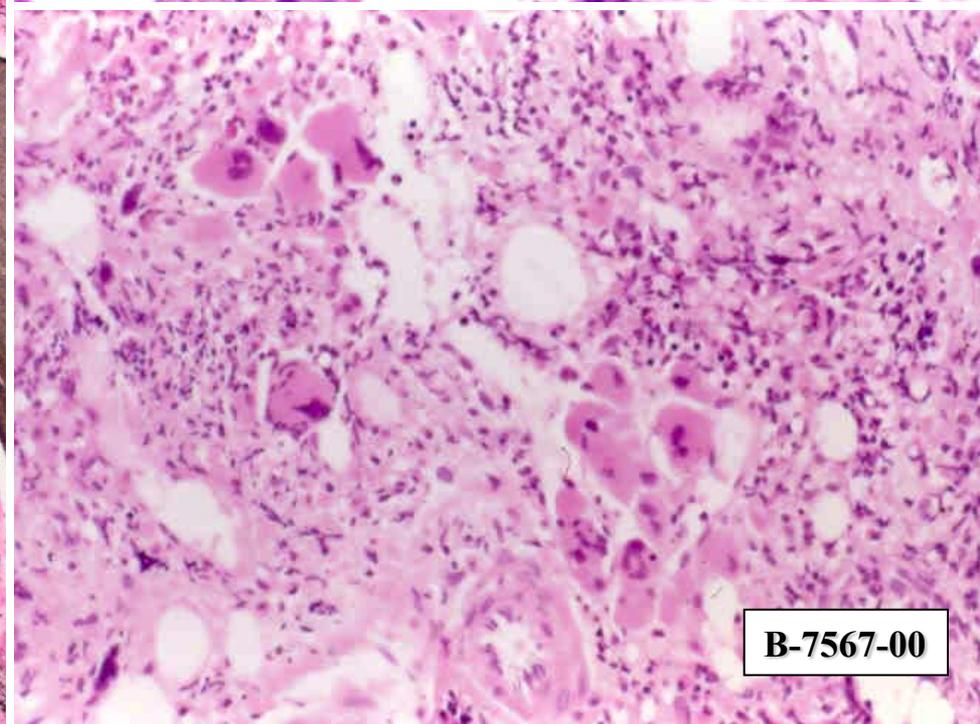
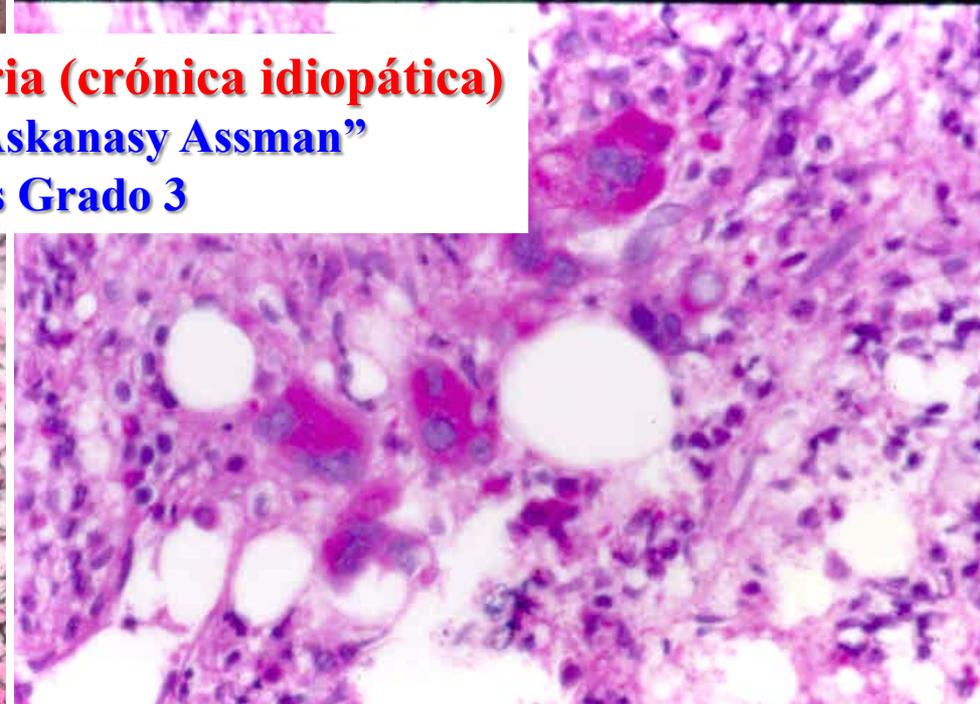
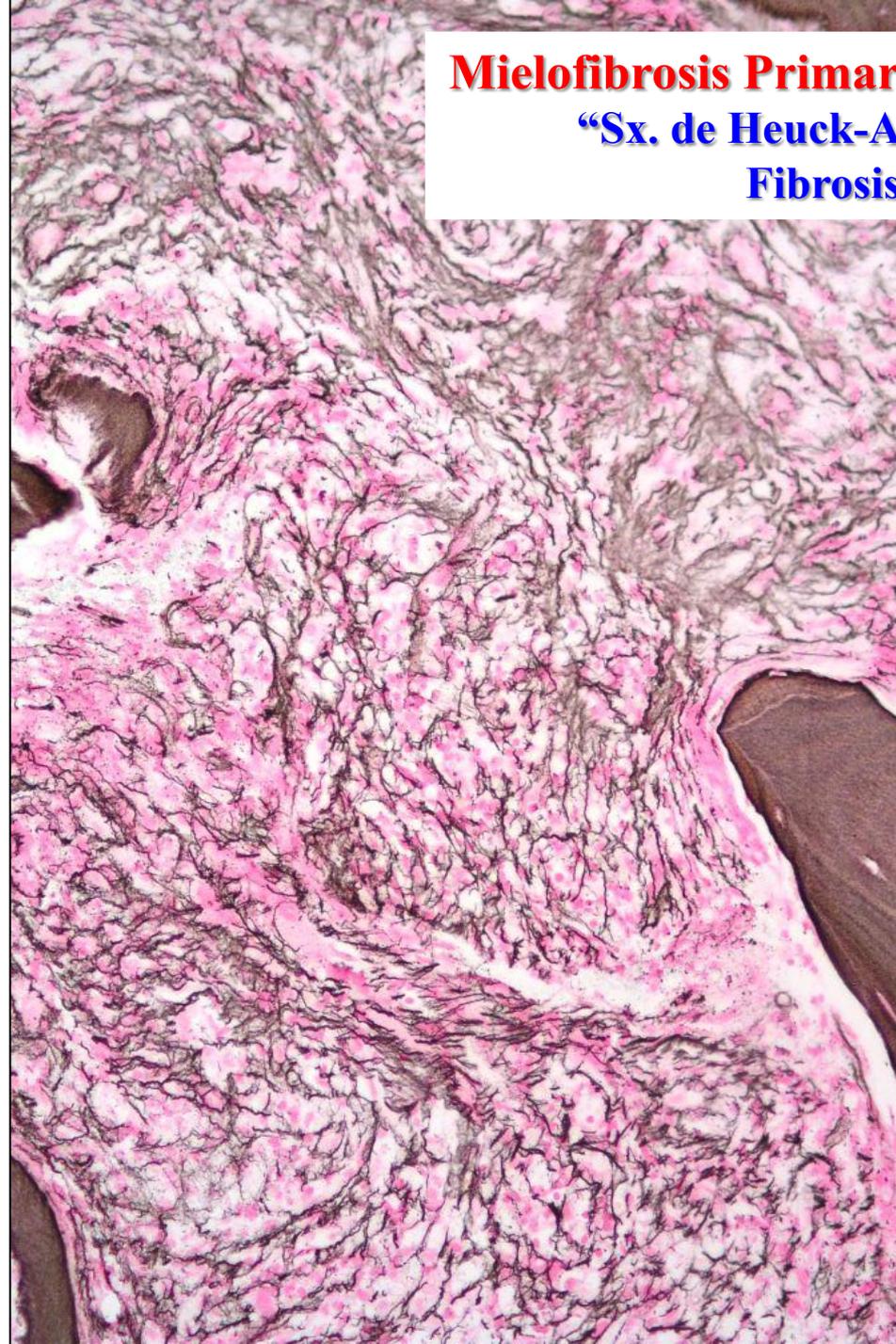


Trombocitemia Esencial
Fibrosis grado I

Grado 1

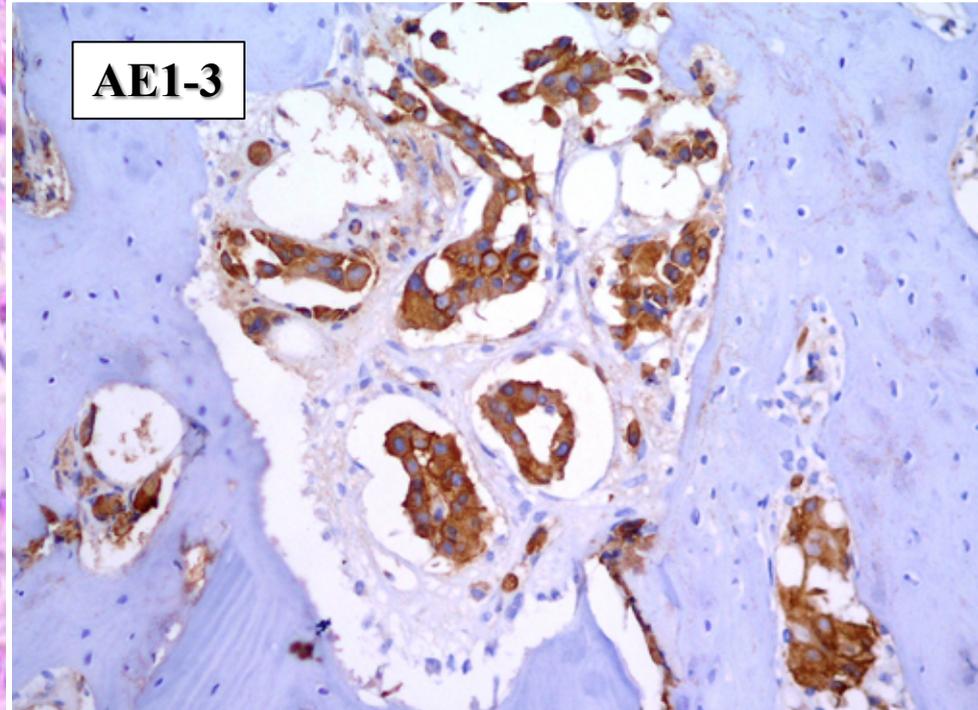
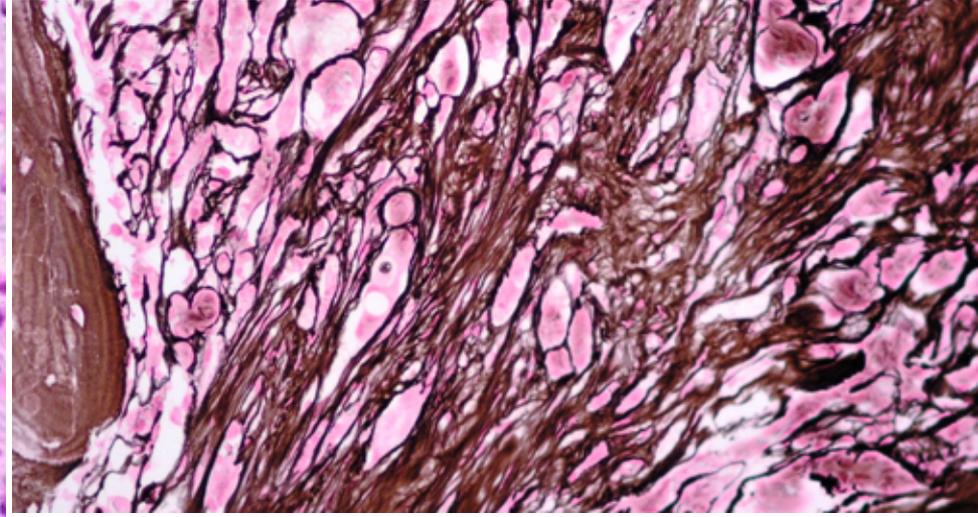
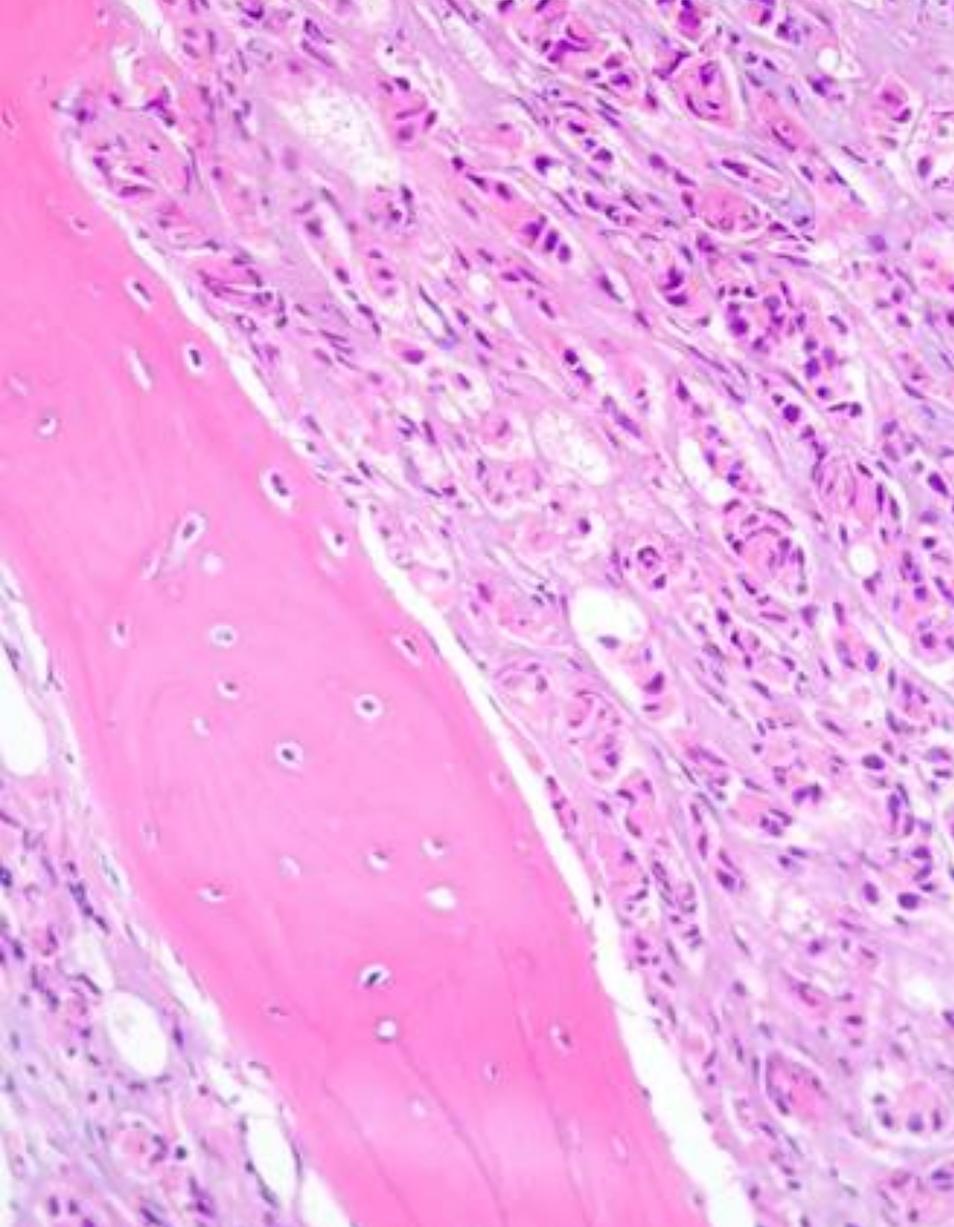


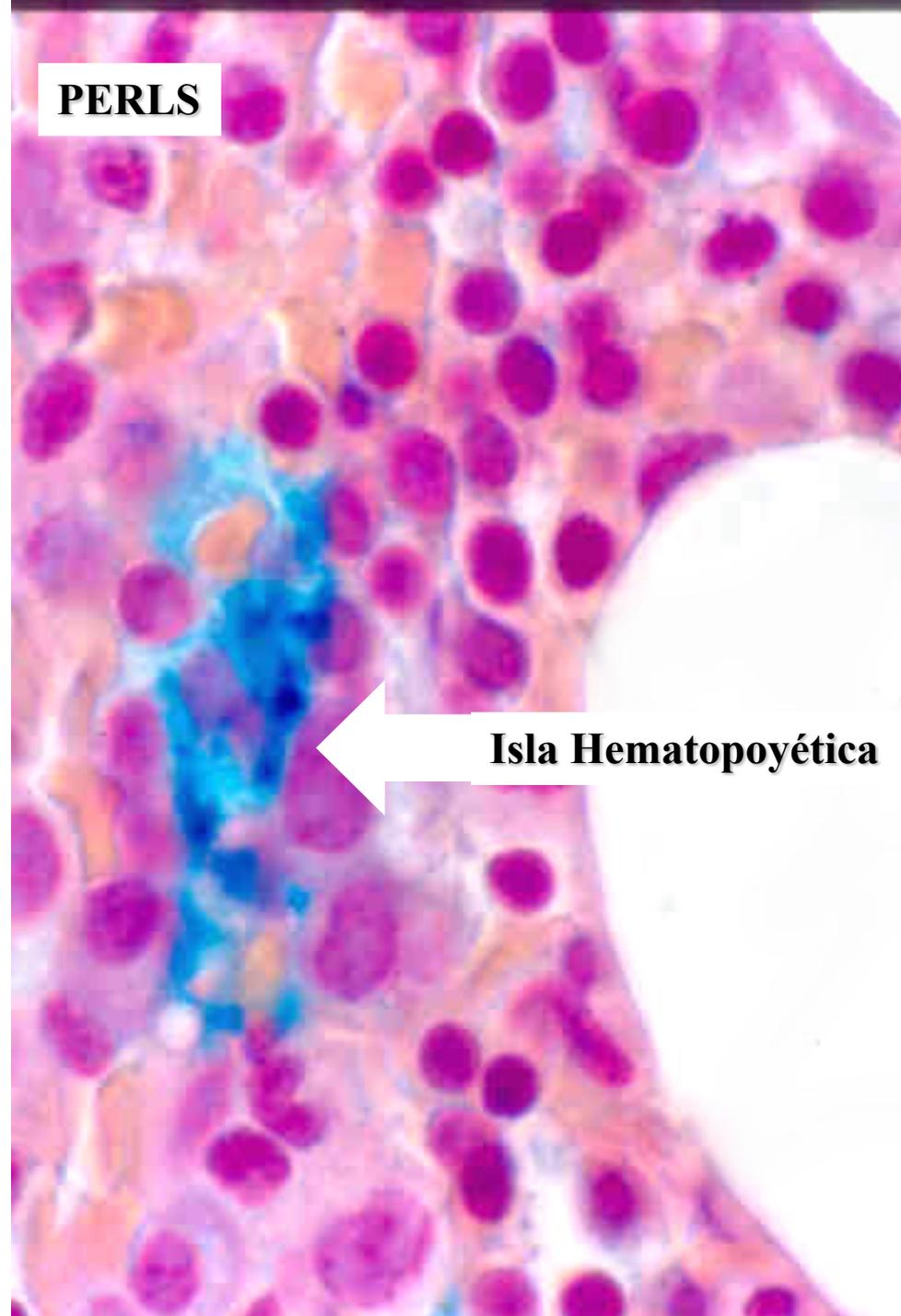
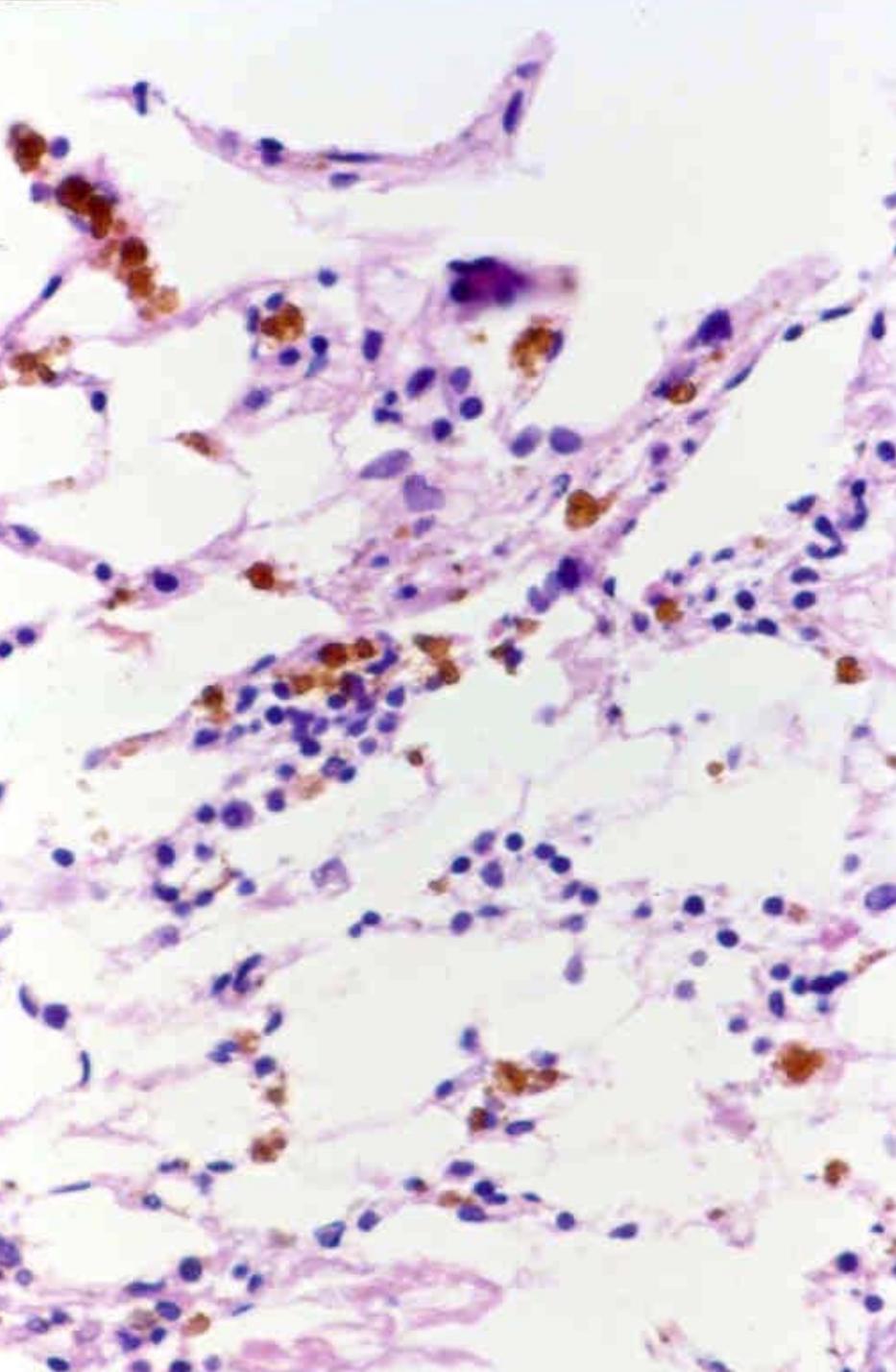
Mielofibrosis Primaria (crónica idiopática)
“Sx. de Heuck-Askanasy Assman”
Fibrosis Grado 3



B-7567-00

Carcinoma ductal mamario metastásico
Fibrosis grado 3





Hemosiderina en Médula ósea

Disminución

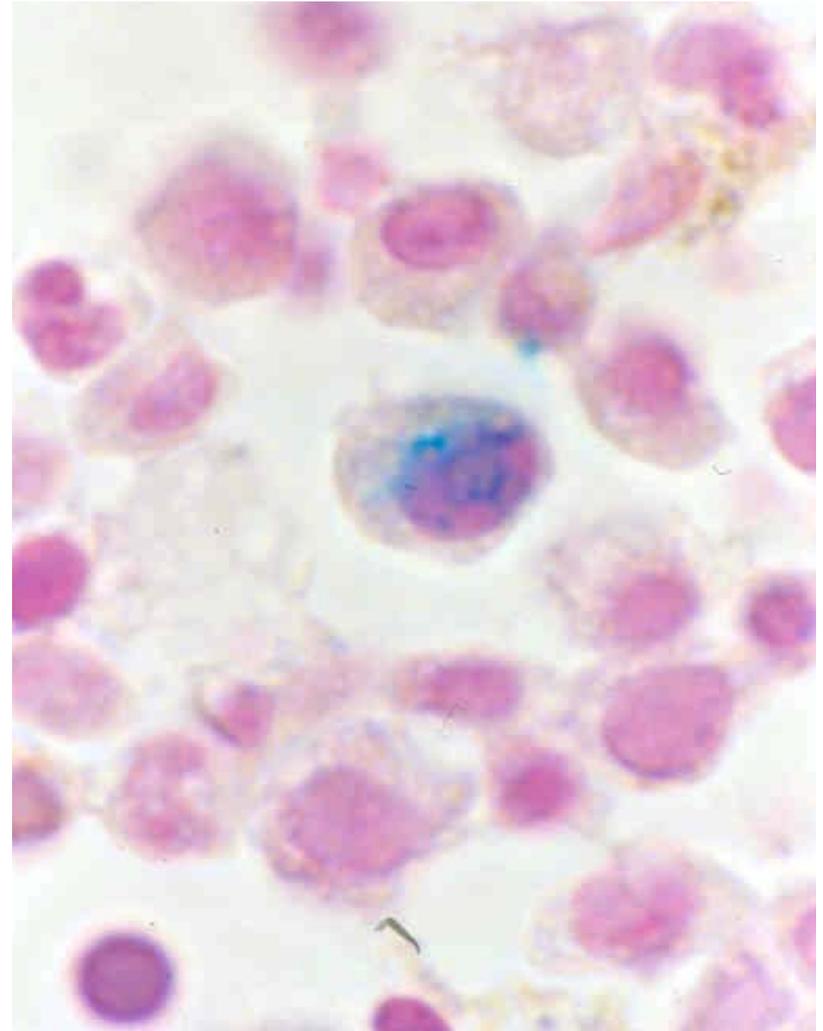
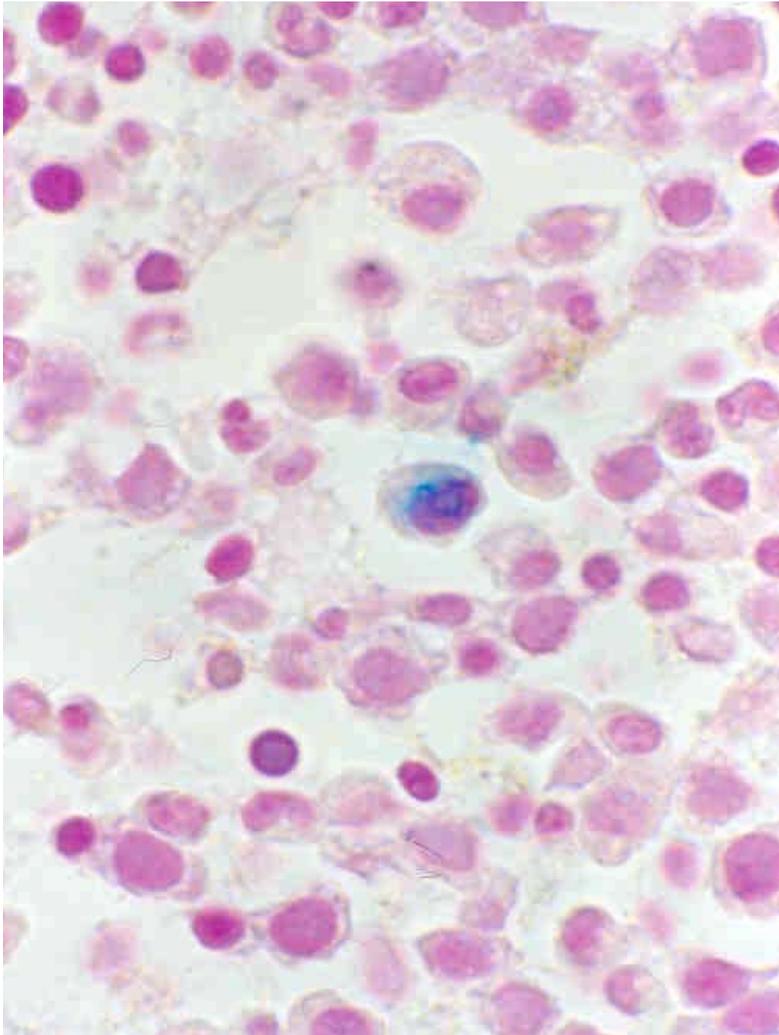
- **Anemia por deficiencia de hierro (microcítica hipocrómica)**
- **Síndromes Mieloproliferativos**
- **Hemoglobinuria Paroxística Nocturna**
- **Hemosiderosis pulmonar**
- **Alteraciones congénitas del metabolismo (atransferrinemia)**
- **Hemolisis Intravascular**

Aumento

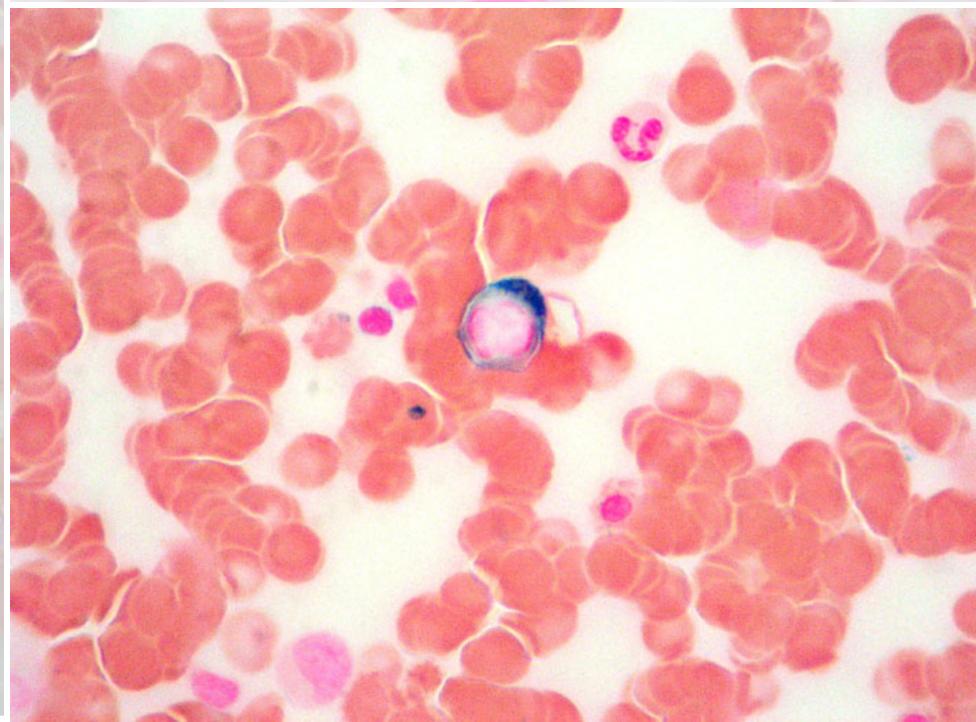
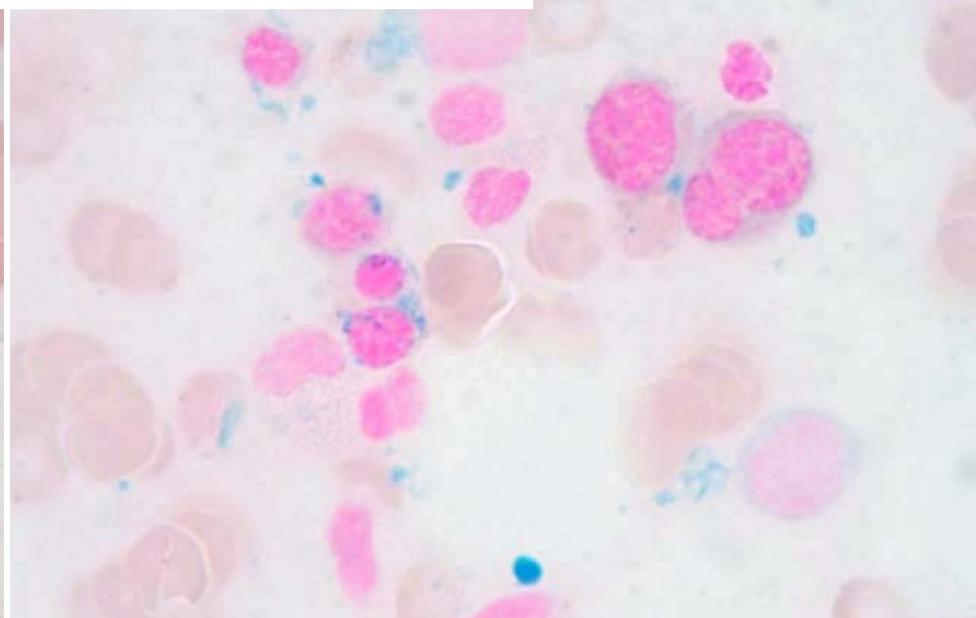
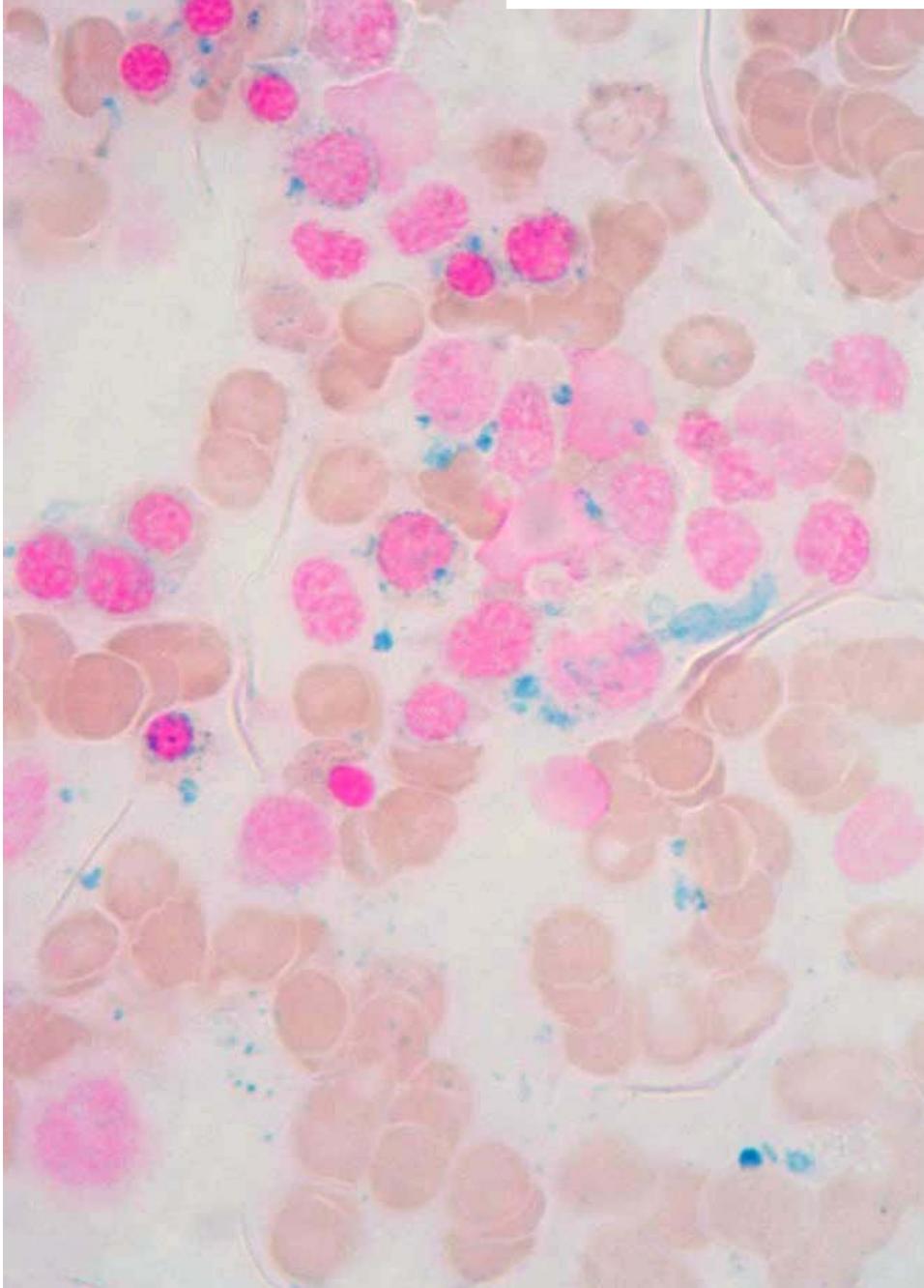
- **Anemias.**
- **Hemocromatosis**
- **Post transfusión.**
- **Porfiria cutánea**
- **Enfermedad de Gaucher.**

SIDEROBLASTOS EN ANILLO

- 10 o más gránulos de hierro que rodean un tercio o más del núcleo



SIDEROBLASTOS EN ANILLO



Informe de Médula ósea

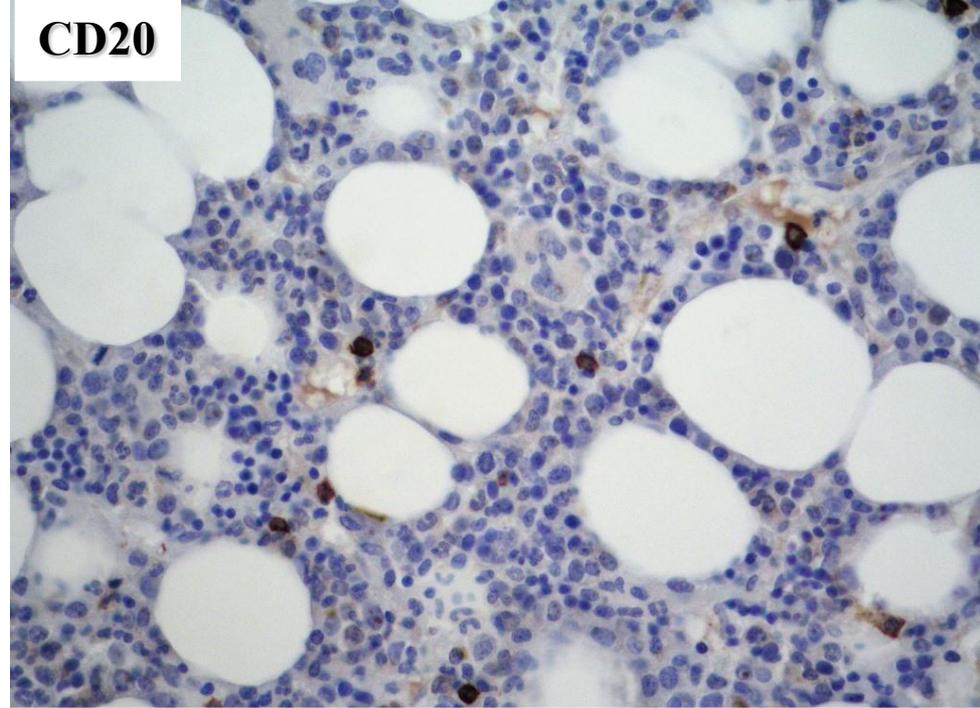
“Otros”

- **Linfocitos**
- **Células plasmáticas**
- **Células cebadas (Mastocitos)**
- **Macrófagos (pseudogaucher)**

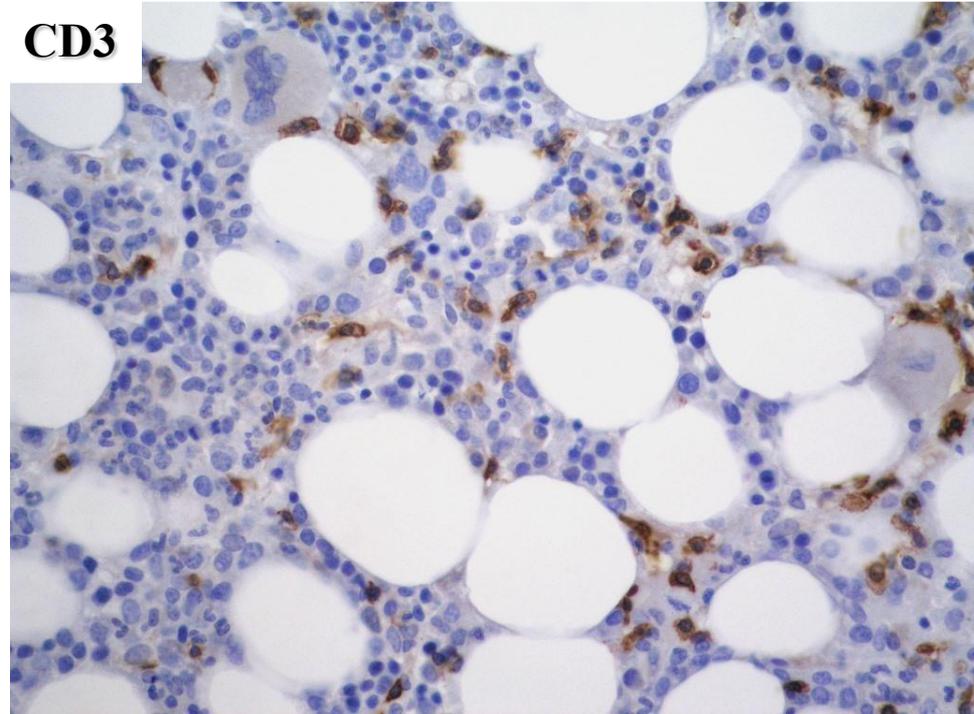
LINFOCITOS

- Normal: **20%** linfocitos
 - En niños hasta **40%**
 - En los tres primeros años hasta **50%**.
- **T:B = 3:1** **CD4:CD8 = 2:1**
- **10% son T/NK.**
- **Tres agregados linfoides, normal.**
Mas de 5 sugiere linfoma.
- **Hiperplasia linfoide:**
 - **Artritis reumatoide,**
hipertiroidismo, anemias hemolíticas.

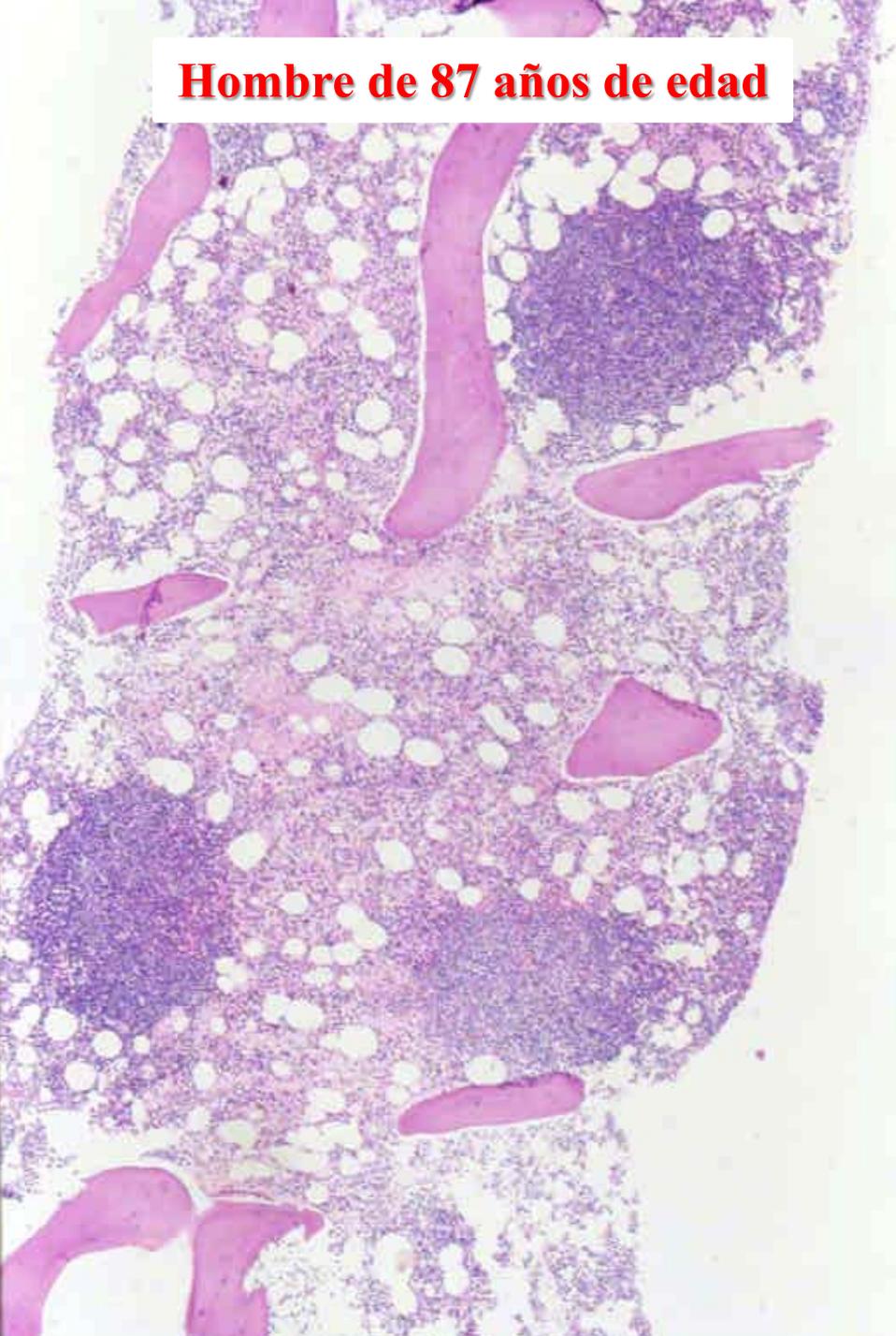
CD20



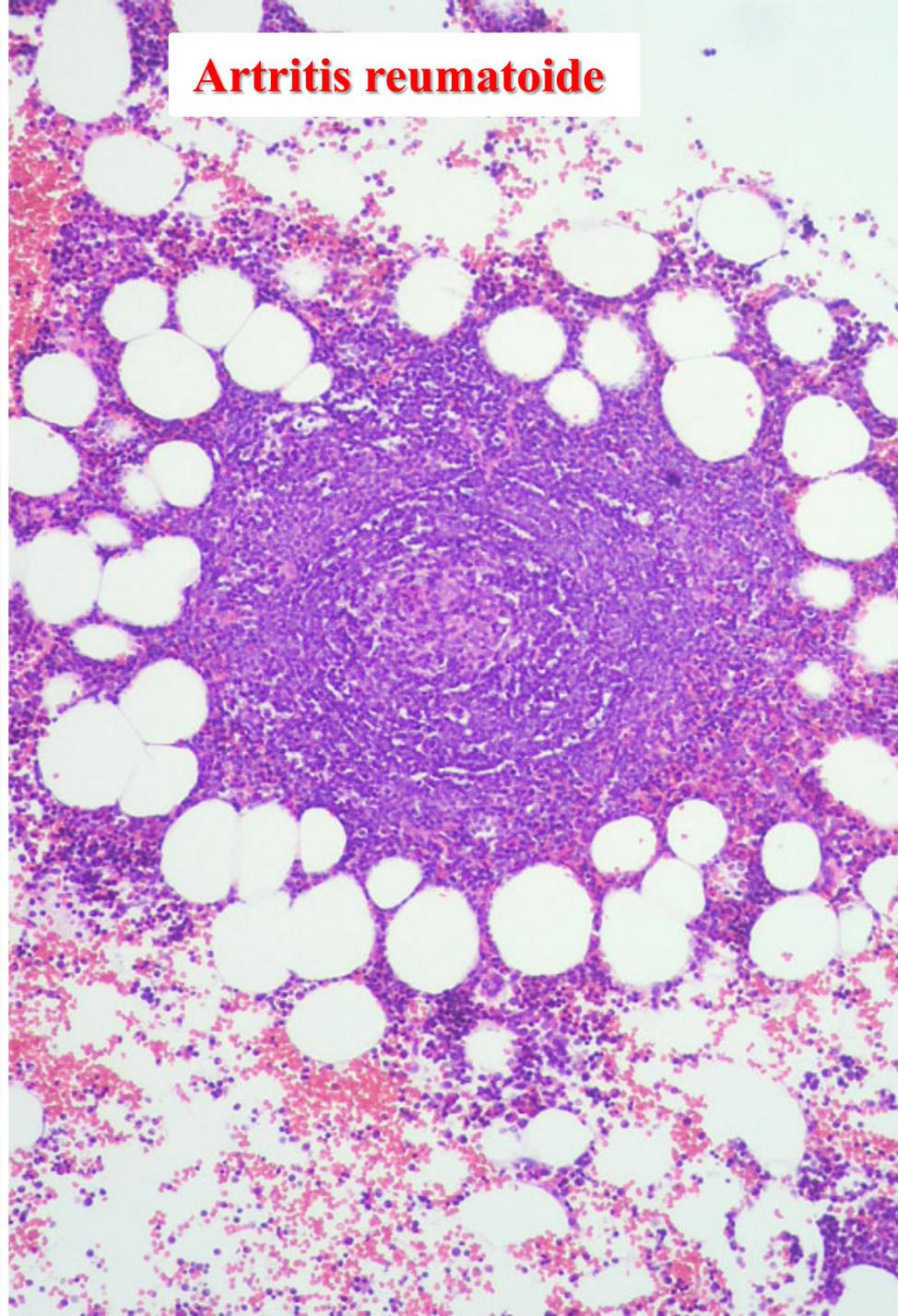
CD3



Hombre de 87 años de edad

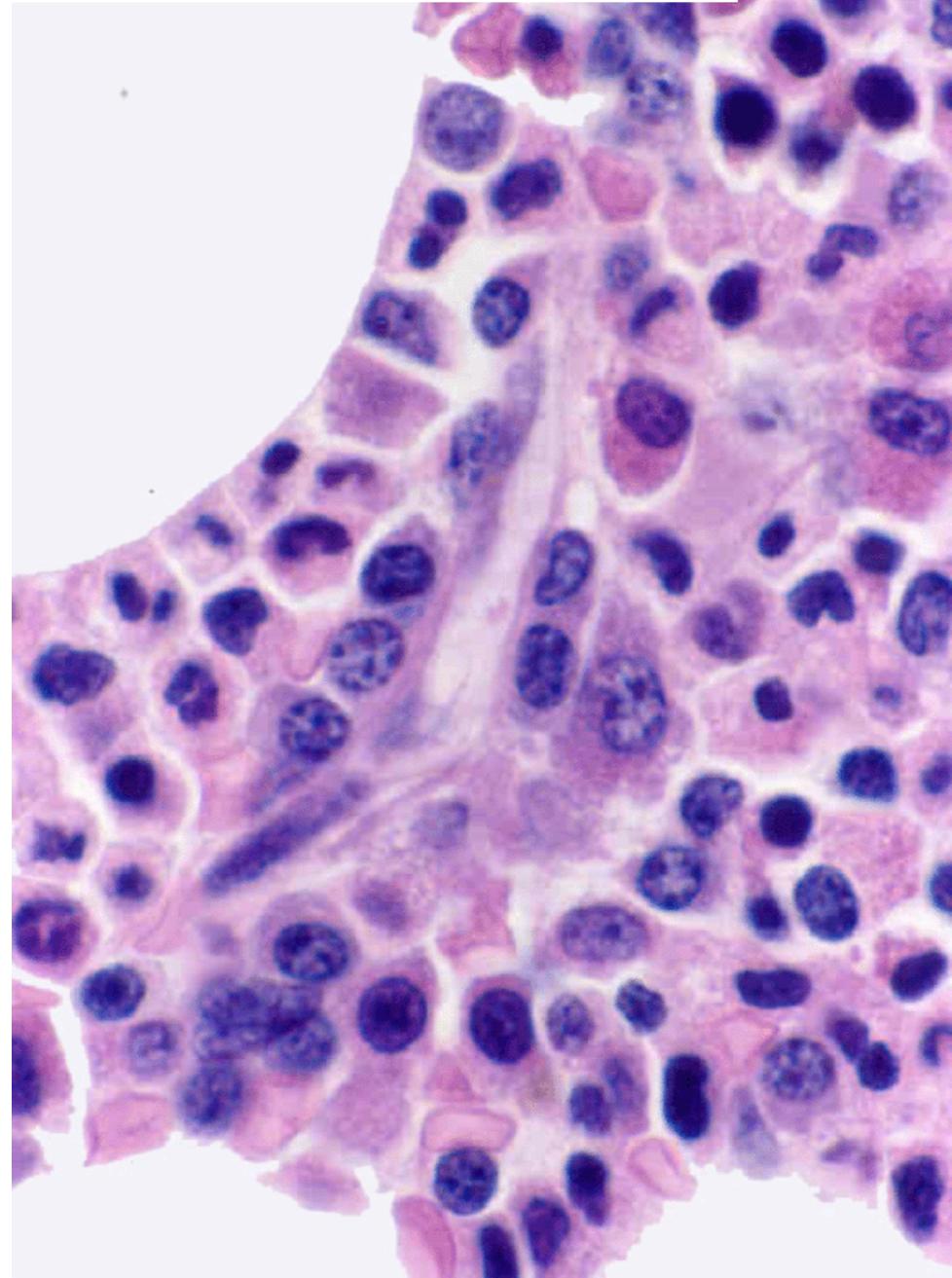
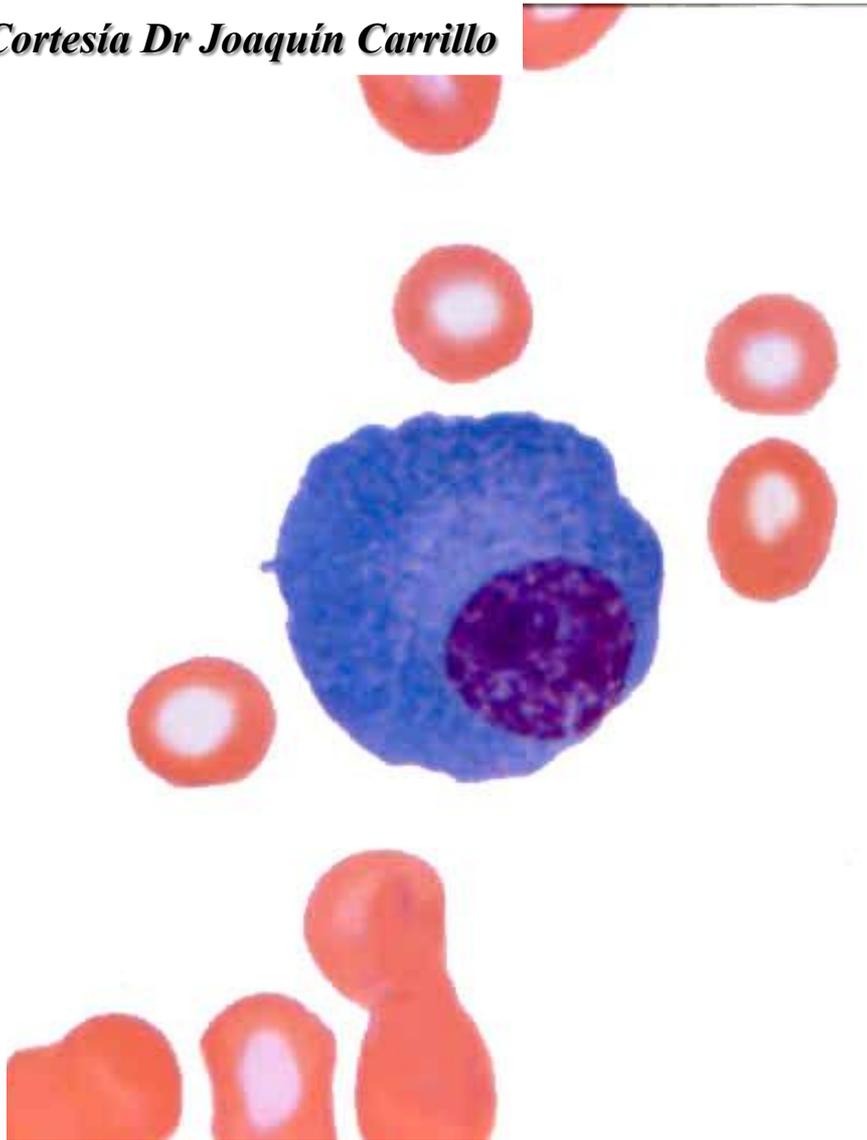


Artritis reumatoide

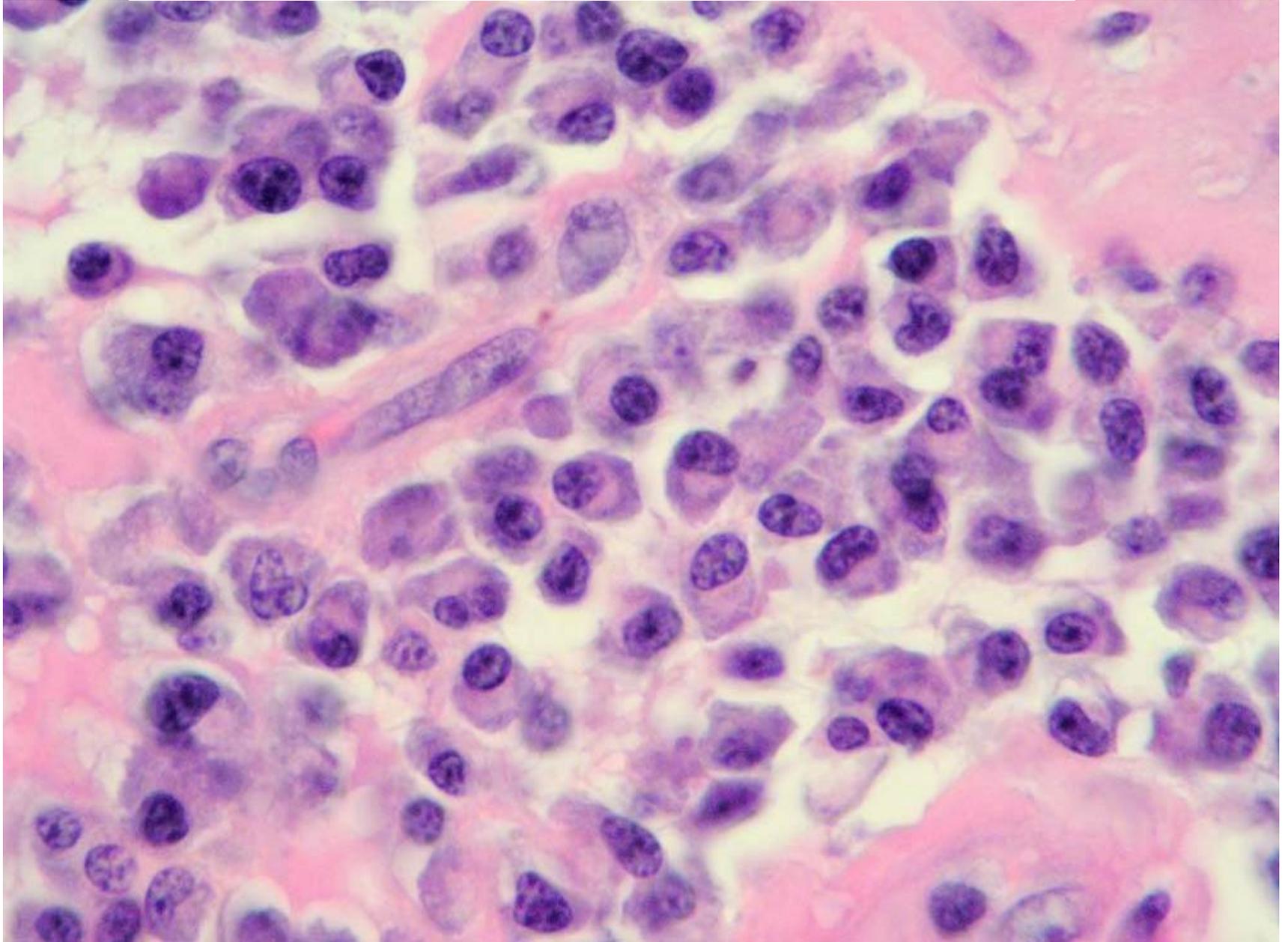


Células plasmáticas (3-6%) perivasculares

Cortesía Dr Joaquín Carrillo

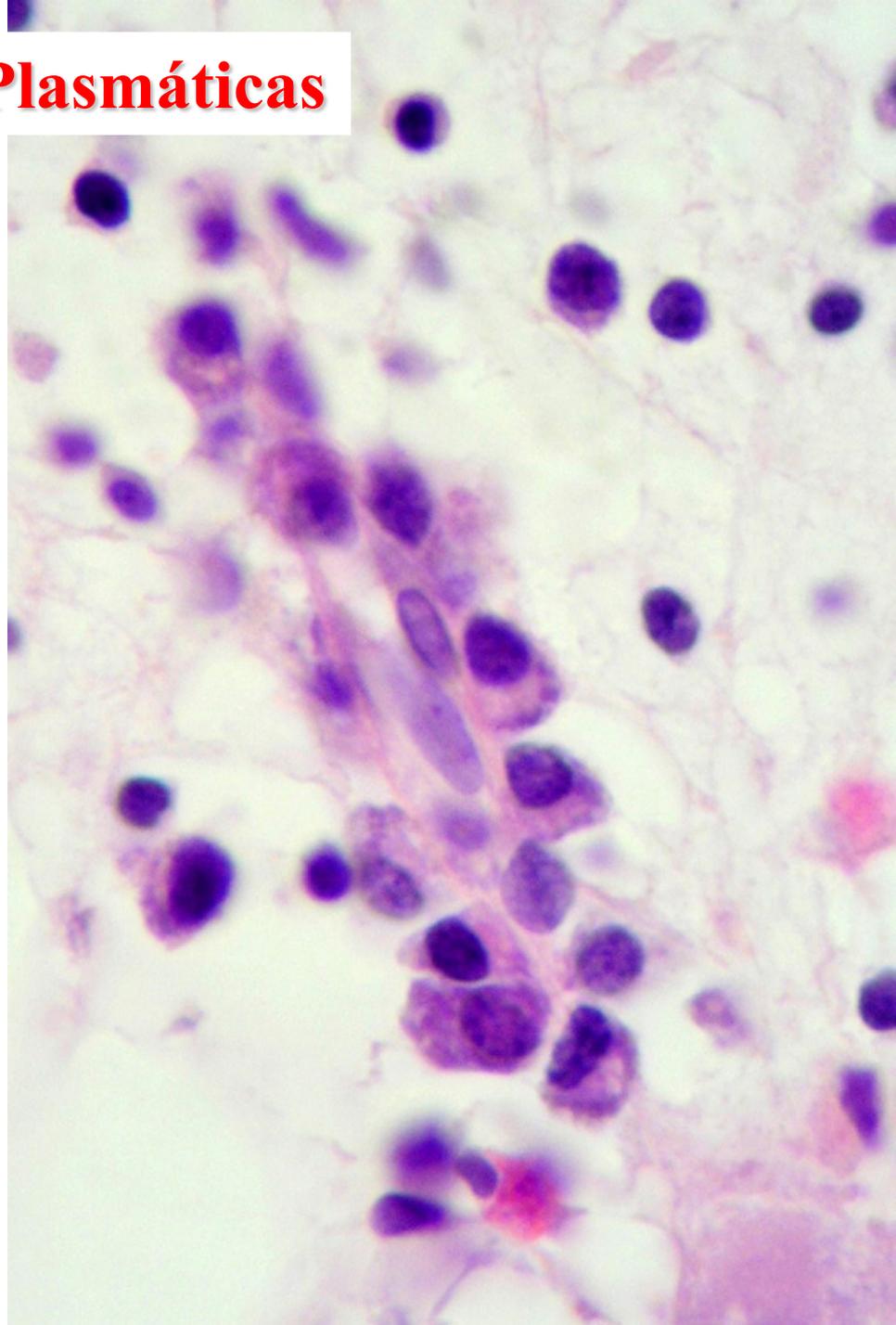
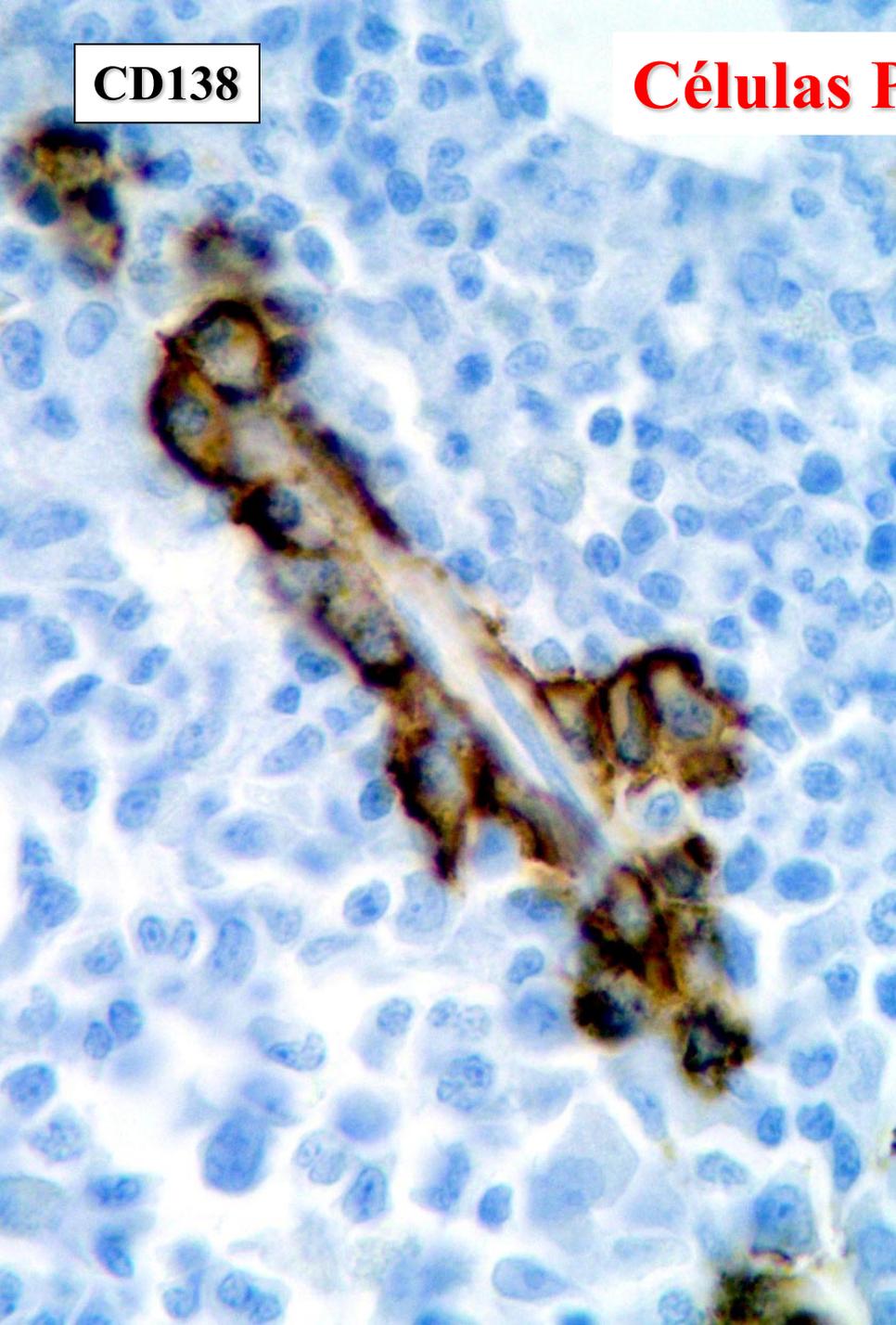


“Células Cianófilas de Cajal”

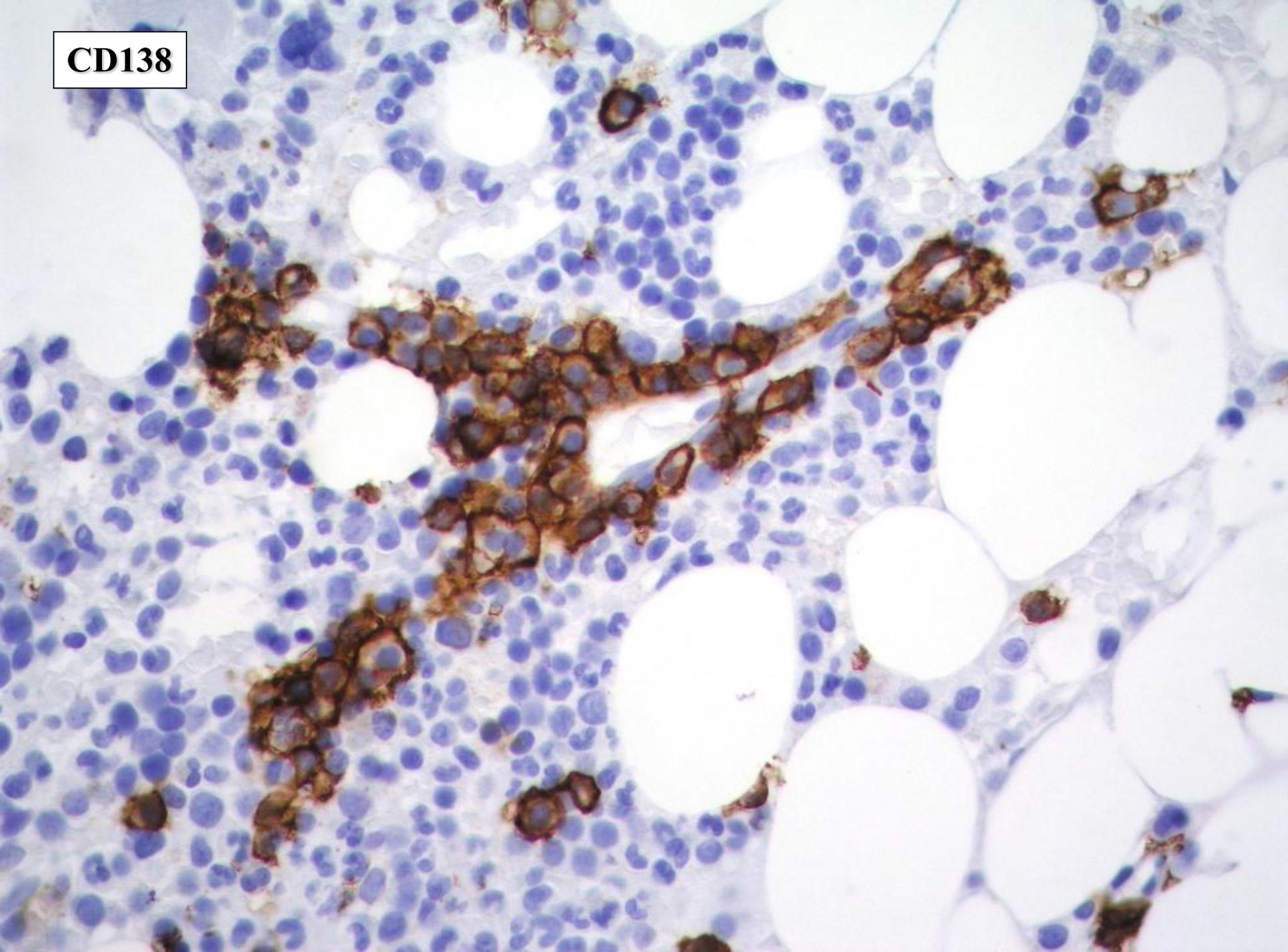


CD138

Células Plasmáticas

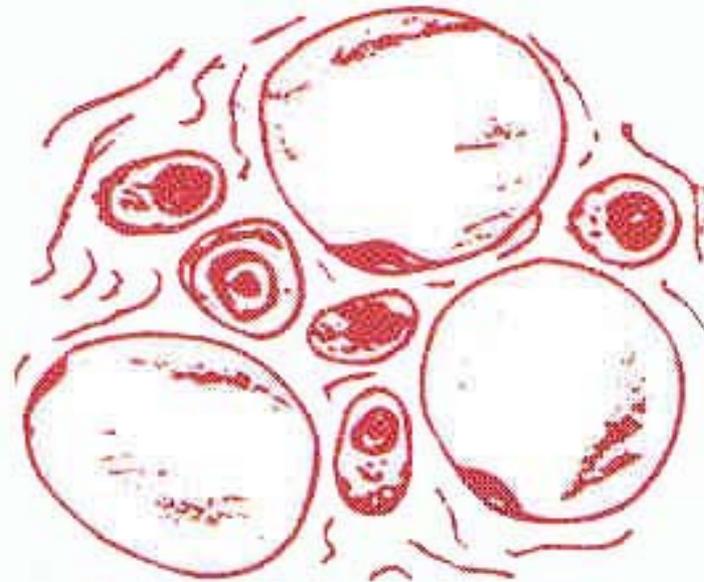
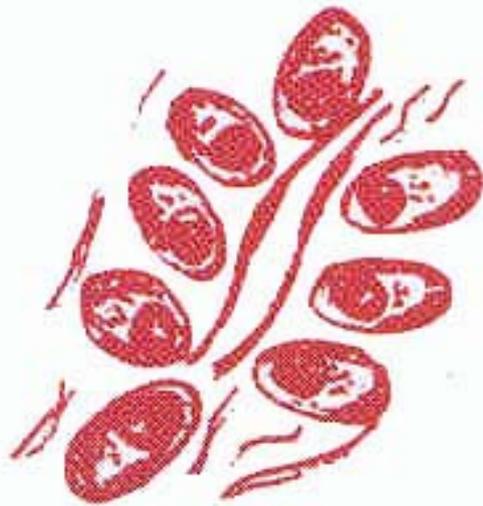


CD138



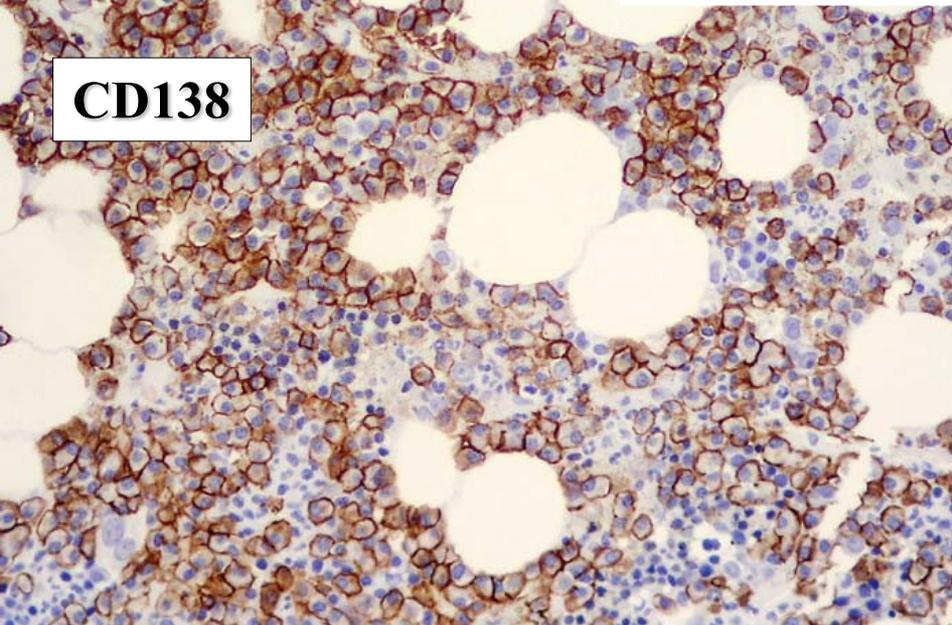
Plasmocitosis Reactiva.
Perivascular

Mieloma
Difuso

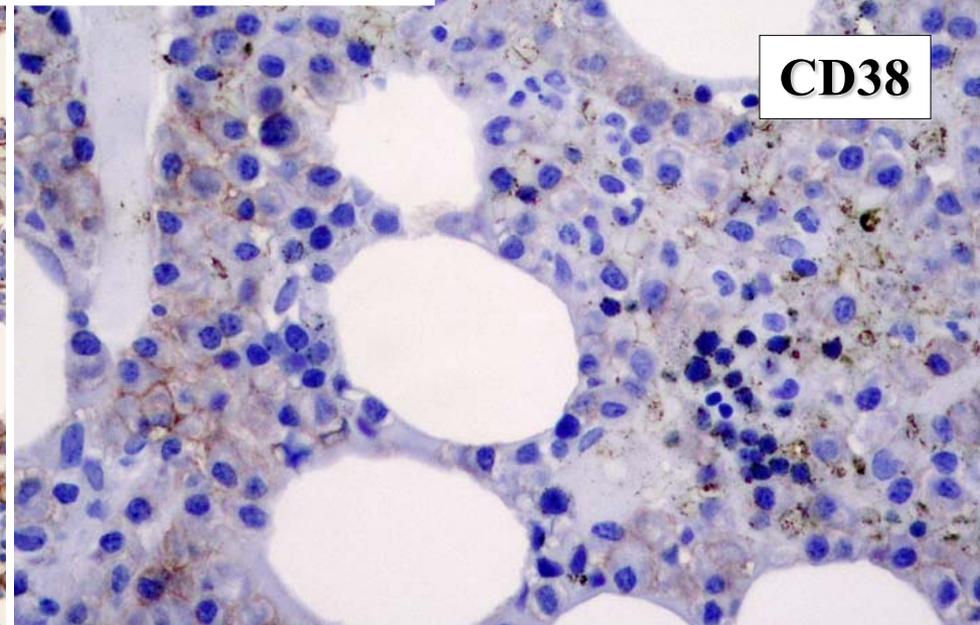


Mieloma de células plasmáticas

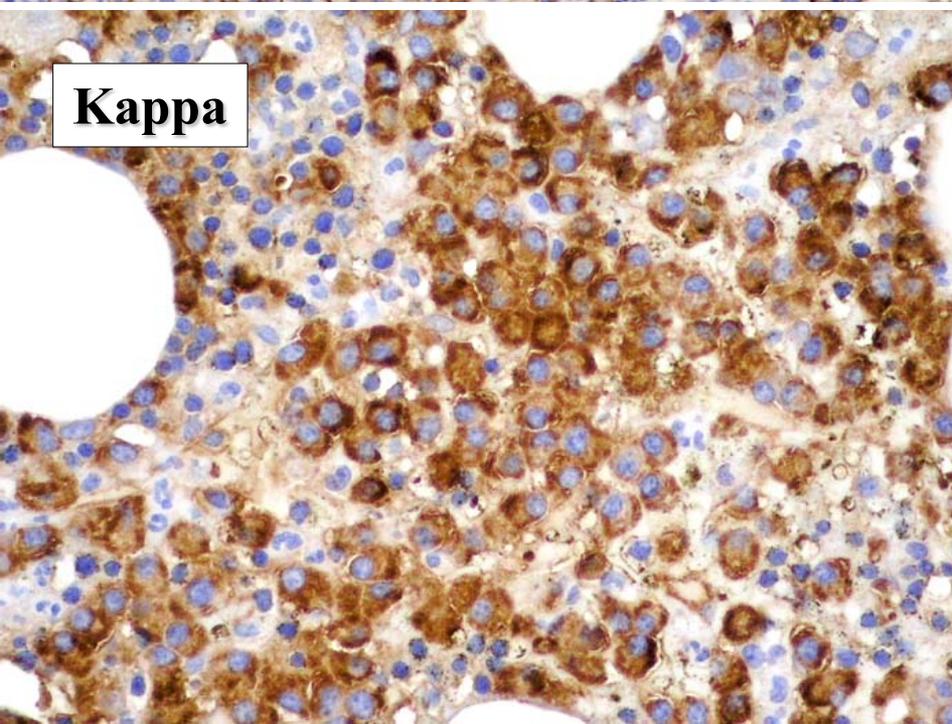
CD138



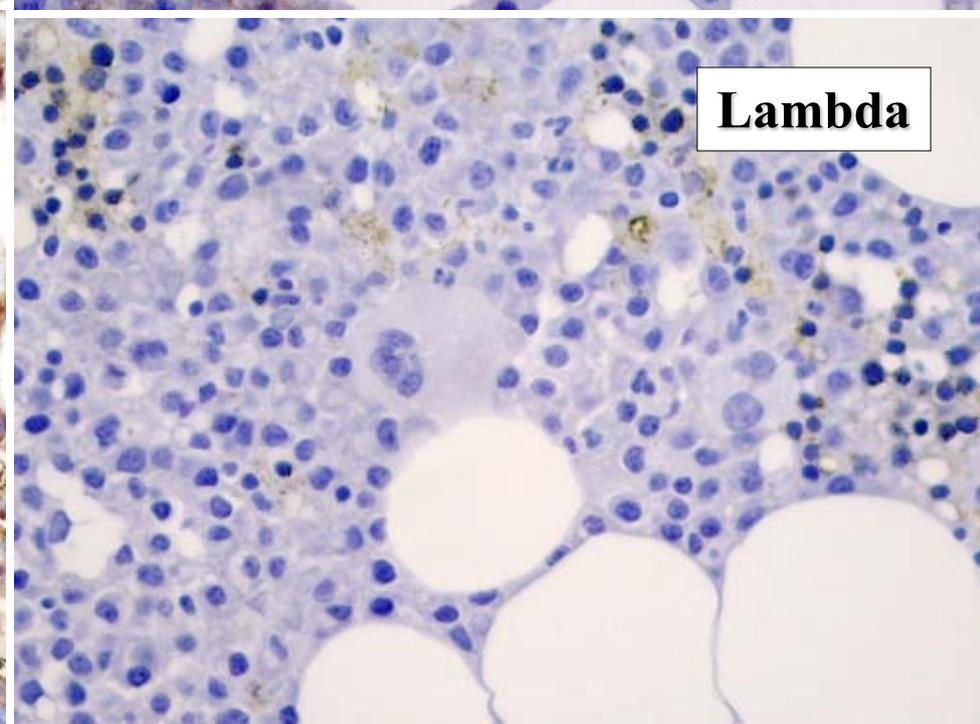
CD38



Kappa



Lambda

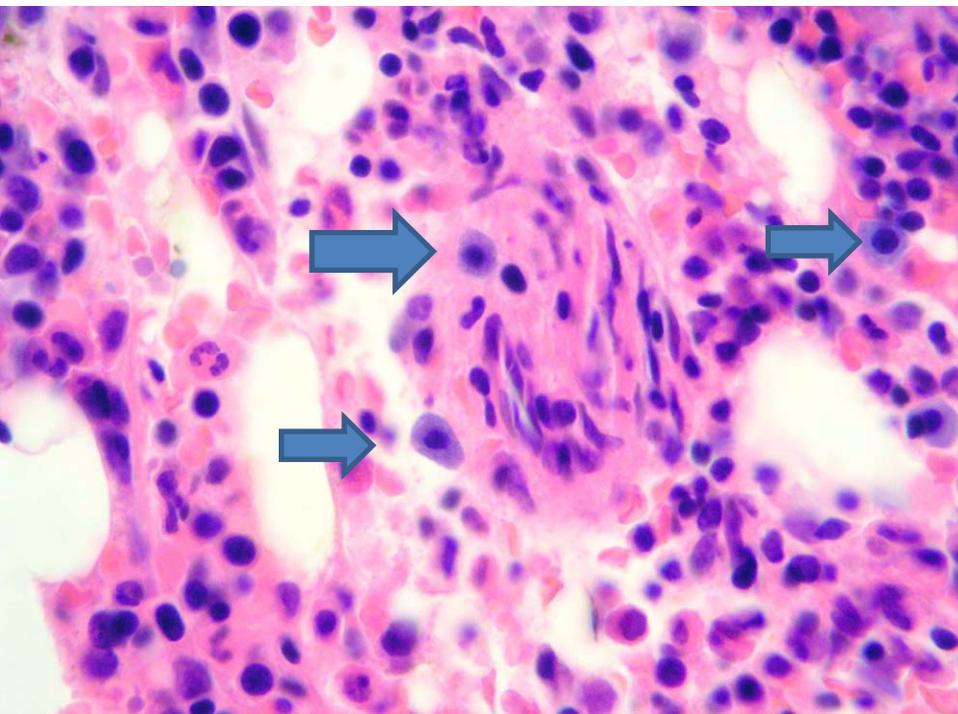
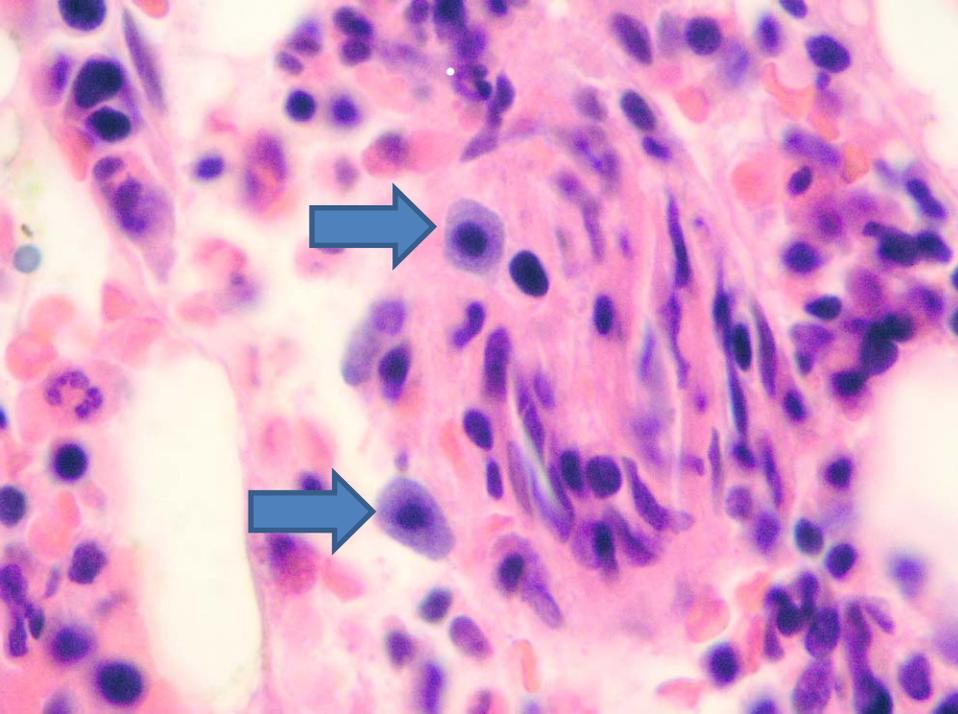


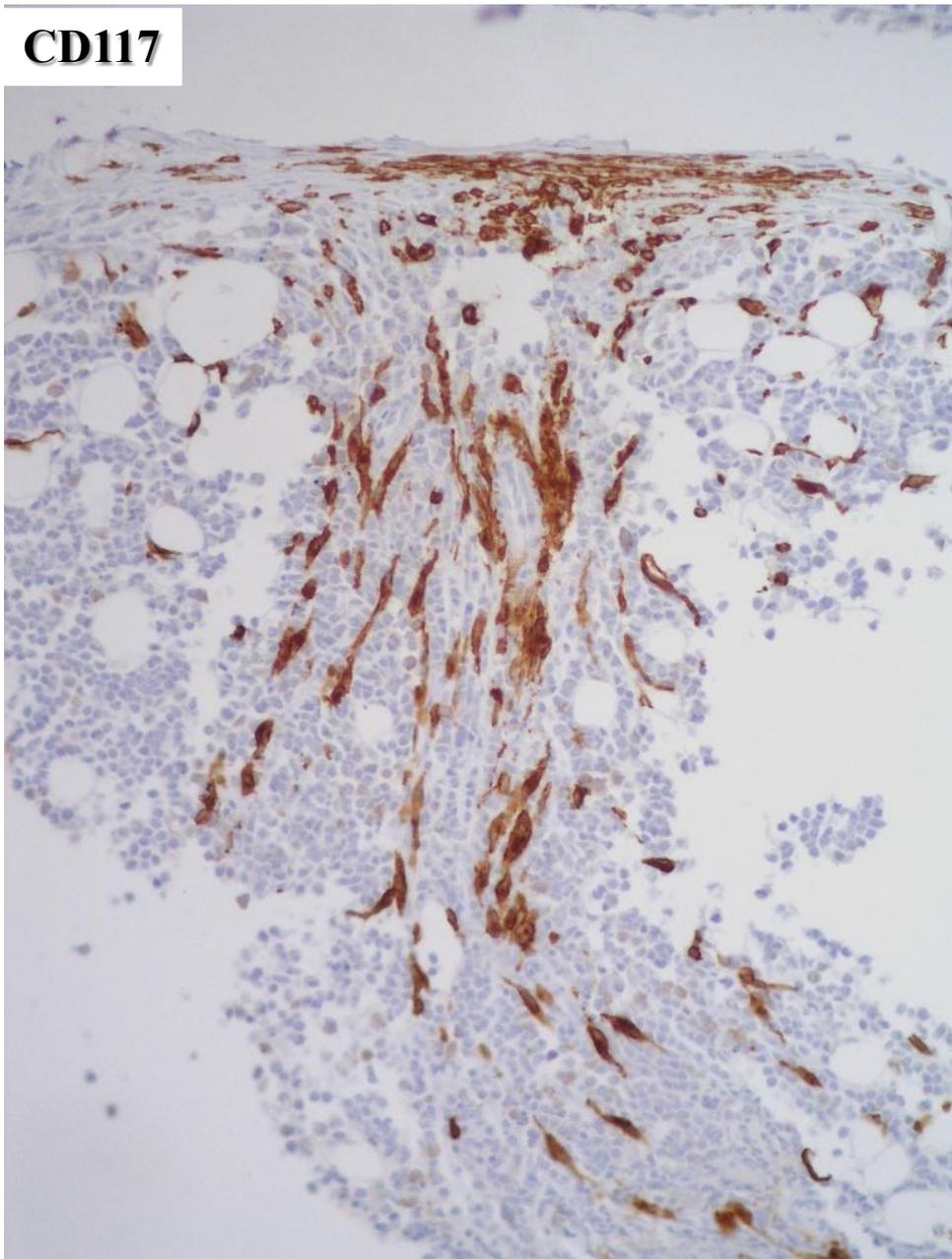
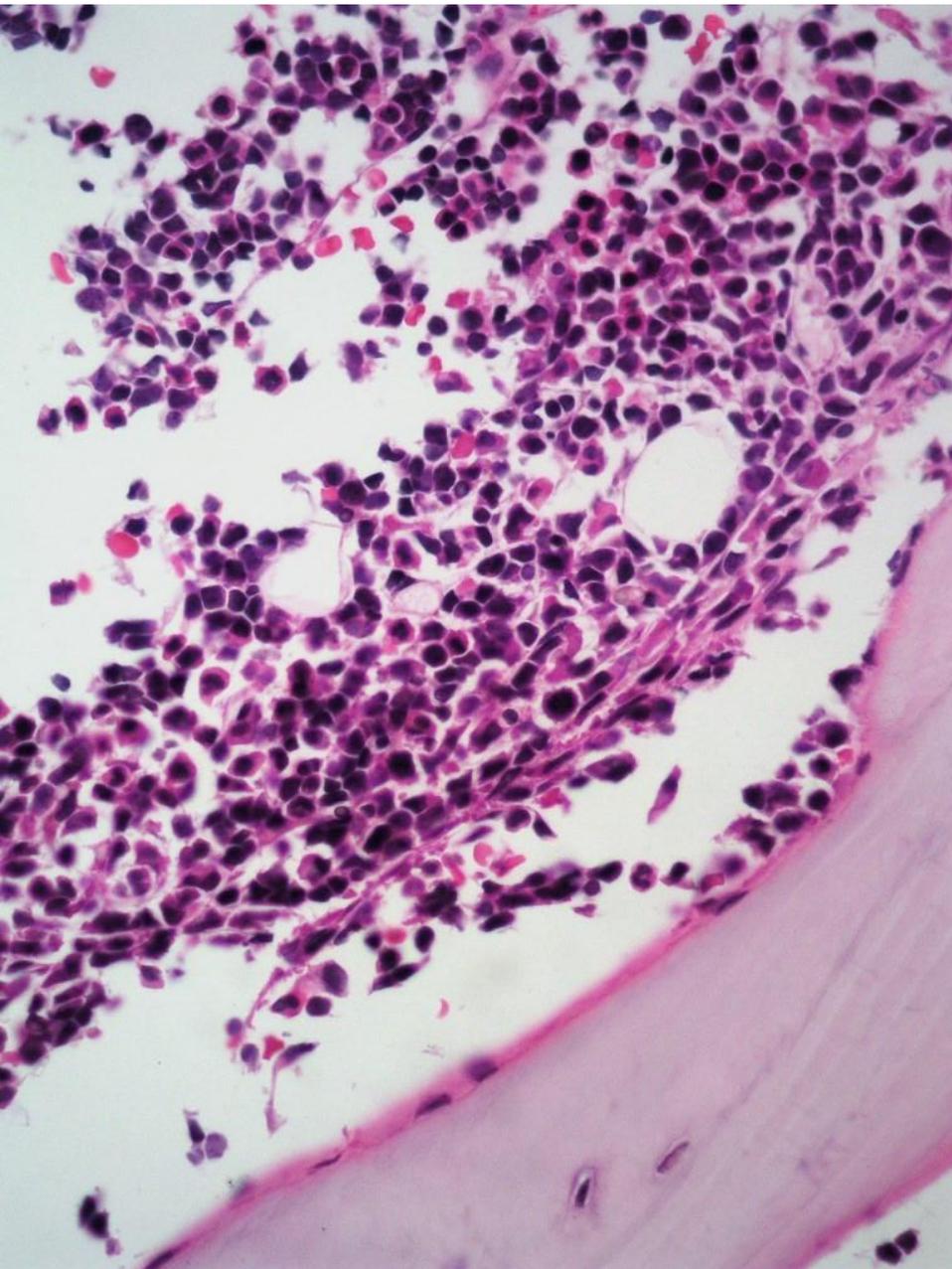
Células Cebadas

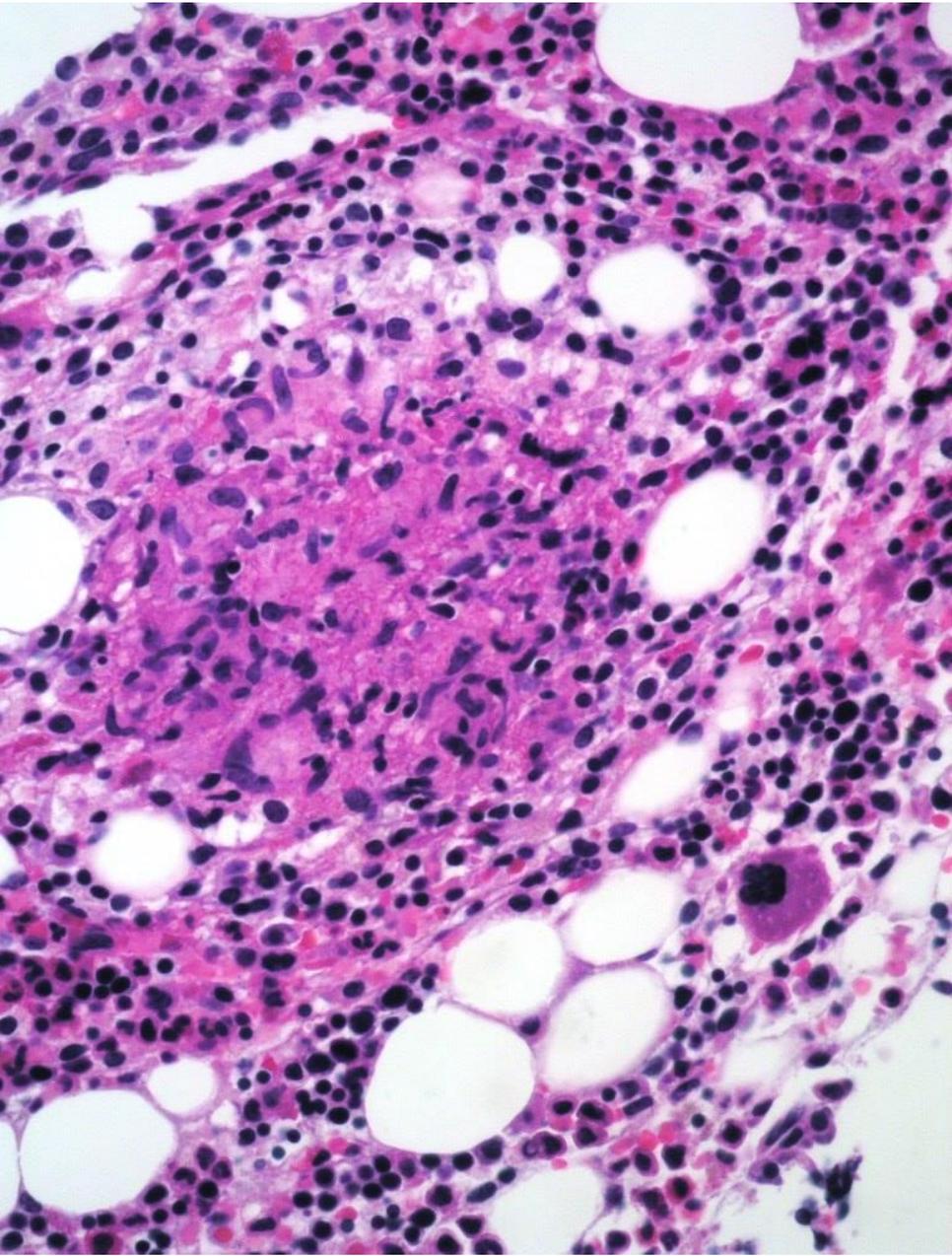
< 2% de la población medular.

- **Alcoholismo**
- **Aplasia medular**
- **Osteodistrofia renal**
- **Estimulación medular.**

- **LLC / LLP***
- **Linfoma Folicular**
- **Leucemia de células peludas**
- **Mieloma**
- **Mielodisplasia**
- **Leucemias agudas.**







GRANULOMAS

INFECCIONES

- **Tuberculosis**
- **Enfermedad de Lyme**
- **Brucellosis**
- **Tifoidea**
- **Rickettsias**
- **Leishmaniasis**
- **Toxoplasmosis**
- **Hongos**
- **Citomegalovirus**
- **EB-V (Mononucleosis infecciosa)**
- **Sarcoidosis**

AUTOINMUNES

- **Cirrosis biliar primaria**
- **Enfermedad de Crohn**
- **Artritis reumatoide**

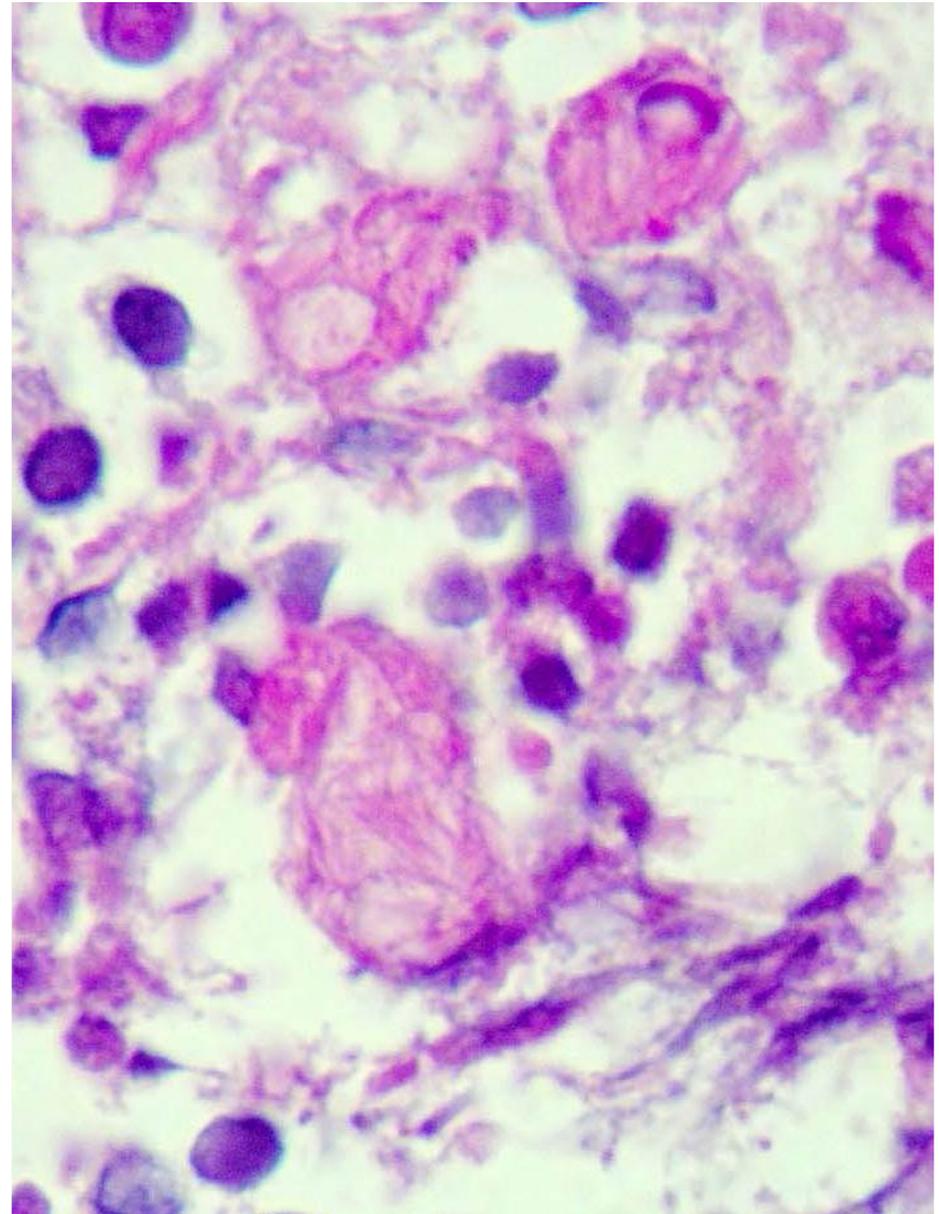
LINFOMAS

MEDICAMENTOS

Hematopoyesis anormal

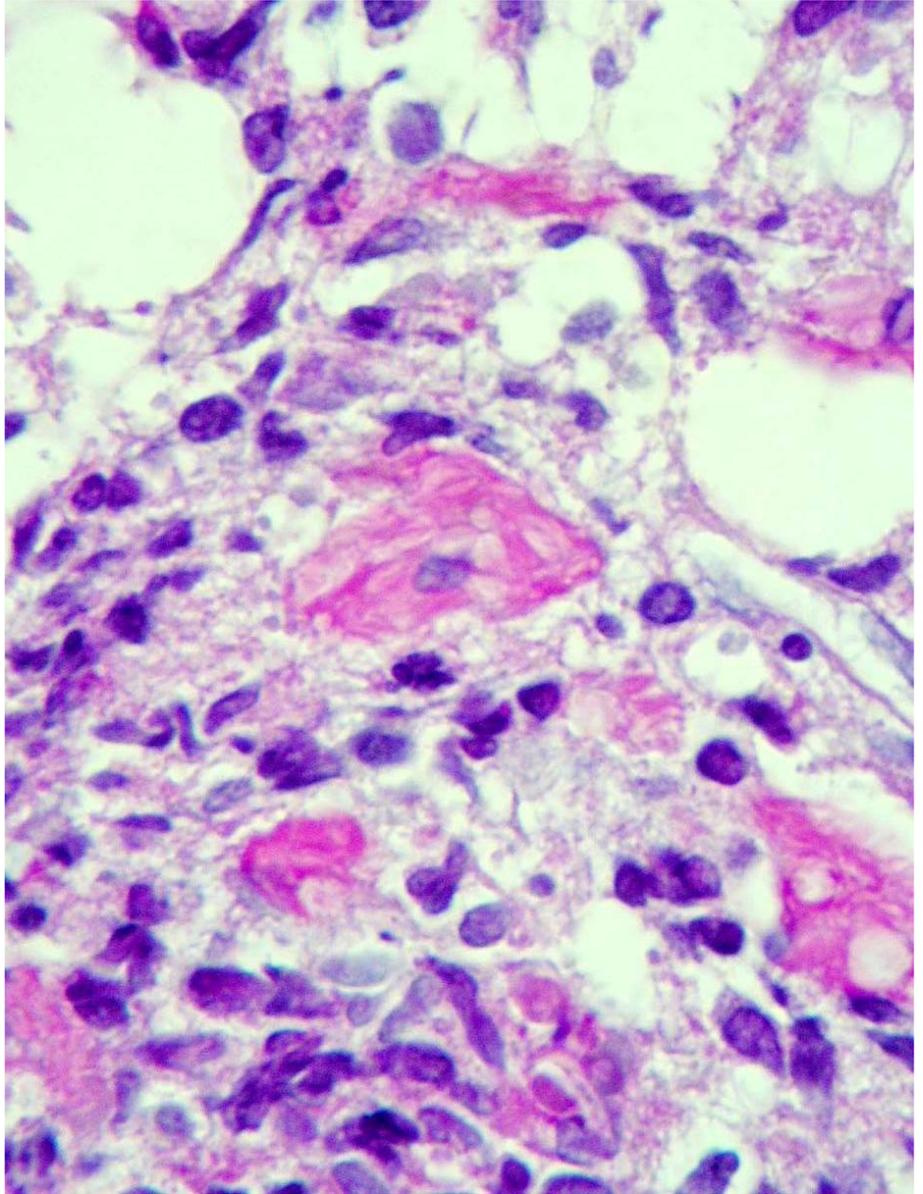
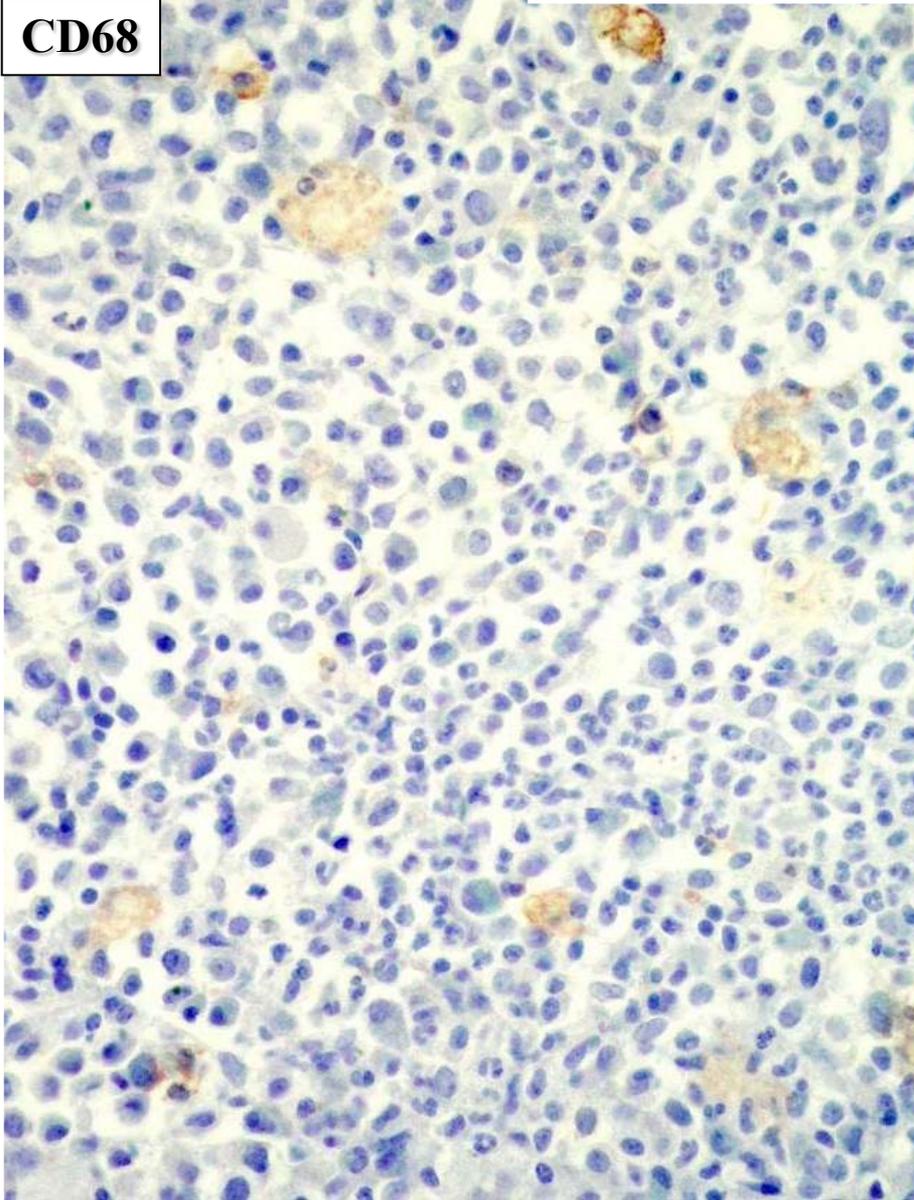
- **Leucemia Mieloide Crónica**
- **Talasemias**
- **Post quimioterapia**
- **Tumores (alto recambio celular)**

Células de pseudoGaucher

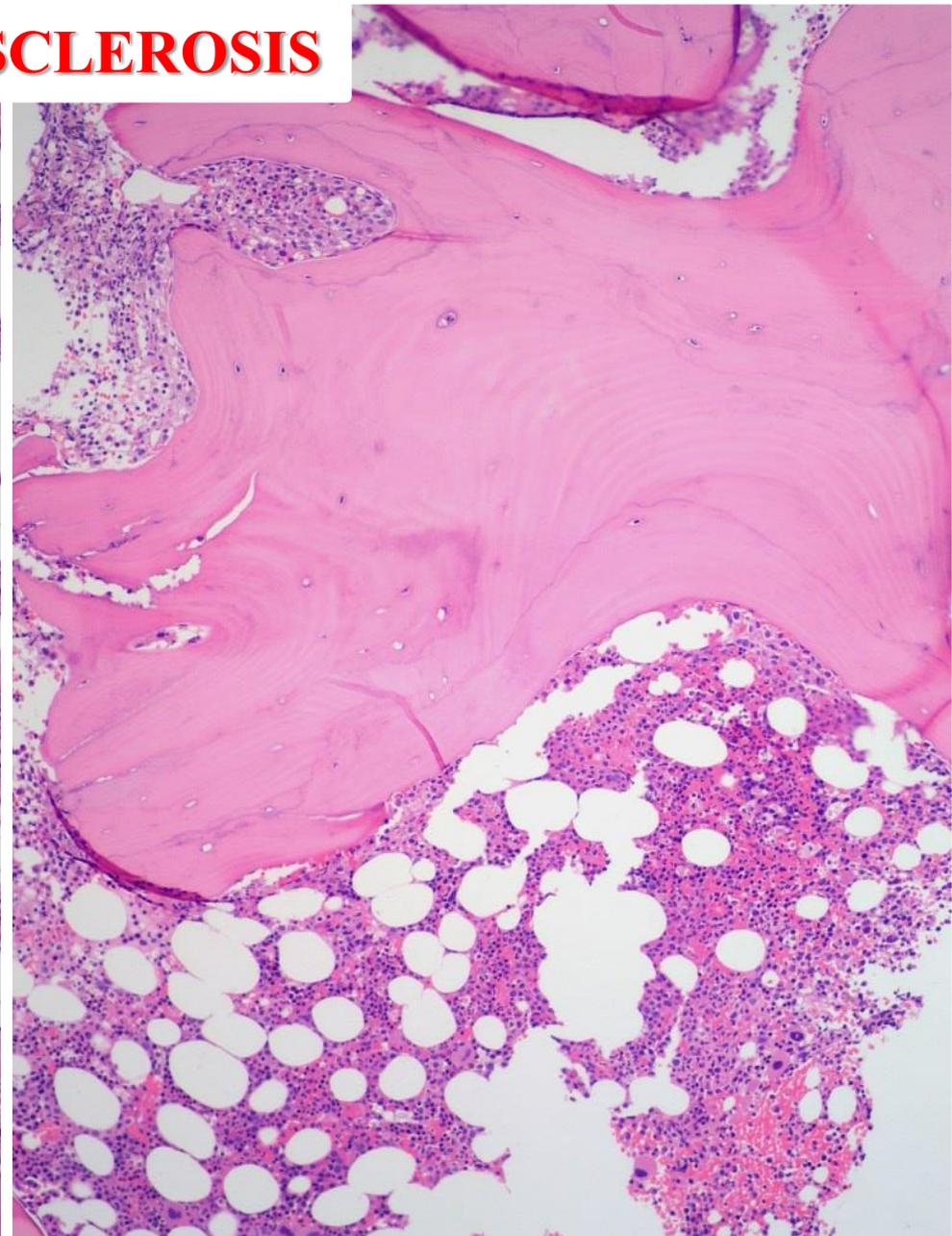
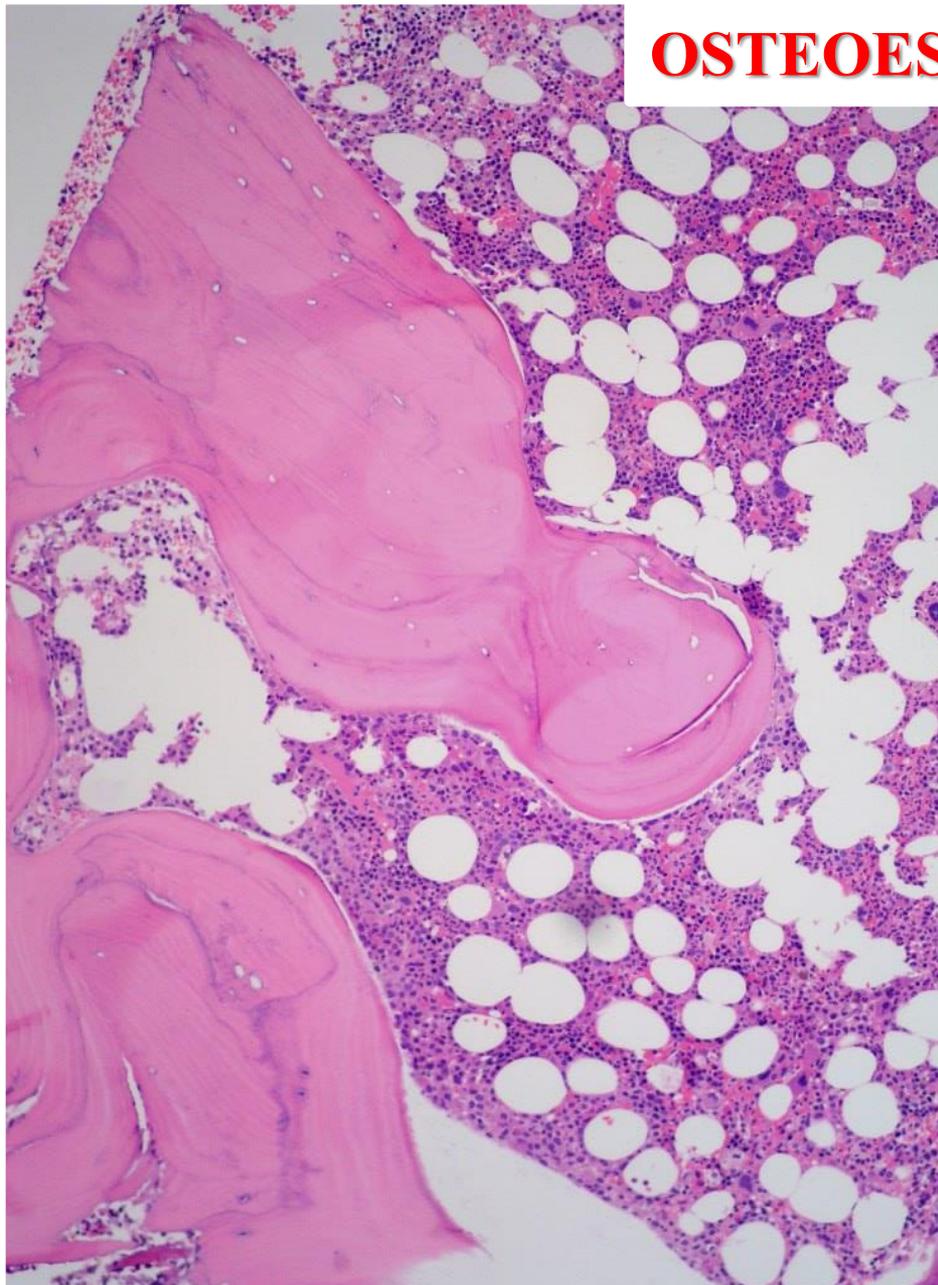


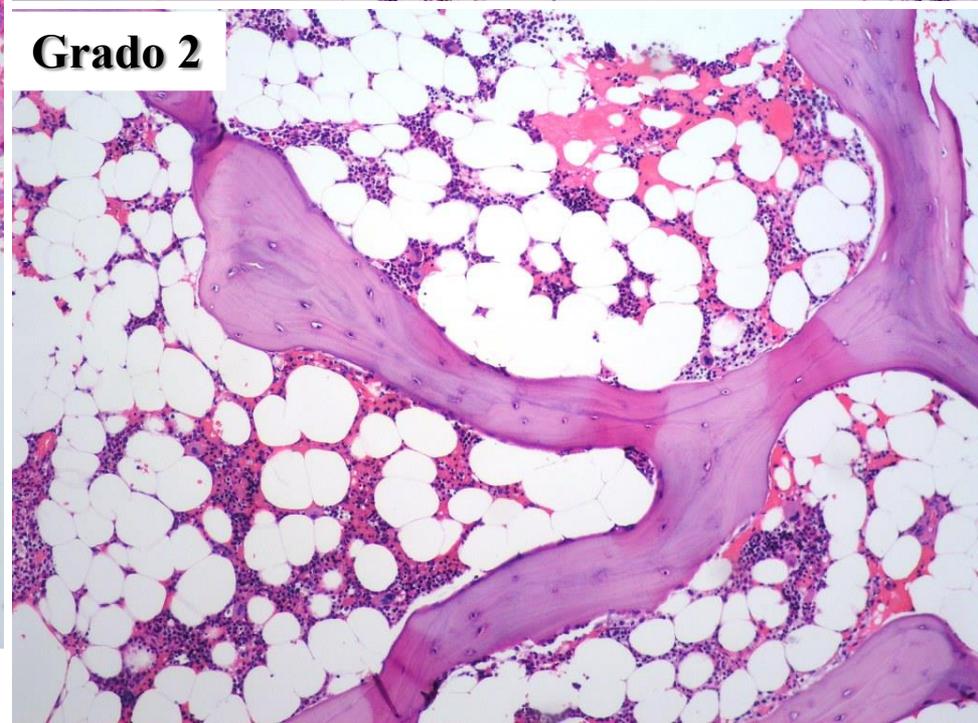
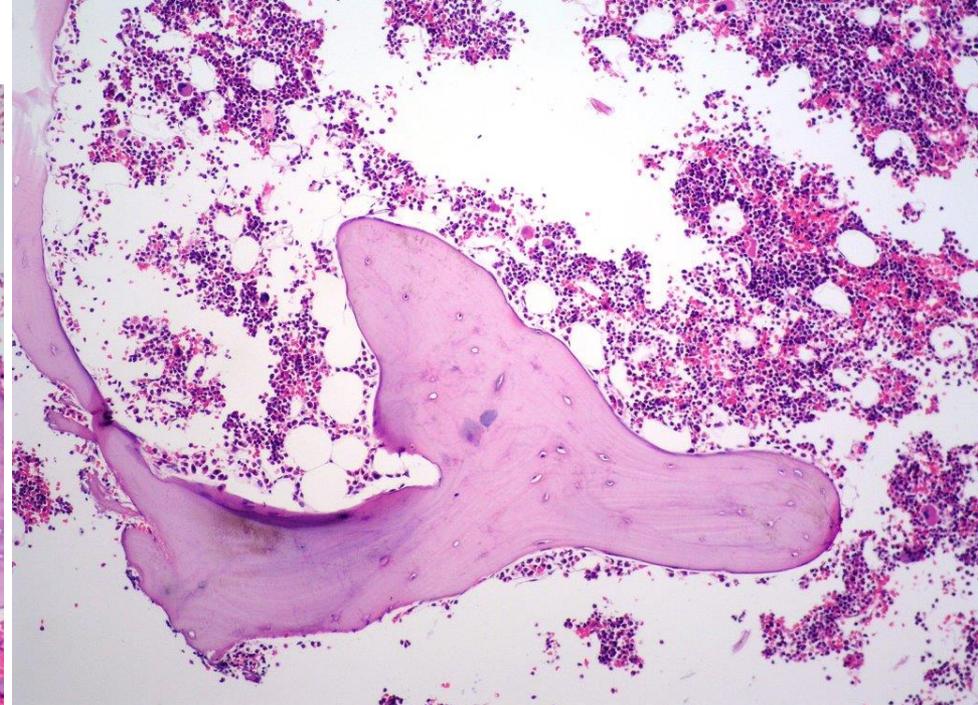
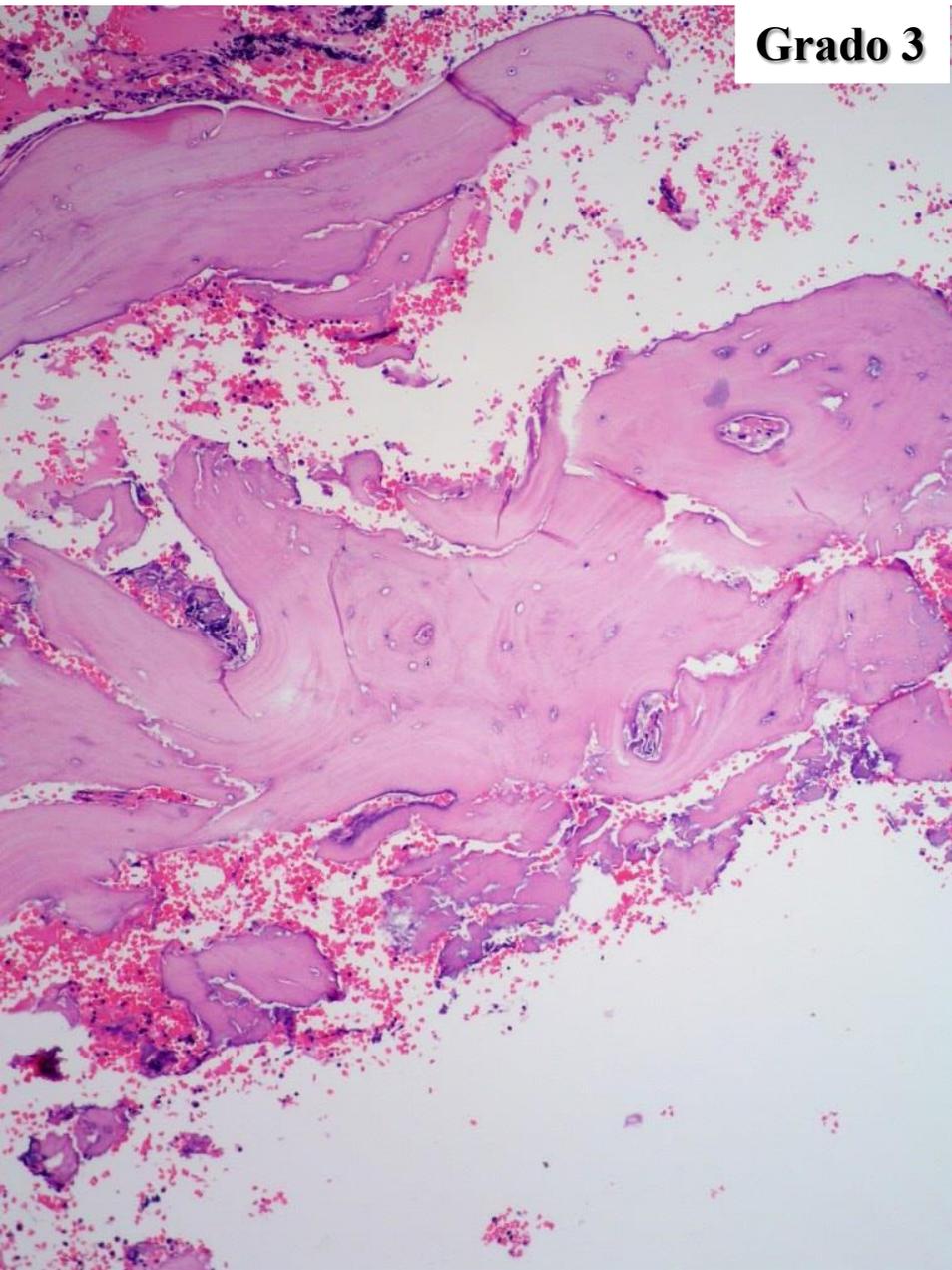
Células de pseudo Gaucher. (Leucemia Mieloide Crónica)

CD68

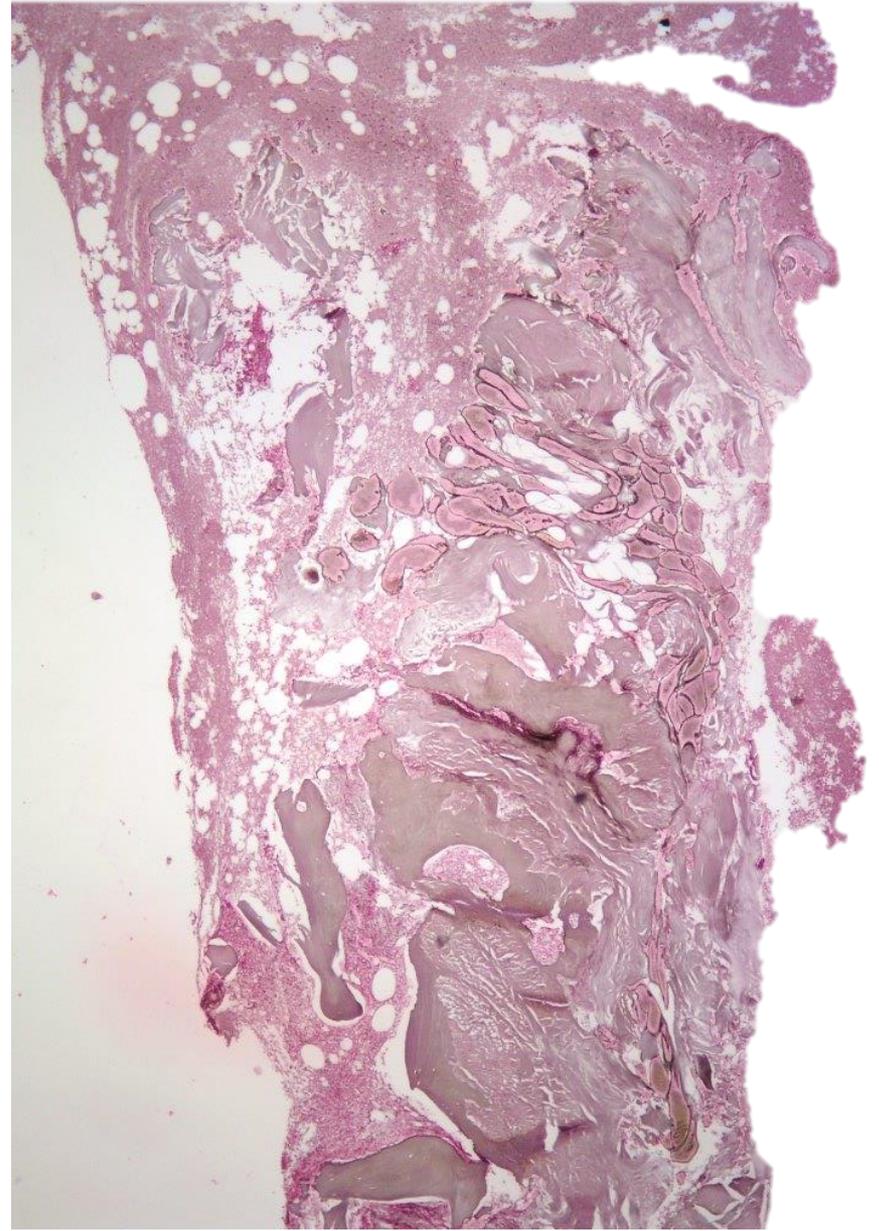
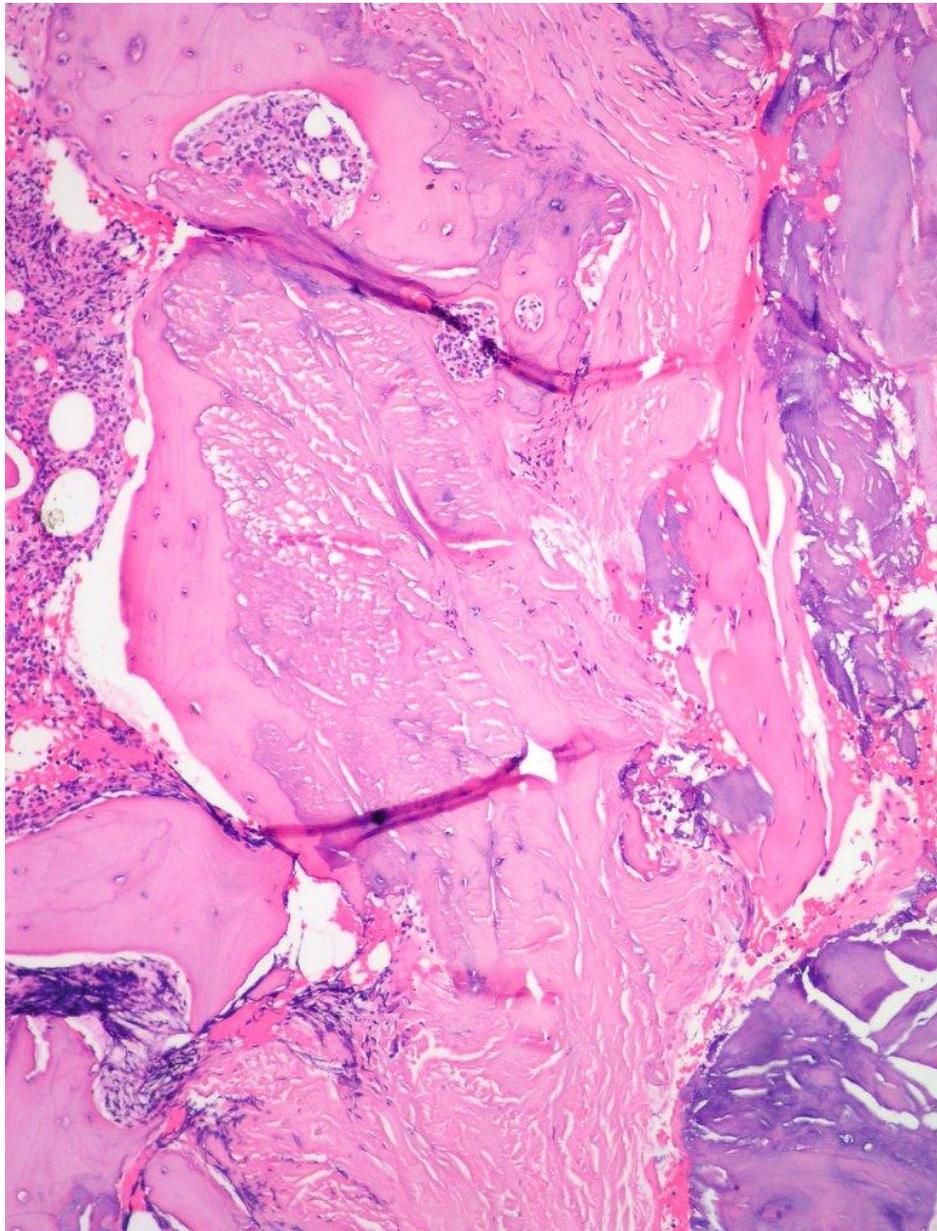


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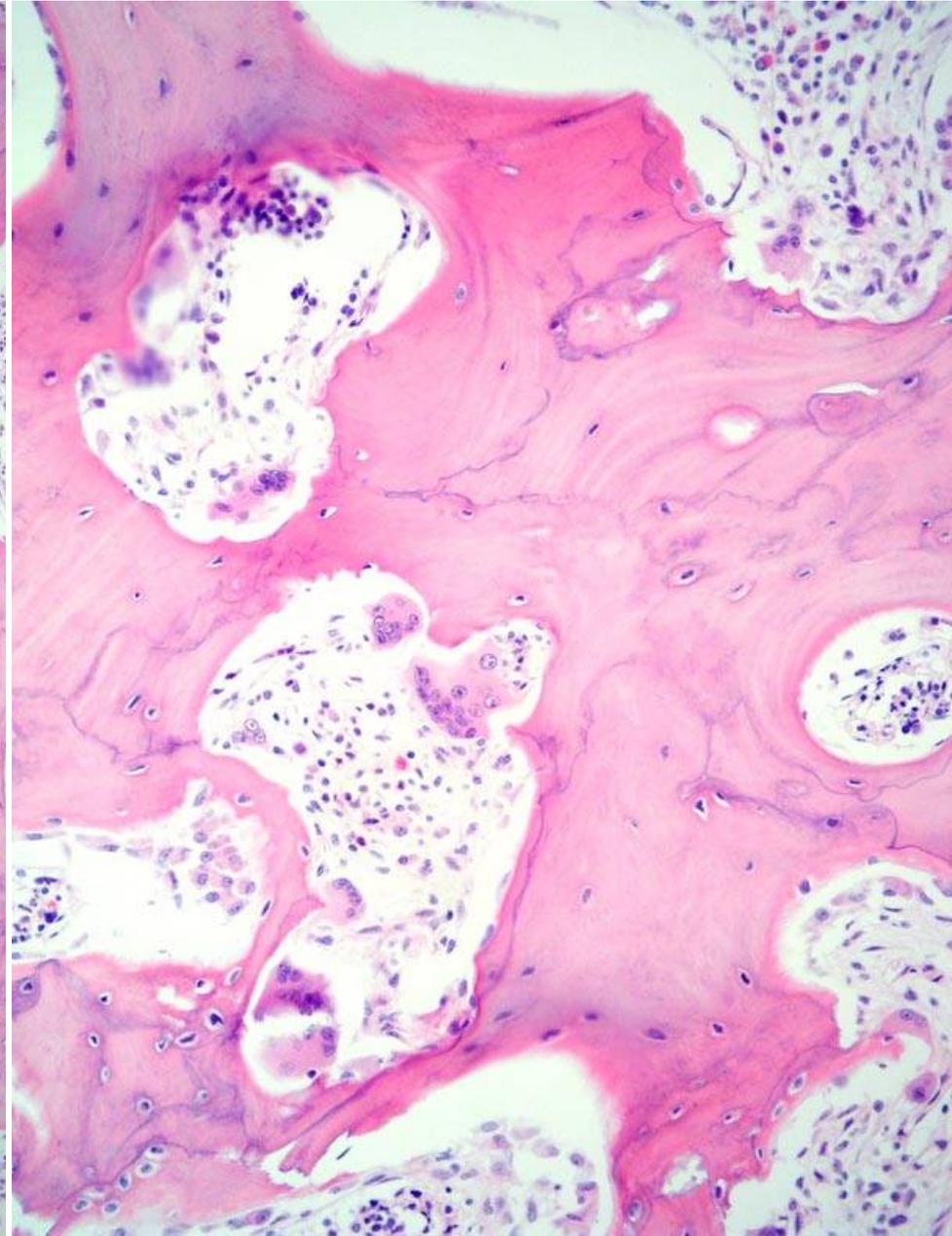
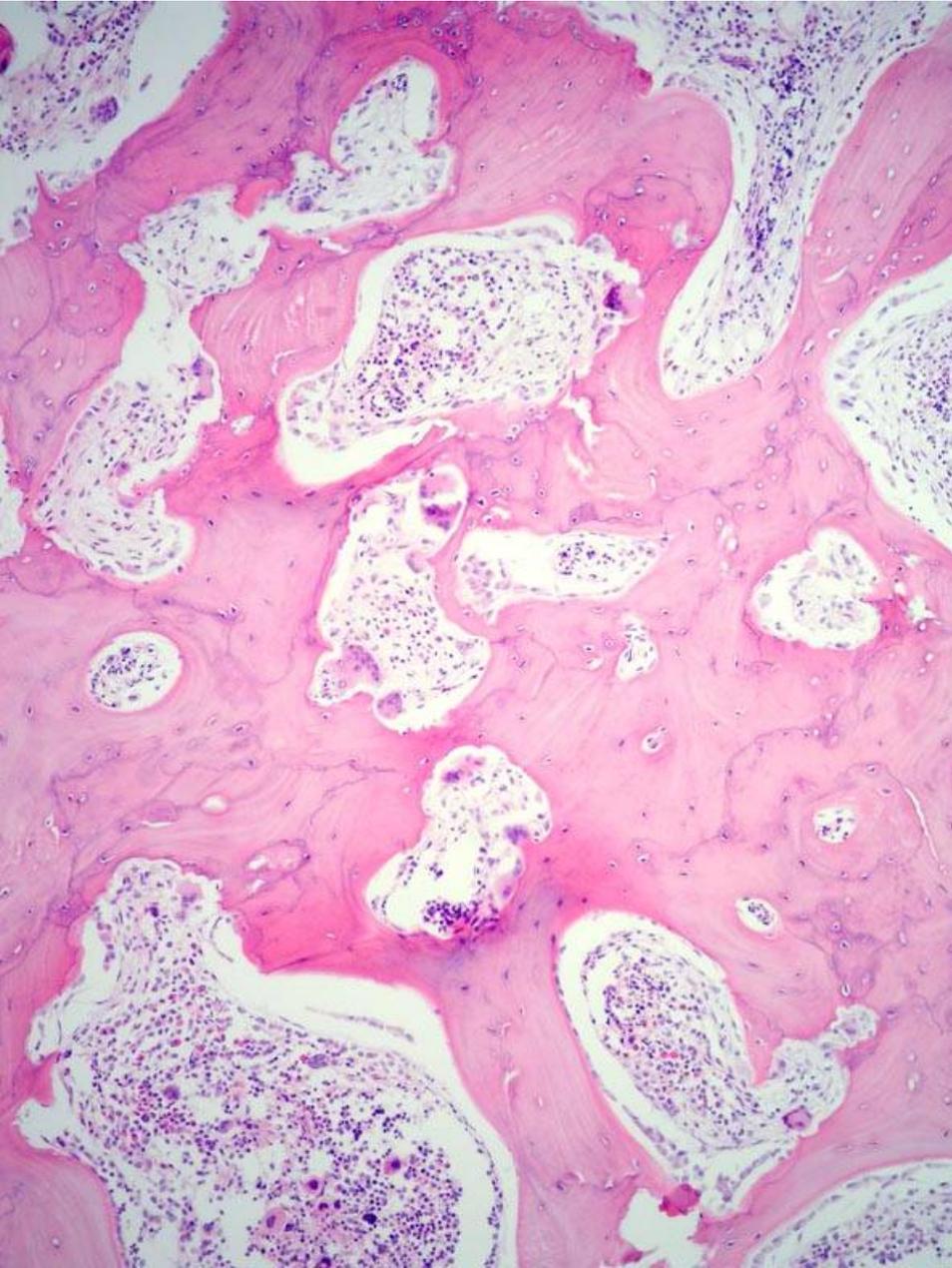




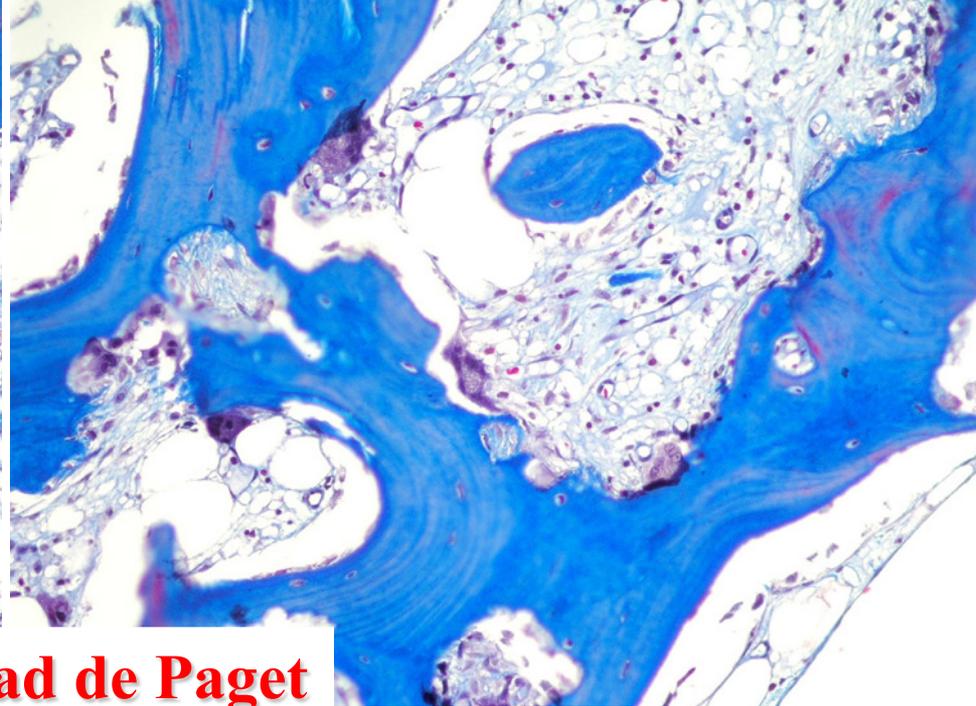
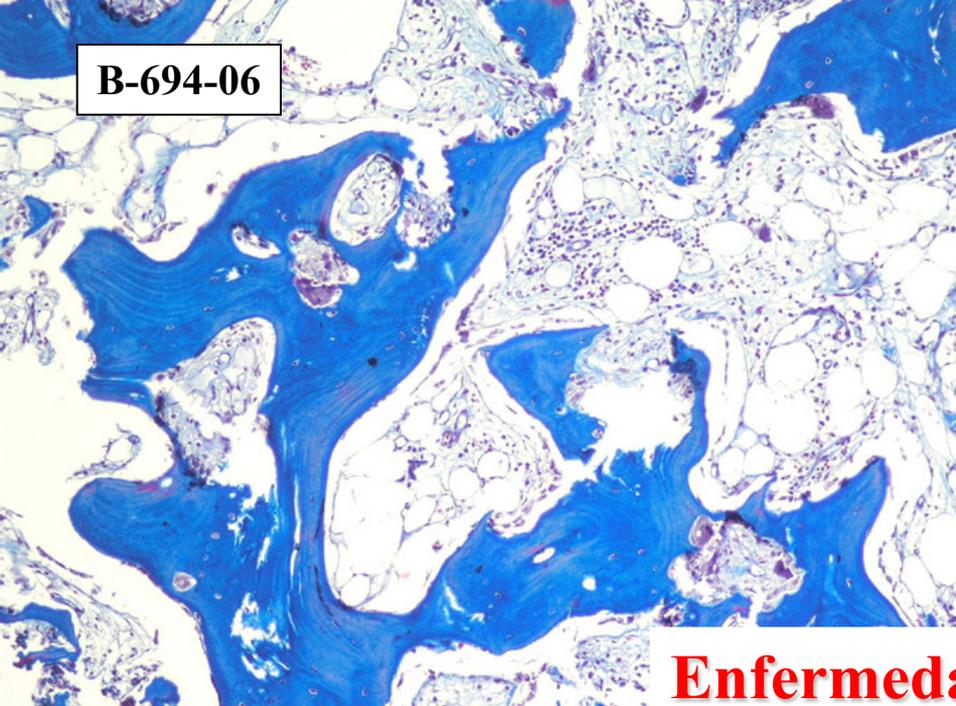
OSTEOESCLEROSIS



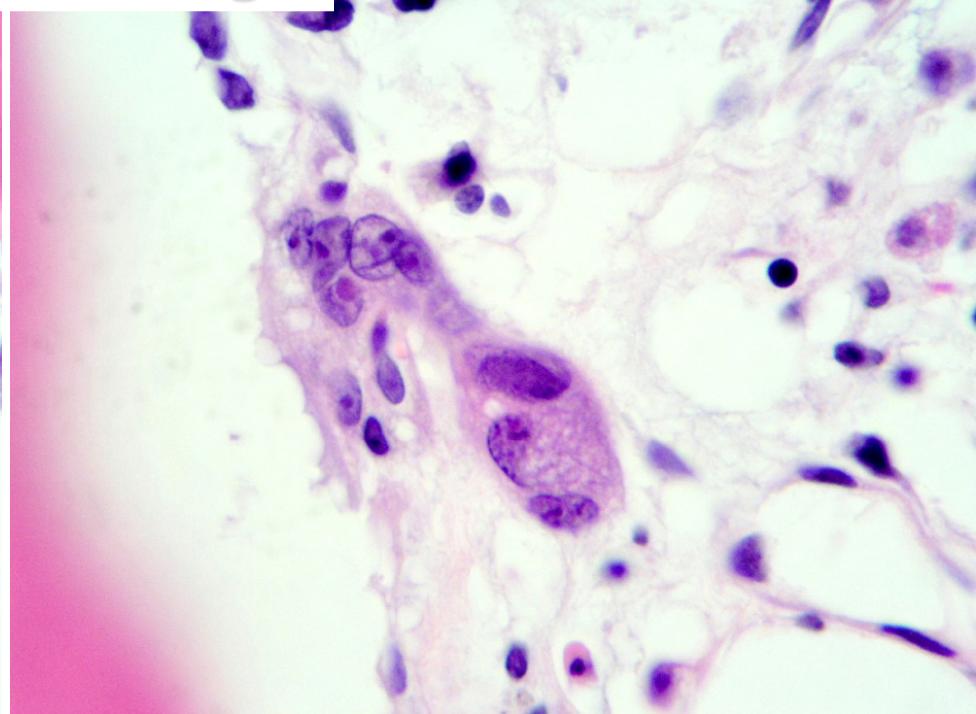
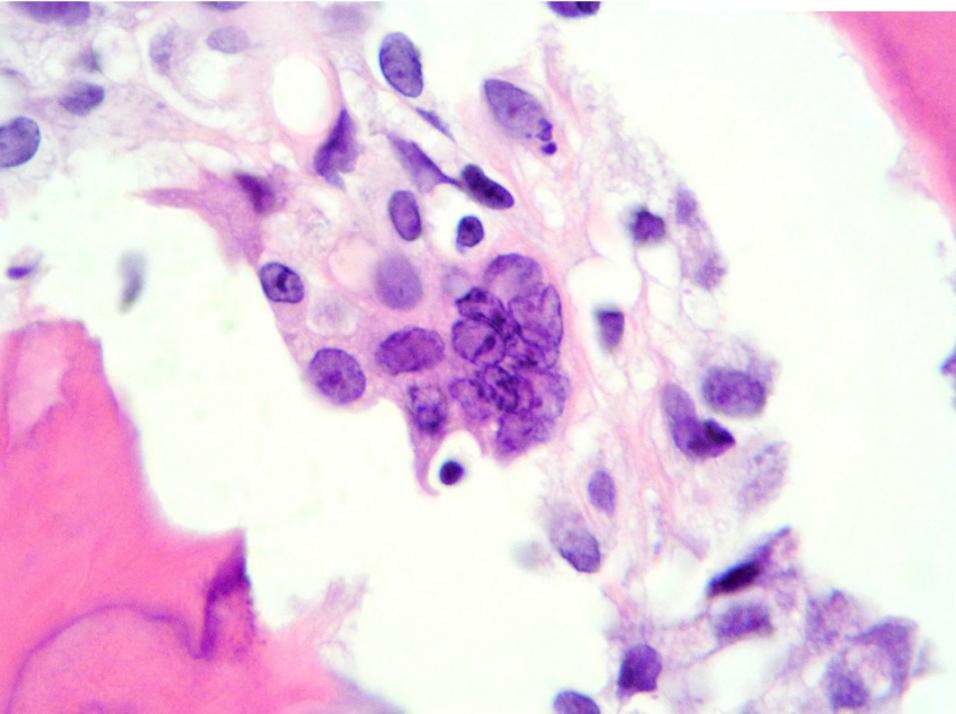
Enfermedad de Paget



B-694-06



Enfermedad de Paget



NEOPLASIAS MIELOPROLIFERATIVAS

Dra. Mónica A. Carrera Álvarez

NMP

- DESORDENES EN EL GEN DE LA TIROSIN CINASA
 - LMC BCR-ABL POSITIVA
 - LNEUTROFILICA CRONICA
 - POLICITEMIA VERA
 - MIELOFIBROSIS PRIMARIA
 - TROMBOCITEMIA ESENCIAL
 - LEUCEMIA EOSINÓFILICA CRÓNICA NOS
 - MASTOCITOSIS
 - NEOPLASIA PROLIFERATIVA NO CLASIFICABLE

LMC BCR-ABL1 POSITIVA

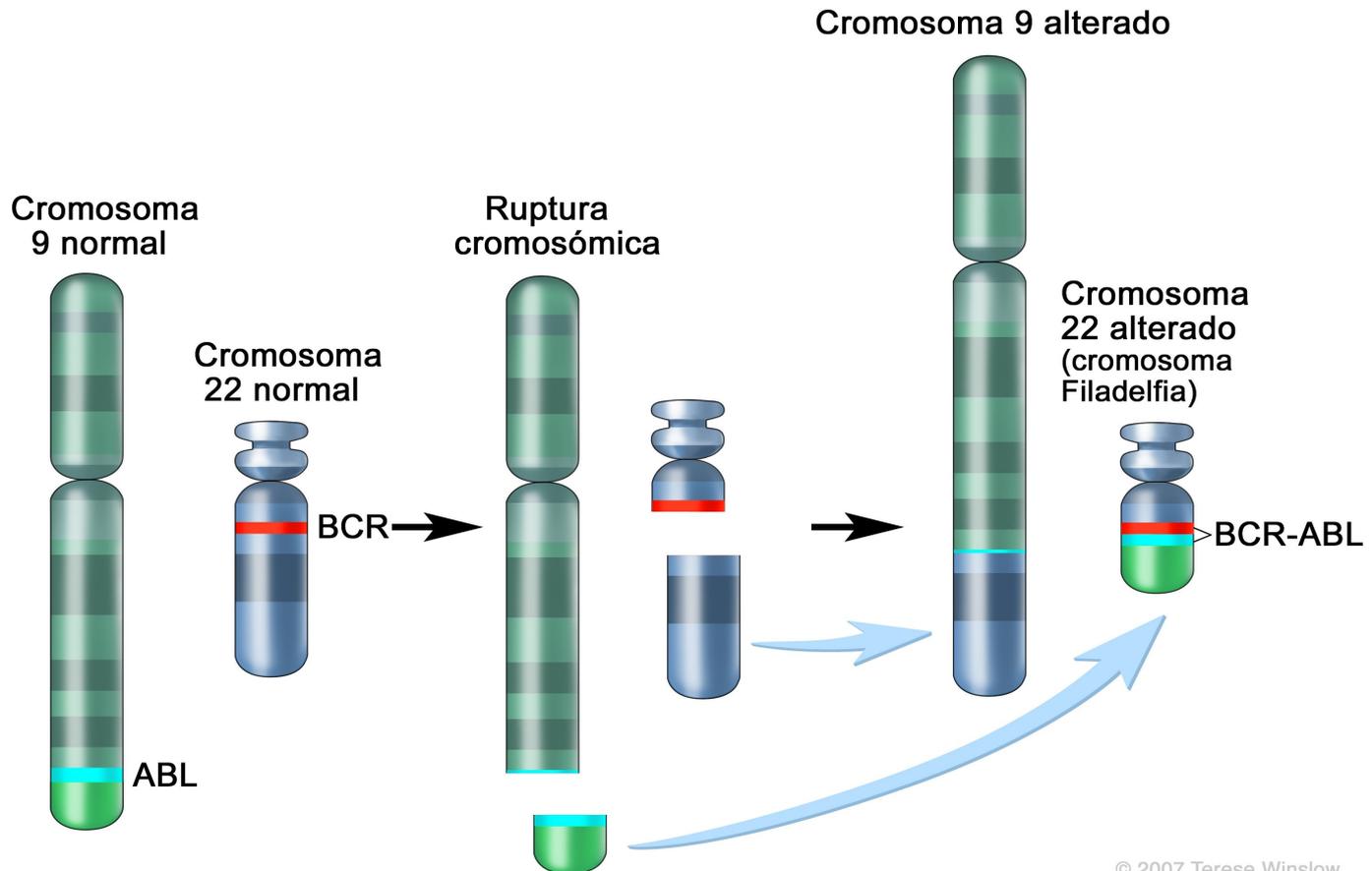
- Origen cel madre
- Proteína quim´wrica BCR-ABL BCR Cr 22 y ABL 9 (Cr Ph)
- Fase indolente
- Fase aguda
- Fase blástica
- Cinasa ABL – vías RAS, JAK/STAT y TC (granulocítica y megacariocítica)

LMC BCR-ABL1 POSITIVA

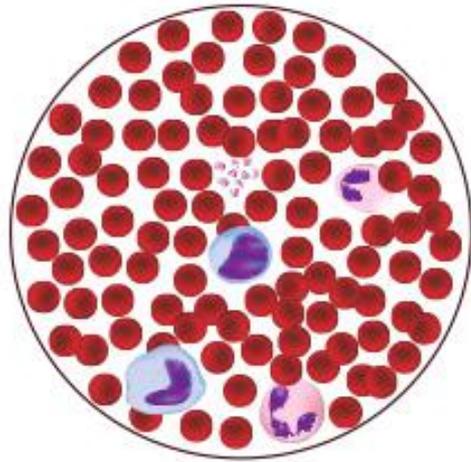
- Fase crónica.- Limitado a MO
- Fase blástica infiltra H, B GL, Piel y TB
- 40% asintomáticos
- 60% fatiga, perdida peso, diagoresis nocturna, esplenomegalia, trombocitopenia y anemia
- MO. Hiperplasia granulocítica, maduración similar en SP, eosinofilia, pocos blastos mieloides, FR. 20% mieloblastos y SP
- Bazo: cel pseudoGaucher
- Rp inhibidores de BCR-ABL1

Definición

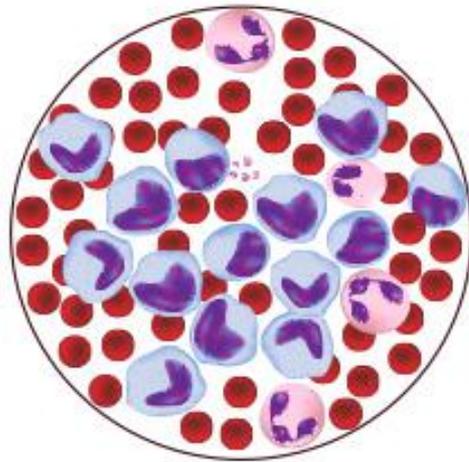
- Trastorno hematológico de la célula madre pluripotente asociado a una traslocación cromosómica específica.



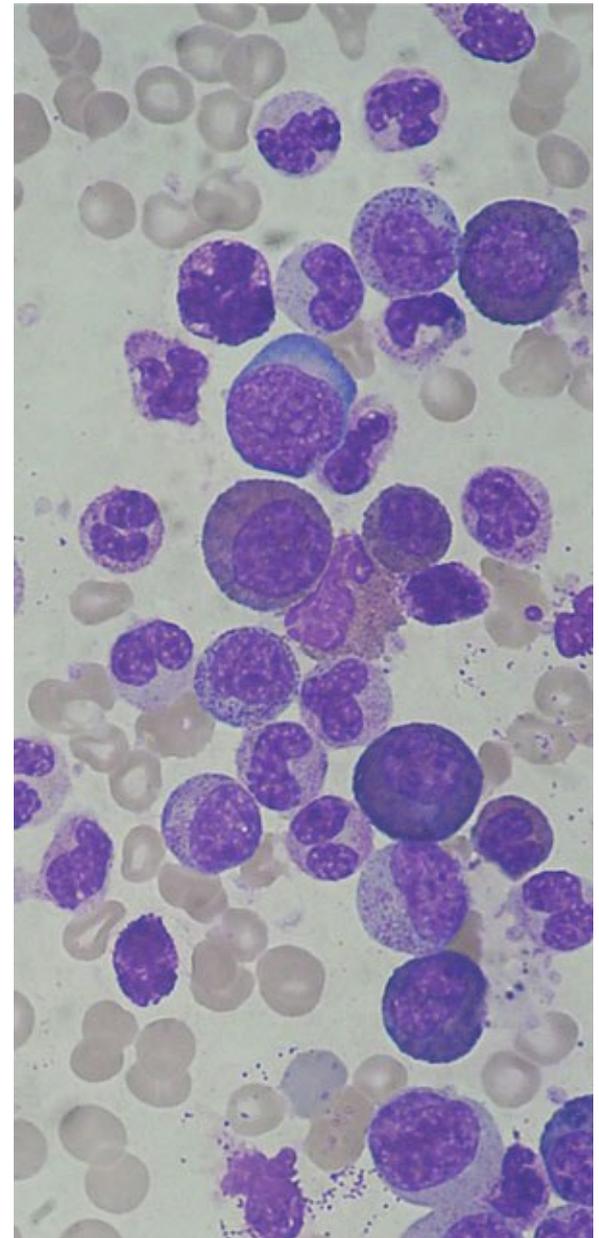
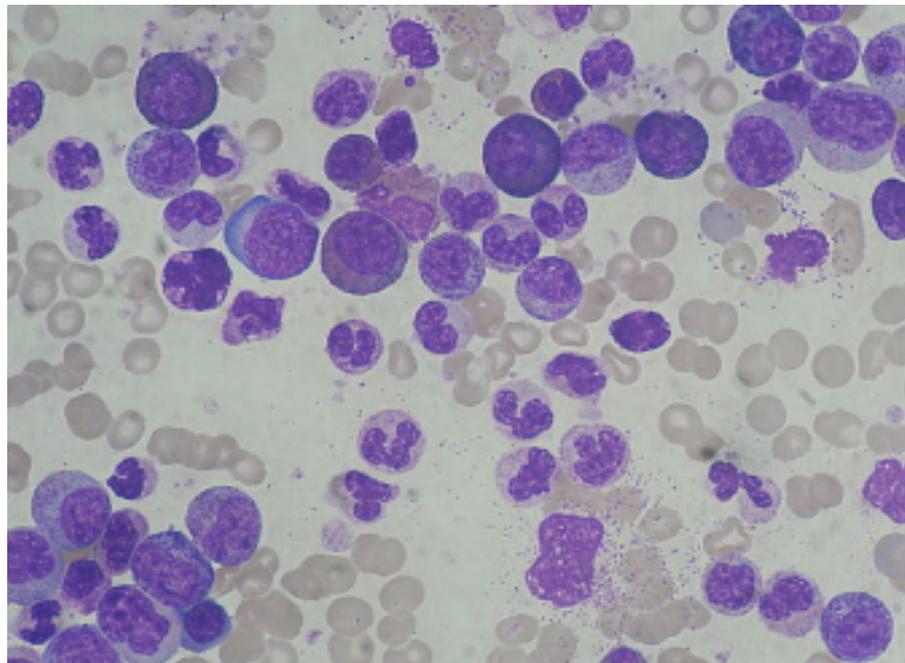
Sangre normal



Leucemia



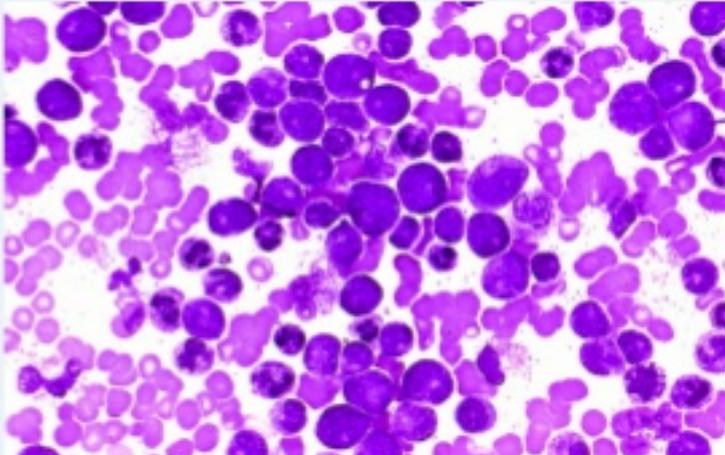
eritrocito neutrófilo limfocito monocito plaquetas



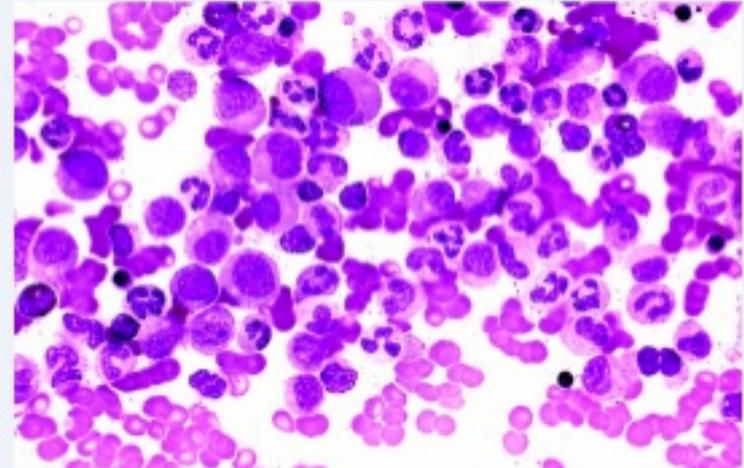
Leucemia neutrofílica crónica

- Neutrofilia periférica (mielocitos, promielocitos y metamielocitos)
- MO hipercelular
- Hepatoesplenomegalia
- Hemorragia gingival y TD de repetición.

Leucemia Mieloide Crónica



Leucemia Neutrofílica Crónica

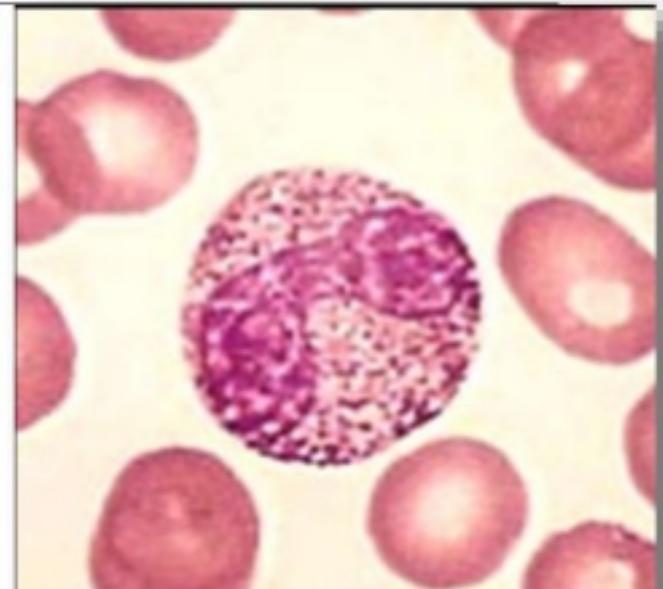


LEUCEMIA NEUTROFÍLICA CRÓNICA

Es un raro trastorno caracterizado por la proliferación granulocítica madura en sangre, médula ósea y la infiltración en los órganos que resultan en hepatoesplenomegalia.

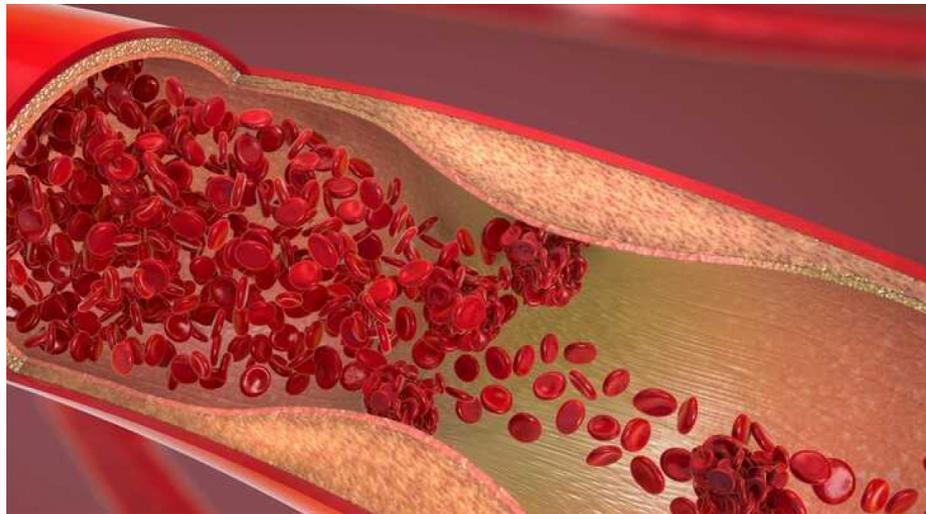
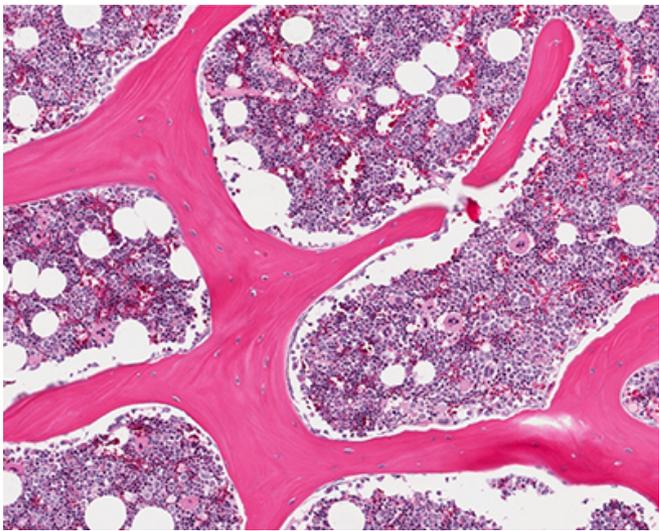
Existen granulaciones tóxicas en los neutrófilos, hipersegmentación nuclear y aumento de la fosfatasa alcalina.

Un subconjunto de pacientes demuestra mutaciones puntuales en el gen *CSF3R*, que codifica el receptor para CSF3, regulación de la producción de neutrófilos.



POLICITEMIA VERA

- Aumento en la producción de eritrocitos (mecanismos distintos)
- FASE AVANZADA: Panmielosis
- Mutación JAK2
- Etiología desconocida (predisposición genética)
- Afecta MO solo (puede irse a Sist FM)
- Alteraciones por las anomalías vasculares por aumento de eritrocitos
- MO hiper celular con aumento de las 3 series
- Estadios avanzados MF grado 1 o 2

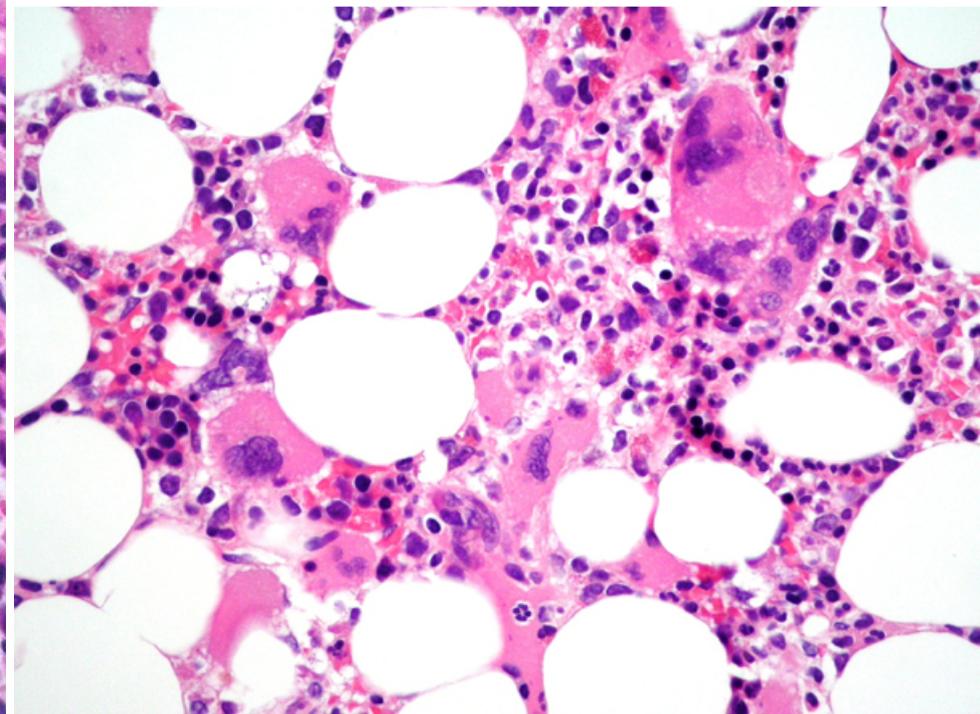
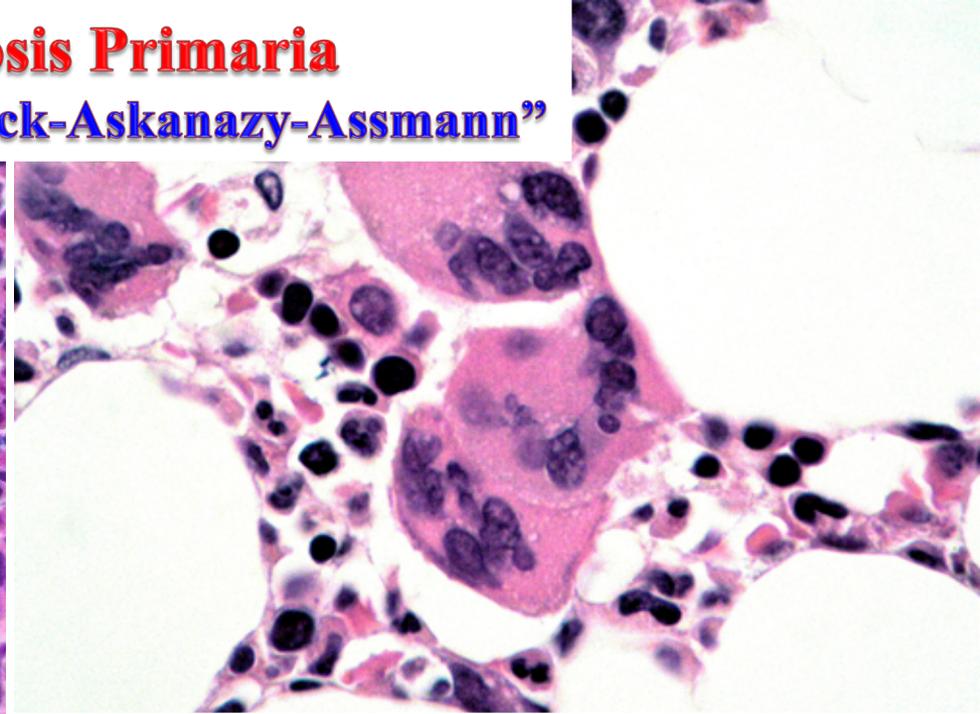
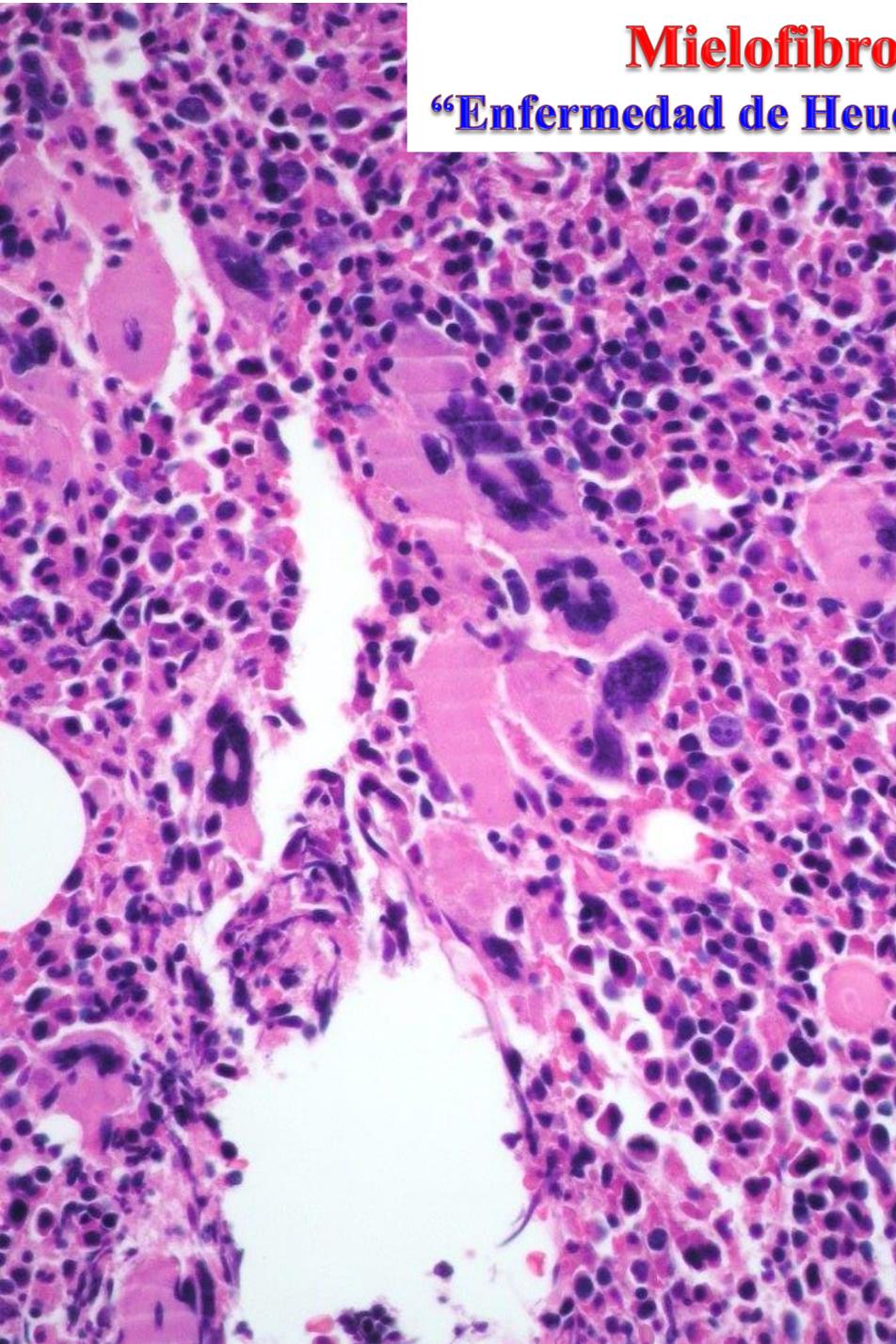


MIELOFIBROSIS PRIMARIA

- Proliferación de megacariocitos y granulocitos de la MO asoc a MF y Hematopoyesis extramedular
- 50% mutaciones de JAK2
- 1/3 asintomaticos
- La > al momento del Dx con esplenomegalia, anemia, leucocitosis y trombocitosis
- MO con MF extensa
- Megacariocitos displásicos y se disponen en grupos
- Hematopoyesis en bazo e hígado

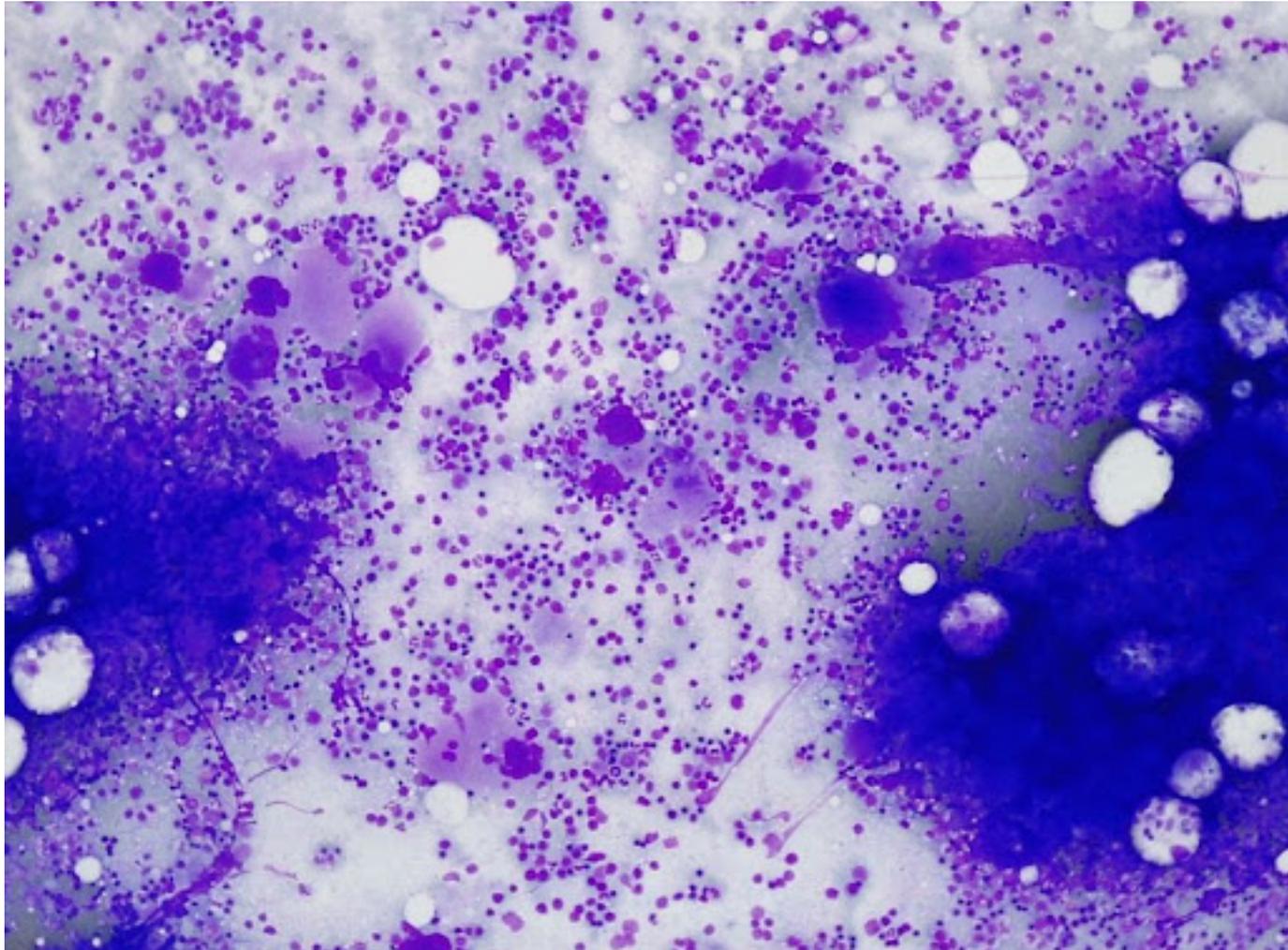
Mielofibrosis Primaria

“Enfermedad de Heuck-Askanazy-Assmann”

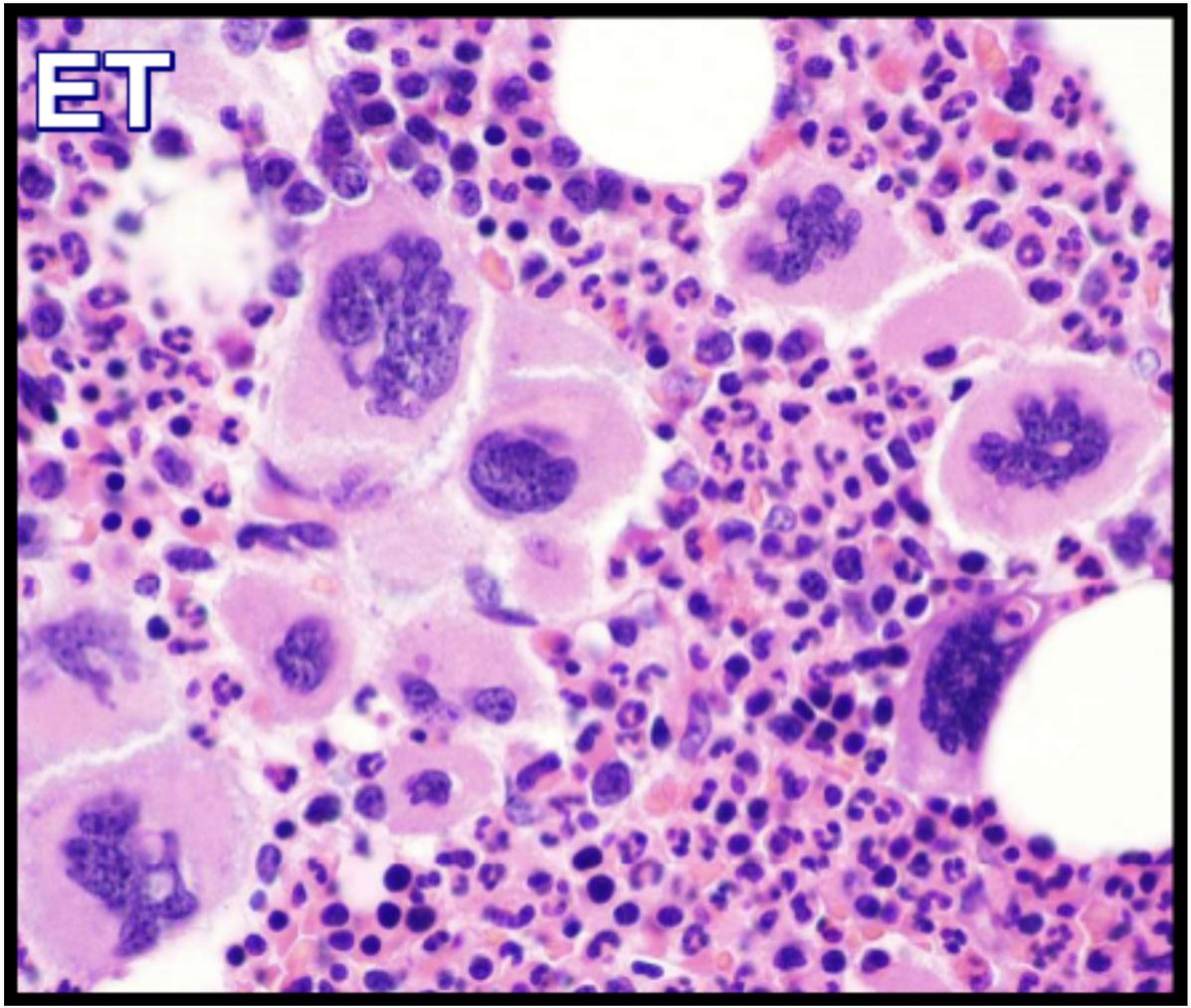


TROMBOCITEMIA ESCENCIAL

- Afección de serie megacariocítica
- Trombocitosis en SP (>450 mil PLT)
- Aumento de megacariocitos maduros en MO
- La >asintomáticos (hallazgo por trombocitemia periférica)
- Alt vasculares, hepato y esplenomegalia
- MO aumento en numero de megacariocitos que pueden ser displasicos y en SP PLT displásicas
- 50% de los pacientes pueden presentar alt JAK2

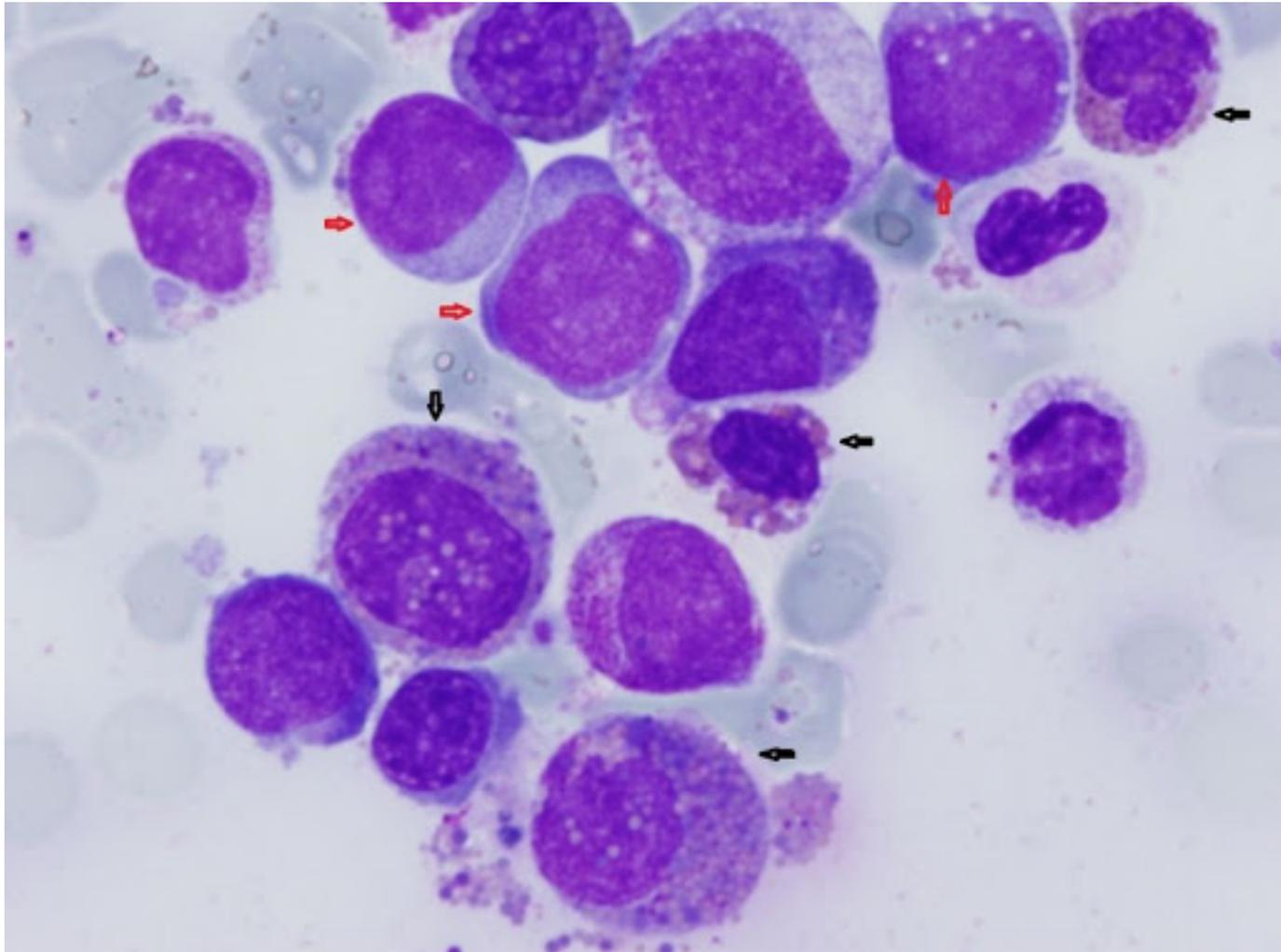


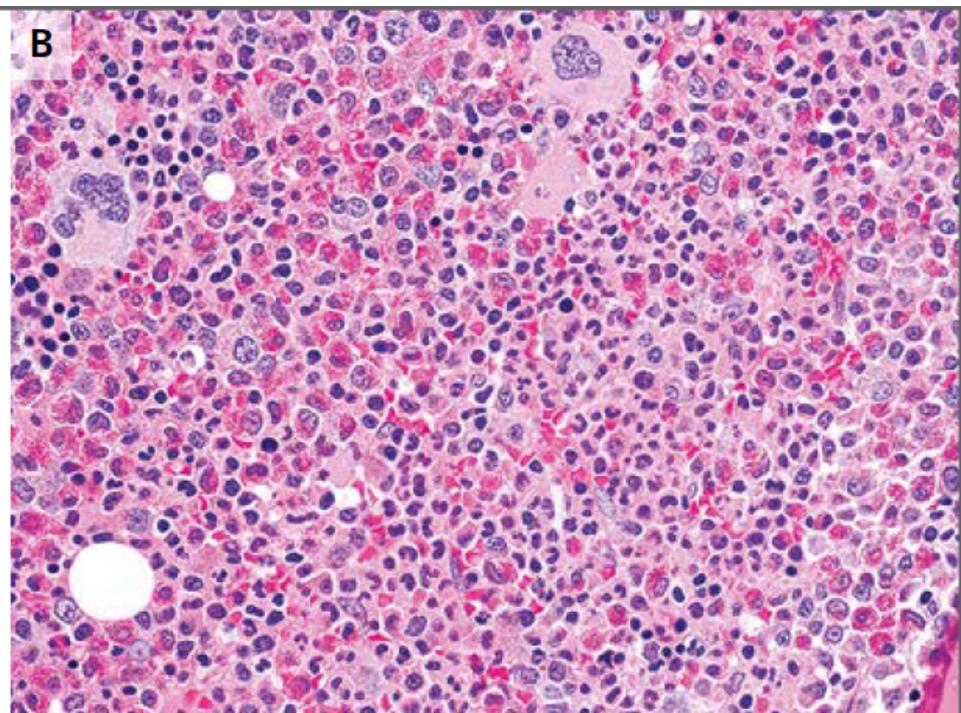
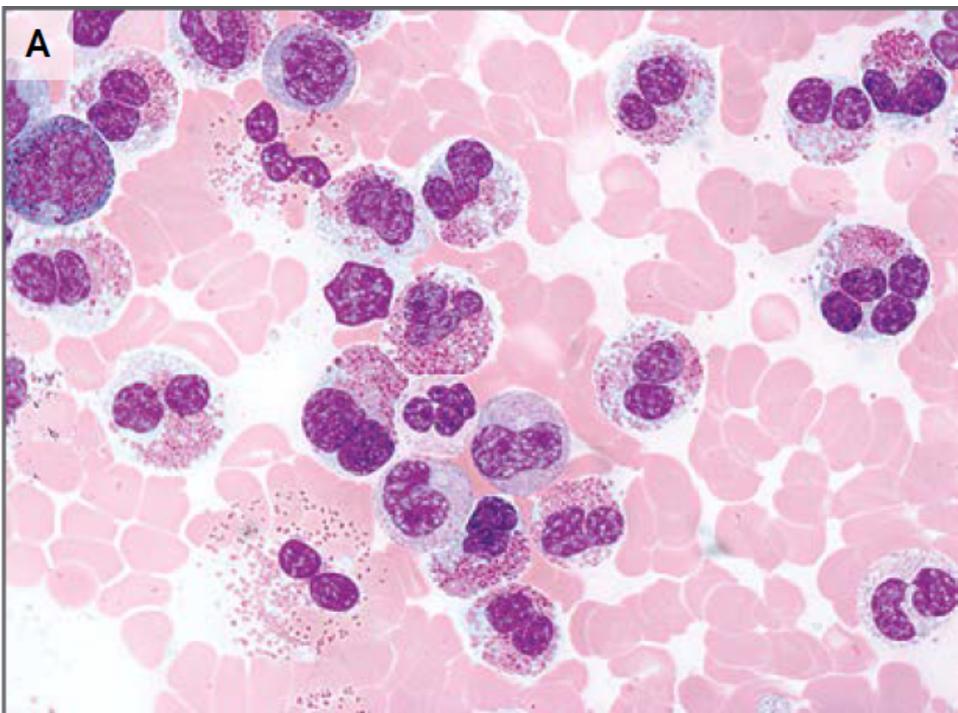
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Leucemia eosinofílica crónica NOS

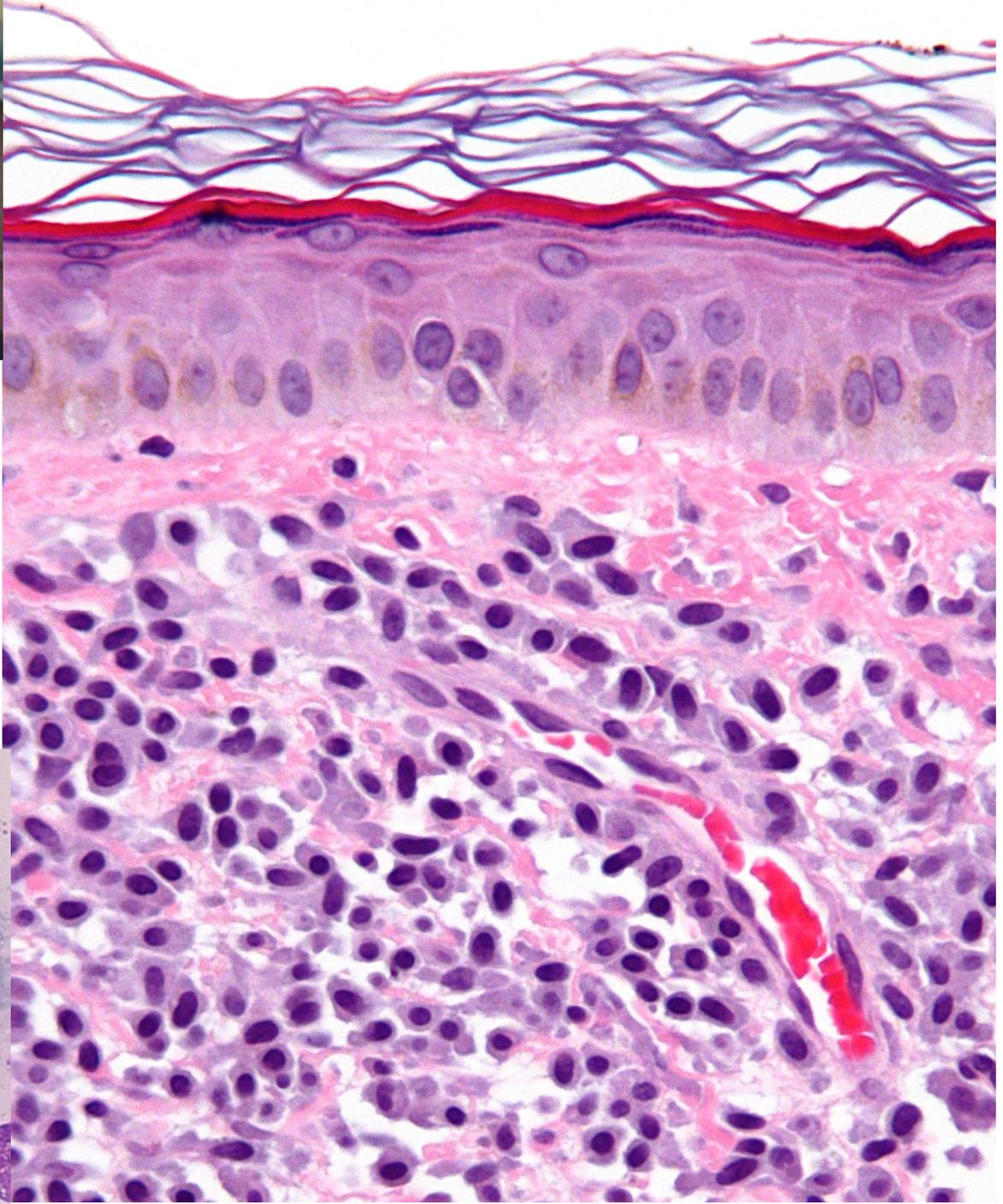
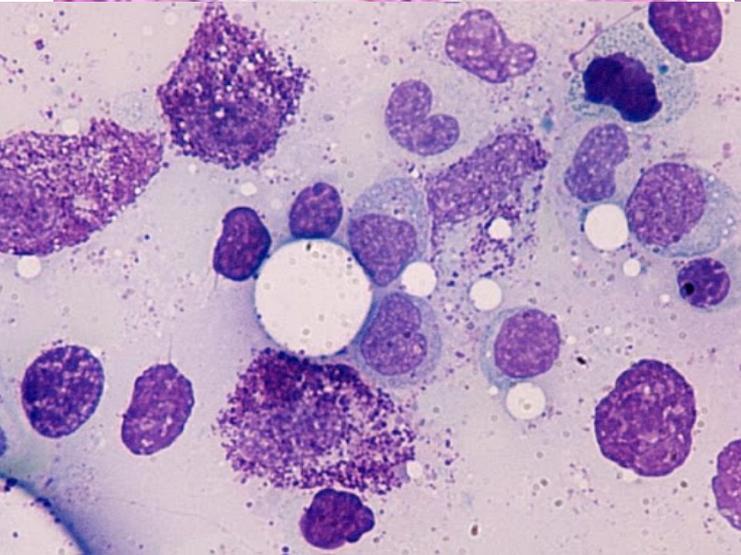
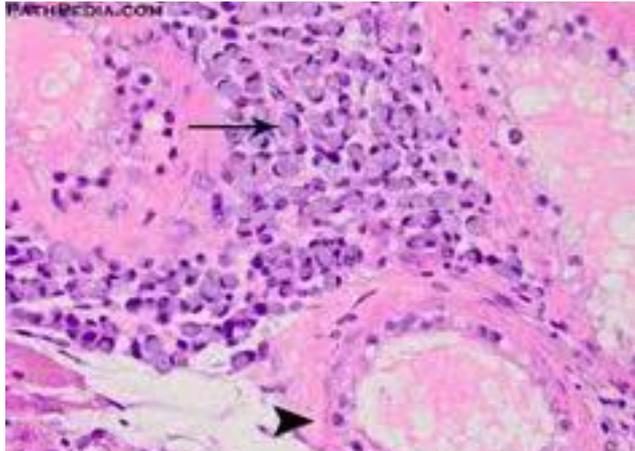
- Proliferación clonal de precursores de eosinófilos con eosinofilia periférica, tisular y medular
- Dx de exclusión por lo que se debe buscar reordenamiento de PDGFRFA, PDGFRB o FGFR1





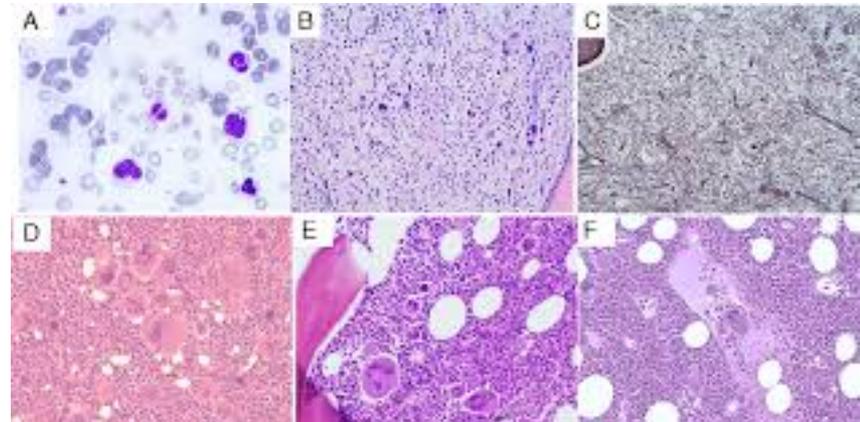
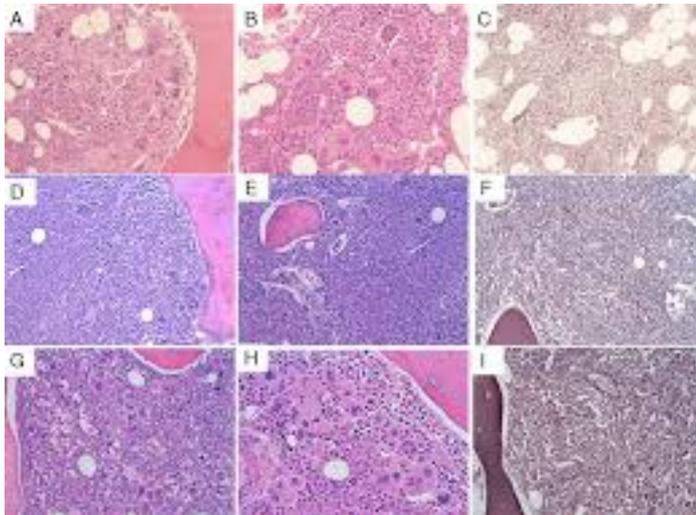
MASTOCITOSIS

- Proliferación neoplásica clonal de mastocitos
- Acumulo en uno o mas órganos
- Mutación puntual en KIT
- Piel o mutisistémica
- Cualquier edad (mas en niños)
- Afecta MO, piel, bazo, hígado y TD
- Anemia, leucocitosis, eosinofilia, neutropenia y trombocitopenia
- Puede evolucionar a Sarcoma o Leucemia de cell mastocíticas
- Dx demostrar las céulas neoplásicas



NEOPLASIA PROLIFERATIVA NO CLASIFICABLE

- Casos en los que no es posible caracterizar una neoplasia mieloproliferativa específica



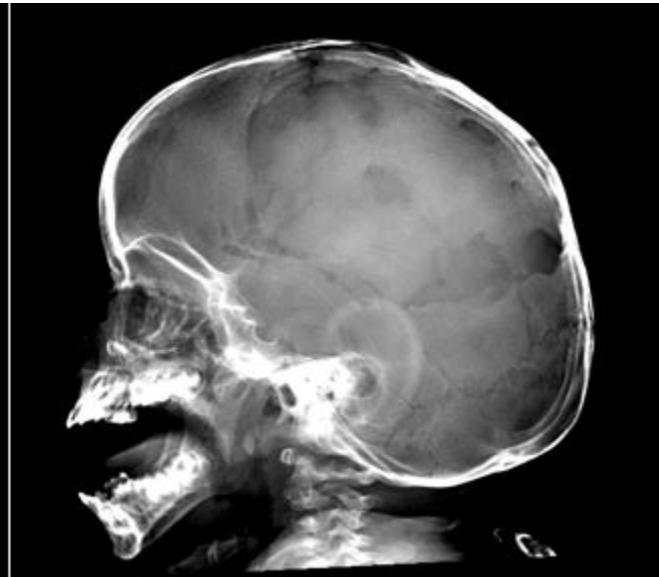
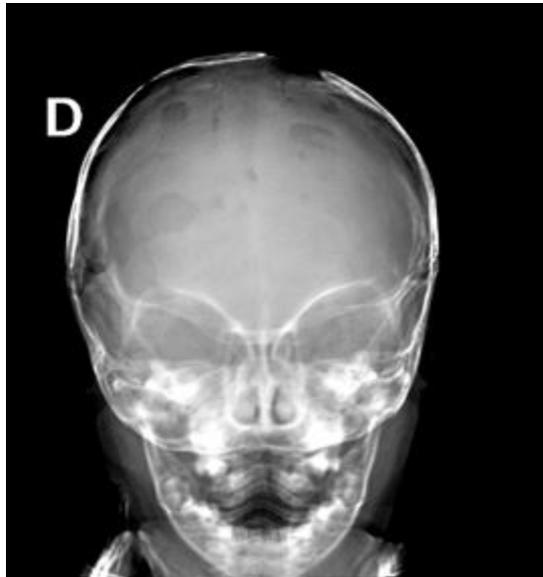
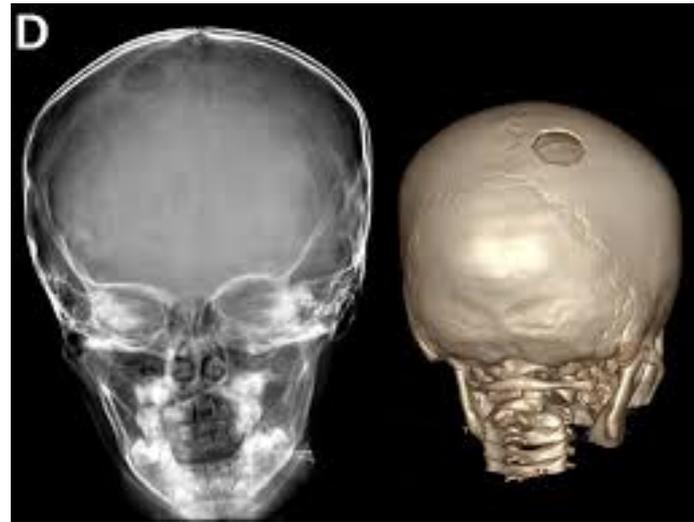
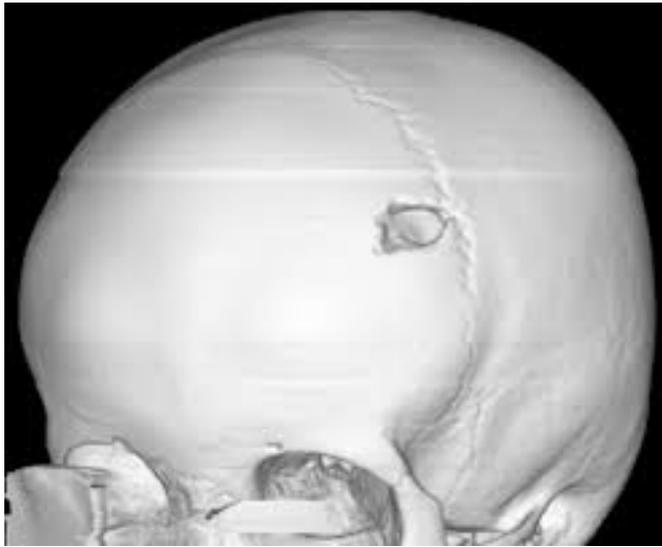
HISTIOCITOSIS DE CÉLULAS DE LANGERHANS

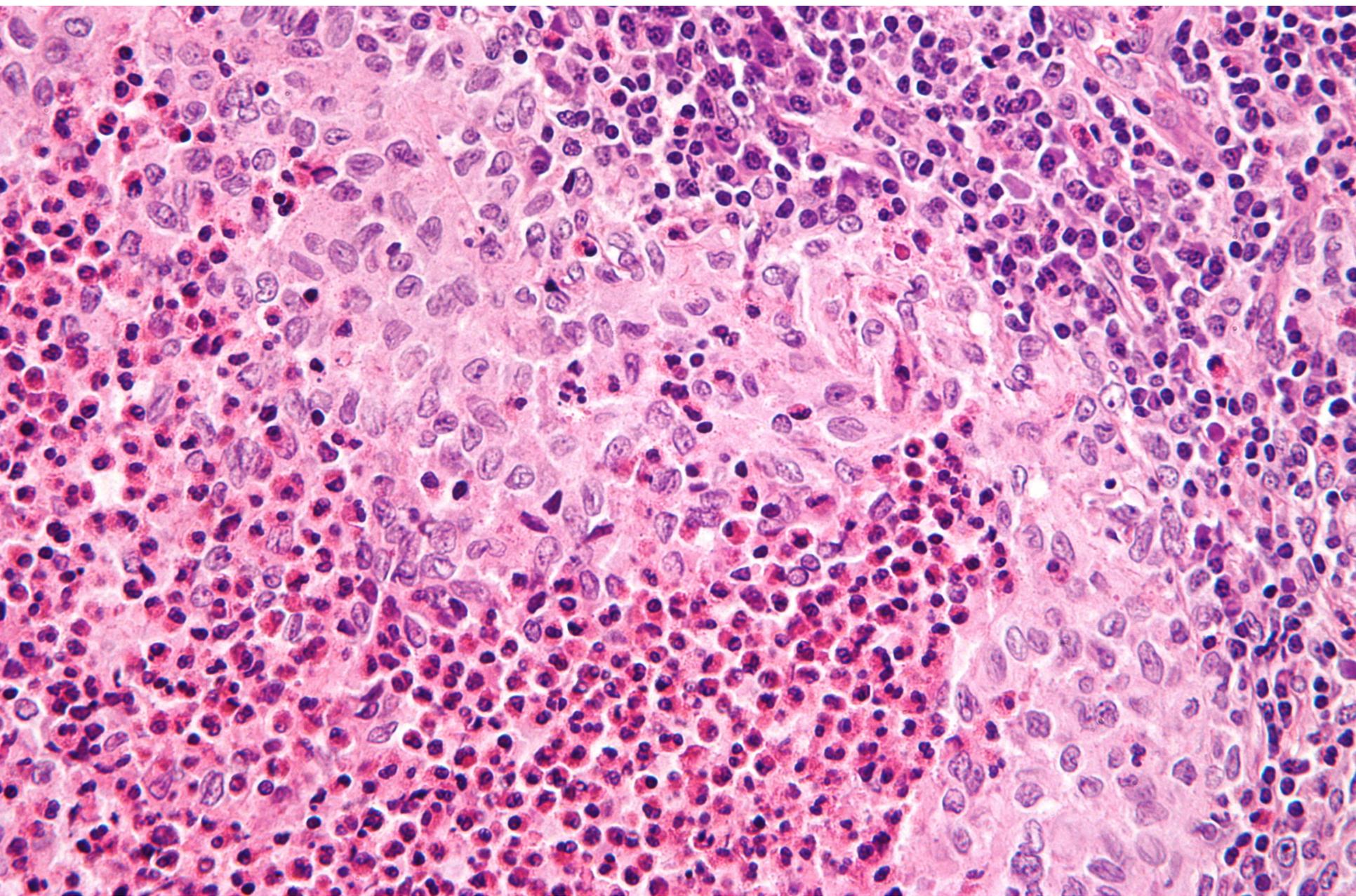
- Proliferación neoplásica clonal de células de Langerhans
- Multifocal: Hand-Schüller-Christian
- Visceral: Letterer-Siwe
- Lx solitarias= Granuloma eosinofílico
- Fcte en niños, adultos en pulmón fumadores
- Huesos del cráneo, vertebras y TB adyacentes. Hígado, bazo y GL

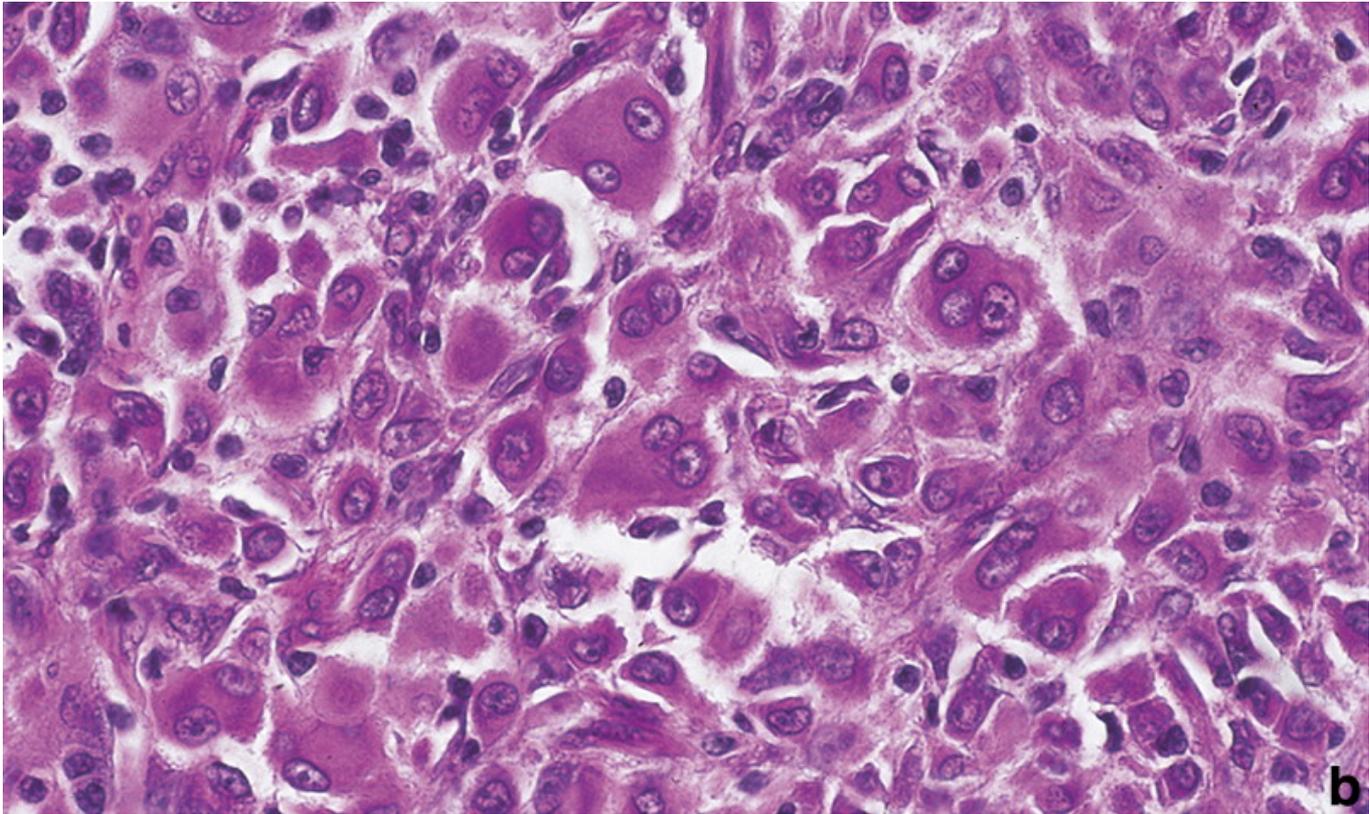
HISTIOCIDITIS DE CÉLULAS DE LANGERHANS

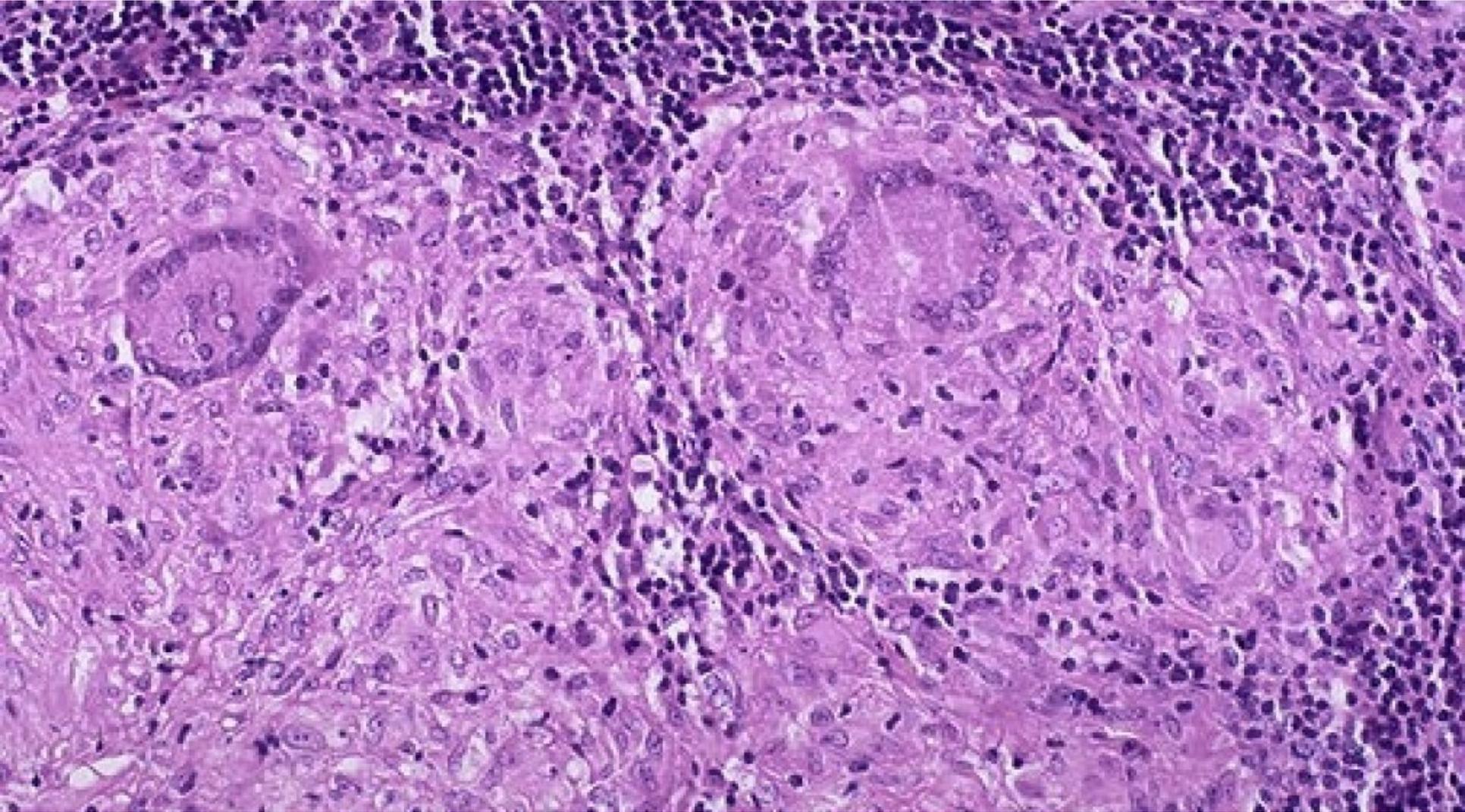
- Lx osteolíticas y citopenias
- Citoplasma amplio eosinófilo, núcleos en granos de café, lobulados y hendidos. Células gigantes multinucleadas tipo Touton y numerosos eosinófilos
- Dx morfológico. S-100, CD1a y Langerina
- Ultraestructura gránulos de Birbeck (cuerpos pentalaminares en forma de raqueta = invaginación de la membrana citoplasmática.)











SD. MIELODISPLÁSICOS

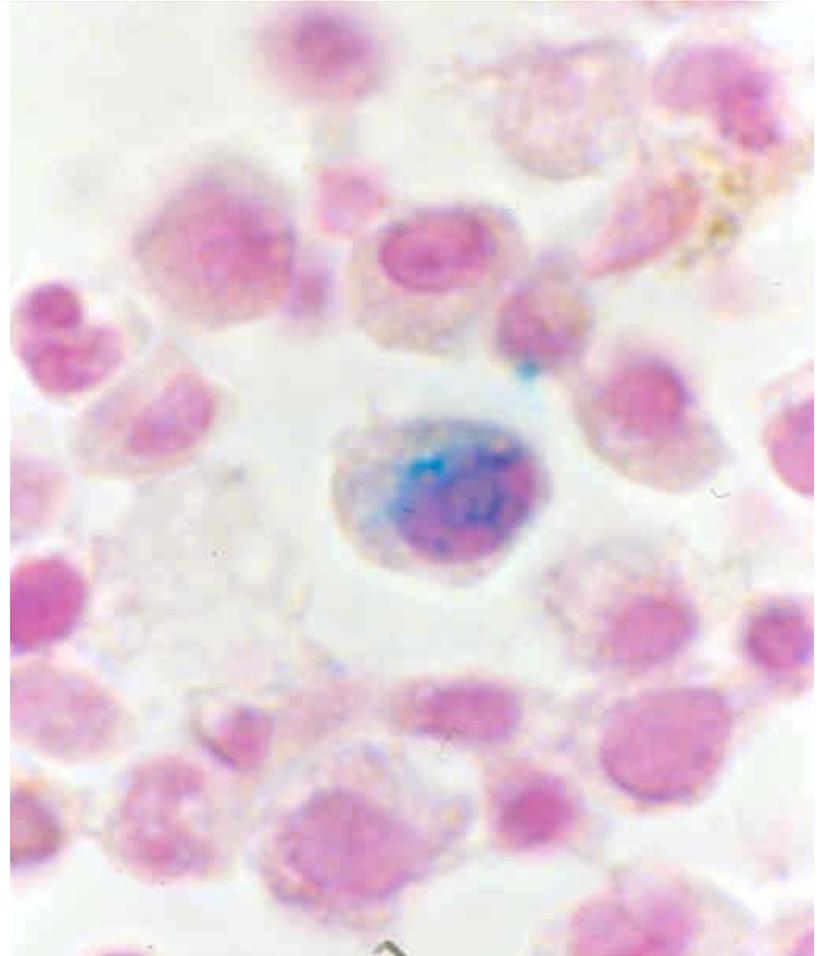
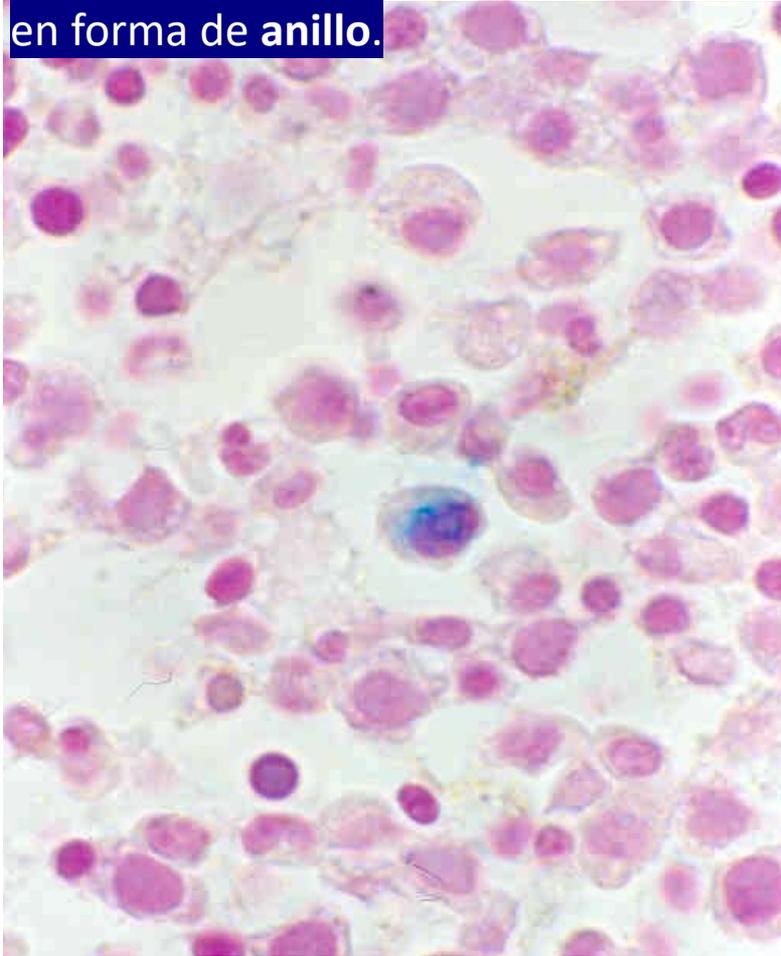
- Gpo. De enf. Hematopoyéticas (HTPY)clonales
- Displasia de una o mas líneas HTPY, HTPY inefectiva y riesgo aumentado de desarrollar LMA
- Ppalmente pacientes ancianos (70 años)
- Cuadro clínico e relación a la línea celular afectada
- Formas primarias (Sin predisponente)
- Forma secundaria (mielotóxicos, rx, becenos, citotóxicos etc)

SD. MIELODISPLÁSICOS

- Algunos Sd relacionados Anemia de Fanconi, disqueratosis congénita
- Clasificación en base a % de blastos en MO y SP, gdo. De displasia y presencia de sideroblastos en anillo

SIDEROBLASTOS EN ANILLO

Los sideroblastos son normoblastos como consecuencia de la acumulación de gránulos de hierro en los normoblastos, que toman una disposición circunnuclear en forma de anillo.



- 10 o más gránulos de hierro que rodean un tercio o más del núcleo

SD. MIELODISPLÁSICOS

- Citopenia refractaria con displasia de una sola línea
- Anemia refractaria con sideroblastos en anillo
- Citopenia refractaria con displasia multilínea
- Anemia refractaria con exceso de blastos
- Sd. Mielodisplásico con deleción aislada 5q
- Sd. Mielodisplásico no clasificable
- Sd. Mielodisplásico en niños

SD. MIELODISPLÁSICOS

- Dx en base a:
- Cuadro clínico
- Cambios displásicos en la MO (diseritropoyesis, disgranulopoyesis, dismegacariopoyesis)
- Se requiere la demostración de las alteraciones moleculares para su clasificación
- Rp de elección es trasplante de MO

Neoplasia de células plasmáticas

- Expansión de una clona secretora de Igs o fcos de Igs
- En gral una Ig monoclonal homogénea denominada paraproteína ó porteína M. = “Gammapatía monoclonal”
 - Plasmocitoma
 - Mieloma múltiple
 - Enf. De cadenas ligeras y pesadas
 - Amiloidosis primaria

MIELOMA MÚLTIPLE

- Neoplasia de cel plasmáticas multifocal asociada a presencia de proteína M en suero u orina
- Dx integral con hallazgos clínicos, pato y Rx
- 1% de todas la neoplasia malignas y 10-15% de las hematológicas
- Adultos promedio 50 años no niños, poco frecuente <30, >H 4:1
- Etiología poco clara (estímulo crónico y rx)

MIELOMA MÚLTIPLE

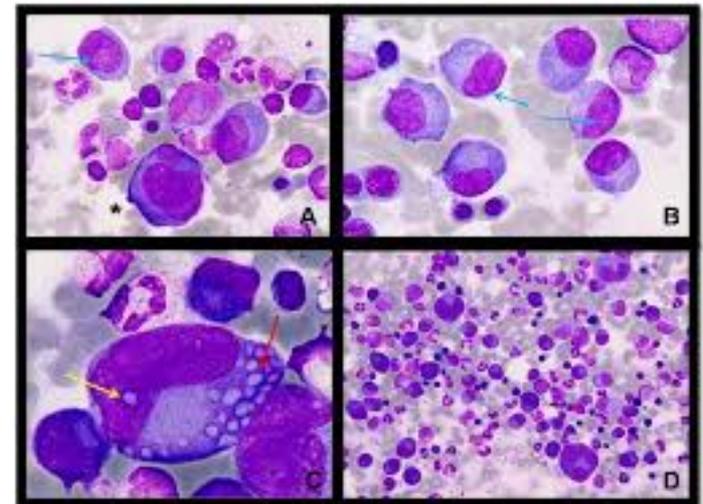
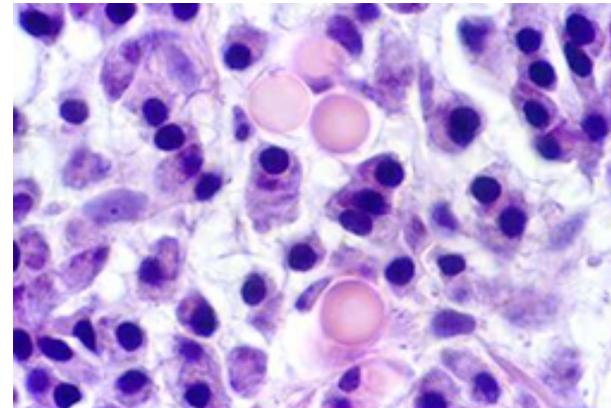
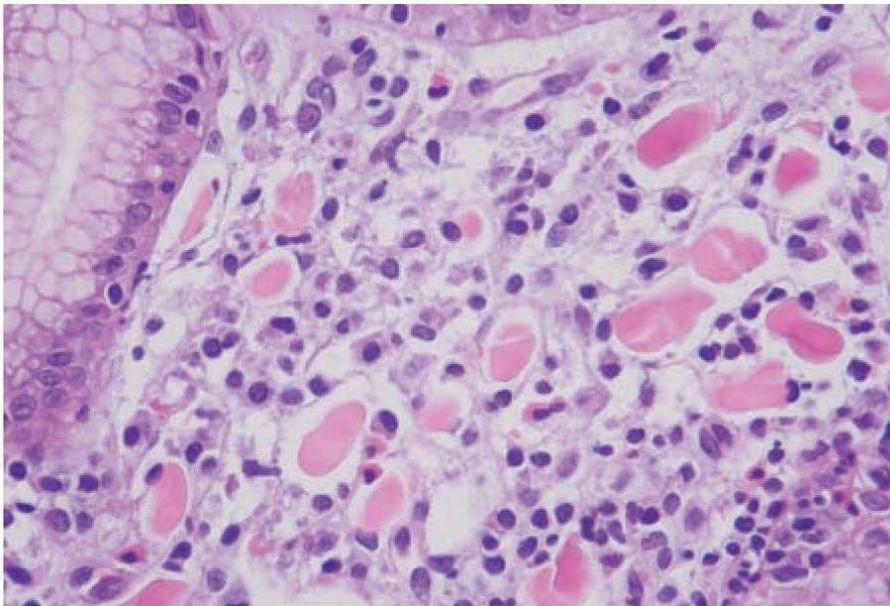
- Síntesis en exceso de cadenas ligeras o pesadas
- Ligeras liberan en orina = proteína de Bence-Jones (determinación diagnóstico) IR
- La > hipermutación somática de los genes de las Igs
- Algunos reordenamiento a genes Cr 14q32 y otras
- También Ciclinas D y lo más frecuente delección del Cr 13q

MIELOMA MÚLTIPLE

- Lx óseas, hipercalcemia, IR y anemia
- 70% Rx lesiones líticas, osteoporosis y fracturas patológicas
- Formas asintomáticas MM esclerosante, no hay proteína de Bence Jones (Mieloma no secretor) Celulas Plasmáticas SP >20% = Leucemia de células plasmáticas
- MO >30% de células plasmáticas, con o sin alteraciones morfológicas

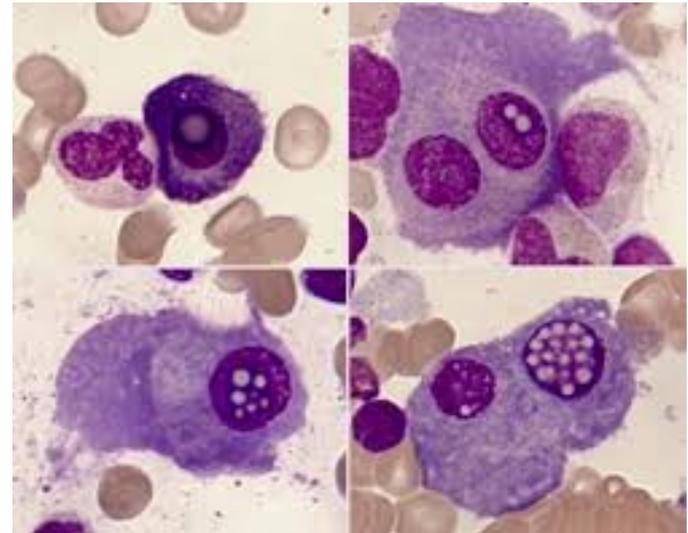
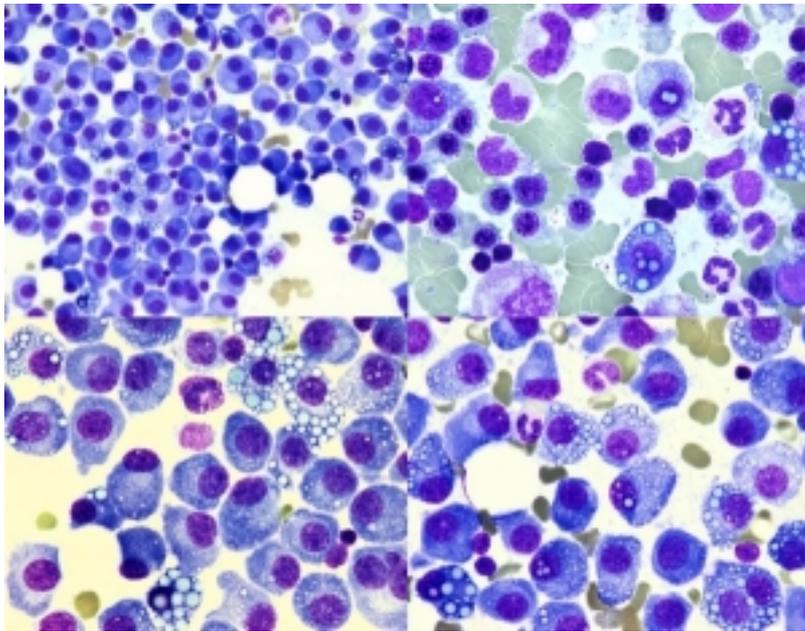
MIELOMA MÚLTIPLE

- Inclusiones citoplasmáticas cuerpos de Russell



MIELOMA MÚLTIPLE

- Inclusiones intranucleares cuerpos de Dutcher



MIELOMA MÚLTIPLE

- Puede infiltrar Hígado, bazo, pulmón, riñón, TB y GL
- Es incurable
- Mal px
- SV 4 a 6 años
- Rp con alquilantes, talidomida, esteroides, y transplante de MO es paliativo, solo prolonga el índice de SV pero no es curativo

PLASMOCITOMA SOLITARIO

- Lx única formada por células plasmáticas
- Intra o extraóseo
- Más vértebras, cráneo, fémur y clavícula, escápula y pelvis
- Extraósea orofaringe
- Similar a MM morfología
- Px excelente libre de enf a 10 años
- Rp con RT

LEUCEMIAS AGUDAS

- LMA
- Neoplasia maligna originada en progenitores hematopoyéticos
- Causada por mutación congénita adquirida que impide diferenciación y maduración
- Se acumulan en MO y sustituye a las normales

LEUCEMIAS MIELOIDES AGUDAS

- Múltiples alteraciones moleculares en genes que codifican factores de transcripción – diferenciación mieloide
- Síntomas de acuerdo a afección y serie más desarrollada
- Anemia, trombocitopenia, neutropenia
- Hemorragias recurrentes de encías, equímosis, petequias
- Susceptibilidad a infecciones sobre todo gramnegativas

LEUCEMIAS MIELOIDES AGUDAS

- MO hiperclular
- >20% de blastos
- Los remanentes hematopoyéticos son displásicos
- Mielofibrosis
- Presencia de sideroblastos en anillo
- Dx morfología y hallazgos de alteración molecular mediante citogenética, FISH y citometría de flujo
- Rp QT convencional y terapia epigenética. En pediátricos con Transplante de células madre

