

Eritropatías

Introducción

Gustavo Chiappe

Función sistema eritroide:

transportar O₂ a los tejidos

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Anemia (insuficiencia eritroide) Definiciones:

1) incapacidad de transportar O₂ a los tejidos para satisfacer sus requerimientos

Función sistema eritroide:

transportar O₂ a los tejidos

Anemia (insuficiencia eritroide) Definiciones:

- 1) **incapacidad de transportar O₂ a los tejidos para satisfacer sus requerimientos**
- 2) **Hb por debajo de valores normales para edad, sexo, raza, residencia** (\neq valores previos)

Función sistema eritroide:

transportar O₂ a los tejidos

Anemia (insuficiencia eritroide) Definiciones:

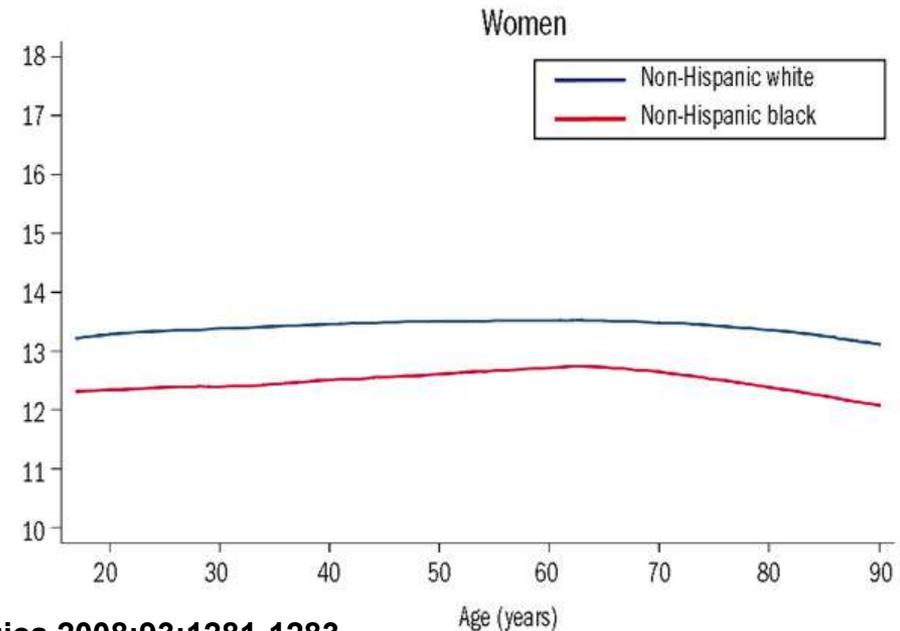
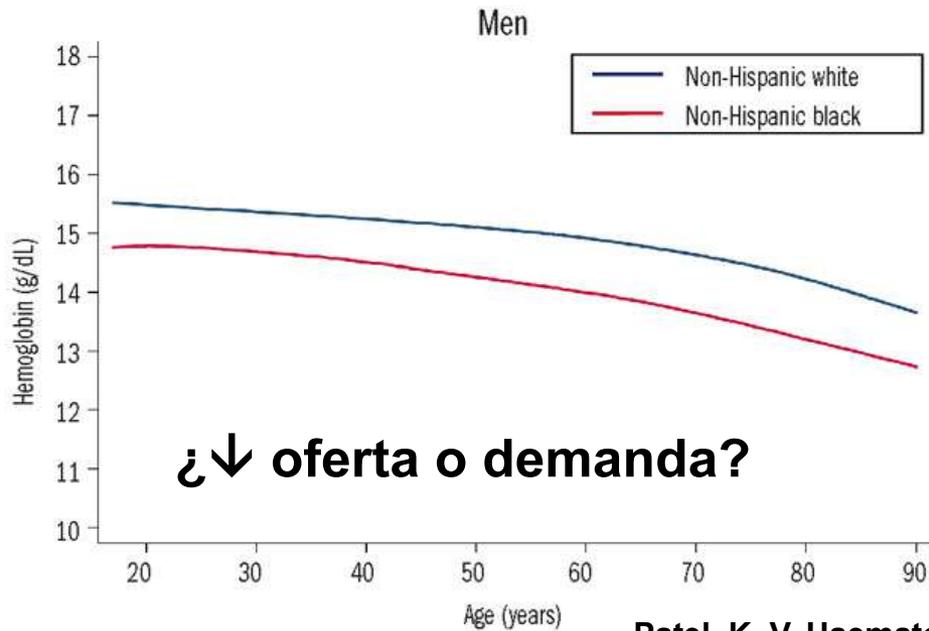
1) incapacidad de transportar O₂ a los tejidos para satisfacer sus requerimientos

2) Hb por debajo de valores normales para edad, sexo, raza, residencia (\neq valores previos)

Limitaciones de la segunda definición:

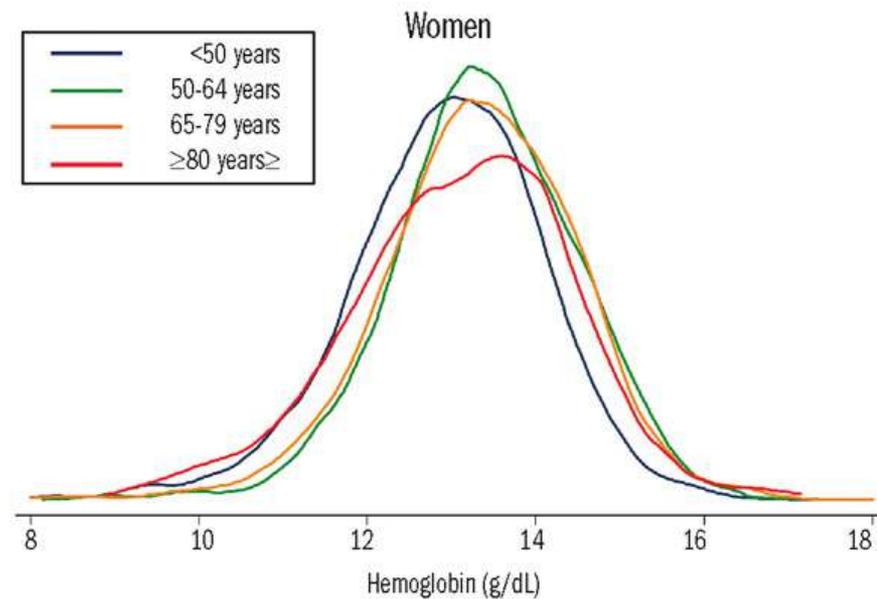
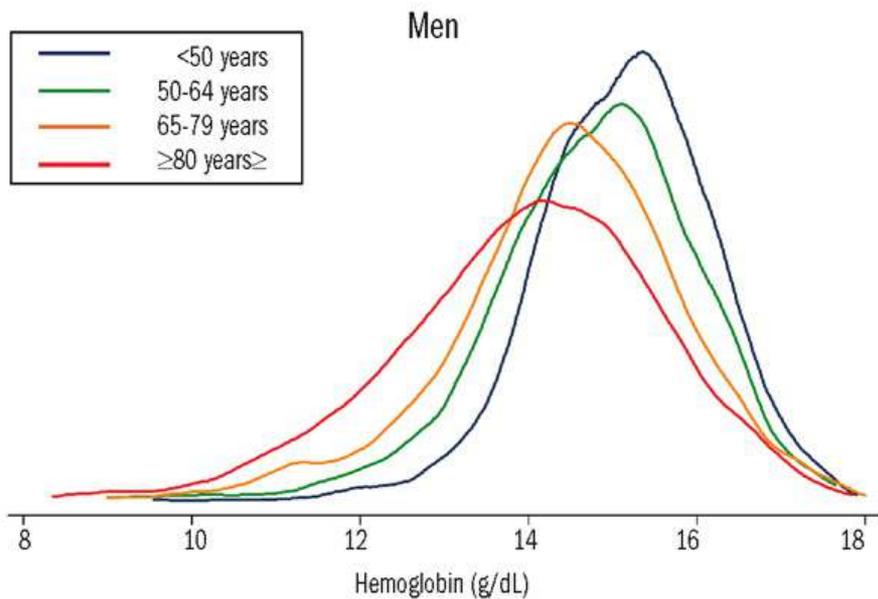
- Hb: concentración de Hb en plasma
hemoconcentración, hemodilución
- Hb: funcional y no funcional
metaHb, carboxiHb, Hb afinidad alterada
- Disponibilidad O₂ variable: EPOC - altura
- Requerimiento O₂ variable: hipotiroidismo

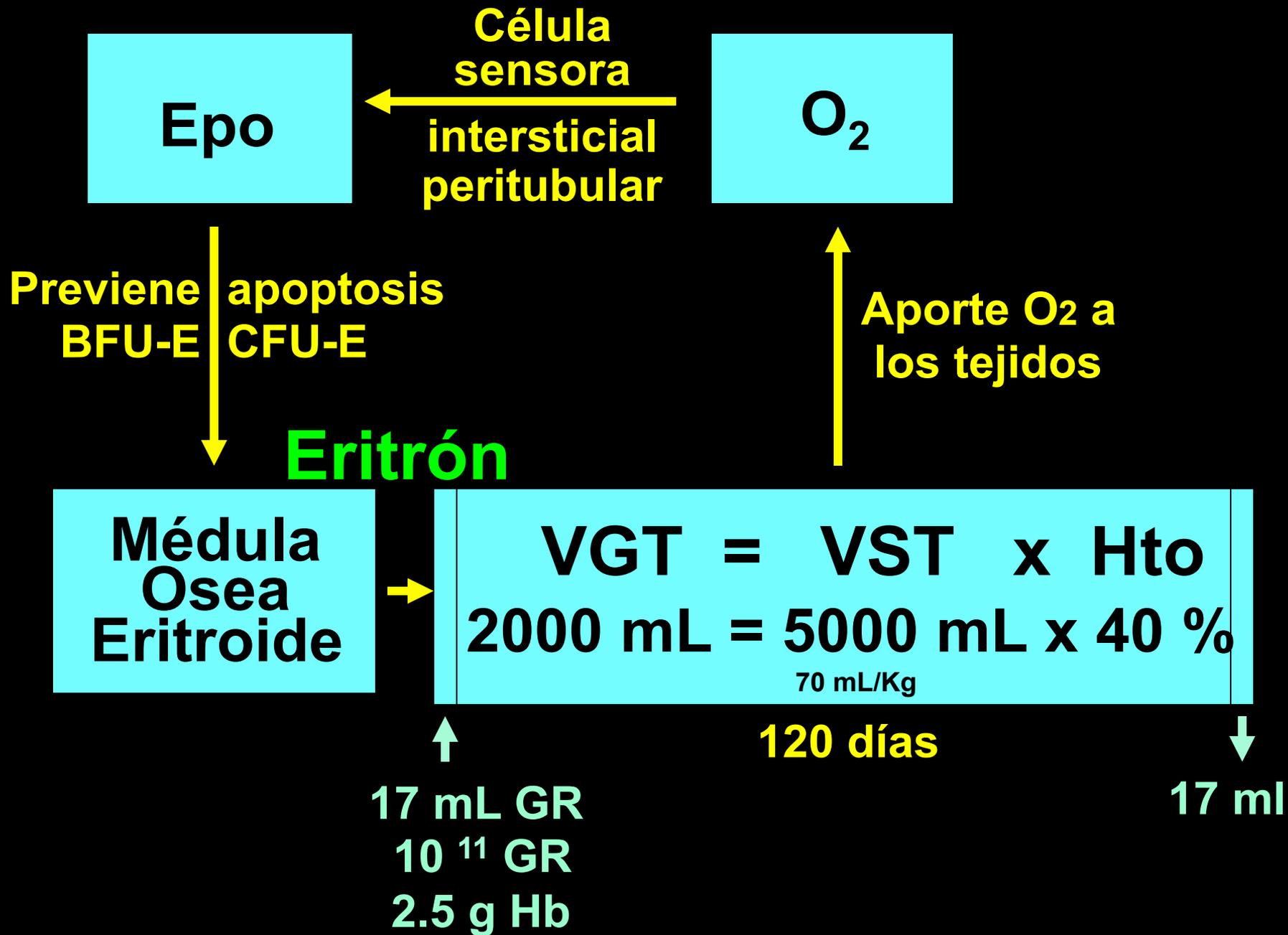
EEU: 1988-1994 Third National Health and Nutrition Examination Survey (N=11,780)

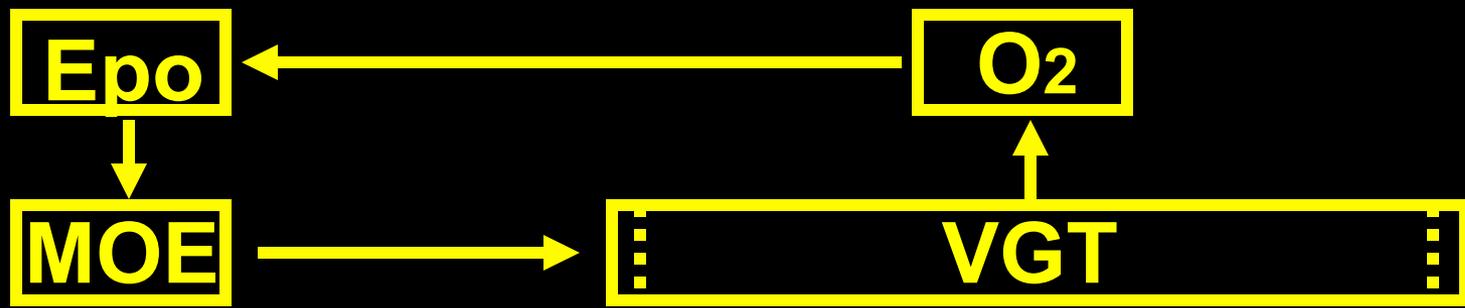


Patel, K. V. Haematologica 2008;93:1281-1283

EEU: 1988-1994 Third National Health and Nutrition Examination Survey (N=17,170)







↓ < **Anemias** ↓ >

Hiporregenerativas		Hiperregenerativas	
Defecto proliferativo	Defecto maduración		
	nuclear	citoplasmático	
<u>-Déficit Epo</u> - IRC - API	<u>Defecto duplicación ADN</u> (megaloblásticas)		<u>Defecto síntesis Hb</u> (hipocrómicas)
<u>-Defecto MOE</u> - aplasia - fibrosis - reemplazo	- def. pirimidinas (B12-folatos) - def. purinas - def. ribonuc. red.	- ferropenia - talasemias - anemia sideroblástica	<u>-Hiperhemólisis</u> - corpuscular - Hb - membrana - enzimas - extracorporeo <u>-Pérdida aguda</u>
hipoproliferativo	macrocíticas		microcíticas
			reticulocitos ↑

Anemias con reticulocitos disminuídos (Hipoproliferativas)

por déficit eritropoyetina

- insuficiencia renal crónica
- anemia de los procesos inflamatorios

por defecto médula ósea eritroide

- anemia aplásica
- aplasia eritroide pura
- (mielofibrosis metaplasia mieloide)
- (reemplazo médula ósea)
- (HPN)

Anemias con VCM-HCM aumentado (Macrocíticas)

Megaloblásticas (x defecto duplicación ADN)

- síntesis pirimidinas (B12 - folatos)
(AZT)
- síntesis purinas (6MP)
- ribonucleótido reductasa (HU)

No megaloblásticas

- reticulocitosis
- esplenectomía (Howell Jolly)
- hepatopatía - etilismo
- hipotiroidismo
- embarazo - neonato
- AA - AEP - SMD - LA

Anemias con VCM-HCM disminuído (Microcíticas)

Anemias hipocrómicas (defecto síntesis Hb)

- anemia ferropénica
- síndromes talasémicos
- anemia sideroblástica (cong)

Anemias con esquistocitos

Anemias con reticulocitos aumentados

- por liberación precoz (policromatofilia)

- por expansión médula ósea eritroide

- pico reticulocitario (+ Fe + B₁₂ - $\begin{array}{c} \text{CH}_3 \\ | \\ \text{CH}_2\text{OH} \end{array}$)

- anemias hiperregenerativas

- por pérdida aguda

- por hiperhemólisis

- causa extracorpuscular

- autoinmune (esferocitos)

- microangiopática (esquistocitos)

- causa corpuscular

- hemoglobinopatía

- membranopatía

- enzimopatía

Componentes

- ferropénico
- inflamatorio
- talasémico
- megaloblástico
- mielodisplásico
- sideroblástico
- hiperhemolítico
 - hipoplásico
- hiperesplénico
- etc.

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- etc.

Anemias multifactoriales

Evaluar todos los
datos clínicos y
bioquímicos
a favor / en contra
de la presencia /
ausencia de cada
componente
responsable de la
anemia

Arsenal diagnóstico

- Interrogatorio. Examen físico
- Hemograma: valores, índices, histogramas
- Morfología eritrocitaria
- Recuento de reticulocitos
- Creatinina, bilirrubina, LDH
- Ferremia / Capacidad de transporte = % sat.
- Ferritina sérica

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- **Dosaje B₁₂, folatos (sérico, eritrocitario)**
 - **Haptoglobina, prueba de Coombs**
 - **Eritropoyetina Interpretación**
 - **Protoporfirina eritrocitaria libre**
 - **Receptor soluble de transferrina**
 - **Medulograma (con coloración de Perls)**
 - **Estudios específicos.....**

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- **Prueba terapéutica**

Paciente asintomático con estos análisis:

- Hb: 7,0 g/dL
- Hto: 21 %
- GR: $1,9 \times 10^6/\mu\text{L}$
- Reticulocitos: 3 %
- Ferremia: 23 $\mu\text{g/dL}$

¿Cuál considera Ud. que es el componente más probable responsable de la anemia?

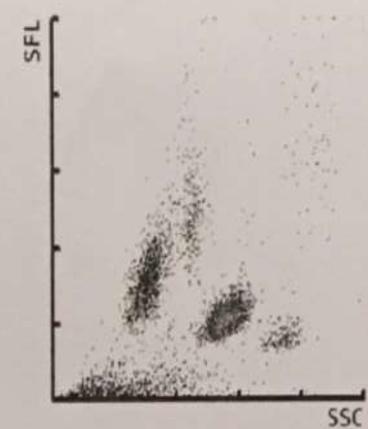
- a) hiperregenerativo por pérdida aguda**
- b) ferropénico por pérdida crónica**
- c) megaloblástico**
- d) hiperregenerativo por hemólisis**

Positive

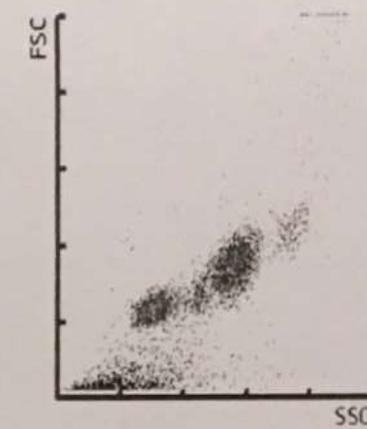
Morph.

WBC	5.98	[10 ³ /uL]		
RBC	3.93	[10 ⁶ /uL]		
HGB	11.2	[g/dL]		
HCT	32.7	[%]		
MCV	83.2	- [fL]		
MCH	28.5	[pg]		
MCHC	34.3	[g/dL]		
PLT	235	[10 ³ /uL]		
RDW-SD	48.9	[fL]		
RDW-CV	16.3	+ [%]		
MPV	10.8	[fL]		
NEUT	3.21	[10 ³ /uL]	53.7	[%]
LYMPH	2.08	[10 ³ /uL]	34.8	[%]
MONO	0.34	[10 ³ /uL]	5.7	[%]
EO	0.23	[10 ³ /uL]	3.8	[%]
BASO	0.03	[10 ³ /uL]	0.5	[%]
IG	0.09	[10 ³ /uL]	1.5	[%]
RET	6.91	[%]	0.271	[10 ⁶ /uL]
IRF		[%]		
RET-He	29.1	[pg]		

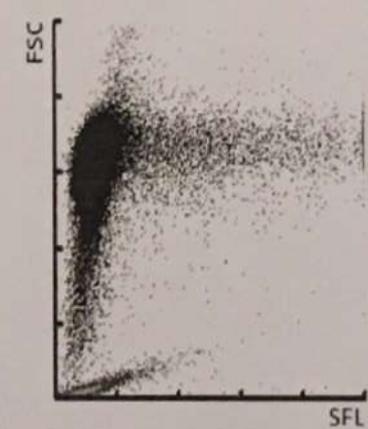
WDF



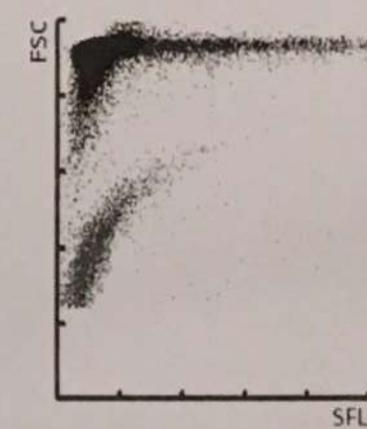
WDF-CBC



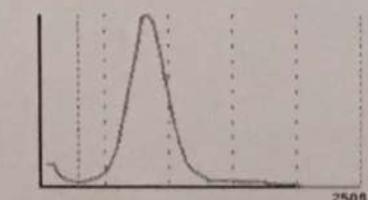
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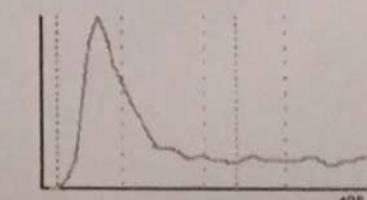
PLT-O



RBC



PLT



Positive

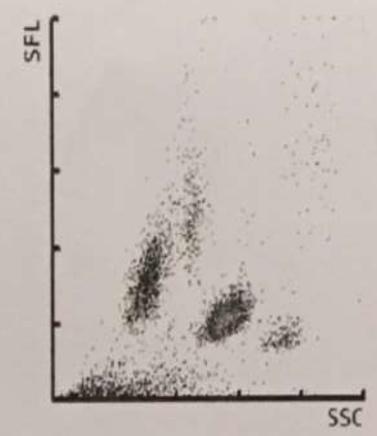
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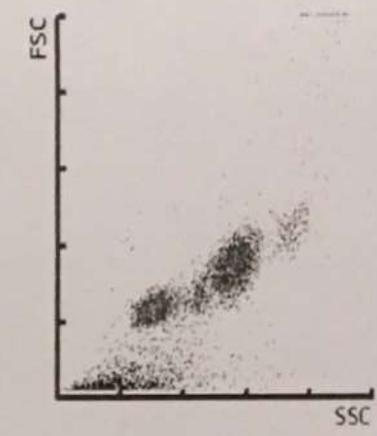
Valores eritrocíticos

53.7 [%]
 34.8 [%]
 5.7 [%]
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 0.5 [%]
 1.5 [%]
 0.271 [10⁶/uL]

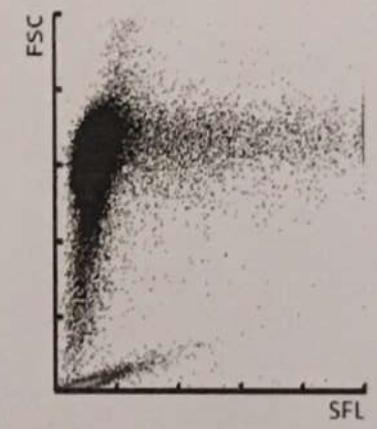
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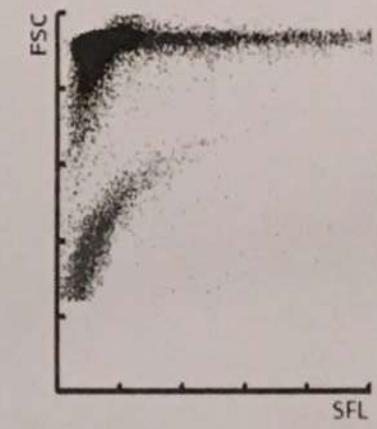
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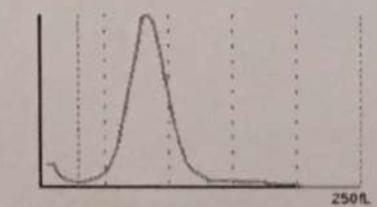
RET



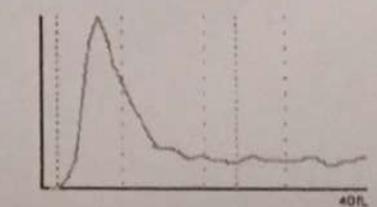
PLT-0



RBC



PLT



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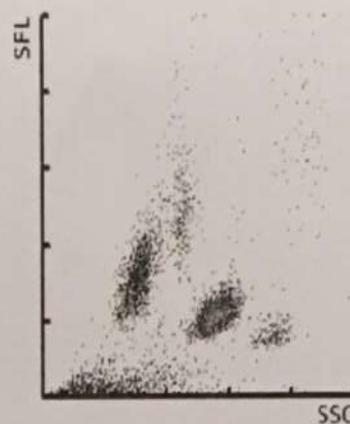
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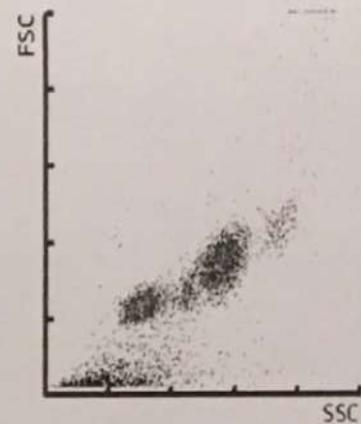
Índices eritrocíticos

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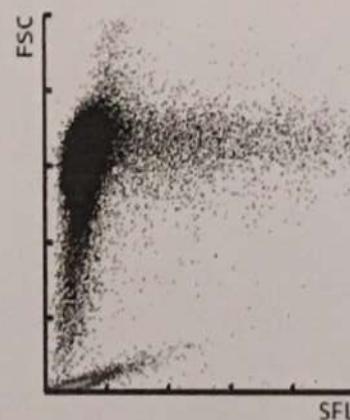
WDF



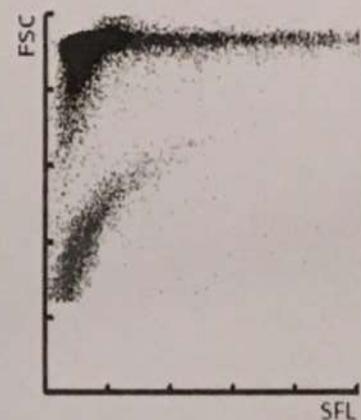
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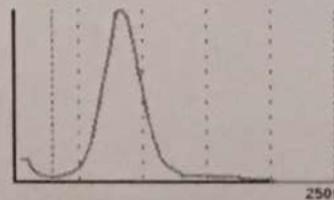
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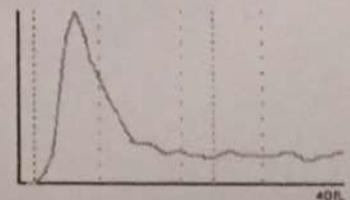
PLT-0



RBC



PLT



Positive

Morph.

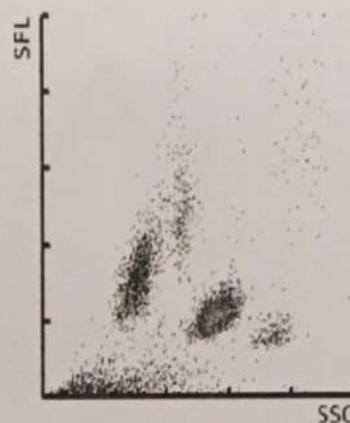
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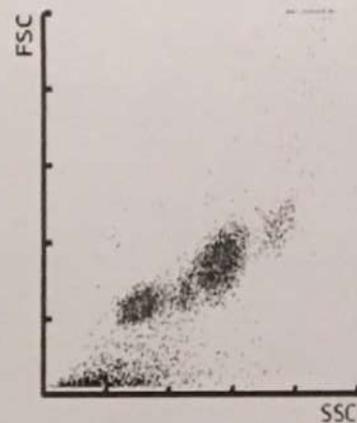
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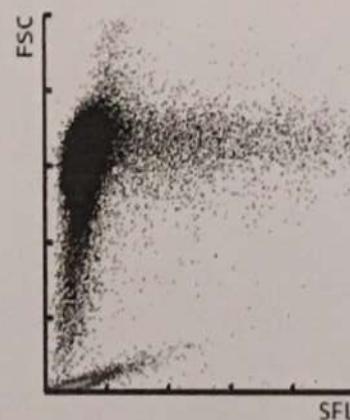
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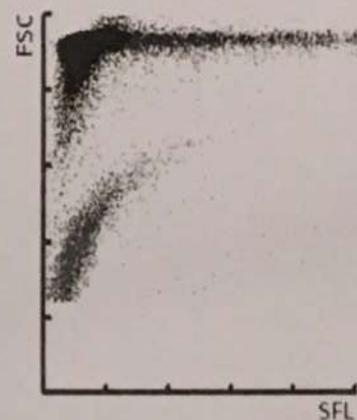
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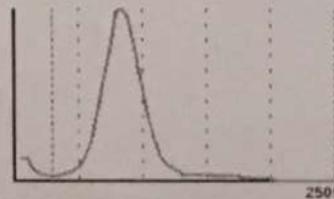


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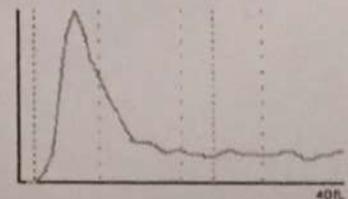


RBC

Histograma de volumen



PLT



Positive

Morph.

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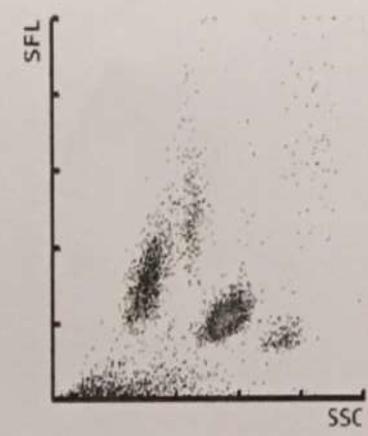
Valores eritrocíticos

Índices eritrocíticos

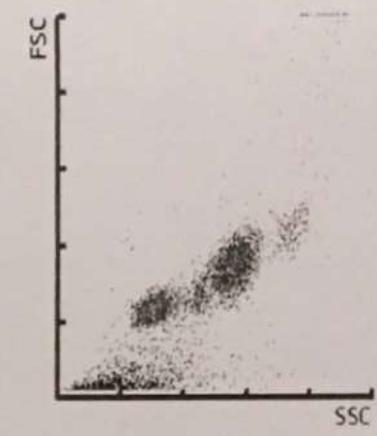
Amplitud distribución eritrocitaria

	53.7	[%]
	34.8	[%]
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	3.8	[%]
	0.5	[%]
	1.5	[%]
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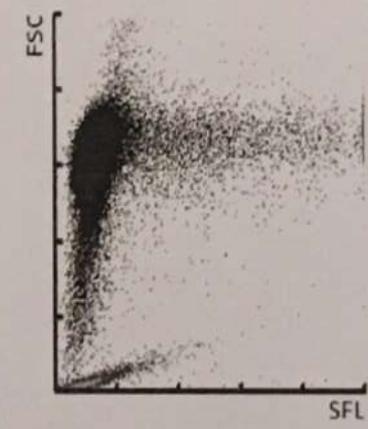
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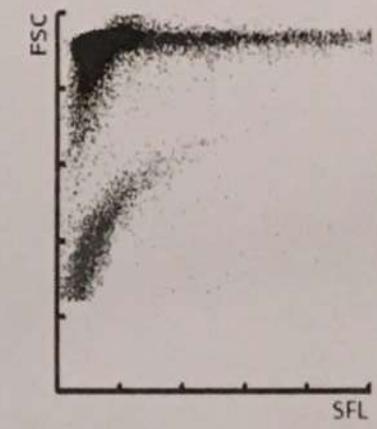
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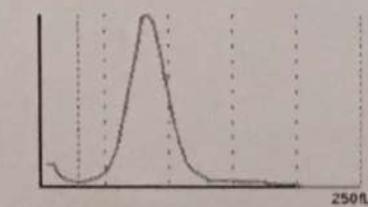


PLT-0

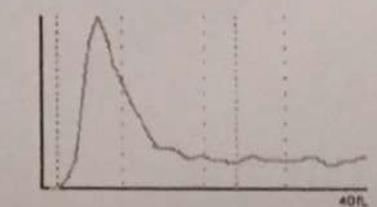


RBC

Histograma de volumen



PLT



Positive

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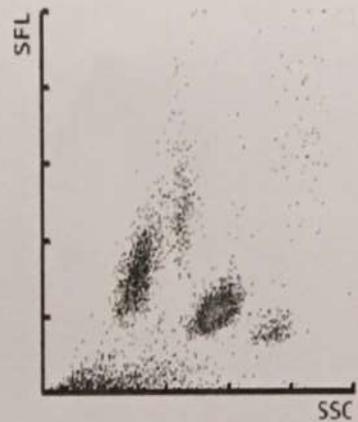
Valores eritrocíticos

Índices eritrocíticos

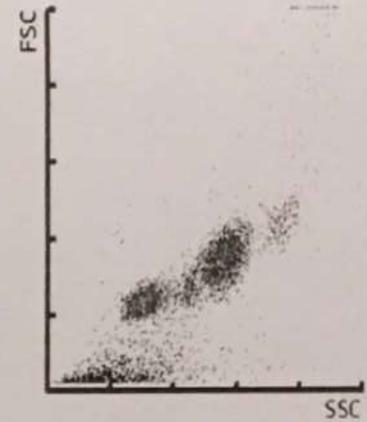
Amplitud distribución eritrocitaria

Reticulocitos
0.271 [10⁶/uL]

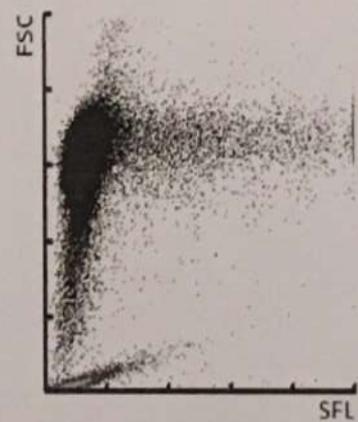
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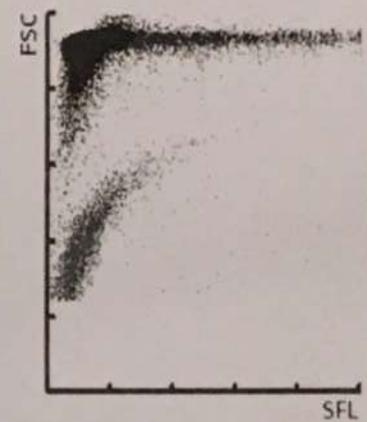
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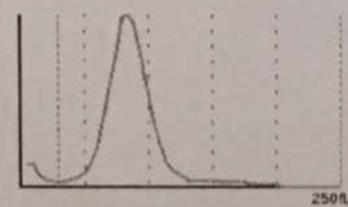


PLT-0

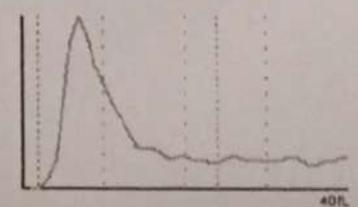


RBC

Histograma de volumen



PLT



Positive

Morph.

WBC	5.98	[10 ³ /uL]
RBC	3.93	[10 ⁶ /uL]
HGB	11.2	[g/dL]
HCT	32.7	[%]
MCV	83.2	- [fL]
MCH	28.5	[pg]
MCHC	34.3	[g/dL]
PLT	235	[10 ³ /uL]
RDW-SD	48.9	[fL]
RDW-CV	16.3	+ [%]
MPV	10.8	[fL]
NEUT	3.21	[10 ³ /uL]
LYMPH	2.08	[10 ³ /uL]
MONO	0.34	[10 ³ /uL]
EO	0.23	[10 ³ /uL]
BASO	0.03	[10 ³ /uL]
IG	0.09	[10 ³ /uL]
RET	6.91	[%]
IRF		[%]
RET-He	29.1	[pg]

Valores eritrocíticos

Índices eritrocíticos

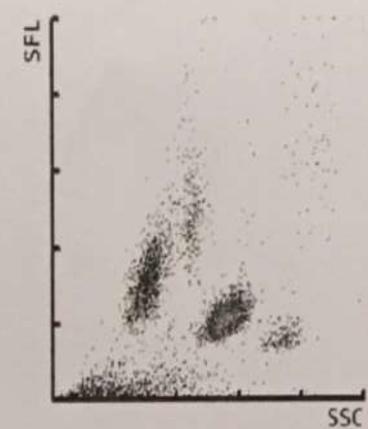
Amplitud distribución eritrocitaria

	53.7	[%]
	34.8	[%]
	5.7	[%]
	3.8	[%]
	0.5	[%]
	1.5	[%]
	0.271	[10 ⁶ /uL]

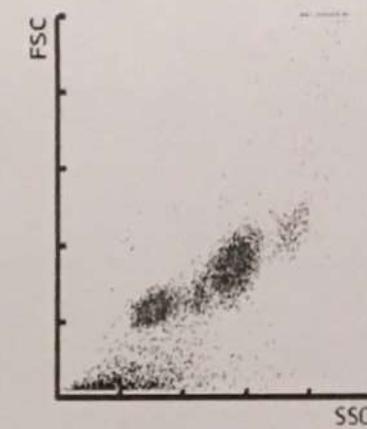
Reticulocitos

Hb reticulocitaria MRH

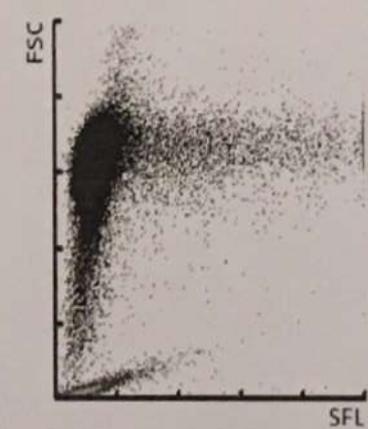
WDF



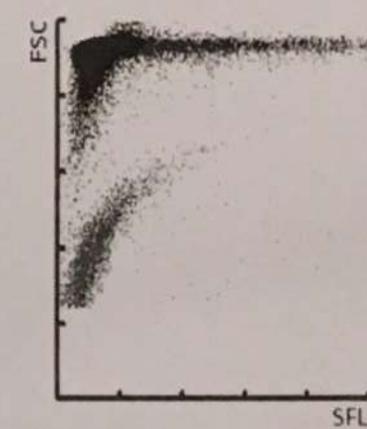
WDF-CBC



RET

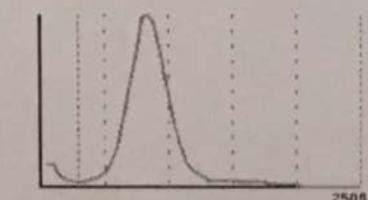


PLT-0

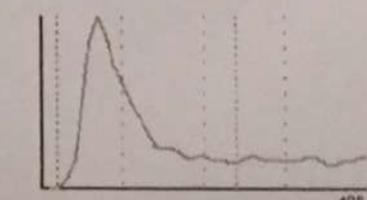


RBC

Histograma de volumen



PLT



Positive

Morph.

WBC	5.98	[10 ³ /uL]
RBC	3.93	[10 ⁶ /uL]
HGB	11.2	[g/dL]
HCT	32.7	[%]
MCV	83.2	- [fL]
MCH	28.5	[pg]
MCHC	34.3	[g/dL]
PLT	235	[10 ³ /uL]
RDW-SD	48.9	[fL]
RDW-CV	16.3	+ [%]
MPV	10.8	[fL]
NEUT	3.21	[10 ³ /uL]
LYMPH	2.08	[10 ³ /uL]
MONO	0.34	[10 ³ /uL]
EO	0.23	[10 ³ /uL]
BASO	0.03	[10 ³ /uL]
IG	0.09	[10 ³ /uL]
RET	6.91	[%]
IRF		[%]
RET-He	29.1	[pg]

Valores eritrocíticos

Índices eritrocíticos

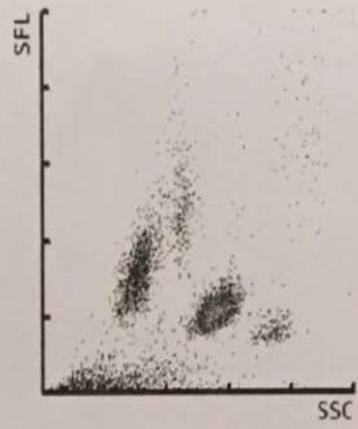
Amplitud distribución eritrocitaria

	53.7	[%]
	34.8	[%]
	5.7	[%]
	3.8	[%]
	0.5	[%]
	1.5	[%]
	0.271	[10 ⁶ /uL]

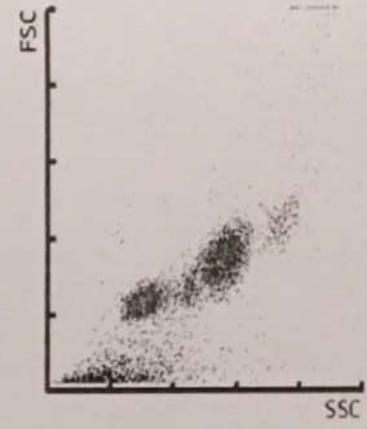
Reticulocitos

Hb reticulocitaria MHR

WDF

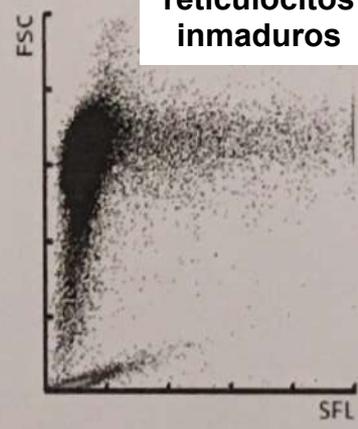


WDF-CBC

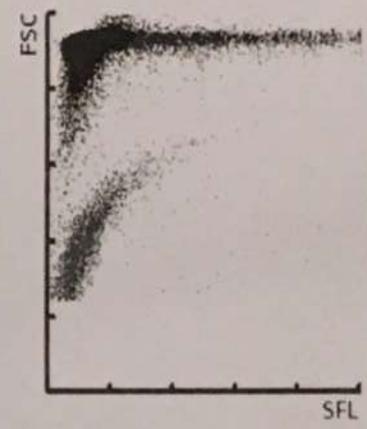


RET

Fracción reticulocitos inmaduros

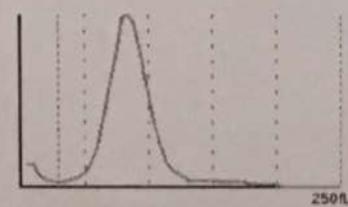


PLT-0

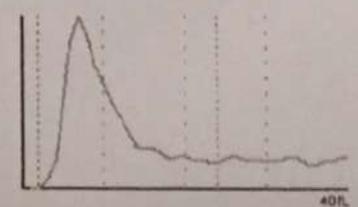


RBC

Histograma de volumen



PLT



Positive

Morph.

WBC	5.98	[10 ³ /uL]
RBC	3.93	[10 ⁶ /uL]
HGB	11.2	[g/dL]
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MCV	83.2	- [fL]
MCH	28.5	[pg]
MCHC	34.3	[g/dL]
PLT	235	[10 ³ /uL]
RDW-SD	48.9	[fL]
RDW-CV	16.3	+ [%]
MPV	10.8	[fL]
NEUT	3.21	[10 ³ /uL]
LYMPH	2.08	[10 ³ /uL]
MONO	0.34	[10 ³ /uL]
EO	0.23	[10 ³ /uL]
BASO	0.03	[10 ³ /uL]
IG	0.09	[10 ³ /uL]
RET	6.91	[%]
IRF		[%]
RET-He	29.1	[pg]

Valores eritrocíticos

Índices eritrocíticos

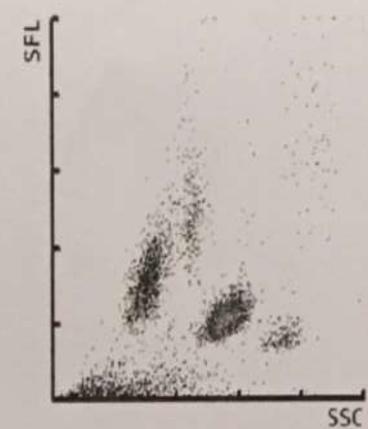
Amplitud distribución eritrocitaria

	53.7	[%]
	34.8	[%]
	5.7	[%]
	3.8	[%]
	0.5	[%]
	1.5	[%]
	0.271	[10 ⁶ /uL]

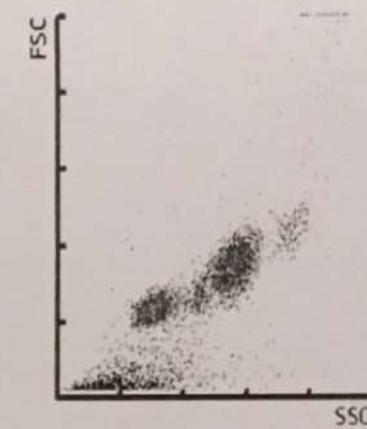
Reticulocitos

Hb reticulocitaria MRH

WDF

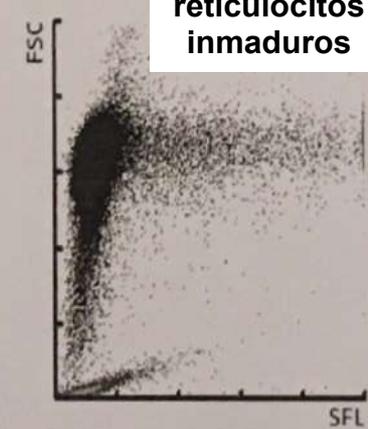


WDF-CBC

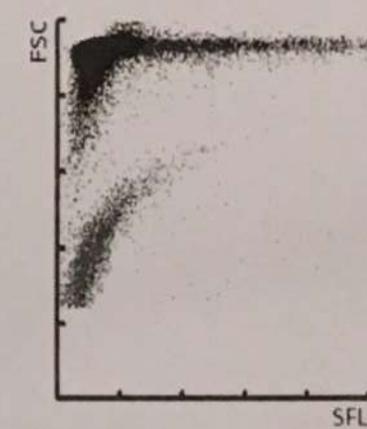


RET

Fracción reticulocitos inmaduros

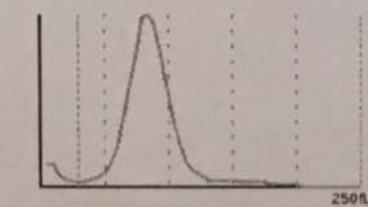


PLT-0

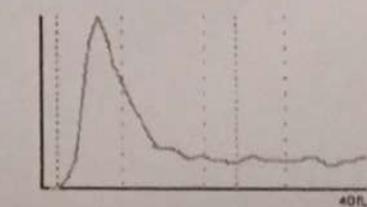


RBC

Histograma de volumen

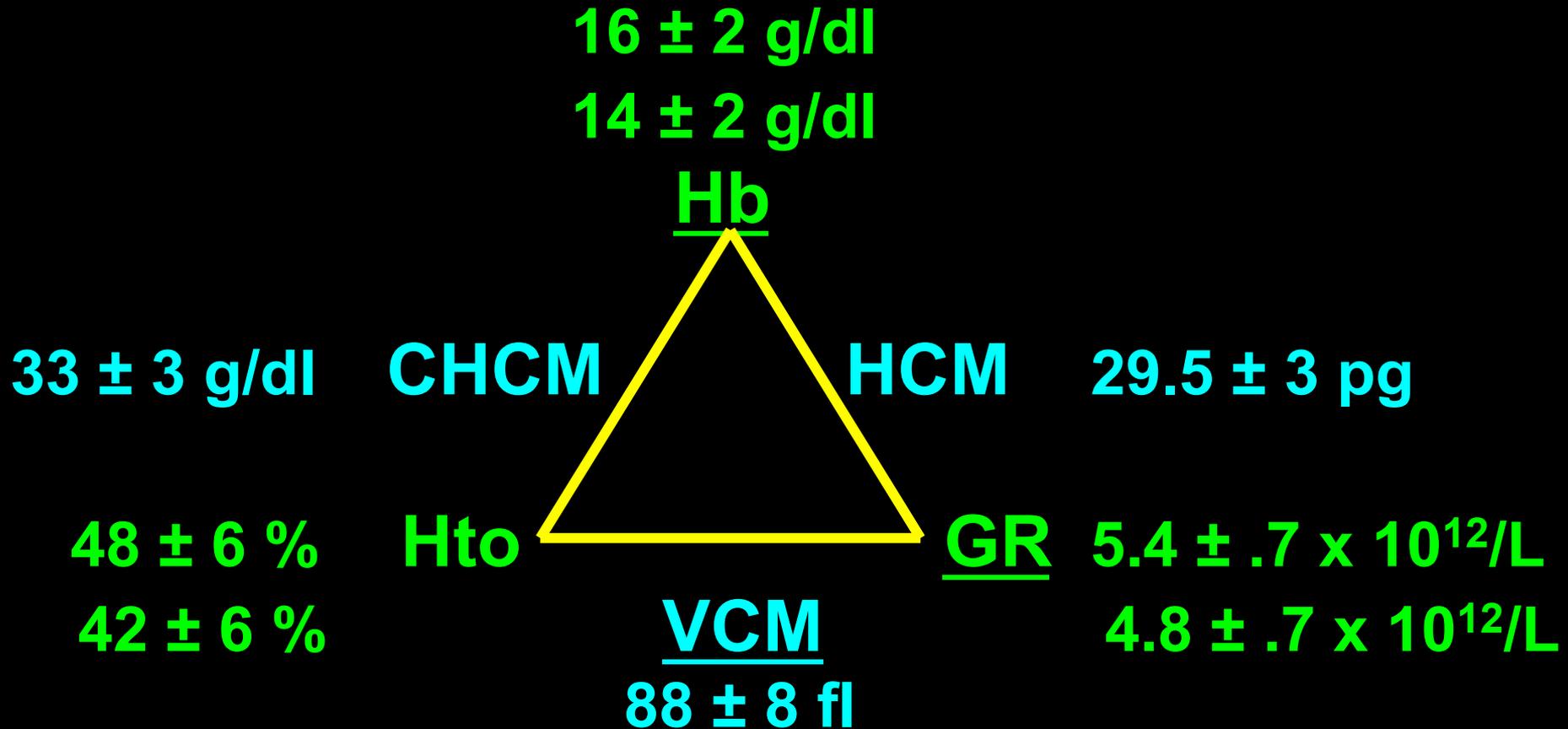


PLT



Hemograma

- **Valores e índices hematimétricos**



- **Recuento y fórmula leucocitaria**
- **Recuento de plaquetas**
- **Morfología (hematíes, leucocitos, plaquetas)**

Positive

Morph.

WBC	5.98	[10 ³ /uL]
RBC	3.93	[10 ⁶ /uL]
HGB	11.2	[g/dL]
HCT	32.7	[%]
MCV	83.2	- [fL]
MCH	28.5	[pg]
MCHC	34.3	[g/dL]
PLT	235	[10 ³ /uL]
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RDW-CV	16.3	+ [%]
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NEUT	3.21	[10 ³ /uL]
LYMPH	2.08	[10 ³ /uL]
MONO	0.34	[10 ³ /uL]
EO	0.23	[10 ³ /uL]
BASO	0.03	[10 ³ /uL]
IG	0.09	[10 ³ /uL]
RET	6.91	[%]
IRF		[%]
RET-He	29.1	[pg]

Valores eritrocíticos

Índices eritrocíticos

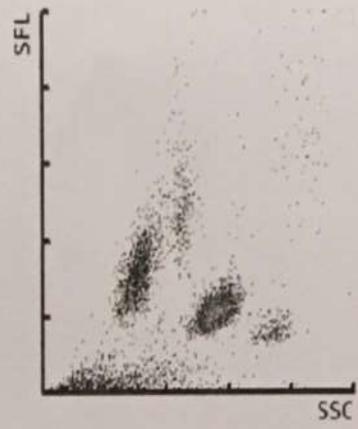
Amplitud distribución eritrocitaria

	53.7	[%]
	34.8	[%]
	5.7	[%]
	3.8	[%]
	0.5	[%]
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	0.271	[10 ⁶ /uL]

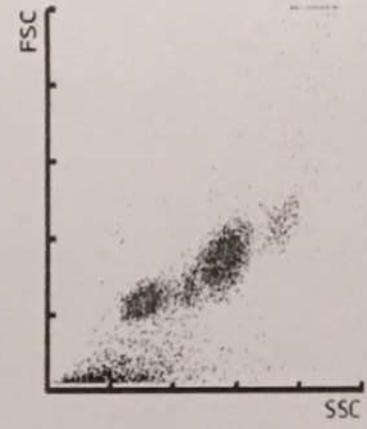
Reticulocitos

Hb reticulocitaria MHR

WDF

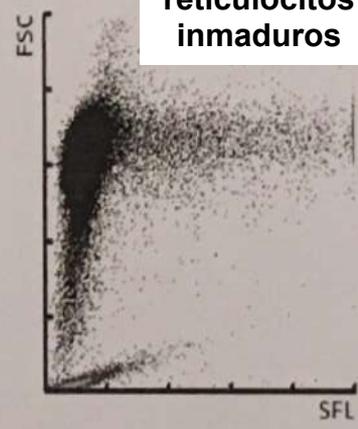


WDF-CBC

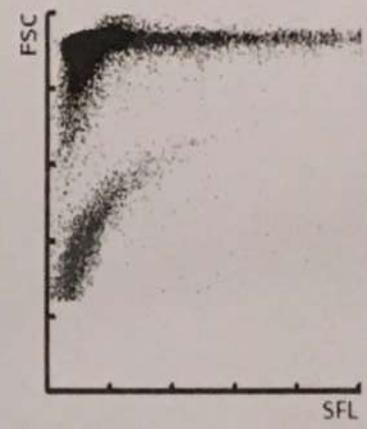


RET

Fracción reticulocitos inmaduros

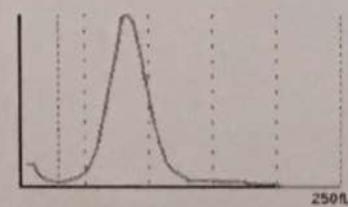


PLT-0

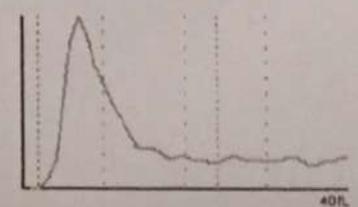


RBC

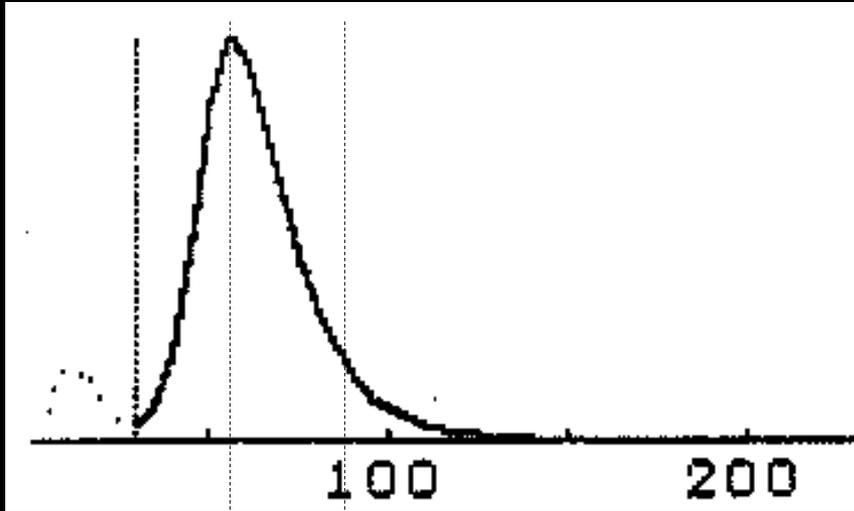
Histograma de volumen



PLT



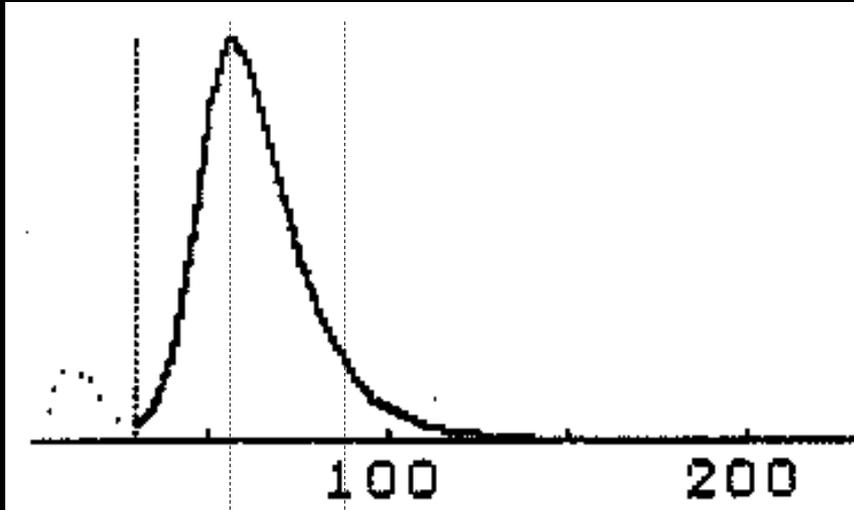
Anemia ferropénica: respuesta al hierro parenteral



Día 0

Hb	4.9	g/dL
Hto	18.4	%
GR	2.93	x 10⁶/μL
VCM	62.8	fL
RDW	17.6	%

Anemia ferropénica: respuesta al hierro parenteral



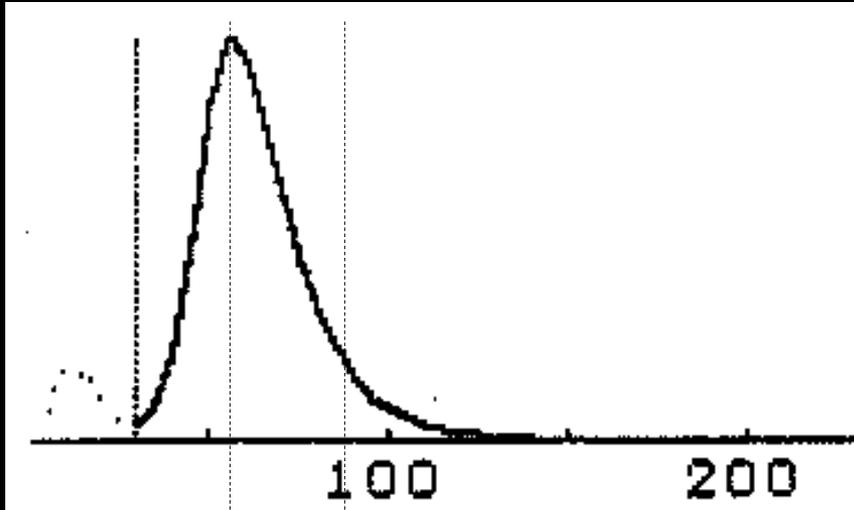
Día 0

Hb	4.9	g/dL
Hto	18.4	%
GR	2.93	$\times 10^6/\mu\text{L}$
VCM	62.8	fL
RDW	17.6	%

Día + 33

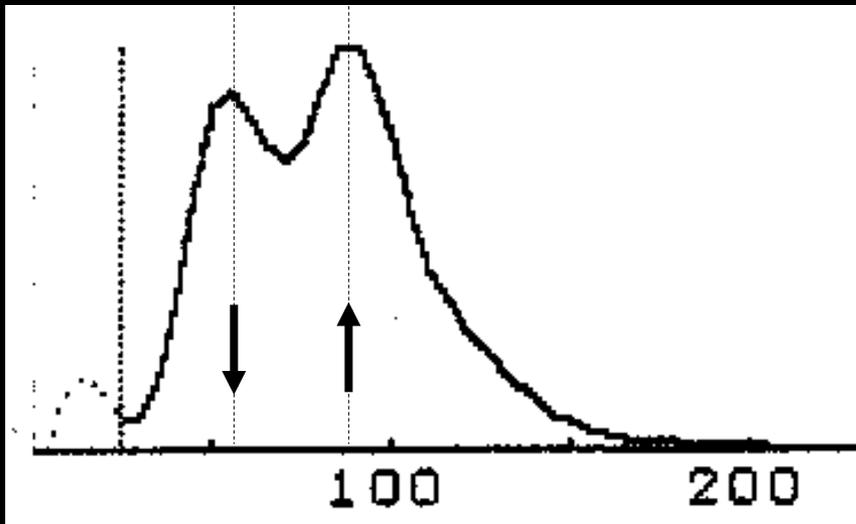
Hb	10.1	g/dL
Hto	34.3	%
GR	4.35	$\times 10^6/\mu\text{L}$
VCM	78.9	fL
RDW	30.2	%

Anemia ferropénica: respuesta al hierro parenteral



Día 0

Hb	4.9	g/dL
Hto	18.4	%
GR	2.93	x 10⁶/μL
VCM	62.8	fL
RDW	17.6	%

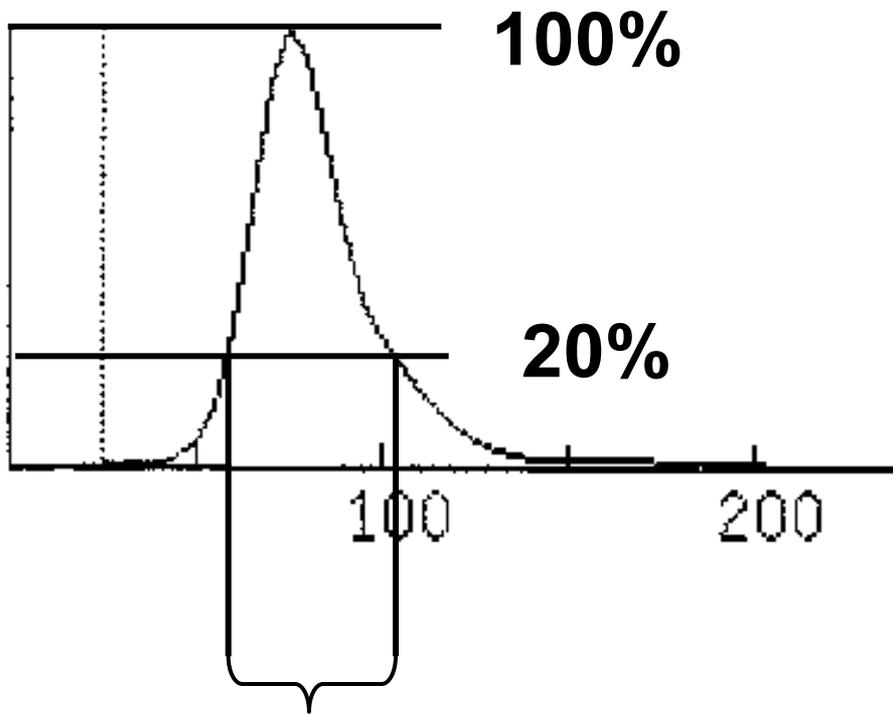


Día + 33

Hb	10.1	g/dL
Hto	34.3	%
GR	4.35	x 10⁶/μL
VCM	78.9	fL
RDW	30.2	%

Amplitud Distribución Eritrocitaria

Desviación estándar

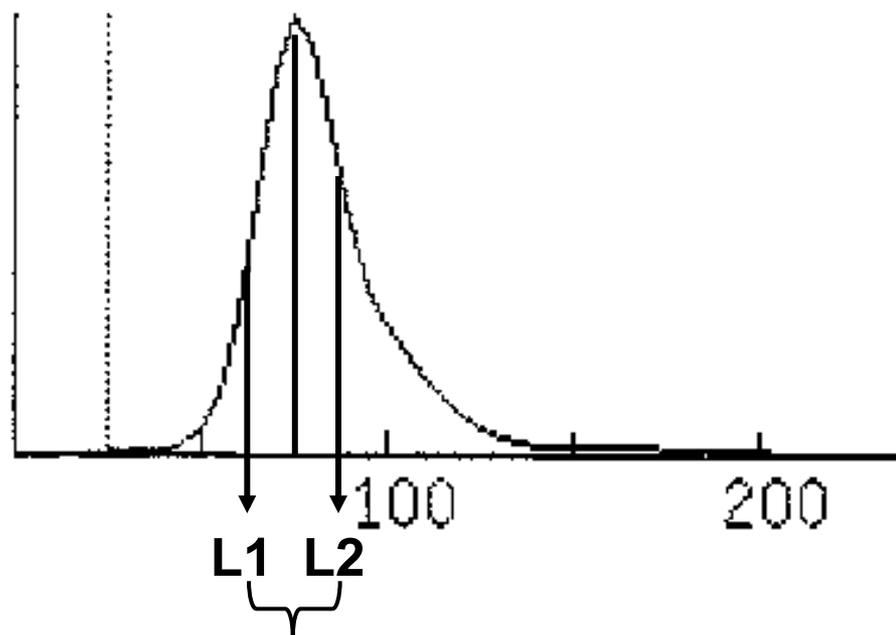


ADE-SD
fL

39 - 46 fL

(Rango normal)

Coefficiente de variación



68.26% del área bajo la curva

$$\text{ADE-CV} = \frac{L2 - L1}{(L2 + L1)/2} \times 100 \%$$

10.6 - 14.7 %

1 DS
VCM

Positive

Morph.

WBC	5.98	[10 ³ /uL]
RBC	3.93	[10 ⁶ /uL]
HGB	11.2	[g/dL]
HCT	32.7	[%]
MCV	83.2 -	[fL]
MCH	28.5	[pg]
MCHC	34.3	[g/dL]
PLT	235	[10 ³ /uL]
RDW-SD	48.9	[fL]
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LYMPH	2.08	[10 ³ /uL]
MONO	0.34	[10 ³ /uL]
EO	0.23	[10 ³ /uL]
BASO	0.03	[10 ³ /uL]
IG	0.09	[10 ³ /uL]
RET	6.91	[%]
IRF		[%]
RET-He	29.1	[pg]

Valores eritrocíticos

Índices eritrocíticos

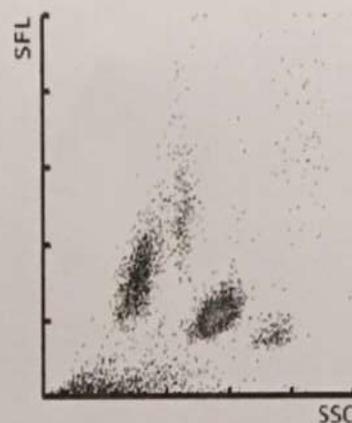
Amplitud distribución eritrocitaria

	53.7	[%]
	34.8	[%]
	5.7	[%]
	3.8	[%]
	0.5	[%]
	1.5	[%]
	0.271	[10 ⁶ /uL]

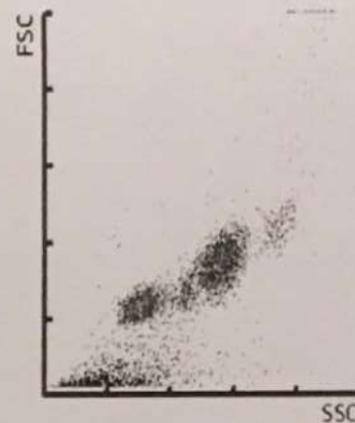
Reticulocitos

Hb reticulocitaria MRH

WDF

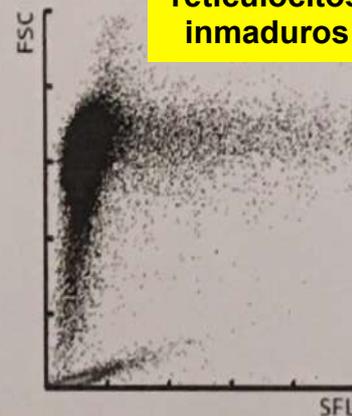


WDF-CBC

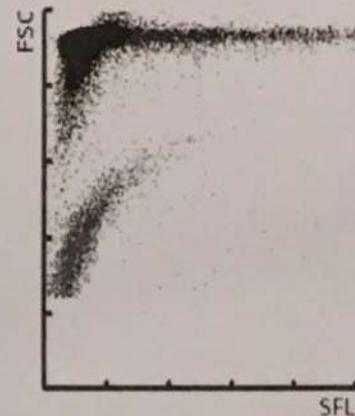


RET

Fracción reticulocitos inmaduros

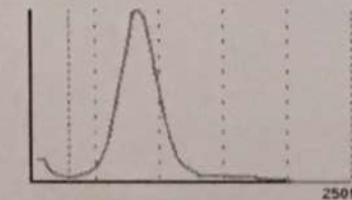


PLT-O

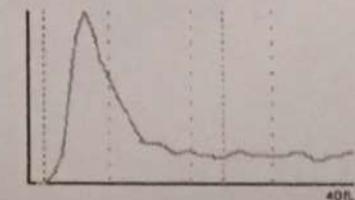


RBC

Histograma de volumen



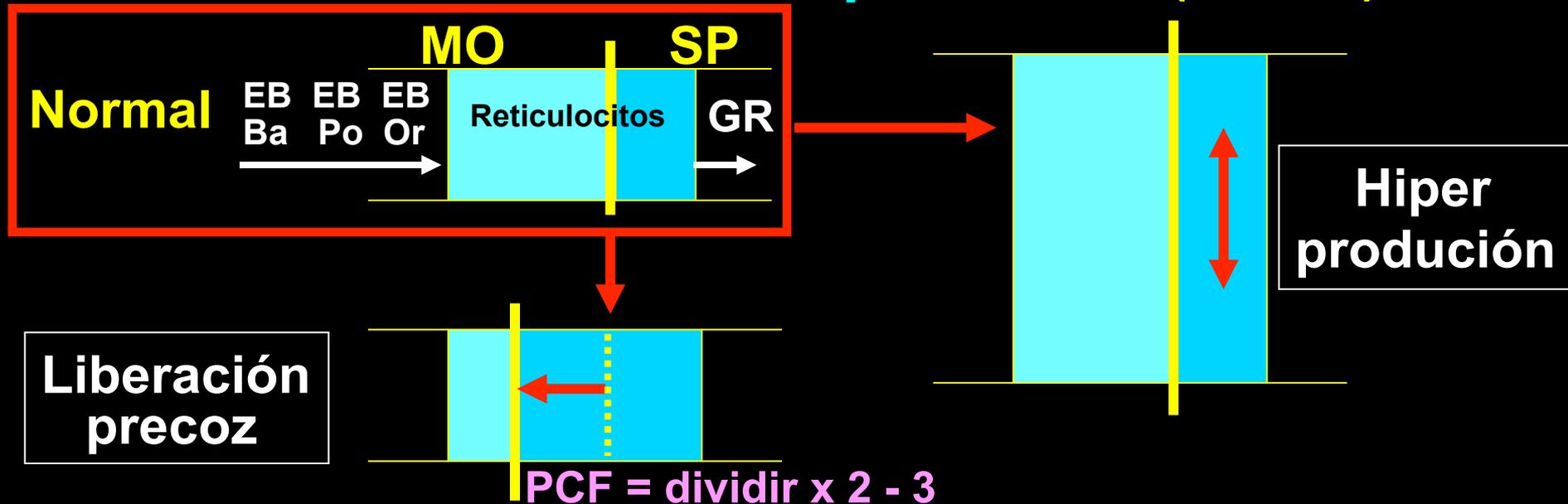
PLT



Reticulocitos: suficiencia medular

1) Valor absoluto: 40.000-60.000/mm³ (1% 5.000.000)

2) Diferenciar: - hiperproducción → ("bueno")
- liberación precoz → ("malo")

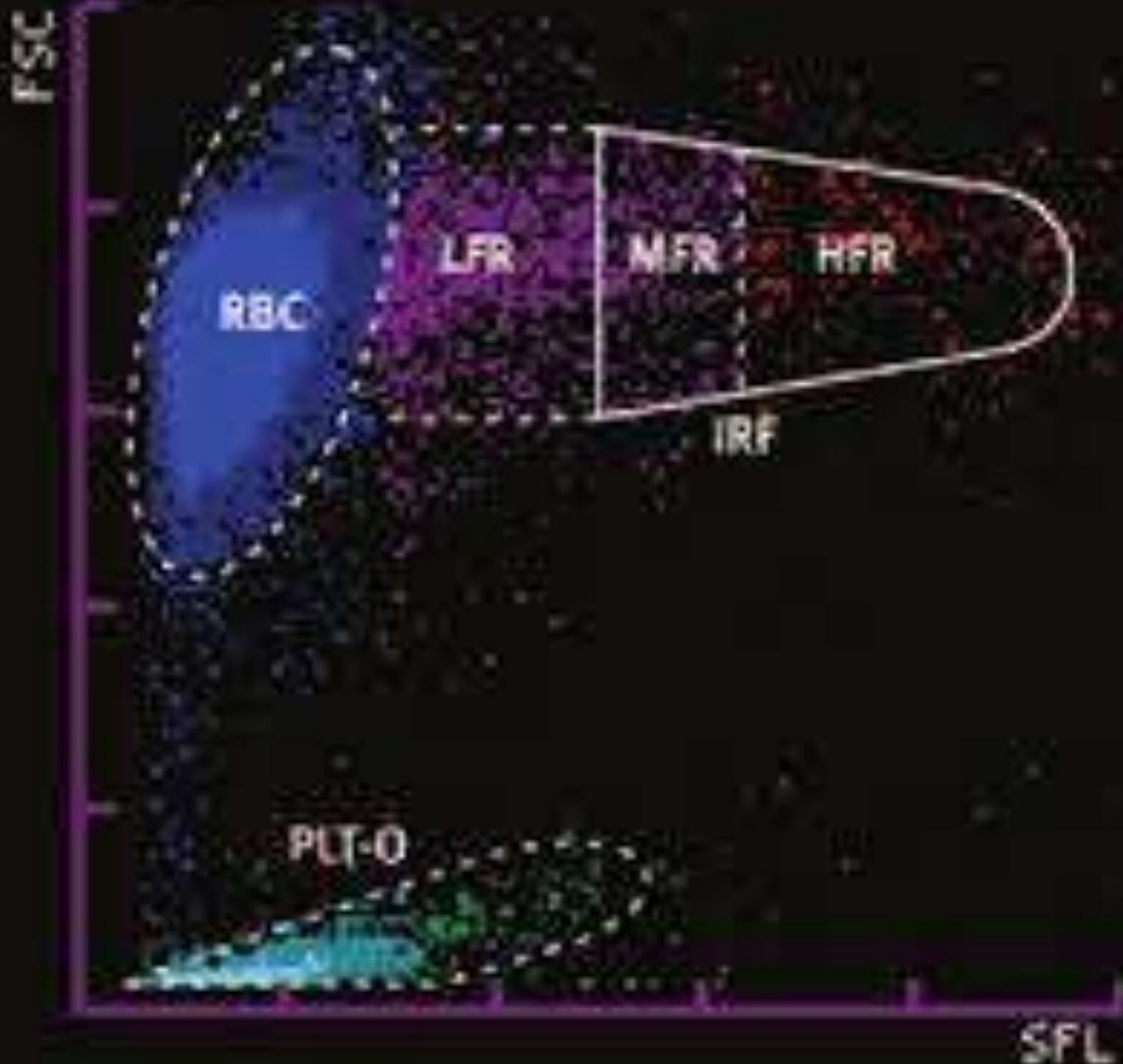


3) Valor esperable según grado de anemia:

- sin anemia: 50.000 /mm³
 - anemia leve: 100.000 /mm³
 - anemia severa: 150.000 /mm³
- } eritropoyesis medular normal

Tamaño celular

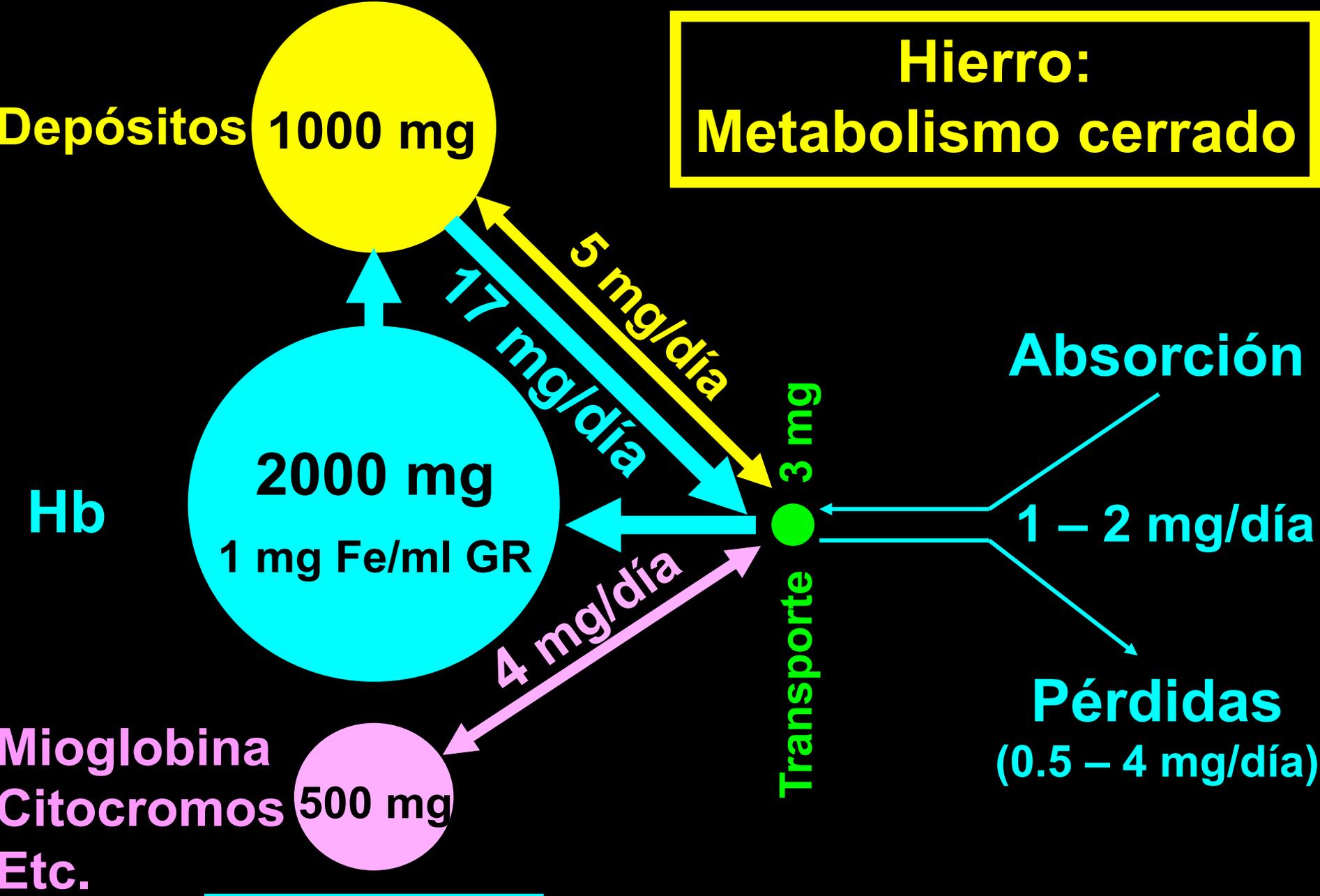
RET



leucocitos
eritroblastos
Howell Jolly

Fluorescencia (polimetina: ADN ARN)

**Hierro:
Metabolismo cerrado**



Total = 3000 - 4000 mg (RN = 250 mg)

Evaluación del hierro del organismo

Ferremia

Hierro sérico

/ capacidad de transporte ($Tf \times 1,27$) **Avidez por el Fe**

= % de saturación de la Tf **% ocupación**

Ferritina sérica $1 \text{ ug/L} \equiv 8 \text{ mg Fe}$

Fe depósito

Evaluación del hierro del organismo

Ferremia

Hierro sérico

/ **capacidad de transporte** ($Tf \times 1,27$) **Aidez por el Fe**

= % de saturación de la Tf **% ocupación**

Ferritina sérica $1 \text{ ug/L} \equiv 8 \text{ mg Fe}$ **Fe depósito**

Receptor soluble de transferrina (sTfR)

Protoporfirina eritrocitaria libre (PEL)

Evaluación del hierro del organismo

Ferremia

Hierro sérico

/ **capacidad de transporte** ($Tf \times 1,27$) **Avidez por el Fe**

= % de saturación de la Tf **% ocupación**

Ferritina sérica $1 \text{ ug/L} \equiv 8 \text{ mg Fe}$ **Fe depósito**

Receptor soluble de transferrina (sTfR)

Protoporfirina eritrocitaria libre (PEL)

Hierro medular (Perls) - **hemosiderina**
- **sideroblastos**

Evaluación del hierro del organismo

Ferremia

Hierro sérico

/ **capacidad de transporte** ($Tf \times 1,27$) **Avidez por el Fe**

= % de saturación de la Tf **% ocupación**

Ferritina sérica $1 \text{ ug/L} \equiv 8 \text{ mg Fe}$ **Fe depósito**

Receptor soluble de transferrina (sTfR)

Protoporfirina eritrocitaria libre (PEL)

Hierro medular (Perls) - **hemosiderina**
- **sideroblastos**

Hierro tisular - **RNM**

Hierro hepático - **RNM** - **PBH**

$$\frac{\text{Ferremia} \times 100}{\text{Capacidad de transporte}} = \% \text{ saturación}$$

Transferrina = 200 - 280 mg/dL

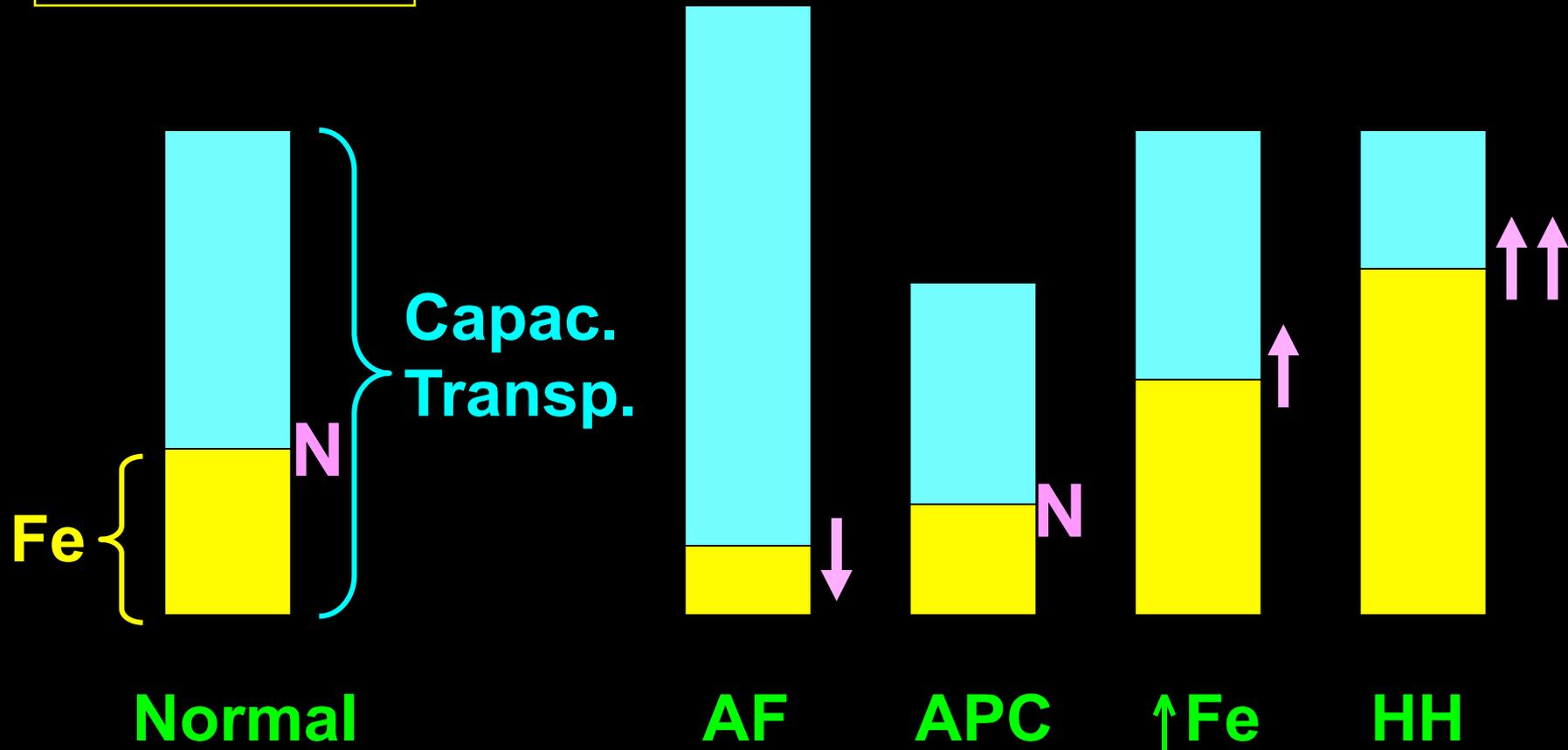
X 1.27

70 - 160 µg/dL
60 - 140 µg/dL

250 - 350 µg/dL

=

24 - 36 %



Ferritina

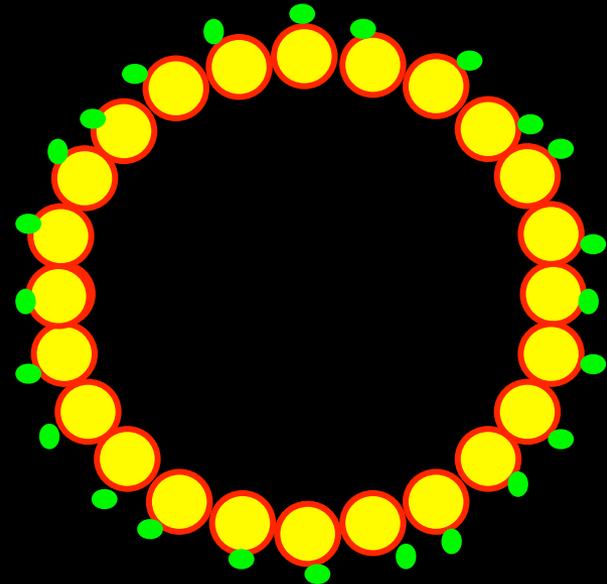
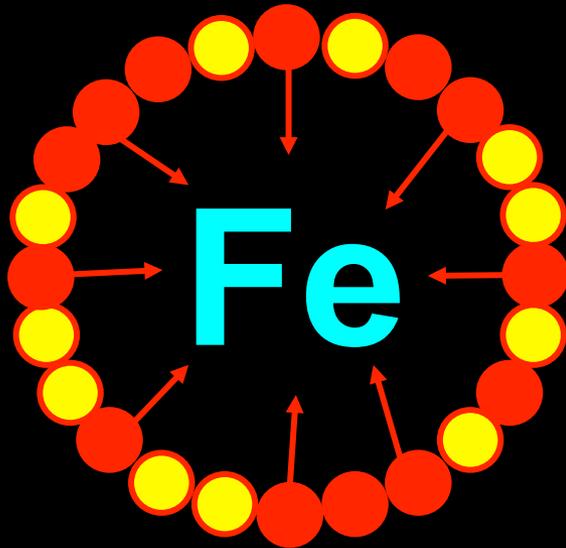
citoplasmática

sérica

8 mg Fe depósito



1 ug/L Ft



Cadena L ●

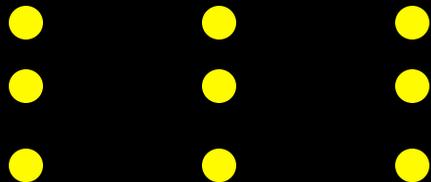
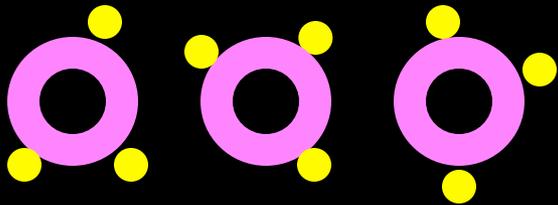


Cadena L glicosilada

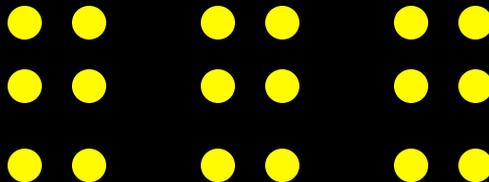
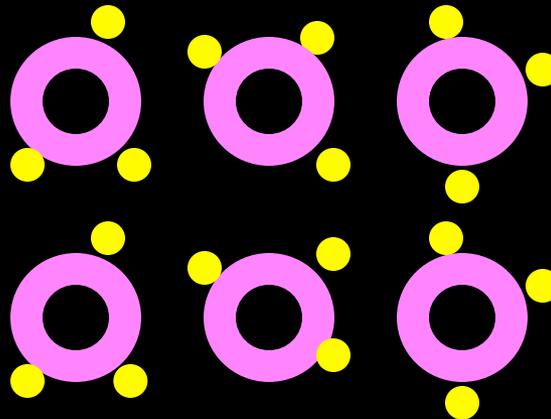
Cadena H ●

Receptor soluble de transferrina

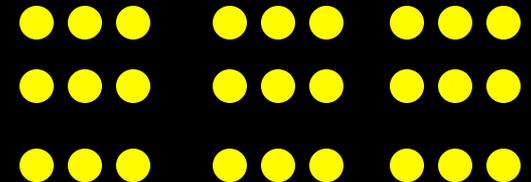
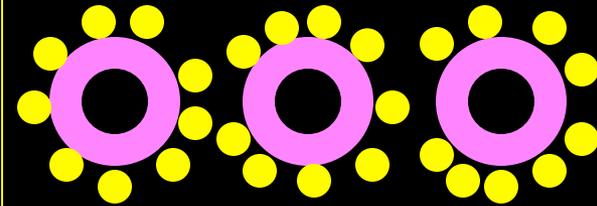
Normal



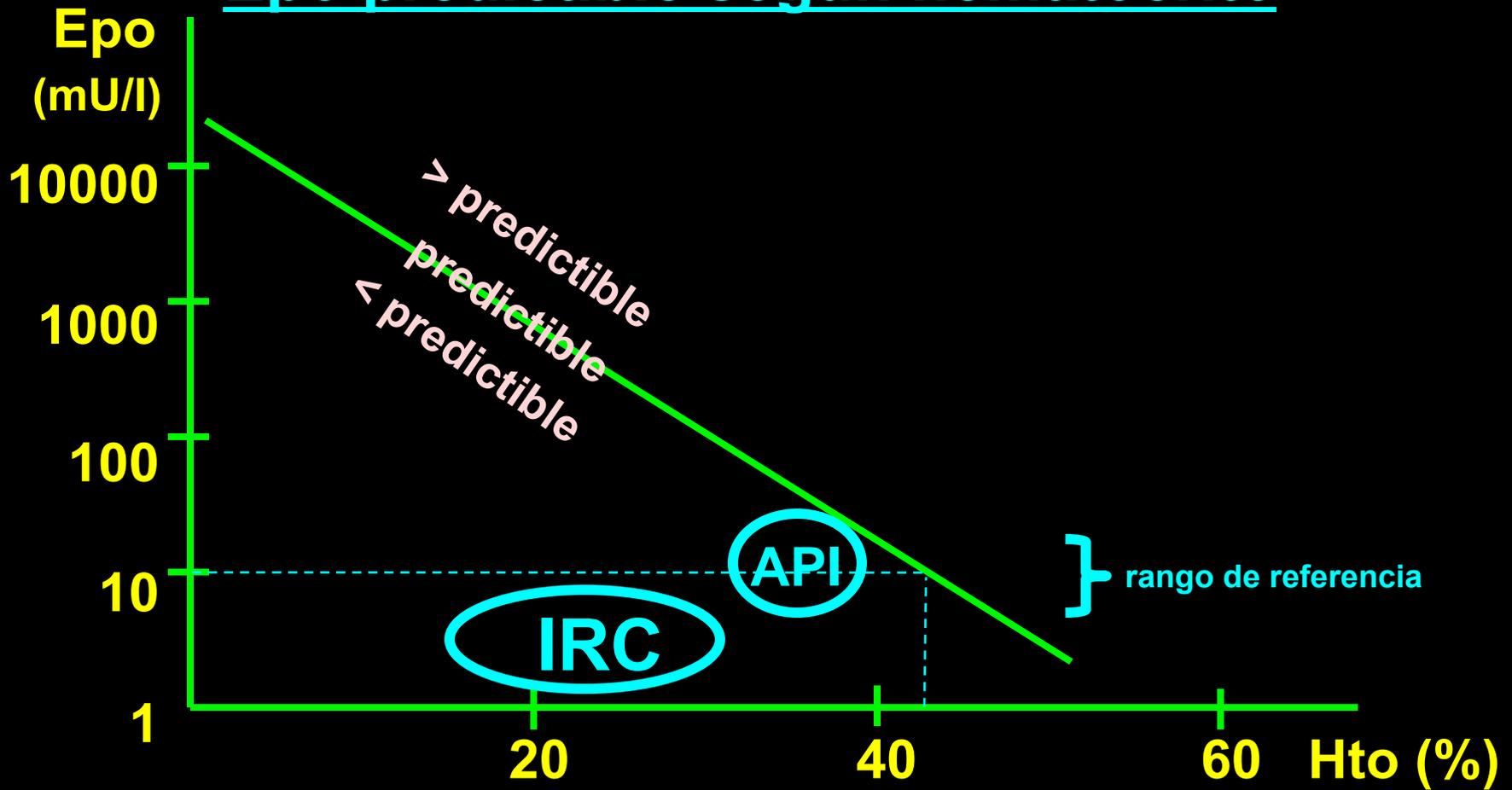
↑ eritropoyesis



Ferropenia



Epo predictable según hematocrito



Anemia

Síntesis (riñón) - Consumo (MOE) = [Epo] sérica

IRC - API

↓

+

< predictable

AAS - AEP - SMD

↑

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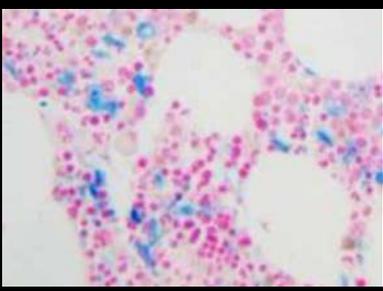
> predictable

AF - AM - AH

↑

+

predictible



Medulograma Reacción de Perls

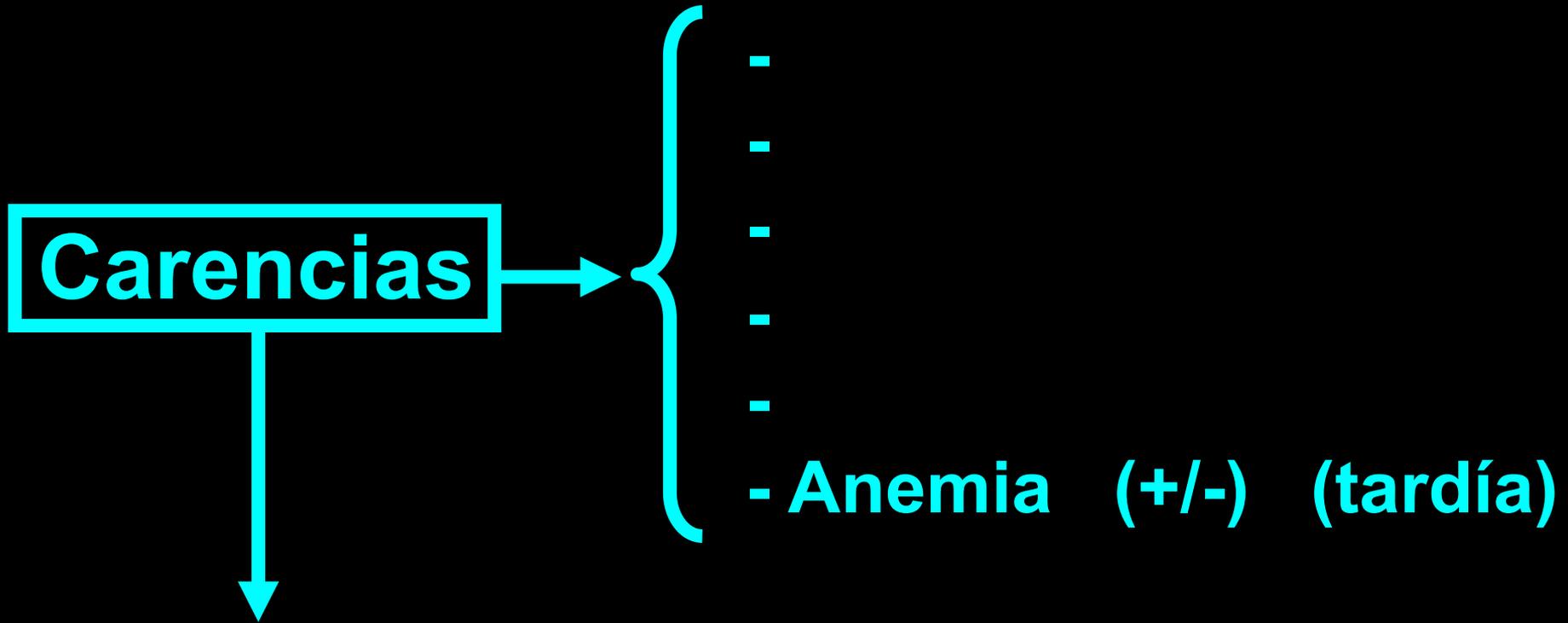
Hemosiderina (grumos)	Sideroblastos 	Ferricianuro de K + CIH 2%
++ / +++	40-60 % 1-3 gr	Normal
-	-	A. ferropénica
+++ / +++++	-	APC
++++	40-60 % 1-3 gr	Sobrecarga Fe
++++	SB en anillo	A. sideroblástica

Prueba terapéutica

Patrón oro

- **hierro** (oral-parenteral) **ferropenia**
- **cobalamina** (oral-parenteral) **cobalaminopenia**
- **ácido fólico** **folatopenia**
- **corticoides - Ig EV** **AHAI**
- **rHuEpo** **IRC**

“Anemias carenciales”

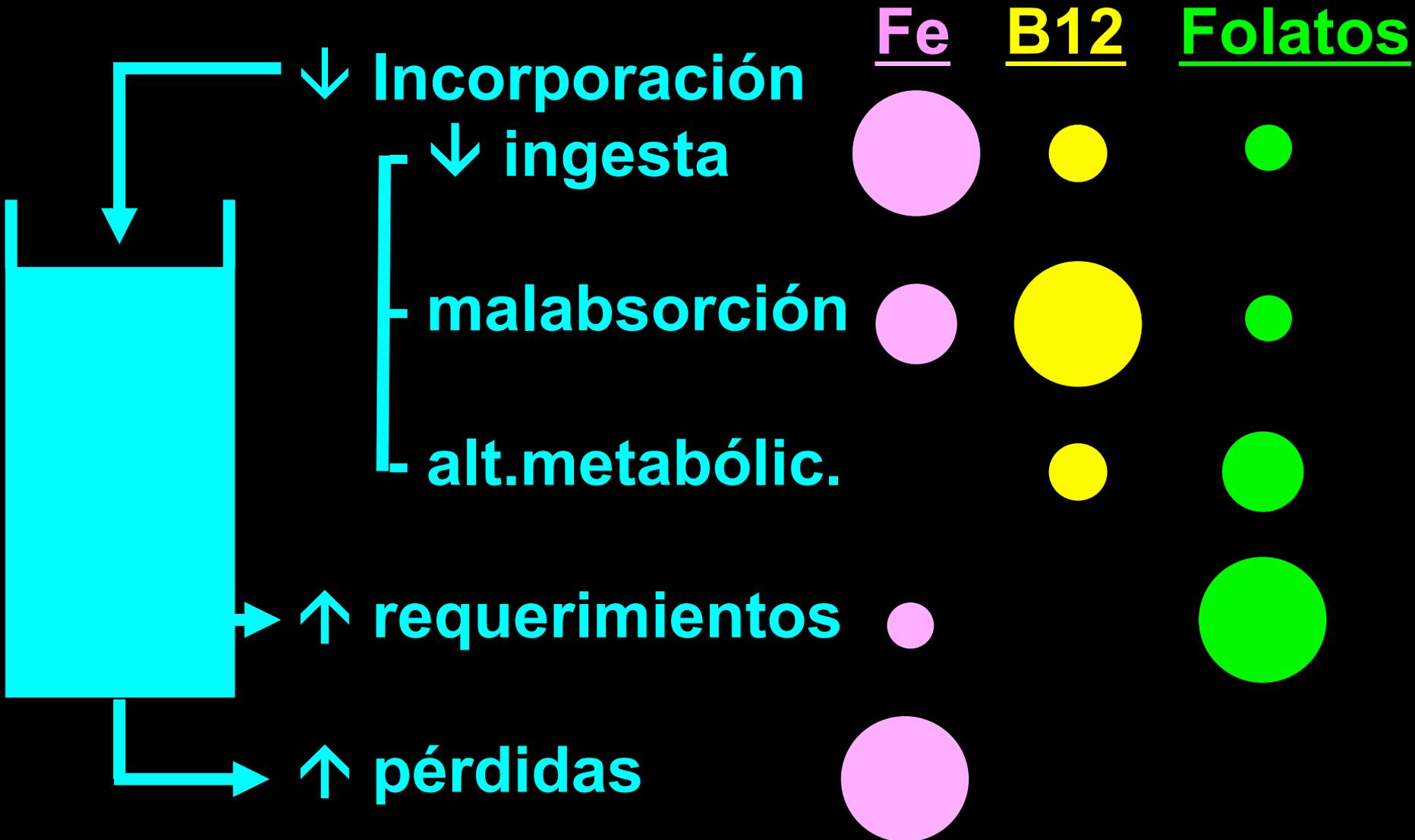


Ferropenia

Cobalaminopenia

Folatopenia

Carencia = balance negativo



Muchas gracias