Instituto Nacional de geriatría

UNIVERSIDAD ANDRES BELLO

XIX Congreso de Geriatría y Gerontología de Chile

IMPLICANCIAS DE LA HIPOALBUMINEMIA EN LA RESPUESTA A FÁRMACOS EN ADULTOS MAYORES

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Sociedad de Geriatría y Gerontología de Chile · 1994

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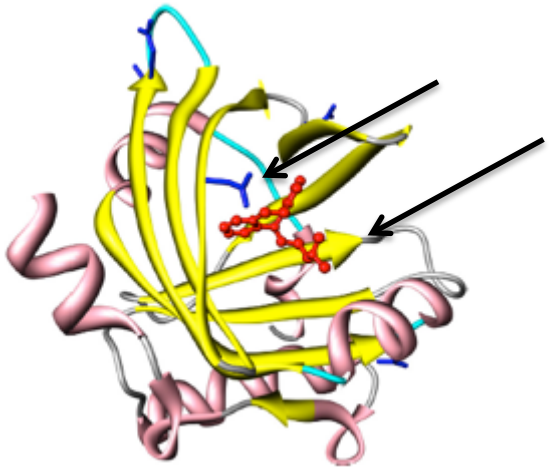
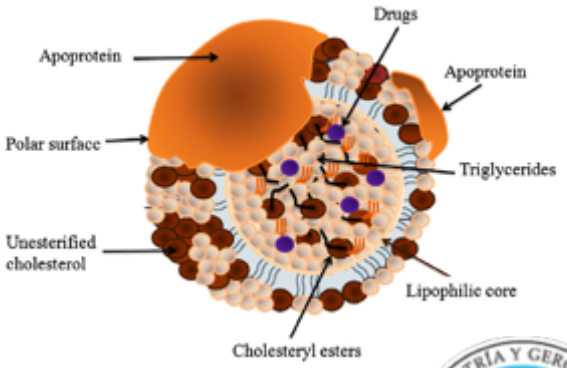
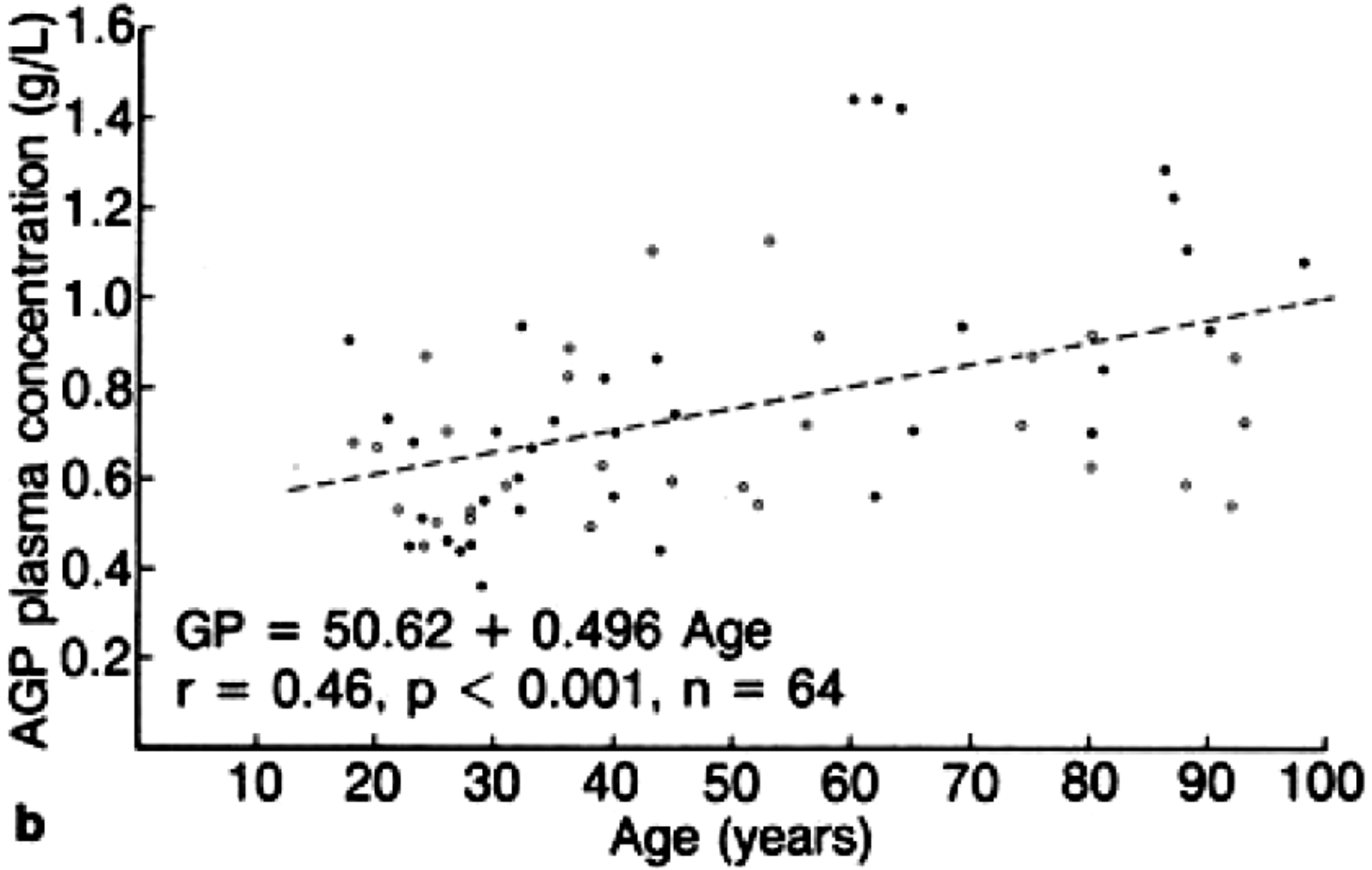




Ascenzi P, et. all. Clinical relevance of drug binding to plasma proteins. Journal of Molecular Structure. Elsevier BV; 2014 Dec;1077:4–13.

Alfa-1-Glucoproteína ácida



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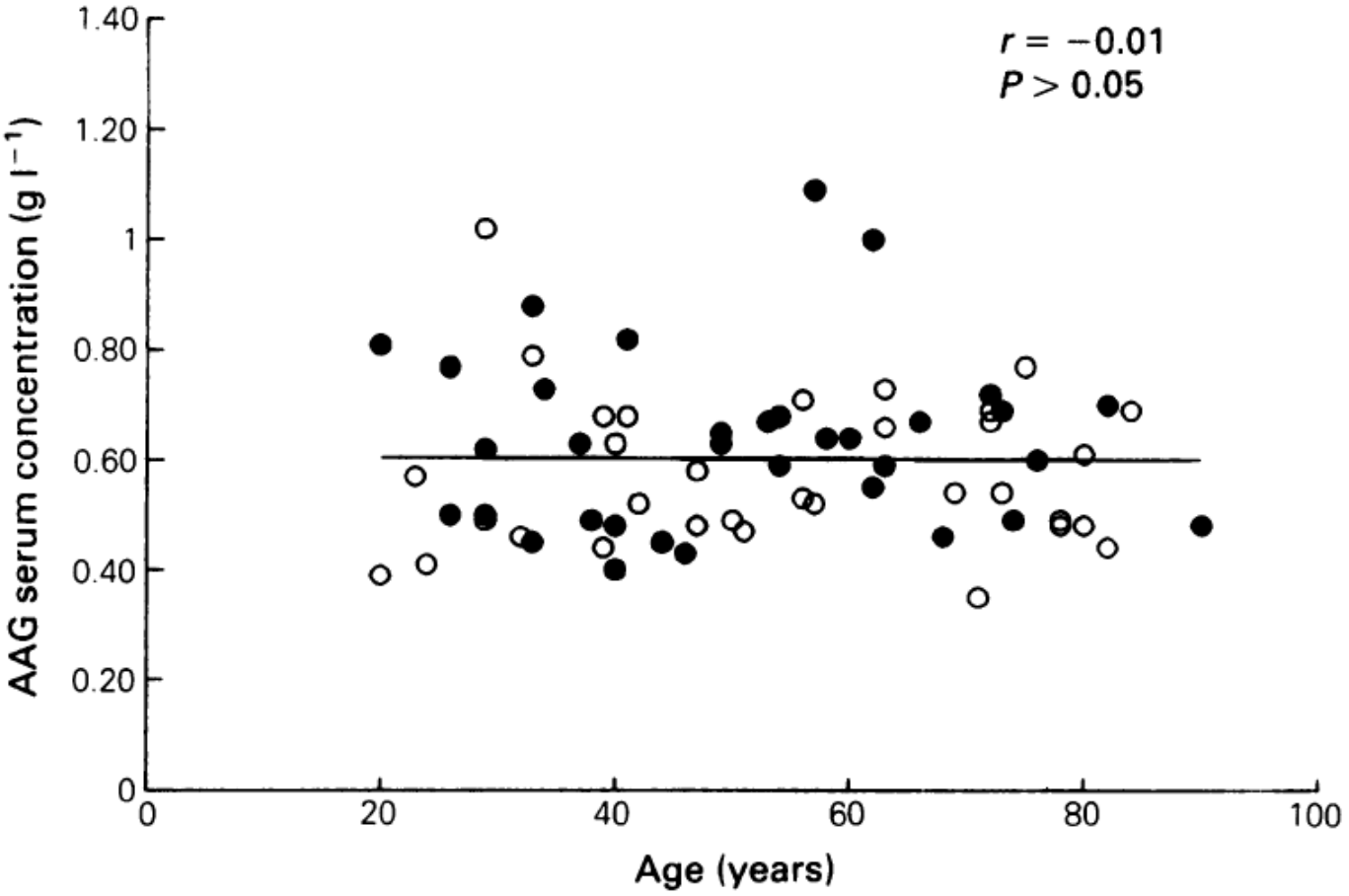
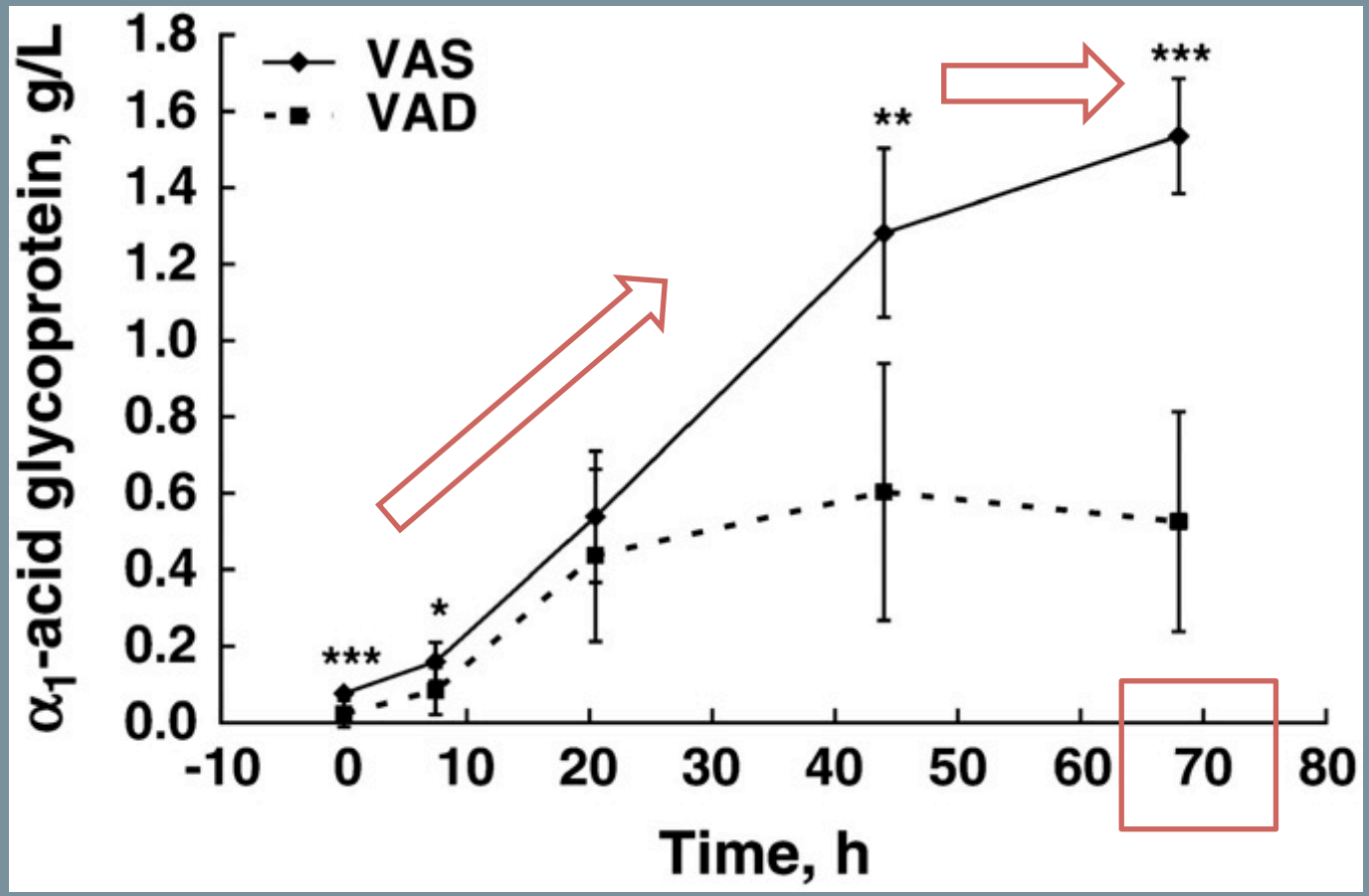


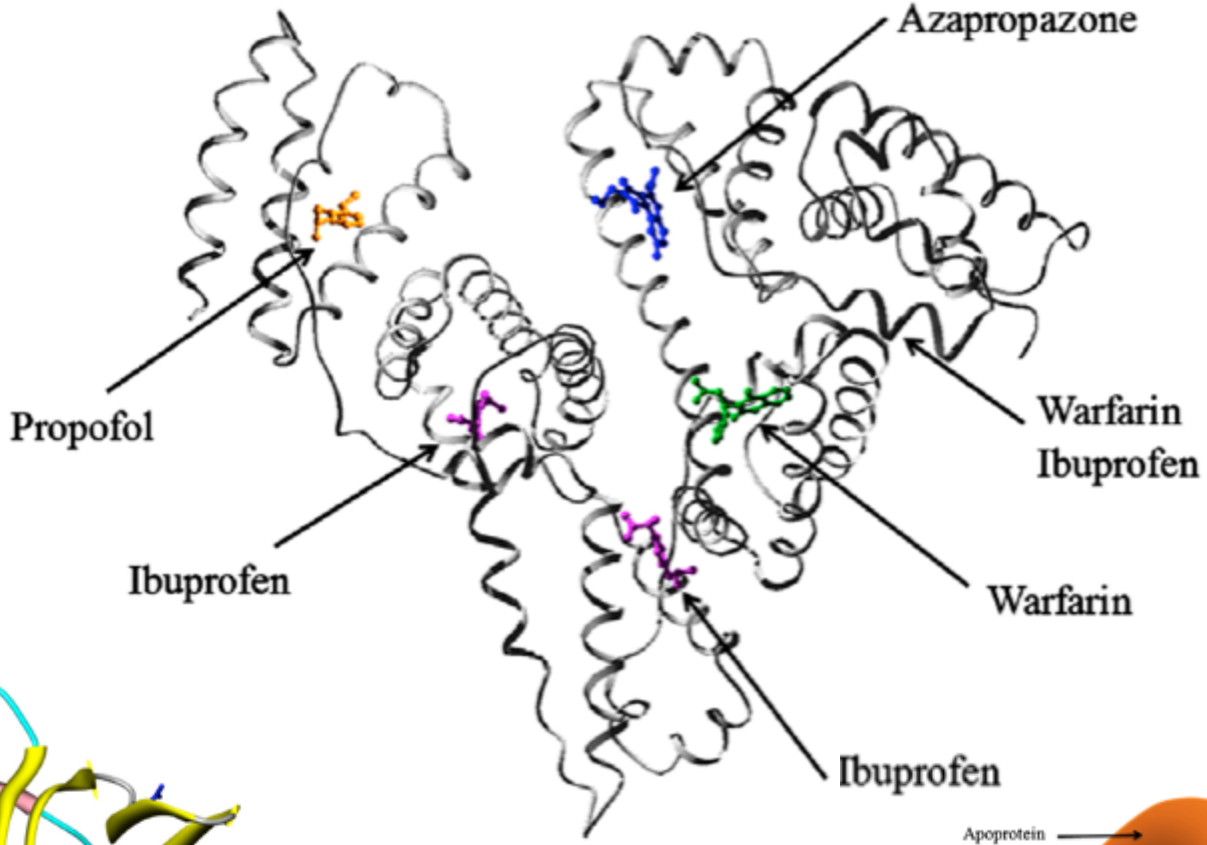
Veering B, Burm A, Souverijn J, Serree J, Spierdijk J. The effect of age on serum concentrations of albumin and alpha 1-acid glycoprotein. British Journal of Clinical Pharmacology. Wiley-Blackwell; 1990 Feb;29(2):201–6.

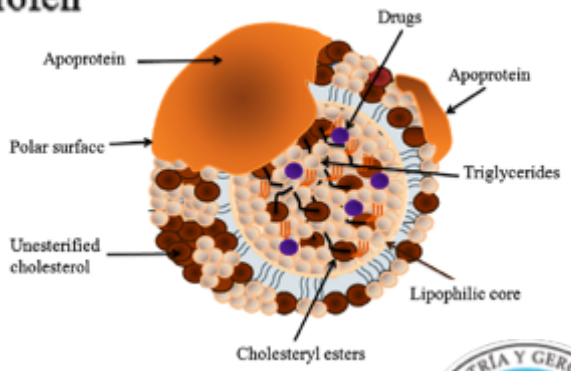
Plasma AGP response to rhIL-6–induced inflammation in VAD and VAS rats. Values are mean 6 SD, n ¼ 4. Asterisks indicate differences between groups:

*P < 0.05; **P < 0.01; ***P < 0.001 (Student's t test).



Gieng SH. Accumulation of retinol in the liver after prolonged hyporetinolemia in the vitamin A-sufficient rat. The Journal of Lipid Research. American Society for Biochemistry & Molecular Biology (ASBMB); 2005 Feb 16;46(4):641–9.





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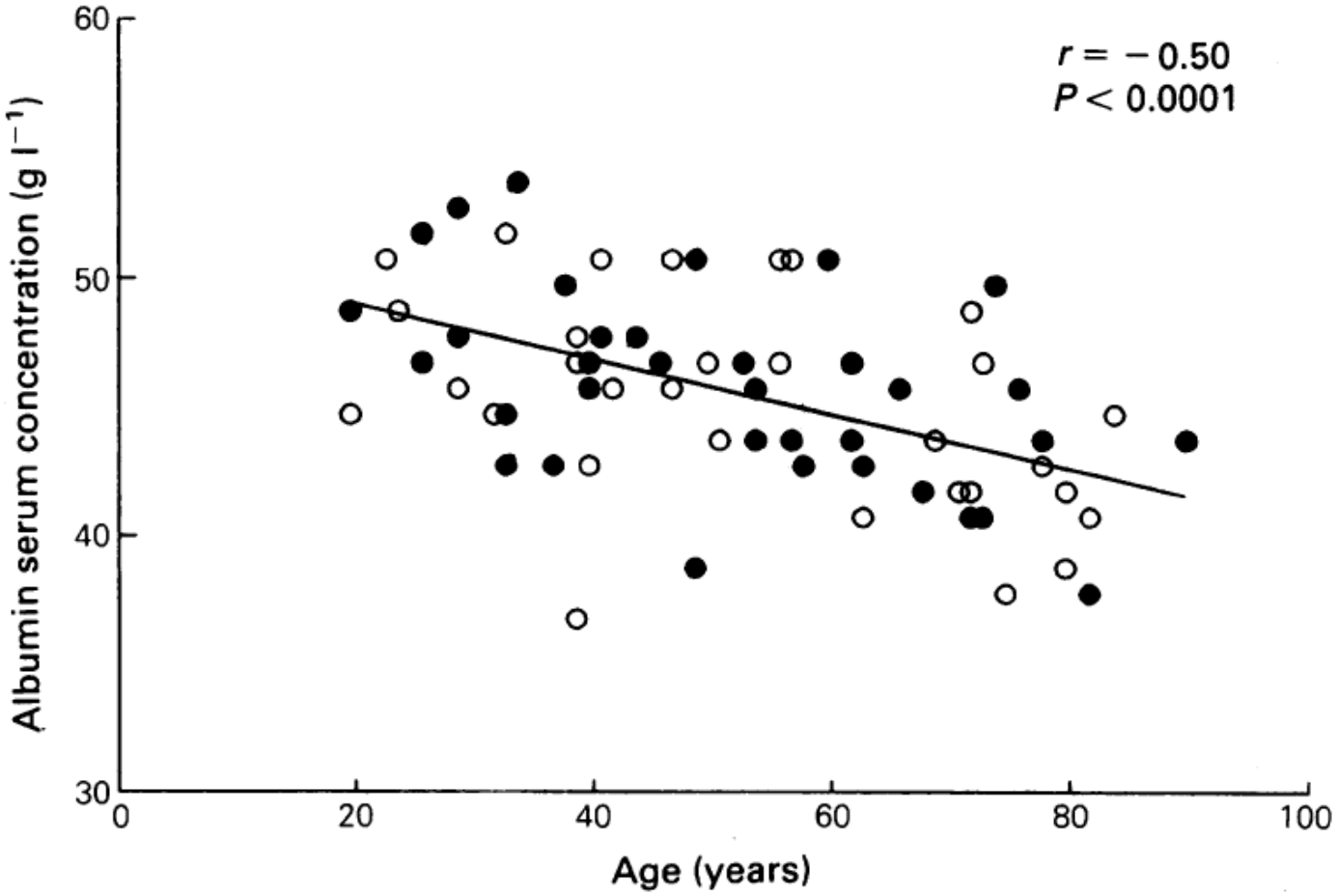
Albumina



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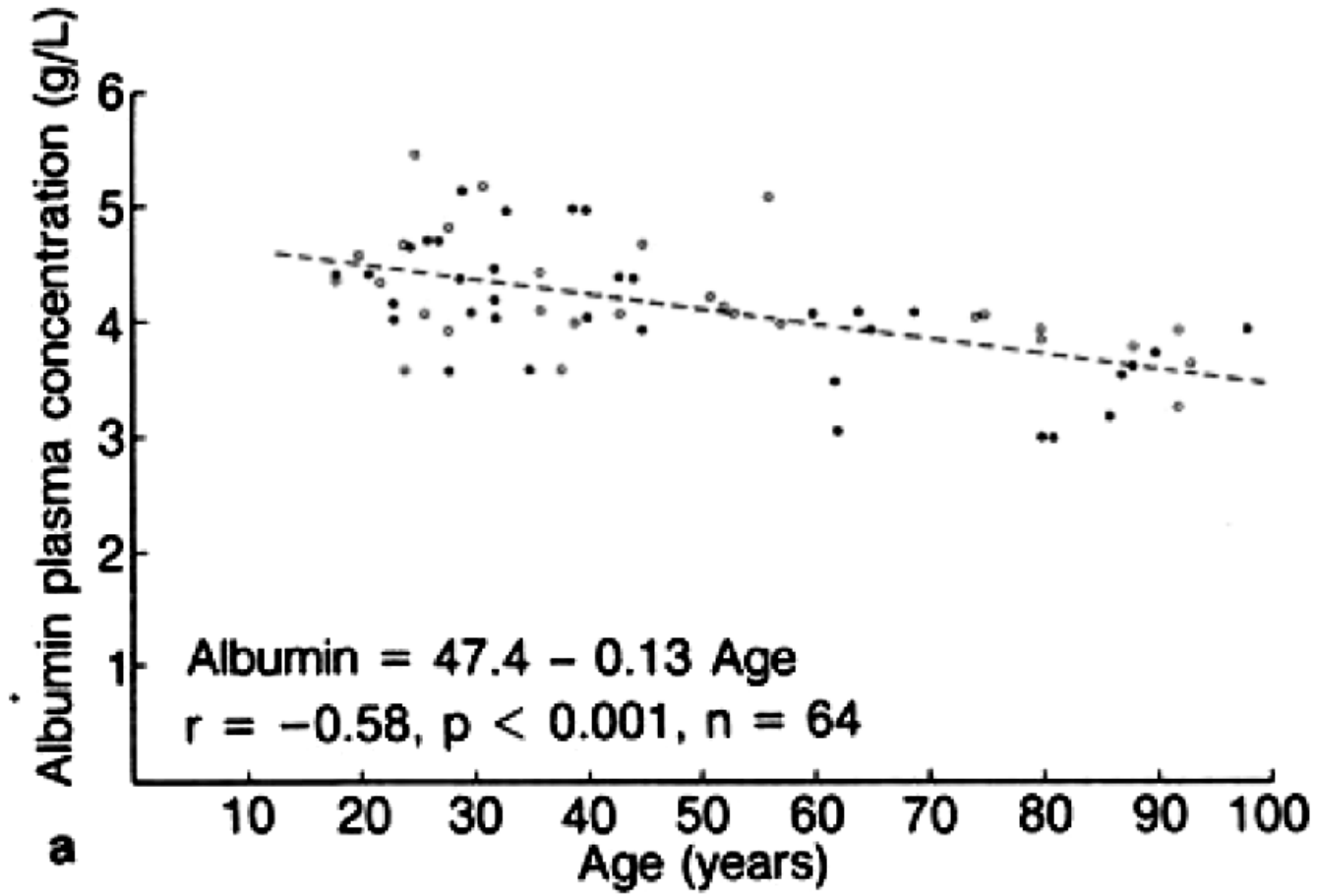
Albumina



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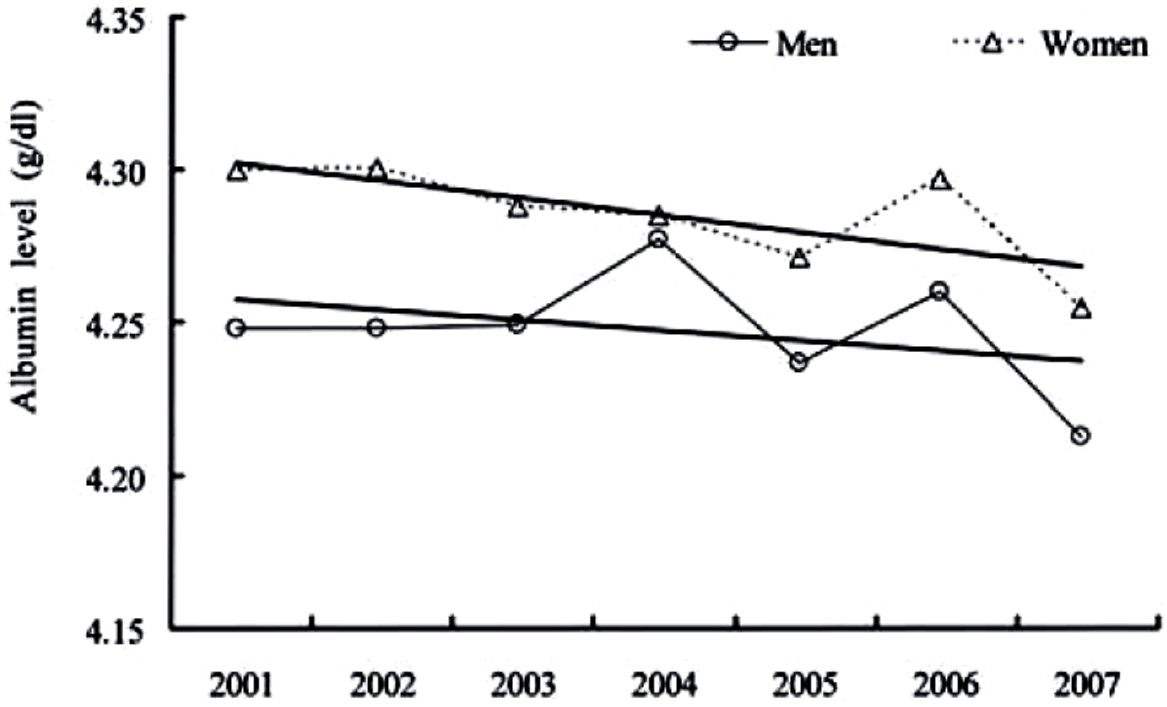


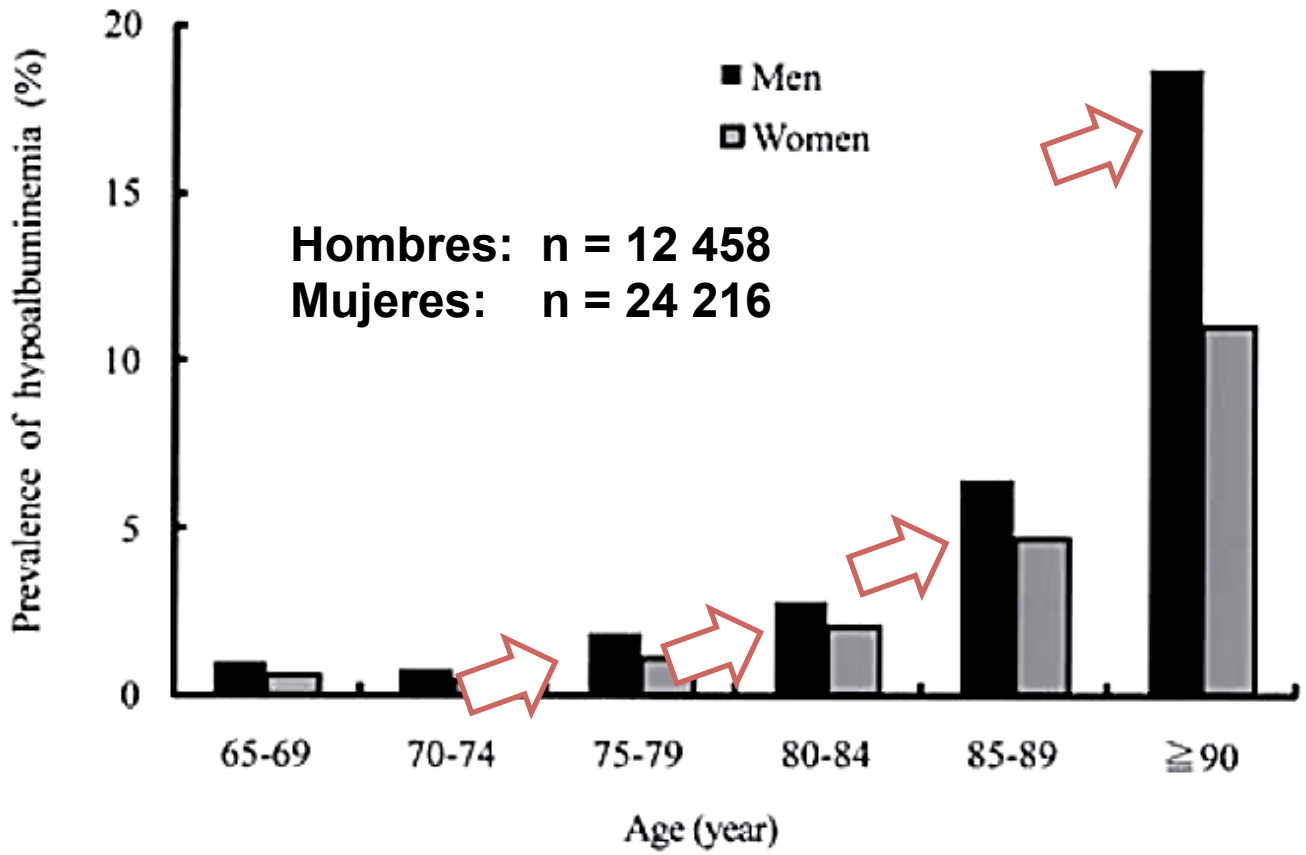
	number of subjects	albumin value (g/dl)		% change in 7 years
		2001	2007	
Men	628	4.25 ± 0.25	4.21 ± 0.23 ***	-0.95%
Women	1,404	4.30 ± 0.23	4.25 ± 0.22 ***	-1.20%

Value are expressed as mean ±SD.

***: p<0.001compared with serum albumin level in 2001and 2007.

Miyake M, et all. Seven-year large cohort study for the association of serum albumin level and aging among community dwelling elderly. J Anal Bio-Sci 2011; 34:4.

Prevalencia Hipoalbuminemia



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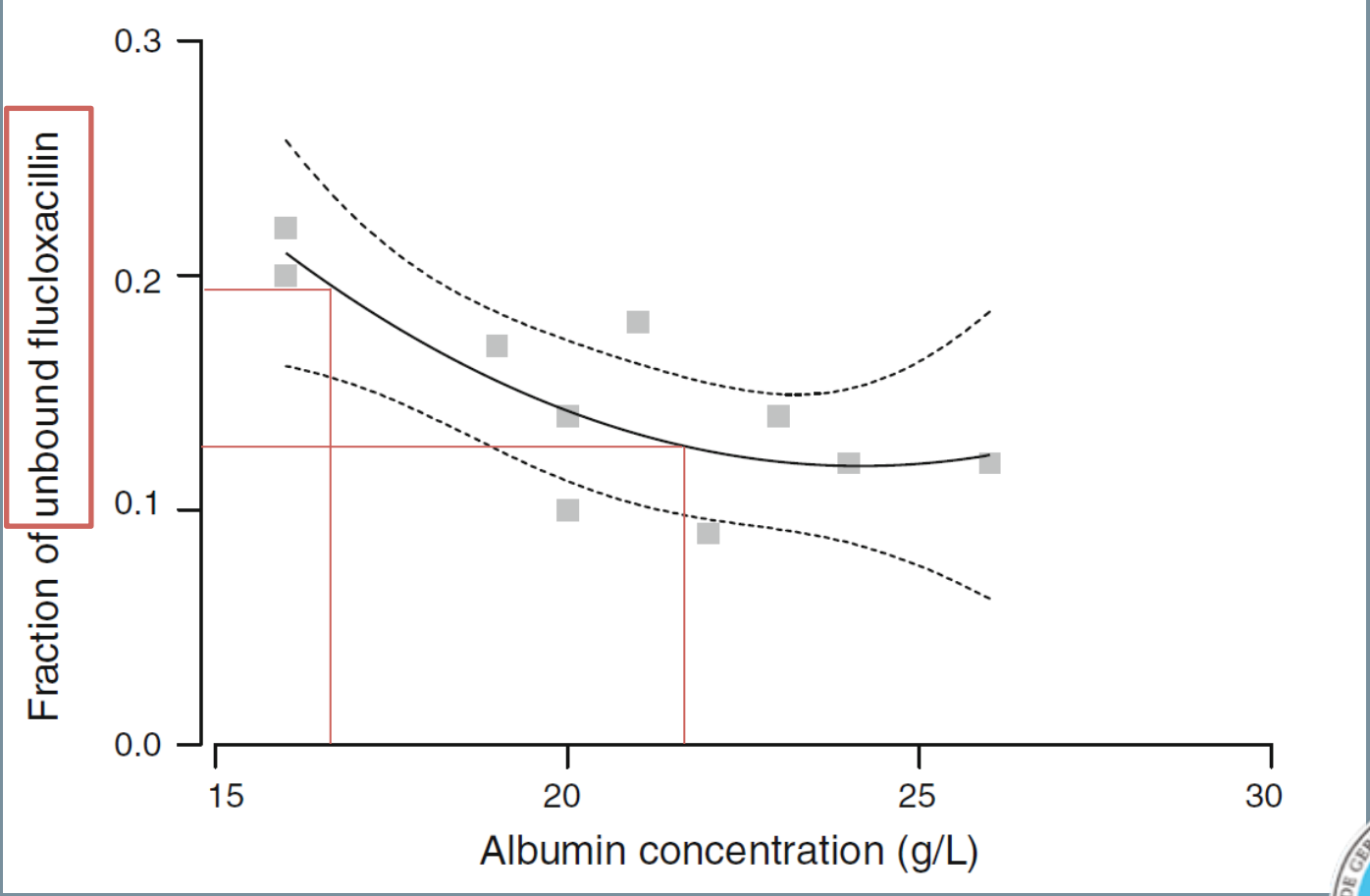
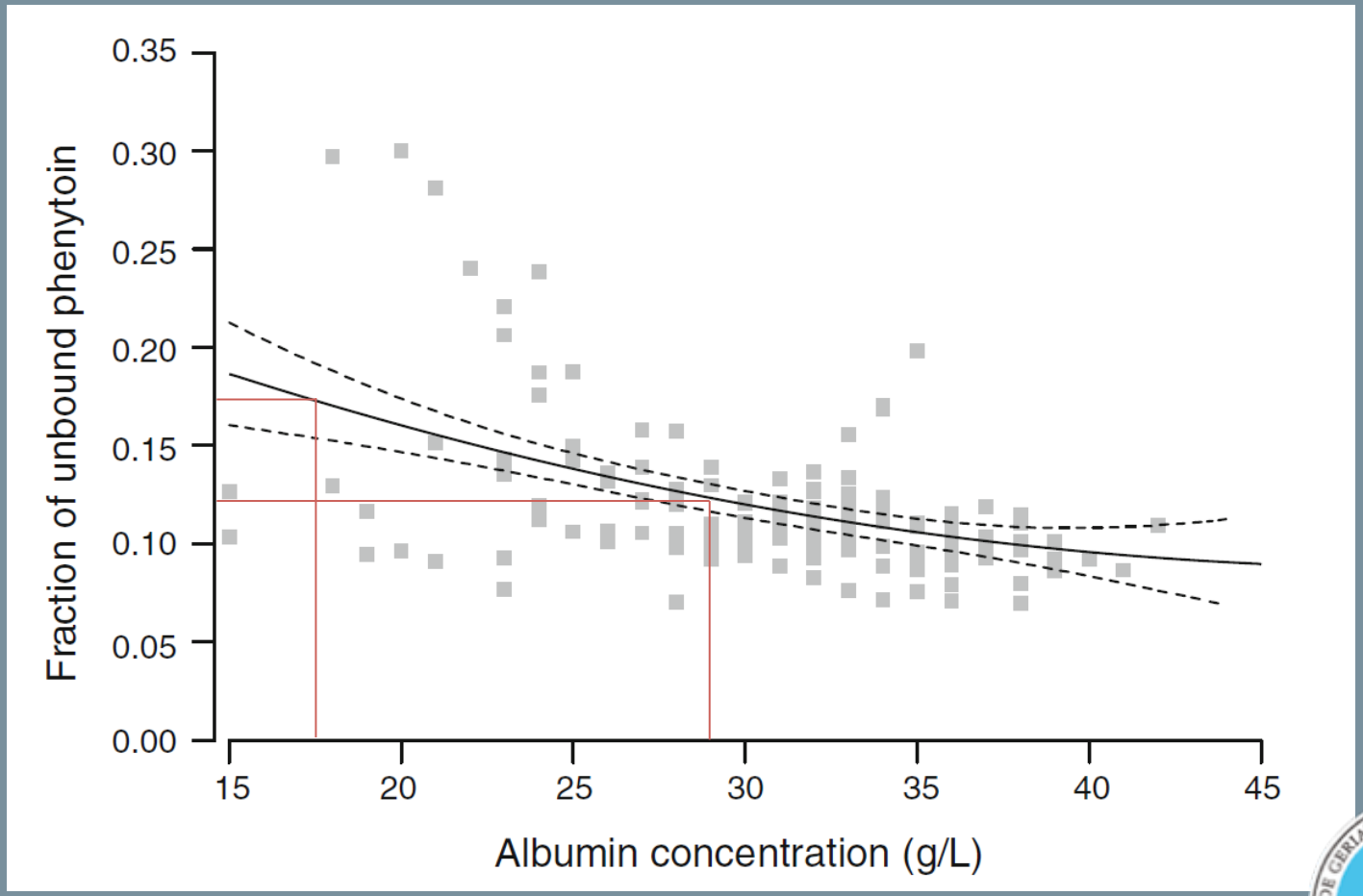
Ejemplo Fármaco Libre



Roberts JA, Pea F, Lipman J. The Clinical Relevance of Plasma Protein Binding Changes. Clinical Pharmacokinetics. 2012 Nov 13;52(1):1–8.

Ejemplo Fármaco Libre



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¿ En que dirección afecta este cambio a los pacientes geriátricos?

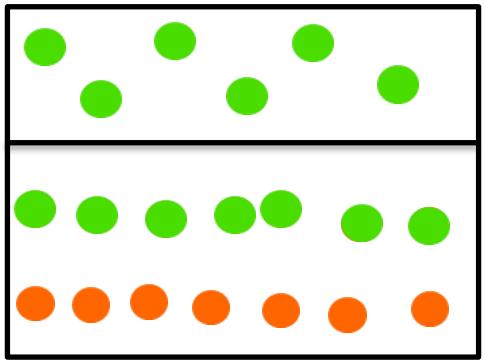
¿Qué acciones podríamos realizar para optimizar nuestras indicaciones terapéuticas?

DC= [L P]
[Lo]

DC= 70%

DC= [P]
K + [P]

K= [L] [P]
[LP]



Cl(h) = Fu x
Cl(int)

$$V_d = \left(\frac{f_u}{f_{uT}}\right) V_T + V_p$$

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CI de Fármaco en Pacientes Adultos & UCI

Table 1 Changes in drug clearance for moderate to highly bound antibacterials in critically ill patients with hypoalbuminaemia compared with healthy volunteer data

Drug	% Protein binding in healthy volunteers	ICU/healthy subjects (*n*)	Change in clearance in ICU patients[a]	Change in V_d in ICU patients[a]
Aztreonam [26, 27]	60	48/7	15 % increase	Nil change
Ceftriaxone [10, 16]	85–95	6/11	99 % increase	32 % increase
Daptomycin [28, 29]	90–93	9/24	151 % increase	10 % increase
Ertapenem [30, 31]	85–95	17/10	113 % increase	200 % increase
Ertapenem [14]	85–95	8/16	462 % increase	624 % increase
Flucloxacillin [13, 32]	95	10/10	10 % increase	57 % increase
Fusidic acid [33, 34]	95–97	6/8	94 % increase	NA
Teicoplanin [8, 35]	90–95	12/6	36 % increase	NA

ICU intensive care unit (critically ill), *NA* not available, V_d apparent volume of distribution

[a] Calculated as (observed value − reference value/reference value) × 100

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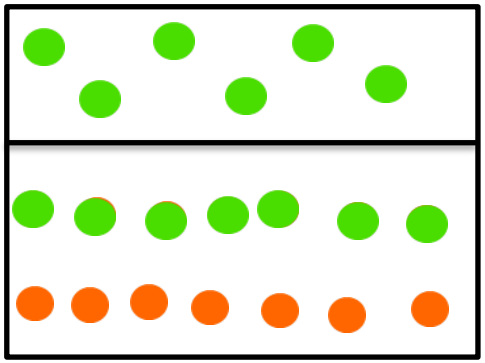
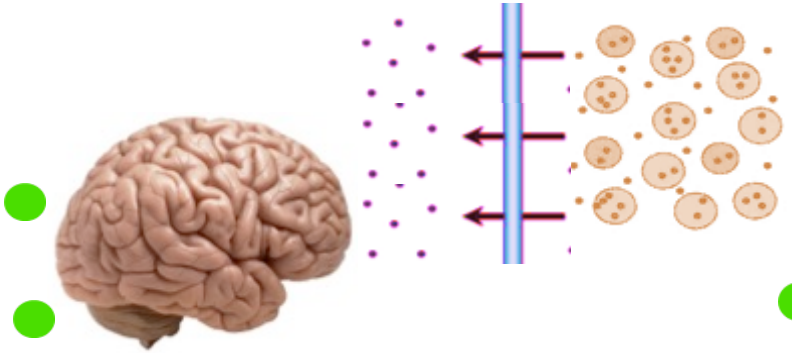


< 50% Cl Fu

Cl(h) = Fu x Cl(int)



< Clcr 60%

< 40%

Cl de Fármaco Libre en Pacientes Geriátricos

Table VI. Summary of evidence for the effect of aging on drug clearance (CL) of capacity-limited drugs with high protein binding

Drug	Free CL	Total CL
Valproic acid	↓[a]	↔[b]
Naproxen	↓[a]	↑[c], ↔[c], ↓[c]
Ibuprofen	↓[b]	↑[c], ↔[c], ↓[c]
Oxaprozin	↓[c]	↓[c]
Phenytoin	↓[c]	↑[c], ↔[c], ↓[c]
Piroxicam	↔[c]	↓[c]
Diazepam	↓[b]	↔[b]
Warfarin	↔[c]	↓[c]
Lorazepam	↓[c]	↓[c]
Temazepam	↓[c]	↔[b]

X = 50 %

a High-level evidence.

b Medium-level evidence.

c Low-level evidence.

↑ indicates increase; ↓ indicates decrease; ↔ indicates unchanged.

Butler JM, Begg EJ. Free Drug Metabolic Clearance in Elderly People. Clinical Pharmacokinetics. Springer Science + Business Media;

Lansoprazol

Claritromicina

Fenitoina

Gemfibrozilo

Lorazepam

Tamoxifeno

Clofibrato

Ceftriaxona

Clordiazepoxido

Rifampicina

Glibenclamida

Prednisolona

Zolpidem

Trazodona

Ciproterano

Clindamicina

Diazepam

Ác. Valpróico

Metadona

Tolbutamida

> 90% unión albumina

< 30 % extracción hepática

Gurevich KG. Effect of blood protein concentrations on drug-dosing regimes: practical guidance. Theoretical Biology and Medical Modelling.

Una Propuesta Cinética Práctica

$$K = \frac{[L]\cdot[P]}{[LP]} \qquad [L_0] = [LP] + [L] \qquad K = \frac{[L_0](1-DC)[P]}{DC[L_0]} = \frac{(1-DC)[P]}{DC}$$

$$DC = \frac{[LP]}{[L_0]} \qquad [LP] = DC[L_0] \qquad DC = \frac{[P]}{K+[P]}$$

$$[L] = [L_0](1-DC)$$

$$[L_1] = [L_{01}](1-DC_1)$$

$$[L_{01}](1-DC_1) = [L_0](1-DC)$$

$$\frac{[L_{01}]}{[L_0]} = \frac{1-DC}{1-DC_1} = \frac{1-DC}{1-\frac{a[P]}{K+a[P]}} \qquad \frac{[L_{01}]}{[L_0]} = \frac{1-DC}{1-\frac{aDC[P]}{(1-DC)[P]+aDC[P]}} = \frac{1-DC}{1-\frac{aDC}{1-DC+aDC}}$$

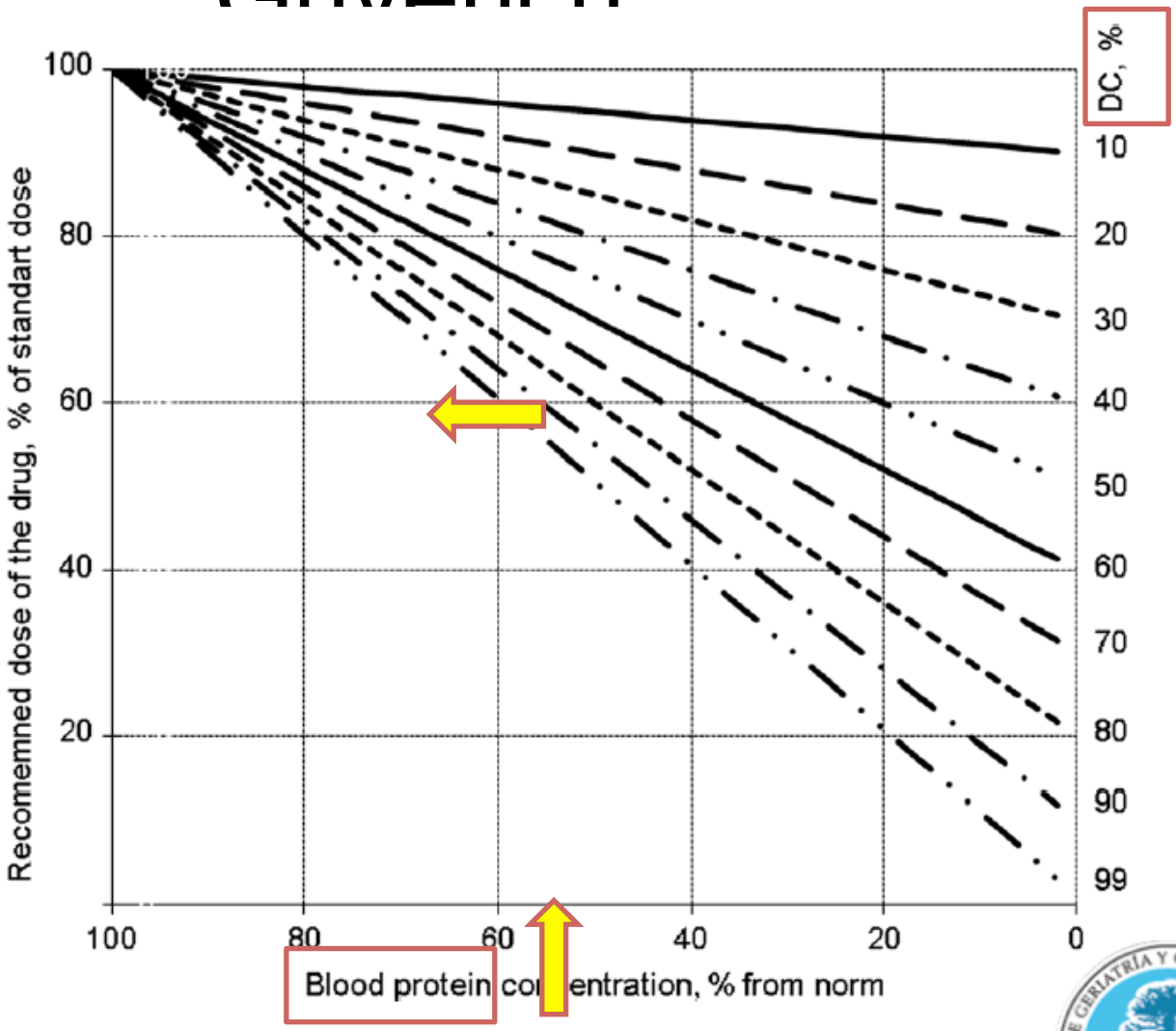
Gurevich KG. Effect of blood protein concentrations on drug-dosing regimes: practical guidance. Theoretical Biology and Medical Modelling. 2013;10(1):20.

Propuesta Cinética Kostantin Guverich

Albumina: 2,0 g/ dL

57% del normal

DC: 85% a 95 %



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muchas gracias.

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