A Coruña 2008
XXIX
Congreso Nacional de la Sociedad Española de Medicina Interna

EPOC:

una Enfermedad Sistémica.

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2008
XXIX
Congreso Nacional
de la Sociedad Española
de Medicina Interna

EPOC:

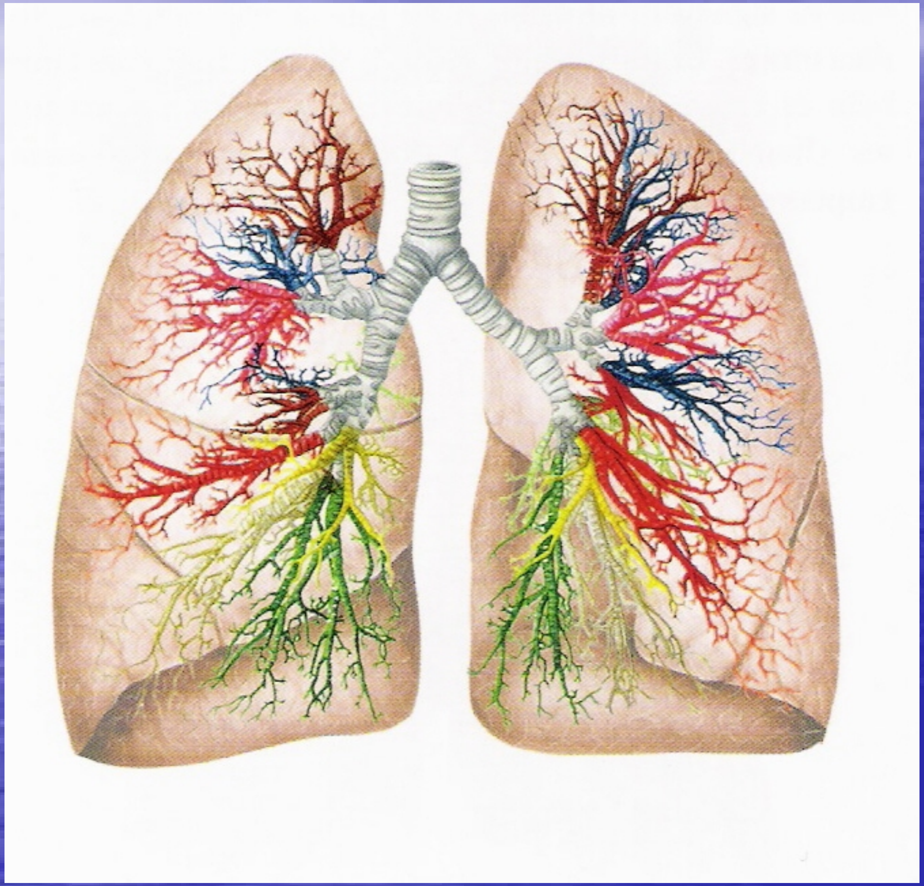
¿ Una Enfermedad Sistémica?

JC Martín Escudero
Hospital Universitario Río Hortega.
Valladolid

Sistémico

- “Perteneciente o relativo al organismo en su conjunto”. Diccionario Real Academia de la Lengua.

EPOC



- El pulmón es el centro del mundo en la EPOC.
- Posiblemente solo sea la víctima principal.

EPOC:

- Las Guías actuales sobre la EPOC, destacan la importancia de la afectación extrapulmonar o sistémica.

1. Pauwels R, Buist SA, Calverley P, Jenkins C, Hurd S. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for chronic obstructive pulmonary disease (**GOLD**). Workshop summary. Am J Respir Crit Care Med. 2001;163:1256-76. Update 2006.
2. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the **ATS/ERS** position paper. Eur Respir J. 2004;23:932-46.
3. Peces-Barba G, Agusti A, Barberá JA, et al. Enfermeda Pulmonar Obstructiva Crónica. Normativa **SEPAR-ALAT.** Arch Bronconeumol. 2008; 44 (5): 271-81.

EPOC etiología

- Múltiples causas pueden determinarla.

EPOC etiología

- Múltiples causas pueden determinarla.

Tabaco

EPOC etiología

- Múltiples [illegible] a.

Tabaco

Tabaco

EPOC etiología

- Múltiples [illegible] a.

Tabaco

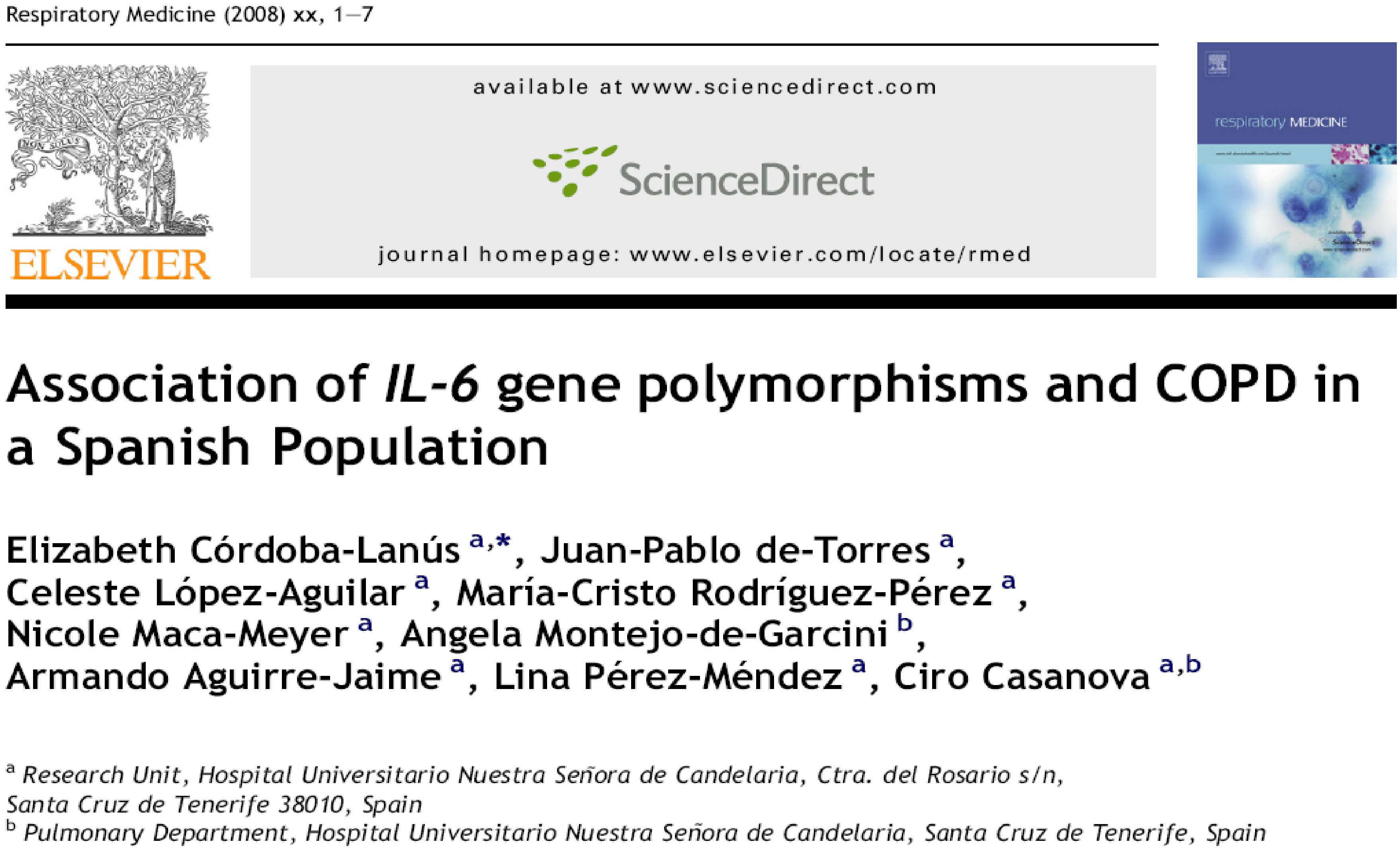
Tabaco

Tabaco

EPOC

- No todos los que fuman tienen EPOC.
- Al menos dos patrones:
  - Inflamación
  - Enfisema

EPOC



Respiratory Medicine (2008) xx, 1–7

available at www.sciencedirect.com

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Association of *IL-6* gene polymorphisms and COPD in a Spanish Population

Elizabeth Córdoba-Lanús [a,*], Juan-Pablo de-Torres [a],
Celeste López-Aguilar [a], María-Cristo Rodríguez-Pérez [a],
Nicole Maca-Meyer [a], Angela Montejo-de-Garcini [b],
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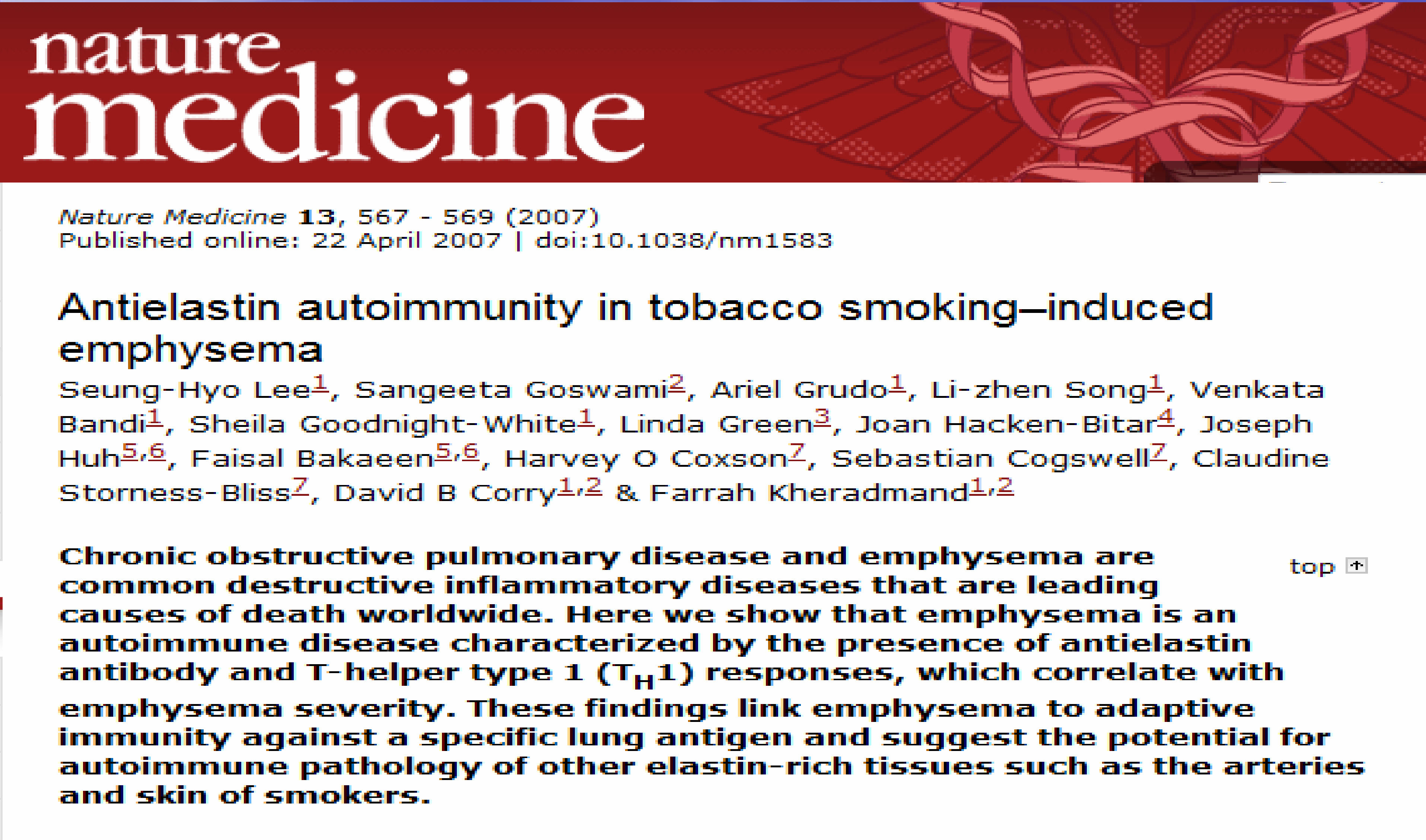
EPOC: tabaco

- Arterioesclerosis: cardiovascular
- Neoplasias.
- Autoinmune.
- Inflamación local y sistémica.

Autoinmune.



nature medicine

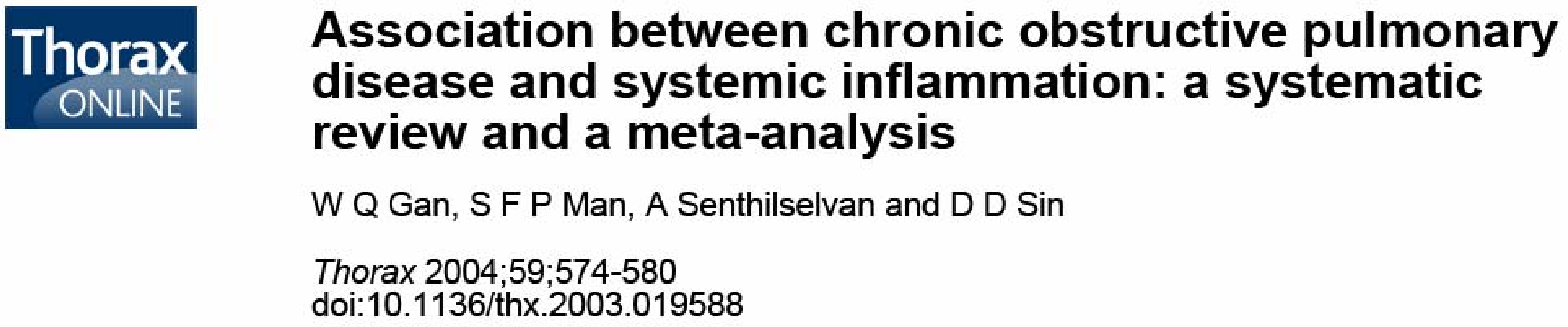
Nature Medicine **13**, 567 - 569 (2007)
Published online: 22 April 2007 | doi:10.1038/nm1583

Antielastin autoimmunity in tobacco smoking–induced emphysema

Seung-Hyo Lee[1], Sangeeta Goswami[2], Ariel Grudo[1], Li-zhen Song[1], Venkata Bandi[1], Sheila Goodnight-White[1], Linda Green[3], Joan Hacken-Bitar[4], Joseph Huh[5,6], Faisal Bakaeen[5,6], Harvey O Coxson[7], Sebastian Cogswell[7], Claudine Storness-Bliss[7], David B Corry[1,2] & Farrah Kheradmand[1,2]

Chronic obstructive pulmonary disease and emphysema are common destructive inflammatory diseases that are leading causes of death worldwide. Here we show that emphysema is an autoimmune disease characterized by the presence of antielastin antibody and T-helper type 1 (T_H1) responses, which correlate with emphysema severity. These findings link emphysema to adaptive immunity against a specific lung antigen and suggest the potential for autoimmune pathology of other elastin-rich tissues such as the arteries and skin of smokers.

Inflamación local y sistémica.



Thorax ONLINE

Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis

W Q Gan, S F P Man, A Senthilselvan and D D Sin

Thorax 2004;59;574-580
doi:10.1136/thx.2003.019588

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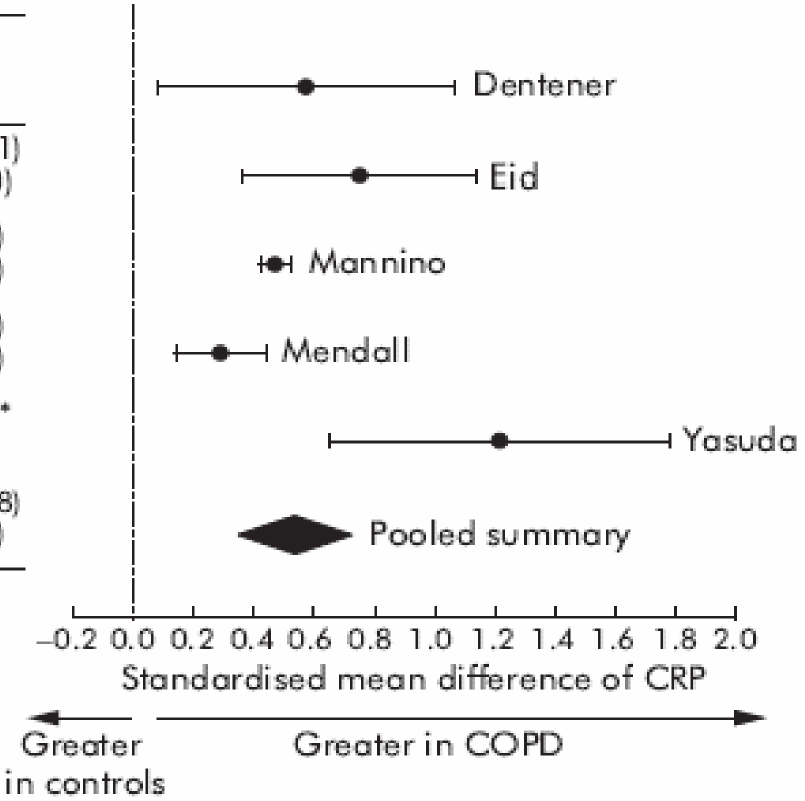
Proteína C Reactiva

Author	Group	N	Age (yr)	FEV_1 (% pred)	Current smoker (%)	Men (%)	CRP (mg/l)
Dentener[18]	COPD	55	69 (4)	36 (14)	NR	100	20.4 (21.1)
	Control	23	64 (3)	110 (17)	NR	70	9.0 (16.0)
Eid[19]	COPD	68	68 (7)	31 (8)	100	57	3.5 (3.4)
	Control	45	NR	NR	33	NR	3.1 (1.9)
Mannino[20]	COPD	2366	64 (16)	78 (20)	32	60	3.3 (2.0)
	Control	8446	40 (17)	103 (13)	21	48	2.7 (1.0)
Mendall[21]	COPD	349*	45–59	NR	NR	100	0.8 (2.8)*
	Control	349*	45–59	NR	NR	100	0 (0)
Yasuda[22]	COPD	39	66 (3)	35 (1)	41	69	18.7 (17.8)
	Control	22	66 (1)	82 (0)	32	68	0.9 (2.8)



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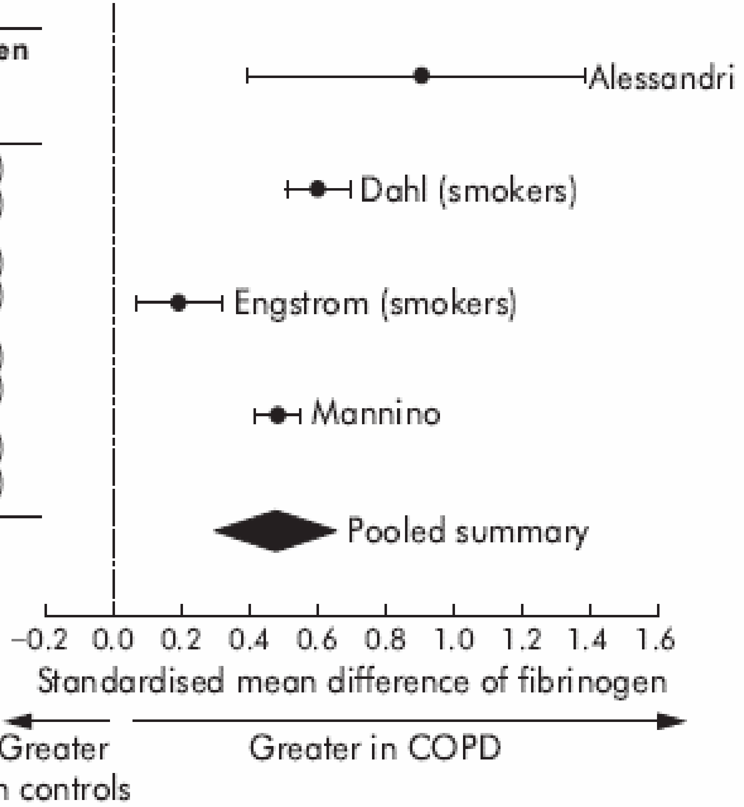
Fibrinógeno

Author	Group	N	Age (yr)	FEV_1 (% pred)	Current smoker (%)	Men (%)	Fibrinogen (g/l)
Alessandri[24]	COPD	37	68 (8)	1.1 (0.5)*	19	73	3.0 (0.9)
	Control	30	58 (10)	NR	20	70	2.3 (0.5)
Dahl[25]	COPD	1427	62 (12)	66 (15)	100	51	3.5 (1.0)
Smokers	Control	785	55 (15)	117 (9)	100	43	3.0 (0.8)
Engstrom[†26]	COPD	720	47 (4)‡	<85	100	NR	3.8 (0.9)
Smokers	Control	449	47 (4)‡	> 105	100	NR	3.6 (0.8)
Mannino[20]	COPD	2065	67 (12)	77 (21)	31	60	3.1 (0.6)
	Control	3488	57 (13)	104 (14)	17	47	2.8 (0.5)



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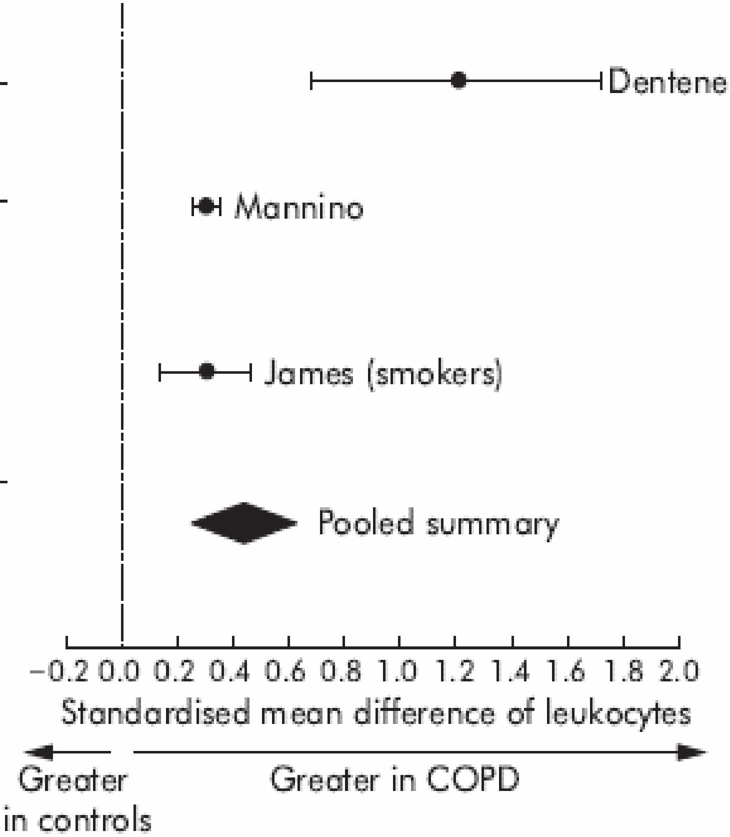
Leucocitos

Author	Group	N	Age (yr)	FEV_1 (% pred)	Current smoker (%)	Men (%)	WBC (10^9/l)
Dentener[18]	COPD	55	69 (4)	36 (14)	NR	100	8.0 (2.7)
	Control	23	64 (3)	110 (17)	NR	70	5.1 (1.2)
Mannino[20]	COPD	2366	68 (16)	78 (20)	32	60	7.1 (1.3)
	Control	8446	40 (17)	103 (13)	21	48	6.7 (1.3)
James*[29]	COPD	294	56 (12)	66 (12)	100	74	7.7 (1.3)
	Control	326	44 (13)	114 (9)	100	58	7.3 (1.3)



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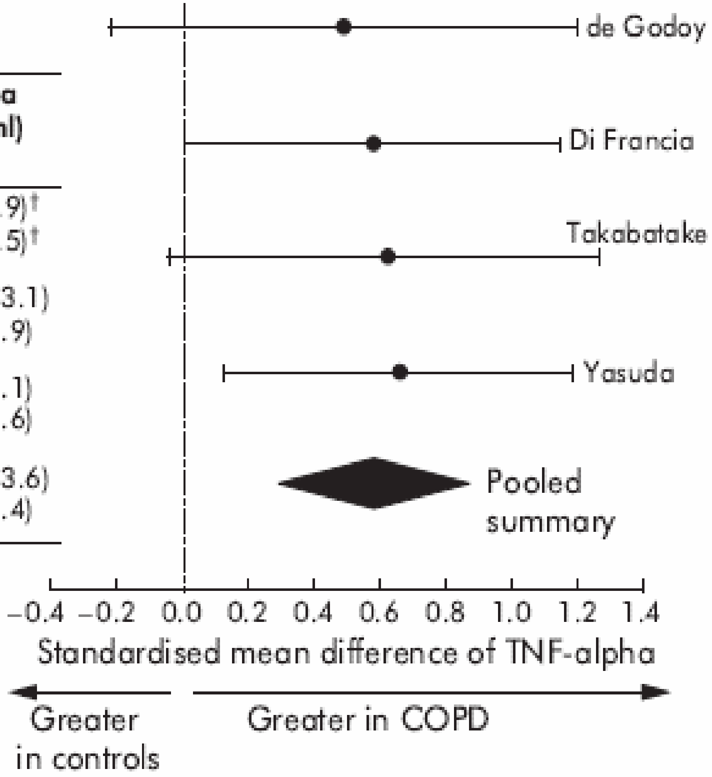
doi:10.1136/thx.2003.019588

TNF-alpha

Author	Group	N	Age (yr)	FEV_1 (% pred)	Current smoker (%)	Men (%)	TNF-α (pg/ml)
de Godoy[31]	COPD	20	69 (9)	69 (13)	NR	70	7.0 (2.9)†
	Control	13	64 (6)	106 (17)	NR	85	5.8 (1.5)†
Di Francia[32]	COPD	30	65 (9)	0.4 (0.1)*	NR	100	40.6 (73.1)
	Control	21	47 (13)	NR	NR	100	7.8 (3.9)
Takabatake[33]	COPD	27	73 (7)	52 (20)	NR	100	6.2 (1.1)
	Control	15	70 (6)	74 (7)	NR	100	5.4 (1.6)
Yasuda[22]	COPD	39	66 (3)	35 (1)	41	69	21.8 (33.6)
	Control	22	66 (1)	82 (0)	30	68	3.9 (2.4)



Thorax 2003;58:73-80

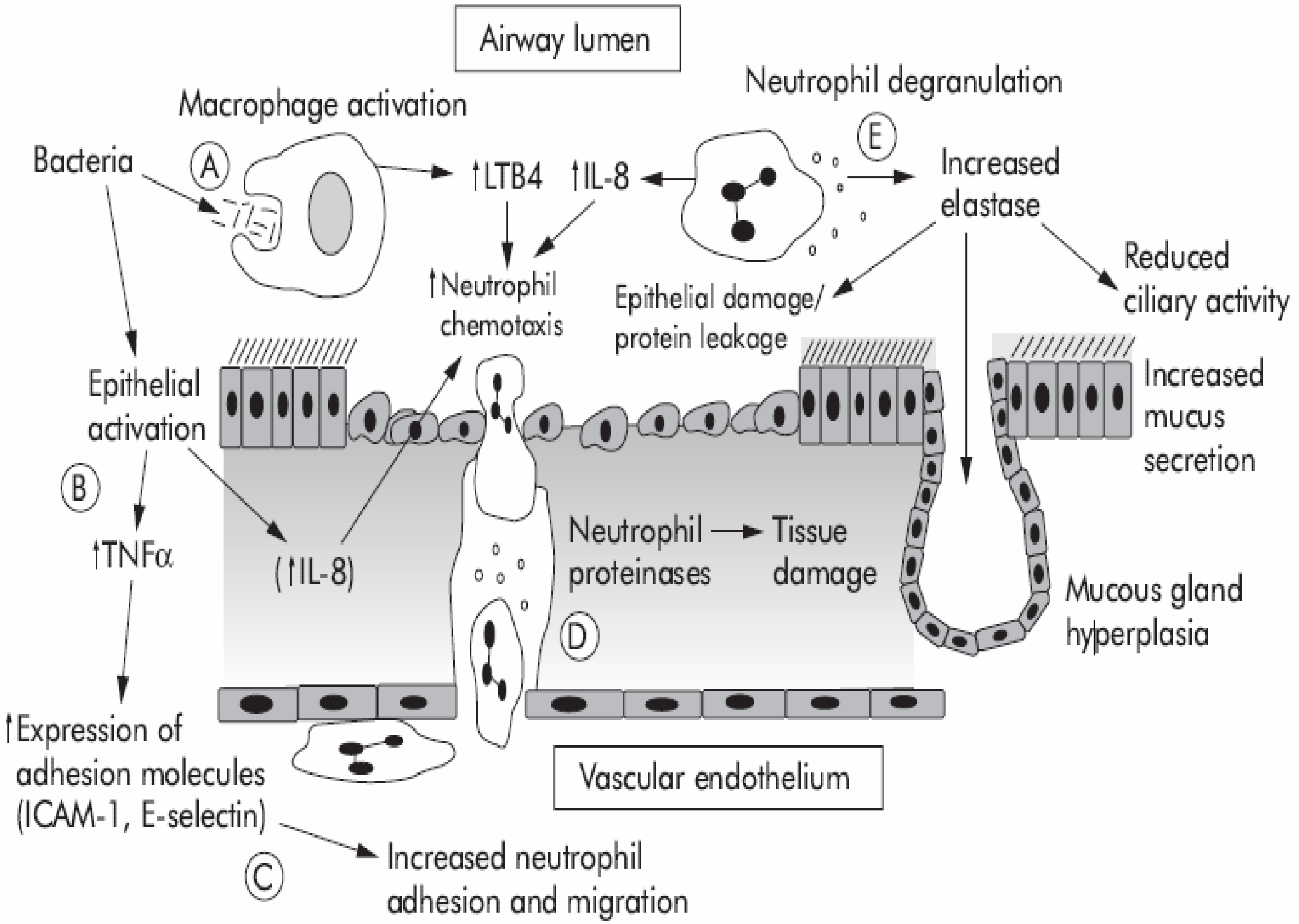
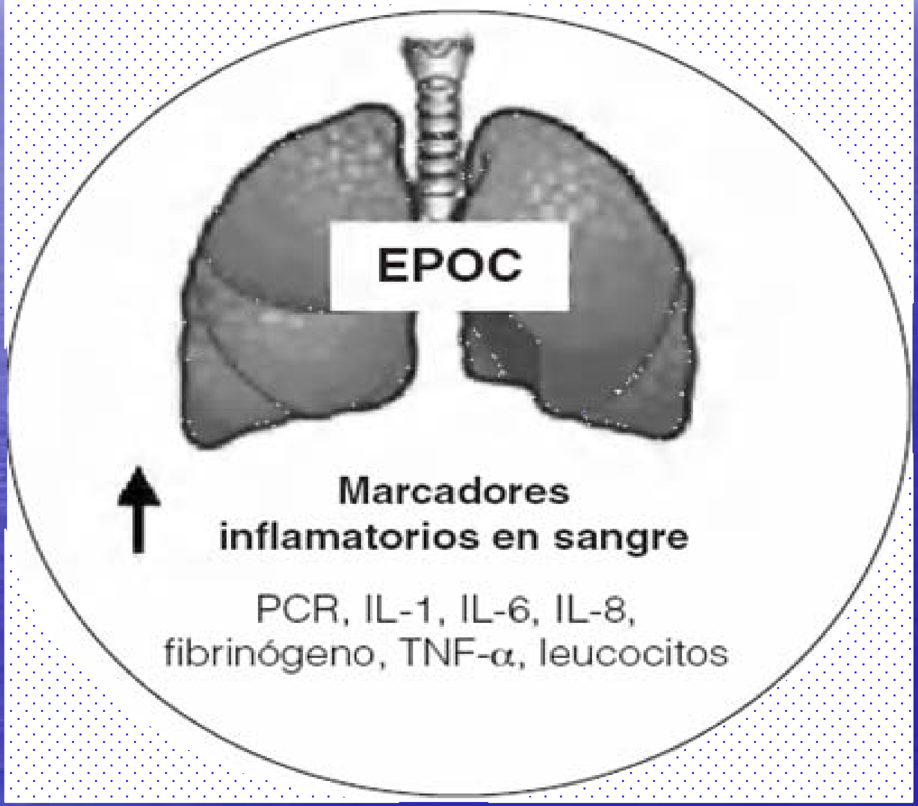
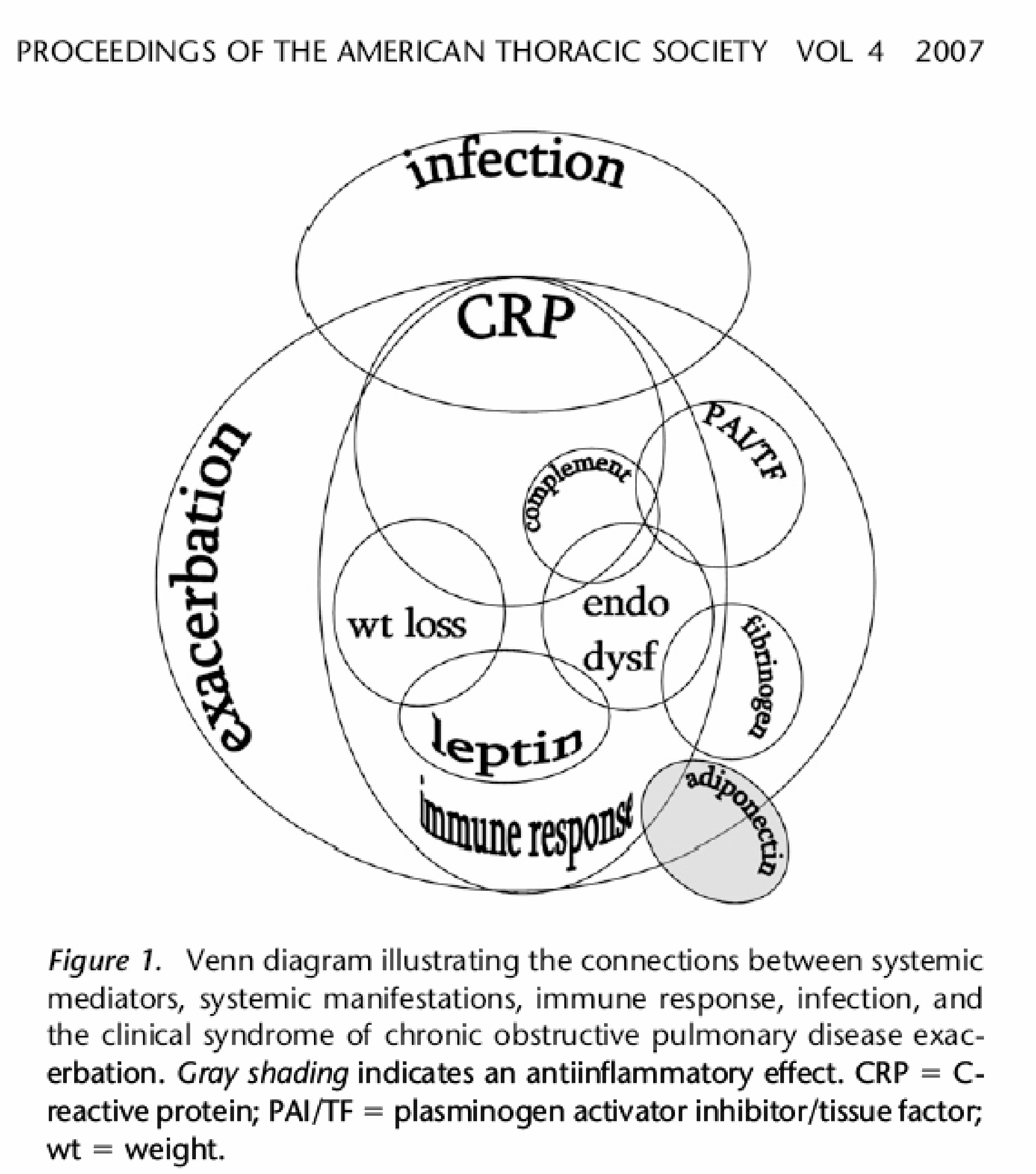

Airway lumen
Macrophage activation
Neutrophil degranulation
Bacteria
A
↑LTB4
↑IL-8
E
Increased elastase
↑Neutrophil chemotaxis
Epithelial damage/ protein leakage
Reduced ciliary activity
Epithelial activation
Increased mucus secretion
B
↑TNFα
(↑IL-8)
Neutrophil → Tissue
proteinases damage
Mucous gland hyperplasia
D
↑Expression of adhesion molecules (ICAM-1, E-selectin)
Vascular endothelium
C
Increased neutrophil adhesion and migration

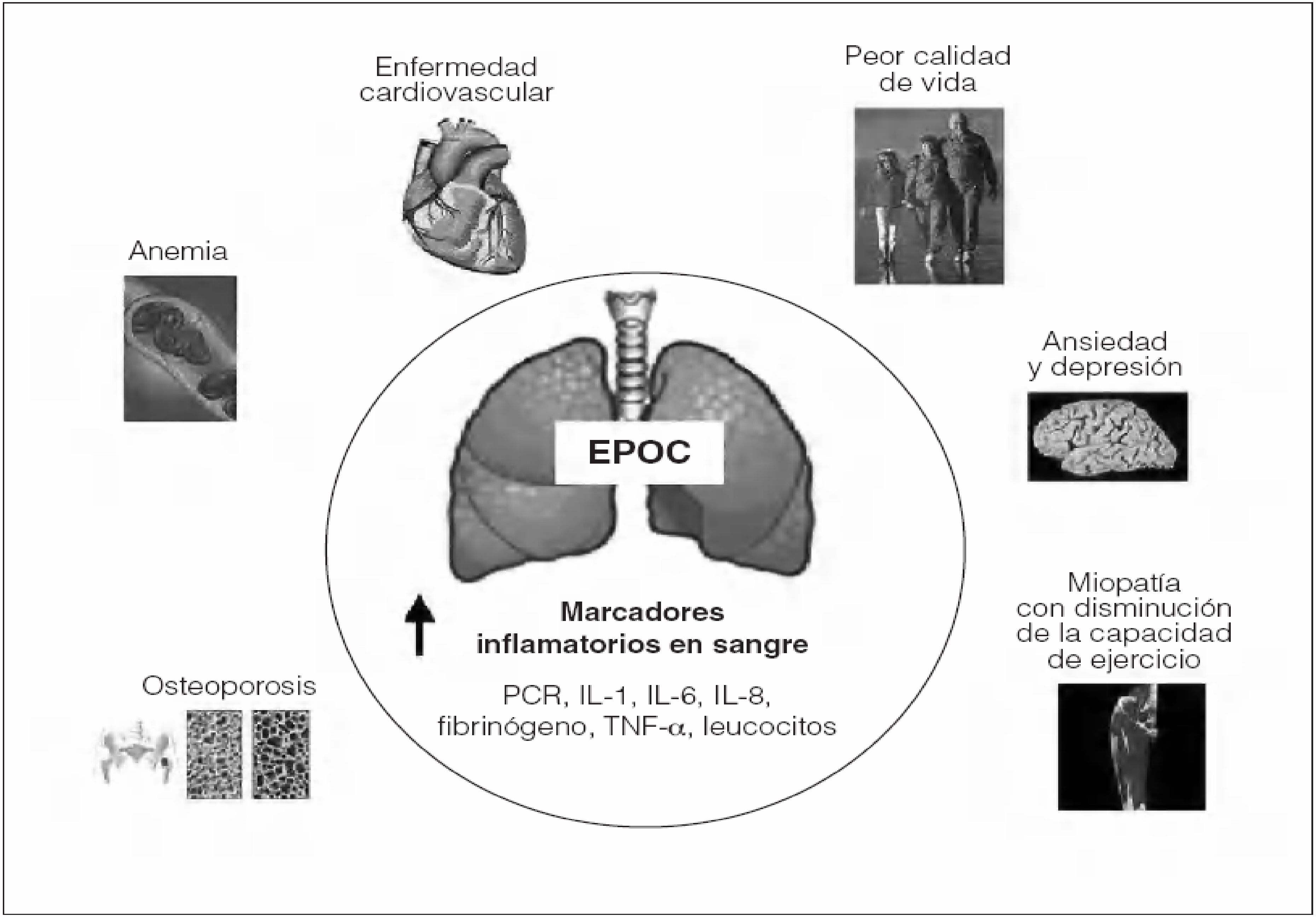
Figure 1 Neutrophilic inflammation during exacerbations of COPD. (A) Phagocytosis/macrophage activation (release of LTB4 and TNFα). (B) Epithelial activation (in response to TNFα and bacterial products, release of TNFα and IL-8). (C) Activation of endothelium (due to TNFα, increase in adhesion molecules). (D) Neutrophil migration (follows from binding to adhesion molecules and IL-8/LTB4 chemotactic gradient, elastase release and tissue damage). (E) Neutrophil elastase release in airway (epithelial damage and protein leakage; increased mucus secretion; reduced mucociliary clearance; associated release of IL-8 and LTB4 resulting in amplification of chemotactic signal). LTB4=leukotriene B4; IL-8=interleukin 8; TNFα=tumour necrosis factor α; ICAM-1=intercellular adhesion molecule 1.


EPOC
↑ Marcadores inflamatorios en sangre
PCR, IL-1, IL-6, IL-8, fibrinógeno, TNF-α, leucocitos



infection
CRP
exacerbation
PAI/TF
complement
wt loss
endo
dysf
fibrinogen
leptin
immune response
adiponectin

Figure 1. Venn diagram illustrating the connections between systemic mediators, systemic manifestations, immune response, infection, and the clinical syndrome of chronic obstructive pulmonary disease exacerbation. *Gray shading* indicates an antiinflammatory effect. CRP = C-reactive protein; PAI/TF = plasminogen activator inhibitor/tissue factor; wt = weight.


Enfermedad cardiovascular
Peor calidad de vida
Anemia
Ansiedad y depresión
EPOC
↑ Marcadores inflamatorios en sangre
PCR, IL-1, IL-6, IL-8, fibrinógeno, TNF-α, leucocitos
Miopatía con disminución de la capacidad de ejercicio
Osteoporosis

Arch Bronconeumol. 2007;43 Supl 3:25-34

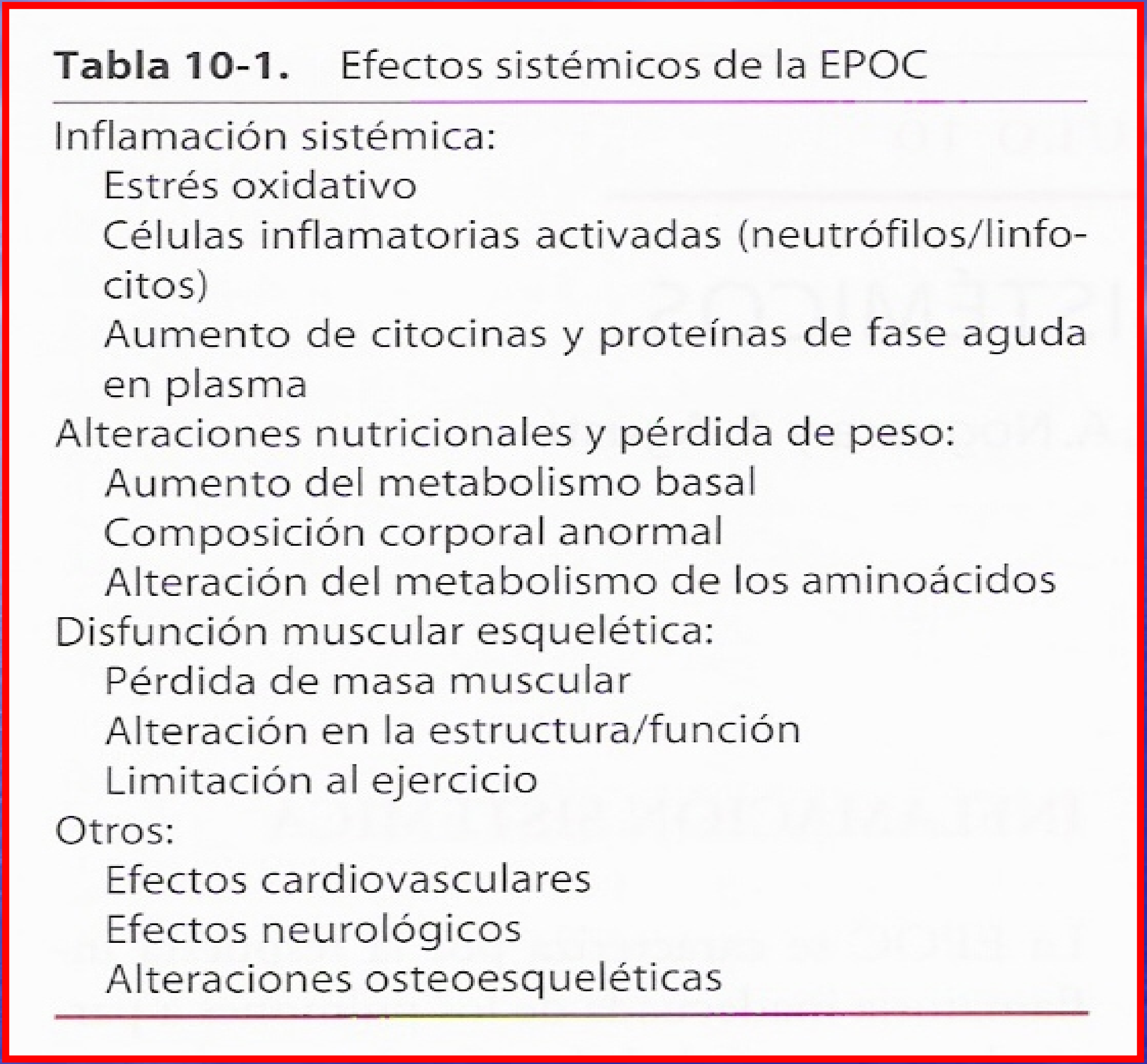


Tabla 10-1. Efectos sistémicos de la EPOC

- Inflamación sistémica:
  - Estrés oxidativo
  - Células inflamatorias activadas (neutrófilos/linfocitos)
  - Aumento de citocinas y proteínas de fase aguda en plasma
- Alteraciones nutricionales y pérdida de peso:
  - Aumento del metabolismo basal
  - Composición corporal anormal
  - Alteración del metabolismo de los aminoácidos
- Disfunción muscular esquelética:
  - Pérdida de masa muscular
  - Alteración en la estructura/función
  - Limitación al ejercicio
- Otros:
  - Efectos cardiovasculares
  - Efectos neurológicos
  - Alteraciones osteoesqueléticas

En: EPOC. A. Agusti, B.Celli. Ed.Masson SA 2005 Barcelona.

Efectos Sistémicos. J.Sauleda, X.Busquets, A.Noguera y A. Agusti. 143-159.

EPOC: una Enfermedad Sistémica.

- Algunos EPOC, tienen inflamación sistémica.
- Algunos EPOC están colonizados.
- Posiblemente juegue un papel en la inflamación.
- Es posible que reducir la inflamación sea favorable.

EPOC: una Enfermedad Sistémica.

- Inflamación y Biomarcadores Sistémicos de la EPOC. Dr. Gabriel Zubillaga
- Colonización, Infección y Agudización Bacteriana. Dr. Pedro Almagro
- Mortalidad en EPOC: factores condicionantes y estrategias terapéuticas. Dr. Juan José Soler Cataluña