MANEJO RACIONAL DE LOS CORTICOIDES

O

…más allá del mg/kg/día

gaIsu

gurutzetako autoinmune sistemikoen ikerketa unitatea

eman ta zabal zazu

GUILLERMO RUIZ-IRASTORZA
GAISU - SERVICIO DE MEDICINA INTERNA
HOSPITAL DE CRUCES
UPV/EHU

CORTICOIDES

Proc Staff Meet Mayo Clin 1949

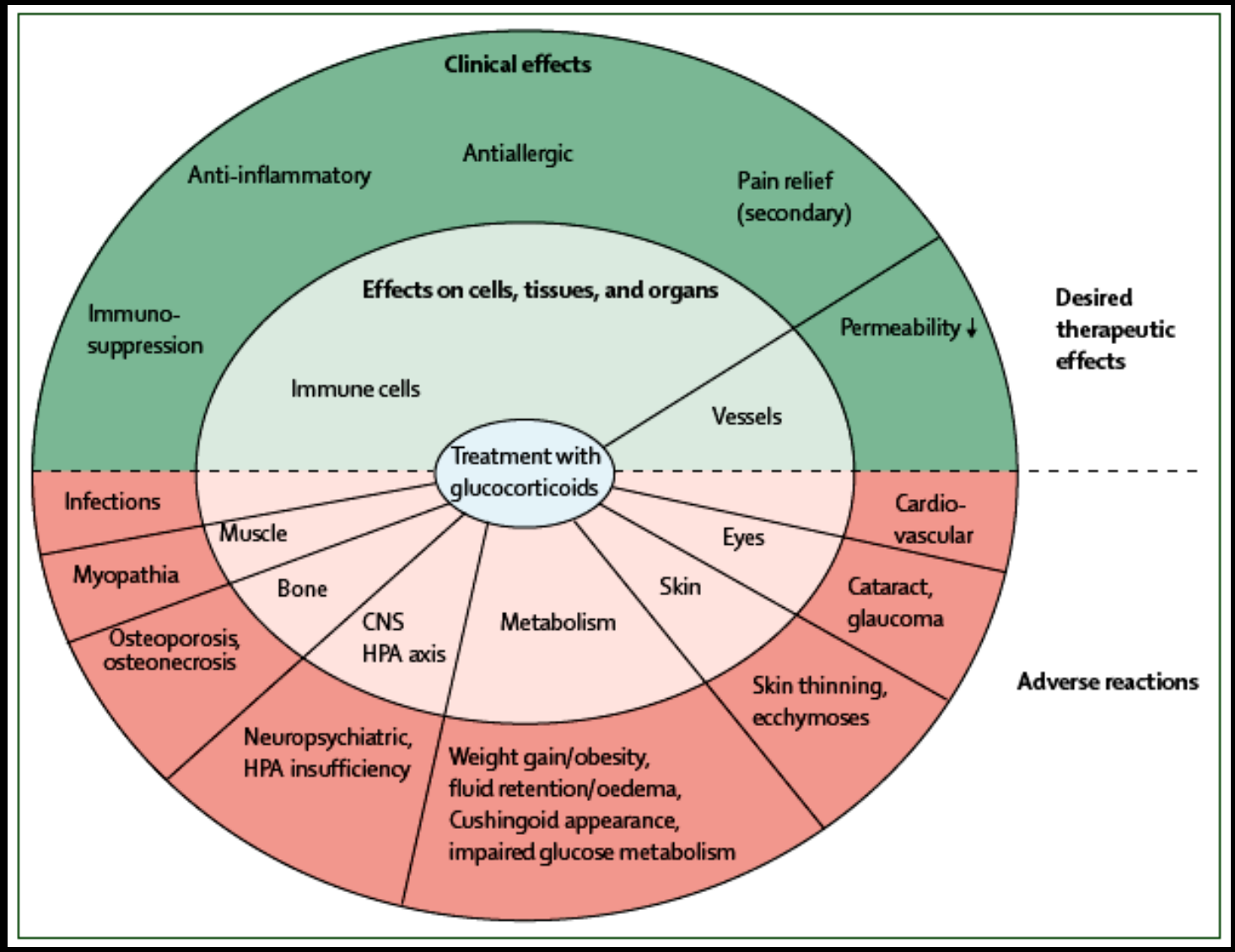
THE EFFECT OF A HORMONE OF THE ADRENAL CORTEX (17-HYDROXY-11-DEHYDROCORTICOSTERONE: COMPOUND E) AND OF PITUITARY ADRENOCORTICOTROPHIC HORMONE ON RHEUMATOID ARTHRITIS*

PRELIMINARY REPORT

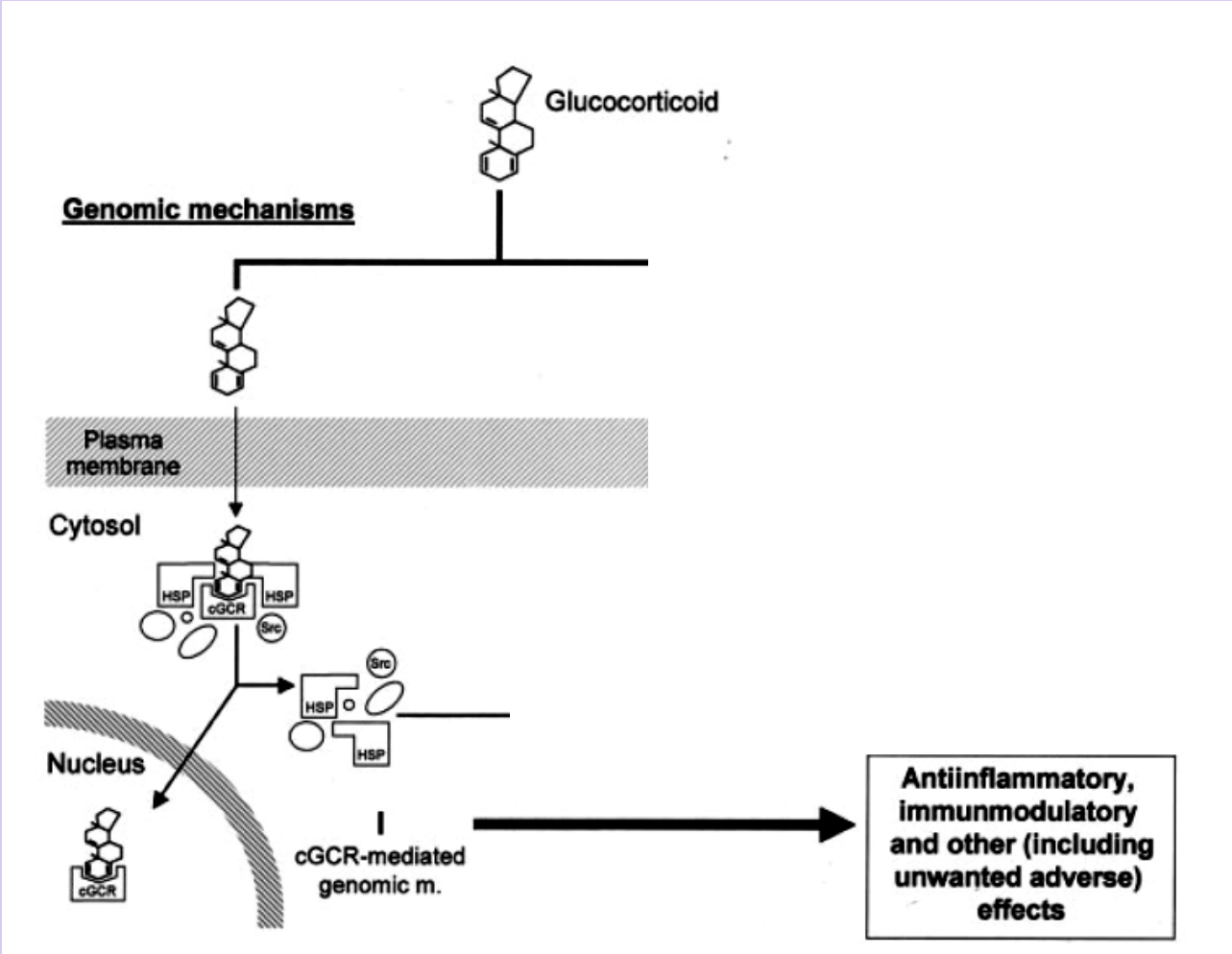
BY

PHILIP S. HENCH, EDWARD C. KENDALL, CHARLES H. SLOCUMB, and HOWARD F. POLLEY

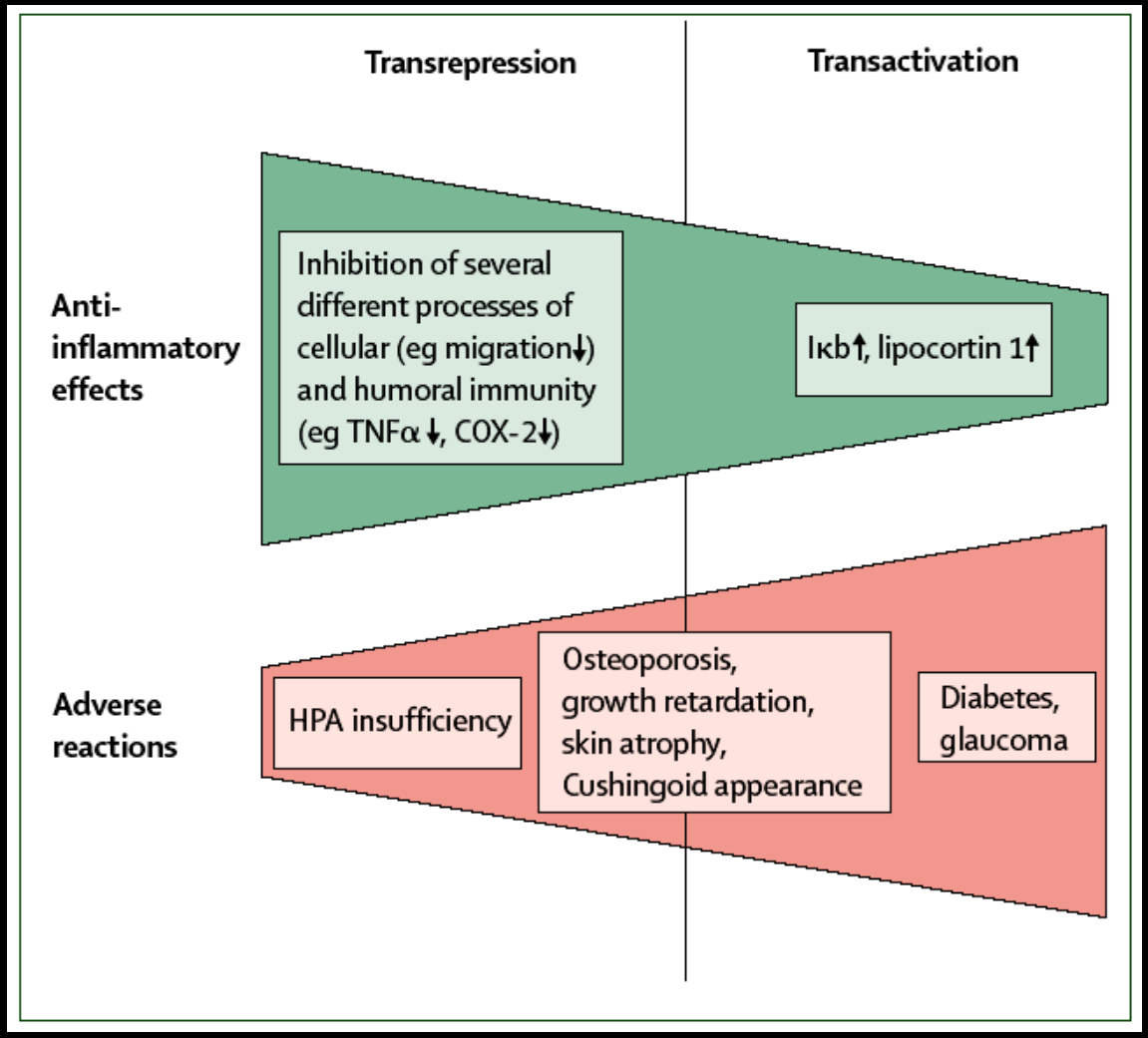
From the Mayo Clinic, Rochester, Minnesota, U.S.A.


Clinical effects
Anti-inflammatory
Antiallergic
Pain relief (secondary)
Immuno-suppression
Effects on cells, tissues, and organs
Permeability ↓
Desired therapeutic effects
Immune cells
Vessels
Treatment with glucocorticoids
Infections
Muscle
Eyes
Cardio-vascular
Myopathia
Bone
Skin
Cataract, glaucoma
CNS HPA axis
Metabolism
Osteoporosis, osteonecrosis
Skin thinning, ecchymoses
Adverse reactions
Neuropsychiatric, HPA insufficiency
Weight gain/obesity, fluid retention/oedema, Cushingoid appearance, impaired glucose metabolism

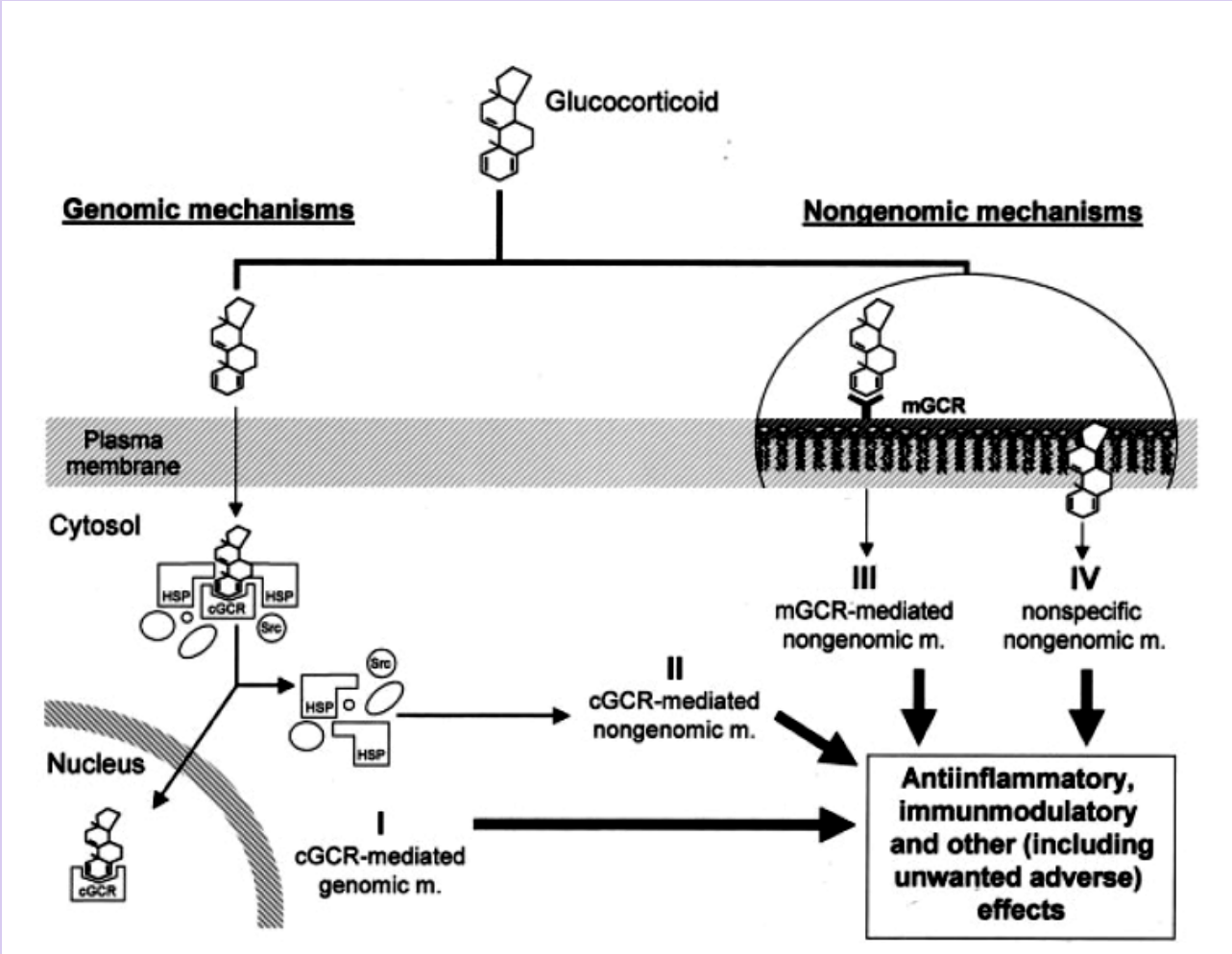
MECANISMO DE ACCIÓN



Buttgereit et al. Arthritis Rheum 2004; 50: 3408-17


Transrepression
Transactivation
Anti-inflammatory effects
Inhibition of several different processes of cellular (eg migration↓) and humoral immunity (eg TNFα↓, COX-2↓)
Iκb↑, lipocortin 1↑
Adverse reactions
HPA insufficiency
Osteoporosis, growth retardation, skin atrophy, Cushingoid appearance
Diabetes, glaucoma

MECANISMO DE ACCIÓN



Buttgereit et al. Arthritis Rheum 2004; 50: 3408-17

MECANISMO DE ACCIÓN

Table 1. Current knowledge on the relationship between clinical dosing and cellular actions of glucocorticoids

Terminology*	Clinical application†	Genomic actions (receptor saturation)‡§	Nongenomic actions§	
			Nonspecific	cGCR-mediated
Low dose (≤7.5 mg/day)	Maintenance therapy for many rheumatic diseases	+ (<50%)	–	?
Medium dose (>7.5 to ≤30 mg/day)	Initial treatment for primary chronic rheumatic diseases	++ (>50 to <100%)	(+)	(+)
High dose (>30 to ≤100 mg/day)	Initial treatment for subacute rheumatic diseases	++(+) (almost 100%)	+	+
Very high dose (>100 mg/day)	Initial treatment for acute and/or potentially life-threatening exacerbations of rheumatic diseases	+++ (almost 100%)	++	+(+?)
Pulse therapy (≥250 mg for 1 or a few days)	For particularly severe and/or potentially life-threatening forms of rheumatic diseases	+++ (100%)	+++	+(++?)

Buttgereit et al. Arthritis Rheum 2004; 50: 3408-17

EL DATO…

Hay más diferencia farmacológica entre 5 y 10 mg/día que entre 35 y 95 mg/día

Y ENTONCES… A QUÉ DOSIS ????

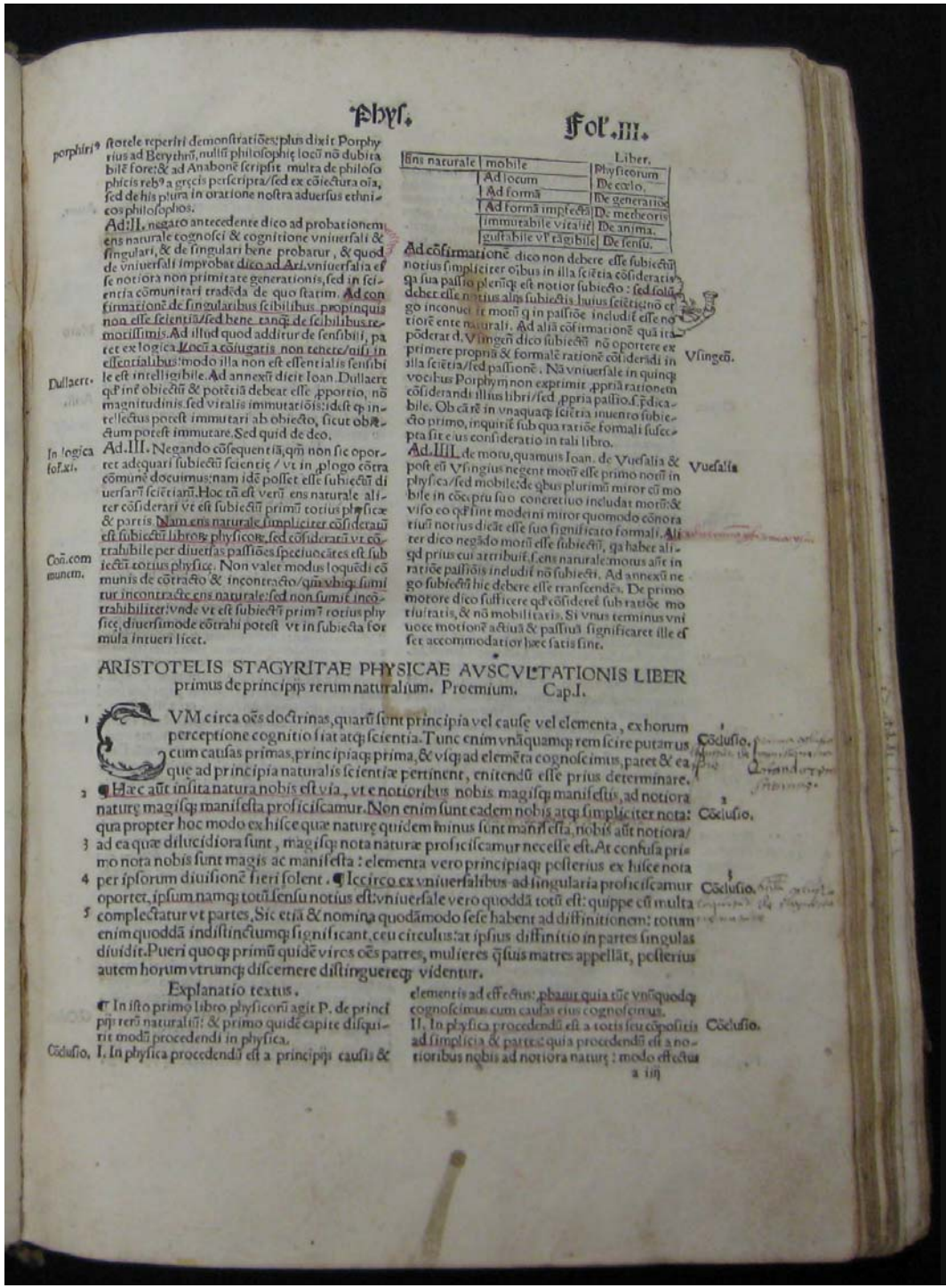
Y ENTONCES… A QUÉ DOSIS ????

LO QUE DICEN LAS FUENTES

UPTODATE:
Systemic glucocorticoids (eg, high doses of 1 to 2 mg/kg/day of prednisone or equivalent or as intermittent intravenous "pulses" of methylprednisolone), used alone or in combination with immunosuppressive agents are generally reserved for patients with significant organ involvement, particularly renal and central nervous system disease.

HARRISON:
The mainstay of treatment for any inflammatory life-threatening or organ-threatening manifestations of SLE is systemic glucocorticoids (0.5-2 mg/kg per day PO or 1000 mg of methylprednisolone sodium succinate IV daily for 3 days followed by 0.5-1 mg/kg of daily prednisone or equivalent).

GUIA CLÍNICA HOSPITAL CLINIC:
Nefropatía tipo III/IV: 1 mg/kg/día durante 1 mes con reducción posterior.



Phys. Fol. III.

porphiri⁹ stotele reperiri demonstratiões: plus dixit Porphyrius ad Berythū, nullū philosophię locū nō dubitabilē fore: & ad Anabonē scripsit multa de philosophicis reb⁹ a grecis perscripta/sed ex cōiectura oīa, sed de his plura in oratione nostra aduersus ethnicos philosophos.

Ad II. negato antecedente dico ad probationem ens naturale cognosci & cognitione vniuersali & singulari, & de singulari bene probatur, & quod de vniuersali improbat dico ad Arī. vniuersalia esse notiora non primitate generationis, sed in scientia cōmunitari tradēda de quo statim. Ad confirmationē de singularibus scibilibus propinquis non esse scientiā/sed bene tanq̄ de scibilibus remotissimis. Ad illud quod additur de sensibili, patet ex logica. Locū a cōiugatis non tenere/nisi in essentialibus: modo illa non est essentialis sensibile est intelligibile. Ad annexū dicit Ioan. Dullaert

Dullaert. qđ inē obiectū & potētiā debeat esse ꝓportio, nō magnitudinis sed viatis immutatiōis: idest q̄ intellectus potest immutari ab obiecto, sicut obiectum potest immutare. Sed quid de deo.

In logica fol. xi. Ad III. Negando cōsequentiā, qm̄ non sic oportet adequari subiectū scientię / vt in ꝓlogo cōtra cōmunē docuimus: nam idē posset esse subiectū diuersarū sciētiarū. Hoc tū est verū ens naturale aliter cōsiderari vt est subiectū primū totius physicæ & partis. Nam ens naturale simpliciter cōsideratū est subiectū libroꝝ physicoꝝ, sed cōsiderarū vt cōtrahibile per diuersas passiões ꝓpriocātes est subiectū totius physicę. Non valet modus loquēdi cō-

Cōm. munem. munis de cōtracto & incontracto/qm̄ vbiq; sumitur incontracte ens naturale: sed non sumit incōtrahibiliter: vnde vt est subiectū primū totius physicę, diuersimode cōtrahi potest vt in subiecta formula intueri licet.

ens naturale	mobile	Liber.
	Ad locum	Physicorum
	Ad formā	De celo.
	Ad formā imperfectā	De generatiõe
	immutabile vitalit	De meteoris
	gustabile vt ꝓgibile	De anima.
		De sensu.

Ad cōfirmationē dico non debere esse subiectū notius simpliciter oībus in illa sciētia cōsideratis qa sua passio plenius̄ est notior subiecto: sed solū debet esse notius alijs subiectis huius sciētię in go inconuenit motū q in passiõe includit esse notiorē ente naturali. Ad aliā cōfirmationē quā itā pōderat d. Vingen dico subiectū nō oportere ex primere propriā & formalē rationē cōsiderādi in alia sciētia/sed passionē. Nā vniuersale in quinq; vocibus Porphym non exprimit ꝓpriā rationem cōsiderandi illius libri/sed ꝓpria passio. f. ꝓdicabile. Ob cāz in vnaquaq; sciētia inuentio subiecto primo, inquirit sub qua ratiõe formali susceꝓta sit eius consideratio in tali libro. Vingen.

Ad IIII. de motu, quamuis Ioan. de Vuesalia & Vuesalia post eū Vingius negent motū esse primo notū in physica/sed mobile: de qbus plurimū miror cū mobile in cōceptu suo concretiuo includat motū: & viso eo qđ sint modi ni miror quomodo cōnotatiuū notius dicāt esse suo significato formali. Aliter dico negādo motū esse subiectū, qa habet aliqđ prius cui attribuit. f. ens naturale: motus aūt in ratiõe passiõis includit nō subiectū. Ad annexū nego subiectū hic debere esse transcendēs. De primo motore dico sufficere qđ cōsidereꝝ sub ratiõe motiuitatis, & nō mobilitatis. Si vnus terminus vniuoce motionē actiuā & passiuā significaret ille esset accommodatior hæc satis sint.

ARISTOTELIS STAGYRITAE PHYSICAE AVSCVLTATIONIS LIBER primus de principijs rerum naturalium. Proemium. Cap. I.

1 CVM circa oēs doctrinas, quarū sunt principia vel cause vel elementa, ex horum perceptione cognitio fiat atq; scientia. Tunc enim vnāquamq; rem scire putamus cum causas primas, principiaq; prima, & vsq; ad elemēta cognoscimus, paret & ea que ad principia naturalis scientiæ pertinent, enitendū esse prius determinare. Cōclusio.

2 ¶ Hæc aūt insita natura nobis est via, vt e notioribus nobis magisq; manifestis, ad notiora naturę magisq; manifesta proficiscamur. Non enim sunt eadem nobis atq; simpliciter nota: qua propter hoc modo ex hisce quæ naturę quidem minus sunt manifesta, nobis aūt notiora/ 3 ad ea quæ dilucidiora sunt, magisq; nota naturæ proficiscamur necesse est. At confusa primo nota nobis sunt magis ac manifesta: elementa vero principiaq; posterius ex hisce nota 4 per ipsorum diuisionē fieri solent. ¶ Iccirco ex vniuersalibus ad singularia proficiscamur oportet, ipsum namq; totū sensu notius est: vniuersale vero quoddā totū est: quippe cū multa 5 complectatur vt partes. Sic etiā & nomina quodāmodo sese habent ad diffinitionem: totum enim quoddā indistinctiusq; significant, ceu circulus: at ipsius diffinitio in partes singulas diuidit. Pueri quoq; primū quidē vires oēs patres, mulieres q̄ suis matres appellāt, posterius autem horum vtrumq; discernere distinguereq; videntur. Cōclusio. Cōclusio. Cōclusio.

Explanatio textus.

¶ In isto primo libro physicorū agit P. de principijs rerū naturaliū: & primo quidē capite disquirit modū procedendi in physica.

Cōclusio. I. In physica procedendū est a principijs causis & elementis ad effectus: ꝓbatur quia tūc vnūquodq; cognoscimus cum causas eius cognoscimus.

II. In physica procedendū est a totis seu cōpositis ad simplicia & partes: quia procedendū est a notioribus nobis ad notiora naturę: modo effectus

a iiij

MEDICINA BASADA EN LA INSISTENCIA

(notoria escasez de ensayos clínicos)

Graham Hughes

Lupus Research Unit - St. Thomas' Hospital

High versus "low" dose corticosteroids in recipients of cadaveric kidneys: prospective controlled trial

J PAPADAKIS, C B BROWN, J S CAMERON, D ADU, M BEWICK, R DONAGHEY, C S OGG, C RUDGE, D G WILLIAMS, D TAUBE

BRITISH MEDICAL JOURNAL VOLUME 286 2 APRIL 1983

Circulation (2008) vol. 118 (6) pp. 667-71

Corticosteroids for Recurrent Pericarditis

High Versus Low Doses: A Nonrandomized Observation

Massimo Imazio, MD; Antonio Brucato, MD; Davide Cumetti, MD; Giovanni Brambilla, MD; Brunella Demichelis, MD; Silvia Ferro, MD; Silvia Maestroni, MD; Enrico Cecchi, MD; Riccardo Belli, MD; Giancarlo Palmieri, MD; Rita Trinchero, MD

Thorax 1989;**44**:280–288

Randomised controlled trial comparing prednisolone alone with cyclophosphamide and low dose prednisolone in combination in cryptogenic fibrosing alveolitis

M A JOHNSON, S KWAN, N J C SNELL, A J NUNN, J H DARBYSHIRE, M TURNER-WARWICK

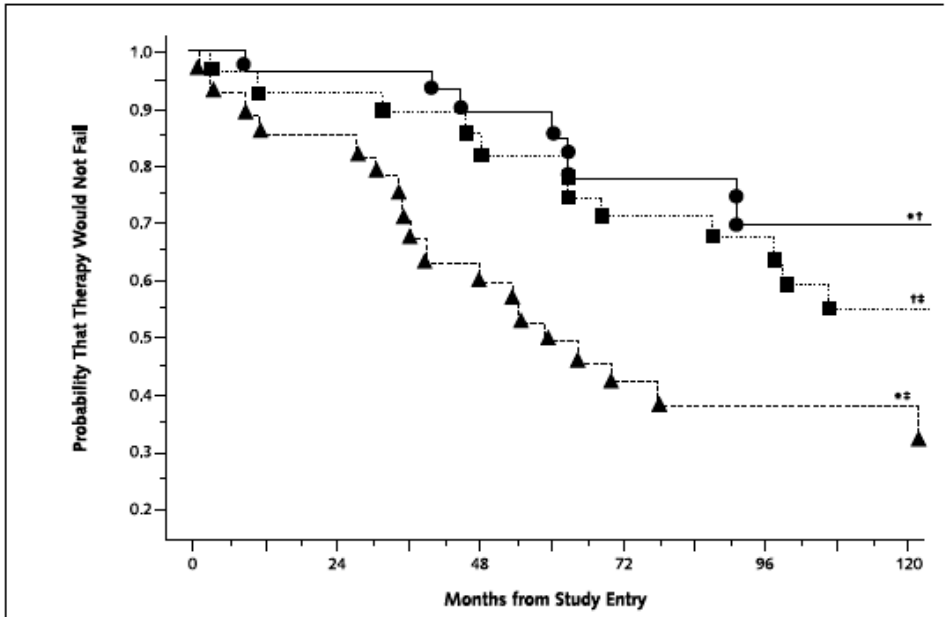
Combination Therapy with Pulse Cyclophosphamide plus Pulse Methylprednisolone Improves Long-Term Renal Outcome without Adding Toxicity in Patients with Lupus Nephritis

Gabor G. Illei, MD; Howard A. Austin III, MD; Marianna Crane, NP; Lee Collins, MS; Mark F. Gourley, MD; Cheryl H. Yarboro, RN; Ellen M. Vaughan, MSN; Takashi Kuroiwa, MD; Carol L. Danning, MD; Alfred D. Steinberg, MD; John H. Klippel, MD; James E. Balow, MD; and Dimitrios T. Boumpas, MD

Ann Intern Med. 2001;135:248-257.

0.5 mg/kg/d

Figure. Kaplan–Meier analysis of failure of therapy with cyclophosphamide plus methylprednisolone (*circles*), cyclophosphamide only (*squares*), or methylprednisolone only (*triangles*).



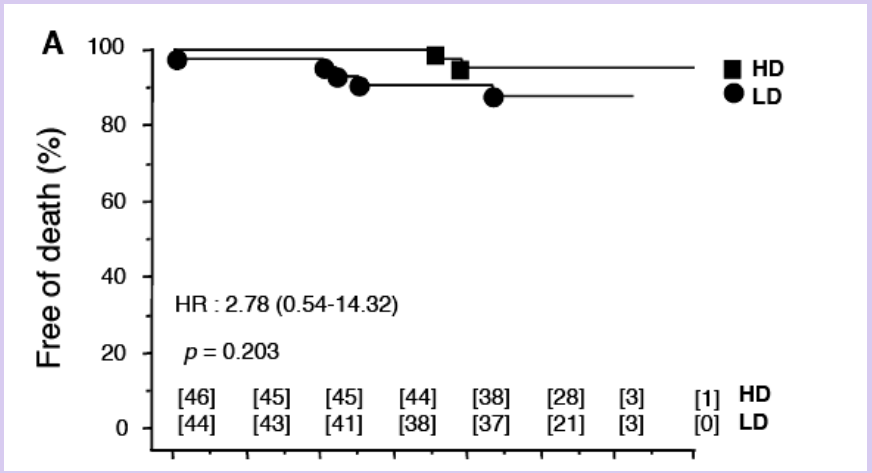
Patients at Risk

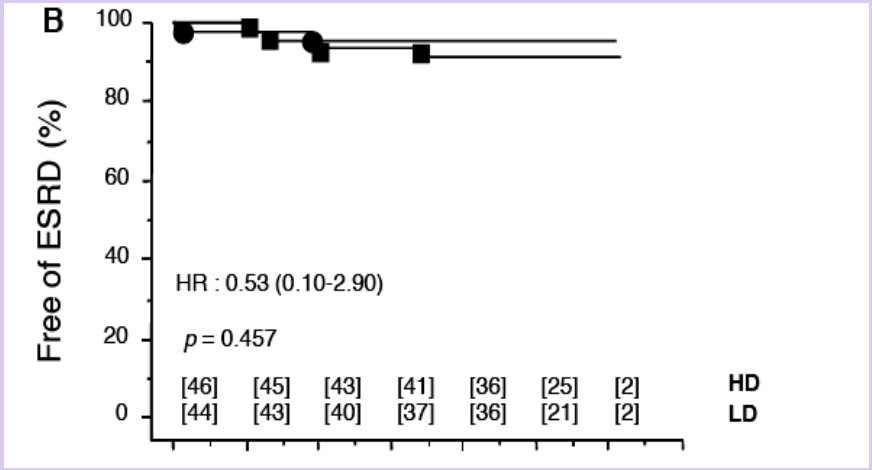
Treatment	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
	←					*n*					→
Cyclophosphamide	27	25	25	24	23	22	18	18	17	11	7
Cyclophosphamide plus methylprednisolone	28	27	27	26	23	23	20	20	17	15	12
Methylprednisolone	27	23	23	19	17	13	11	10	10	8	6

The 10-year follow-up data of the Euro-Lupus Nephritis Trial comparing low-dose versus high-dose intravenous cyclophosphamide

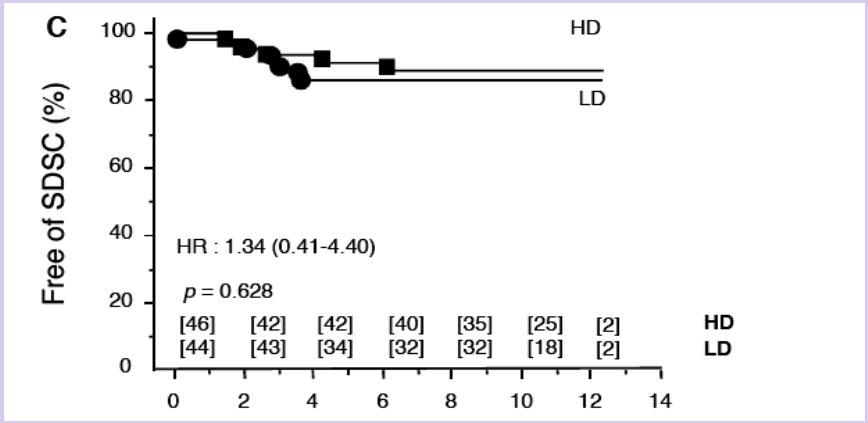
Frédéric A Houssiau, Carlos Vasconcelos, David D'Cruz, Gian Domenico Sebastiani, Enrique de Ramon Garrido, Maria Giovanna Danieli, Daniel Abramovicz, Daniel Blockmans, Alberto Cauli, Haner Direskeneli, Mauro Galeazzi, Ahmet Gül, Yair Levy, Peter Petera, Rajko Popovic, Radmila Petrovic, Renato A Sinico, Roberto Cattaneo, Josep Font, Geneviève Depresseux, Jean-Pierre Cosyns and Ricard Cervera

Ann Rheum Dis published online 20 Jan 2009;
doi:10.1136/ard.2008.102533





Prednisona inicial 0.5 mg/kg/día



EULAR randomised controlled trial of pulse cyclophosphamide and methylprednisolone versus continuous cyclophosphamide and prednisolone followed by azathioprine and prednisolone in lupus nephritis

C-S Yee, C Gordon, C Dostal, P Petera, J Dadoniene, B Griffiths, B Rozman, D A Isenberg, G Sturfelt, O Nived, J H Turney, A Venalis, D Adu, J S Smolen, P Emery

Ann Rheum Dis 2003;**63**:525–529. doi: 10.1136/ard.2002.003574

Table 2 Summary of outcomes in the pulse therapy (n = 13) and continuous therapy (n = 16)

Outcomes	Continuous therapy (%)	Pulse therapy (%)
Doubled serum creatinine	1 (6.3)	0
Dialysis	2 (12.5)	0
Neutropenia	3 (18.8)	1 (7.7)
Infections	4 (25)	5 (38.5)
Nausea/vomiting	1 (6.3)	3 (23.1)
Haemorrhagic cystitis	1 (6.3)	0
Malignancy	0	1 (7.7)
Permanent amenorrhoea	1 (6.3)	1 (7.7)
Withdrawn from therapy	7 (43.8)	7 (53.8)
Death	1 (6.3)	2 (15.4)

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C-S Yee, C Gordon, C Dostal, P Petera, J Dadoniene, B Griffiths, B Rozman, D A Isenberg, G Sturfelt, O Nived, J H Turney, A Venalis, D Adu, J S Smolen, P Emery

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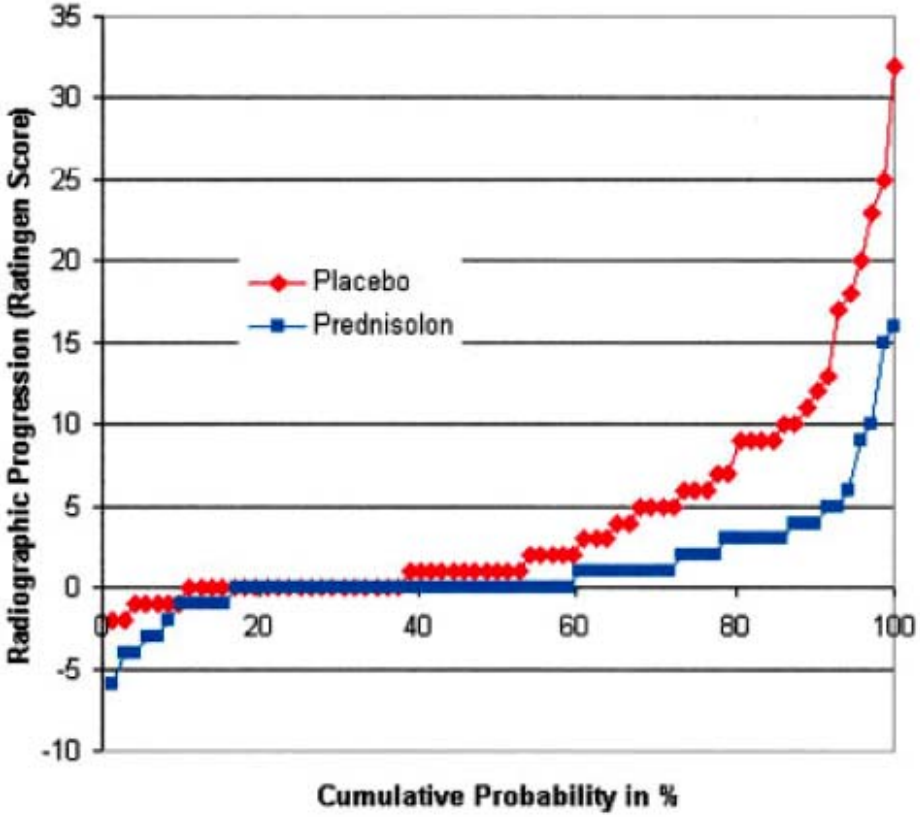
Malignancy	0	1 (7.7)
Permanent amenorrhoea	1 (6.3)	1 (7.7)
Withdrawn from therapy	7 (43.8)	7 (53.8)
Death	1 (6.3)	2 (15.4)
	0.85 mg/kg/d	**0.3 mg/kg/d**

ARTHRITIS & RHEUMATISM
Vol. 52, No. 11, November 2005, pp 3371–3380

Very Low-Dose Prednisolone in Early Rheumatoid Arthritis Retards Radiographic Progression Over Two Years

A Multicenter, Double-Blind, Placebo-Controlled Trial

Siegfried Wassenberg,[1] Rolf Rau,[1] Paul Steinfeld,[2] and Henning Zeidler,[3] for the Low-Dose Prednisolone Therapy Study Group



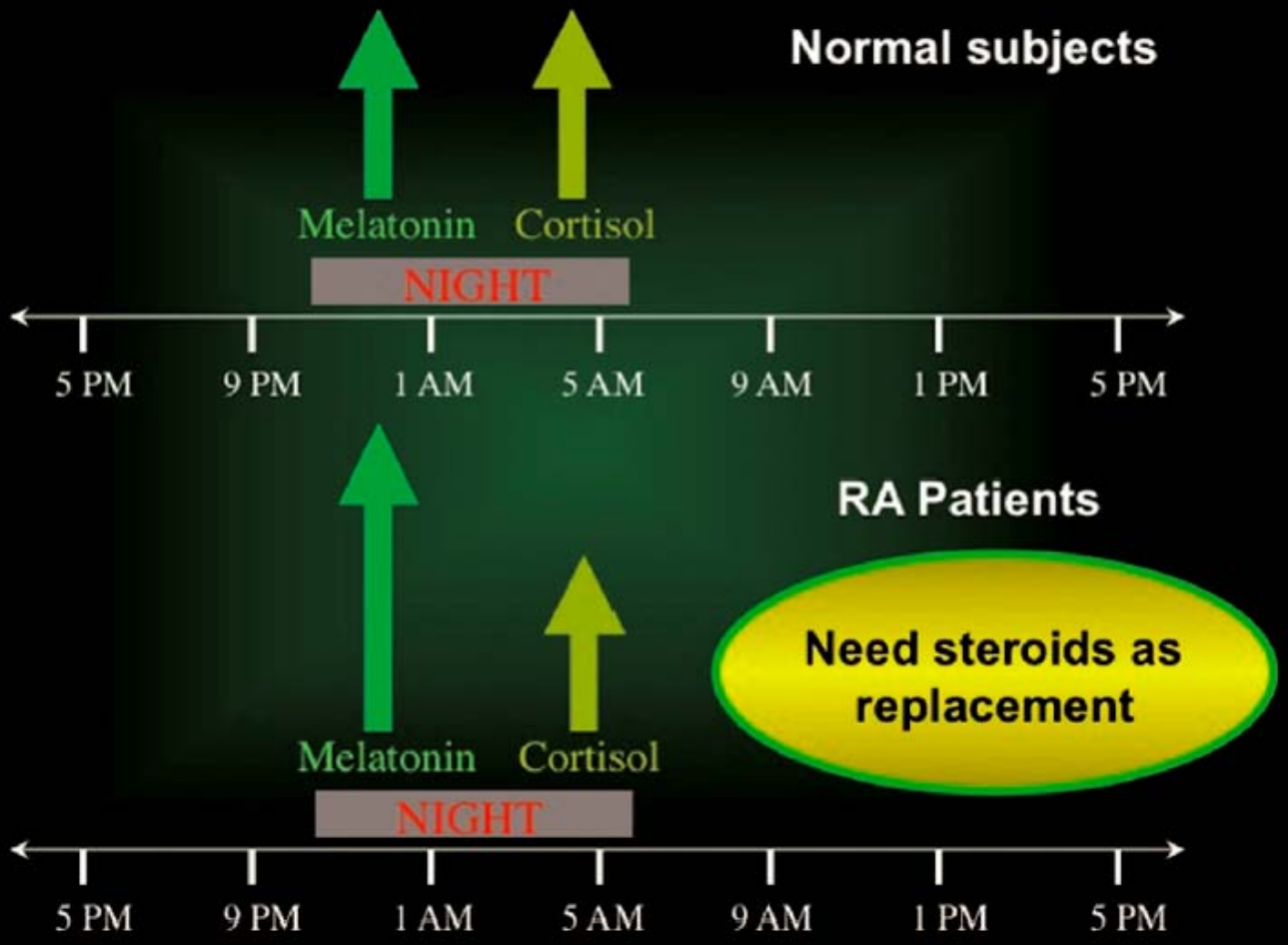
5 mg/d x 24 meses

Arthritis Research & Therapy 2009, 11:218

Review

Insights into endocrine-immunological disturbances in autoimmunity and their impact on treatment

Maurizio Cutolo[1] and Rainer H Straub[2]



ES DECIR…

Dosis menores a 30 mg/día pueden ser igualmente eficaces en situaciones agudas graves.

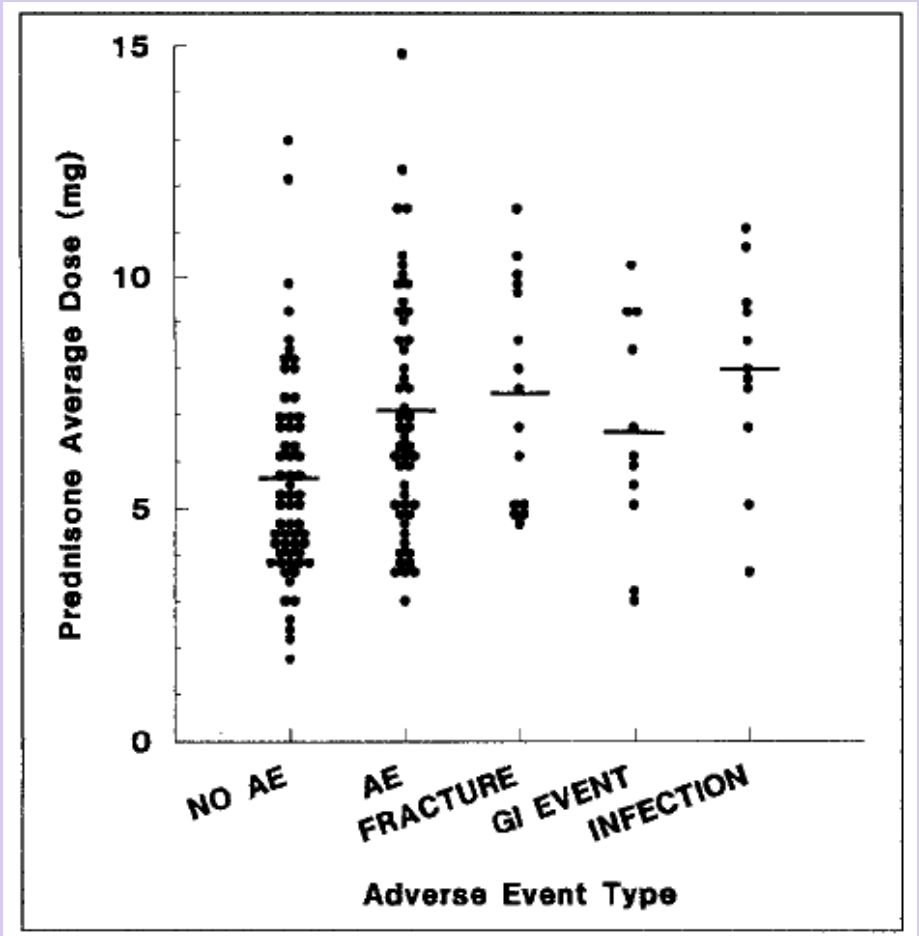
Dosis de 2.5 - 5 mg/día pueden tener un efecto de reposición “fisiológica”.

¿A qué dosis aparecen efectos adversos?

Low Dose Long-Term Corticosteroid Therapy in Rheumatoid Arthritis: An Analysis of Serious Adverse Events

KENNETH G. SAAG, M.D., ROCHELLE KOEHNKE, R.N., *Iowa City, Iowa,* JACQUES R. CALDWELL, M.D., *Daytona Beach, Florida,* RICHARD BRASINGTON, M.D., *Marshfield, Wisconsin,* LEON F. BURMEISTER, PH.D., BRIDGET ZIMMERMAN, PH.D., JAMES A. KOHLER, M.A., *Iowa City, Iowa,* DANIEL E. FURST, M.D., *Seattle, Washington*

Am J Med 1994; 96: 115-23



Low Dose Long-Term Corticosteroid Therapy in Rheumatoid Arthritis: An Analysis of Serious Adverse Events

KENNETH G. SAAG, M.D., ROCHELLE KOEHNKE, R.N., *Iowa City, Iowa,* JACQUES R. CALDWELL, M.D., *Daytona Beach, Florida,* RICHARD BRASINGTON, M.D., *Marshfield, Wisconsin,* LEON F. BURMEISTER, PH.D., BRIDGET ZIMMERMAN, PH.D., JAMES A. KOHLER, M.A., *Iowa City, Iowa,* DANIEL E. FURST, M.D., *Seattle, Washington*

Am J Med 1994; 96: 115-23

TABLE III

Risk Factors for the First Adverse Event

Final Model Variables*	Odds Ratio	95% CI	p Value
Average prednisone			
>10–15 mg/d	32.3	4.6, 220	0.0004
5–10 mg/d	4.5	2.1, 9.6	0.0001
>0–<5 mg/d	1.9	0.8, 4.7	0.15
Rheumatoid nodules	3.9	1.9, 8.0	0.0001
Bony erosions	2.4	1.2, 4.7	<0.02
Job: farmer/laborer	2.4	1.1, 5.6	<0.04
GI protectives: drug years	0.6	0.4, 0.9	<0.02

Taking Glucocorticoids by Prescription Is Associated with Subsequent Cardiovascular Disease

Li Wei, MB, MSc; Thomas M. MacDonald, MD, FRCPE; and Brian R. Walker, MD, FRCPE

Ann Intern Med. 2004;141:764-770.

Table 2. **Influence of Dose of Glucocorticoids on All Cardiovascular Events**

Steroid Exposure	Events, *n*	Unadjusted Rate Ratio (95% CI)	Adjusted Rate Ratio (95% CI)*	Adjusted Rate Ratio (95% CI)†
Comparator	4383	1.00	1.00	1.00
Low dose	3521	1.30 (1.24–1.36)	1.00 (0.95–1.05)	1.00 (0.95–1.05)
Medium dose	1380	1.60 (1.50–1.70)	1.03 (0.96–1.10)	1.04 (0.95–1.14)
High dose	167	4.50 (3.86–5.25)	2.56 (2.18–2.99)	3.09 (2.51–3.80)

Tiempo de tratamiento 1-5 años

Low dose: rectal o inhalados

Medium dose: < 7.5 mg/día

High dose: ≥ 7.5 mg/día

Taking Glucocorticoids by Prescription Is Associated with Subsequent Cardiovascular Disease

Li Wei, MB, MSc; Thomas M. MacDonald, MD, FRCPE; and Brian R. Walker, MD, FRCPE

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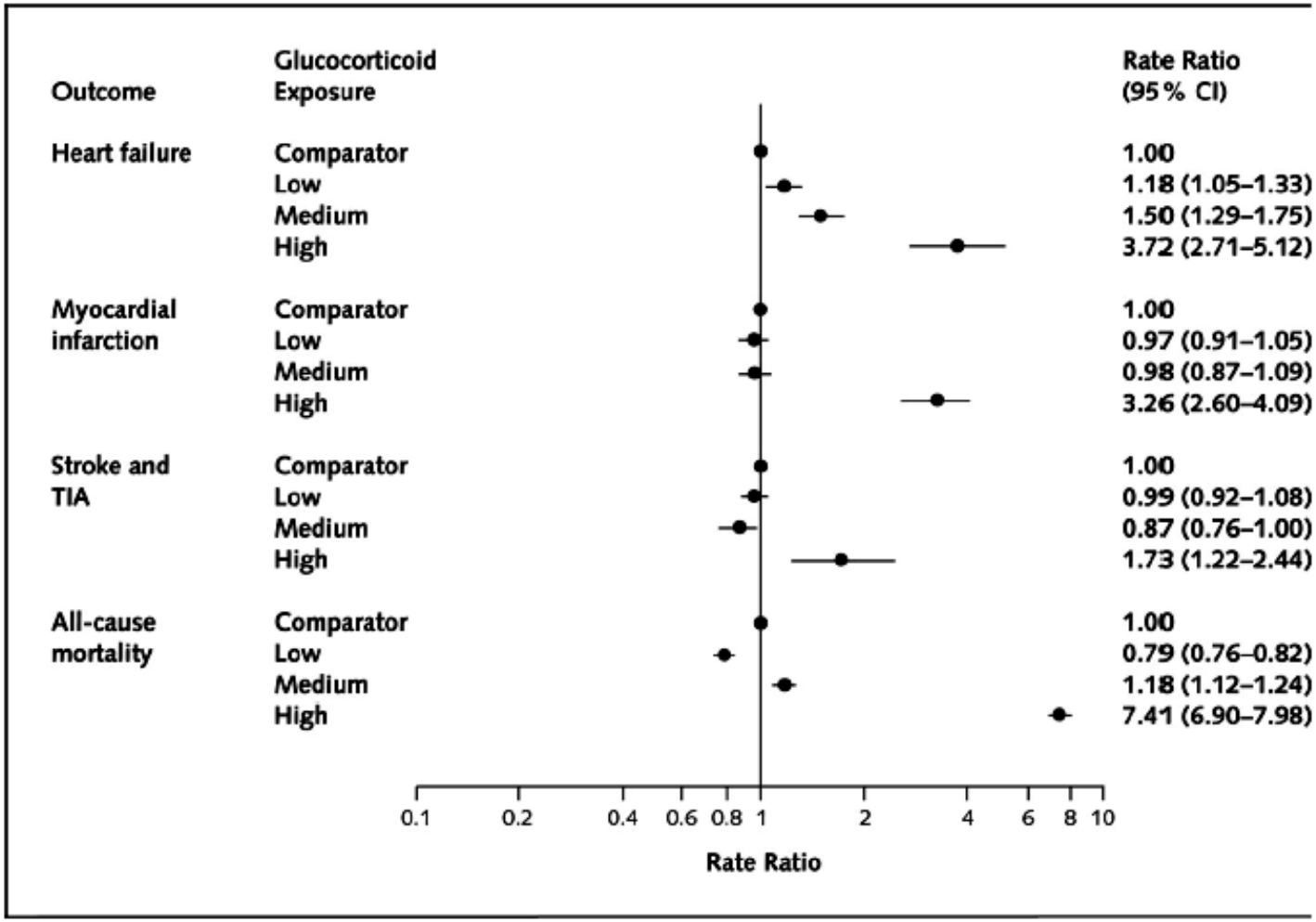

REVIEW

Safety of low dose glucocorticoid treatment in rheumatoid arthritis: published evidence and prospective trial data

J A P Da Silva, J W G Jacobs, J R Kirwan, M Boers, K G Saag, L B S Inês, E J P de Koning, F Buttgereit, M Cutolo, H Capell, R Rau, J W J Bijlsma

Ann Rheum Dis 2006;**65**:285–293. doi: 10.1136/ard.2005.038638

Efectos adversos que no aparecen (o lo hacen en menor medida) con dosis de prednisona < 7.5 mg/d:

- **Osteoporosis**
- **Osteonecrosis**
- **Miopatía**
- **Cushing**
- **Diabetes**
- **Enfermedad cardiovascular**
- **Psicosis**
- **Depresión**

J Rheumatol 2009;36:560–4;

Prednisone, Lupus Activity, and Permanent Organ Damage

MAE THAMER, MIGUEL A. HERNÁN, YI ZHANG, DENNIS COTTER, and MICHELLE PETRI

Table 4. Hazard ratio of organ damage (n = 141) by cumulative average dose of prednisone.

Cumulative Average Prednisone Dose (mg/mo)	% of Patient-mos	No. of Events	Unadjusted Model HR	Unadjusted Model 95% CI	Conventionally-Adjusted Model* HR	Conventionally-Adjusted Model* 95% CI	Weighted Model* HR	Weighted Model* 95% CI
0	35.9	34	Ref		Ref		Ref	
> 0–180	37.0	49	1.58	1.00, 2.50	2.01	1.11, 3.63	1.16	0.54, 2.50
> 180–360	14.9	29	2.10	1.24, 3.55	2.46	1.17, 5.16	1.50	0.58, 3.88
> 360–540	6.7	18	3.04	1.67, 5.53	3.54	1.55, 8.12	1.64	0.58, 4.69
> 540	5.5	21	4.19	2.35, 7.47	4.10	1.74, 9.65	2.51	0.87, 7.27

*Adjusted for age, sex, race/ethnicity, baseline prednisone dose, baseline SLE activity, baseline organ damage, and time-varying covariates. HR: hazard ratio.

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Prednisone, Lupus Activity, and Permanent Organ Damage

MAE THAMER, MIGUEL A. HERNÁN, YI ZHANG, DENNIS COTTER, and MICHELLE PETRI

Table 4. Hazard ratio of organ damage (n = 141) by cumulative average dose of prednisone.

Cumulative Average Prednisone Dose (mg/mo)		% of Patient-mos	No. of Events	Unadjusted Model HR	Unadjusted Model 95% CI	Conventionally-Adjusted Model* HR	Conventionally-Adjusted Model* 95% CI	Weighted Model* HR	Weighted Model* 95% CI
0		35.9	34	Ref		Ref		Ref	
> 0–180	0-6	37.0	49	1.58	1.00, 2.50	2.01	1.11, 3.63	1.16	0.54, 2.50
> 180–360	6-12	14.9	29	2.10	1.24, 3.55	2.46	1.17, 5.16	1.50	0.58, 3.88
> 360–540	12-18	6.7	18	3.04	1.67, 5.53	3.54	1.55, 8.12	1.64	0.58, 4.69
> 540	> 18	5.5	21	4.19	2.35, 7.47	4.10	1.74, 9.65	2.51	0.87, 7.27

*Adjusted for age, sex, race/ethnicity, baseline prednisone dose, baseline SLE activity, baseline organ damage, and time-varying covariates. HR: hazard ratio.

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DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS ASSOCIATION WITH CORTICOSTEROIDS

ABRAHAM ZONANA-NACACH, SUSAN G. BARR, LAURENCE S. MAGDER, and MICHELLE PETRI

Table 5. Relative risk of damage in SLE associated with cumulative prednisone, high-dose prednisone, and pulse methylprednisolone

Damage item	Cumulative prednisone*		High dose prednisone†		Pulse methylprednisolone‡	
	Adjusted RR (95% CI)	*P*	Adjusted RR (95% CI)	*P*	Adjusted RR (95% CI)	*P*
Osteoporotic fracture	2.5 (1.7, 3.7)	0.0001	0.8 (0.7, 1.0)	0.08	1.3 (1.0, 1.8)	0.07
Coronary artery disease	1.7 (1.1, 2.5)	0.008	1.0 (0.8, 1.2)	0.9	1.1 (0.7, 1.8)	0.8
Cataracts	1.9 (1.4, 2.5)	0.0001	0.9 (0.8, 1.1)	0.3	1.0 (0.7, 1.4)	0.9
Avascular necrosis	1.1 (0.8, 1.5)	0.6	1.2 (1.1, 1.4)	0.0002	1.2 (0.9, 1.6)	0.2
Stroke	0.9 (0.5, 1.5)	0.7	1.2 (1.0, 1.5)	0.02	0.9 (0.5, 1.5)	0.7
Diabetes mellitus	1.4 (0.8, 2.4)	0.2	1.0 (0.9, 1.3)	0.5	0.8 (0.4, 1.6)	0.6
Hypertension	1.0 (0.7, 1.3)	0.9	1.1 (0.9, 1.2)	0.3	1.0 (0.8, 1.3)	0.9
Pulmonary fibrosis	1.6 (1.0, 2.8)	0.1	1.1 (0.8, 1.3)	0.7	0.7 (0.3, 1.9)	0.5
Venous insufficiency	1.1 (0.5, 2.1)	0.9	1.1 (0.9, 1.5)	0.4	No events	–
Cognitive impairment/psychosis	1.3 (0.6, 2.9)	0.5	1.1 (0.9, 1.4)	0.3	1.5 (1.1, 2.0)	0.02
Renal failure	1.3 (0.8, 2.1)	0.3	1.0 (0.8, 1.2)	0.7	1.3 (0.8, 2.0)	0.3
Joint deformity/erosion	1.2 (0.8, 1.7)	0.4	0.9 (0.8, 1.1)	0.5	1.3 (0.9, 1.8)	0.1
Scarring alopecia	1.5 (0.9, 2.6)	0.1	0.7 (0.4, 1.1)	0.09	1.2 (0.8, 1.7)	0.4
Pulmonary hypertension	0.7 (0.3, 1.5)	0.4	1.2 (0.9, 1.5)	0.3	1.0 (0.5, 1.8)	0.9
Malignancy	1.1 (0.6, 2.0)	0.8	0.4 (0.1, 2.0)	0.3	1.0 (0.4, 2.5)	0.9

Research article

Open Access

Predictors of major infections in systemic lupus erythematosus

Guillermo Ruiz-Irastorza, Nerea Olivares, Ioana Ruiz-Arruza, Agustin Martinez-Berriotxoa, Maria-Victoria Egurbide and Ciriaco Aguirre

Arthritis Research & Therapy 2009, 11:R109

Table 4

Logistic regression, final model (dependent variable, major infection)

Variable	Odds ratio	95% confidence interval
Lung involvement at study point	4.41	1.06 to 18.36
Prednisone dose (mg/day)	1.12	1.04 to 1.19
Antimalarials	0.06	0.02 to 0.18
Antiphospholipid antibodies	1.88	0.66 to 5.32
Antiphospholipid antibodies × antimalarials	2.21	0.52 to 9.33
Antiphospholipid antibodies × prednisone dose	0.98	0.88 to 1.11

Antiphospholipid antibodies × antimalarials and antiphospholipid antibodies × prednisone dose are interaction variables.

O SEA…

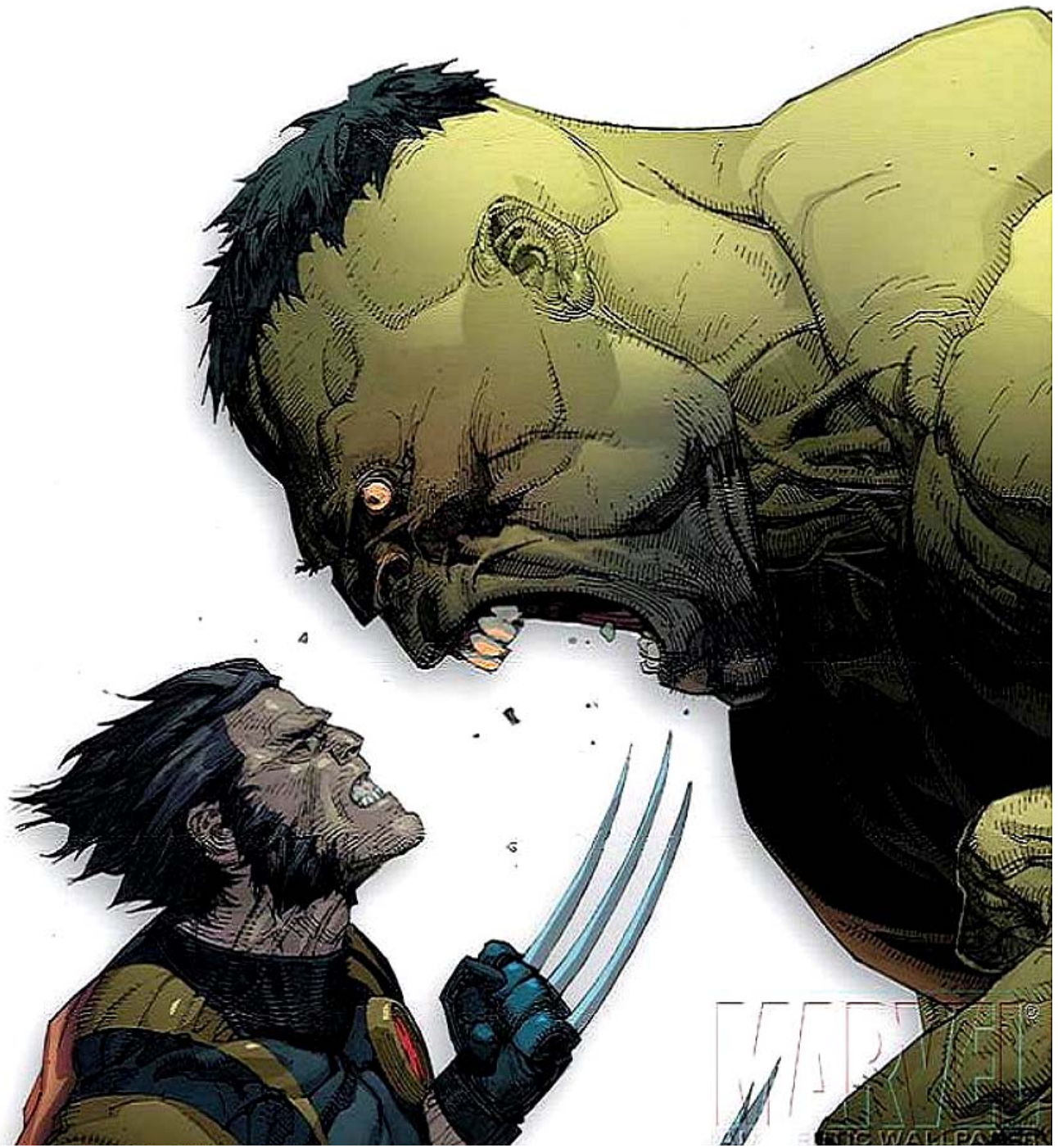
Efectos adversos importantes y dosis dependientes

La toxicidad empieza con dosis superiores a 5 mg/día

Efectos genómicos máximos a partir de 30 mg/día

Efectos no genómicos a partir de 100 mg/día

DONDE ESTÁN LOS KILOS????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Intravenous Pulses of Methylprednisolone for Systemic Lupus Erythematosus

Humeira Badsha and Christopher J. Edwards

Table 3: Selected Clinical Trials Using Pulse MEP for SLE

Author (Reference)	Year	Study Design	n	Disease Manifestation	Response to Therapy
Cathcart (28)	1976	Open label	7	Nephritis	Improved
Dosa (64)	1978	Open label	4	Nephritis	Improved
Eyanson (44)	1980	Open label	2	Coma, idiopathic thrombocytopenia purpura, anemia	Improved
Leibling (65)	1982	DB, PC	9	Nephritis	Monthly IV; MEP improved
Isenberg (37)	1982	Open label	20	Various	Improved
Ballou (66)	1985	Open label	11	Various	No sustained improvement
Edwards (39)	1987	DB	21	Various	No difference 100 or 1000 mg
Mackworth-Young (40)	1988	DB, PC	25	Various	Response not sustained
Howe (49)	1990	Retrospective	39	Various	Increased infection
Rose (67)	1991	Open label	35	Pediatric nephritis	30 mg/kg
Honma (35)	1994	DB	91	Nephritis	MEP 400 mg/day better than high-dose oral prednisolone
Bertoni (68)	1994	Open label	12	Nephritis	Improved
Gourley (33)	1996	DB, PC	82	Nephritis	IV cyclophosphamide + MEP more effective than MEP or cyclophosphamide alone
Badsha (27)	2001	Retrospective	55	Various	500 mg/day effective, fewer infections

LA RECETA

Pulsos de M-Pred en situaciones agudas

En formas graves, dosis iniciales de prednisona en torno a 20-30 mg/d

Descenso rápido y mantenimiento 2.5-5 mg/d

2.5-5 mg/d pueden ser suficientes en situaciones leve-moderadas

Asociar inmunosupresores de forma precoz

HCQ siempre

Biológicos si la cosa no va

CONSENSO MEDICINA INTERNA-NEFROLOGIA HOSPITAL DE CRUCES PARA EL TRATAMIENTO DE LA NEFRITIS LÚPICA

- **Prednisona 15-30 mg/día x 2 semanas**
- **Descenso cada 2 semanas (30-20-15-10)**
- **10 mg/día 1 mes**
- **7.5 mg/día un mes, con reducción posterior hasta dosis de mantenimiento de 2.5 mg/día**

- **Tipo III-IV: 3 pulsos de 250-500 mg de metil-prednisolona al inicio. Ciclofosfamida 500 mg quincenales, precedidos de 125-250 mg iv de metil-prednisolona.**
- **Tipo V: MMF, Tacrolimus**
- **Tipo II: Azatioprina**

- **HCQ, calcio + vit D en todos**

NUESTRA EXPERIENCIA

11 pacientes (8 III-IV, 1 II, 1 V, 1 no biopsia)

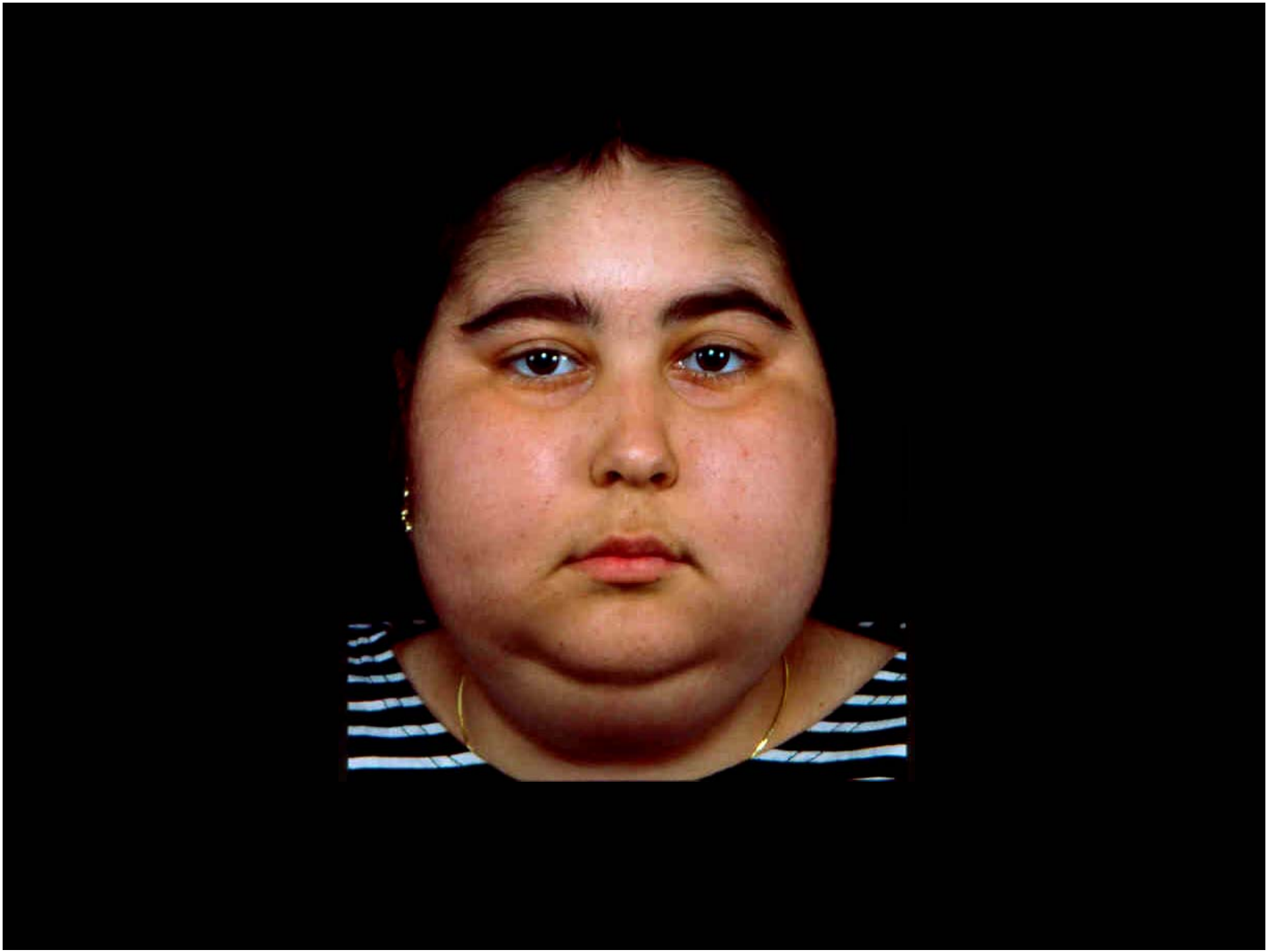
- **CFM en 8**
- **MMF en 2**
- **AZA en 2**
- **M-pred en 8**
- **HCQ en 11**

NUESTRA EXPERIENCIA

	INICIAL	6 MESES	FIN SEGUIMIENTO
Pr/Cr	1.9	0.6	0.26
GFR	80.7	90	85
C3	45.8	81.7	94
Status		RC: 3 RP: 8	RC: 6 RP: 4 NR: 1 (GFR 46, Pr/Cr 0.46)

NUESTRA EXPERIENCIA

Dosis máxima de prednisona:	**5-30 mg/día**
Dosis media de prednisona en 6 meses:	**10 mg/día**
Tiempo medio hasta prednisona 5 mg/día:	**19 semanas**
Necesidad de prednisona > 5 mg/día tras 6 meses:	**1 paciente**
Efectos adversos:	**DM (1 paciente)**




NUNCA MÁIS