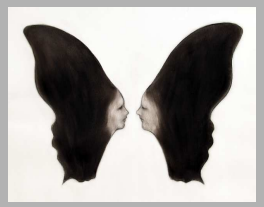
LOS GLUCOCORTICOIDES…..

EN SU JUSTA MEDIDA



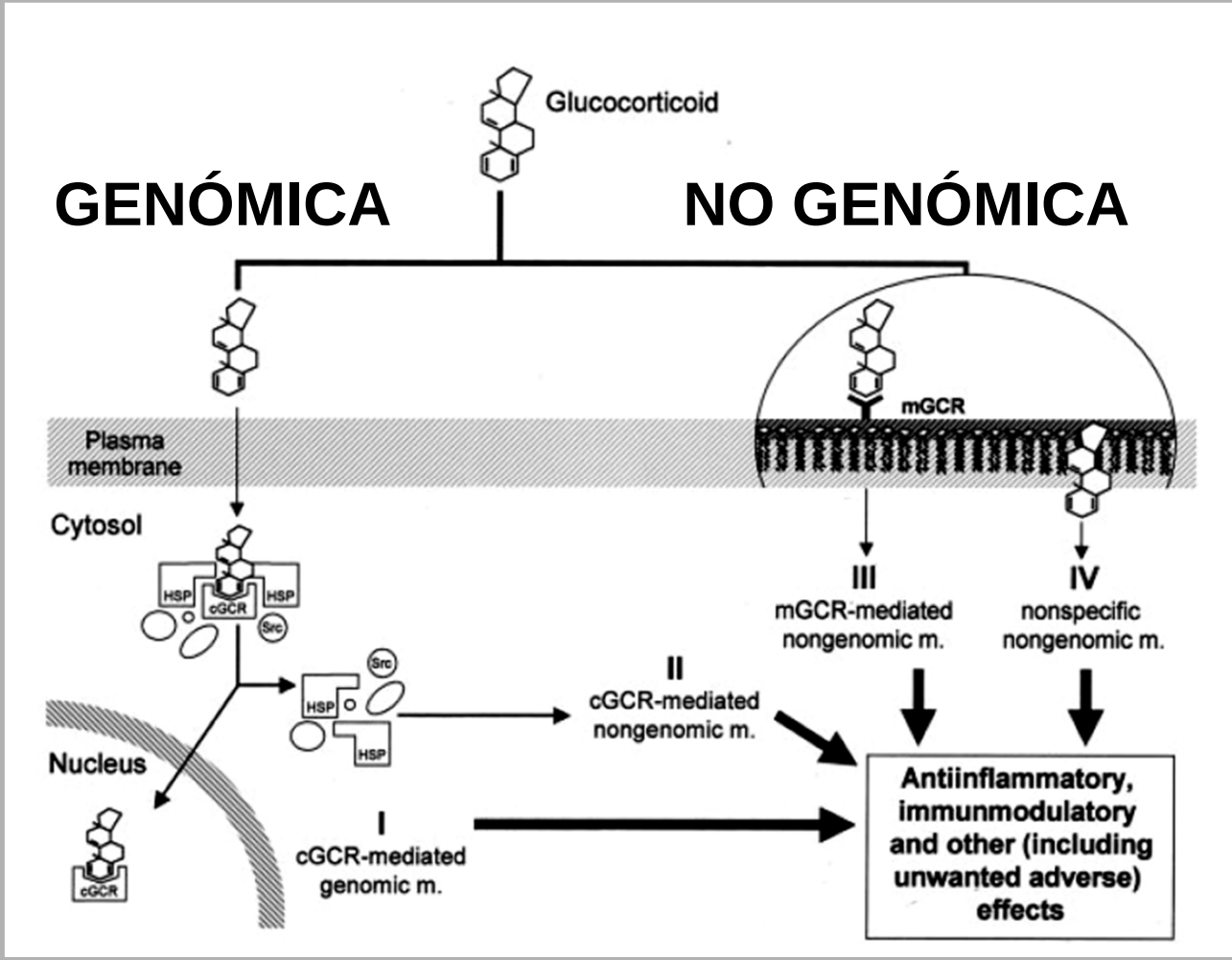
UNIDAD DE INVESTIGACIÓN DE
ENFERMEDADES AUTOINMUNES

BioCruces
HEALTH RESEARCH INSTITUTE

eman ta zabal zazu

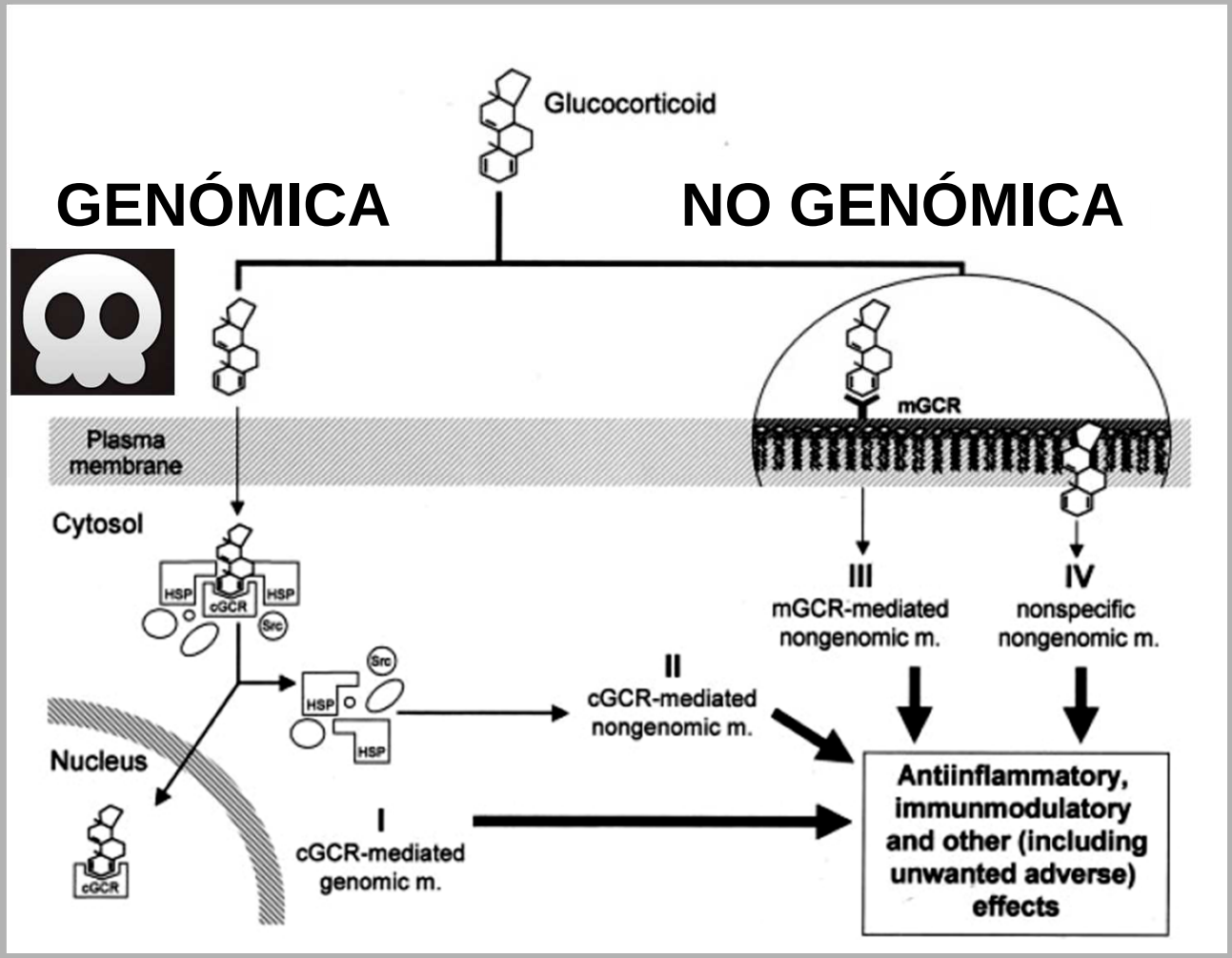
Guillermo Ruiz-Irastorza
Unidad de Investigación de Enfermedades Autoinmunes
Servicio de Medicina Interna
BioCruces Health Research Institute
Hospital Universitario Cruces
Universidad del País Vasco / Euskal Herriko Unibertsitatea

¿ COMO FUNCIONAN ?



Buttgereit et al. Arthritis Rheum 2004

¿ COMO FUNCIONAN ?



Buttgereit et al. Arthritis Rheum 2004

DOSIS DE PREDNISONA Y EFECTO

Dosis bajas: Hasta 7.5 mg/día — **SATURACIÓN VIA GENÓMICA <50%**

Dosis medias: Hasta 30 mg/día

Dosis altas: > 30 mg/día — **EFECTOS GENÓMICOS MÁXIMOS**

Dosis muy altas: ≥ 100 mg/día — **EMPIEZA A FUNCIONAR VIA NO GENÓMICA**

Pulso: ≥ 250 mg/día — **EFECTOS NO GENÓMICOS MÁXIMOS**

Buttgereit et al. Arthritis Rheum 2004

Y ENTONCES… A QUÉ DOSIS ????

Y ENTONCES… A QUÉ DOSIS ????


PREDNISONA


ACTIVIDAD
DAÑO

J Rheumatol 2003;30:1955–9

Accrual of Organ Damage Over Time in Patients with Systemic Lupus Erythematosus

DAFNA D. GLADMAN, MURRAY B. UROWITZ, PROTON RAHMAN, DOMINIQUE IBAÑEZ, and LAI-SHAN TAM

ARTHRITIS & RHEUMATISM
Vol. 43, No. 8, August 2000, pp 1801–1808

DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS ASSOCIATION WITH CORTICOSTEROIDS

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

Original article

doi:10.1093/rheumatology/keu148

Glucocorticoids and irreversible damage in patients with systemic lupus erythematosus

Ioana Ruiz-Arruza[1], Amaia Ugarte[1], Ivan Cabezas-Rodriguez[1], Jose-Alejandro Medina[1], Miguel-Angel Moran[1] and Guillermo Ruiz-Irastorza[1]

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

ARTHRITIS & RHEUMATISM
Vol. 43, No. 8, August 2000, pp 1801–1808

DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS ASSOCIATION WITH CORTICOSTEROIDS

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

	Cumulative prednisone*		High dose prednisone†		Pulse methylprednisolone‡	
Damage item	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

Original article

doi:10.1093/rheumatology/keu148

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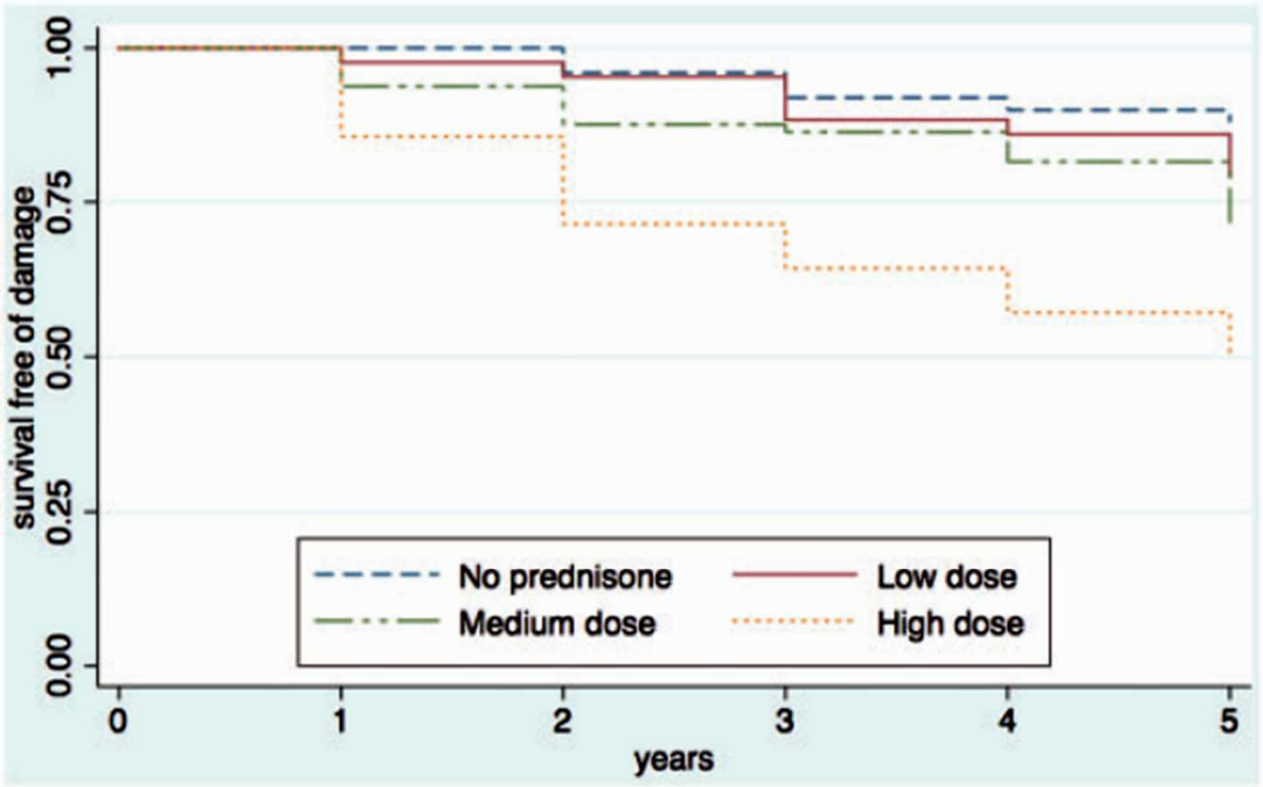
TABLE 5 Prednisone dose category and damage accrual at 5 years: multivariable analysis

		Any damage at year 5 [a], OR (95% CI)	Glucocorticoid-related damage at year 5 [b], OR (95% CI)
Prednisone-4 dose category	No prednisone	Reference	Reference
	Low dose	1.65 (0.53, 5.10)	1.71 (0.17, 17)
	Medium–high dose	5.39 (1.59, 18.27)	9.9 (1.1, 84)

[a]Adjusted by gender, age at diagnosis, calendar year of diagnosis, mean SLEDAI, presence of early damage, proliferative nephritis and months on antimalarials at the end of the fourth year. [b]Adjusted by gender, age at diagnosis, weeks on vitamin D at the end of fourth year, aPL and calendar year of diagnosis. OR: odds ratio; prednisone-4: prednisone at the end of the fourth year of follow-up.

FIG. 1 Kaplan–Meier survival free-of-damage curves according to prednisone dose received during the first year of follow-up



Low dose: ⩽7.5 mg/day; medium dose: ⩽30 mg/day; high dose: >30 mg/day.

Ruiz-Arruza et al. Rheumatology 2014

Original article

doi:10.1093/rheumatology/keu148

Glucocorticoids and irreversible damage in patients with systemic lupus erythematosus

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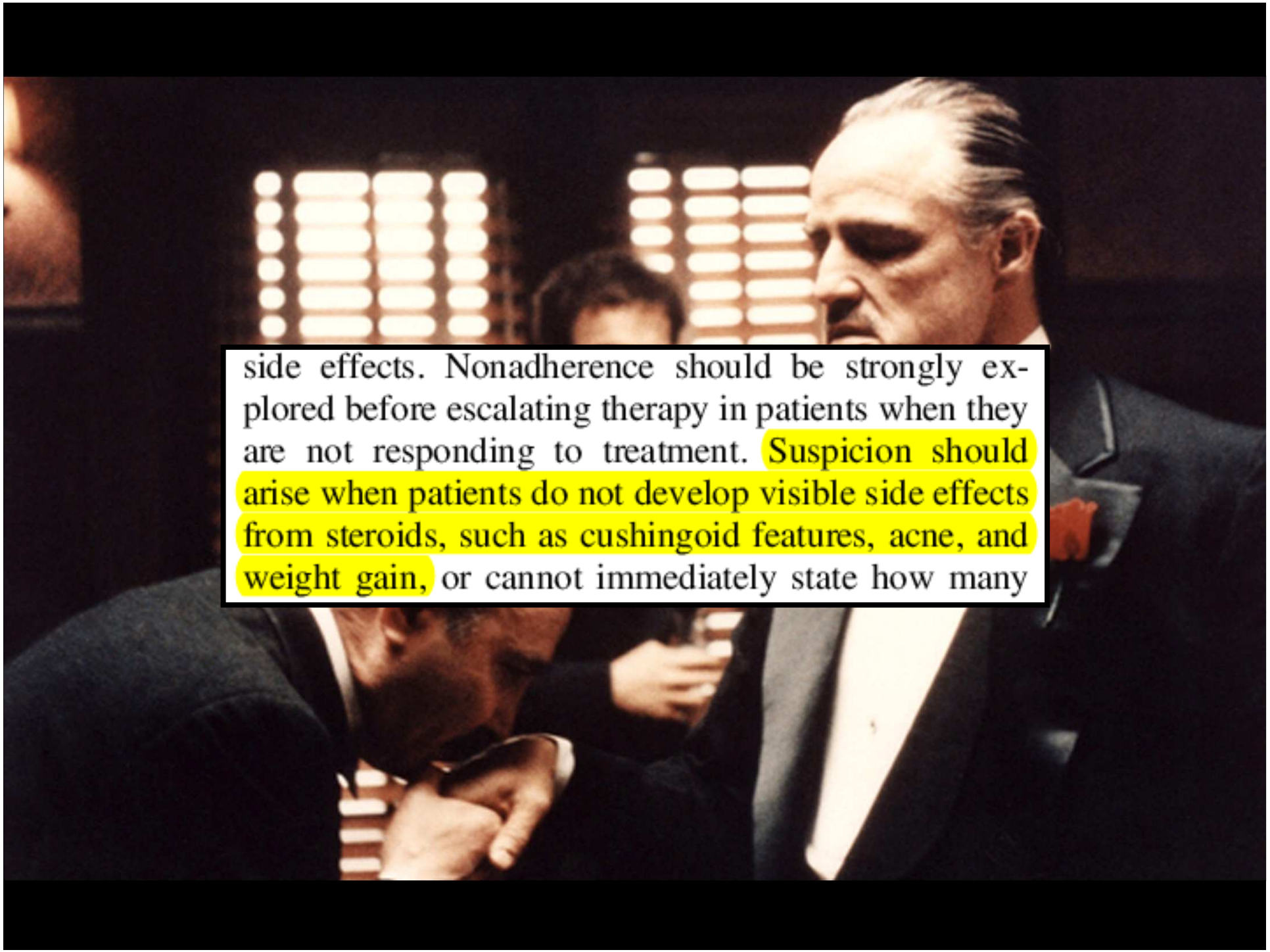
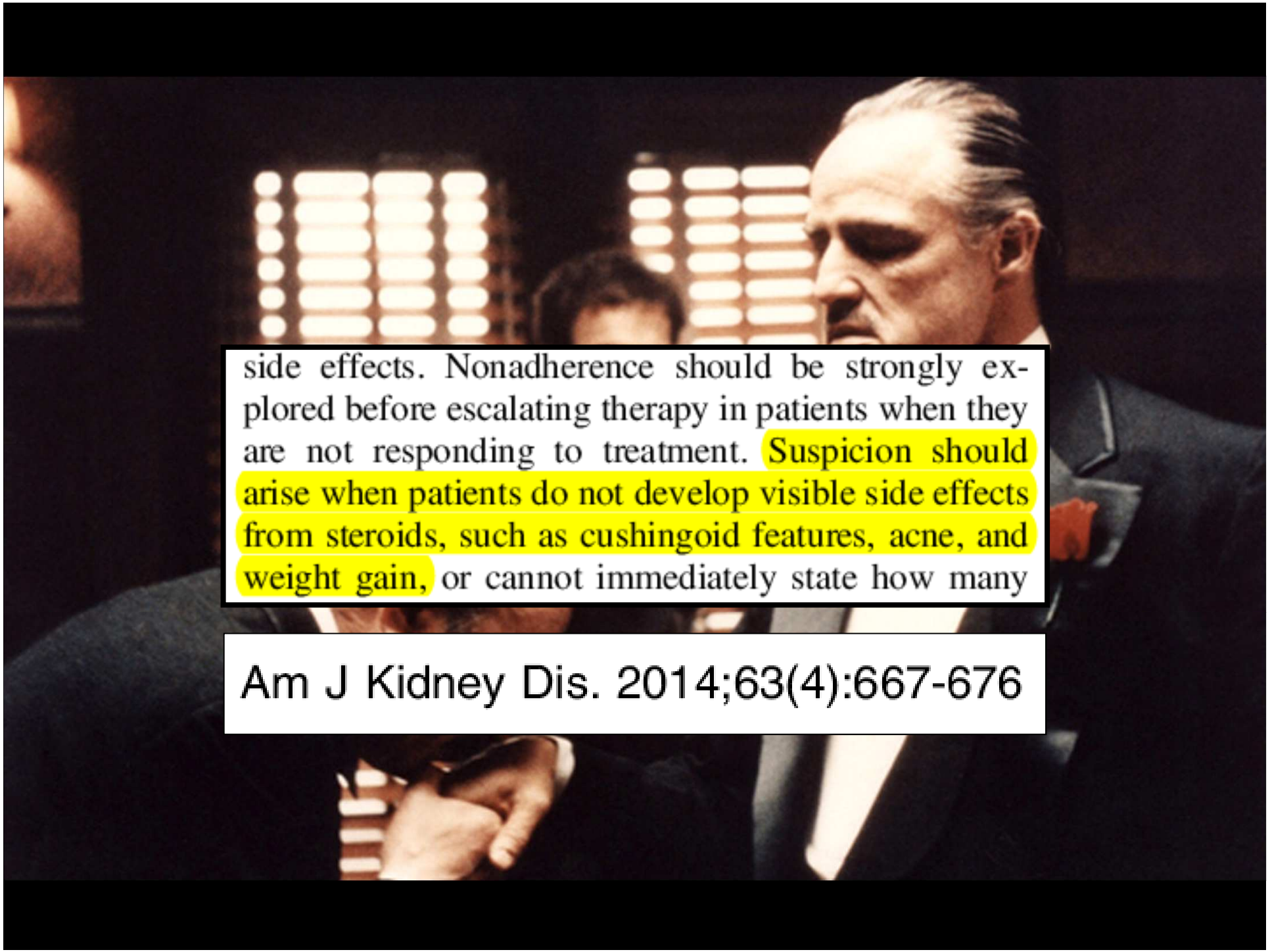
Rheumatology key messages

- Prednisone therapy is associated with damage accrual in patients with SLE.
- Doses of prednisone <7.5 mg/day do not cause global or glucocorticoid-related damage in patients with SLE.
- Methylprednisolone pulses are not related to new damage accrual in patients with lupus.


side effects. Nonadherence should be strongly explored before escalating therapy in patients when they are not responding to treatment. Suspicion should arise when patients do not develop visible side effects from steroids, such as cushingoid features, acne, and weight gain, or cannot immediately state how many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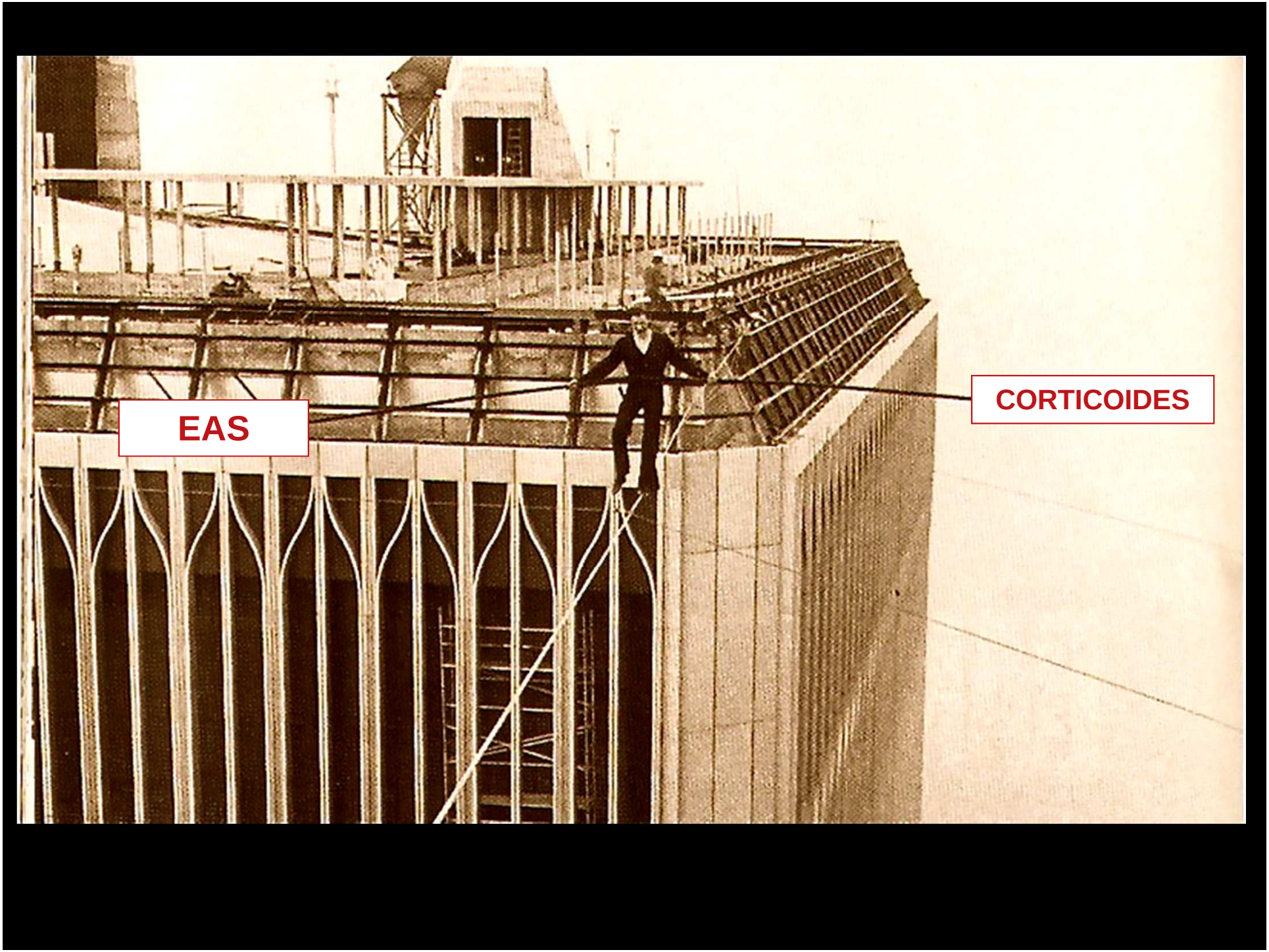
Am J Kidney Dis. 2014;63(4):667-676


EAS
CORTICOIDES

Graham Hughes. Clin Rheum Dis 1982

..aggressive treatment of these patients leads to a greater morbidity from treatment than from the underlying disease.

..attempts at dosage reduction following the initial high dose given for active disease should be conscientious.

Lupus (2011) 20, 1484–1493
http://lup.sagepub.com

PAPER

Efficacy and safety of enteric-coated mycophenolate sodium in combination with two glucocorticoid regimens for the treatment of active lupus nephritis

M Zeher[1], A Doria[2], J Lan[3], G Aroca[4], D Jayne[5], I Boletis[6], F Hiepe[7], H Prestele[8], P Bernhardt[8] and Z Amoura[9]

The Journal of Rheumatology 2012; 39:11;

Renal Outcome in Patients with Lupus Nephritis Using a Steroid-free Regimen of Monthly Intravenous Cyclophosphamide: A Prospective Observational Study

REBECCA FISCHER-BETZ, GAMAL CHEHAB, OLIVER SANDER, STEFAN VORDENBÄUMEN, ADINA VOICULESCU, RALPH BRINKS, and MATTHIAS SCHNEIDER

Ann Rheum Dis 2013;**72**:1280–1286.

EXTENDED REPORT

Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids

Marie B Condon,[1] Damien Ashby,[1] Ruth J Pepper,[1] H Terence Cook,[1,2] Jeremy B Levy,[1] Megan Griffith,[1] Tom D Cairns,[1] Liz Lightstone[1,2,3]

Autoimmunity Reviews 13 (2014) 206–214

Prednisone in lupus nephritis: How much is enough?

Guillermo Ruiz-Irastorza [a,b,*], Alvaro Danza [a,c,d], Isabel Perales [a,e], Irama Villar [a,b], Miriam Garcia [a], Sonia Delgado [f], Munther Khamashta [g]

Table 3
Treatment received within the first six months.

	Cruces-protocol cohort (CPC) (n = 15)	Historic cohort (HC) (n = 30)	P value
Prednisone initial daily doses, mg/d median (range)	20 (5–30)	50 (15–90)	<0.001
Cumulative prednisone doses, g median (range)	1.65 (0.9–2.9)	4.2 (1.7–11.9)	<0.001
Weeks to prednisone 5 mg/d median (range)	16 (0–40)	87 (29–800)	<0.001
Number of intravenous methylprednisolone pulses median (range)	8 (0–13)	0 (0–6)	<0.001
Methylprednisolone cumulative dose, g median (range)	1.5 (0–2.4)	0 (0–1)	<0.001
Cyclophosphamide cumulative doses, g median (range)	3 (0–4.5)	5 (0–16.8)	<0.001
Number of patients treated with hydroxychloroquine (%)	15 (100)	10 (33)	<0.001

Autoimmunity Reviews 13 (2014) 206–214

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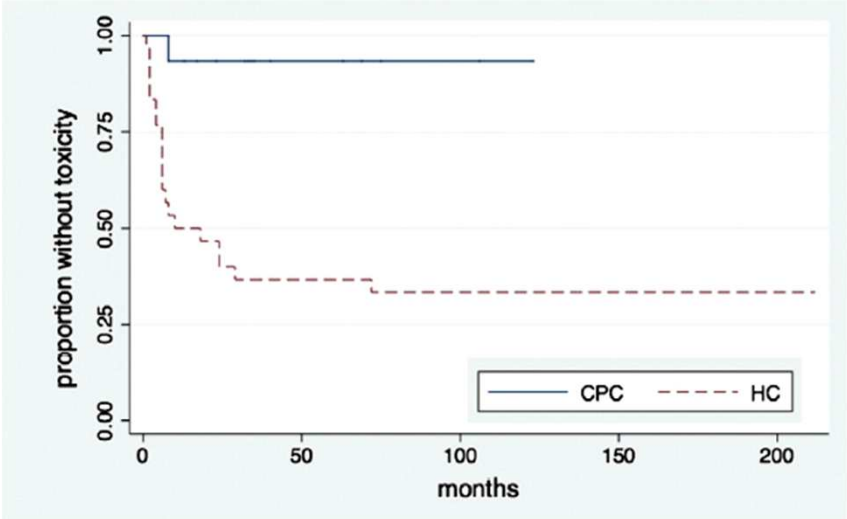

Fig. 2. Survival free of corticosteroid-associated toxicity. Footnotes: CPC: Cruces protocol cohort HC: Historic cohort.

Autoimmunity Reviews 13 (2014) 206–214

Prednisone in lupus nephritis: How much is enough?

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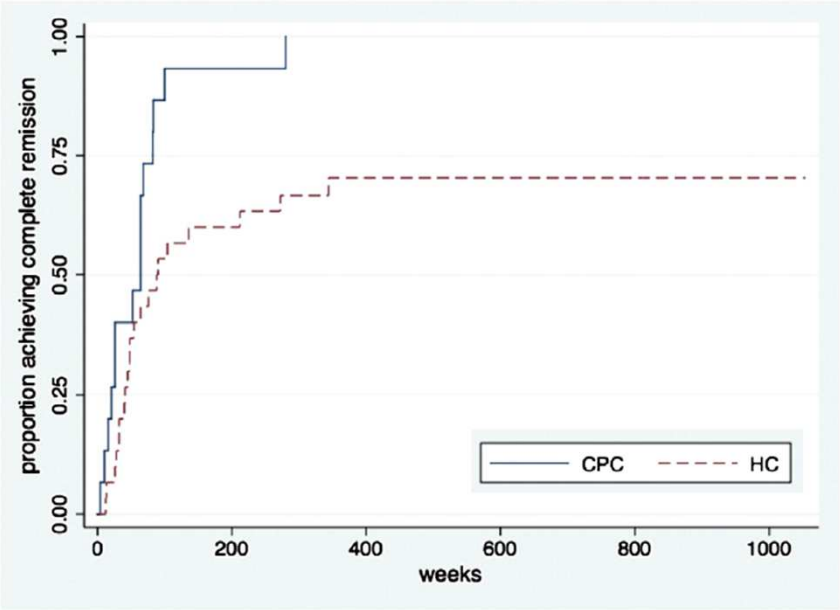

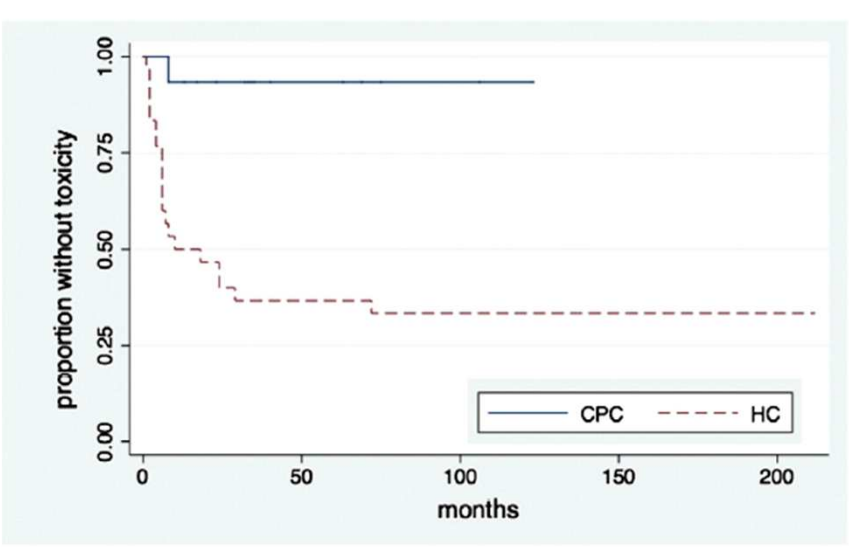

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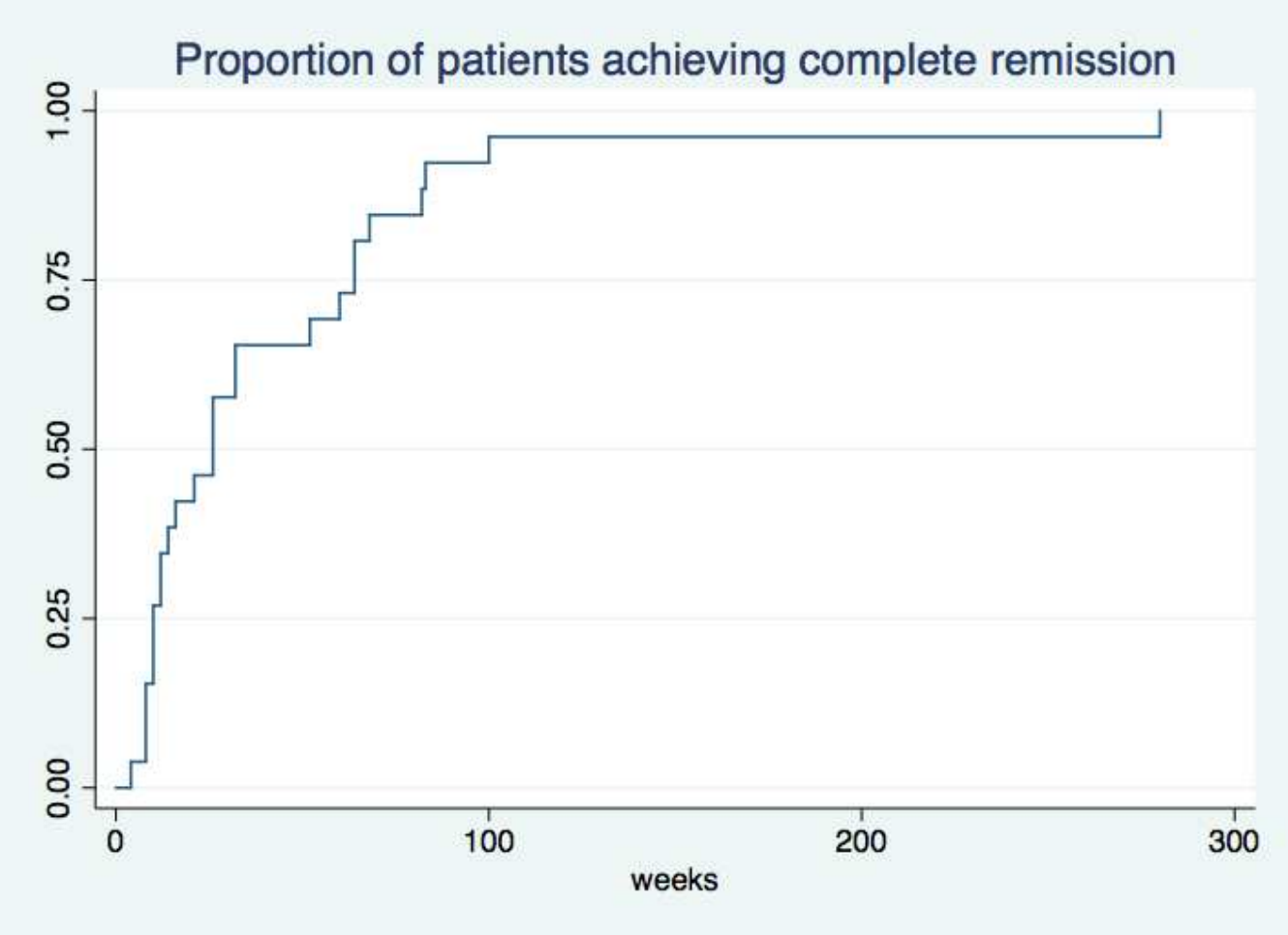
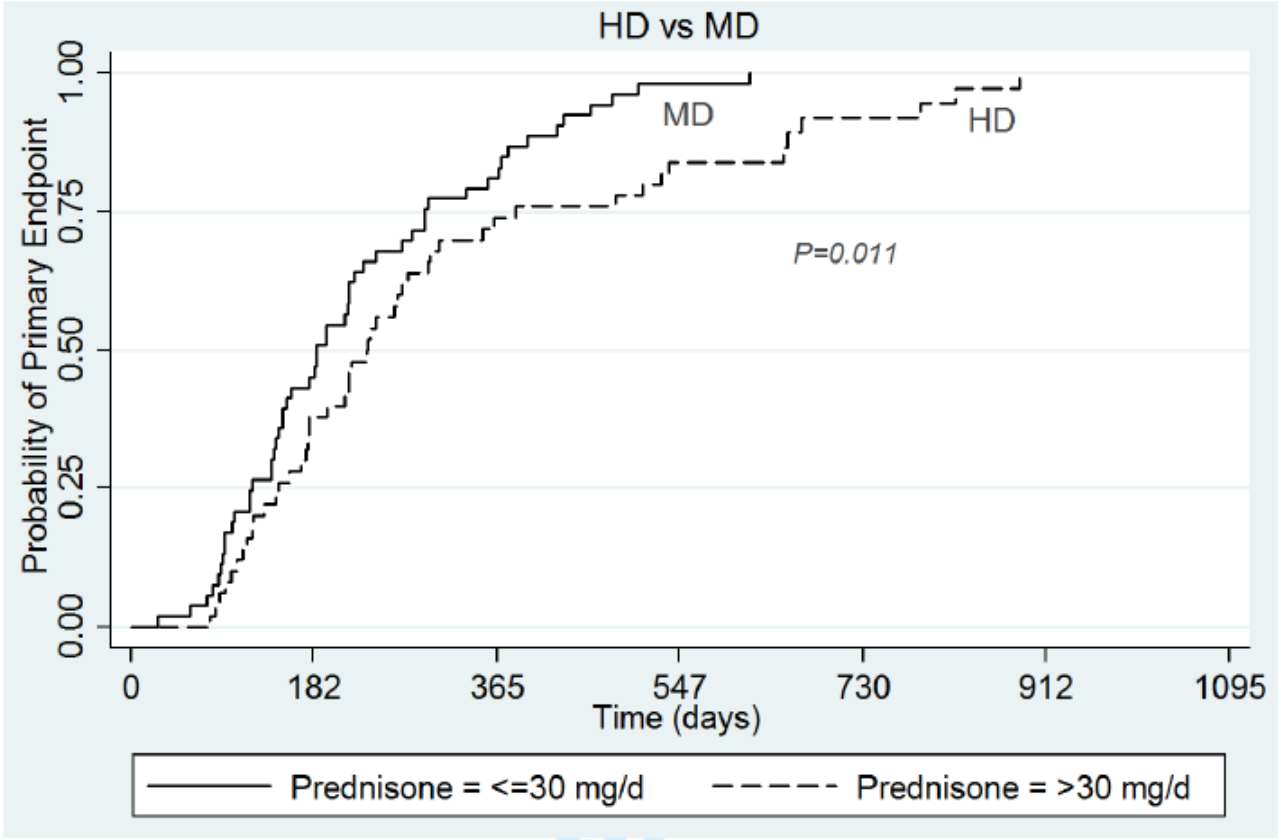


n = 26

Efectos adversos asociados a corticoides = 2 (DM, aumento de peso)

Y PARECIDO EN ARTERITIS TEMPORAL

FIG. 1 Kaplan-Meier probability of achieving clinical and biological remission while receiving ≤7.5 mg/day of prednisone in MD and HD groups.



Les I, et al. EAS-Cruces

LA RECETA

Hidroxicloroquina SIEMPRE en LES

Pulsos de Urbasón (125, 250, 500) en situaciones agudas

En formas graves, dosis iniciales de prednisona en torno a 20-30 mg/día Y NUNCA MÁS DE 30 mg/día

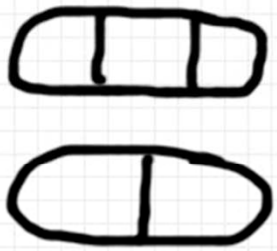
Descenso rápido y mantenimiento 2.5-5 mg/día

2.5-5 mg/día suficientes en brotes leve-moderados

Asociar inmunosupresores de forma precoz:
- Brotes graves
- Dosis de mantenimiento > 5 mg/día

Biológicos si la cosa no va

LA PASTILLA DE DACONTIN



30, 20, 15, 10

7.5, 5, 2.5

Mayo 2013: varón de 15 años que acude para segunda opinión....

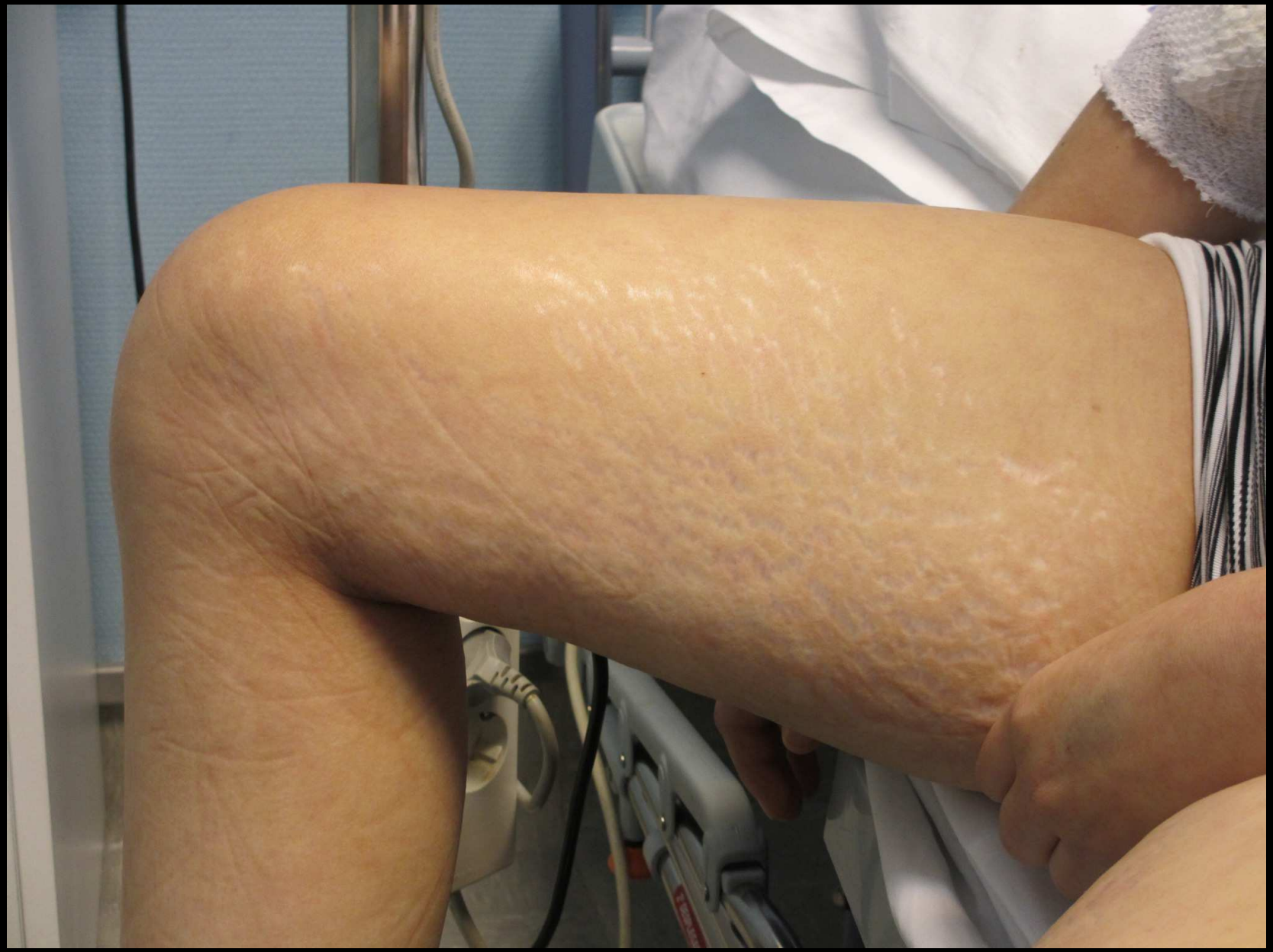
Mayo 2013: varón de 15 años que acude para segunda opinión....

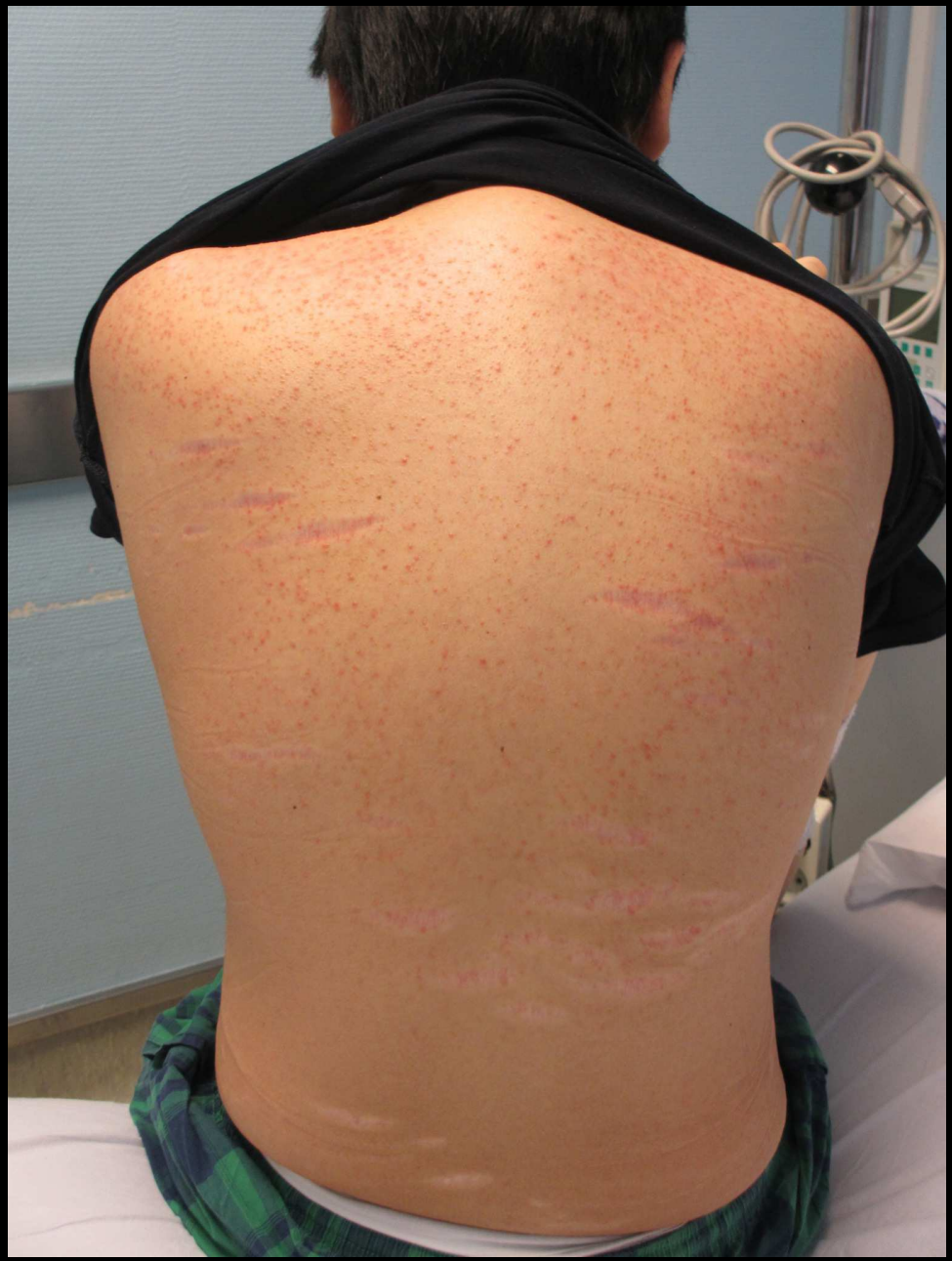
Lupus eritematoso sistémico dignosticado en marzo 2013:

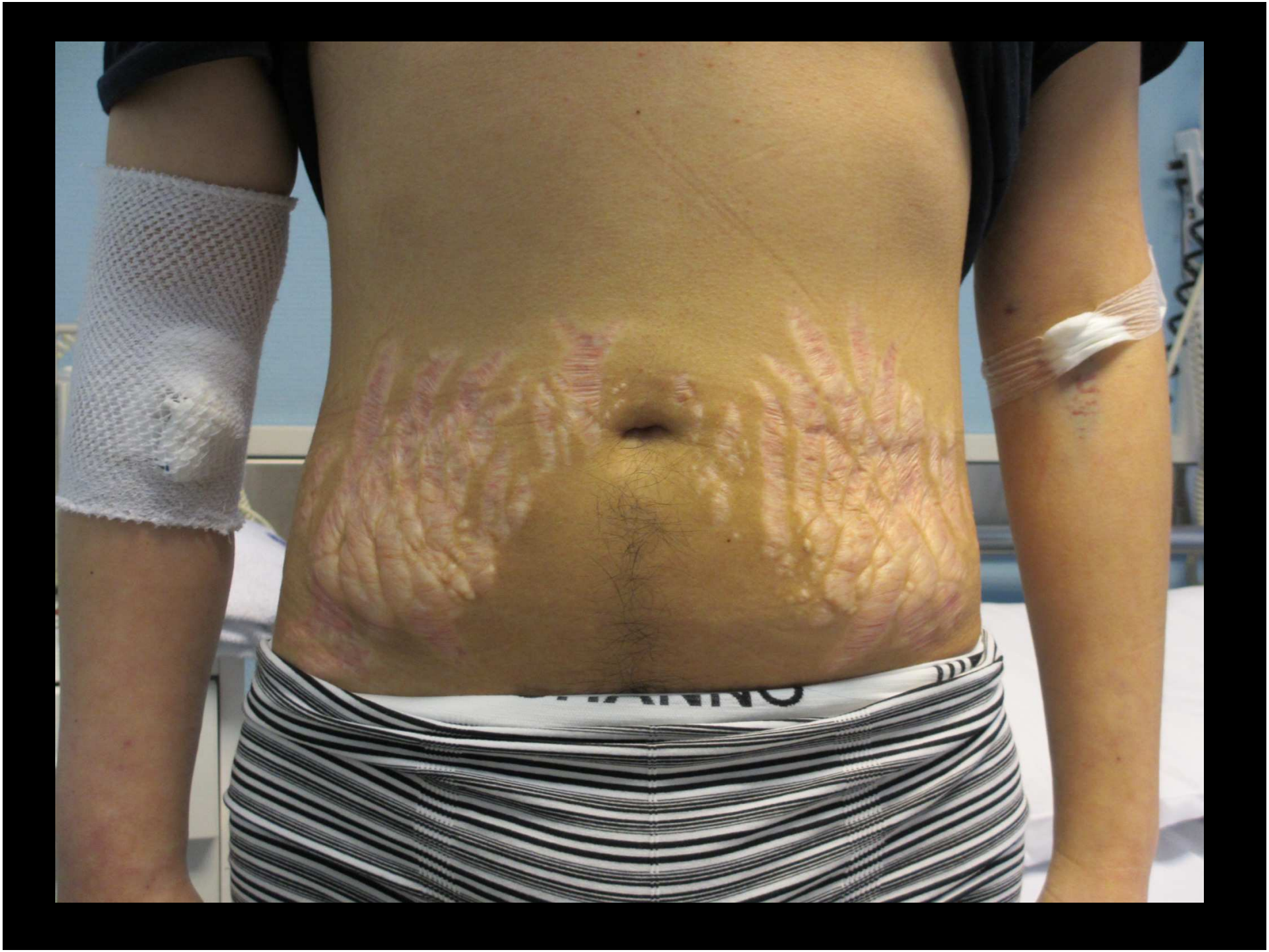
- **Síndrome nefrótico, hipocomplementemia, anti-DNA**
- **Biopsia renal: NL clase IV**

HCQ 200, Prednisona 50 mg/d, MMF 500-0-500

Mes y medio despues MMF 1000-0-1000







Y la nefritis....

Y la nefritis....

- **Hb 8**
- **C3 y C4 normales**
- **Albumina 1.7**
- **IgG total 162**
- **Proteinuria 9.8 gr/24h**

Qué hicimos:

- **M-Pred 250 x3**
- **IGIV**
- **Prednisona 30, 20, 15, 10 (cada 2 semanas)**
- **CFM 500 + M-Pred 125 (cada 2 semanas)**
- **HCQ**
- **IECAS**

Julio-2013

Pred 10, CFM 500 x 4, etc…

- **Hb 11**
- **C3 y C4 normales**
- **Albumina 3.8**
- **Pr/Cr 0.41**

Septiembre-2014

Pred 2.5, MMF 1000-0-1000, HCQ 200

- **Hb 12.1**
- **C3 y C4 normales**
- **Albumina 4.6**
- **Pr/Cr 0.08**

22 year old girl

SLE presenting in July 2009:

- **Widespread rash and alopecia**
- **Severe oral ulcers**
- **Severe class IV lupus nephritis**

  Urine Pr/Cr 3.46

  Serum albumina 2.2

  anti-DNA highly positive

  C3 20, C4 3

SLEDAI = 15

M-Prednisolone 250x3

Prednisone 30, 20, 15, 10 (every two weeks), 7.5, 5 (every 4 weeks)

HCQ

Cyclophosphamide 500 mg (+ m-pred 125) fornightly x9, then MMF

Calcium + vitamin D

Enalapril

AT SIX MONTHS:

Pr/Cr 0.56

Serum albumin 4

C3 92, C4 12

No smoking, normal blood pressure

SLEDAI = 2

AT SIX MONTHS:

Mean dose of prednisone 9 mg/d

No GC-related side effects

AT SIX MONTHS:

Mean dose of prednisone 9 mg/d

No GC-related side effects

TODAY:

Prednisone 2.5 mg/d, HCQ, MMF

LN in complete remission

SDI = 0