# ENFERMEDADES AUTOINMUNES Y EMBARAZO

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EUSKAL HERRIKO UNIBERTSITATEA


DOUBLE TROUBLE
LYNYRD SKYNYRD
ROLL GYPSY ROLL


**COMPLICACIONES EAS-EMBARAZO**

**EMBARAZOS DE ALTO RIESGO**

**MANEJO GENERAL DEL EMBARAZO**

**FARMACOS EN EL EMBARAZO**

**TRATAMIENTO DEL SAF EN EL EMBARAZO**

**PREECLAMPSIA-NEFROPATIA**

**EPIDURAL**

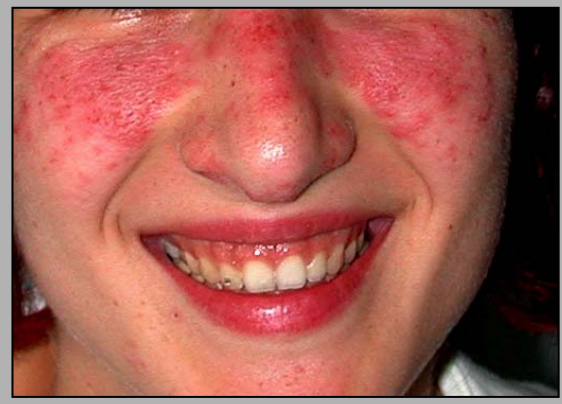
**PUERPERIO Y LACTANCIA**

**REPRODUCCION ASISTIDA**

# LES Y EMBARAZO

**Actividad lúpica**

- **aumenta en el embarazo y el puerperio**
- **aumenta en las que abandonan HCQ**
- **aumenta si brote reciente**
- **más actividad, peor pronóstico fetal**



**Nefropatía**

- **aumento de riesgo de HTA y toxemia**
- **aumento de riesgo de prematuridad y CIR**
- **riesgo de recidiva o deterioro de función renal**

**Bloqueo cardiaco congénito**

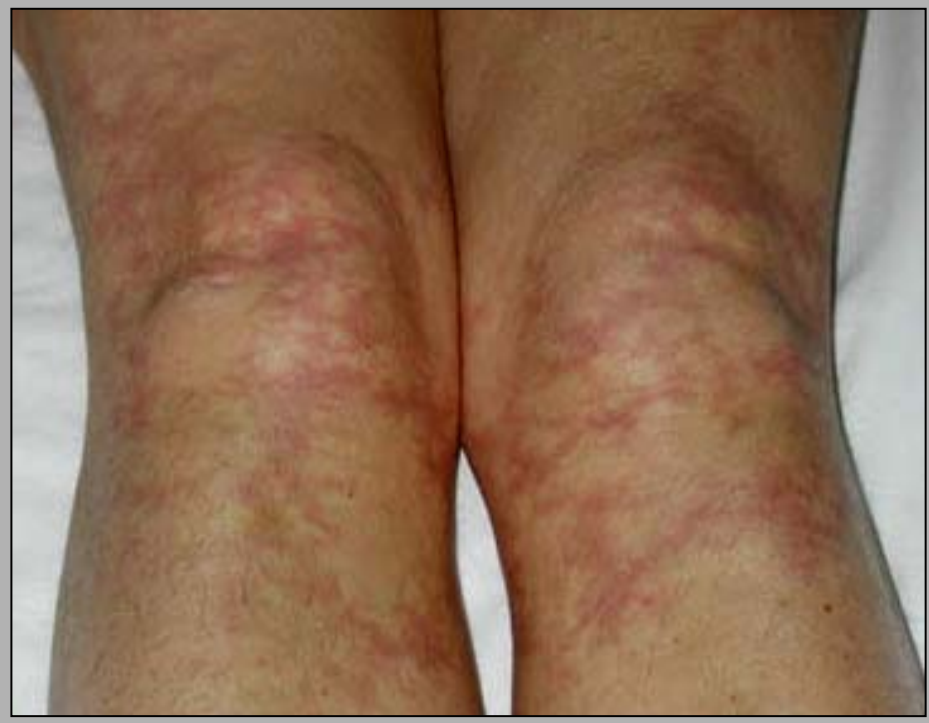
- **2% de hijos de madres anti-Ro (+)**
- **Riesgo de recurrencia 20%**

# SINDROME ANTIFOSFOLIPIDO Y EMBARAZO

**Trombosis materna**

**Complicaciones obstétricas**

- **Muertes fetales**
- **Prematuridad**
- **Bajo peso**
- **Preeclampsia**
- **Abortos**



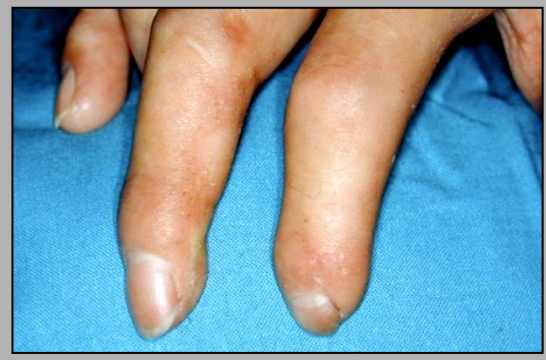
# ESCLERODERMIA Y EMBARAZO

**Menos frecuente (por prevalencia y edad de comienzo)**

**Raynaud mejora**

**RGE empeora**

**Problemas de distensibilidad cutanea**



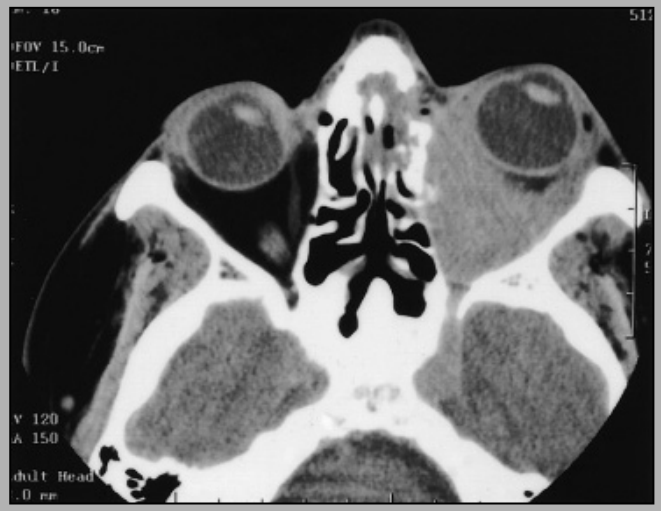
**PELIGRO!!**

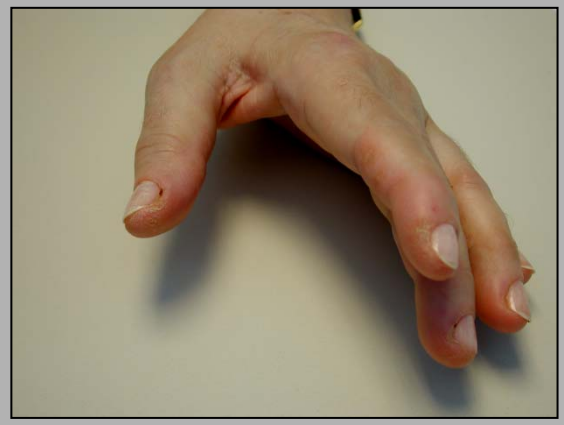
- **HTP**
- **Neumopatía restrictiva**
- **Crisis renal previa**
- **Formas difusas de reciente diagnóstico**

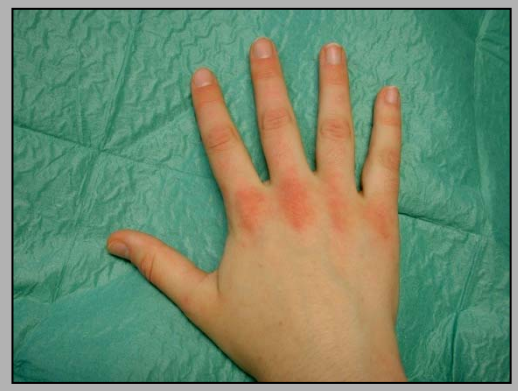
# OTROS (VASCULITIS, MIOPATÍAS)

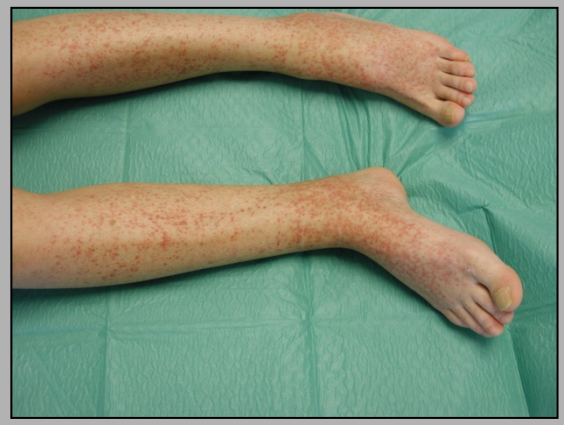
**Complicaciones en función de actividad y afección orgánica:**

- **Riñón**
- **Músculo**
- **Pulmón**
- **Corazón**









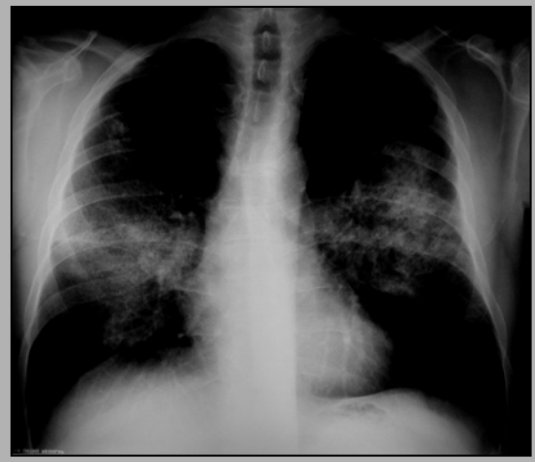


**Table 2**
High-risk lupus pregnancy.

| |
|---|
| Previous poor obstetric history |
| Lupus nephritis |
| Renal failure |
| Heart failure |
| Pulmonary hypertension |
| Interstitial lung disease |
| Active disease |
| High degree of irreversible organ damage |
| High-dose steroid therapy |
| Presence of anti-phospholipid antibodies/syndrome |
| Presence of anti-Ro/La antibodies |
| Multiple pregnancy |
| Age over 40 years |

**Ruiz-Irastorza & Khamashta. Best Pract Res Clin Rheumatol 2009; 23: 575-82**

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**ESCLEROSIS SISTEMICA DIFUSA DE RECIENTE COMIENZO**

**Ruiz-Irastorza & Khamashta. Best Pract Res Clin Rheumatol 2009; 23: 575-82**

**Table 3**
Contraindications to pregnancy in women with SLE.

| |
|---|
| Severe pulmonary hypertension (estimated systolic PAP $>$ 50 mm Hg or symptomatic) |
| Severe restrictive lung disease (FVC $<$ 1 litre) |
| Heart failure |
| Chronic renal failure (Cr $>$ 2.8 mg $dl^{-1}$) |
| Previous severe pre-eclampsia or HELLP despite therapy with aspirin and heparin |
| Stroke within the previous six months |
| Severe lupus flare within the previous six months |

Ruiz-Irastorza & Khamashta. Best Pract Res Clin Rheumatol 2009; 23: 575-82

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**ESCLEROSIS SISTEMICA DIFUSA DE RECIENTE COMIENZO**

**Ruiz-Irastorza & Khamashta. Best Pract Res Clin Rheumatol 2009; 23: 575-82**

# HIGH RISK PREGNANCY MANAGEMENT

MEDICAL-
OBSTETRIC
COORDINATION

WELL DEFINED
MANAGEMENT
PROTOCOL

GOOD
NEONATAL
UNIT

# CUIDADO DEL EMBARAZO

antes

durante


después

# DADO DEL EMBARAZO

antes

durante


después

**Table 1**
Pre-conceptional visit checklist.

| |
|---|
| Age |
| Any previous pregnancy? |
| Previous pregnancy complications? |
| SLE organ involvement |
| Degree of irreversible damage |
| Recent or current SLE activity? |
| Presence of anti-phospholipid antibodies/syndrome? |
| Positivity of anti-Ro/anti-La? |
| Current treatment: any 'forbidden' drugs? |

Ruiz-Irastorza & Khamashta. Best Pract Res Clin Rheumatol 2009; 23: 575-82

**Table 4** Management plan

| |
|---|
| Coordinated care by a medical-obstetric team with experience in autoimmune diseases and high-risk pregnancies |
| Fully equipped neonatal unit |
| Full autoantibody profile available before pregnancy |
| Visits more frequent as pregnancy progresses |
| Blood pressure and urine dipstick on every visit |
| Uterine artery Doppler study at 20 weeks in patients with aPL, renal disease, hypertension or history of preeclampsia. Repeat at 24 weeks if abnormal |
| Umbilical artery Doppler study from 20 weeks, with frequency according to medical and obstetric course, in women with aPL, renal disease, active disease or previous complicated pregnancy |
| Foetal echocardiogram from 20th week in women with anti-Ro and/or anti-La antibodies |

Ruiz-Irastorza & Khamashta. Lupus 2008; 17: 416-20

# PROTOCOLO CONSULTA AUTOINMUNES Y EMBARAZO
# HOSPITAL DE CRUCES

| SEMANA | 8 | 12 | 16 | 20 | 24 | 28 | 30 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | COMENTARIOS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TA | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | TODAS |
| HRF y perfil | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | | ■ | | ■ | | ■ | | ■ | TODAS |
| Sedimento orina | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | TODAS |
| Orina 24 h | | | | | | | | | | | | | | | | | Sedimento + |
| DNA, C3, C4 | ■ | | ■ | | ■ | | ■ | | | ■ | | | | ■ | | | LES |
| Eco | ■ | ■ | | ■ | ■ | ■ | | ■ | | ■ | | ■ | | ■ | | | TODAS |
| Doppler Umbilical | | | | ■ | ■ | ■ | | ■ | | ■ | | ■ | | ■ | | | aFL, NEFROPATÍA HTA |
| Doppler Uterinas | | | | ■ | ■ | | | | | | | | | | | | TODAS |
| Ecocardio fetal | | | | ■ | ■ | ■ | ■ | | | | | | | | | | Ro y /o La + |
| CTG | | | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | TODAS |

Review

# Anti-inflammatory and immunosuppressive drugs and reproduction

Monika Østensen[1], Munther Khamashta[2], Michael Lockshin[3], Ann Parke[4], Antonio Brucato[5], Howard Carp[6], Andrea Doria[7], Raj Rai[8], Pierluigi Meroni[9], Irene Cetin[10], Ronald Derksen[11], Ware Branch[12], Mario Motta[13], Caroline Gordon[14], Guillermo Ruiz-Irastorza[15], Arsenio Spinillo[16], Deborah Friedman[17], Rolando Cimaz[18], Andrew Czeizel[19], Jean Charles Piette[20], Ricard Cervera[21], Roger A Levy[22], Maurizio Clementi[23], Sara De Carolis[23], Michelle Petri[24], Yehuda Shoenfeld[25], David Faden[26*], Guido Valesini[27] and Angela Tincani[28]

*Arthritis Research & Therapy* 2006

# LOS BUENOS

**HCQ**

**AZA**

**AAS**

**Heparina**

**Calcio + D**

**Sildenafilo**

**Epoprostenol?**

**Paracetamol**

# LOS MALOS

**CFM**

**MTX**

**Micofenolato**

**Sintrom (sem. 6-10)**

**Bosentan**

**Iloprost**

**Alprostadilo**

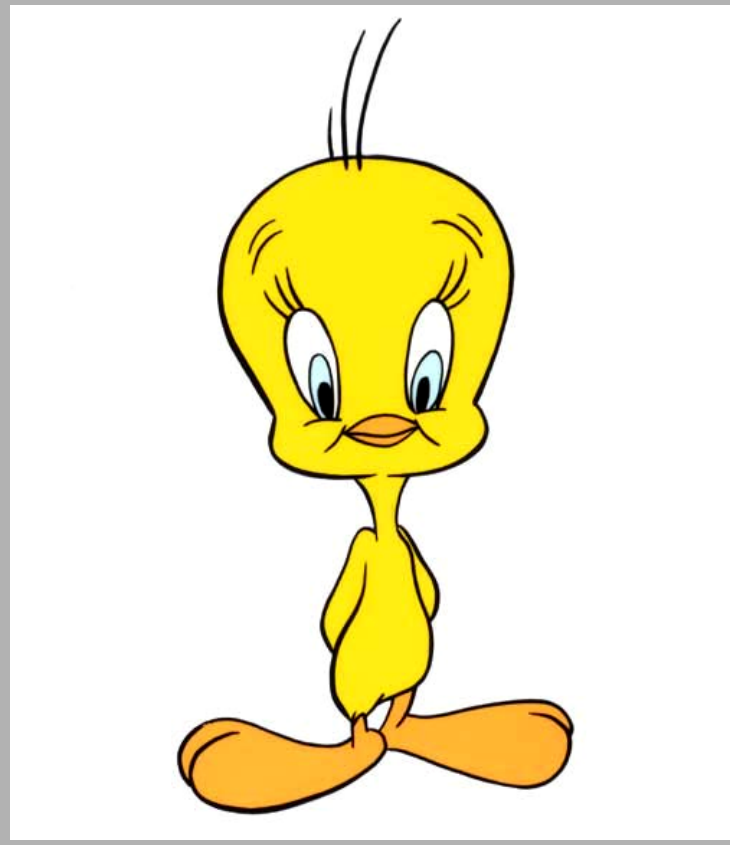
**IECAs, ARA 2**

# LOS QUE PARECEN BUENOS, PERO….

**AINES**

- **Cierre prematuro del ductus**
- **Insuficiencia renal fetal**
- **HTA e insuficiencia renal materna**

**STOP A PARTIR DE SEMANA 30-32**



**PREDNISONA**

- **Segura para el feto**
- **Complicaciones maternas (HTA, DM, rotura prematura..)**

**DOSIS < 7.5 mg/d (O PULSOS)**

ARD ONLINE

## Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review

Guillermo Ruiz-Irastorza, Manuel Ramos-Casals, Pilar Brito-Zeron and Munther A Khamashta

*Ann Rheum Dis* published online 22 Dec 2008;
doi:10.1136/ard.2008.101766

**MAS DE 300 EMBARAZOS PUBLICADOS (Y MUCHOS MÁS NO PUBLICADOS…) EN MUJERES CON LES EN TRATAMIENTO ANTIPALUDICO (LA MAYORIA HCQ)**

**NO MALFORMACIONES ASOCIADAS**

**NO TOXICIDAD FETAL**

**RIESGO DE REACTIVACION SI SE SUSPENDE**

Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 61, No. 5, May 15, 2009, pp 587–592
DOI 10.1002/art.24462


SPECIAL ARTICLE: BIOLOGIC AGENTS IN THE
TREATMENT OF RHEUMATIC DISEASES—THE FIRST DECADE

# Biologic Therapy and Pregnancy Outcomes in Women With Rheumatic Diseases

EVELYNE VINET,[1] CHRISTIAN PINEAU,[1] CAROLINE GORDON,[2] ANN E. CLARKE,[1] AND SASHA BERNATSKY[1]

**Anti-TNF:** **663 embarazos. Parecen seguros. No en lactancia.**

**Rituximab:** **9 embarazos. Leucopenia 4/5. No en lactancia**

**Abatacept:** **No hay datos**

**Anakinra:** **No hay datos**

*Am J Gastroenterol* 2009; 104:1541–1545

CME

REVIEW

# The Safety of Proton Pump Inhibitors (PPIs) in Pregnancy: A Meta-Analysis

Simerpal K. Gill[1,2], Lisa O'Brien[1,3], Thomas R. Einarson[4] and Gideon Koren, MD, FRCPC[1,2,3]

Review: PPI and malformations
Comparison: 1 malformation
Outcome: 3 malformations after any PPI exposure using adjusted ORs from studies

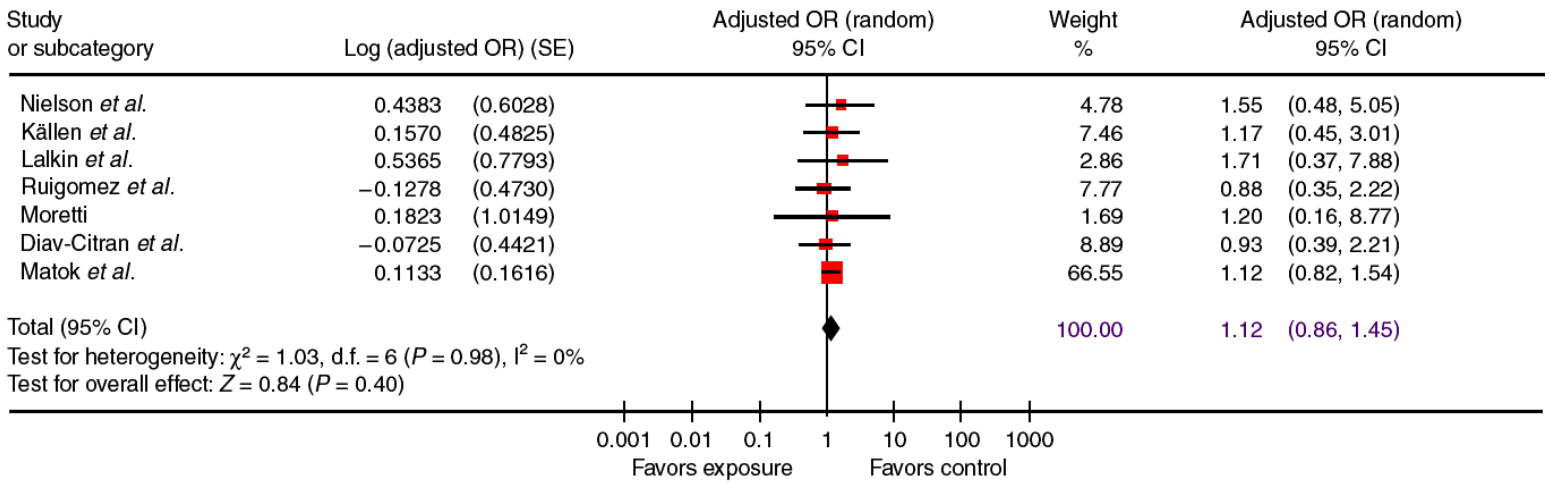



**Figure 1.** Overall effect of the incidence of major congenital malformations after *in utero* exposure to PPIs. CI, confidence interval; OR, odds ratio; PPI, proton pump inhibitor; SE, standrad error.

**On the basis of these results, PPIs are not associated with an increased risk for major congenital birth defects, spontaneous abortions, or preterm delivery. The narrow range of 95% CIs is further reassuring, suggesting that PPIs can be safely used in pregnancy.**

# Management of RA medications in pregnant patients

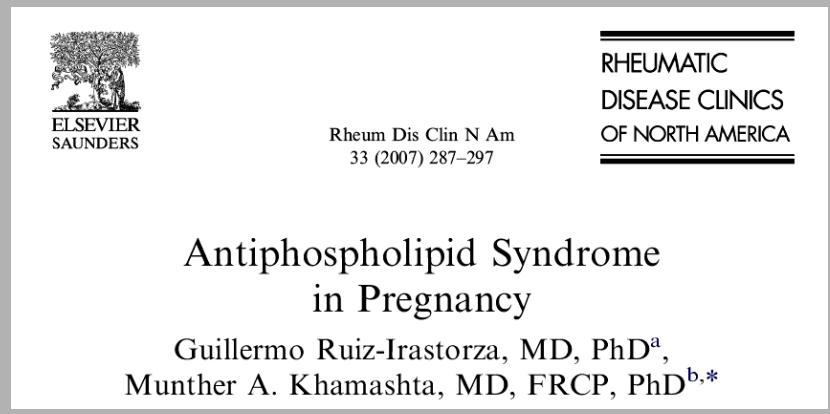
*Monika Østensen and Frauke Förger*

*Nat. Rev. Rheumatol.* **5**, 382–390 (2009)

## Bisphosphonates

*Recommendation*

The limited evidence of bisphosphonate use before and during human pregnancy does not show a significantly increased risk for congenital anomalies. Bisphosphonates given by infusion or injection during pregnancy might lead to hypocalcemia in the neonate. Hypocalcemia did not occur in neonates exposed to oral bisphosphonates;[42] therefore, oral rather than other formulations of bisphosphonates might be safer for patients planning a pregnancy. In the absence of long-term follow-up data in children exposed to bisphosphonates *in utero*, discontinuing bisphosphonates once pregnancy is recognized is advised.




- **Trombosis previas**

  **Heparina (Fragmin ó Clexane) dosis altas + AAS**

- **Abortos recurrentes (tempranos)**

  **AAS**

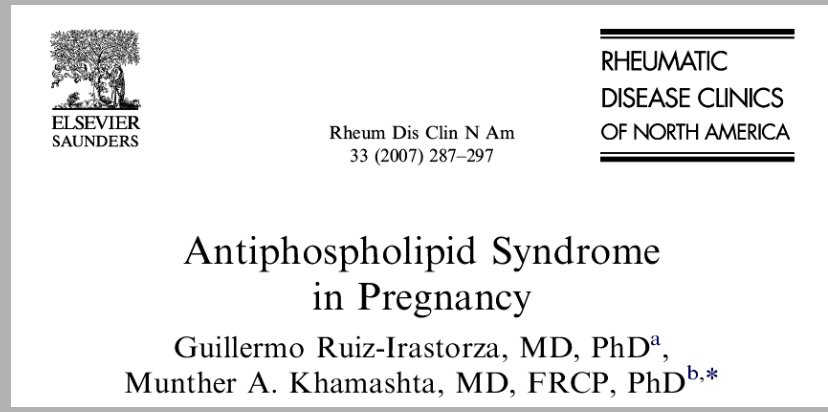
  **Heparina (Fragmin ó Clexane) dosis bajas + AAS**

- **Muertes fetales (tardías) / pre-eclampsia grave / CIR**

  **Heparina (Fragmin ó Clexane) dosis bajas + AAS**

- **Anticuerpos sin trombosis ni problemas obstétricos**

  **AAS**

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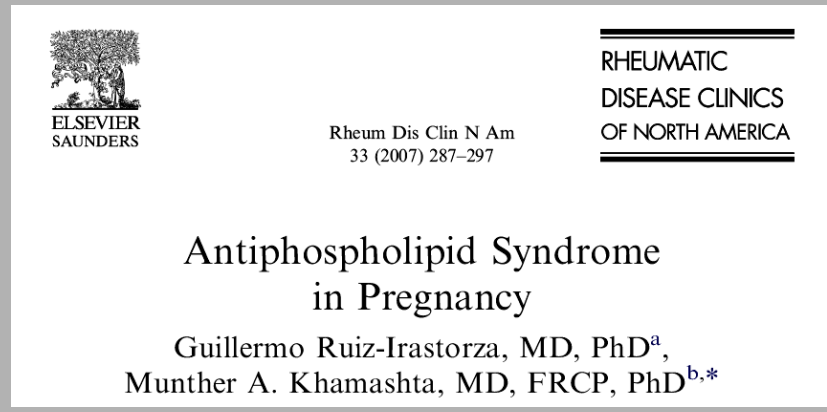



**Prevención de trombosis postparto en todas las mujeres con anticuerpos antifosfolípido**

- **HBPM dosis bajas 4-6 semanas si no trombosis**
- **Sintrom en puerperio inmediato si trombosis previas**

**Calcio + vitamina D durante el embarazo hasta fin de lactancia si se toma heparina**

# PREECLAMPSIA

## High risk for preeclampsia:

- Previous preeclampsia
- Arterial hypertension
- Age over 40
- Obesity
- Multiple pregnancy
- Renal disease
- Antiphospholipid antibodies

# DIAGNOSTICO / TRATAMIENTO

**Diagnóstico diferencial preeclampsia / nefritis lúpica /crisis renal**

- **Acido úrico (preeclampsia)**
- **Proteinuria (preeclampsia, LES)**
- **Sedimento activo (LES)**
- **Anemia microangiopática (preeclampsia, esclero)**

**Tratamiento HTA**

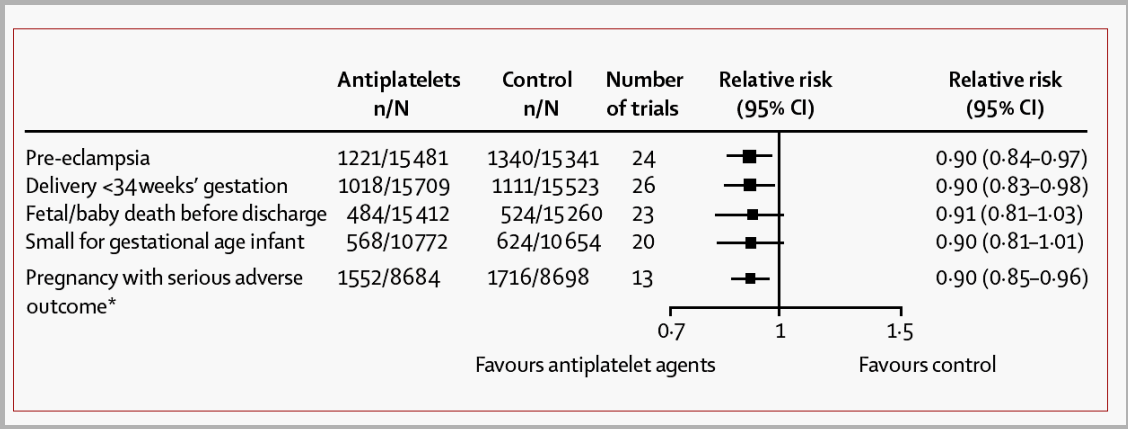
- **Alfa-metil-dopa**
- **Labetalol**
- **Calcio antagonistas**
- **IECAs si crisis renal esclero**

**EL UNICO TRATAMIENTO EFECTIVO DE LA PREECLAMPSIA ES EL FINAL DEL EMBARAZO (AGUANTAR HASTA SEMANA 28 !!)**

*Lancet* 2007; 369: 1791–98

# Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data

*Lisa M Askie, Lelia Duley, David J Henderson-Smart, Lesley A Stewart, on behalf of the PARIS Collaborative Group**




| | Sample baseline event rate | PARIS relative risk (95%CI) | Number needed-to-treat (95% CI) |
|---|---|---|---|
| Pre-eclampsia | 18% | 0·90 (0·84–0·97) | 56 (35–185) |
| | 6% | | 167 (104–556) |
| | 2% | | 500 (313–1667) |
| Preterm <34 weeks | 20% | 0·90 (0·83–0·98) | 50 (29–250) |
| | 10% | | 100 (59–500) |
| | 2% | | 500 (294–2500) |
| Perinatal death | 7% | 0·91 (0·81–1·03) | 159 (75–476) |
| | 4% | | 278 (132–833) |
| | 1% | | 1111 (526–3333) |
| Small for gestational age baby | 15% | 0·90 (0·81–1·01) | 67 (35–667) |
| | 10% | | 100 (53–1000) |
| | 1% | | 1000 (526–10 000) |
| Pregnancy with serious adverse outcome | 25% | 0·90 (0·85–0·96) | 40 (27–100) |
| | 15% | | 67 (44–167) |
| | 7% | | 143 (95–357) |

***Table 4:*** **PARIS number needed-to-treat with sample baseline event rates**

*Lancet* 2007; 369: 1791–98

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| | Antiplatelets n/N | Control n/N | Number of trials | Relative risk (95% CI) | Relative risk (95% CI) |
|---|---|---|---|---|---|
| Pre-eclampsia | 1221/15481 | 1340/15341 | 24 | | 0·90 (0·84–0·97) |
| Delivery <34 weeks' gestation | 1018/15709 | 1111/15523 | 26 | | 0·90 (0·83–0·98) |

**AAS EN TODAS LAS PACIENTES CON ANTIFOSFOLIPIDO, PREECLAMPSIA PREVIA, HTA Y/O NEFROPATÍA**

| | | | |
|---|---|---|---|
| | 10% | | 100 (59–500) |
| | 2% | | 500 (294–2500) |
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# ANTITROMBOTICOS Y EPIDURAL

(Rev. Esp. Anestesiol. Reanim. 2001; 48: 270-278) **ARTÍCULOS ESPECIALES**

## Fármacos que alteran la hemostasia y técnicas regionales anestésicas: recomendaciones de seguridad. Foro de consenso

J.V. Llau[a], J. de Andrés[b], C. Gomar[c], A. Gómez[d], F. Hidalgo[e], J. Sahagún[f] y L.M. Torres[g]

Servicio de Anestesiología, Reanimación y terapéutica del Dolor.
[a]Hospital Clínico Universitario. Valencia. [b]Hospital General Universitario. Valencia. [c]Hospital Clínico. Barcelona. [d]Hospital Clínico Universitario. Málaga. [e]Clínica Universitaria de Navarra. Pamplona. [f]Hospital 12 de Octubre. Madrid. [g]Hospital Puerta del Mar. Cádiz.

**HBPM a dosis profiláctica: STOP 12 horas antes**

**HBPM a dosis terapeútica: STOP 24 horas antes**

# ¿ QUE HAY QUE HACER CON EL BEBE ?

**Si está bien, nada**

**ECG si madre anti-Ro**


AAS, SINTROM,
HEPARINA,
HCQ, PREDNISONA, AZA,
IECAs
NO ME AFECTAN
CFM, MMF, MTX, BOSENTAN,
SILDENAFILO, ARA2
ME HACEN DAÑO

# NO OLVIDARSE DE LA MADRE !!!

**Trombosis**

**Sangrado**

**Brote LES**

**HTA**

**…**

# Ovarian stimulation for ovulation induction and in vitro fertilization in patients with systemic lupus erythematosus and antiphospholipid syndrome

*José Bellver, M.D., and Antonio Pellicer, M.D.*

Instituto Valenciano de Infertilidad, Universidad de Valencia, Valencia, Spain

Fertil Steril® 2009

**TABLE 5**

**Guidelines for ovarian stimulation in women with SLE or antiphospholipid syndrome.**

| |
|---|
| Friendly ovarian stimulation |
| Clomiphene citrate: drug of choice in ovulation induction |
| Prevent ovarian hyperstimulation syndrome |
| Single embryo transfer |
| Coadjuvant therapy: anticoagulation, corticosteroids, immunosuppressants |
| Transfer of frozen embryos and ovum donation |
| Natural cycles better than treated cycles |
| Natural $E_2$ better than synthetic estrogens |
| Transdermal route better than oral route |
| Luteal phase support |
| Progesterone better than hCG |
| Natural P better than synthetic progestogens |
| Vaginal route better than oral route |

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| Progesterone better than hCG |
| Natural P better than synthetic progestogens |
| Vaginal route better than oral route |

**LES en remisión**

**No trombosis recientes**

**HTA controlada**

# Ovarian stimulation for ovulation induction and in vitro fertilization in patients with systemic lupus erythematosus and antiphospholipid syndrome

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**TABLE 5**

**Guidelines for ovarian stimulation in women with SLE or antiphospholipid syndrome.**

Friendly ovarian stimulation
- Clomiphene citrate: drug of choice in ovulation induction

Prevent ovarian hyperstimulation syndrome

Single embryo transfer

Coadjuvant therapy: anticoagulation, corticosteroids, immunosuppressants

Transfer of frozen embryos and ovum donation
- Natural cycles better than treated cycles
- Natural $E_2$ better than synthetic estrogens
- Transdermal route better than oral route

Luteal phase support
- Progesterone better than hCG
- Natural P better than synthetic progestogens
- Vaginal route better than oral route

**aFL +, no trombosis:**

- **HBPM tras transferencia ( no antes)**

**aFL+, trombosis previa**

- **HBPM + AAS: Stop AAS 3-5 días y HBPM 12 horas antes de toma de ovocito. Reiniciar 12 horas despues y mantener**

**aFL -, no trombosis**

- **No tromboprofilaxis**

# LAS REGLAS DE ORO

## Control coordinado

**Estabilidad previa al embarazo**

**Valoración de riesgo: decir NO si hay que decir no**

**Valoración de riesgo de reproducción asistida**

**Prever complicaciones:**

- **Tensión arterial**
- **Proteinuria**
- **Doppler**

# LAS REGLAS DE ORO

**HCQ en LES**

**Aspirina en riesgo de preeclampsia (antifosfolípido, nefropatía, HTA…)**

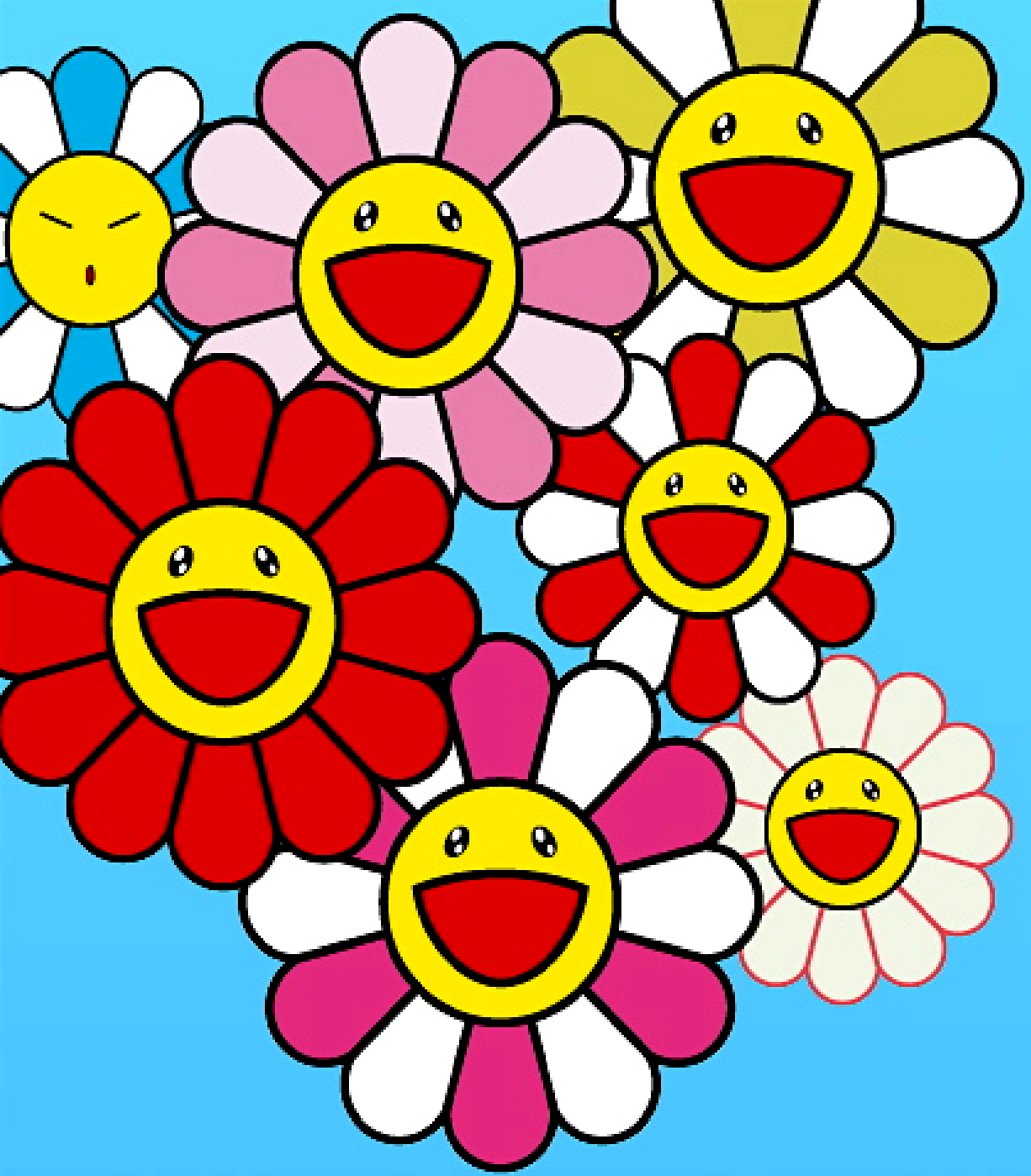
**Tromboprofilaxis en antifosfolípido**

**Madre primero: en situaciones graves, fin de embarazo**

**Niño mejor a partir de la semana 28**

**No olvidarse de la madre postparto**

**Buena Unidad Neonatal**



SI LAS COSAS SE HACEN BIEN, *SUELEN* SALIR BIEN


OR BUST
CURRY