

**ACTUALIZACIÓN EN EL
SÍNDROME ANTIFOSFOLIPÍDICO**

MANIFESTACIONES CLÍNICAS: Evidentes, inusuales y silentes

**LECCIONES DEL PROYECTO
“EURO-PHOSPHOLIPID”**

Ricard Cervera
Servicio de Enfermedades Autoinmunes
Hospital Clínic
Barcelona



SÍNDROME ANTIFOSFOLIPÍDICO (1983-2008)

25 años

BRITISH MEDICAL JOURNAL VOLUME 287 8 OCTOBER 1983

Thrombosis in systemic lupus erythematosus: striking association with the presence of circulating lupus anticoagulant

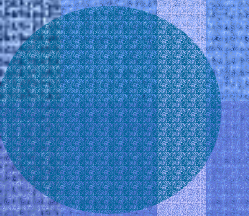
W L BOEY, C B COLACO, A E GHARAVI, K B ELKON, S LOIZOU, G R V HUGHES

SÍNDROME ANTIFOSFOLIPÍDICO

Epidemiología

- **20%** de las trombosis venosas profundas
- **10%** de los abortos de repetición
- **30%** de los accidentes vasculares cerebrales en <50 años

NIH, 2001



SÍNDROME ANTIFOSFOLIPÍDICO

Epidemiología

ESTIMACIONES

- Incidencia: **5** nuevos casos/100.000 hab./año
- Prevalencia: **50** casos/100.000 hab.

SAF-2008: MANIFESTACIONES CLÍNICAS: Evidentes, inusuales y silentes

ARTHRITIS & RHEUMATISM
Vol. 42, No. 7, July 1999, pp 1309-1311
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Arthritis & Rheumatism

Official Journal of the American College of Rheumatology

SPECIAL ARTICLE

INTERNATIONAL CONSENSUS STATEMENT ON PRELIMINARY CLASSIFICATION CRITERIA FOR DEFINITE ANTIPHOSPHOLIPID SYNDROME

Report of an International Workshop

WENDELL A. WILSON, AZZUDIN E. GHARAVI, TAKAO KOIKE, MICHAEL D. LOCKSHIN,
D. WARE BRANCH, JEAN-CHARLES PIETTE, ROBIN BREY, RONALD DERKSEN, E. NIGEL HARRIS,
GRAHAM R. V. HUGHES, DOUGLAS A. TRIPLETT, and MUNTER A. KHAMASHTA

SÍNDROME ANTIFOSFOLIPÍDICO

Criterios de Sapporo, 1998

Criterios clínicos

- Trombosis arteriales/venosas/microcirculación: ≥ 1 episodio
- Morbilidad en el embarazo:
 - Abortos (<10 sem.): ≥ 3
 - Muertes fetales (≥ 10 sem.): ≥ 1
 - Prematuros (≤ 34 sem.): ≥ 1

Criterios de laboratorio

- Anticuerpos anticardiolipina (IgG/IgM): ≥ 2 determ.
- Anticoagulante lúpico: ≥ 2 determ.

Diagnóstico: 1 criterio clínico+1criterio de laboratorio

Euro-Phospholipid on Line

Official Web-site of the "European Forum on Antiphospholipid Antibodies"

- [Organization](#)
- [Membership Directory](#)
- [Workshops and Meetings](#)
- [Multicentre Studies](#)
- [The World of Antiphospholipid Antibodies and Systemic Autoimmune Diseases in Internet](#)
- [News on Antiphospholipid Antibodies](#)



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Dirección  http://www.med.ub.es/MIMMUN/FORUM/STUDIES.HTM



Ir a

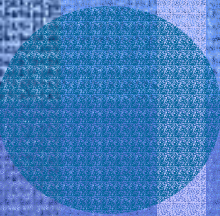
Vínculos

Euro-Phospholipid on Line

Official Web-site of the "European Forum on
Antiphospholipid Antibodies"

MULTICENTRE STUDIES

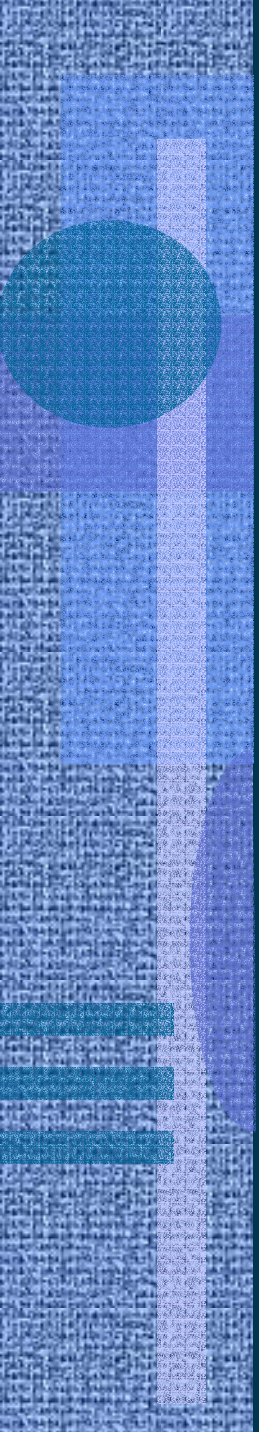
-  [Euro-Phospholipid project](#)
-  [Familial Antiphospholipid Syndrome](#)
-  [Warfarin in the Antiphospholipid Syndrome \(WAPS\)](#)
-  [Pulmonary Hypertension and Antiphospholipid](#)



PROYECTO "EURO-PHOSPHOLIPID"

COORDINADORES:

Ricard Cervera, Josep Font, Marie-Claire Boffa,
Jean-Charles Piette, Munther A. Khamashta y
Graham R.V. Hughes en representación del
*European Forum on Antiphospholipid
Antibodies*



PROYECTO "EURO-PHOSPHOLIPID"

FINALIDAD:

Evaluar prospectivamente las manifestaciones clínicas y serológicas, así como la evolución a largo plazo, del SAF en Europa, mediante el estudio durante 10 años de 1.000 pacientes procedentes de 20 centros universitarios.

SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes

ARTHRITIS & RHEUMATISM

Vol. 46, No. 4, April 2002, pp 1019–1027

DOI 10.1002/art.10187

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Antiphospholipid Syndrome

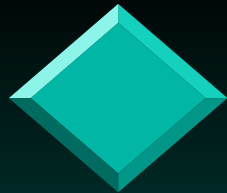
Clinical and Immunologic Manifestations and Patterns of Disease Expression in a Cohort of 1,000 Patients

Ricard Cervera,¹ Jean-Charles Piette,² Josep Font,¹ Munther A. Khamashta,³
Yehuda Shoenfeld,⁴ María Teresa Camps,⁵ Soren Jacobsen,⁶ Gabriella Lakos,⁷ Angela Tincani,⁸
Irene Kontopoulou-Griva,⁹ Mauro Galeazzi,¹⁰ Pier Luigi Meroni,¹¹
Ronald H. W. M. Derksen,¹² Philip G. de Groot,¹² Erika Gromnica-Ihle,¹³ Marta Baleva,¹⁴
Marta Mosca,¹⁵ Stefano Bombardieri,¹⁵ Frédéric Houssiau,¹⁶ Jean-Christophe Gris,¹⁷
Isabelle Quéré,¹⁷ Eric Hachulla,¹⁸ Carlos Vasconcelos,¹⁹ Beate Roch,²⁰
Antonio Fernández-Nebro,²¹ Marie-Claire Boffa,² Graham R. V. Hughes,³ and
Miguel Ingelmo,¹ for the Euro-Phospholipid Project Group

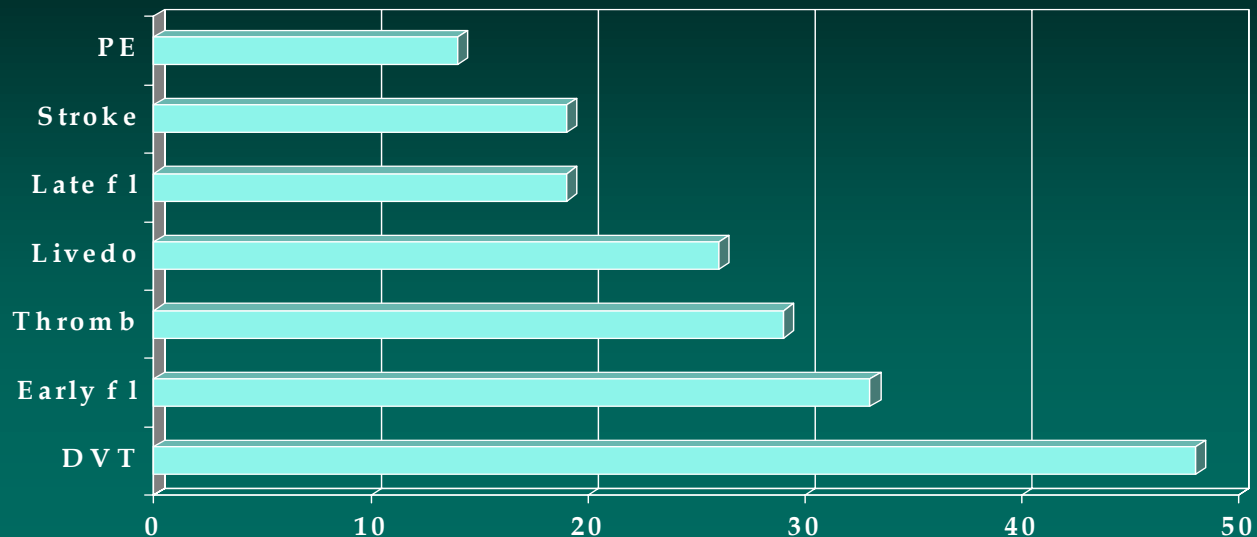
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MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT Cumulative manifestations



SAF - 2008:

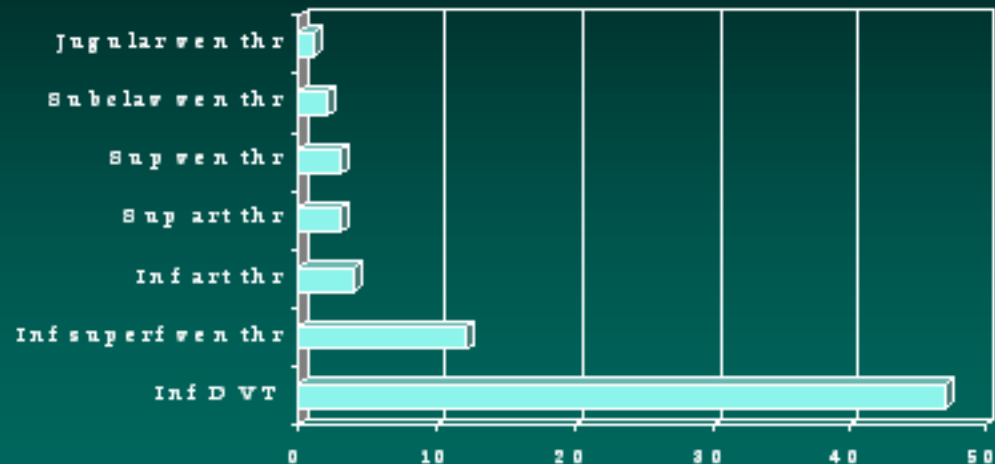
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Thrombosis in extremities



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

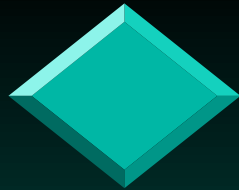
Evidentes, inusuales y silentes



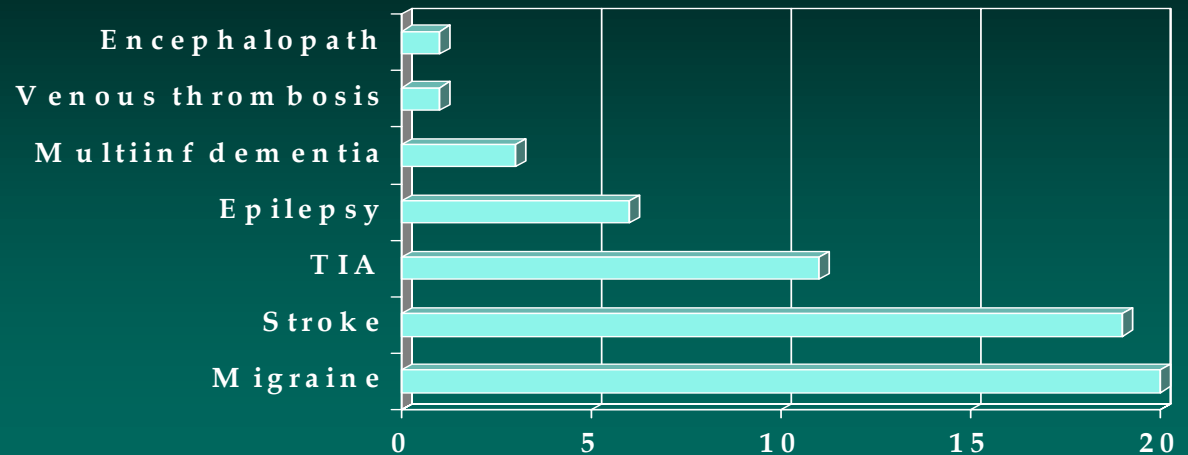
SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



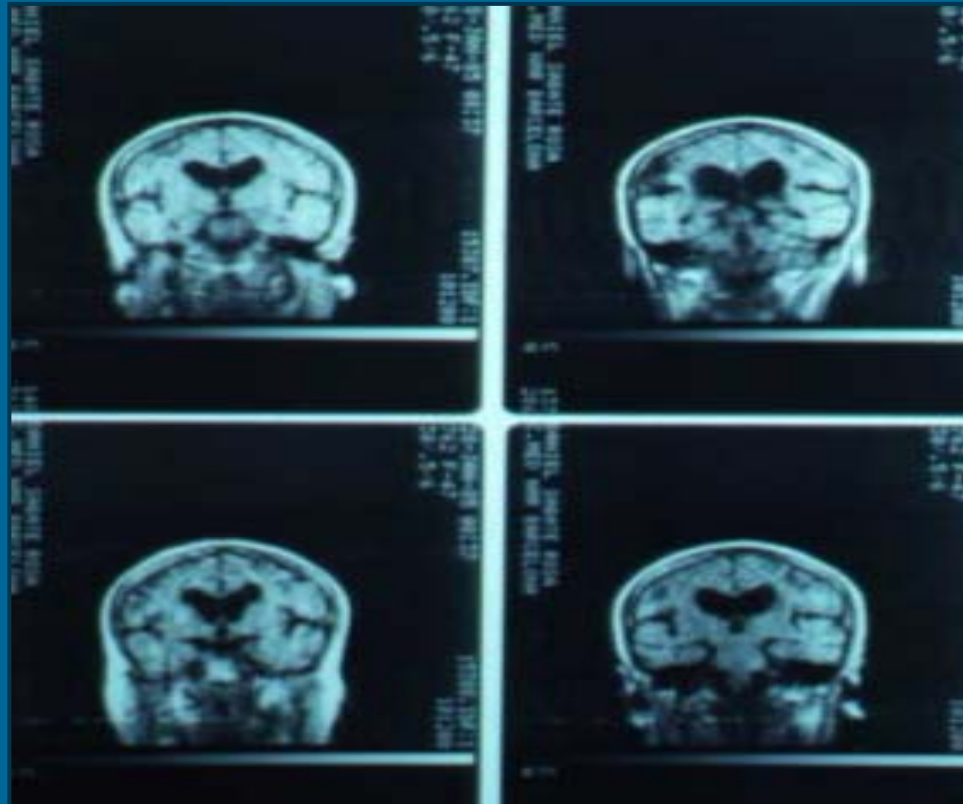
EURO-PHOSPHOLIPID PROJECT Neurologic manifestations



SAF - 2008:

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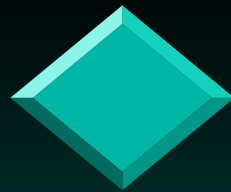
Evidentes, inusuales y silentes



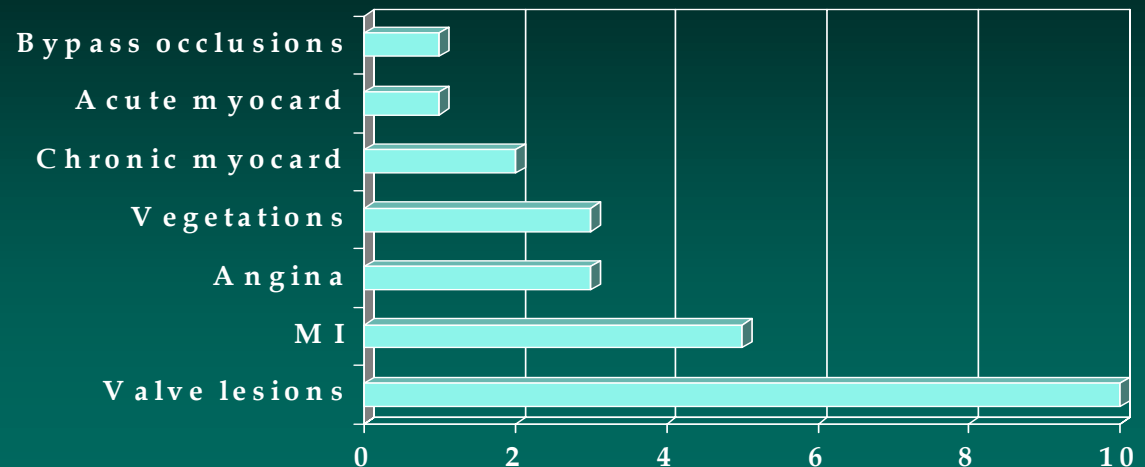
SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT Cardiac manifestations



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MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

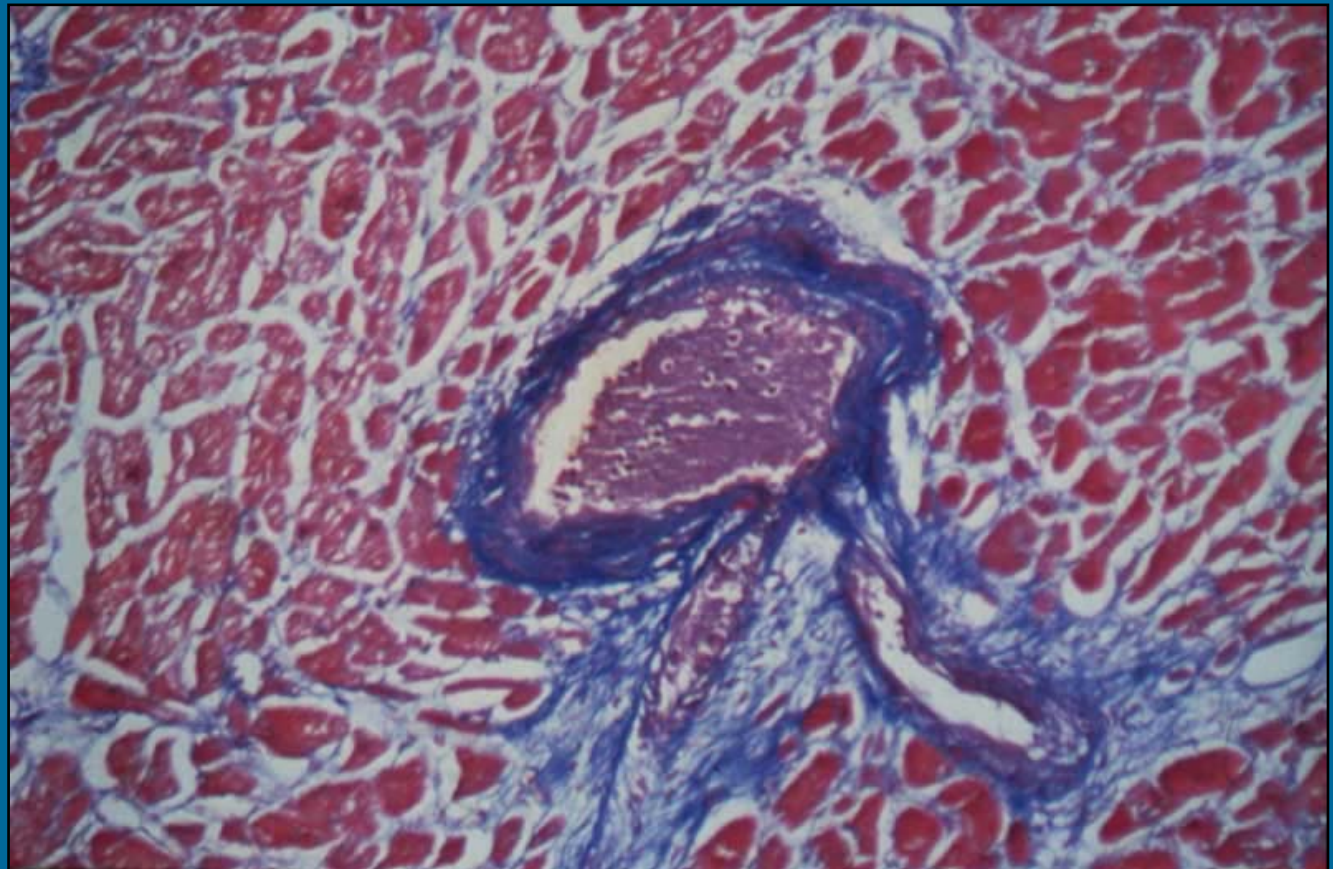
Evidentes, inusuales y silentes



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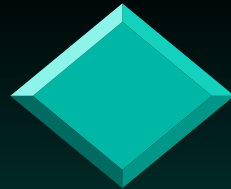
Evidentes, inusuales y silentes



SAF - 2008:

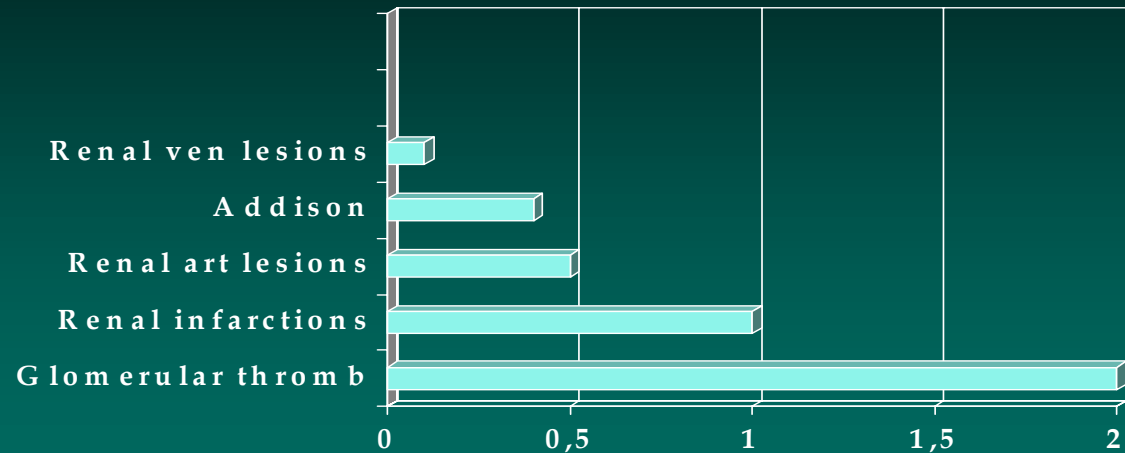
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

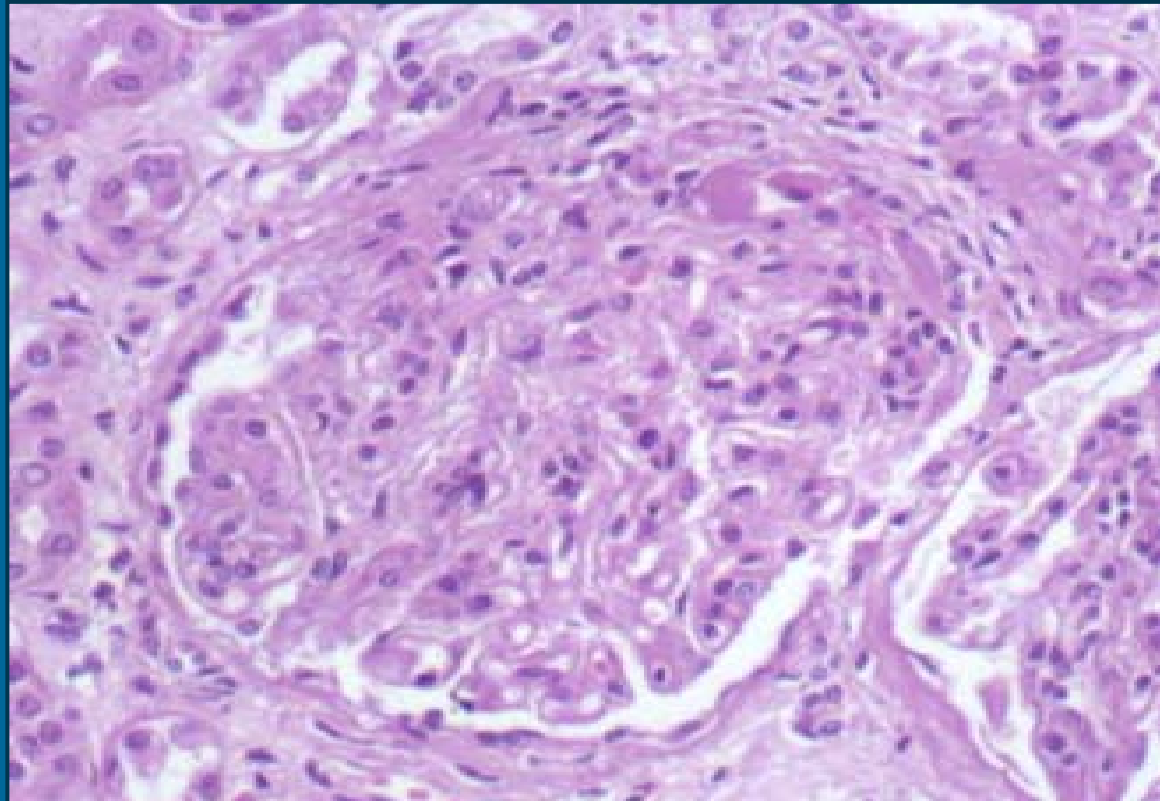
Renal and adrenal manifestations



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

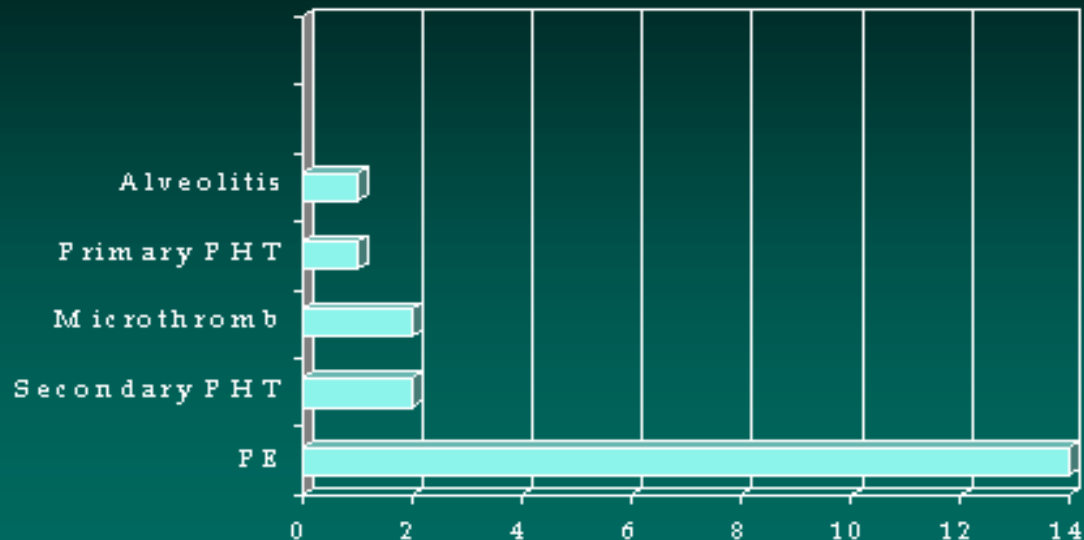
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Pulmonary manifestations



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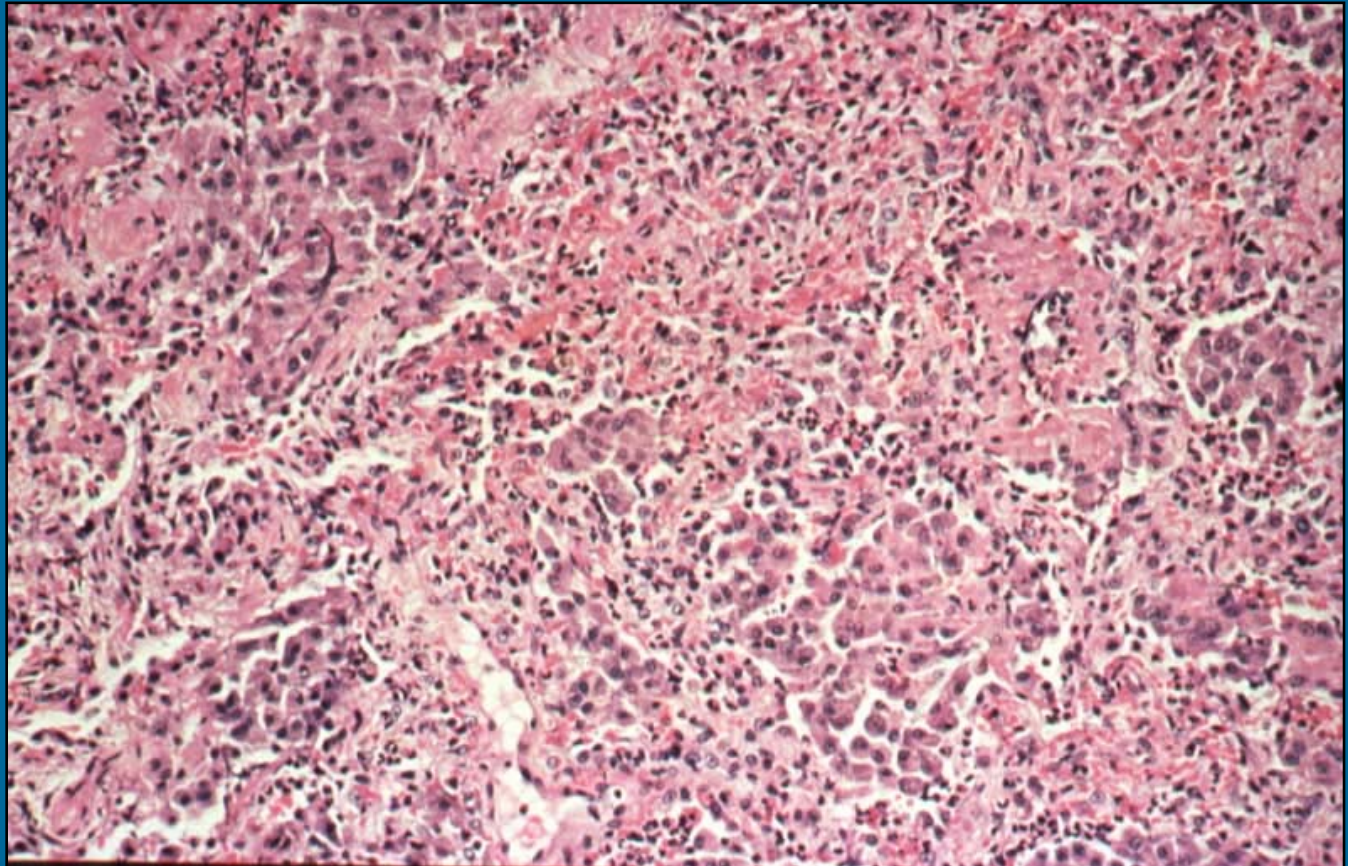
Evidentes, inusuales y silentes



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

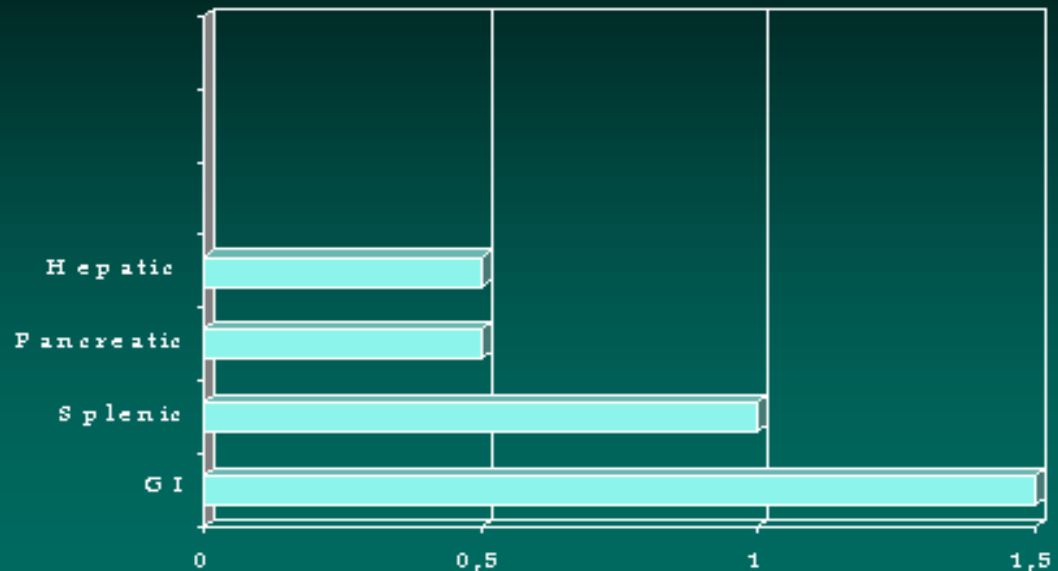
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

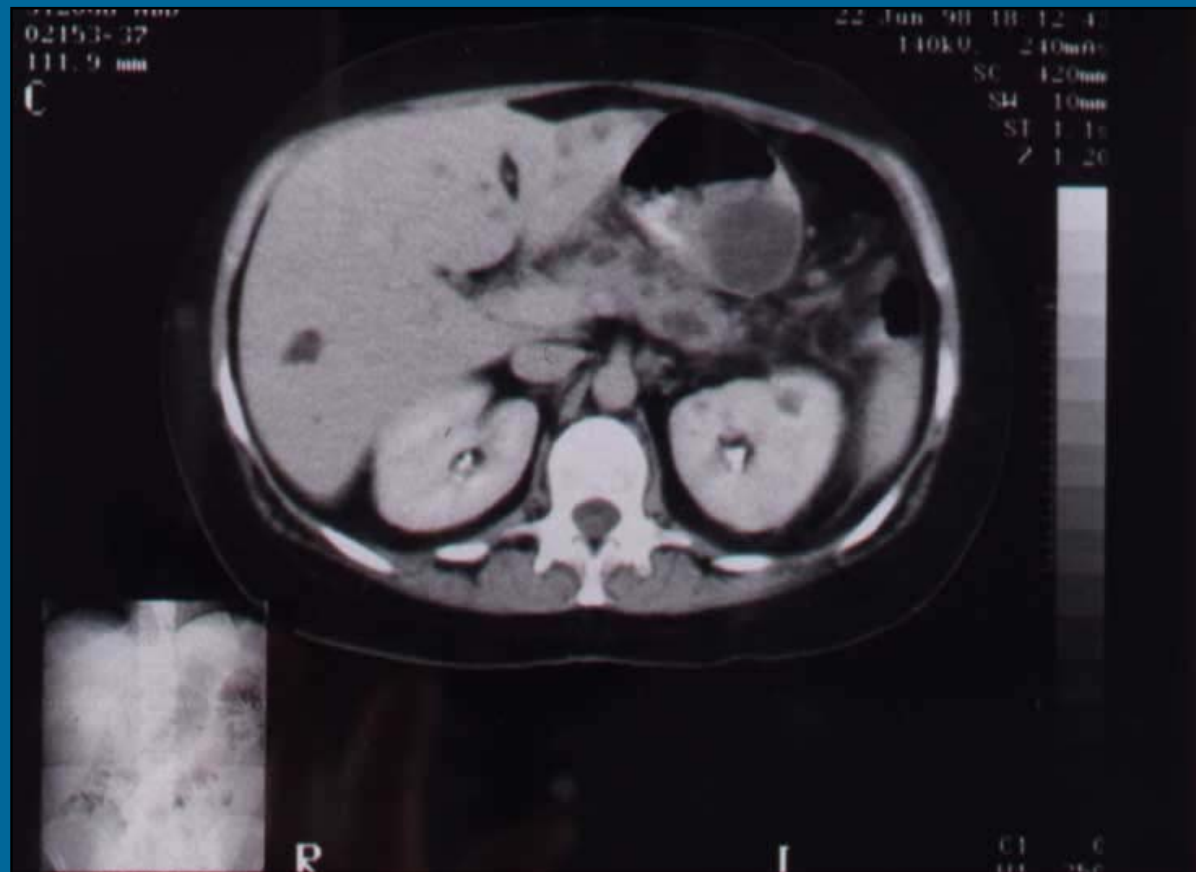
Digestive manifestations



SAF - 2008:

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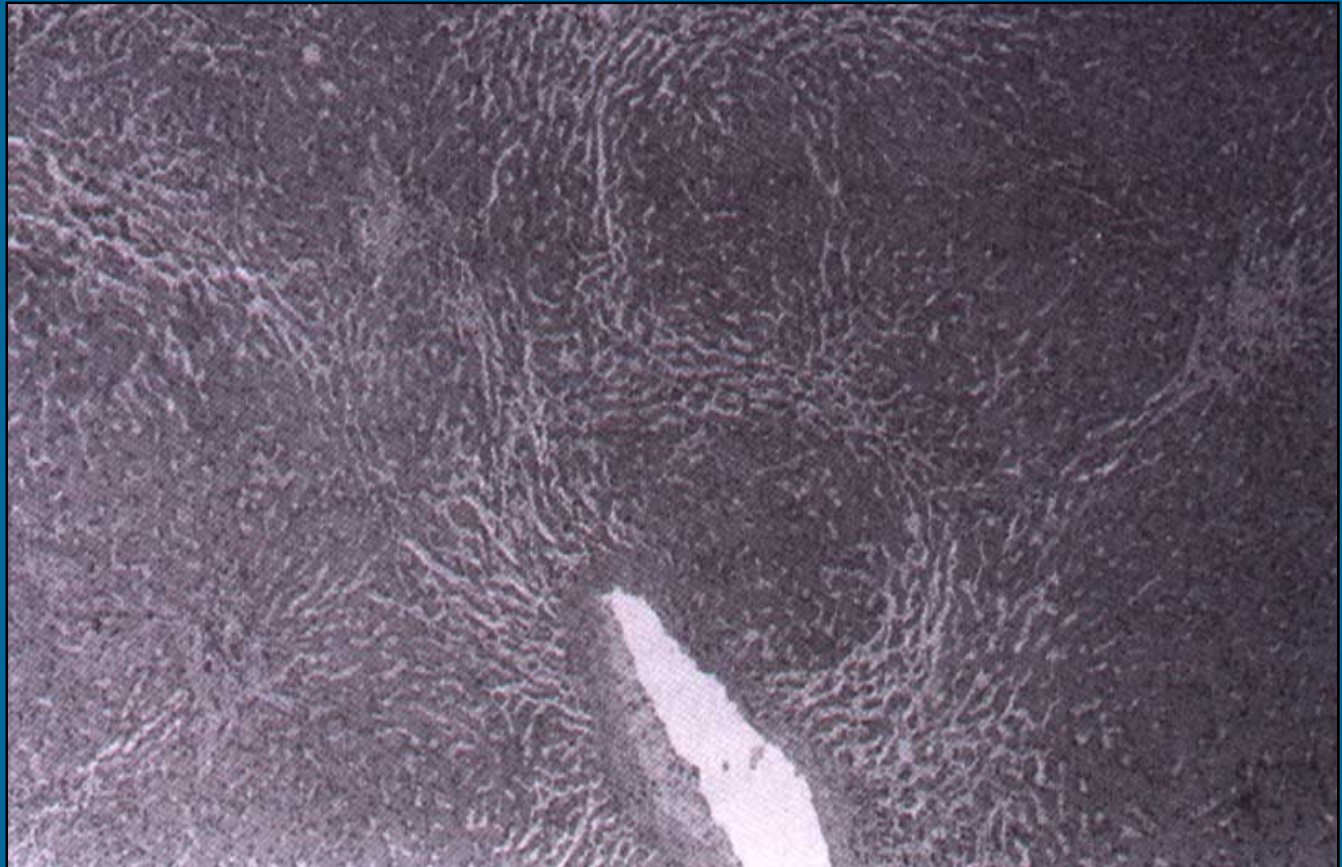
Evidentes, inusuales y silentes



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

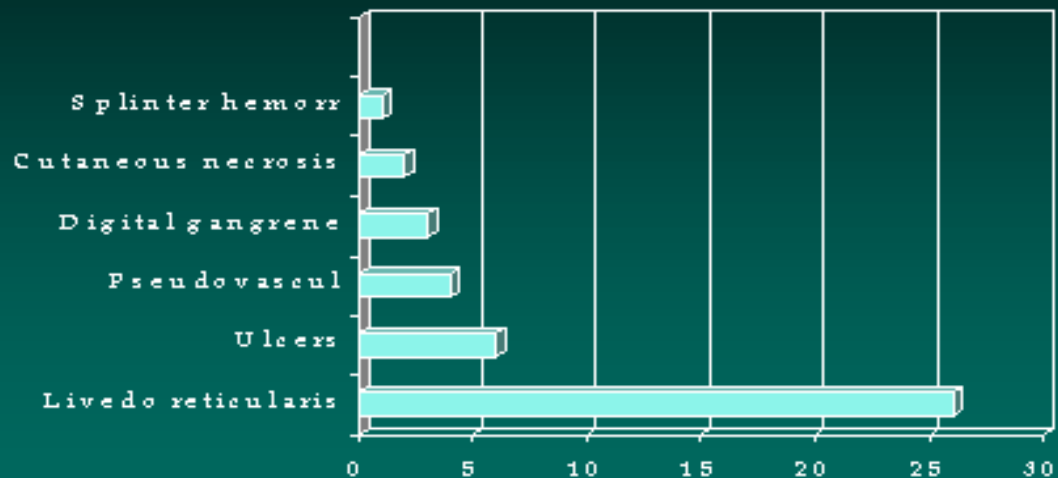
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Dermatologic manifestations



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



SAF - 2008:

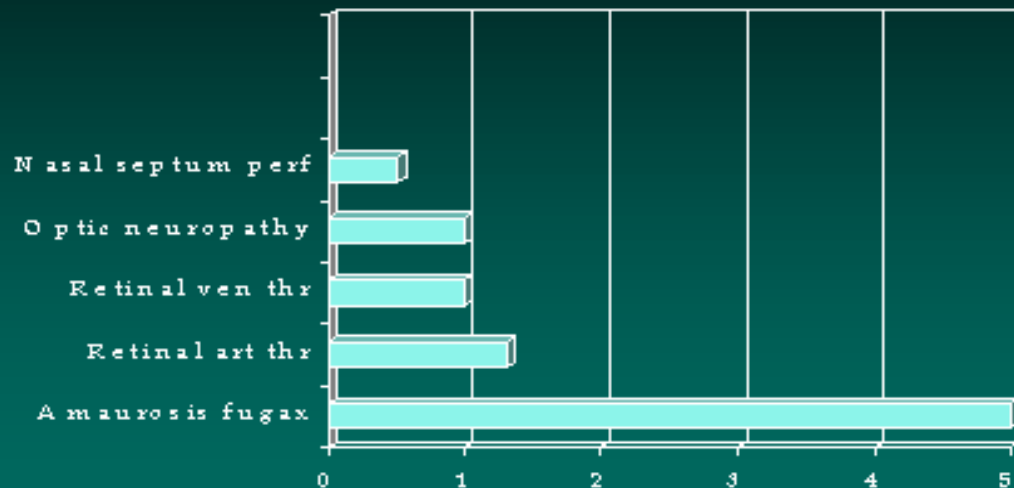
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Ophthalmologic and ENT manifestations



SAF - 2008:

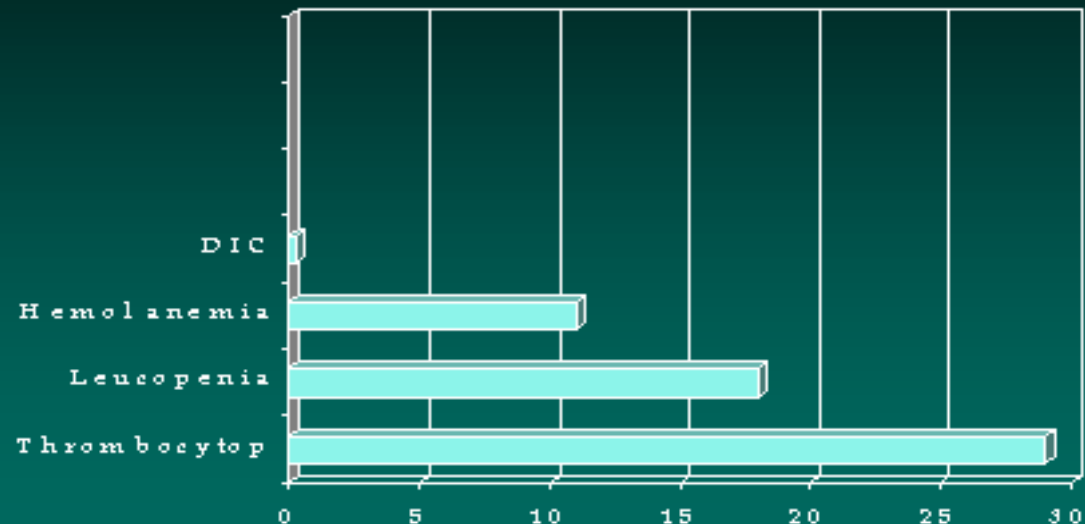
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Hematologic manifestations



CONCISE REPORT

Disseminated intravascular coagulation in catastrophic antiphospholipid syndrome: clinical and haematological characteristics of 23 patients

R A Asherson, G Espinosa, R Cervera, J A Gómez-Puerta, J Musuruana, S Bucciarelli, M Ramos-Casals, A L Martínez-González, M Ingelmo, J C Reverter, J Font, D A Triplett, for the Catastrophic Antiphospholipid Syndrome Registry Project Group*

Ann Rheum Dis 2005;**64**:943–946. doi: 10.1136/ard.2004.026377

EXTENDED REPORT

Thrombotic microangiopathic haemolytic anaemia and antiphospholipid antibodies

G Espinosa, S Bucciarelli, R Cervera, M Lozano, J-C Reverter, G de la Red, V Gil, M Ingelmo, J Font, R A Asherson

Ann Rheum Dis 2004;**63**:730–736. doi: 10.1136/ard.2003.007245

ALTERACIONES DE LA HEMOSTASIA

- **CID:** 14.9 %

- **AHMT:** 8.6 %

SAF - 2008:

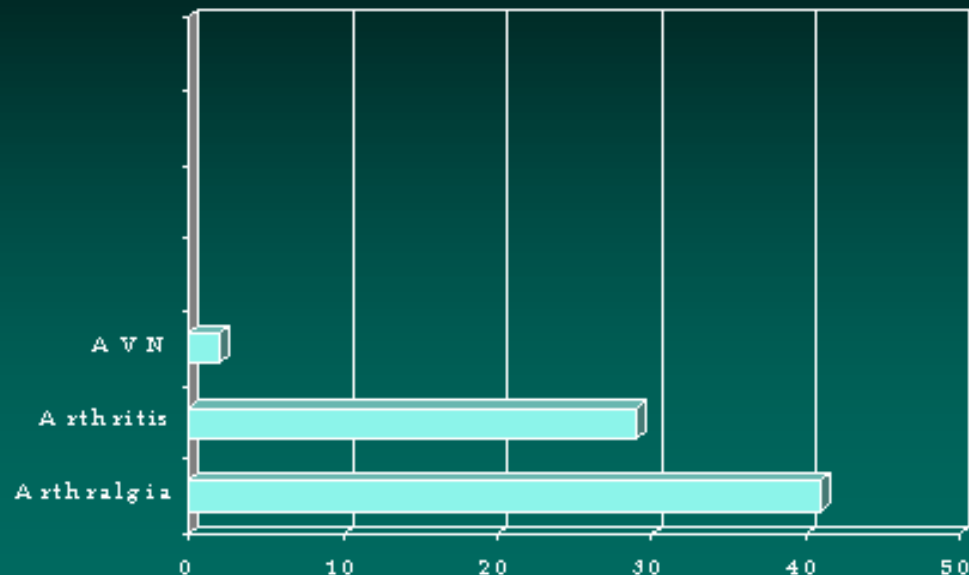
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Osteo-articular manifestations



SAF - 2008:

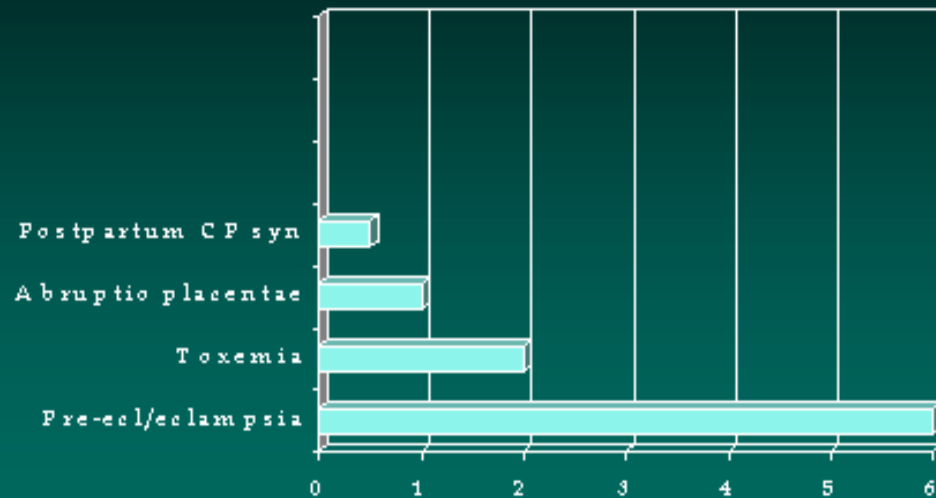
MANIFESTACIONES CLÍNICAS :

Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Obstetric maternal manifestations



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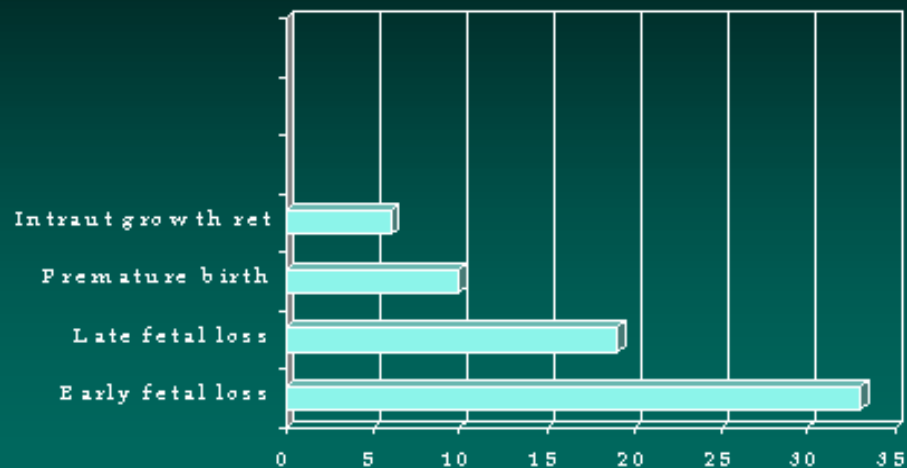
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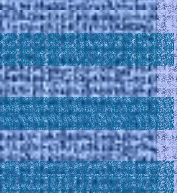
Evidentes, inusuales y silentes



EURO-PHOSPHOLIPID PROJECT

Fetal manifestations







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Autoimmunity Reviews 2 (2003) 140–151



www.elsevier.com/locate/autrev

The antiphospholipid syndrome: multiple faces beyond the classical presentation

Ronald A. Asherson^a, Ricard Cervera^{b,*}

^a*Rheumatic Diseases Unit, Department of Medicine, University of Cape Town School of Medicine, Cape Town, South Africa*

^b*Department of Autoimmune Diseases, Hospital Clínic, Villarroel 170, 08036 Barcelona, Catalonia, Spain*

Received 10 November 2002; accepted 11 December 2002

TROMBOSIS VENOSA YUGULAR → **AVC**

LESIONES VALVULARES

EMBOLISMO PULMONAR

BUDD-CHIARI

MICROANGIOPATIA RENAL

MORBILIDAD FETAL

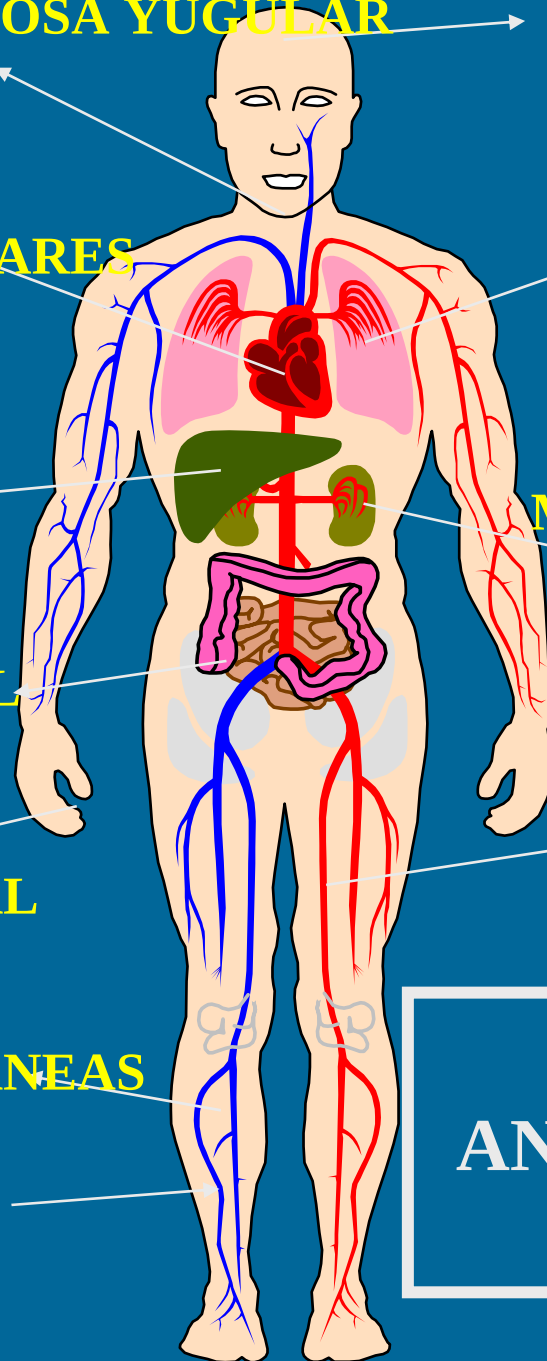
LIVEDO RETICULARIS

ISQUEMIA DIGITAL

ULCERAS CUTÁNEAS

TVP

**SÍNDROME
ANTIFOSFOLIPÍDICO
“SISTÉMICO”**



PRE-CONGRESS SESSION: THERAPY CONSENSUS

Supported by an unrestricted educational grant from American Autoimmune Related Diseases Association, Inc., USA (AARDA)

Chairpersons:

Y. Shoenfeld, Israel
M. Khamashta, UK

PROPHYLAXIS

D. Alarcon-Segovia, A.S. Roubey, D. Triplett, W. Wilson, Mexico, USA

THROMBOEMBOLISM

J.A. McIntyre, J.M.M.C. Arnout, T. Koike, P.L. Meroni, J-C. Piette, USA, Belgium, Japan, Italy, France

STROKE

R.L. Brey, J. Chapman, R. Derksen, T. Exner, E.N. Harris, S.R. Levine, USA, Israel, The Netherlands, Australia

PREGNANCY

A. Tincani, D.W. Branch, H.J.A. Carp, M. Khamashta, R.A. Levy, R. Rai, Italy, USA, Israel, UK, Brazil

OTHER CNS

J.H. Rand, R.L. Brey, **J. Chapman**, T. Exner, D. Smith, USA, Israel, Australia, Canada

CARDIAC

M. Lockshin, L. Carreras, S.A. Krilis, G. McCarty, M. Petri, UK, Argentina, Australia, USA

CATASTROPHIC

R.A. Asherson, M-C. Boffa, R. Cervera, P. De Groot, D. Erkan, South Africa, France, Spain, The Netherlands, USA

Catastrophic antiphospholipid syndrome: international consensus statement on classification criteria and treatment guidelines

**RA Asherson¹, R Cervera^{2*}, PG de Groot³, D Erkan⁴, M-C Boffa⁵, J-C Piette⁵, MA Khamashta⁶ and Y Shoenfeld⁷
for the Catastrophic Antiphospholipid Syndrome Registry Project Group[†]**

¹Rheumatic Diseases Unit, University of Cape Town School of Medicine, Cape Town, South Africa; ²Department of Autoimmune Diseases, Institut Clínic d'Infeccions i Immunologia, Hospital Clínic, Barcelona, Catalonia, Spain; ³Thrombosis and Haemostasis Laboratory, Department of Haematology, University Medical Center Utrecht, Utrecht, The Netherlands; ⁴Hospital for Special Surgery, Weill Medical College of Cornell University, New York, USA; ⁵Department of Internal Medicine, Hôpital Pitié-Salpêtrière, Paris, France; ⁶Lupus Unit, The Rayne Institute, St. Thomas' Hospital, London, UK; ⁷Center for Autoimmune Diseases, Chaim Sheba Medical Center, Tel-Hashomer, Israel

SAF CATASTRÓFICO

Criterios clasificatorios preliminares

1. Evidencia de trombosis que afectan **3 o más órganos**, sistemas o tejidos.
2. Desarrollo de las manifestaciones en un período **<1 semana**
3. Confirmación **anatomopatológica** de la oclusión de los vasos de pequeño calibre en algún órgano.
4. Confirmación **serológica** de la presencia de anticuerpos antifosfolipídicos.

» **SAFC definitivo**: 4 criterios

» **SAFC probable**: 4 criterios (2 órganos)

Criterios 1,2 y 4

Criterios 1,3,4 y 2 (<1 mes)

Lupus 2003; 12: 530-534

11th International Congress on Antiphospholipid Antibodies

Sydney, Australia - 14th to 18th November 2004



**Pre-Congress Workshop: Update on the
International Classification Criteria for the APS**

SPECIAL ARTICLE

International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)

S. MIYAKIS, * M. D. LOCKSHIN, † T. ATSUMI, ‡ D. W. BRANCH, § R. L. BREY, ¶ R. CERVERA, ** R. H. W. M. DERKSEN, †† P. G. DE GROOT, †† T. KOIKE, ‡ P. L. MERONI, ‡‡ G. REBER, §§ Y. SHOENFELD, ¶¶ A. TINCANI, *** P. G. VLACHOYIANNOPOULOS ††† and S. A. KRILIS *

*St George Hospital, University of New South Wales, Sydney, Australia; †Hospital for Special Surgery, Cornell Medical Center, New York, NY, USA; ‡Hokkaido University, Sapporo, Japan; §University of Utah Health Sciences Center, Salt Lake City, UT; ¶University of Texas Health Science Center, San Antonio, TX, USA; **Hospital Clinic, Barcelona, Spain; ††University Medical Center, Utrecht, The Netherlands; ‡‡Istituto Auxologico Italiano, University of Milan, Milan, Italy; §§University Hospital, Geneva, Switzerland; ¶¶Sheba Medical Center, Tel-Hashomer and Tel Aviv University, Israel; ***Spedali Civili, University of Brescia, Italy; and †††Department of Pathophysiology, University of Athens, Greece

J Thromb Haemostas 2006; 4:295-306

Criterios revisados de SAF-2006

Criterios clínicos

- Trombosis vascular : ≥ 1 episodio
- Morbilidad en el embarazo :
 - Abortos (<10 sem.): ≥ 3
 - Muertes fetales (≥ 10 sem.): ≥ 1
 - Prematuros (≤ 28 sem.): ≥ 1

Criterios de laboratorio

- Anticuerpos anticardiolipina (IgG/IgM): ≥ 2 determ.
- Anticoagulante lúpico : ≥ 2 determ.
- Anti-beta-2-glicoproteína I (IgG/IgM) : ≥ 2 determ.

SAF Definitivo: 1 criterio clínico + 1 criterio de laboratorio

ADDENDUM

Manifestaciones asociadas con el SAF (pero no incluidas en los criterios de clasificación)

- Lesiones valvulares cardíacas
- *Livedo reticularis*
- Trombocitopenia
- Nefropatía
- Manifestaciones neurológicas
- AAC IgA
- Anti-beta-2-GPI IgA
- Anti-PS
- Anti-PE
- Anti-PT
- Anti-PS/PT



European Forum on Antiphospholipid Antibodies