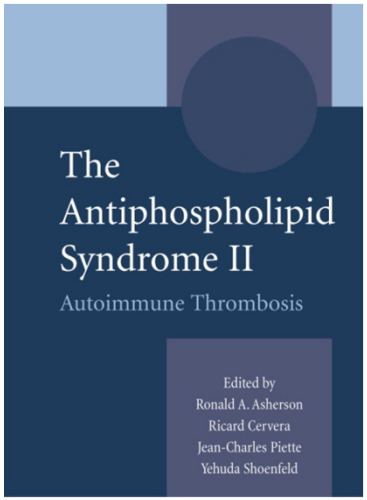
The risk of Thrombosis in Patients with Antiphospholipid Syndrome

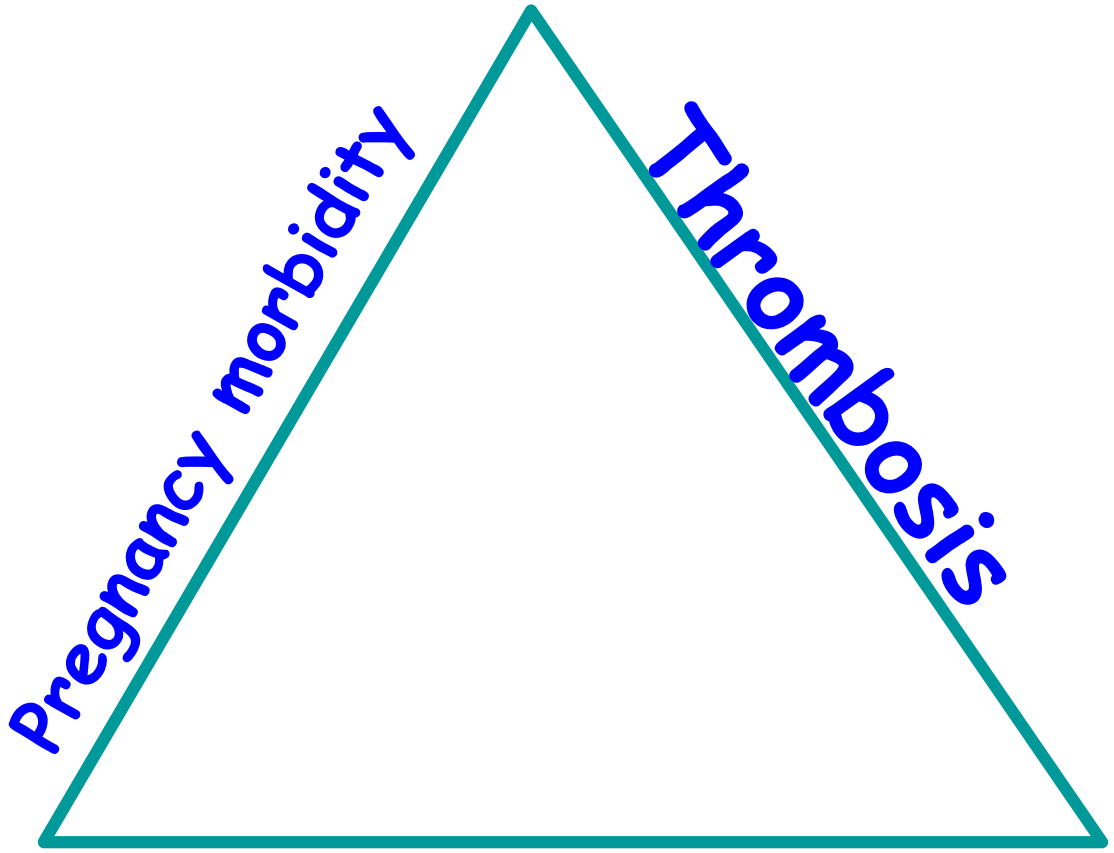
Influence of Antiphospholipid Antibody Type and Levels

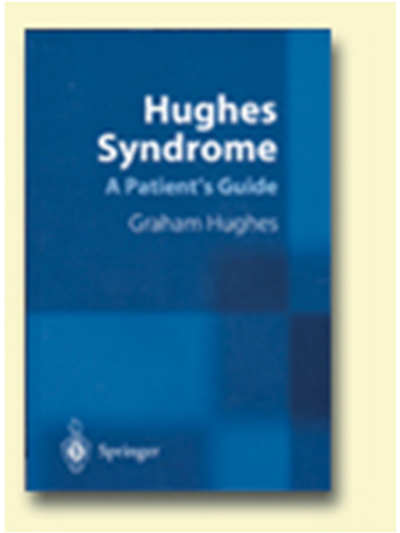
Ljudmila Stojanovich

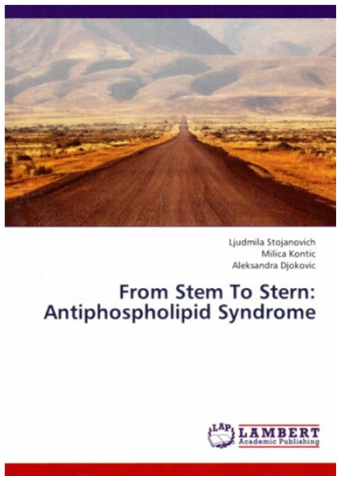
"Bezanijska Kosa",
University Medical Center, Belgrade, Serbia

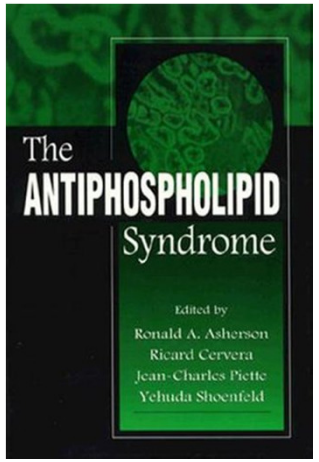


Antiphospholipid Syndrome









Stojanovich L, MD, PhD

ANTIPHOSPHOLIPID SYNDROME

Very frequent Sy:

- ✓ 1 / 5 YOUNG WITH CVI
- ✓ 1 / 5 DVT
- ✓ 1 / 5 PREGNANCY LOSS

Stojanovich L, MD, PhD

Factors Predicting Autoimmune Diseases

Hormonal and Environmental Factors Involved in Autoimı Diseases – 2008

Yehuda Shoenfeld MD[1], Gisele Zandman-Goddard MD[2], Ljudmila Stojanovich MD[3], Maurizio Howard Amital MD[5], Yair Levy MD[6], Mahmoud Abu-Shakra MD[7], Ori Barzilai MD[1], Yackov Be Miri Blank PhD[9], Joselio Freire de Carvalho MD[10], Andrea Doria MD[11], Boris Gilburd PhD[9], Uri Ilan Krause MD[12], Pnina Langevitz PhD[13], Hedi Orbach MD[14], Vitor Pordeus MD[15], Maya Ram[9] Elias Toubi MD[16] and Yaniv Sherer MD[1]

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Autoimmunity Reviews 7 (2008) 209–213

Stress as a trigger of autoimmune disease

Ljudmila Stojanovich *, Dragomir Marisavljevich
"Bezhanijska Kosa" University Medical Center, Belgrade University, Serbia

Changeable factors

- Psychological stress
- Infection
- Vaccination
- Smoking
- Obesity
- Ultraviolet light exposure
- Drugs…

Unchangeable factors

- Genetic
- Hormonal
- Immune deficiency state
- Gender

Autoimmunity Reviews 9 (2010) A271–A276

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Stress and autoimmunity

Ljudmila Stojanovich *
"Bezhanijska Kosa", University Medical Center, Belgrade University, Serbia

Sapporo Criteria on Antiphospholipid Syndrome (1998)

Clinical criteria

- ✓ Vascular thrombosis
- ✓ Pregnancy morbidity

Laboratory criteria

- ✓ Lupus anticoagulant
- ✓ Anticardiolipin antibody

  dependent of β_2*-GPI*

The Sapporo APS classification criteria (1998, published in 1999) were replaced by the Sydney criteria in 2006

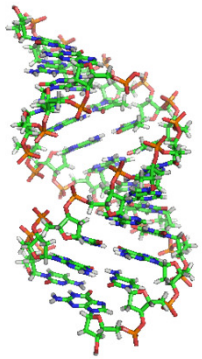
Clinical:

- **A documented episode of arterial, venous, or small vessel thrombosis — other than superficial venous thrombosis — in any tissue or organ by objective validated criteria with no significant evidence of inflammation in the vessel wall, and/or**
- **1 or more unexplained deaths of a morphologically normal fetus (documented by ultrasound or direct examination of the fetus) at or beyond the 10th week of gestation and/or 3 or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded or at least 1 premature birth of a morphologically normal neonate before the 34th week of gestation due to eclampsia or severe pre-eclampsia according to standard definitions, or recognized features of placental insufficiency plus**

Miyakis S, Lockshin MD, Atsumi T et al. (February 2006). "International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)". J. Thromb. Haemost. 4 (2): 295–306.

The Sapporo APS classification criteria (1998, published in 1999) were replaced by the Sydney criteria in 2006

- Laboratory:
  - Anti-cardiolipin IgG and/or IgM measured by standardized, non-cofactor dependent ELISA on 2 or more occasions, not less than 12 weeks apart; medium or high titer (i.e., > 40 GPL or MPL, or > the 99th percentile) and/or
  - Anti-β2 glycoprotein I IgG and/or IgM measured by standardized ELISA on 2 or more occasions, not less than 12 weeks apart; medium or high titer (> the 99th percentile) and/or
  - Lupus anticoagulant detected on 2 occasions not less than 12 weeks apart according to the guidelines of the International Society of Thrombosis and Hemostasis.

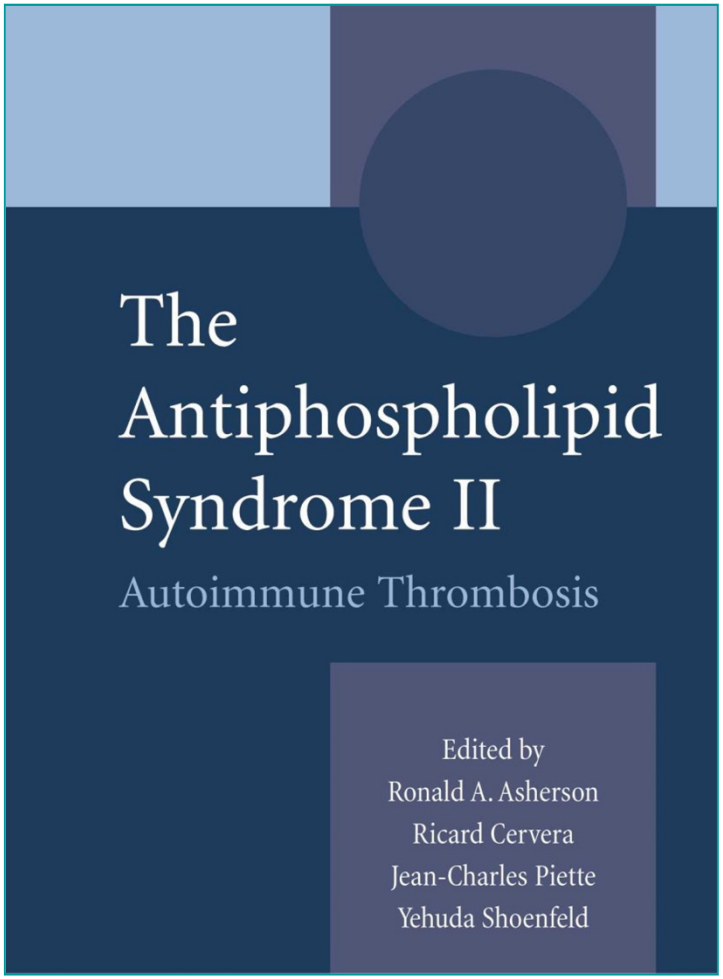


Mechanisms of thrombosis in the APS

TABLE I. Possible mechanisms of autoantibody-mediated thrombosis in antiphospholipid syndrome

Inhibition of anticoagulant reactions
Inhibition of the protein C pathway
Inhibition of protein C activation
Inhibition of activated protein C
Inhibition of antithrombin activity
Displacement of annexin A5
Inhibition of β_2GPI anticoagulant activity
Cell-mediated events
On monocytes
Expression of tissue factor
Enhanced endothelial cell procoagulant activity
Expression of tissue factor
Expression of adhesion molecules
Impaired fibrinolysis
Dysregulation of eicosanoids
Decreased endothelial cell prostacyclin production
Increased platelet thromboxan A_2 production
Enhanced platelet activation/aggregation

Adapted from: Roubey RAS. Tissue factor, protein C pathway, and other haemostasis abnormalities in the pathogenesis of the antiphospholipid syndrome. In: Asherson RA, Cervera R, Piette J-C, and Shoenfeld Y, eds. The antiphospholipid syndrome II. Autommune thrombosis, Elsevier 2002.



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Systemic APS by Shoenfeld Y

Lupus. 2003

1) Skin (livedo reticularis)
2) Heart (non-verrucal endocarditis)
3) Kidneys (renal artery stenosis)
4) Circulation (hypertension, atherosclerosis)
5) Lung (pulmonary hypertension)
6) Brain (cognitive impairment)
7) Brain Vasculature (migraine)
8) Blood elements (AIHA, thrombocytopenia)
9) Bones (osteonecrosis)
10) Adrenals (apoplexy)
11) Placenta (insuficiency, fetal death)
12) Pregnancy (eclampsia, pregnansy loss)
13) Coagulation (hypercoagulable state)
14) Blood vessels (accelerated atherosclerosis)
15) Eyes (amaurasis fugox, optic neuritis)
16) Ears (acute hearing loss)
17) GI involvement (spleen, Budd Chiari)

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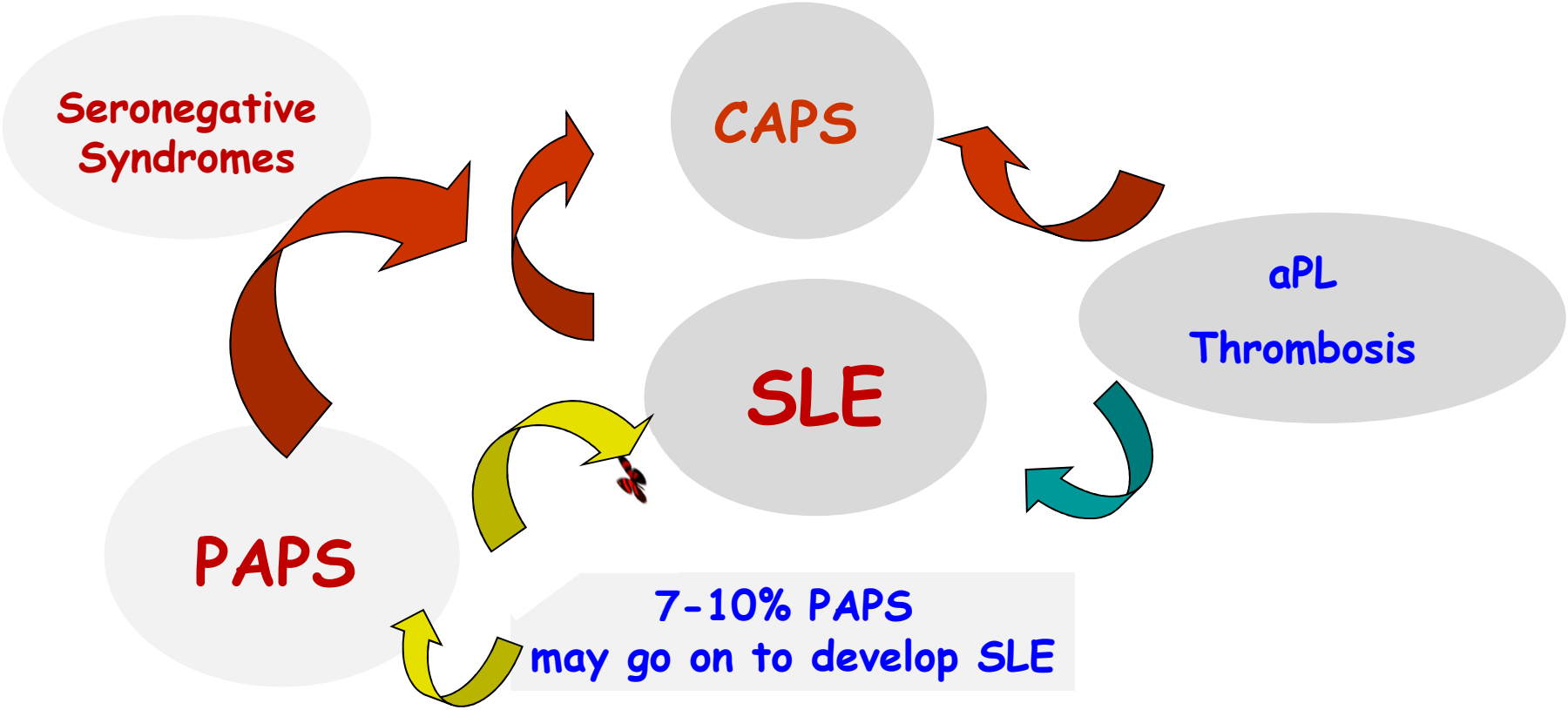
Evolution of APS/ SUBSETS

1 % APS may go on to develop CAPS



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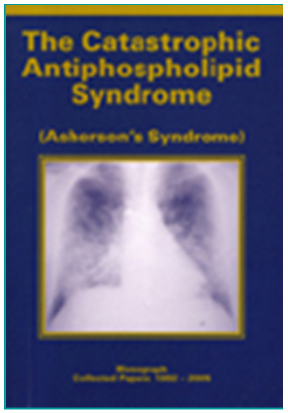

A TRIBUTE TO THE LATE RONALD A. ASHERSON

"CAPS REGISTRY"
International Registry of Patients with Catastrophic APS

www.med.ub.es/MIMMUN/FORUM/CAPS.HTM

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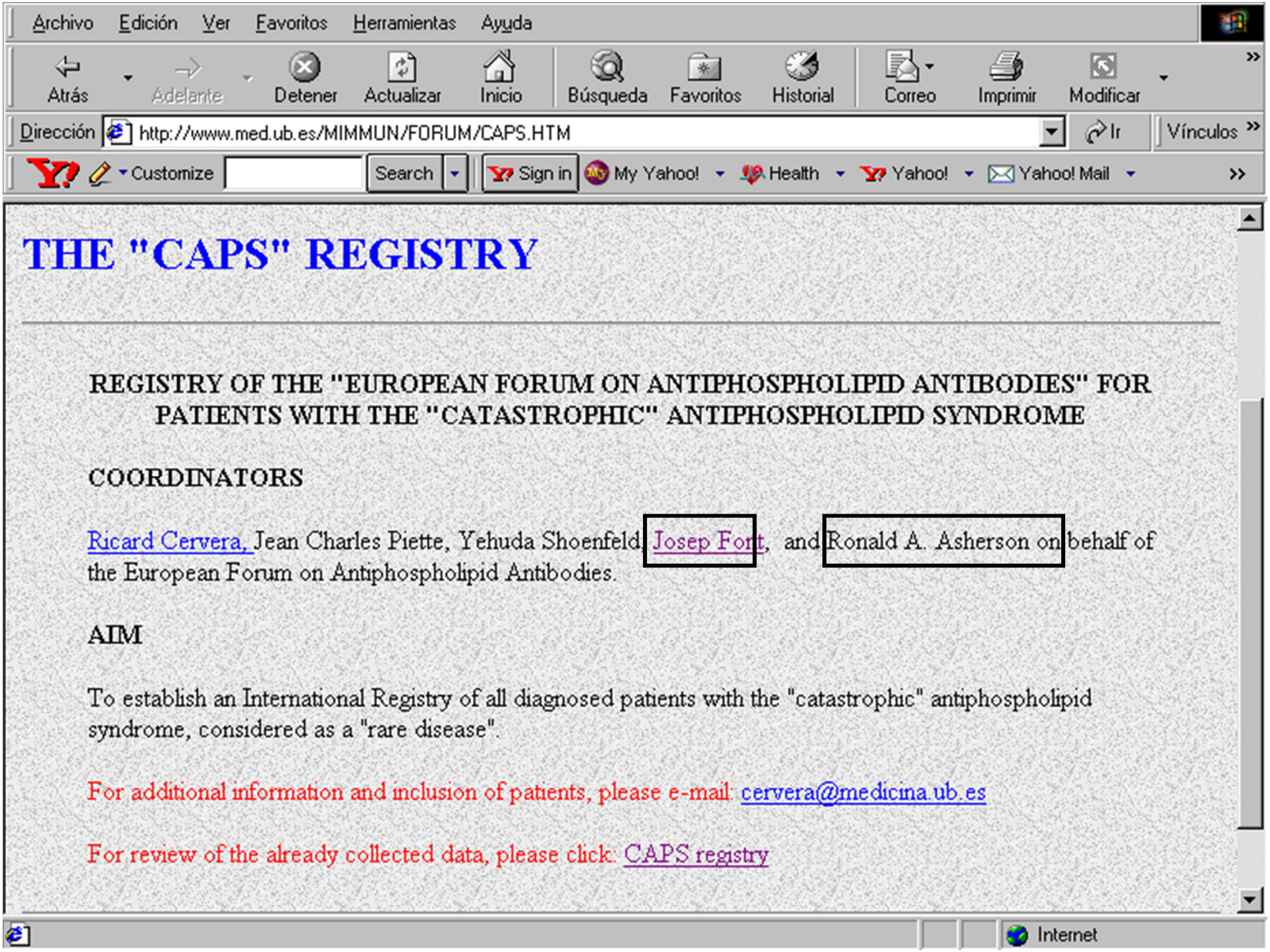
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THE "CAPS" REGISTRY
REGISTRY OF THE "EUROPEAN FORUM ON ANTIPHOSPHOLIPID ANTIBODIES" FOR PATIENTS WITH THE "CATASTROPHIC" ANTIPHOSPHOLIPID SYNDROME
COORDINATORS
Ricard Cervera, Jean Charles Piette, Yehuda Shoenfeld, Josep Font, and Ronald A. Asherson on behalf of the European Forum on Antiphospholipid Antibodies.
AIM
To establish an International Registry of all diagnosed patients with the "catastrophic" antiphospholipid syndrome, considered as a "rare disease".
For additional information and inclusion of patients, please e-mail: cervera@medicina.ub.es
For review of the already collected data, please click: CAPS registry
Internet

MORTALITY IN CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

Catastrophic APS represents 1% of all patients with APS
Cervera R, Piette JC et al Arthritis Rheum 2002; 46:1019-1027

They are usually in a life-threatening situation

The mortality rate is around 50%
Asherson RA, Cervera R et al. Medicine (Baltimore) 1998; 77:195-207
Asherson RA, Cervera et al. Medicine (Baltimore) 2001; 80:355-376

The causes and prognostic factors of this high mortality are still unknown

Stojanovich L, MD, PhD

Precipitating factors to CAPS

Clinic Rev Allerg Immunol (2009) 36:98–103
DOI 10.1007/s12016-008-8102-1

The Catastrophic Antiphospholipid Syndrome in Serbia: Diagnostic and Management Problems

Ljudmila Stojanovich

- Infection was identified in 50% of CAPS patients
- Cigarette smoking found in 41.7% of CAPS patients
- Prolonged stress situations, including the 1999 NATO bombing of Serbia, lead to CAPS in 33.3% CAPS patients
- CAPS resulted from discontinuation of prescribed anticoagulant therapy in 25.0% patients.
- Surgical procedure precipitated CAPS development in 16.6% patients

Stojanovich L, MD, PhD

Clinic Rev Allerg Immunol (2009) 36:74–79
DOI 10.1007/s12016-008-8108-8

Clinical and Laboratory Features of the Catastrophic Antiphospholipid Syndrome

Ljudmila Stojanovich · Dragomir Marisavljevic · Jozef Rovensky · Aleksandra Djokovich · Darina Kozáková · Nikola Milinic

ClinicalManifestations:

- **RENAL** **73%**
- **PULMONARY** **68%**
- **CEREBRAL** **65%**
- **SKIN** **52%**
- **CARDIAC** **51%**
- **HEPATIC** **34%**
- **GASTROINTESTINAL** **24%**

Stojanovich L, MD, PhD

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- Familial Antiphospholipid Syndrome
- Warfarin in the Antiphospholipid Syndrome (WAPS)
- Pulmonary Hypertension and Antiphospholipid Antibodies
- Standardization of the Antiphospholipid Antibodies
- Cerebral Ischaemia in the Primary Antiphospholipid Syndrome: Source of Thrombi European Study (STEP)
- FcgRIIa polymorphism in the Antiphospholipid Syndrome
- The CAPS Registry
- Future projects

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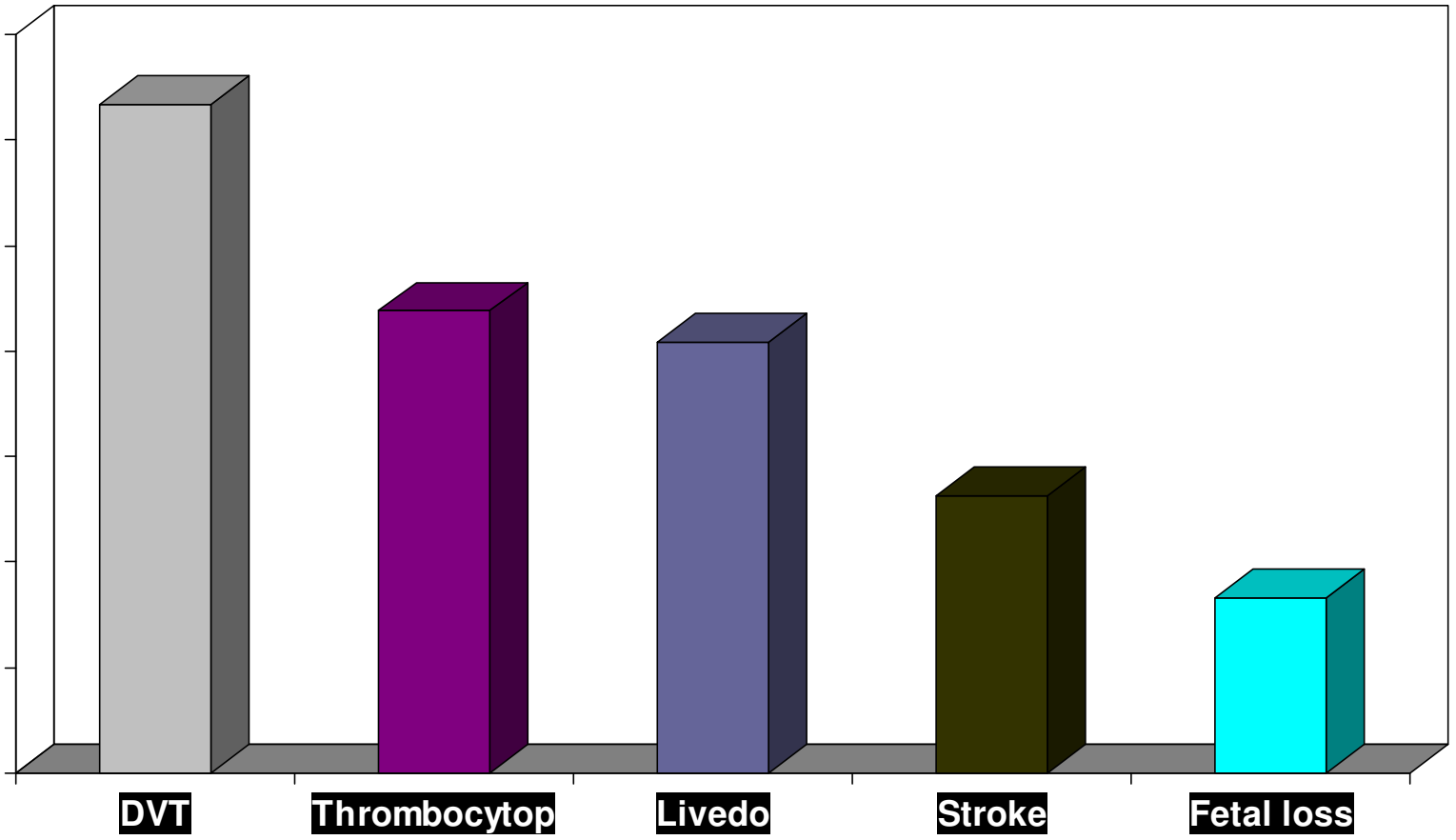
Programas

Lessons from the Euro-Phospholipid Project



Cervera et al. A & Rheum 46:12002

Project
Issued by the Ministry of Science of the Republic of Serbia

Issued by the Ministry of Science of the Republic of Serbia:

- ***Grant number 145020 for 2006-2010:***

Multi-disciplinary Study of Risk Factors for the Development of Thromboses in APS

- ***Grant number 175041 for 2011-2014:***

Multidisciplinary study of genetic and acquired abnormalities of the immune response for the occurrence of systemic antiphospholipid syndrome manifestations

Stojanovich L, MD, PhD

Research Goal

1. To determine prevalence and types of aPL titer (LA, ACL, β2GPI) in patients with thrombotic and non-thrombotic manifestations of the disease.
2. Analisys of gene polymorphisms that are important for the T (H) 17 and regulatory T cells differentiation in APS patients, and their corellation with the disease.
3. Determination of aPL association with the innate Thrombophilia (defficiency of AT, PC, PS, FXII, polymorphisms FV Leiden, prothrombin 20210 and MTHFR) and clinical expression.
4. Determination of aPL role in the development of induced atherosclerosis, including subclinical forms of the disease using the latest technology methods such as multi sliced computed tomography (64 MSCT), which would present the extent and location of changes in blood vessels.
5. To determine the importance of oxidative stress, markers of inflammation, endothelial adhesion receptor molecules induction and activation, as additional factors in the complicated pathophysiology and multifactorial etiology of APS thrombosis.
6. To continue in obtaining the national APS patients registry with the possibilities of its participating in international studies.
7. To overview the patient outcomes with various APS therapeutic protocols.

Stojanovich L, MD, PhD

Goals

- Aim of this study was to observe and investigate association between thrombotic in prospective study of APS patients.
- Differences between patients with primary and secondary APS were also analyzed.
- This study presents the results from our national cohort.

Patient Group Description

501/383 patients:

358/ 260 PAPS patients:

- 201 female and 59 male
- mean age 45.2 + 13.7 years

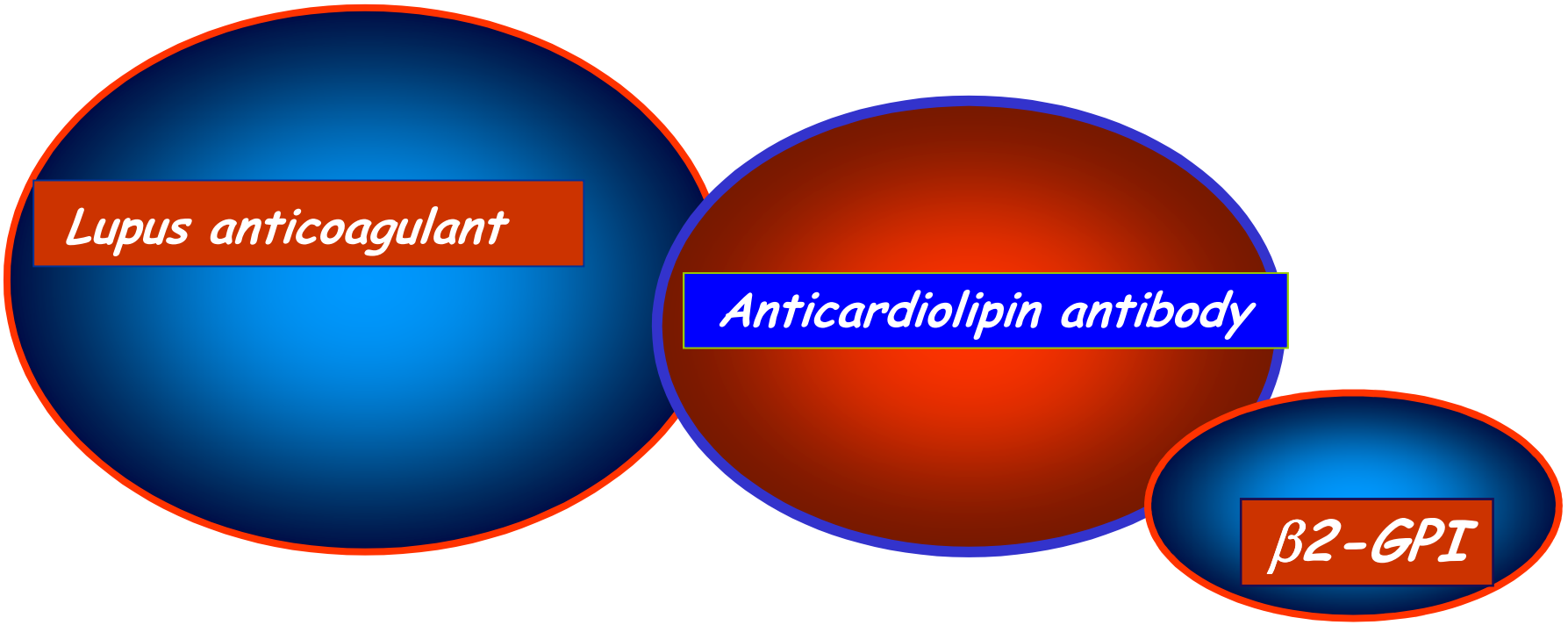
143/ 114 SLE patients with secondary APS

- 106 female and 9 male
- mean age 46.9 + 15.9 years

14 (4.5%) patients with CAPS: 7 SLE+ 7 PAPS

Stojanovich L, MD, PhD

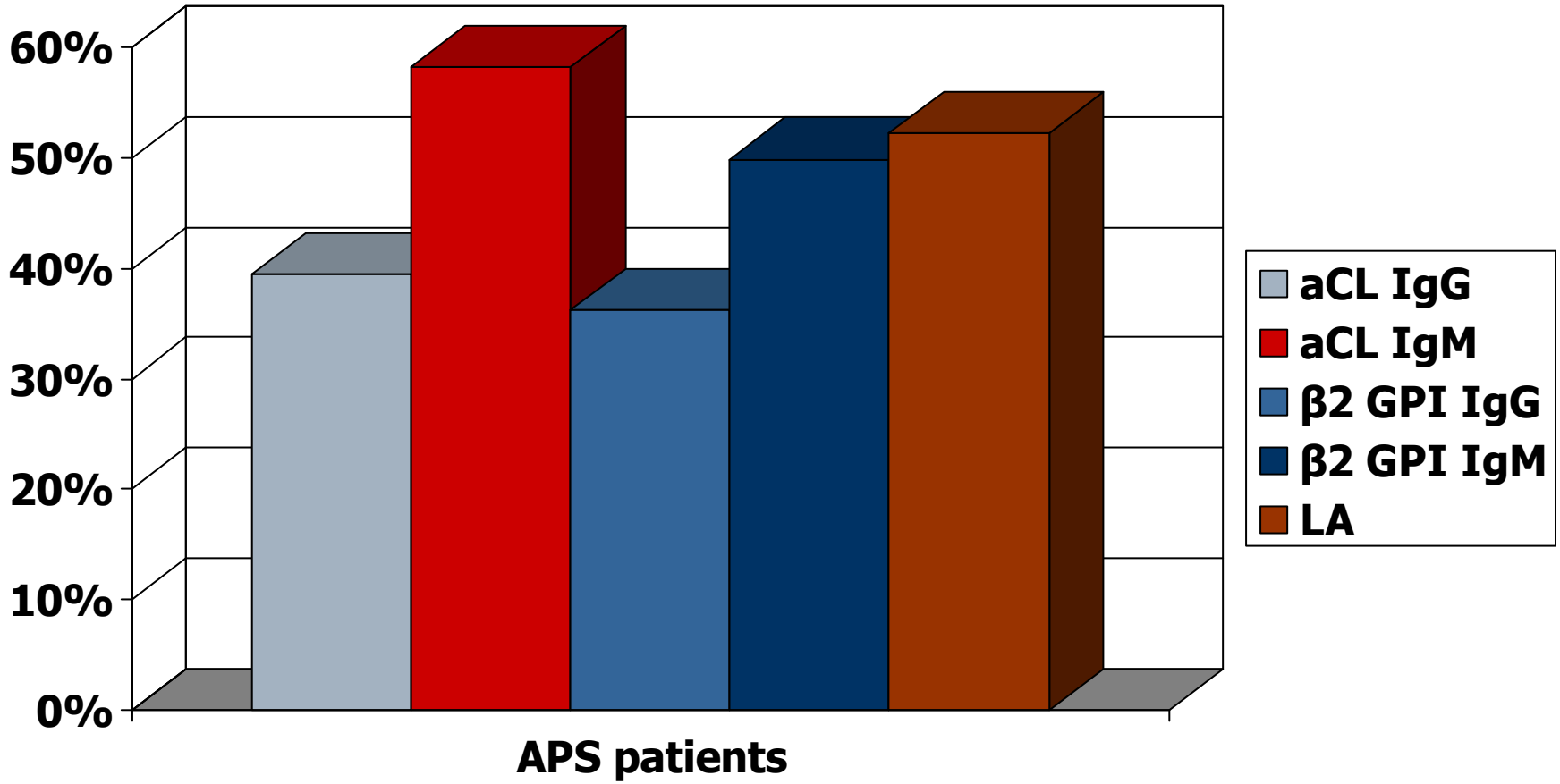
Methodology



by positive levels:

- ✓ *low (10-30)*
- ✓ *medium (31-99)*
- ✓ *high (>100PLU/ml)*

Break-down of Patients According to the Type of aPL



Stojanovich L, MD, PhD

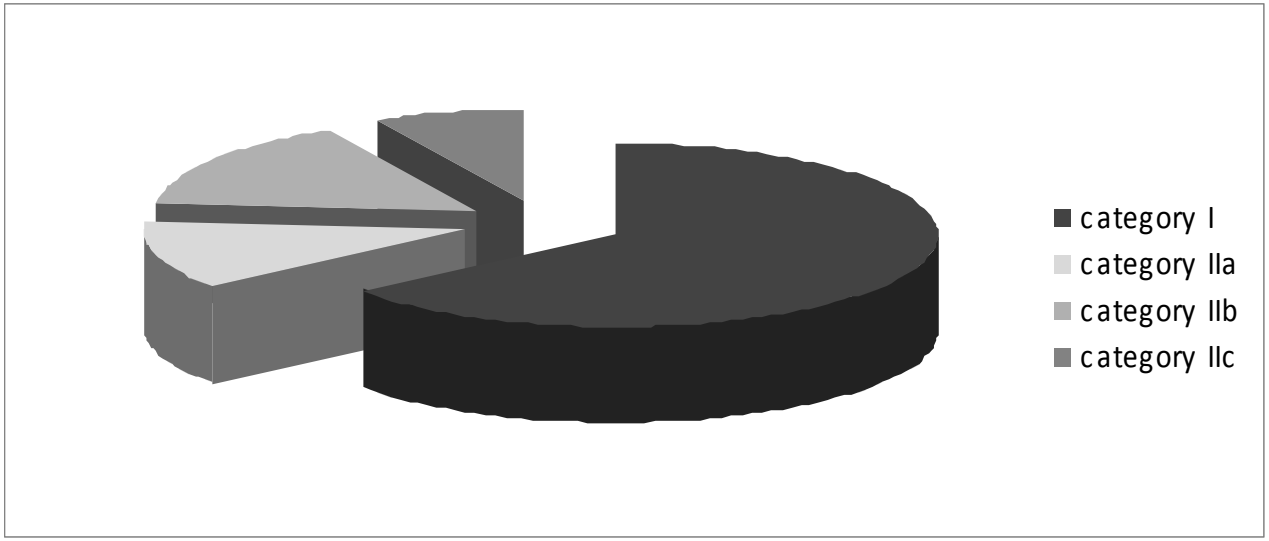
Distribution of aPL in PAPS and SAPS

Table 2. Distribution of aPL in the PAPS and SAPS groups

aPL type/ aPLcategory	PAPS (N=260)	SAPS (N=114)	p value
aCL IgG	95 (36.5)	68 (59.6)	**0.0001**
aCL IgM	141 (54.2)	73 (64.0)	**0.049**
ß$_2$GPI IgG	83 (31.9)	49 (43.0)	**0.027**
ß$_2$GPI IgM	98 (37.7)	51 (44.7)	0.122
LA	133 (51.2)	56 (49.1)	0.402
I	160 (61.5)	81 (71.1)	
IIa	41 (15.8)	5 (4.4)	
IIb	46 (17.7)	23 (20.2)	p=0.020
IIc	13 (5.0)	5 (4.4)	

Legend: PAPS= primary antiphospholipid syndrome, SAPS= secondary antiphospholipid syndrome, aCL= anticardiolipin antibodies,ß$_2$ GPI=anti- ß$_2$ glycoprotein I antibodies, LA= lupus anticoagulant, aPL= antiphospholipid antibodies
Categories: I-more than one aPL present, IIa LA present alone, IIb-aCL present alone, IIc- anti-β2GPI present alone

Distribution of patients according to antibody category



- More than one type of antibodies (category I) was present in 64.5%
- Lupus anticoagulant was present alone in 12.1% patients (category IIa)
- aCL antibodies were present alone in 16% patients (category IIb)
- anti-β2GPI antibodies were present alone in 7.4% patients (category IIc)

PengoV et al.
Antibody profiles for the diagnosis of APS.
Thromb Haemost 2005

Results
APS Manifestations

- ✓ Pregnancy loss: 41% pts
- ✓ Venous thrombosis: 28% pts
- ✓ Arterial thrombosis: 51% pts

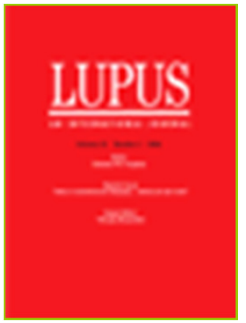
Diagnostic of vascular APS manifestations

Lupus (2014) 0, 1–5
http://lup.sagepub.com

REVIEW

Tomography and blood vessels in Hughes syndrome

L Stojanovich and A Djokovic
Internal Medicine, "Bezanijska Kosa," University Medical Center, Belgrade, Serbia



- Physical examination
- X-ray diagnosis of chest
- Vascular ultrasonography (Doppler)
- Peripheral angiography
- Vascular magnetic resonance imaging/ MRA angiography
- Computed tomographic angiography (CTA)
- 64-multi slice CT - *whole body angiography*

  can allow us excellent visualization of all major and minor blood vessels

Autoimmunity Reviews 10 (2011) 233–237
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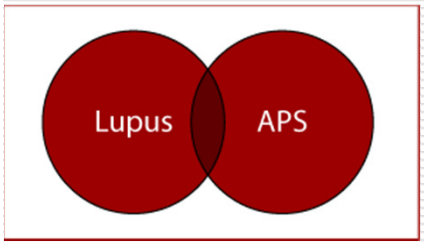
Review

Systemic vascular diseases in the antiphospholipid syndrome. What is the best diagnostic choice?

Jovica Saponjski *,1, Ljudmila Stojanovich 1, A. Djokovic, M. Petkovic, D. Mrda
Internal medicine, "Bezanijska Kosa", University Medical Center, Belgrade, Serbia



Thrombosis

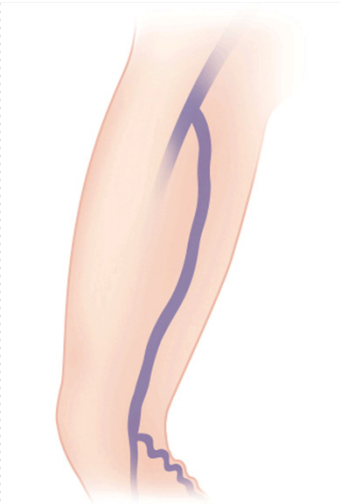
Thrombosis was diagnosed:

- ✓ 83 (51.2%) PAPS patients
- ✓ 36 (38.3%) SLE patients

p = 0.045

Results

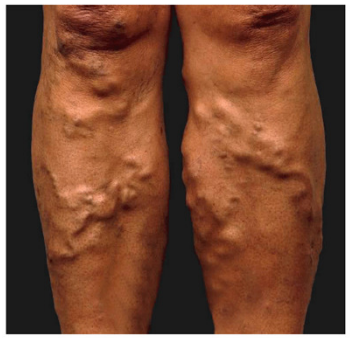
- ✓ Arterial Thrombosis : 51% pts
- ✓ Venous thrombosis: 28% pts



Arterial Thrombosis

- ✓ 35% PAPS patients
- ✓ 34% SLE patients

p = 0.932

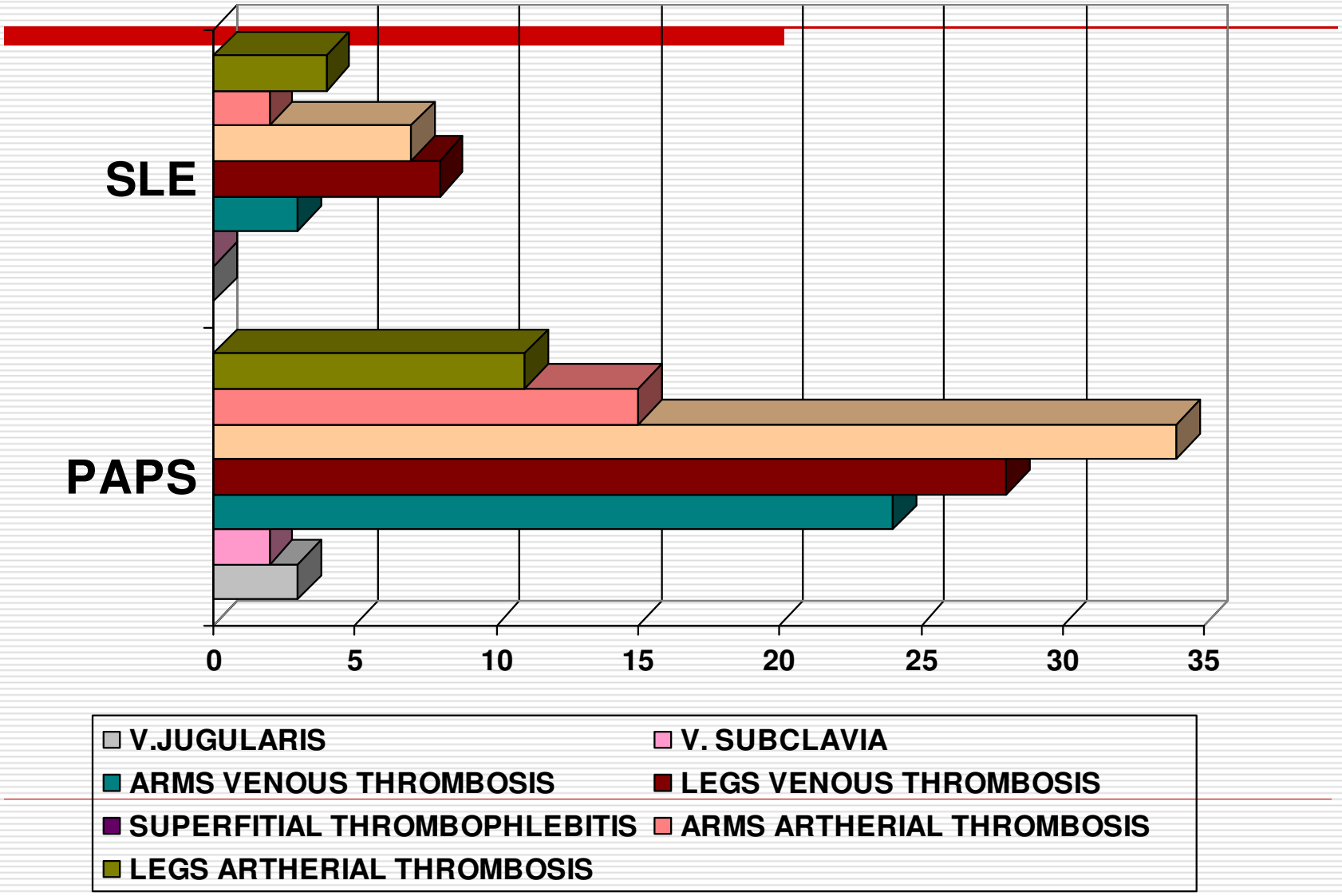


Venous thrombosis

- ✓ 25.9% PAPS patients
- ✓ 8.5% SLE patients

p = 0.001

Incidence of thrombosis in APS pts in Serbia



Distribution of aCL IgG/IgM levels in PAPS patients with arterial and venous thrombosis

PAPS	Level of aCL IgG				Level of aCL IgM			
	Low	medium	high	p	low	medium	high	p
Thrombosis	50.0	65.2	46.7	0.520	60.6	56.3	37.9	0.069
AT	33.3	52.2	26.7	0.253	45.1	28.1	25.9	0.095
VT	25.9	26.1	26.1	0.553	28.2	37.5	17.2	0.195

Distribution of aCL IgG/IgM levels in SAPS patients with arterial and venous thrombosis

Secondary APS	Level of aCL IgG				Level of aCL IgM			
	low	medium	high	p	low	medium	high	P
Thrombosis	29.8	37.5	51.6	0.256	26.7	35.5	51.5	0.094
AT	25.5	37.5	45.2	0.298	26.7	25.8	48.5	0.119
VT	4.3	0	19.4	0.054	6.7	12.9	6.1	0.484

Distribution of β_2GPI IgG/IgM levels in patients with PAPS

PAPS	β_2GPI-IgG				β_2GPI-IgGM			
	low	medium	high	p	low	medium	high	p
Thrombosis	50.0	65.2	46.7	0.882	48.9	42.9	64.1	0.201
AT	33.3	52.2	26.7	0.898	30.9	28.6	48.7	0.088
VT	25.9	26.1	26.7	0.973	27.7	17.9	28.2	0.645

Distribution of β_2GPI IgG/IgM levels in patients with SAPS

Secondary APS	β_2GPI-IgG				β_2GPI-IgGM			
	low	medium	high	p	low	medium	high	p
Thrombosis	32.7	33.3	50.0	0.270	42.6	33.3	34.8	0.275
AT	28.8	25.0	46.7	0.107	40.4	25	30.4	0.298
VT	9.6	8.3	6.7	0.952	8.5	12.5	4.3	0.324

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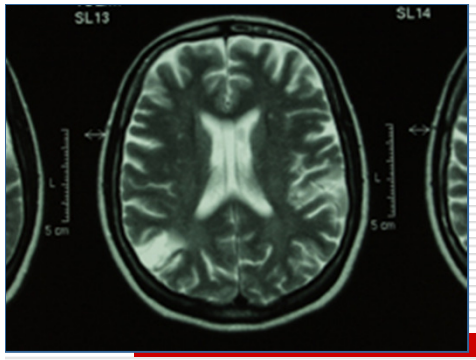
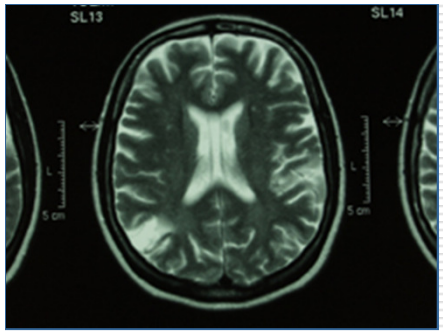


CVI in PAPS

There was a correlation between:

CVI and:

- pts with $ß_2$GPI-IgM — *p=0.008*
- pts with LA — *p=0.009*



CVI in SLE

There was a correlation between:

CVI and:

- ✓ pts with $ß_2$GPI — *p=0.008*
- ✓ pts with LA — *p=0.009*

Analysis of aPL and localization of thrombosis

There was no correlation between:

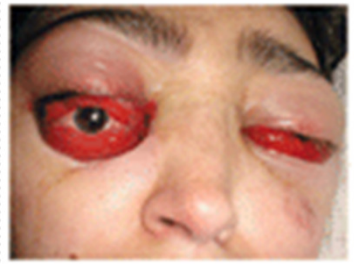
other localization of arterial thrombosis and the type of aPL

$p > 0.05$

Thrombosis in PAPS was significantly more frequent than in SLE:

- ✓ superior extremity *p=0.004*
- ✓ inferior extremity deep vein *p=0.027*
- ✓ inferior extremity superficial thrombophlebitis *p=0.004*

Analysis of aPL and localization of thrombosis



- ✓ aCL-IgM and cerebral venous sinus thrombosis
- ✓ aCL-IgM and jugular venous thrombosis

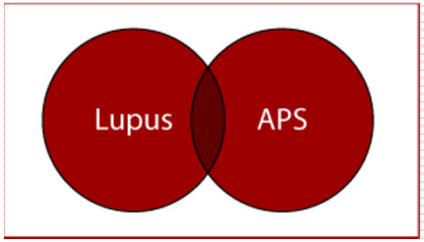
p= 0.040

Analysis of aPL and localization of thrombosis

There was no correlation between:

other localization of venous thrombosis and the type of aPL

$p > 0.05$



Distribution of arterial and venous thrombosis in PAPS and SAPS patients under and over 45 years of age

Age	PAPS		Secondary APS	
	AT	VT	AT	VT
≤45 years	17 (28.5%)	20 (24.15%)	14 (25.5%)	4 (7.3%)
>45 years	39 (49.2%)	22 (27.8%)	18 (46.2%)	4 (10.3%)
	p=0.028	p=0.238	p=0.031	p=0.439

Analysis of localization of thrombosis and age

Age was a significant risk factor for:

- CVI: 51.92 and 41.97 years, respectively p=0.001
- MI: 56.6 and 43.6 years, respectively p=0.0001

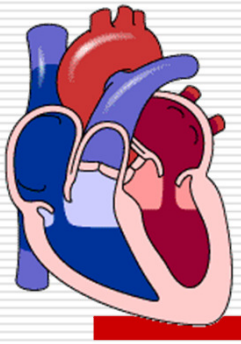
Analysis of activity of SLE (SLEDAI) and thrombosis

The median SLEDAI score was 9 in patients without thrombosis.

The median SLEDAI score was 13.5 in patients with thrombosis.

p=0.03

The activity of SLE was in significant correlation with the prevalence of thrombosis.



CARDIOLOGICAL MANIFESTATIONS

The heart is one of the major target organs in APS and heart valve abnormalities (vegetations and/or thickening) are the most common cardiac manifestations of APS.

Silbiger JJ. The cardiac manifestations of antiphospholipid syndrome and their echocardiographic recognition. J Am Soc Echocardiogr 2009; 22: 1100–1108.

- **Prevalence: 40 %**
- **Morbidity: 4-6%**

ARTHRITIS & RHEUMATISM
Vol. 46, No. 4, April 2002, pp 1019–1027
DOI 10.1002/art.10187

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

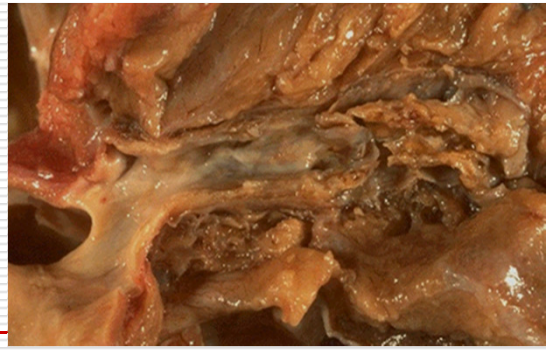
Results

There was no correlation between APS cardiac manifestations and:

- ✓ cardiovascular risk factors (including diabetes)
- ✓ SLE activity (SLEDAI) and other parameters

$p > 0.05$

Results



There was a correlation between:

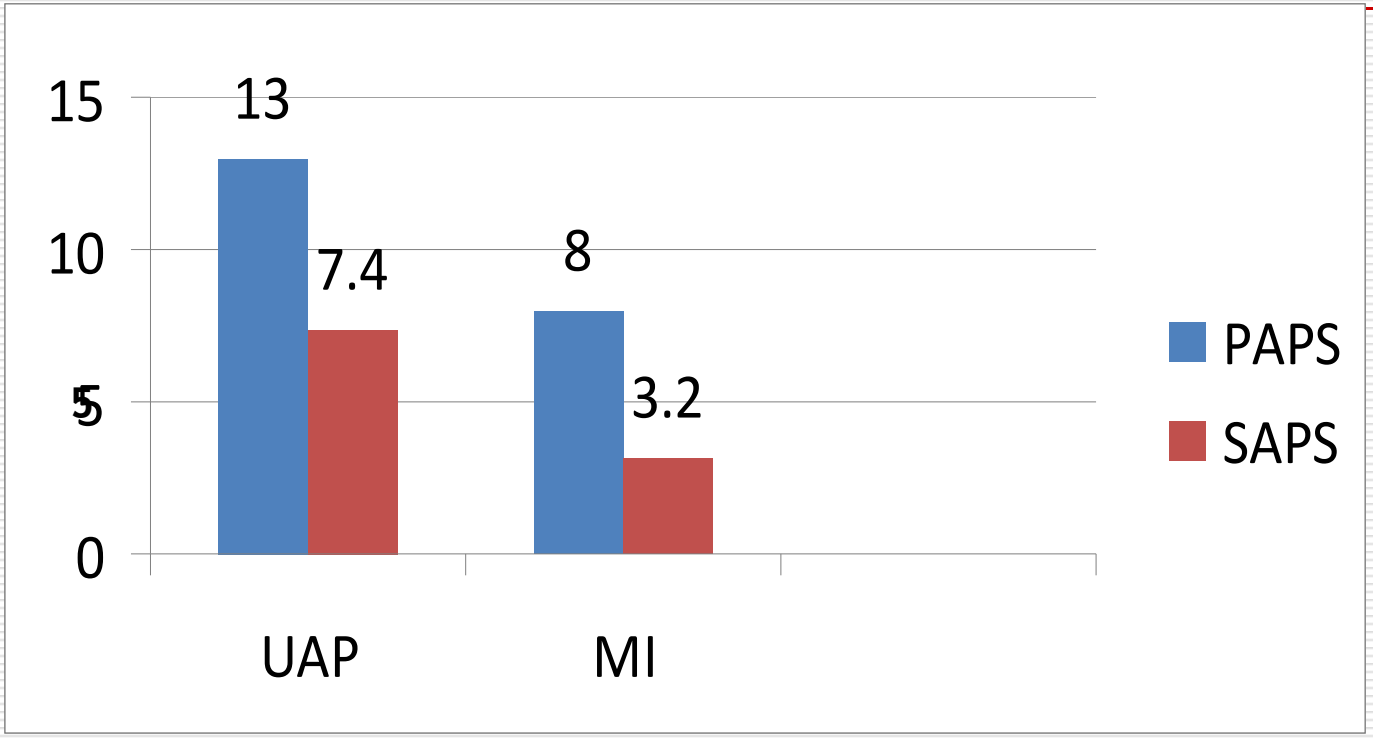
Patients with aCL – IgM and:

- ***CABG/PTCA (p=0.026)***

coronary artery bypass grafting/ percutaneus coronary artery angioplasty

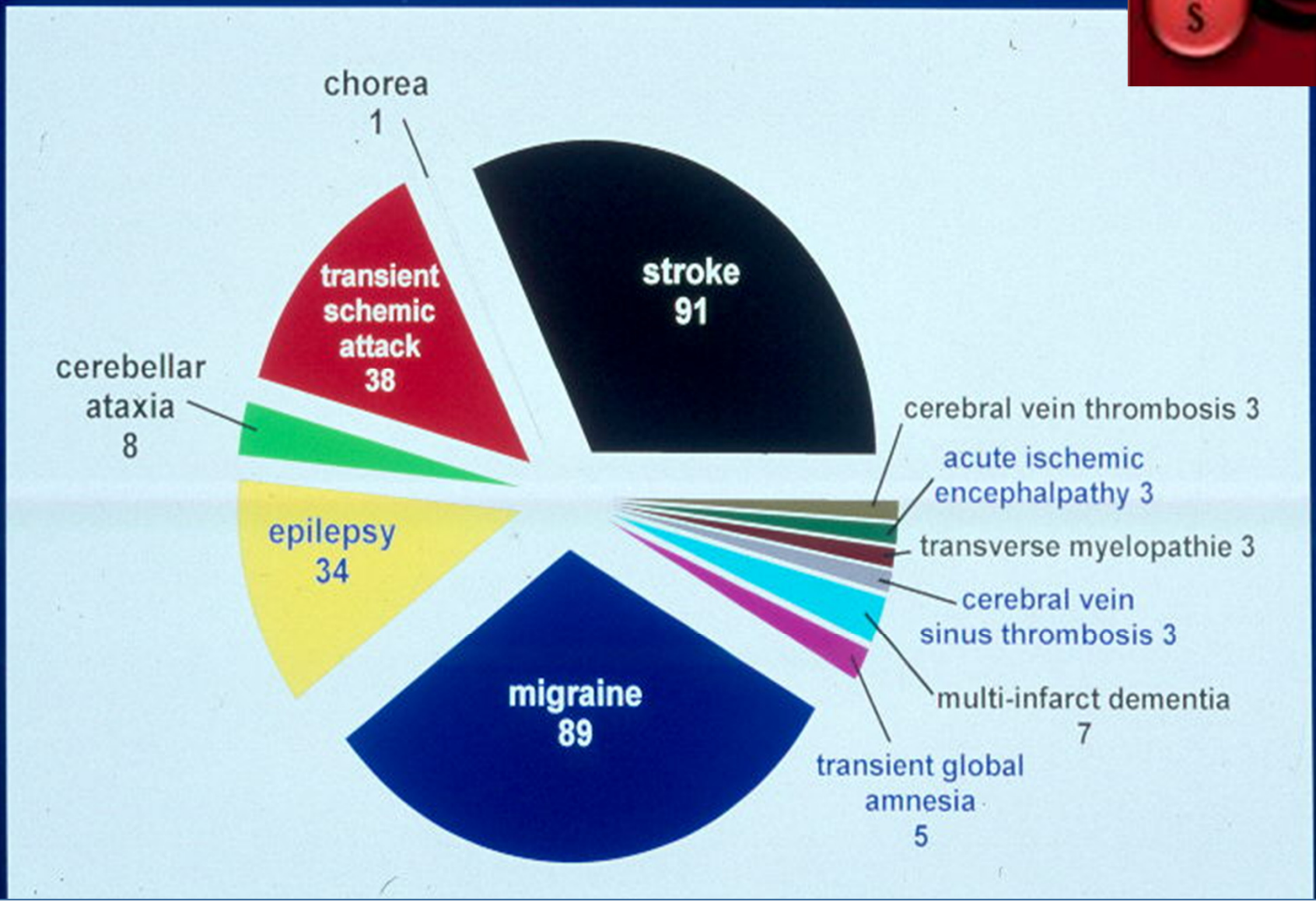
- **Pseudoinfective endocarditis *(p=0.037)***

Results

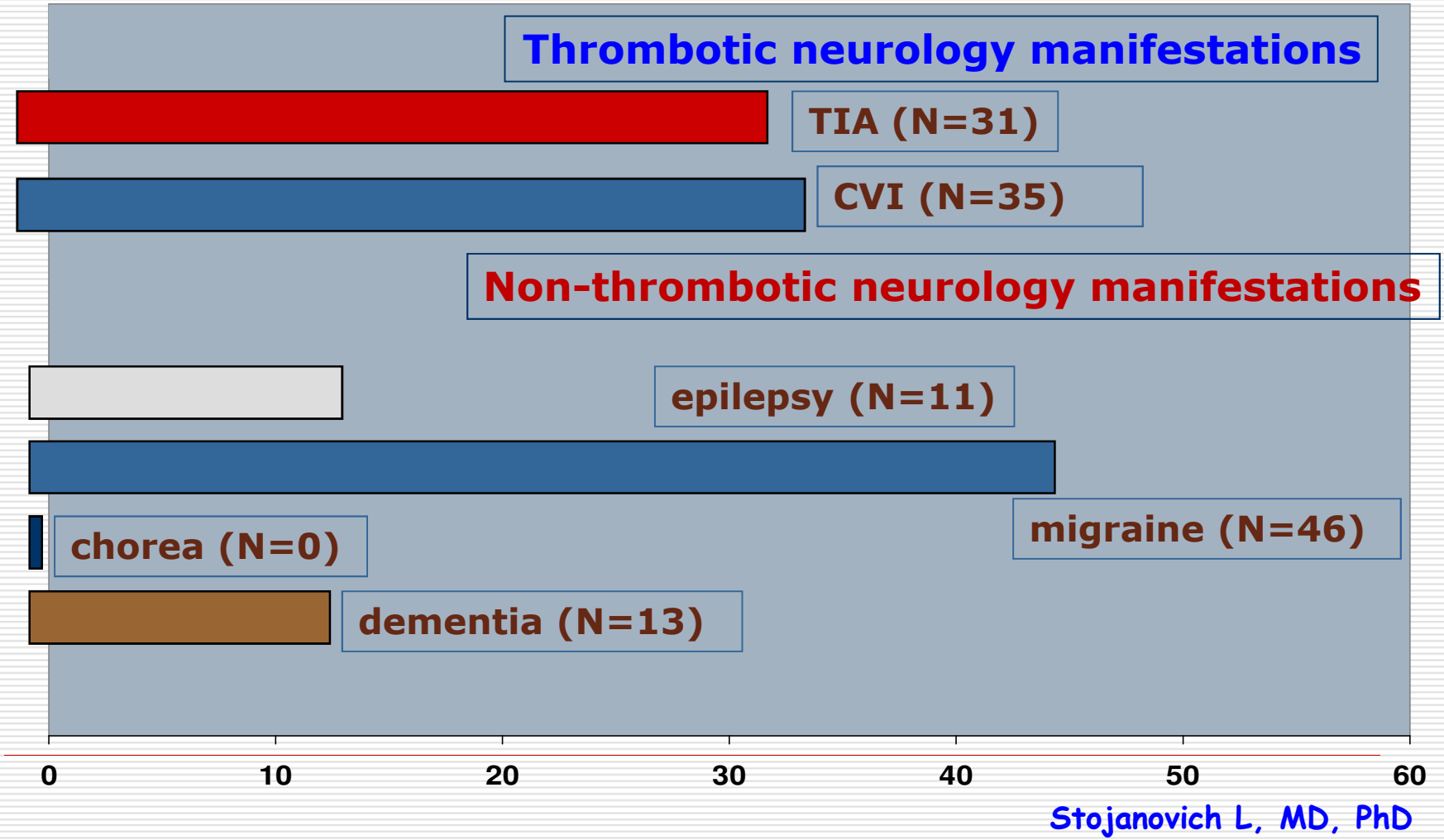


PAPS and SLE patients did not differ among themselves with regard to the occurrence of MI (p = 0,102) and UAP (p = 0.123) *unstable angina pectoris (UAP)*

Neurological Manifestations



Frequency of Neurology Manifestations in PAPS patients



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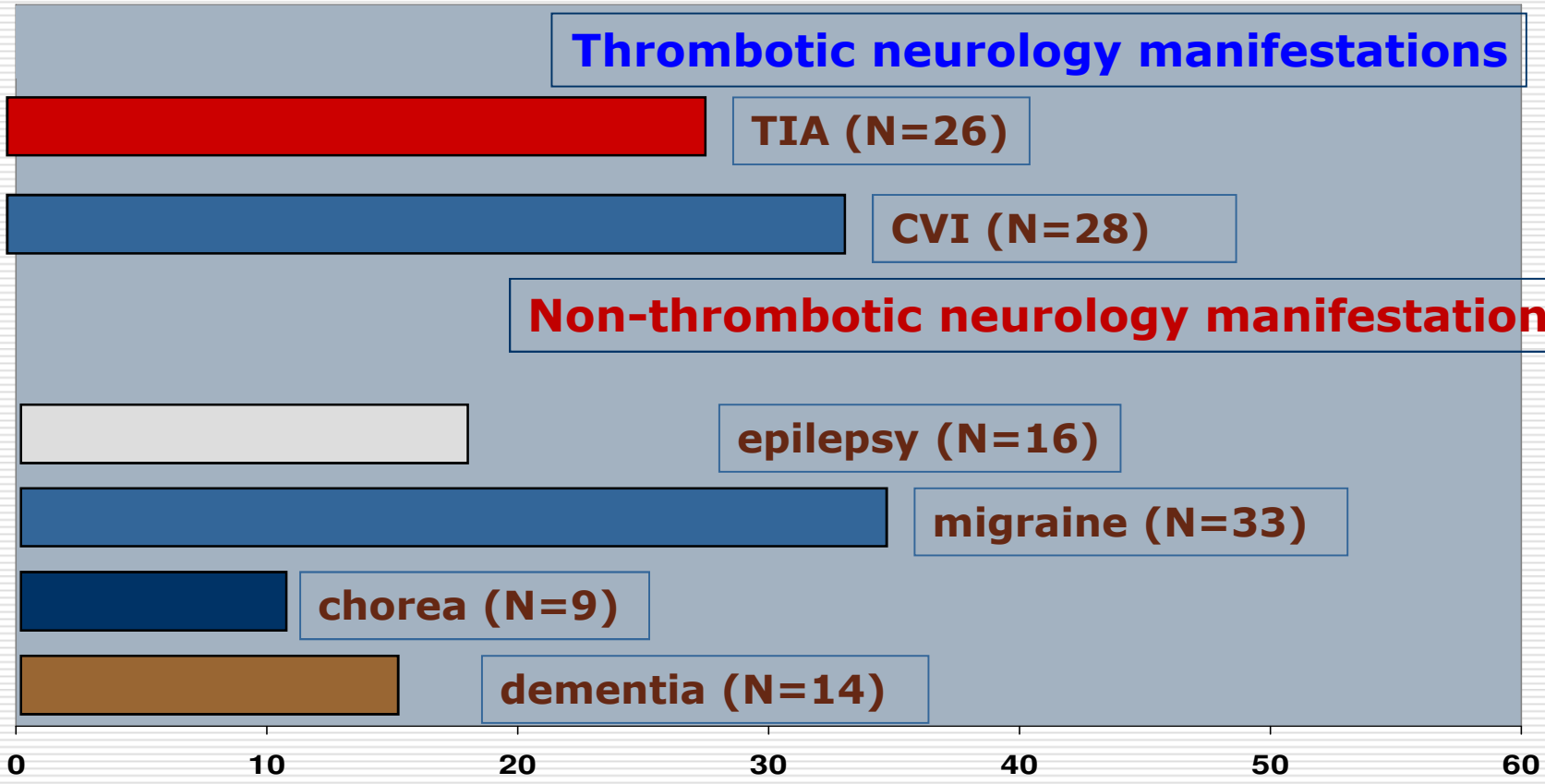
Frequency of Neurology Manifestations in SLE patients



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Comparison of frequency of neurological manifestations between PAPS and SAPS pts

	PAPS	SAPS	p
Transient ischemic attack	21.6%	27%	0.237
Chorea	0%	7.8%	0.000*
Epilepsy	5%	19.1%	0.001*
Migraine	28%	34.8%	0.026*
Transient global amnesia	1.4%	1.7%	0.769
Acute ischemic encehalopathy	1.4%	4.3%	0.305
Anterior spinal artery syndrome	0%	0.9%	0.550
Cehalea	24%	13.9%	0.031*
Vertigo	8.3%	3.5%	0.093
Sy depressivum	3.7%	0%	0.037*

Stojanovich L, MD, PhD

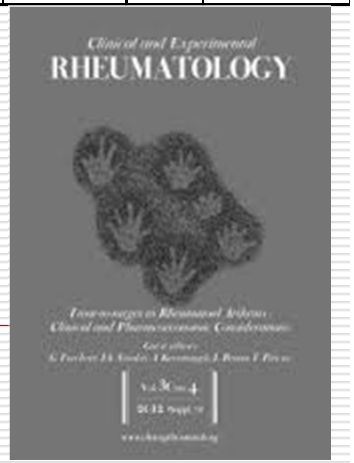
Correlation between neurological and cardiac manifestations in PAPS

PAPS patients		Transient ischemic attack			Epilepsy			Transient global amnesia			Depression		
		-	+	p	-	+	p	-	+	p	-	+	p
Non stable angina pectoris	-	158	36	0.002*	187	7	0.006*	193	1	0.002*	187	6	0.217
	+	13	11		20	4		22	2		22	2	
Valve vegetations	-	160	40	0.064	193	7	0.001*	198	2	0.285	15	3	0.002*
	+	11	7		14	4		17	1		194	5	

Association between non-thrombotic neurological and cardiac manifestations in patients with antiphospholipid syndrome

L. Stojanovich[1], M. Kontic[2], D. Smiljanic[3], A. Djokovic[1], B. Stamenkovic[4]
D. Marisavljevic[1,5]

[1]Internal Medicine, "Bezanijska Kosa", University Medical Centre, Belgrade, Serbia;
[2]Clinic for Pulmonology, Clinical Center of Serbia, University in Belgrade, Serbia;
[3]Department of Neurology, Clinical-Hospital Centre (KBC) Zemun, Belgrade, Serbia;
[4]Rheumatology Clinic, Institute Niska Banja, Medical Faculty, University of Nis;
[5]Faculty of Medicine, University of Belgrade, Belgrade, Serbia.



Correlation between neurological and cardiac manifestations in SAPS

SAPS patients		Transient ischemic attack			Acute ischemic encephalopathy		
		Present	Not present	p	Present	Not present	p
Non stable angina pectoris	not present	80	24	0.004*	102	2	0.000*
	present	4	7		8	3	

International Conference on Cardiology
(Cardiology'11)
(part of Summer WORLDMED)
Prague, Czech Republic, September 26-28, 2011

Plenary Lecture 3:

Non-Thrombotic Neurological and Cardiac Manifestations in Antiphospholipid Syndrome
by **Prof. Ljudmila Stojanovich**, Belgrade University, SERBIA.

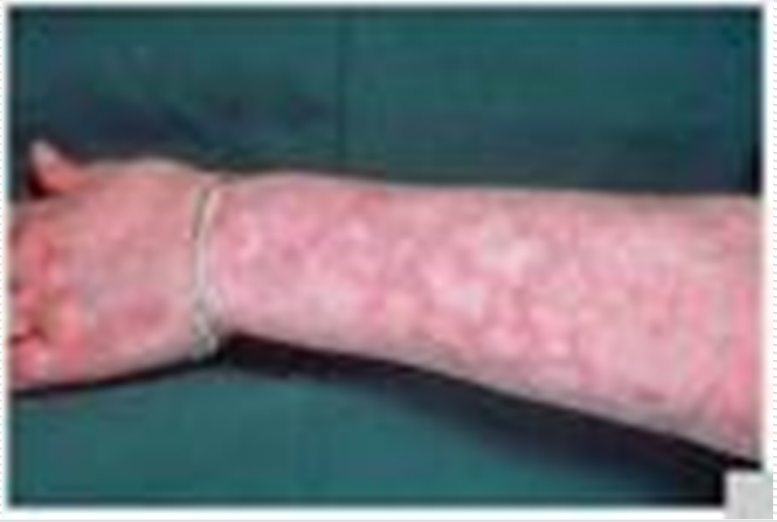
Clinical and Experimental
RHEUMATOLOGY
Free to view
Quality of care in Rheumatolog: opportunities and challenges
Vol. 25 no.6 (suppl.47) 2007

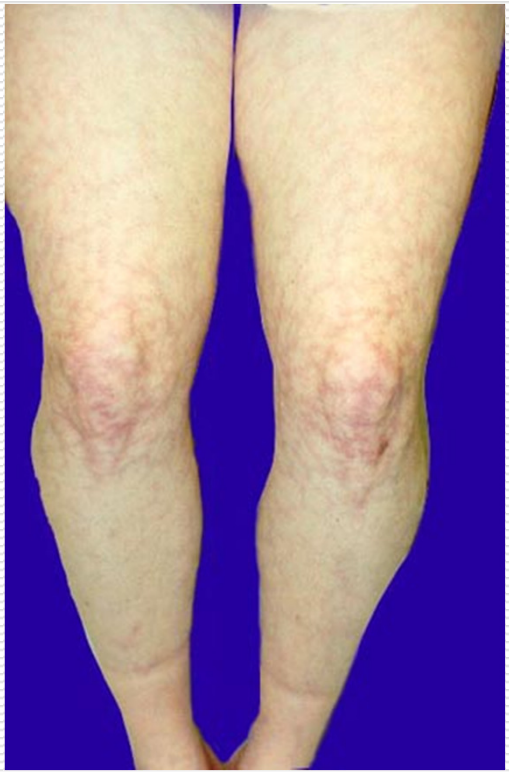
Livedo reticularis is a marker for predicting multi-system thrombosis in antiphospholipid syndrome

E. Toubi[1], I. Krause[2,3], A. Fraser[3], S. Lev[3], L. Stojanovich[4], J. Rovensky[5], M. Blank[2], Y. Shoenfeld[2]

[1]Division of Allergy and Clinical Immunology, Bnai Zion Medical Center, Haifa; [2]Department of Internal Medicine B and Center of Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer; [3]Department of Medicine E, Rabin Medical Center, and Sackler Faculty of Medicine, Tel-Aviv University, Israel; [4]Department of Rheumatology and Hospital Center, Bezanijskakosa, Belgrade, Serbia; [5]Research Institute of Rheumatic Diseases, Piestany, Slovakia.

31% pts had Livedo Reticularis





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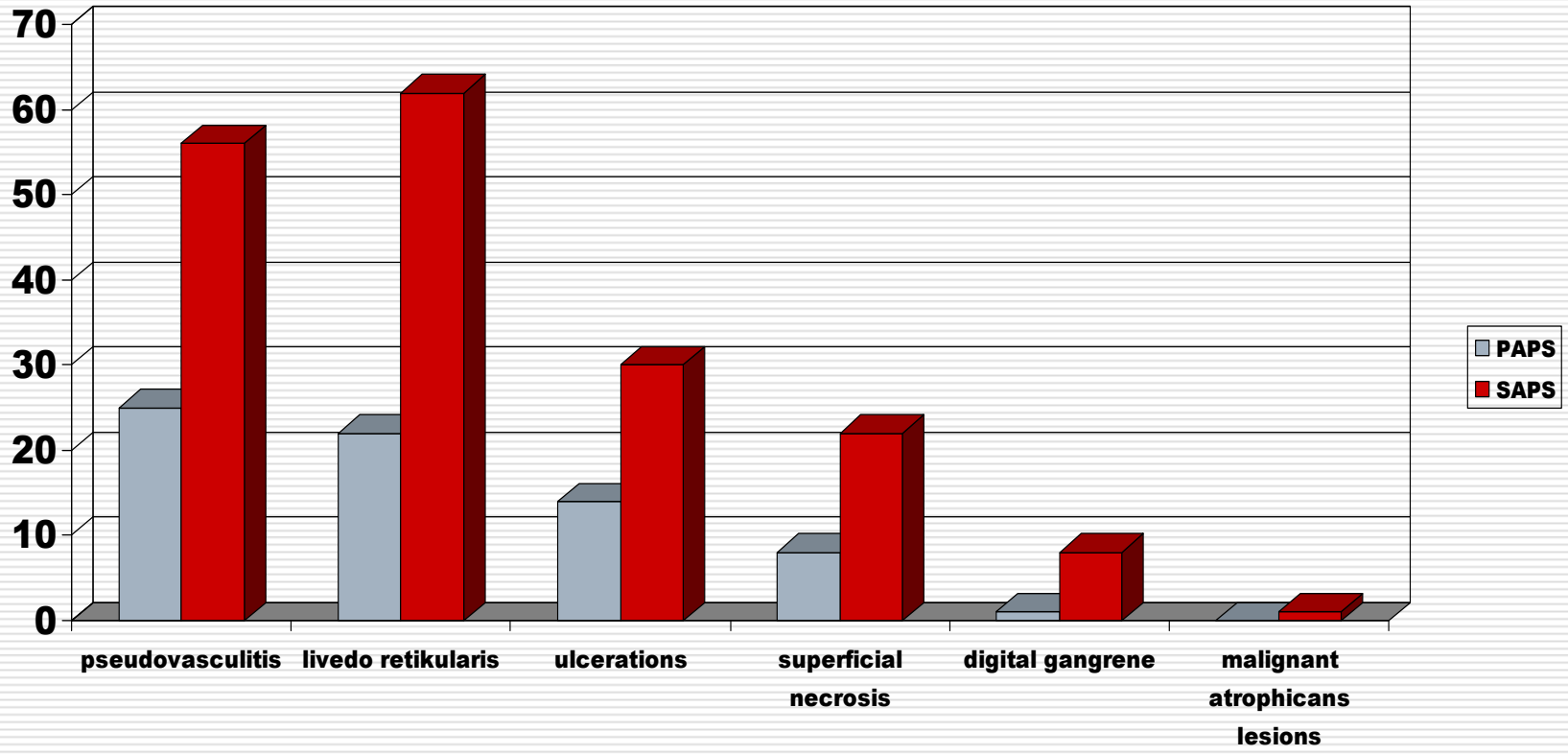
Skin manifestations



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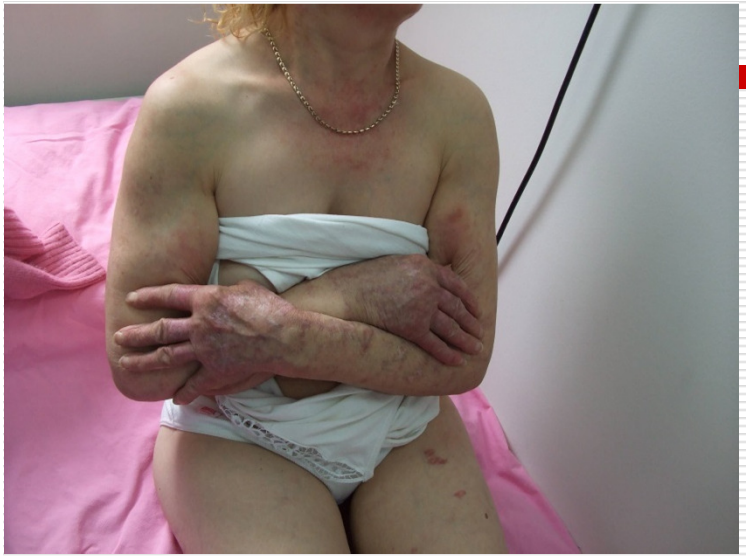
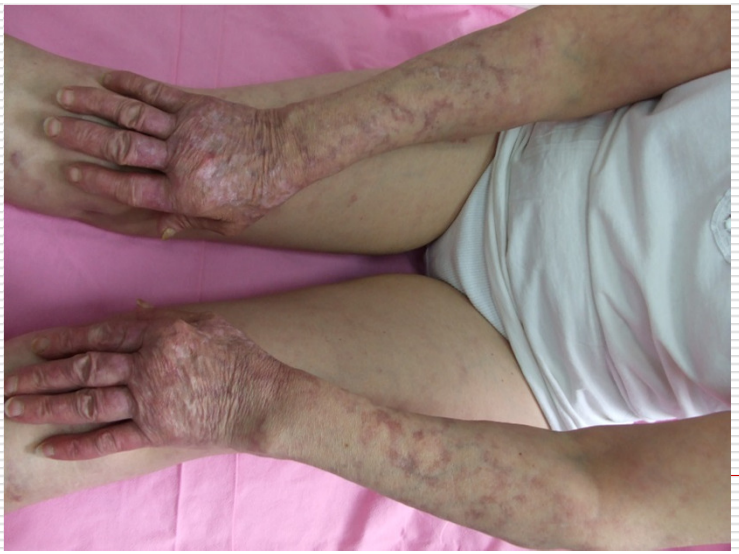
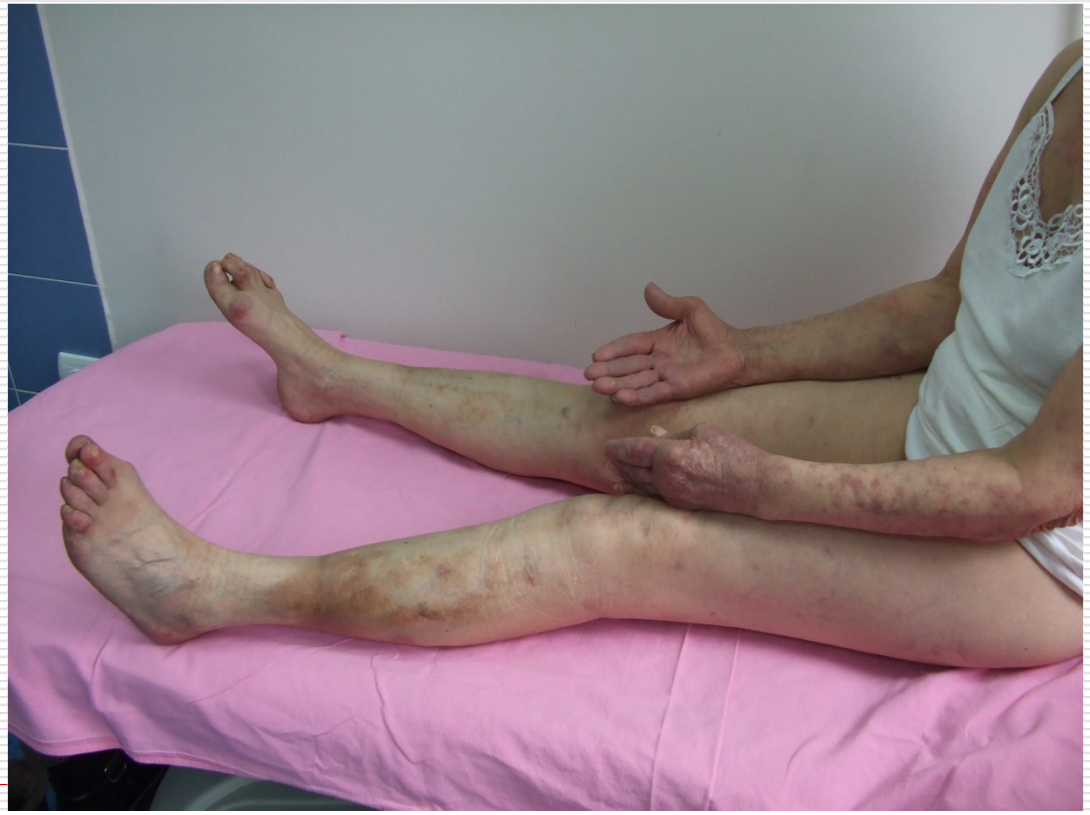
Combination of different skin manifestations in APS

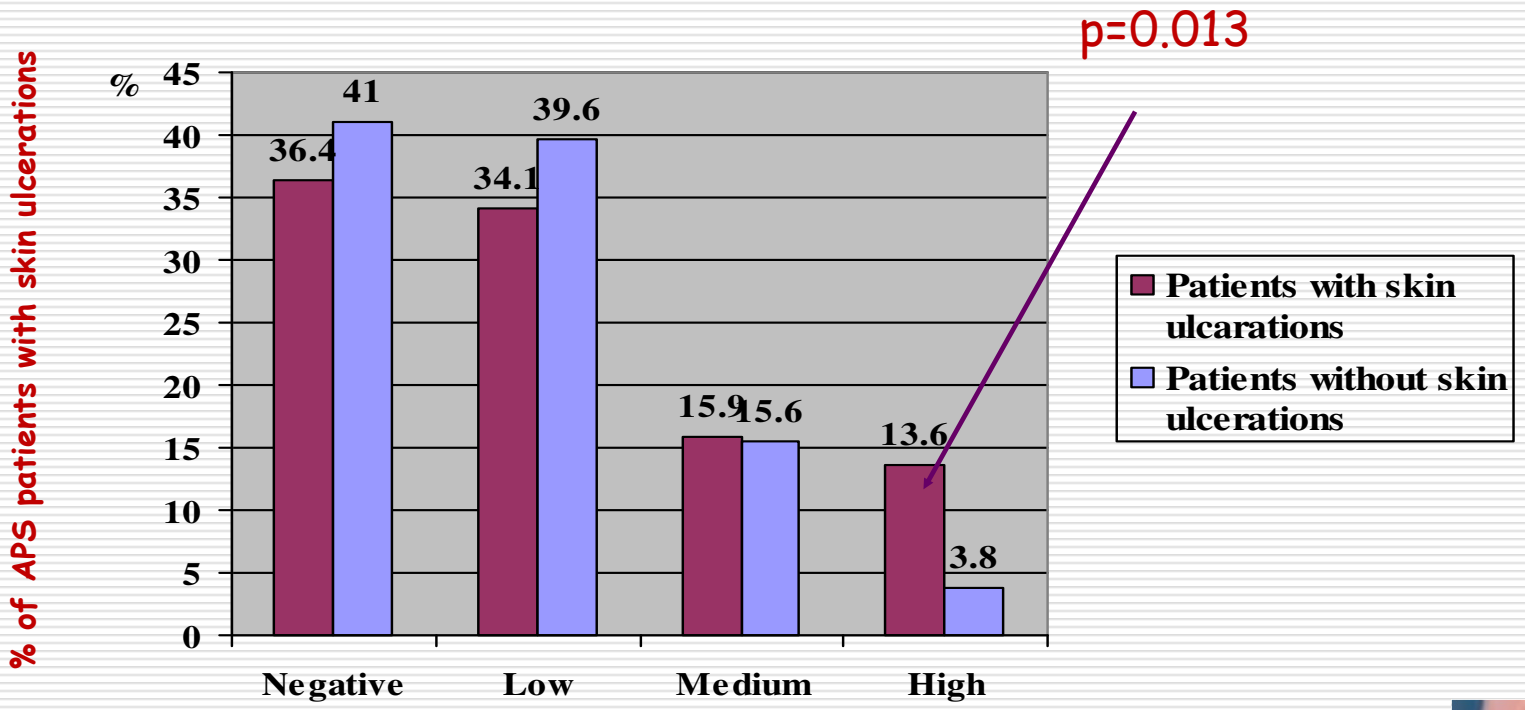


- ✓Livedo reticularis
- ✓Skin ulcerations
- ✓Pseudovasculitis





aCL IgM levels in APS with and without skin ulcerations



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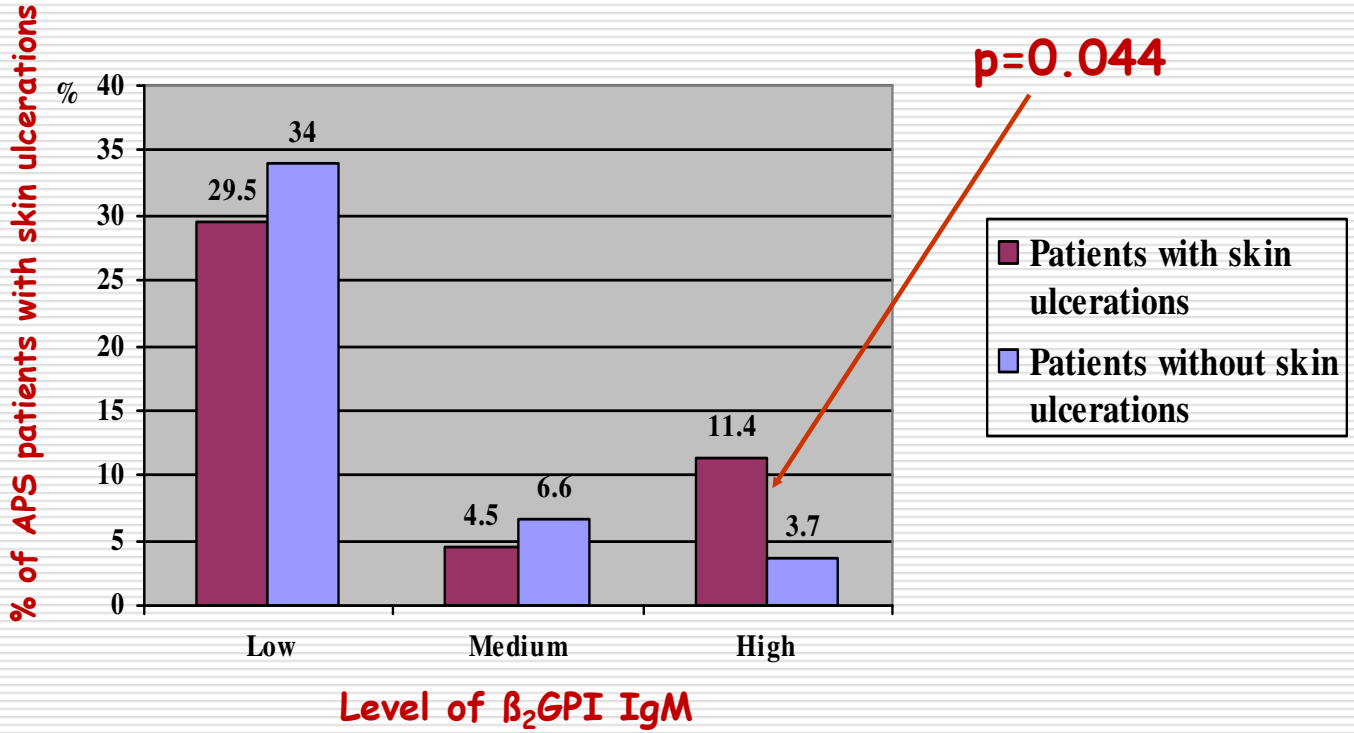
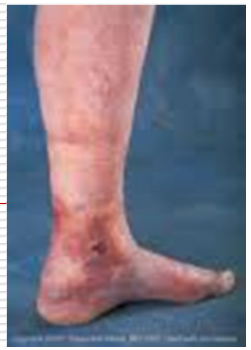
ß$_2$GPI IgM levels in APS with and without skin ulcerations





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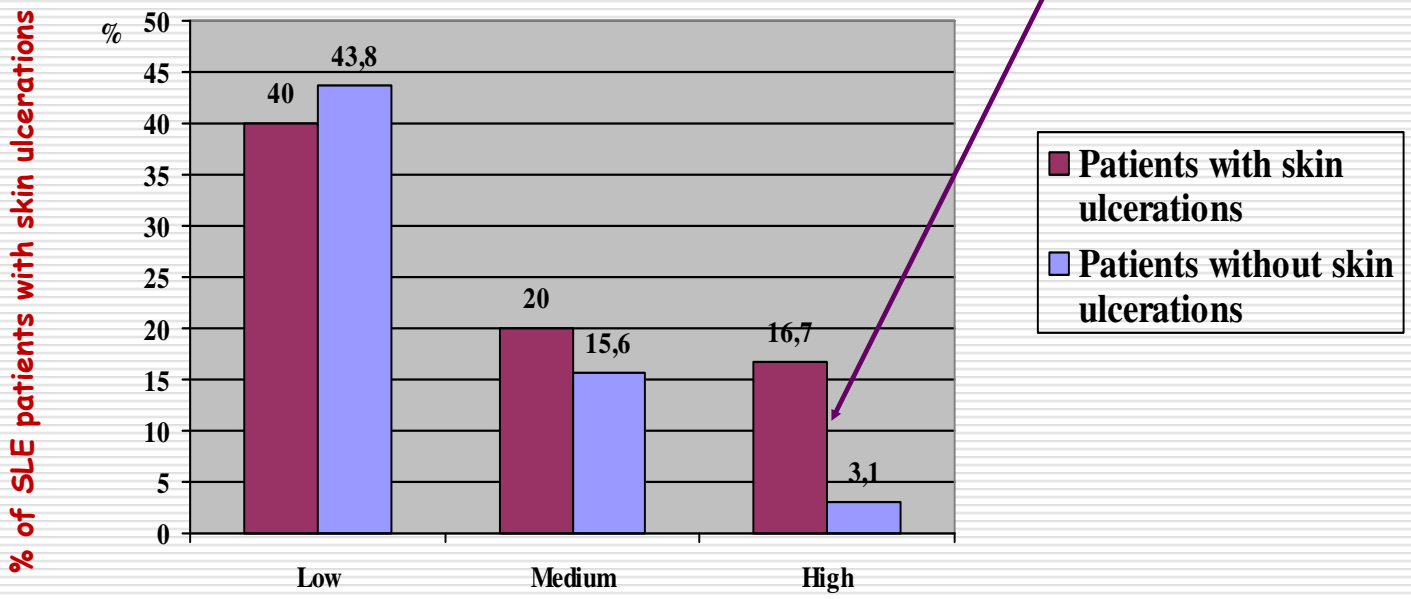
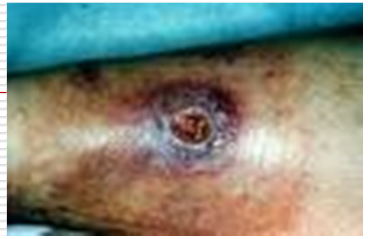
aCL IgM levels in SLE with and without skin ulcerations

p=0.049



Level of aCL IgM



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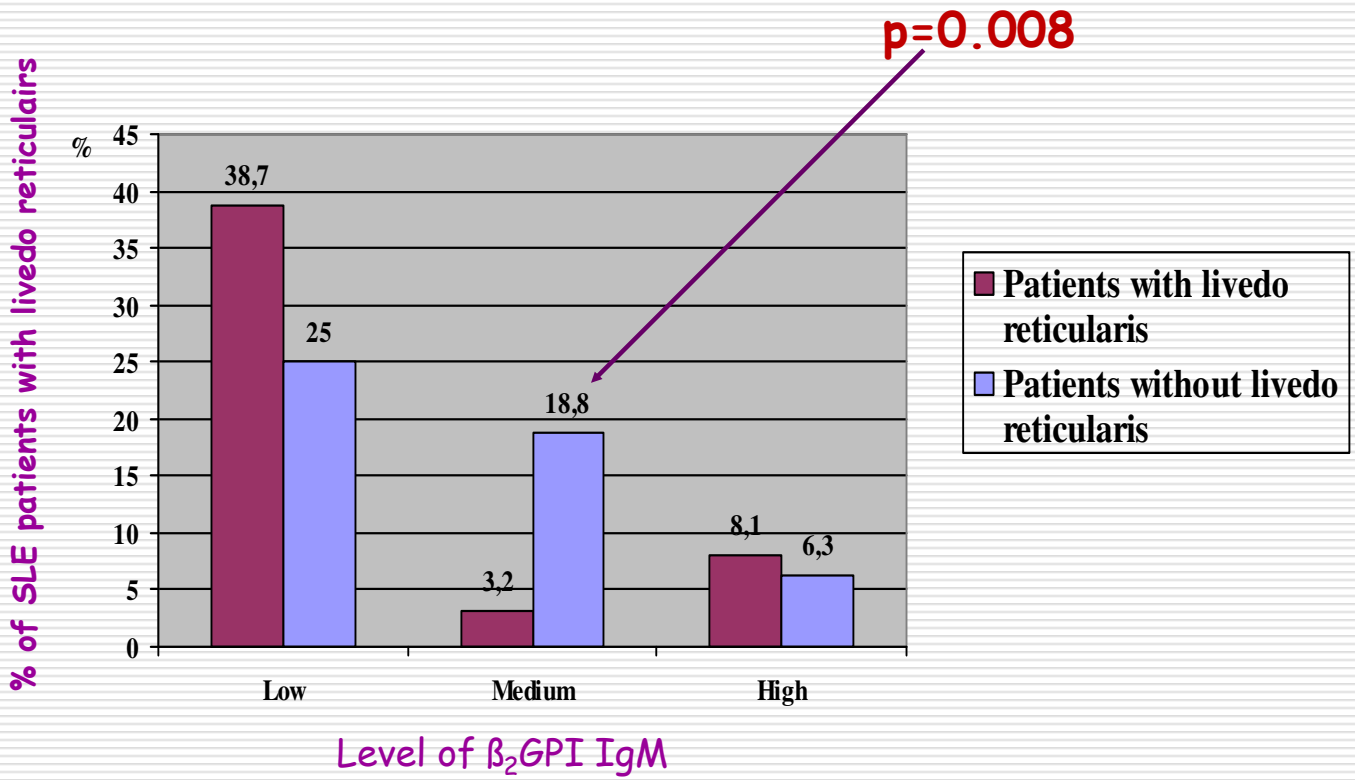
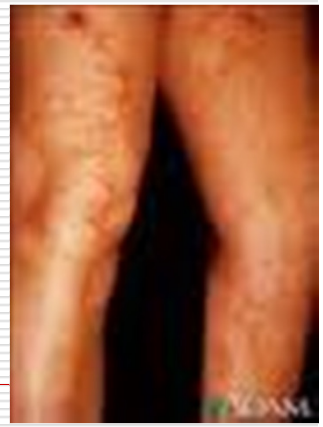
ß$_2$GPI IgM levels in SLE with and without livedo reticularis





Stojanovich L, MD, PhD

Comparisons between Pulmonary Manifestations and Gender in PAFS

	Male N=54	Female N=159	p
Pulmonary embolism and infarction	18.5%	13.2%	0.464
Primary pulmonary hypertension	1.9%	1.3%	0.999
Secondary pulmonary hypertension	13%	3.2%	0.019*
Major pulmonary arterial thrombosis	3.7%	1.9%	0.814
Pulmonary microthrombosis	24.1%	13.3%	0.099
Acute respiratory distress syndrome	5.6%	1.3%	0.203

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Autoimmunity Reviews 5 (2006) 344–348

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Review

Pulmonary manifestations in antiphospholipid syndrome

Ljudmila Stojanovich *

Medical Center "Bezhanijska Kosa", Belgrade University, Department of Internal Medicine/Rheumatology, Belgrade 11080, Bezanijski put bb, Serbia

Received 18 January 2006; accepted 6 February 2006
Available online 3 March 2006

Comparisons between Pulmonary Manifestations and Gender in SAFS

	Male N=13	Female N=99	P
Pulmonary embolism and infarction	15.4%	7.1%	0.621
Primary pulmonary hypertension	0	0	/
Secondary pulmonary hypertension	0%	2%	0.999
Major pulmonary arterial thrombosis	0%	2%	0.999
Pulmonary microthrombosis	23.1%	6.1%	0.114
Acute respiratory distress syndrome	0%	3%	0.999

Scand J Rheumatol 2012;iFirst article:1–4

Pulmonary events in antiphospholipid syndrome: influence of antiphospholipid antibody type and levels

L Stojanovich[1], M Kontic[2], A Djokovic[1], N Ilijevski[3], N Stanisavljevic[1], D Marisavljevic[1]

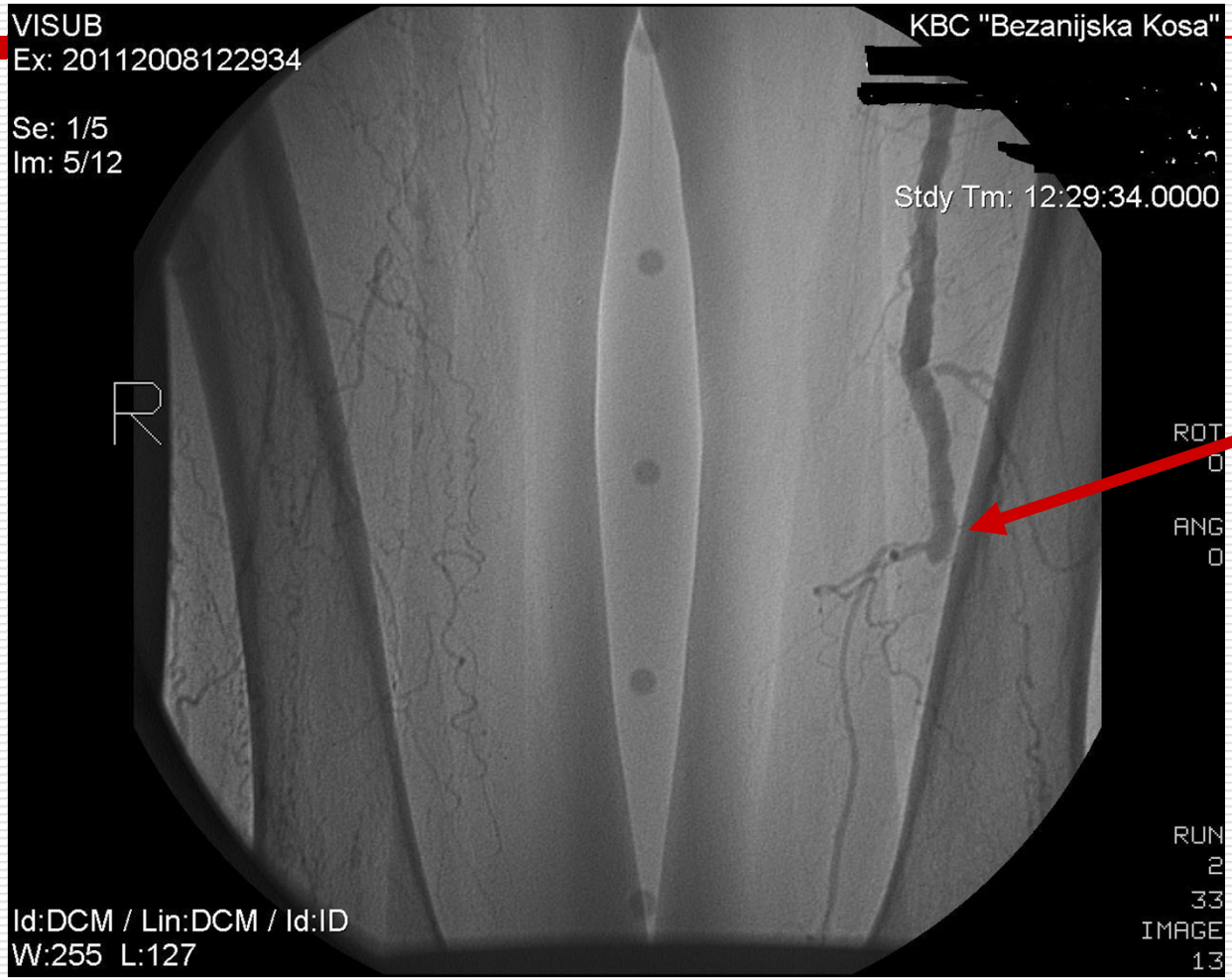
[1]Internal Medicine, 'Bezanijska Kosa', University Medical Centre, Belgrade, [2]Pulmonology Clinic, Clinical Centre of Serbia, University in Belgrade, and [3]Institute of Cardiovascular Disease 'Dedinje', Belgrade, Serbia

Patient Outcome
After 10 years follow-up

Stable condition	367pts from *383* pts	96.9%
Exitus letalis *	16pts from *383* pts	2.8%

*5 with CAPS

Trombosis *a.femoris superfic.lat.sin.* in APS /MSCT-angiography



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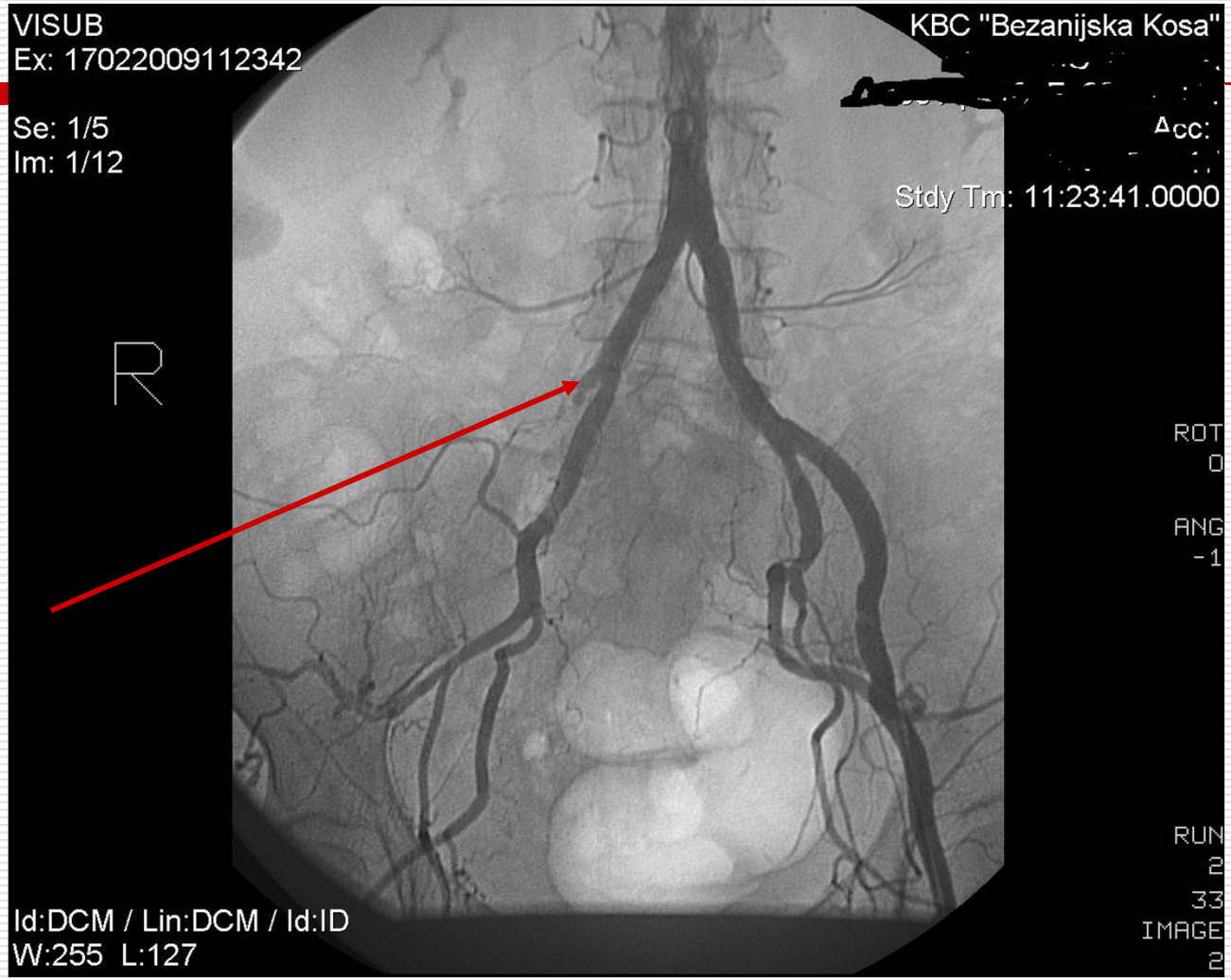
Thrombosis *a.iliaca esterna lat.dex* in APS/MSCT-angiography



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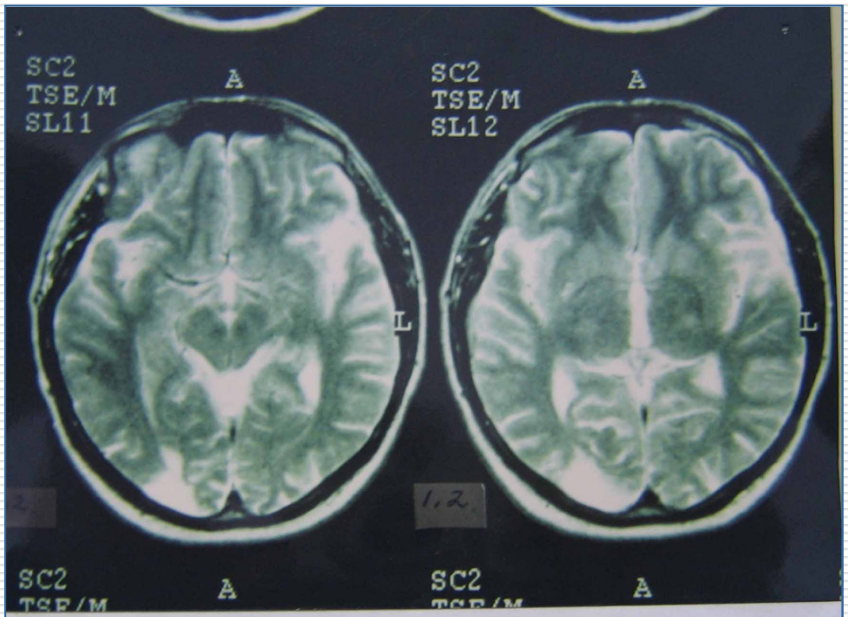
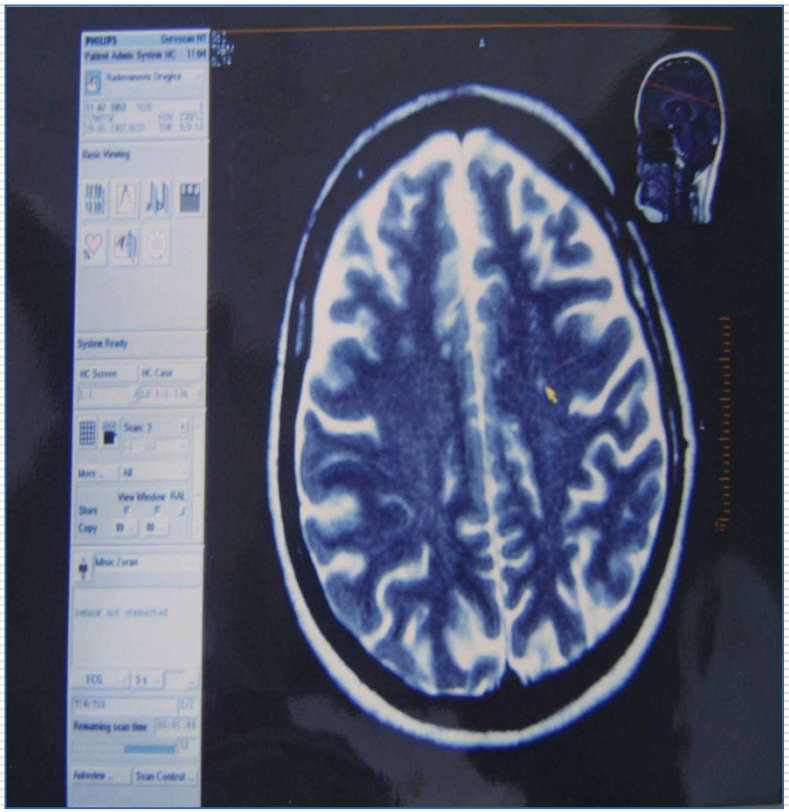
Multiple cerebral infarctions in APS pts



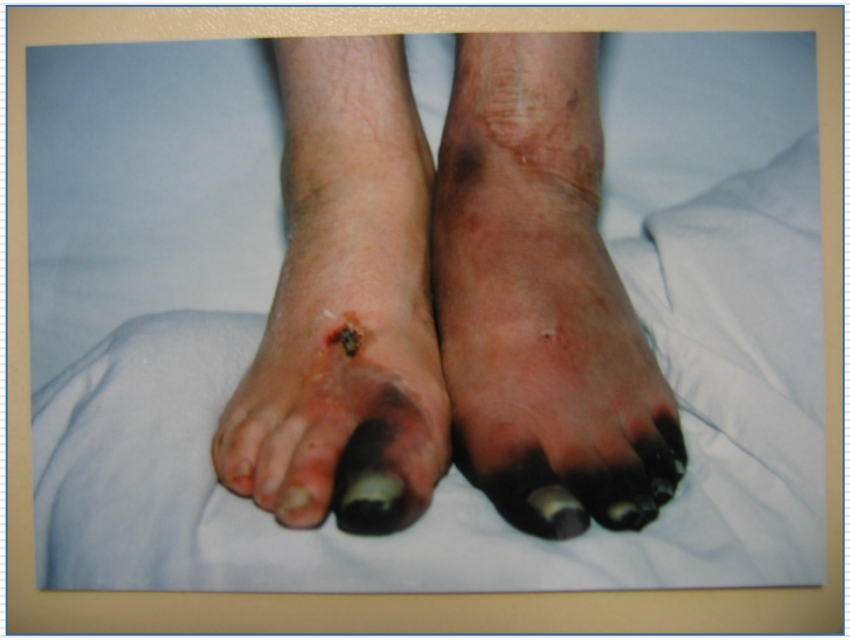
An axial T_2-w image of the brain supraventricular section of a 32–year-old man with a clinical presentation of chorea, livedo reticularis, and antiphospholipid antibodies. This T_2-weighted image shows old left and right cerebral infarctions.

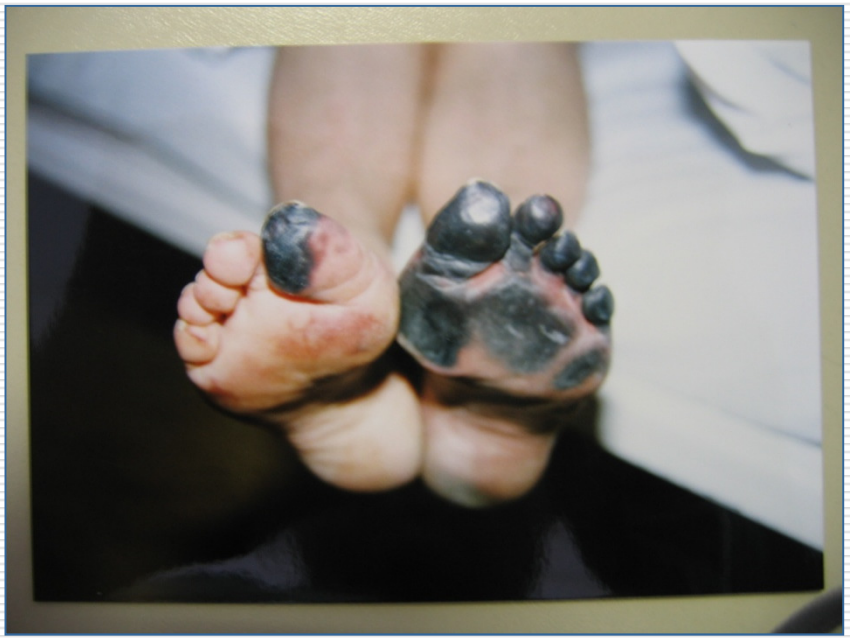


Stojanovich L, MD, PhD

Peripheral Arterial Thrombosis
(*foot arterial*)

Patients with Digital Gangrene





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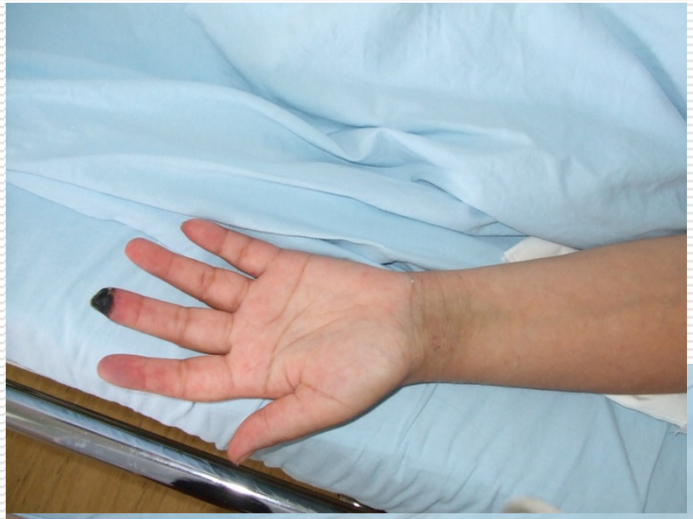
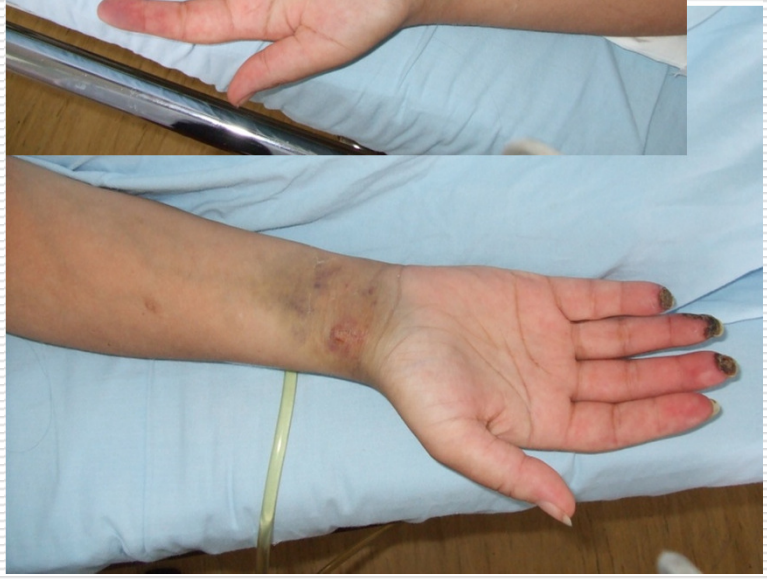
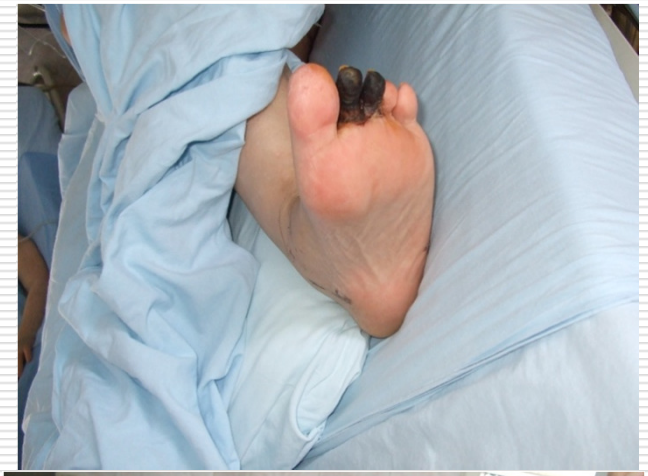
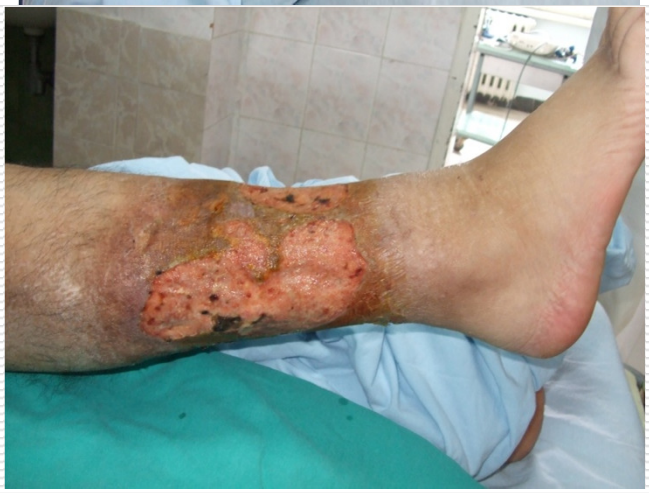
Peripheral Thrombosis
Patient with Digital Gangrene/CAPS









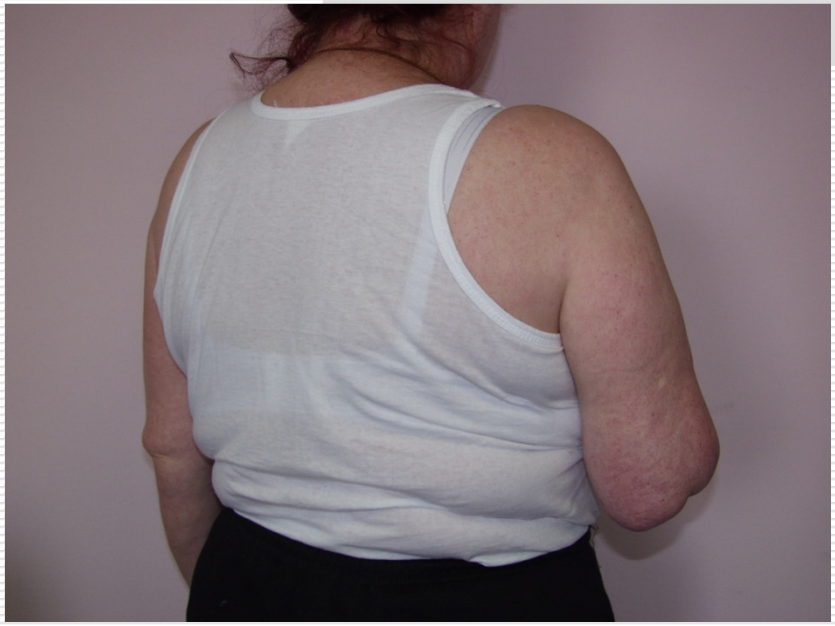
Stojanovich L, MD, PhD

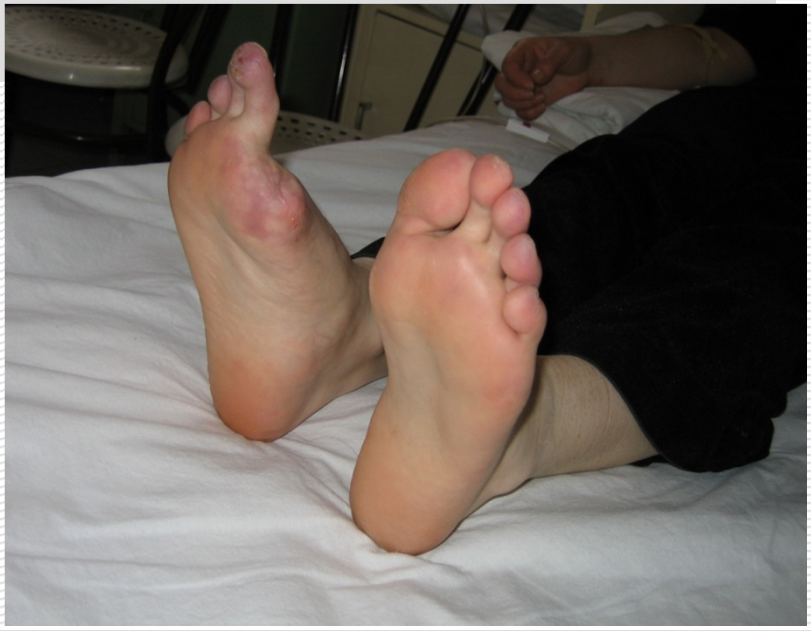
VASCULITIS AND VASCULOPATHY

Amputation of Digits or Limbs in Patients with Antiphospholipid Syndrome

Ronald A. Asherson, MD, FACP, FRCP,*
Ricard Cervera, MD, PhD, FRCP,† Evandro Klumb, MD,‡
Ljudmila Stojanovic, MD,§ Piercarlo Sarzi-Puttini, MD,¶ Janet Yinh, MD,‖
Silvia Bucciarelli, MD, PhD,† Gerard Espinosa, MD, PhD,†
Roger Levy, MD,** and Yehuda Shoenfeld, MD, FRCP††

Digital gangrene/with amputations





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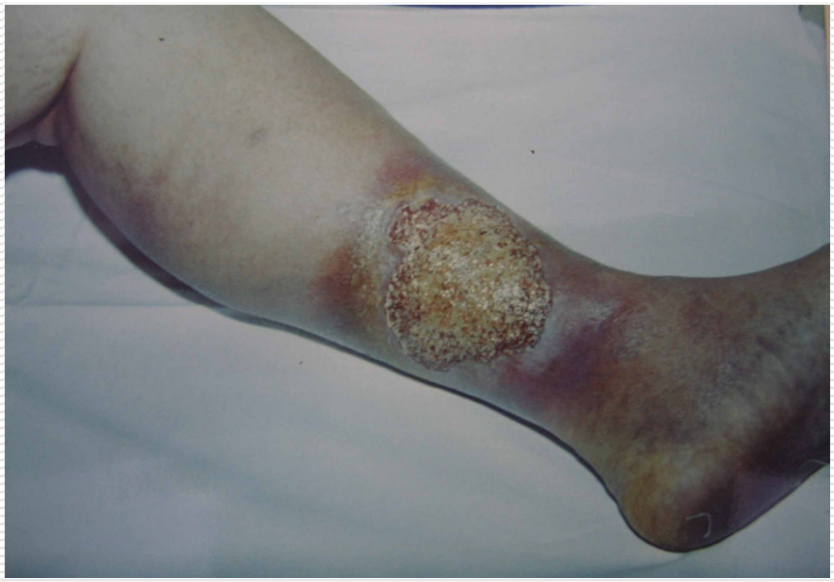
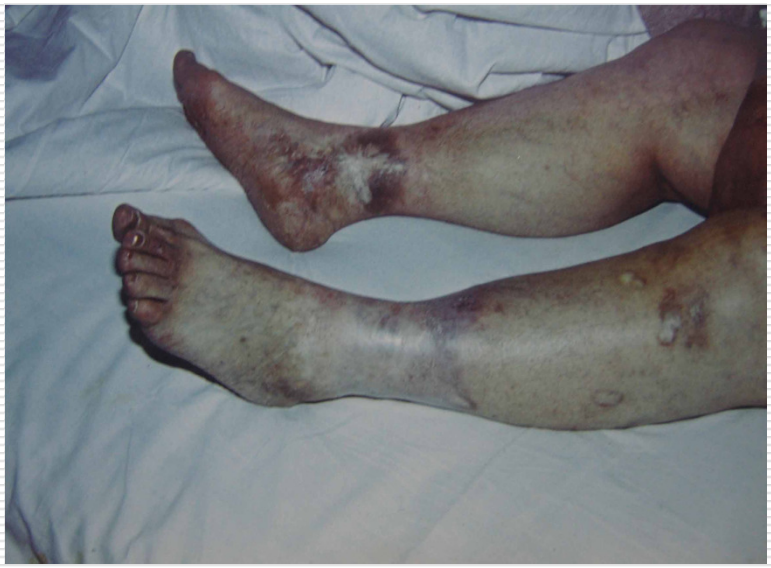
APS Patients with Deep Venous Thrombosis





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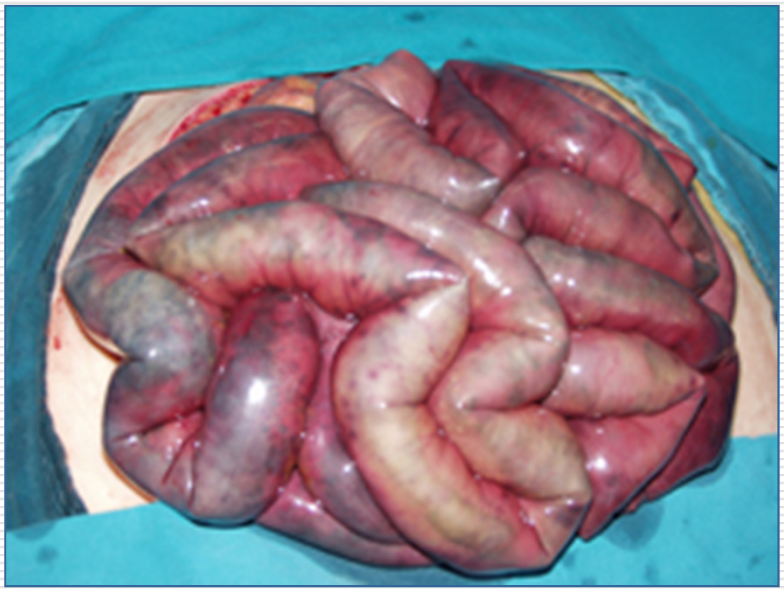
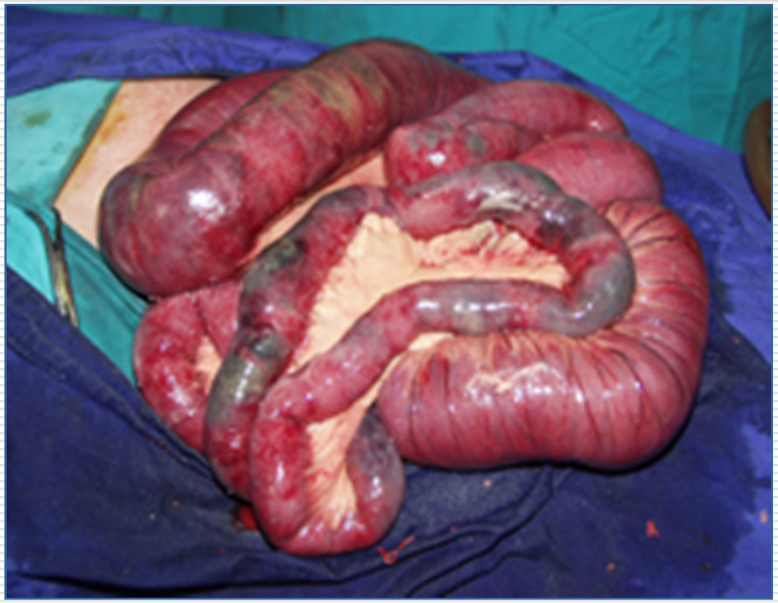
APS Patient with *Mesenteries Thromboses*





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Wrapping up

- ✓ The Serbian National APS Registry allowed us to ascertain a significantly increased incidence of thrombosis in PAPS patients, as compared to SLE patients with secondary APS.
- ✓ CAPS is 4 times more common in our national registry group of patients than in others. This may be due to prolonged stress, and to a high number of smoking patients.
- ✓ Patients over 45 years of age were at a higher risk for arterial thrombosis, particularly for cerebral ischemic attack and myocardial infarction.

Wrapping up

- ✓ LA positivity was a risk factor for deep venous thrombosis and CVI in PAPS patients, and for CVI and pulmonary embolism in SLE patients.
- ✓ The activity of SLE (SLEDAI) was in significant correlation with the prevalence of thrombosis.

Wrapping up

- ✓ The prevalence of thrombosis was similar in all antibody category groups. Any aPL level and type is risk factor for thrombotic event in ours APS patients.
- ✓ After 10 years follow-up, we observed no thrombotic manifestations in any patients with high aPL levels. *All patients were treated according to international protocols*

Lupus (2011) 0, 1–8

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Influence of antiphospholipid antibody levels and type on thrombotic manifestations: results from the Serbian National Cohort Study

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Acknowledgements

With grateful thanks to my colleagues












Questions?

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