CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

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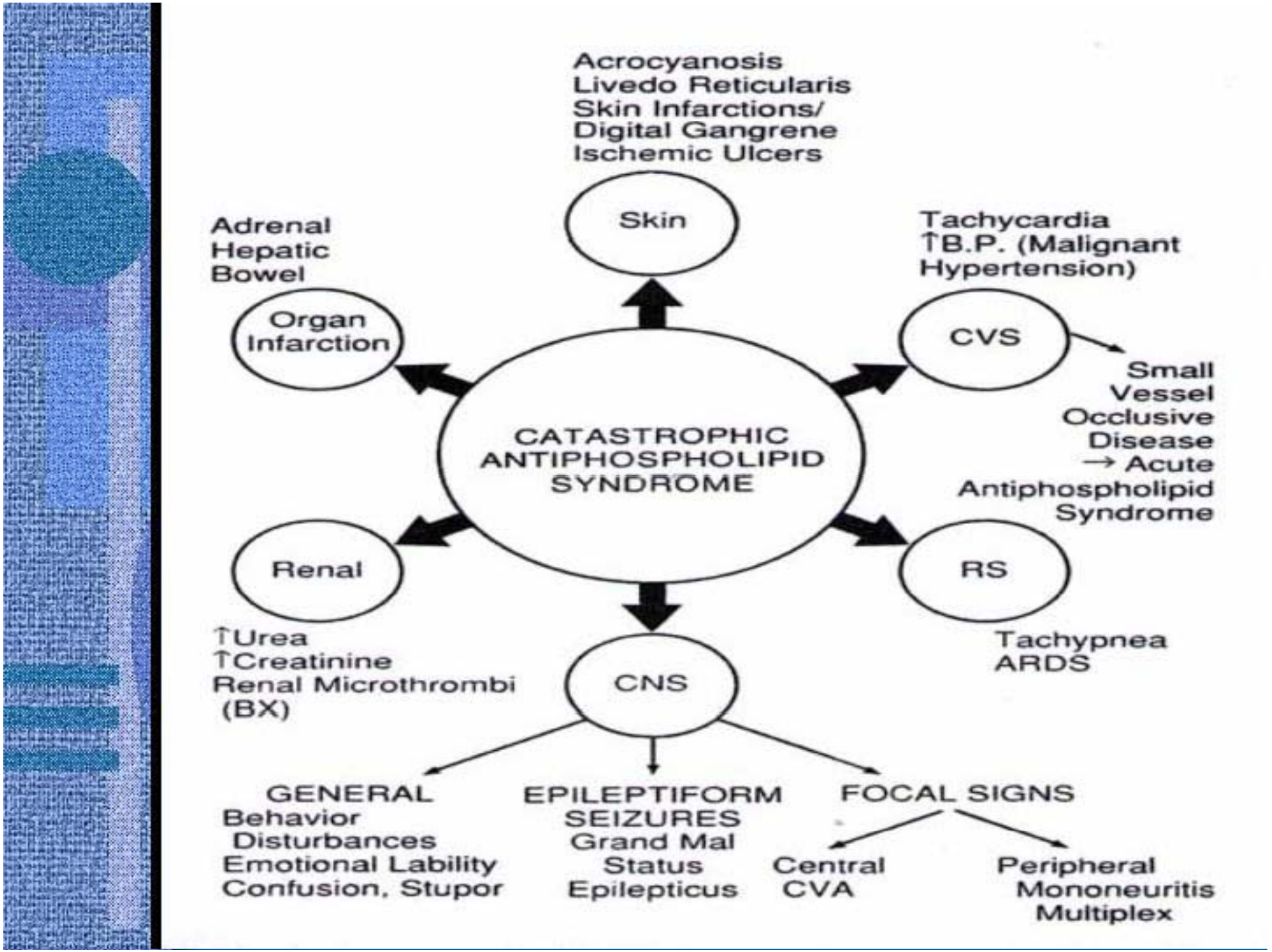
Servei de Malalties Autoimmunes
1995-2005


Acrocyanosis
Livedo Reticularis
Skin Infarctions/
Digital Gangrene
Ischemic Ulcers
Skin
Adrenal
Hepatic
Bowel
Organ
Infarction
Tachycardia
↑B.P. (Malignant
Hypertension)
CVS
Small
Vessel
Occlusive
Disease
→ Acute
Antiphospholipid
Syndrome
CATASTROPHIC
ANTIPHOSPHOLIPID
SYNDROME
Renal
↑Urea
↑Creatinine
Renal Microthrombi
(BX)
RS
Tachypnea
ARDS
CNS
GENERAL
Behavior
Disturbances
Emotional Lability
Confusion, Stupor
EPILEPTIFORM
SEIZURES
Grand Mal
Status
Epilepticus
FOCAL SIGNS
Central
CVA
Peripheral
Mononeuritis
Multiplex

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME
Epidemiology

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

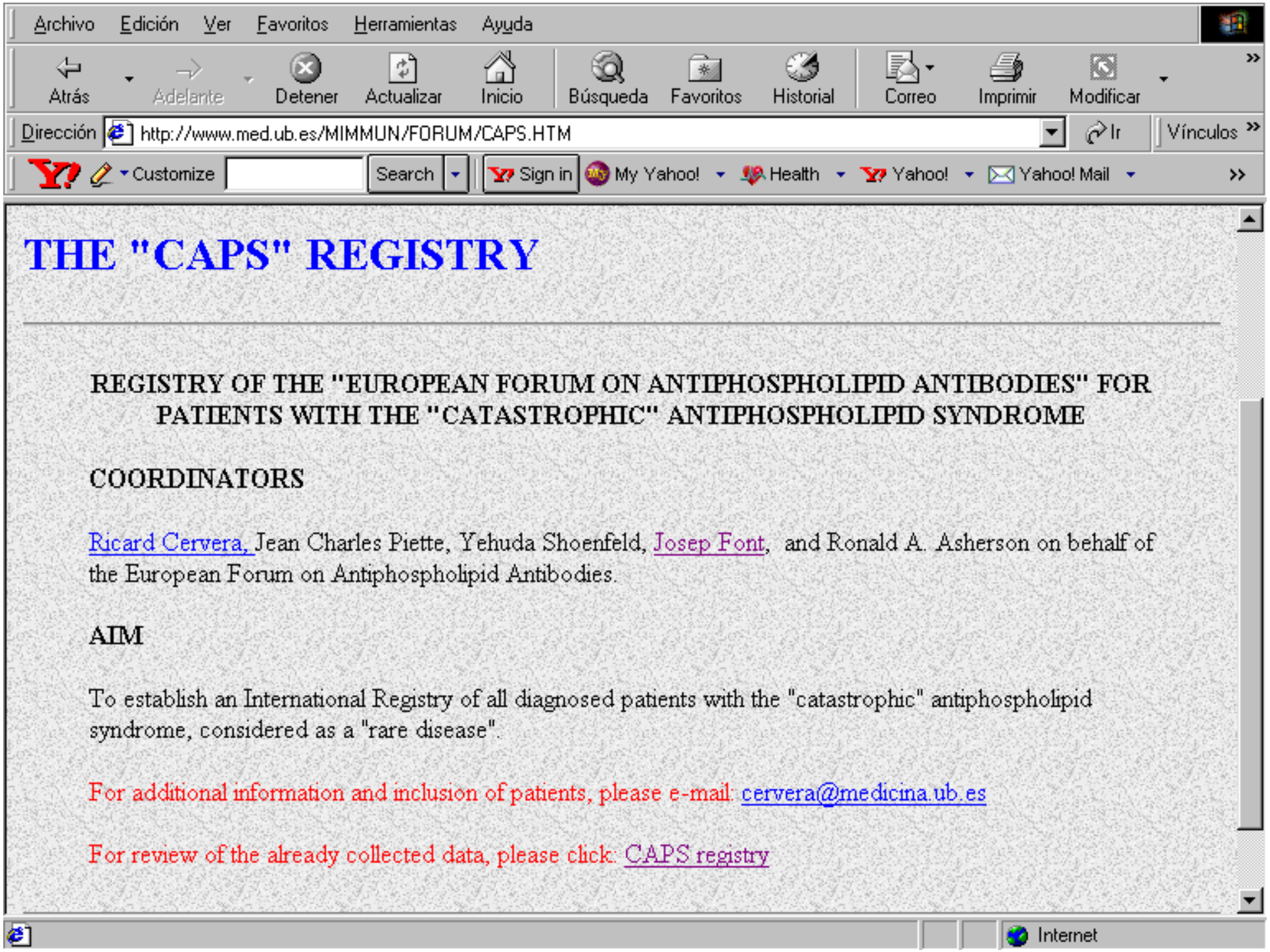
CAPS: 1% of APS

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

UPDATE IN DIAGNOSIS

THE "CAPS" REGISTRY
International Registry of Patients with Catastrophic APS

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


Archivo Edición Ver Favoritos Herramientas Ayuda
Atrás Adelante Detener Actualizar Inicio Búsqueda Favoritos Historial Correo Imprimir Modificar
Dirección http://www.med.ub.es/MIMMUN/FORUM/CAPS.HTM
Ir Vínculos
Customize Search Sign in My Yahoo! Health Yahoo! Yahoo! Mail
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

CATASTROPHIC APS:
Presenting Manifestations (I)

CARDIOPULMONARY INVOLVEMENT	**25%**
Acute respiratory failure/dyspnea	**13%**
Chest pain	**5%**
Pulmonary embolism	**4%**
Cardiac failure	**3%**
Myocardial infarction	**1%**
CNS INVOLVEMENT	**22%**
ABDOMINAL PAIN	**22%**
RENAL INVOLVEMENT	**14%**
Renal failure	**13%**
Hematuria	**1%**

CAPS Registry, 2005

CATASTROPHIC APS:
Presenting Manifestations (II)

CUTANEOUS INVOLVEMENT	**9%**
Digital necrosis/gangrene	**5%**
Ulcers	**3%**
Purpura	**1%**
FEVER	**10%**
OTHER MANIFESTATIONS	
Leg pain	**4%**
Arterial thrombosis	**1%**
Multiple organ thrombosis	**1%**
Adrenal failure	**1%**

CAPS Registry, 2005

CATASTROPHIC APS
Frequency of System Involvement (I)

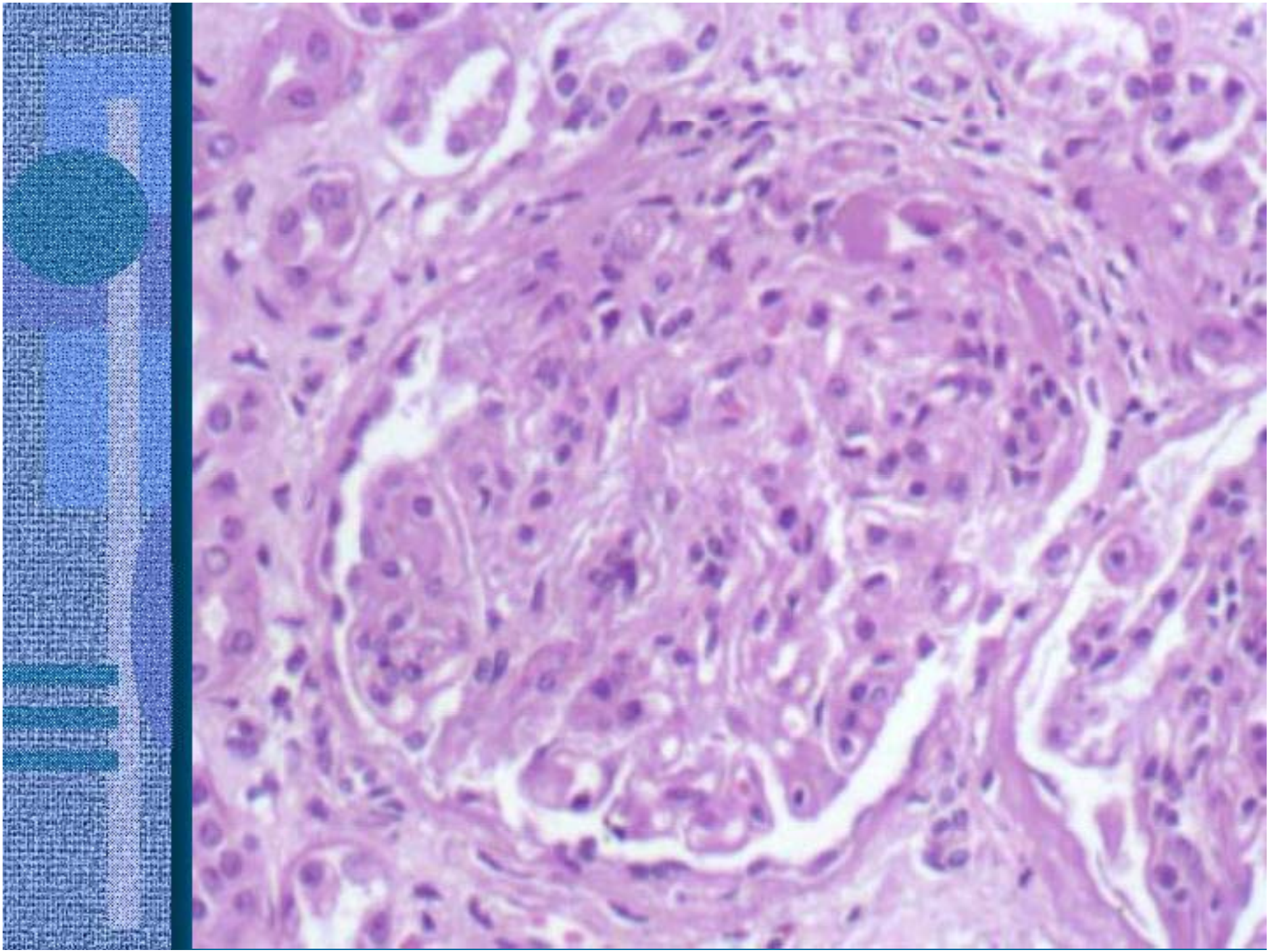
INTRAABDOMINAL	**83%**
Renal	**72%**
Hepatic	**37%**
Splenic	**17%**
Gastrointestinal	**14%**
Pancreatic	**11%**
Adrenal	**10%**

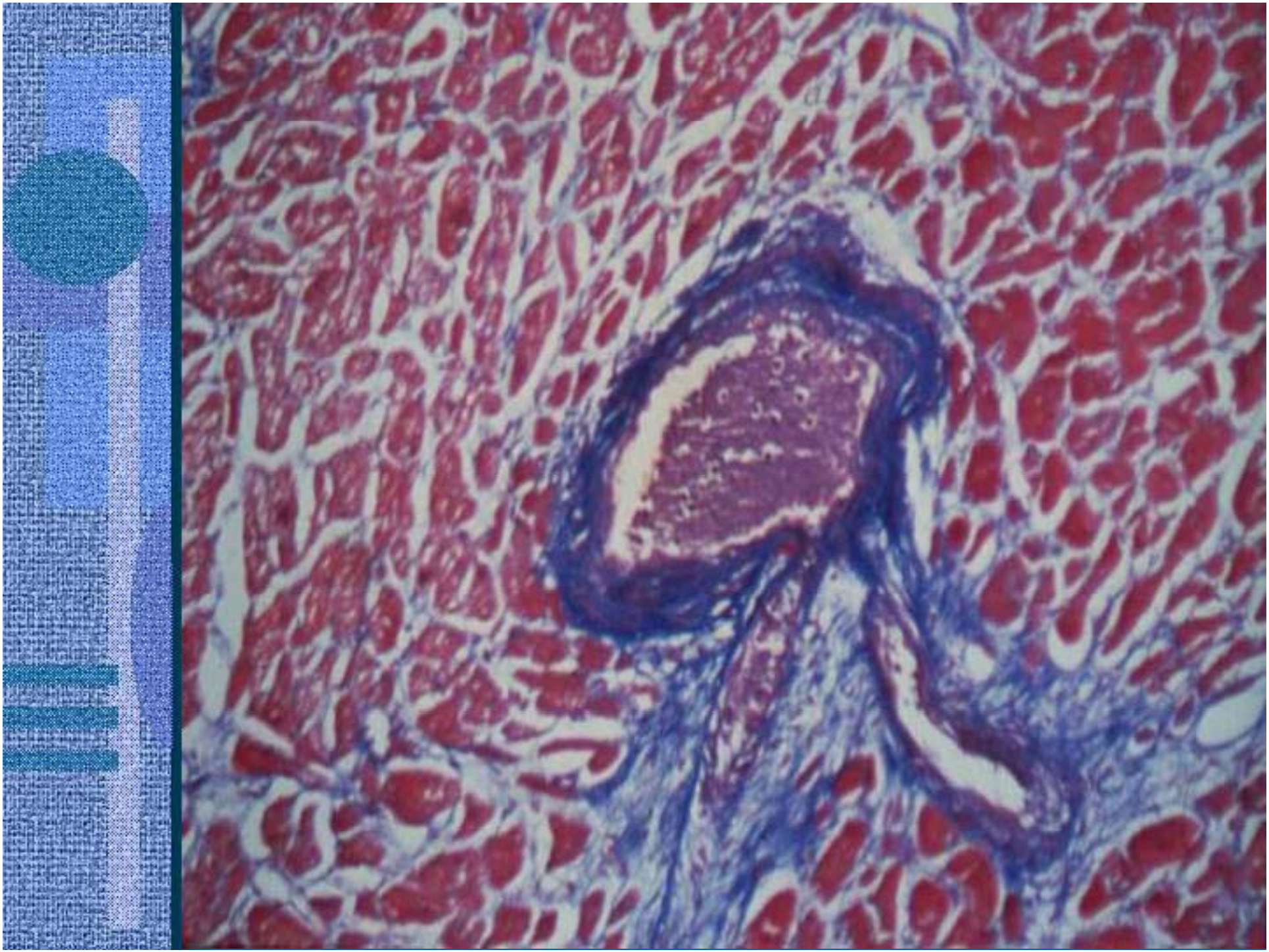
CAPS Registry, 2005

CATASTROPHIC APS
Frequency of System Involvement (II)

PULMONARY	**64%**
CEREBROVASCULAR	**61%**
CARDIAC	**55%**
CUTANEOUS	**52%**
OTHER	
Venous thrombosis	**27%**
Peripheral arterial thromb.	**11%**
Bone marrow necrosis	**10%**

CAPS Registry, 2005





Lupus (2003) 12, 530–534
www.lupus-journal.com

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

RA Asherson[1], R Cervera[2]*, PG de Groot[3], D Erkan[4], M-C Boffa[5], J-C Piette[5], MA Khamashta[6] and Y Shoenfeld[7]
for the Catastrophic Antiphospholipid Syndrome Registry Project Group[†]

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

CATASTROPHIC APS

International consensus for classification criteria

1. Clinical evidence of vessel occlusions affecting 3 or more organs or systems.
2. Development of the manifestations simultaneously or in less than a week.
3. Confirmation by histopathology of small vessel occlusion in at least one organ.
4. Serological confirmation of the presence of aPL (LA and/or aCL).

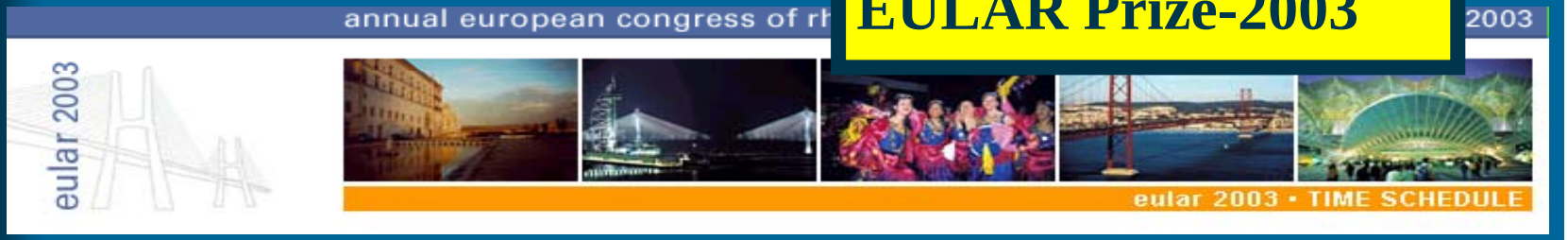
-**Definite catastrophic APS**: All 4 criteria.

-**Probable catastrophic APS**:

-1, 2 & 4

-1, 3 & 4 and the development of the third event in more than a week but less than a month, despite anticoagulation

EULAR Prize-2003



ANALYSIS OF THE INTERNATIONAL CONSENSUS STATEMENT ON PRELIMINARY CLASSIFICATION CRITERIA FOR CAPS USING THE "CAPS REGISTRY"

Cervera R and Asherson RA, for the "CAPS Registry Project Group".

"Definite" CAPS: 72/147 (49%)

"Probable" CAPS: 60/147 (41%)

Sensitivity: 89%

Specificity: 100%.

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

UPDATE IN TREATMENT

CATASTROPHIC APS
Treatment (I)

Anticoagulation (IV Heparin followed by coumadin)	84%
Steroids (high dose IV)	80%
Cyclophosphamide	35%
Plasma exchange	20%
IV Gammaglobulin	19%

CAPS Registry, 2005

CATASTROPHIC APS
Treatment (II)

Hemodialysis	6%
Fibrinolytics	6%
Prostacyclin	5%
Azathioprine	1%
Danazol	1%
Splenectomy	1%
Cyclosporine	1%

CAPS Registry, 2005

CATASTROPHIC APS
Outcome (I)

DEATH	**50%**
SLE	**67%**
Primary APS	**46%**
Hemolytic anemia	**62%**
Microangiopathic anemia	**57%**
Thrombocytopenia	**47%**
DIC	**43%**

CAPS Registry, 2005

CATASTROPHIC APS Outcome (II)

RECOVERY	**50%**	
Plasma exchange		**65%**
Anticoagulants		**63%**
Steroids		**54%**
IV Gammaglobulins		**50%**
Cyclophosphamide		**41%**
AC+St+Pl/IV-GG	**70%**	
AC+St+Pl/IV-GG+Cyclo	**50% (p=0.02)**	

CAPS Registry, 2005

Lupus (2003) 12, 530–534
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Catastrophic antiphospholipid syndrome: international consensus statement on classification criteria and treatment guidelines

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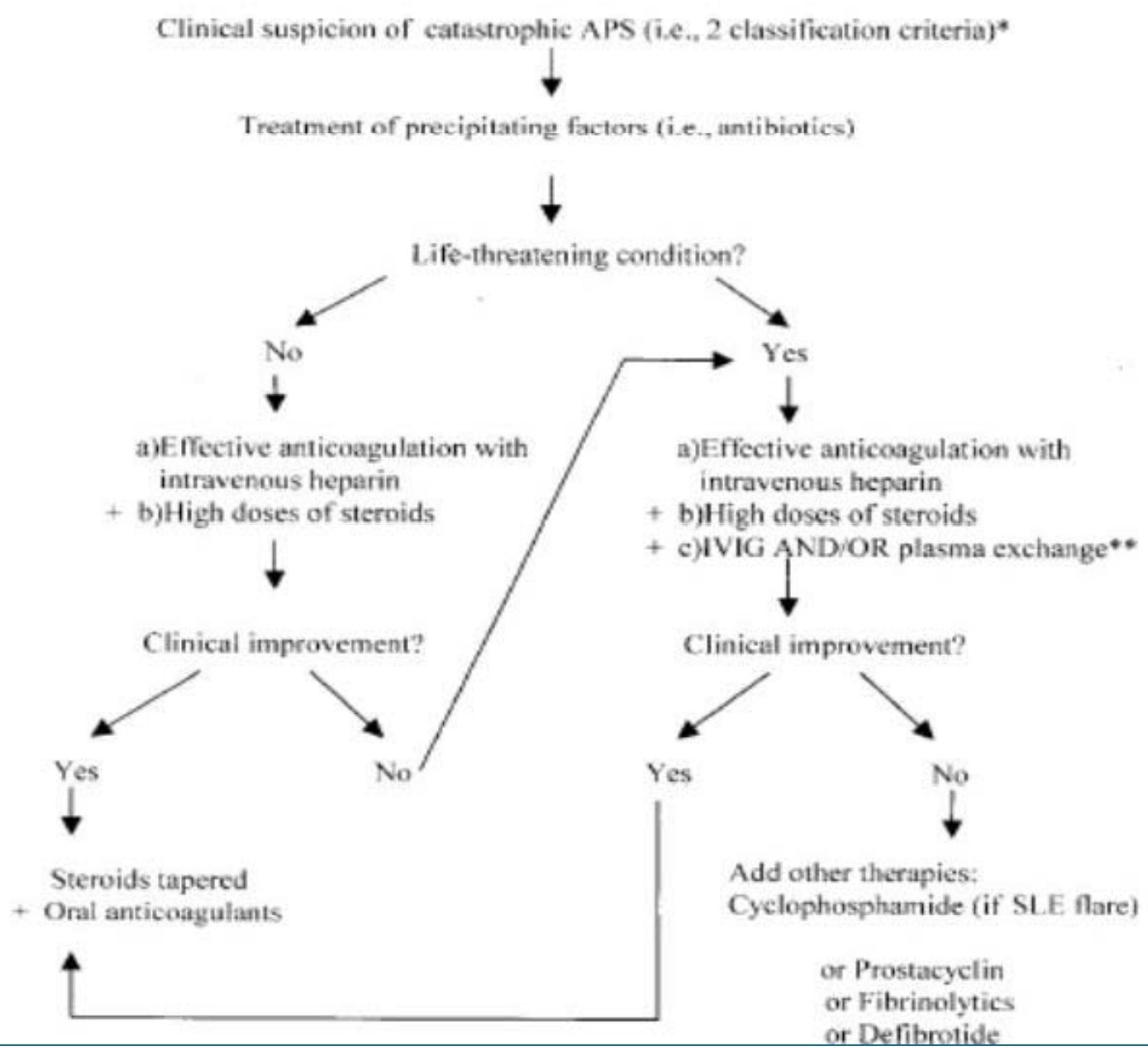

Clinical suspicion of catastrophic APS (i.e., 2 classification criteria)*
Treatment of precipitating factors (i.e., antibiotics)
Life-threatening condition?
No
Yes
a)Effective anticoagulation with intravenous heparin
+ b)High doses of steroids
a)Effective anticoagulation with intravenous heparin
+ b)High doses of steroids
+ c)IVIG AND/OR plasma exchange**
Clinical improvement?
Clinical improvement?
Yes
No
Yes
No
Steroids tapered
+ Oral anticoagulants
Add other therapies:
Cyclophosphamide (if SLE flare)
or Prostacyclin
or Fibrinolytics
or Defibrotide

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

UPDATE IN PATHOGENESIS

CATASTROPHIC APS:
Precipitating Factors (I)

INFECTIONS	**35%**
Respiratory tract	**15%**
Cutaneous	**8%**
Urinary tract	**6%**
Sepsis	**3%**
Gastrointestinal	**1%**
Other	**9%**

CAPS Registry, 2005

CATASTROPHIC APS:

Precipitating Factors (II)

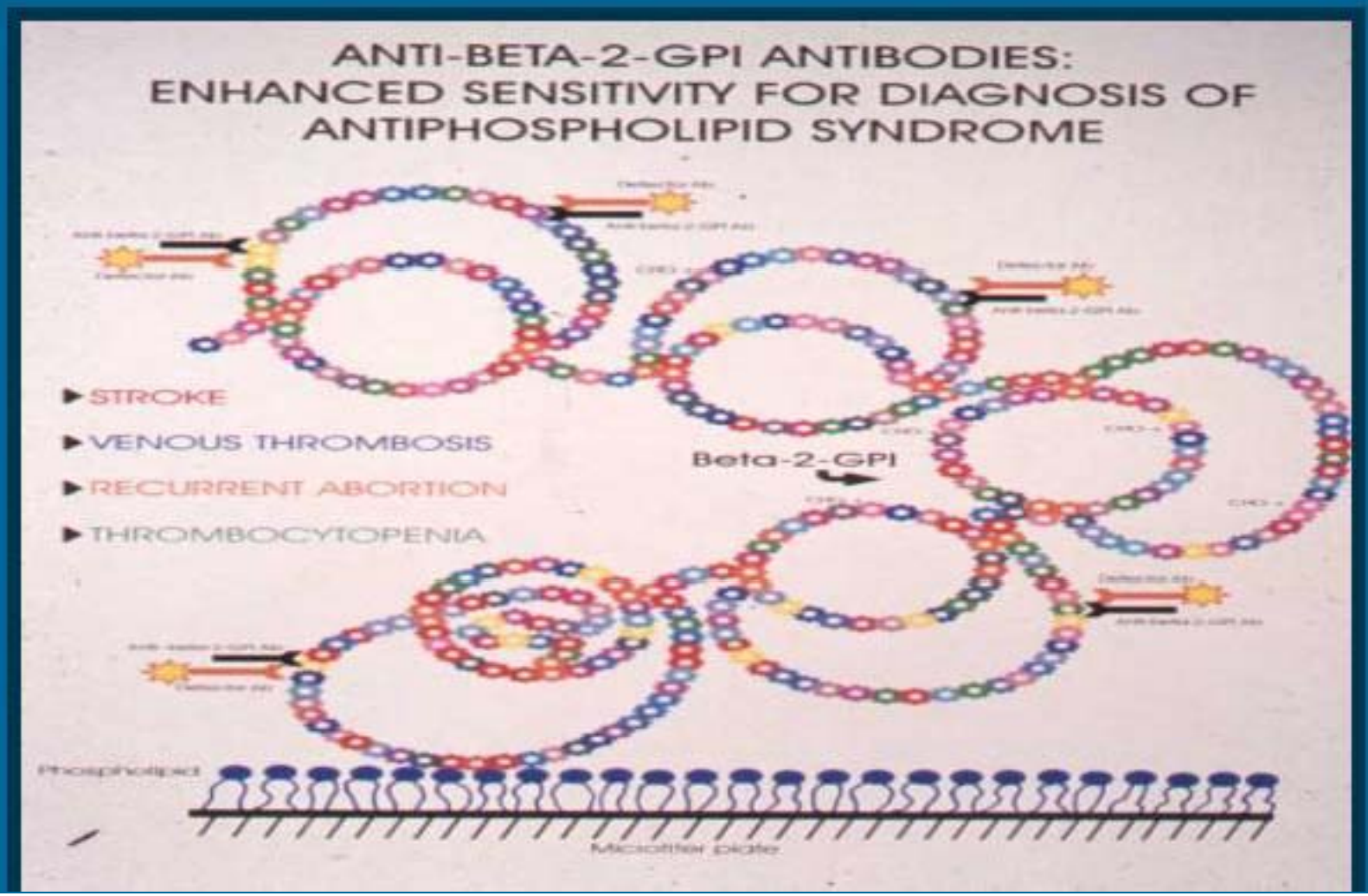
SURGERY, TRAUMA & INVASIVE PROCEDURES	13%
NEOPLASIA	8%
ANTICOAGULATION WITHDRAWAL /LOW INR	8%
OBSTETRIC COMPLICATIONS	6%
SLE FLARES	5%
ORAL CONTRACEPTIVES	3%

NO FACTOR IDENTIFIED	35%

CAPS Registry, 2005

UPDATE IN PATHOGENESIS

Role of Infections



UPDATE IN PATHOGENESIS

Role of Infections

Journal of Clinical Immunology, Vol. 23, No. 5, September 2003 (© 2003)

Prevalence and Clinical Correlations of Antibodies Against Six β2-Glycoprotein-I-Related Peptides in the Antiphospholipid Syndrome

Y. SHOENFELD,[1,21] I. KRAUSE,[1] F. KVAPIL,[1] J. SULKES,[2] S. LEV,[1] P. VON LANDENBERG,[1,3] J. FONT,[4] J. ZAECH,[1,3] R. CERVERA,[4] J. C. PIETTE,[5] M. C. BOFFA,[6] M. A. KHAMASHTA,[6] M. L. BERTOLACCINI,[6] G. R. V. HUGHES,[6] P. YOUINOU,[7] P. L. MERONI,[8] V. PENGO,[9] J. D. ALVES,[10] A. TINCANI,[11] G. SZEGEDI,[12] G. LAKOS,[12] G. STURFELT,[13] A. JÖNSEN,[13] T. KOIKE,[14] M. SANMARCO,[15] A. RUFFATTI,[16] Z. ULCOVA-GALLOVA,[17] S. PRAPROTNIC,[18] B. ROZMAN,[18] M. LORBER,[19] V. B. VRIEZMAN,[20] and M. BLANK[1]

UPDATE IN PATHOGENESIS

Role of Infections

Antibodies against	Entire APS population (n=503)	Primary APS (n=276)	SLE with secondary APS (n=184)
Peptide A	36.2	37.3	34.2
Peptide B	47.5	47.8	45.1
Peptide C	16.7	19.2	14.1
P274-280	59.0	66.2	50.3
P244-264	62.0	63.0	60.2
P276-290	52.1	53.6	52.5

J Clin Immunol 2003

UPDATE IN PATHOGENESIS

Role of Infections

RESULTS

- **Anti-peptide C Abs** were significantly correlated with **recurrent abortions** (35.8% vs. 19.8%, $p<0.005$).

- **Anti-P274-280 Abs** were associated with **toxemia** (12.4% vs. 5.6%, $p<0.03$) and with **recurrent abortions** (25.7% vs. 15.2%, $p<0.02$).

- **Anti-P244-264** were associated with **cardiac valves abnormalities** (19.0% vs. 11.5%, $p<0.05$).

J Clin Immunol 2003

UPDATE IN PATHOGENESIS

Role of Infections

Journal of Clinical Immunology, Vol. 24, No. 1, January 2004 (© 2004)

Antiphospholipid Syndrome Infectious Origin

M. BLANK, R. A. ASHERSON, R. CERVERA, and Y. SHOENFELD[1,4]

J Clin Immunol 2004; 24: 12-23

Table III. Antiphospholipid Abs Detected in Diverse Infections and β2GPI Peptide Homologies Shared with Structures in These Pathogens

	Infections associated with circulating anti-PL Abs	TLRVYK (38)[a]	LKTPRV (38)	KDKATF (38)	GDKVSFF (49)	GRTCPKP-DDLP (53)
Viral						
CMV	+		+		+	
EBV	+	+				
HIV	+	+2[b]	+			
Hepatitis C	+					
Parvovirus B19	+					
Adenovirus	+		+			
Varicella	+					
Vaccinia	+	+2				
Mumps	+					
Rubella	+					
HTLV-1	+					
Herpesvirus	−				+	
Bacterial						
Leprosy	+					
Tuberculosis	+	+	+			
M. pneumoniae, M. penetrans	+					
Salmonella	+	+, *typhi*				
Staphylococci	+	+	+	+		
Streptococci	+	+, *pyogenes*	+, *pyogenes*	+		
Chlamydia	−			+	+	
Trypanosome brucei rhodesiense	−	+				
Coxiella burnetii (riccecia, Q fever)	+		+	+		
Porphyromonas gingivalis	−	+				
Helicobacter pylori	+	+	+2			+3
Haemophilus influenzae	−	+		+		

J Clin Immunol 2004; 24: 12-23

Table III. Antiphospholipid Abs Detected in Diverse Infections and β2GPI Peptide Homologies Shared with Structures in These Pathogens

	Infections associated with circulating anti-PL Abs	TLRVYK (38)[a]	LKTPRV (38)	KDKATF (38)	GDKVSFF (49)	GRTCPKP-DDLP (53)
Spirochete						
Treponema palidum (syphilis)	+					
Leptospira	+					
Borrelia burgdorferi	+	+	+			
Parasite						
Kala-azar	+					
Schistosoma mansoni	−		+			
Toxoplasmosis	+					
Yeast						
Saccharomyces cervevisiae (Crohn)	+	+	+	+		
Candida albicans	−	+				
Streptomyces lividans	−	+				
Mycoplasma	+		+, *pulmonis, genitalium,*	+, *pneumoniae, capricolum, genitalium, pulmonis*		

J Clin Immunol 2004; 24: 12-23

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

?

Therapeutic Vaccines