

Guy's and St Thomas' Hospital

NHS Trust



**KING'S**  
*College*  
**LONDON**

University of London

# **Situaciones estresantes en el lupus**

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**Director, Lupus Research Unit**

**Barcelona, Noviembre 2008**

# What is Lupus?

GEAS-SEMI



**Lupus is a neurological  
disease and sometimes  
affects other organs**

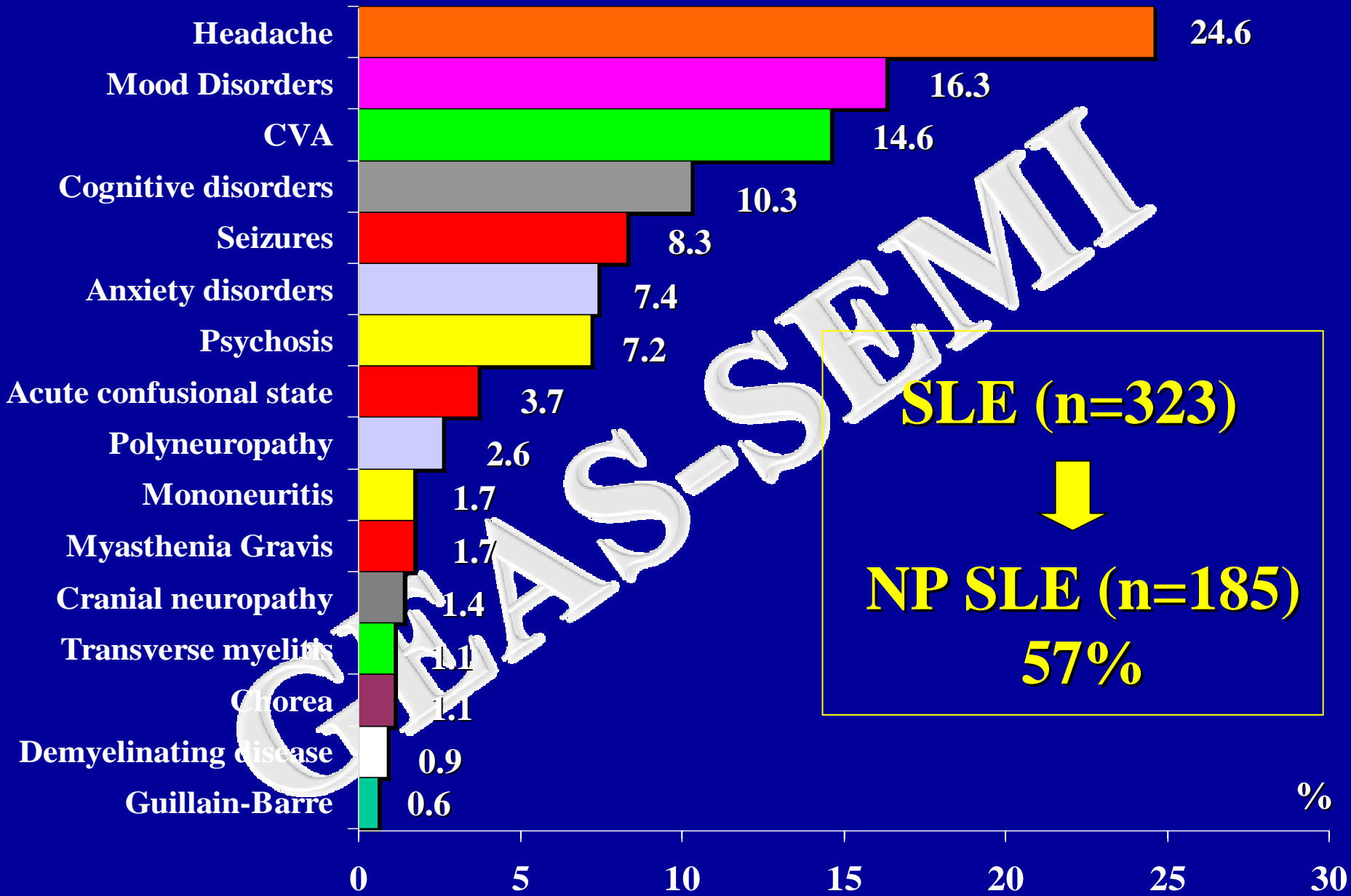
**Prof G Hughes**

# ACR Classification for Neuropsychiatric SLE

- Aseptic meningitis
- Cerebrovascular disease
- Demyelinating syndrome
- Headache
- Movement disorder
- Myelopathy
- Seizure disorders
- Acute confusional state
- Anxiety disorder
- Cognitive dysfunction
- Mood disorder
- Psychosis
- Guillain-Barre syndrome
- Autonomic disorder
- Mononeuropathy
- Myasthenia gravis
- Neuropathy
- Plexopathy
- Polyneuropathy

Arthritis Rheum 1999





# CNS lupus

## Significance of aPL

(Multivariate analysis)

	<u>Odds ratio</u>	<u>95% CI</u>	<u>p value</u>
CVA	6.11	2.79-13.36	<0.00001
Seizures	3.06	1.24-7.57	0.015
Headache	1.82	1.03-3.22	0.039

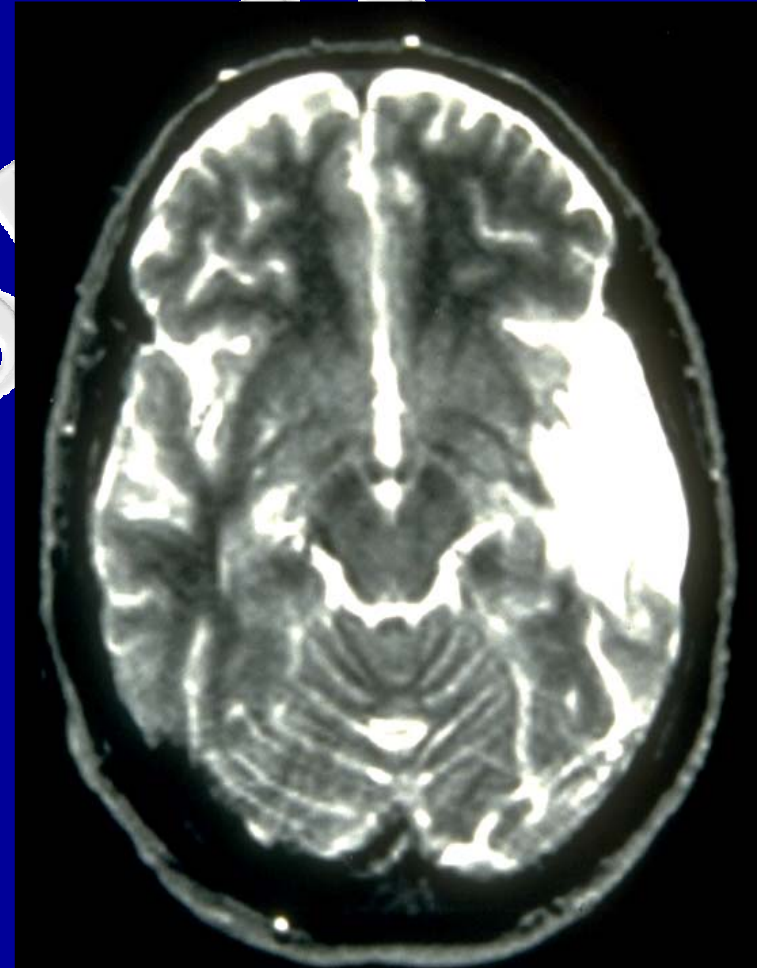
# Stroke in APS

- **Most common neurological complication**
- **Most frequent arterial thrombosis**
- **1:5 in young people (<45 years)**

Nencini et al. Stroke 1992

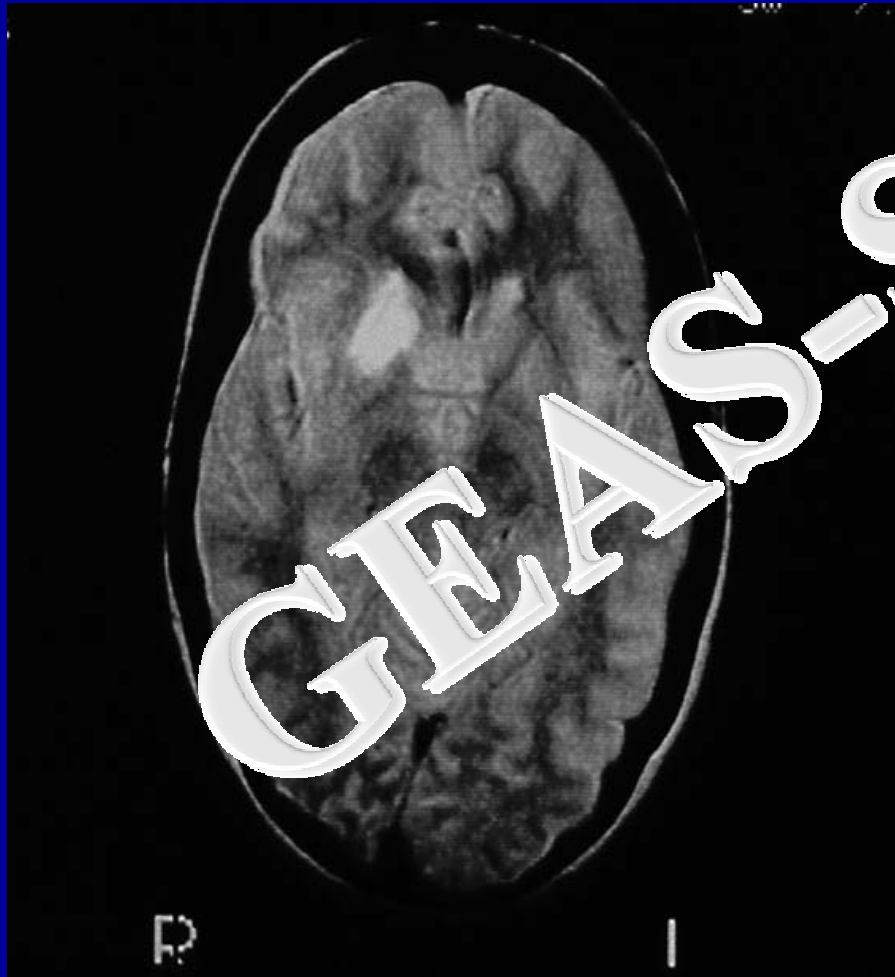
- **Recurrent events frequent**

Levine et al. Ann Neurol 1995





# Sneddon's or APS?



GEAS SEMI

# MS or APS?

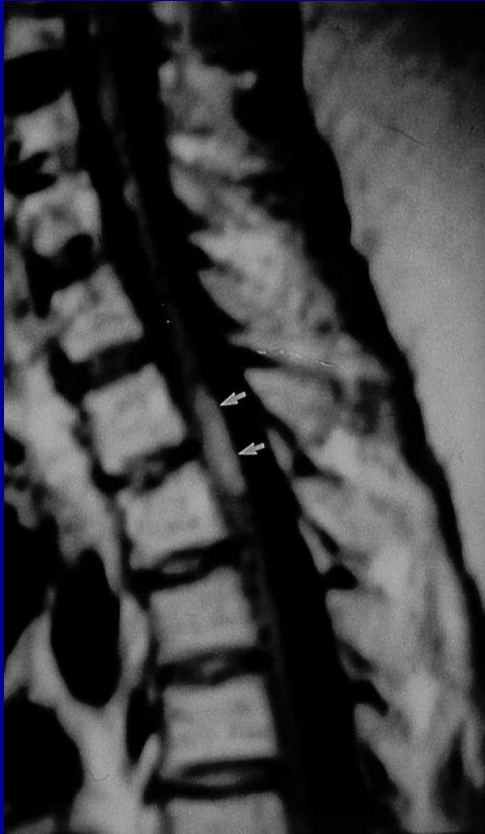


Cuadrado et al. Medicine 2000

# aPL and white matter hyperintensity lesions -“small vessel disease”?



# Transverse myelitis and aPL

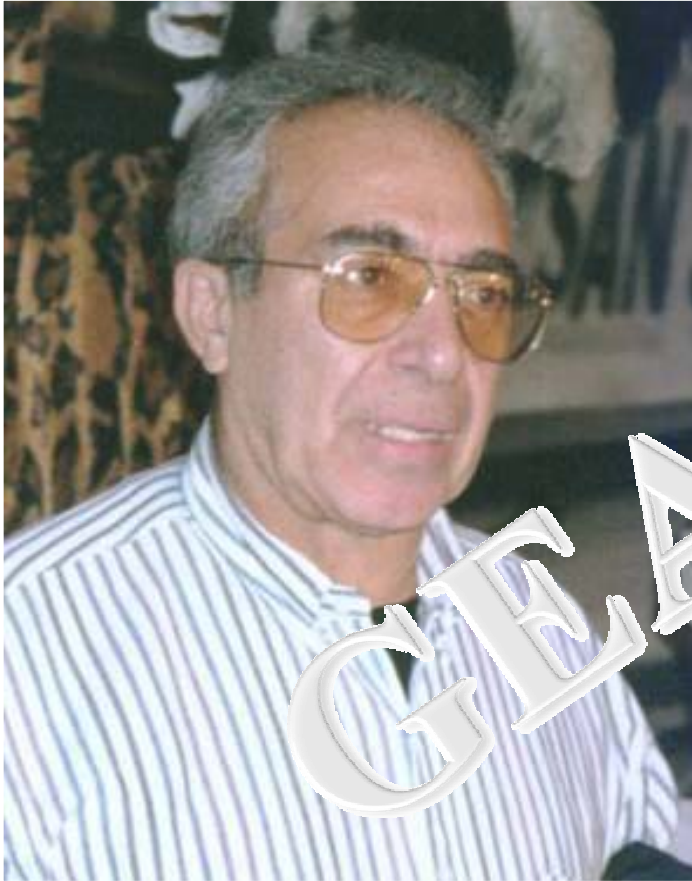


- 15 SLE with TMI as 1<sup>st</sup> manifestation
- 11 (73%) aPL +ve
- Good response to immunosuppressant
- Antiplatelet / anticoagulant in aPL+ve

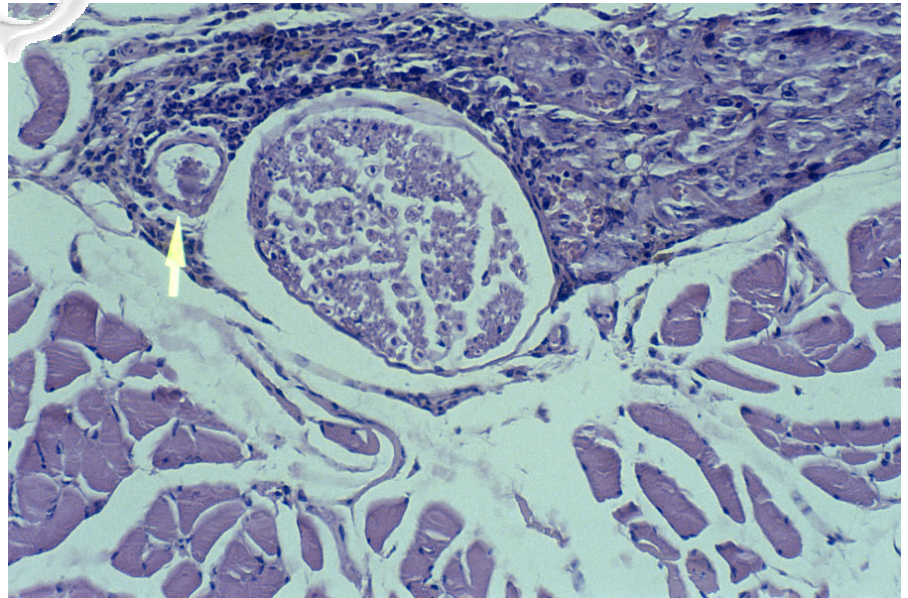


# Transverse myelitis: animal model

**Aziz Gharavi**



**1938 - 2004**



GEAS-SEMI

# **Pulse cyclophosphamide in the treatment of neuropsychiatric systemic lupus erythematosus**

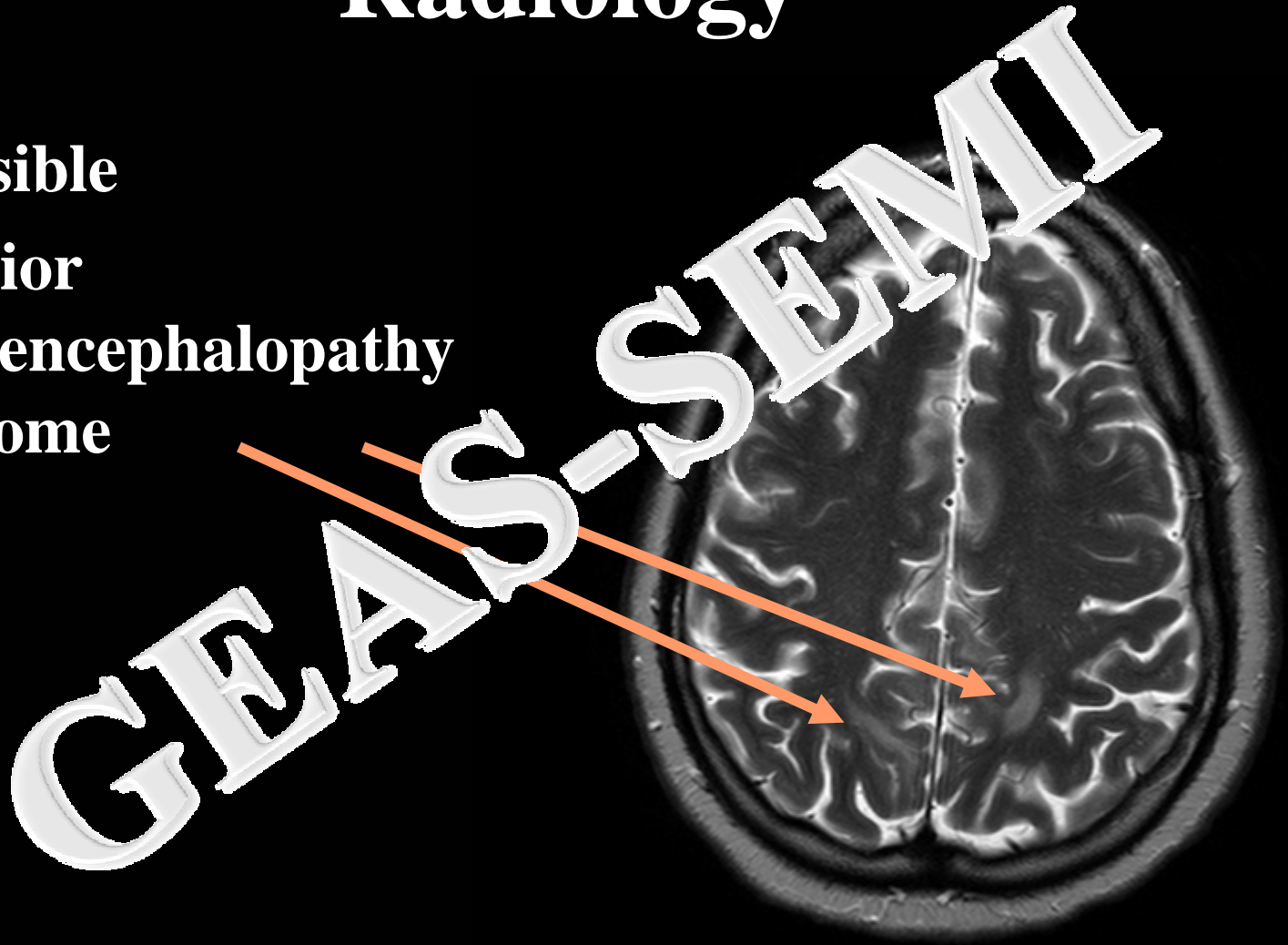
**Ramos PC, Mendez MJ, Ames PR, Khamashta MA, Hughes GR**

**Clin Exp Rheumatol 1996; 14: 295-9**



# Radiology

- Reversible  
Posterior  
Leukoencephalopathy  
Syndrome







# The NEW ENGLAND JOURNAL of MEDICINE

Volume 334:494-500 [February 22, 1996](#) Number 8

## **A Reversible Posterior Leukoencephalopathy Syndrome**

*Judy Hinchey, M.D., Claudia Chaves, M.D., Barbara Appignani, M.D., Joan Breen, M.D., Linda Pao, M.D., Annabel Wang, M.D., Michael S. Pessin, M.D., Catherine Lamy, M.D., Jean-Louis Mas, M.D., and Louis R. Caplan, M.D.*

# Reversible Posterior Leukoencephalopathy Syndrome

- **Acutely rapidly evolving clinical condition characterised by**
  - Headache
  - Nausea & vomiting
  - Abnormalities of visual perception (blurred vision, hemianopia, visual neglect, cortical blindness)
  - Altered alertness and behaviours
  - Mental state abnormalities
  - Seizure (usually generalised)
  - Focal neurological signs

# Reversible Posterior Leukoencephalopathy Syndrome

- Described in
  - Pre-eclampsia/eclampsia
  - Hypertension
  - Hypertensive encephalopathy
  - Renal disease with HTN
  - Immunosuppressive therapy
  - Autoimmune connective tissue disease
  - TTP
  - HIV syndrome
  - Acute intermittent porphyria
  - Organ transplantation
  - Hypercalcaemia



seminars in  
Arthritis and  
Rheumatism

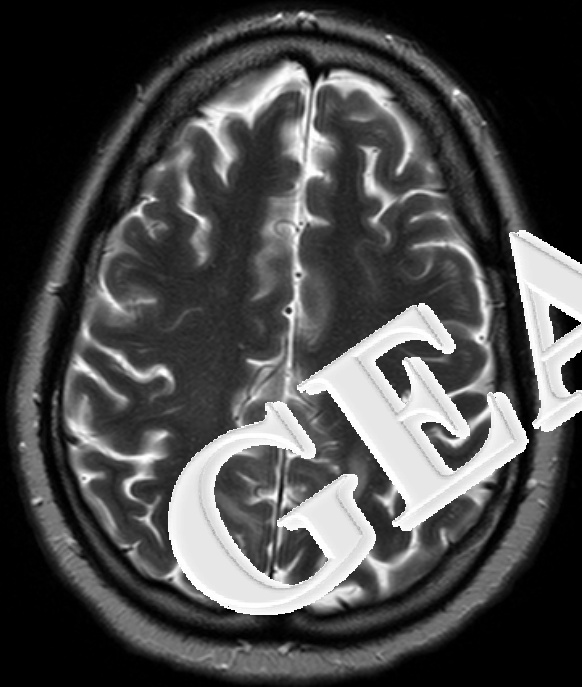
## Reversible Posterior Leukoencephalopathy in Patients with Systemic Lupus Erythematosus

Molly D. Magnano,\* Thomas M. Cash,<sup>†</sup> Ivonne Herrera,<sup>‡</sup> and Roy D. Altman<sup>§</sup>

Semin Arthritis Rheum, 2006 35:296-402

# MRI imaging

- Parieto-occipital subcortical white matter and corresponding cortical regions



# MRI imaging

- **Differential diagnosis**
  - » Sinus thrombosis
  - » Ischemic cerebrovascular pathology



# Pathophysiology

- **Vasogenic oedema**
  - Disruption of auto regulatory mechanism (brain-capillary leak syndrome)
- **Sympathetic innervation**
  - Antero-posterior gradient
  - Reduced innervation of posterior circulation

# Therapy

- Empirical
- Based on clinical experience
- Lack of controlled randomized trials



# Therapeutic approach

## Mild CNS disease

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### Symptomatic therapy

- Analgesic / NSAIDs / calcium antagonists
- Ergotamine
- Anxiolytics
- Antidepressant
- Anticonvulsants
- Antipsychotics
- Low dose corticosteroids

# Therapeutic approach

## Severe CNS disease

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### Diffuse / nonthrombotic

- High-dose corticosteroids
- IV pulse methylprednisolone
- IV pulse cyclophosphamide
- Plasmapheresis
- IV immunoglobulins
- Methotrexate (? intrathecal)
- Azathioprine
- Mycophenolate mofetil
- Rituximab

# Therapeutic approach

## Severe CNS disease

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### Focal / thrombotic – aPL associated

- **Prophylaxis**
  - Low-dose aspirin / Clopidogrel
- **Thrombosis**
  - Long-term warfarin  
INR (3.0 – 4.0)