



<b>Title</b>	<b>Increased apoptotic blood neutrophils and macrophages and decreased clearance of apoptotic neutrophils in systemic lupus erythematosus</b>
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## G-RI-1

### Neuropsychiatric Manifestations in Southern Chinese Patients with Systemic Lupus Erythematosus (SLE) According to the 1999 ACR Nomenclature and Their Clinical Associations

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**Objectives:** To study the prevalence of neuropsychiatric (NP) manifestations in a large cohort of southern Chinese SLE patients according to the new ACR case definitions and their clinical associations.

**Method:** Patients with SLE who were followed between 1984 to 2000 were retrospectively reviewed. NP manifestations were ascertained and classified. The association of NP manifestations with other clinical features and autoantibodies (Ro, La, Sm, nRNP, anticardiolipin antibodies and lupus anticoagulant [LA]) was studied by both univariate and multivariate analysis.

**Results:** 518 SLE patients were studied. The female to male ratio was 7.8 to 1 and the mean age of disease onset was 29.5 (9-80) years. The mean duration of follow up was 7.3 (0.3-23) years. 96 patients (19%) had 133 NP events and the mean number of events / patient was 1.39 (1-4). In decreasing order of frequency, these events were: seizure disorder (28%), cerebrovascular disease (19%), acute confusional state (14%), psychosis (11%), myelopathy (8%), mood disorder (6%), headache (4%), movement disorder (2%), cranial neuropathy (3%), demyelinating syndrome (1.5%), anxiety disorder (1.5%), mononeuritis multiplex / mononeuropathy (1.5%), aseptic meningitis (1%) and polyneuropathy (1%). Cognitive dysfunction was not classified because of the lack of standard neuropsychological testing for all patients. Univariate analysis (Chi<sup>2</sup> test) revealed that NP-SLE was associated with a positive LA (p = 0.001), leucopenia (p=0.01), lymphopenia (p=0.03), thrombocytopenia (p=0.03) and pulmonary involvement (p=0.03). Multivariate analysis using logistic regression demonstrated that only a positive LA was significantly associated with NP manifestations in our patients (RR; 2.6 [1.2-5.4], p=0.01). Cerebrovascular disorder was especially associated with the presence of LA (OR; 2.8 [1.0-7.87], p = 0.04).

**Conclusions:** The prevalence of NP manifestations in our cohort of SLE patients was 19%, which was likely to be under-estimated because cognitive dysfunction was not classified. Seizure and cerebrovascular disorders were the most common NP features. The presence lupus anticoagulant was significantly associated with NP manifestations, in particular cerebrovascular disorders.

## G-RI-2

### Increased Apoptotic Blood Neutrophils and Macrophages and Decreased Clearance of Apoptotic Neutrophils in Systemic Lupus Erythematosus

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**Objectives:** Apoptosis and phagocytosis of apoptotic cells may play important roles in the pathogenesis of systemic lupus erythematosus (SLE). In the present study we compared 20 SLE patients with 10 health subjects in the apoptosis of blood neutrophils and monocyte-derived macrophages (Mph), and phagocytosis of apoptotic neutrophils by Mph.

**Method:** Human neutrophils and monocytes were isolated from fresh blood and cultured in the presence of different sources of human serum. Apoptotic Mph and neutrophils were examined by annexin V binding and morphology on May-Giemsa stained cytopreparations at different time points. The secondary necrotic neutrophils were verified by trypan blue.

**Results:** First, the percentage of apoptotic neutrophils at 5 and 24 hours cultured in the presence of autologous sera was significantly higher in SLE patients (9.0%± 5.9%, 71.5%± 18.1%) when compared with healthy subjects (2.4%± 3.2%, 56.6%± 15.5% respectively) (p<0.05). Second, the percentage of secondary necrotic neutrophils was increased in SLE patients to 18.3% (SE=7.1%) at 24 hours and 64.0% (SE=14.5%) at 48 hours, which were much higher than 10.8% (SE=5.6%) (p<0.05) and 44.8% (SE=8.3%) (p<0.05) at the two respective time points in healthy subjects. Third, SLE sera were found to be able to accelerate the apoptosis and secondary necrosis of neutrophils from healthy subjects. Regarding the apoptosis of Mph and phagocytosis of intact apoptotic neutrophils by Mph, the percentage of apoptotic Mph was significantly increased in SLE patients (19.8%± 3.5%) as compared with healthy subjects (2.3%± 1.1%) (p<0.05). Sera from SLE patients not only significantly increased Mph apoptosis of healthy subjects but also remarkably downregulated the clearance of apoptotic neutrophils by Mph from healthy subjects. Sera from healthy subjects can significantly rescue the phagocytosis of apoptotic neutrophils by Mph from SLE patients.

**Conclusion:** The observed increase of apoptotic neutrophils and Mph and poor ability of Mph to phagocytose apoptotic bodies in SLE patients may indicate an impaired clearance mechanism. This may be mediated by factors in the serum.