# Are antinuclear antibodies useful in neurologic patients? A retrospective analysis based on 545 cases

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**Summary**

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In this retrospective analysis determination of antinuclear antibodies had no positive or negative predictive value for diagnosing neuropsychiatric systemic lupus erythematosus (NPSLE). A history suggestive of antiphospholipid syndrome, of unusual symptoms for the patient's age and/or signs of non-neurological manifestations of systemic lupus erythematosus in a female patient were typical of NPSLE.

*Keywords: neuropsychiatric; systemic lupus erythematosus; antinuclear antibodies*

## Introduction

Systemic lupus erythematosus (SLE) is one of the diseases familiar to practitioners from a wide range of specialities [1]. Various laboratory markers and clinical manifestations define the disease [2, 3]. Four of 11 criteria have to be present, serially or simultaneously, to classify the patient as having systemic lupus erythematosus: four dermatologic manifestations, arthritis (arthralgia), serositis, renal disorder, neurologic disorder, haematologic disorder, immunologic disorder (antiphospholipid antibodies, antibodies against dsDNA and/or Sm nuclear antigen) and/or antinuclear antibodies (ANA) in the absence of drugs known to be associated with a drug-induced lupus syndrome.

The neurologic disorder was previously defined as seizures or psychosis in the absence of offending drugs or known metabolic derangements. This category has now been expanded to include 19 so-called neuropsychiatric syndromes of the peripheral and central nervous system (NPSLE) [1, www.rheumatology.org/ar/1999/aprilappendix.html].

To determine whether these neurologic manifestations – that cover practically every category of neurologic disease – are part of the spectrum of NPSLE or not, alternative causes have to be excluded.

This article examines the diagnostic yield of determining ANA titres in neurologic patients and discusses the implications of using such a test as a screening tool for NPSLE (positive predictive value). Previous studies have shown that testing for antinuclear antibodies has a high negative predictive value for systemic lupus erythematosus [3].

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## Methods and results

This retrospective study included all patients of the Department of Neurology at the University Hospital of Zurich who had at least one laboratory test for antinuclear antibodies in 2002. The total number of patients was 545; 278 were males (51%) and 267 (49%) were females. The age range for males was 16 to 84 years and 18 to 84 years for females; 73% of male patients and 72% of females were over the age of 40. Patients were identified with the help of a computer search. ANA titre, age and sex were recorded; the computerised medical records were reviewed to determine whether patients met the accepted criteria for systemic lupus erythematosus and for NPSLE.

190 of 278 male patients (68%) and 136/267 female patients (51%) had titres of 1:40 or lower, which are considered negative by general consensus [4]. The data confirmed a well-known observation that older – and in particular female – patients tend to have higher ANA titres than younger and male patients [5].

Six of 545 patients (1.1%) met the diagnostic criteria for systemic lupus erythematosus and NPSLE. Case vignettes: *Patient 1:* Female, 54 years, ANA 1:640, embolic stroke due to aseptic endo-

carditis ("serositis"), thrombocytopenia, antiphospholipid and anti-dsDNA antibodies; history of cranial neuropathy and cognitive dysfunction. *Patient 2:* Female, 42 years, ANA 1:5120, ischaemic stroke (possibly embolic), malar rash; history of photosensitivity, polyarthralgia and anti-Sm antibodies. *Patient 3:* Female, 34 years, antinuclear antibodies 1:320, transient ischaemic attacks with vertigo and diplopia, positive titre for antibodies against dsDNA; because of previous history of arthralgia and other criteria the patient was diagnosed with systemic lupus erythematosus and already treated with antimalarial drugs. *Patient 4:* Female, 41 years, ANA titre 1:320, multiple ischaemic strokes (probably due to antiphospholipid syndrome), malar rash, antibodies against dsDNA; history of arthritis and photosensitivity. *Patient 5:* Female, 62 years, antinuclear antibodies negative, ischaemic stroke (despite therapy with steroids, antimalarials, cyclophosphamide and aspirin); ≥10-year history of primary antiphospholipid syndrome, seizures, cognitive dysfunction and movement disorder (chorea) followed by a history of typical skin manifestations of systemic lupus erythematosus (discoid rash) and transiently positive antinuclear antibodies (but not at initial presentation). *Patient 6:* Male, 35 years, antinuclear antibodies negative, antibodies against dsDNA and transiently increased antinuclear antibodies and antiphospholipid antibodies (but both not at initial presentation); history of unspecific sensory symptoms and vertigo (associated with multiple white matter lesions in cerebral MRI). During follow-up he reported gonarthritis (responding to non-steroidal anti-inflammatory drugs). In patients 5 and 6 only titre changes of more than one dilution were deemed to be significant.

The number of patients with known systemic lupus erythematosus and (new) neurologic symptoms, but without testing for antinuclear antibodies during 2002, could not be determined. Also, the number of systemic lupus erythematosus patients with neurologic symptoms (NPSLE) that were seen in other hospital departments is not known.

## Discussion

Roughly 1% out of 545 patients met criteria for NPSLE (5 females and one male). The spectrum of ANA titres ranged from negative to 1:5120 in these patients. By history 3 of these 6 patients had non-neurologic signs and symptoms suggestive of systemic lupus erythematosus prior to development of NPSLE, and 3 had neurologic symptoms as the primary manifestation of systemic lupus erythematosus (of these latter patients at least 2 had a negative ANA titre initially). Although a generalisation with such a small sample of NPSLE patients is hardly possible, it seems that at least in this patient population neither a positive ANA titre nor the value of the titre itself have any positive predictive value. Likewise, a negative titre does not have a negative predictive value.

This observation is in line with reports that a high ANA titre (defined as 1:640 or higher) does not readily predispose to systemic lupus erythematosus and that the pre-test probability of systemic lupus erythematosus on history and physical examination is vital in interpreting the test results [4, 5]. Although a certain percentage of healthy persons with positive antinuclear antibodies and other autoantibodies, that appear in a distinct time course, do finally develop systemic lupus erythematosus, this information has so far no therapeutic or prophylactic consequences [6, 7].

Previous publications have stressed that a negative test for antinuclear antibodies has a high negative predictive value although this is not supported in this sample (albeit with clear limitations due to the small number of patients diagnosed with NPSLE) [3].

Overall it is clear that the diagnostic yield of antinuclear antibodies is low for NPSLE in terms of the numbers screened and actual diagnosis. As there is no specific neurological syndrome which defines that the patient has NPSLE, it is the context in which it appears that should alert the physician to the possibility of NPSLE.

A history suggestive of antiphospholipid (antibody) syndrome or unusual neurologic symptoms for the patient's age, unusual findings in routine stroke work-up (echocardiography) or a positive history and physical examination for non-neurological manifestations of systemic lupus erythematosus in a female patient were typical of NPSLE in this series [8].

## References


1 Ruiz-Irastorza G, Khamashta MA, Castellino G, Hughes GRV. Systemic lupus erythematosus. Lancet 2001;357:1027–32.

2 Hochberg HC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.

3 Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–7.

4 Myckatyn SO, Russel AS. Outcome of positive antinuclear antibodies in individuals without connective tissue disease. J Rheumatol 2003;30:736–9.

5 Blumenthal DE. Tired, aching, ANA-positive: does your patient have lupus or fibromyalgia? Cleve Clin J Med 2001;69:143–52.

6 Shmerling RH. Autoantibodies in systemic lupus erythematosus – there before you know it. N Engl J Med 2003;349:1499–500.

7 Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. N Engl J Med 2003;349:1526–33.

8 Lockshin MD, Erkan D. Treatment of the antiphospholipid syndrome. N Engl J Med 2003;349:1177–9.