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# Antinuclear antibodies-negative systemic lupus erythematosus – does it exist?

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**TITLE** Antinuclear antibody-negative lupus as a distinct diagnosis entity – does it no longer exist?

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**LIST OF ABBREVIATIONS** Antinuclear antibodies (ANA), immunoglobulin G (IgG), systemic lupus erythematosus (SLE)

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## SUMMARY

Systemic lupus erythematosus is a multi-system autoimmune disorder with protean manifestations. The diagnosis of SLE was considerably eased by the demonstration of ANA and it has become an important diagnostic criterion for the diagnosis of SLE. It was reported previously that approximately 5% of patients with lupus were ANA-negative. The paper analysed a total of 19 papers describing 169 patients with ANA-negative lupus identified between the periods 1976–2003. The authors found that pertinent data are often lacking in the published reports, which makes comprehensive review of the clinical cases difficult. However, they highlighted a number of confounding factors that should be considered before accepting a diagnosis of ANA-negative lupus. They are:

1 Influence of antigenic deficiency in testing substrate on ANA status: Usage of human substrates like Hep-2 cells reduce spuriously negative ANA results.
2 Concurrent immunosuppressive treatment.
3 Persistent profound proteinuria with associated renal loss of IgG produced spuriously negative ANA results.

## OPINIONS

The authors accept that the published data are incomplete in their reporting of clinical features, laboratory data and therapeutic intervention, and as such there are difficulties drawing conclusions from limited data. In addition to the confounding factors mentioned could be poor tissue fixation and inadequate fluorescent microscopy. In addition, other ANA-negative multisystem disorders can mimic SLE, and early undifferentiated connective tissue disease can evolve into systemic sclerosis rather than ANA-positive SLE.

It is true that negative lupus is very rare with the advent of using Hep-2 cells substrate for ANA testing. At present the ANA-negative SLE cases we come across are probably in the early phase of the disease process. With time, if left alone, some of these patients may become ANA-positive. However, due to other clinical features (especially arthritis, renal and central nervous system features), clinicians treat these patients with steroids and other immunosuppressive agents. The treatment may falsely keep these patients in negative ANA status, making them persistent ANA-negative SLE.

As suggested by the authors, it is time to maintain a registry of cases to make definite conclusions about ANA-negative lupus. This condition could be more common than is realised as many clinicians use ANA as a screening test to exclude SLE.