Antinuclear Antibody Testing

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KEYWORDS

• Antinuclear antibodies • Systemic lupus erythematosus • Immunofluorescence
• Sensitivity • Specificity • Diagnostic testing • Autoimmune • Autoantibody

HOSPITAL MEDICINE CLINICS CHECKLIST

1. The American College of Rheumatology recommends the immunofluorescent assay (rather than a solid-phase assay) as the gold standard for antinuclear antibody (ANA) testing.
2. The results of ANA testing are not sufficient to make the diagnosis of systemic lupus erythematosus (SLE); they must always be interpreted within the clinical context.
3. The ANA test should be ordered if the clinician feels there is a reasonable suspicion of SLE based on the symptoms, history, physical examination, and other laboratory testing. The ANA test should not be used as a screening test in the absence of suspecting an ANA-associated disease.
4. Serial titers of ANA are not necessary and do not correlate with disease activity.
5. Five percent to 30% of healthy adults may have a positive ANA test in the absence of an ANA-associated illness. An even higher percentage may be positive among the elderly and family members of patients with SLE.
6. Given the high sensitivity of the ANA in SLE, a negative ANA makes SLE highly unlikely.
7. ANA could be ordered if one suspects other ANA-associated disease such as drug-induced lupus, progressive systemic sclerosis (scleroderma), Sjögren syndrome, mixed connective tissue disease, polymyositis or dermatomyositis, or autoimmune liver or thyroid disease.
8. The different types of ANA may be helpful for specific clinical manifestations, such as anti-Smith, anti–double-stranded DNA, anti-Ro, and antiribonucleoprotein.

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1. What is antinuclear antibody?

Antinuclear antibody (ANA) describes the group of autoantibodies directed at various nuclear antigens. These antibodies have the capacity to bind and destroy certain structures within the nucleus, which may lead to phagocytosis of the nucleus and destruction of the cell. Autoantibodies to specific nuclear antigens, such as anti–double-stranded DNA (anti-dsDNA), anti-Smith (anti-Sm), antiribonucleoprotein (anti-RNP), anti-Ro, anti-La, or antihistone, may assist in the diagnosis of a systemic rheumatic disease in the appropriate clinical context. Antibodies directed at any of these antigens can produce a positive ANA. ANA is present in nearly every patient with systemic lupus erythematosus (SLE) and is considered a hallmark of the disease. This test, however, is not specific for SLE. ANA has been detected in the serum of patients with many rheumatic and nonrheumatic diseases as well as in healthy individuals.

Tags: autoantibodies, ANA, SLE.

2. How is ANA testing performed?

There is no single standardized methodology for ANA testing.[1] Most laboratories use a human epithelial tumor cell line substrate (HEp-2 cell line) with immunofluorescent (IF) labeling for routine ANA testing. This substrate has higher sensitivity, but lower specificity, than the previously used rodent tissue substrate. Thus, patients without ANA-associated rheumatic disease and even healthy individuals may have positive ANA results. Laboratories also report the dilution, or titer, at which nuclear immunofluorescence disappears. In HEp-2 ANA testing, up to 30% of normal persons have an ANA titer of 1:40 or greater and approximately 5% have an ANA titer of 1:160 or greater.[2] For this reason, a reported titer of at least 1:160 is often used as the cutoff for a positive ANA test.

An enzyme immunoassay (EIA, or rapid-throughput solid-phase ANA) may be used for broad screening of several different nuclear antigens because of its ease of use and lower cost. For example, the ANA, anti-dsDNA, anti-Ro (SS-A), and anti-La (SS-B) can all be rapidly tested on a single sample. However, this approach has not been examined in large populations and has been reported to produce high false-negative and high false-positive rates. In one review, up to 35% of patients with SLE and a positive ANA by IF were negative on solid-phase assays.[1] At present, rapid-throughput solid-phase ANA testing is not the preferred methodology for ANA testing.[3,4]

Tags: autoantibodies, ANA, immunofluorescence, solid phase assay.

3. How important is the titer of the ANA?

A positive ANA is defined as the level or titer of antinuclear antibody exceeding that found in 95% of the normal population. Each laboratory determines its own cutoff for a positive result, so there is variability between laboratories. When HEp-2 cells are used as the substrate, a common cutoff for a positive titer is 1:160 or greater. In general, the higher the titer, the more likely the result is a true-positive (ie, a positive result in a patient with SLE or another ANA-associated disease).[5] However, a significant minority of patients with SLE have low-titer positive results. If lower titers are used to define a positive result, up to 30% of healthy patients may have a positive ANA.[6]

Tags: ANA, titer.

4. What is the LE cell test?

After its discovery in 1948, the LE cell became the method of choice for assessing the presence of ANAs. The LE cell, named for its association with lupus erythematosus, is