THE ANTINUCLEAR ANTIBODY (ANA) TEST

ANA for Diagnosing Lupus, Arthritis, and other Autoimmune Disorders
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The test for antinuclear antibodies (ANA test) has value in helping diagnose specific autoimmune disorders. It’s useful, as well, as a way to rule out specific conditions, for instance to rule out the possibility of systemic lupus in a patient with early vague symptoms. The ANA test, when it is positive, is also used to monitor disease progression, remission and treatment response.

Autoimmune diseases are defined as conditions caused by an autoimmune response. However, this definition can be vague, since the actual cause of a specific disorder may be difficult to pinpoint.

And while finding the presence of antinuclear and other autoantibodies is often the first step in diagnosing autoimmune disorders, autoantibodies may not be the actual cause of the disease. A positive antinuclear antibody (ANA) test result can occur in systemic as well as organ-specific autoimmune diseases and also a variety of infections. In addition, a positive ANA can occur in normal individuals.

Clinical Usefulness of the ANA Test
The ANA test has value in the following instances:
- Helping set up a diagnosis in patients with clinical symptoms suggestive of an autoimmune or connective tissue disorder
- Ruling out autoimmune or connective tissue disorders in patients with few or uncertain clinical findings
- Sub-classifying disease in a patient with an established diagnosis of an autoimmune or connective tissue disorder
- Monitoring disease progression, remission, relapse, and treatment response

The Positive ANA Result
The titer of ANA and the specific ANA pattern can help determine if a positive ANA test result is associated with an autoimmune disease and which disease.

Sensitivity in Arthritic Disorders
A positive ANA result varies in sensitivity in different disorders and is most sensitive in systemic lupus erythematous (SLE).
- SLE- sensitivity, 93 percent
- Scleroderma- 85 percent
- Mixed connective tissue disease - 93 percent
- Polymyositis/dermatomyositis- 61 percent
Rheumatoid arthritis - 41 percent
Sjogren’s syndrome - 48 percent
**Drug-induced lupus** - 100 percent
**Discoid lupus** - 15 percent
Pauciarticular juvenile chronic arthritis - 71 percent

**Sensitivity in Specific organ-specific diseases**
Hashimoto’s thyroiditis - 46 percent
Graves’ disease - 50 percent
**Autoimmune hepatitis** - 63-91 percent
**Primary biliary cirrhosis** - 10-40 percent
Idiopathic pulmonary arterial hypertension - 40 percent
Other conditions associated with a positive ANA titer include chronic infectious diseases such as mononucleosis, hepatitis B, hepatitis C, HIV infection, subacute bacterial endocarditis, tuberculosis and some lymphoproliferative diseases.

**Types of ANAs**
The different types of ANA are named by the antigens they target, for instance double-stranded (ds) DNA or RNA protein complexes. Specific ANAs are associated with specific disorders.

- **dsDNA antibodies**—very specific for systemic lupus erythematosus and **lupus nephritis**; seen after certain drug exposures, such as heroin abuse, and occasionally in other connective tissue diseases such as rheumatoid arthritis
  - Histone antibodies—antibodies to H1 and H2 B histones are seen in SLE, whereas antibodies to H3-H4 histones are seen in drug related and idiopathic SLE.
  - RNA complex and other nuclear protein antibodies—Antibodies to U1-RNP are seen in mixed connective tissue disease and rarely in localized scleroderma; seen in 30-40 percent of patients with SLE in conjunction with antibodies to Smith antigen.
  - Smith antibodies—very specific for SLE but only occur in 25 percent of patients.
  - Ro/SSa and La/SSb antibodies are seen in Sjogren’s syndrome and to a lesser extent in subacute cutaneous lupus.
  - Topoisomerase (Scl-70) antibodies seen in systemic sclerosis

**Limitations of the ANA test**
Different serum dilutions can produce varying nuclear patterns, and one pattern may obscure and prevent the detection of other patterns when several antibodies are present. Nuclear patterns aren’t specific or sensitive. Therefore, no single pattern denotes a single disease, and several diseases may produce a particular pattern. High titers (greater than 1:640) are relevant and patients without a specific diagnosis should be followed for the emergence of a possible illness, although such high titers can occur in the absence of disease. Titers higher than 1:80 are seen in 13 percent of the normal population and titers greater than 1:320 are seen in 3 percent of the normal population.

**Resource:**
Shu-Ling Liang, Advances in ANA Testing, Advance for Administrators of the Laboratory, January 2008.
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