



CLINICAL SIGNIFICANCE AND INTERPRETATION OF ANTINUCLEAR ANTIBODIES (ANA)

Antinuclear antibodies are a spectrum of autoantibodies that react with various nuclear molecules including DNA, RNA, Histones, Acidic Nuclear Proteins and complexes of the molecular elements. The presence of antinuclear antibodies in serum is associated with various factors including genetic predisposition, environmental agents such as ultraviolet light, viruses, intravenous drug use and other chemicals. They are also associated with estrogen-androgen balance, chronic infections, neoplasms and advancing age.

Aging cannot be overemphasized as a factor associated with the presence of antinuclear antibodies. Several studies have shown that as much as 20% of otherwise healthy persons older than 65 years had a positive ANA test.

Primary care physicians often see patients with rheumatic complaints such as joint pains, muscle weakness and other symptoms suggestive of “connective tissue” disease. When this occurs it is usual to order a variety of “rheumatic disease” tests including ANA. If the ANA test result is positive it is assumed that there is a rheumatic disease, particularly lupus erythematosus. Unfortunately, the interpretation of a positive ANA is a complex issue, further complicated by the fact that laboratories in Jamaica are now offering a menu of tests for antibodies to a variety of more specific antigens. There are many such antibodies. At least thirty have been identified so far and without question, further research will identify many more in the future. The common ones tested for in Jamaica are double stranded DNA, Anti-Sm, Anti-Ro (anti SSA & SSB Sjogren’s), Anti-RNP and Antihistone.

The presence of these autoantibodies in serum does not always mean that a patient has SLE. These antibodies may appear in other immunologic disorders including immunopathic chronic and active hepatitis. There is also strong evidence that ds-DNA plays a direct role in the pathogenesis of nephritis in patients with SLE. In general, the role of autoantibodies in the pathogenesis of rheumatic disorders is still not fully understood.

When Should You Order an ANA

There are only three diseases that include, or require, a positive antinuclear test in their diagnostic criteria. The tests are:

- 1 **Systemic Lupus Erythematosus (SLE)**
- 2 **Mixed Connective Tissue Disorders (MCTD) and**
- 3 **Drug Induced Lupus Erythematosus (DLE)**

The diagnosis of SLE is a clinical diagnosis; laboratory findings are mere adjuncts to the physicians' impressions. If a doctor does not suspect one of the three conditions mentioned above, there is no need to order the ANA tests.

In 1982 the American Rheumatism Association established criteria for diagnosing patients with suspected SLE.

A The patient will present with symptoms of SLE and the ANA test will be positive.

B Either the LE prep or the DNA test will be positive

C Either the Sm antigen or the VDRL will be positive.

As useful as these criteria may appear, they do not address the fact the diagnosis of SLE may be quite difficult for the physician. Individuals who are afflicted with this illness can suffer a myriad of varying manifestations that can affect almost any part of the body. The manifestations can be quite minimal or extremely severe, even life threatening, and can appear and disappear with frustrating unpredictability, lasting anywhere from a few days to several months or more. Thus, those with the illness frequently can go for months or even years while physicians vainly try to make the diagnosis. It is not uncommon, especially in milder cases, for such patients to be labeled as neurotic or chronic complainers.

The criteria were also developed before the significance of newly studied autoantibodies was realized. The diagnosis and management of SLE will unquestionably improve with the current menu of autoantibody test availability.

95% of all patients with SLE will have a positive ANA. 100% of patients with MCTD or DLE will have a positive ANA. The attached table characterizes the sensitivity and specificity of the common antinuclear antibodies. Those available at Microlabs are highlighted.

ANTINUCLEAR ANTIBODY	SENSITIVITY	SPECIFICITY	DISEASE
Anti-nDNA	SLE 60% - 70%	High	SLE (>90%) if present in high titre
Antihistone	Drug-Induced SLE 100%	Low	
	RA 15% - 20%		
	SLE 30%		
Anti-Sm	SLE 30% - 40%	High	SLE 98%
Anti-nRNP	MCTD 100%	Low	
	SLE 30%		
	Scleroderma 20% - 30%		
	Rheumatoid Arthritis 10%		
	Discoid Lupus 20% - 30%		
Anti-Ro (Anti-SSA)	SLE 30% - 40%	Low	
	Sjogren's Syndrome 60% - 70%		
	RA 10%		
Anti-LA (Anti-SSB)	SLE 10% - 15%	Low	
	Sjogren's Syndrome 50% - 60%		
Anticentromere	Scleroderma 10% - 15%	High	Scleroderma or a closely related disease such as CREST or Raynaud's Disease - 10% - 30%
	CREST 50% - 90%		
	Raynaud's Disease >95%		
Anti-Sc170	Scleroderma 15% - 20%	High	Scleroderma >95%
Anti-PM-Scl	Polymyositis 10%	Unknown	? Polymyositis
Anti-Jo 1	Polymyositis 30%	Unknown	? Myositis
	Dermatomyositis <10%		

CREST = Calcinosis, Raynaud's phenomenon, Esophageal dysfunction, Sclerodactyly and Telangiectasia.

Criteria for the Classification of Systemic Lupus Erythematosus

The American College of Rheumatology establishes criteria for the diagnosis of lupus. The presence of four (4) of the eleven (11) criteria is required to classify a patient as having SLE. As noted in the criteria, the laboratory abnormalities are important in making and confirming the diagnosis.

Criterion	Frequency (%)
Malar rash	40-64
Discoid rash	17-31
Photosensitivity	17-41
Oral Ulcers	15-36
Arthritis	86-100
Serositis	
Pleuritis	30-60
Pericarditis	17-23
Renal Disorder	
Proteinuria	>25
Cellular casts	17-48
Neurologic	
Psychosis, convulsions	16-20
Hematologic	
Hemolytic anemia	14-54
Leukopenia	40-47
Lymphopenia	>40
Thrombocytopenia	11-14
ANA	99
Immunologic	
Anti-DNA	90-100
Anti-Sm	30-40
LE cells	49-92
False positive VDRL/RPR	8-20