

# GUIDELINES & PROTOCOLS

## ADVISORY COMMITTEE

### Antinuclear Antibody (ANA) Testing for Connective Tissue Disease

Effective Date: July 1, 2001

#### Scope

This guideline describes appropriate use of antinuclear antibody (ANA) testing (fee item 90280) in the diagnosis of connective tissue disease (CTD), also referred to as “systemic rheumatic disease”. It applies only to individuals 17 years of age and over. The guideline does not address ANA testing in the investigation of unexplained infertility, adverse pregnancy outcomes, liver disease or thrombotic disorders.

#### RECOMMENDATION 1:

#### ANA testing not indicated

ANA testing should not be ordered unless a connective tissue disease is a significant clinical possibility.

ANA testing is not helpful in confirming a diagnosis of rheumatoid arthritis or osteoarthritis.

ANA testing should not be used to evaluate fatigue, back pain or other musculoskeletal pain unless accompanied by one or more of the clinical features listed in Recommendation 2.

#### RECOMMENDATION 2:

#### ANA testing indicated

ANA testing is a useful diagnostic adjunct if the clinical history and physical examination show symptoms and signs of CTD consistent with systemic lupus erythematosus (SLE), scleroderma, Sjögren’s syndrome or polymyositis/dermatomyositis. Such patients typically\* present with at least one of the following clinical criteria, unexplained by other causes:

- arthritis
- pleurisy or pericarditis
- photosensitive rash
- laboratory evidence of renal disorder
- hemolytic anemia, immune thrombocytopenia or neutropenia
- skin changes of scleroderma, dermatomyositis or vasculitis
- clinical and laboratory evidence of myositis
- Raynaud’s phenomenon
- neurologic signs

CTD is uncommon, occurs almost exclusively in women, and typically presents before 50 years of age.

\* Atypical clinical presentations of CTD are seen by various specialty groups. Clinical judgement should guide ANA testing in these cases.

#### RECOMMENDATION 3:

#### Repeat testing rarely indicated

ANA testing should usually be ordered only once.

Positive ANA tests do not need to be repeated. Changes in the ANA titre do not correlate with disease activity. Negative tests rarely need to be repeated. If there is a strong suspicion of an evolving CTD or a change in the patient’s illness suggesting the diagnosis should be revised, repeat testing may be indicated.

## Rationale

This guideline is intended to clarify the role of ANA testing in evaluating connective tissue disease. The recommendations are designed to cover the vast majority of cases where ANA testing would be appropriate. More selective ordering of ANA tests would not only improve the test's predictive value, but also reduce the volume of tests, unnecessary referrals, and even misdiagnosis or inappropriate therapy.

Antinuclear antibodies are autoantibodies directed against a variety of components of the cell nucleus.<sup>1,2</sup> Detection of antinuclear antibodies is a diagnostic adjunct in patients with suspected CTD.<sup>1,3</sup> The usefulness of the ANA test results depends on the clinical situation. The likelihood that a positive test will provide useful information is proportional to the probability that CTD is present.<sup>4-7</sup> If the clinical history and physical examination reveal symptoms or signs suggestive of SLE or other CTD, a positive ANA test contributes to the diagnosis. In the absence of such symptoms and signs, a positive ANA test only confounds the diagnosis. ANA testing provides little useful information in the evaluation of complaints such as chronic fatigue or musculoskeletal pain in the absence of more specific symptoms or findings.<sup>4</sup>

Interpreting ANA test results may be difficult. A positive ANA test can be seen in healthy individuals, particularly the elderly, who never develop CTD. Positive ANA may also be seen in a wide range of diseases other than CTD, where it has no diagnostic or prognostic value.<sup>2,3,8</sup> The ANA titre provides useful information.<sup>3</sup> As a general rule, the higher the titre, the more likely that a connective tissue disease is present.<sup>4</sup> However, ANA titre is not a marker of disease activity.

A positive ANA test will show a particular staining pattern that may have diagnostic value in differentiating between types of CTD, but only in conjunction with clinical evaluation.<sup>5</sup>

Repeating ANA tests is rarely useful. There is no role for serial monitoring of ANAs since ANA titre does not correlate with disease activity.<sup>2,6,9</sup>

The ANA test is frequently requested. More than 68,800 ANA tests were performed in B.C. in fiscal year 1999/00 (at a cost of \$2.1 million). The number of tests ordered greatly exceeded the small number of new cases of CTD expected per annum (see Table). This volume of testing suggests that ANA tests are being ordered for patients with little chance of having ANA-associated CTD.

### Incidence and Estimated New Cases in B.C. for Selected CTDs

	Incidence per million	Estimated new cases in B.C. per annum*
SLE	56 <sup>†</sup>	226
Scleroderma	19 <sup>‡</sup>	77
Dermatomyositis & polymyositis	<10 <sup>§</sup>	<40

\* Based on population of 4,038,900: BC Stats 1999/2000 spanned average updated postcensal estimate.

<sup>†</sup> Uramoto KM, Michet CJ Jr, Thumboo J, Sunku J, O'Fallon WM, Gabriel SE. Trends in the incidence and mortality of systemic lupus erythematosus. 1950-1992. *Arthritis Rheum* 1999;42(1):46-50.

<sup>‡</sup> Mayes MD. Scleroderma epidemiology. *Rheum Dis Clin North Am* 1996;22(4):751-764.

<sup>§</sup> Kovacs SO, Kovacs SC. Dermatomyositis. *J Am Acad Dermatol* 1998;39(6):899-920.

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## Sponsors

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This guideline is based on scientific evidence current as of the effective date.

Guidelines and Protocols Advisory Committee  
PO Box 9642 STN PROV GOVT  
Victoria BC V8W 9P1

Phone: (250) 952-1347

Fax: (250) 952-1417

E-mail: [hlth.guidelines@gov.bc.ca](mailto:hlth.guidelines@gov.bc.ca)

Web site: [BCGuidelines.ca](http://BCGuidelines.ca)

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