



Antinuclear Antibody (ANA) Testing Protocol

Effective Date: June 1, 2013

Scope

This guideline describes the appropriate use of antinuclear antibody (ANA) testing in the diagnosis of connective tissue disease (CTD) in adults aged ≥ 19 years. The guideline does NOT address ANA testing in the investigation of unexplained infertility, adverse pregnancy outcomes, liver disease or thrombotic disorders.

Key Recommendations

- ANA testing need only be ordered once.
- ANA testing is NOT indicated unless a connective tissue disease (e.g., systemic lupus erythematosus (SLE), scleroderma, Sjogren's syndrome, polymyositis/dermatomyositis) is a significant clinical possibility.
- ANA testing is NOT indicated as a screening test to evaluate fatigue, back pain, or other musculoskeletal pain without other clinical indications.
- ANA testing is NOT indicated to confirm a diagnosis of rheumatoid arthritis (RA) or osteoarthritis (OA).

Epidemiology

The ANA test is frequently ordered. More than 94,000 ANA tests were performed in B.C. in fiscal year 2011/12 at a cost of \$2.24 million annually (\$23.82 per test). The number of tests ordered greatly exceeds the small number of new cases of CTD expected per annum (see Table 1). This volume of testing suggests that ANA tests are being ordered for patients with little chance of having ANA-associated CTD.

Table 1: Incidence and Estimated New Cases in B.C. for Selected CTDs

Connective Tissue Disease	Disease incidence per million population ¹⁻³	Estimated new BC cases/year *
Systemic lupus erythematosus (SLE)	56	259
Scleroderma	19	88
Dermatomyositis & polymyositis	< 10	< 46

Eighteen percent of first-time tested outpatients underwent unnecessary repeat testing in 2010/2011. In 57.2% of the repeat testing, both the initial and the repeat ANA tests were ordered by a GP. In 24.8% the initial test was ordered by a GP and the repeat test was ordered by a specialist, and in 10.2% both the initial and the repeat test were ordered by the same specialist.**

The sensitivity and specificity of ANA has been reported as 40% and 66% (PPV = 29%, NPV = 77%) in a study looking at the diagnosis of any CTD as requested by primary care.⁴ More selective ordering of ANA tests would not only improve the predictive value of the test, but also reduce the volume of tests performed, unnecessary referrals, misdiagnosis, and inappropriate therapy.⁵

* Based on an estimated BC population of 4.6 million, third quarter 2012. Available at: www.bcstats.gov.bc.ca/DATA

** Antibody Testing Update on Test Utilization Fiscal Year 2011/12, provided by Laboratory Office, Laboratory, Diagnostic and Blood Services Branch, BC Ministry of Health

Testing

ANAs are autoantibodies directed against a variety of components of the cell nucleus.^{6,7} Detection of ANAs is a diagnostic adjunct in patients with suspected CTD.^{6,8} The usefulness of the ANA test results depends on the clinical situation. If the clinical history and physical examination reveal symptoms or signs suggestive of SLE, scleroderma, Sjögren's syndrome or polymyositis/dermatomyositis, then ordering ANA is appropriate and a positive test contributes to the diagnosis.⁹⁻¹² ANA testing is not indicated for diagnosis of RA or OA.

Such CTD patients typically present with at least one of the following clinical findings 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

In the absence of such symptoms and signs, a positive ANA test only confounds the diagnosis because positive ANAs are commonly found in the normal population. The prevalence of ANAs in healthy individuals is about 3-15%.¹³ The production of these autoantibodies is strongly age-dependent, increasing to 10-37% in healthy persons over the age of 65.

Positive ANA tests may also be seen in a wide range of diseases other than CTD where they have no diagnostic or prognostic value.^{7,8,14} Individuals with viral infections can have positive ANA for a short time. Some medications (e.g., some statins, β -blockers, ACE inhibitors and NSAIDs) and conditions, i.e., cancer, can also cause a positive ANA.

The higher the ANA titre, the more likely that a CTD is present.⁹ However, there is no role for serial monitoring of ANAs and repeat ANA testing is rarely indicated. Atypical clinical presentations of CTD do occur and clinical judgment should guide ANA testing in these cases. CTD is uncommon, occurs almost exclusively in women, and typically presents at less than fifty years of age.

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.⁹

The very low specificity of a positive ANA in the absence of clinical findings of a CTD precludes its use as a screening test for disease in the general healthy population.¹⁰

► ANA testing is NOT indicated:

- unless a CTD is a significant clinical possibility.
- to confirm a diagnosis of rheumatoid arthritis or osteoarthritis.
- to evaluate fatigue, back pain, or other musculoskeletal pain unless accompanied by one or more of the clinical findings listed above.

► Repeat ANA testing is RARELY indicated:

- In general, ANA testing need only be ordered once.
- Positive tests need not be repeated and there is no role for serial monitoring of ANAs since changes in ANA titres do not correlate with disease activity.^{6,10,14}
- Negative tests rarely need to be repeated except when there is a strong suspicion of an evolving CTD or a change in the patient's illness suggesting revision of diagnosis.

Resources

► References

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15. Kavanaugh A, Tomar R, Reveille J, Solomon DH, Homburger HA. Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens. American College of Pathologists. *Arch Pathol Lab Med.* 2000;124:71-81.

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► Resources

BC Guidelines: www.bcguidelines.ca - Rheumatoid Arthritis: Diagnosis, Management and Monitoring

HealthlinkBC – Health information, translation services and dieticians, www.healthlinkbc.ca or by telephone 811.

Community Healthcare and Resource Directory (CHARD) - Information on healthcare specialists and resources www.info.chardbc.ca or Toll Free: 1-877-330-7322

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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