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Quality Assurance for the Indirect Immunofluorescence Test for Autoantibodies to Nuclear Antigen (IF-ANA); Approved Guideline

This document addresses the criteria for immunofluorescence ANA testing, including test components, quantification of results, and classification criteria.

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Quality Assurance for the Indirect Immunofluorescence Test for Autoantibodies to Nuclear Antigen (IF-ANA); Approved Guideline

Abstract

Quality Assurance for the Indirect Immunofluorescence Test for Autoantibodies to Nuclear Antigen (IF-ANA); Approved Guideline (NCCLS document I/LA2-A) provides guidance for laboratorians who perform immunofluorescence tests for autoantibodies to nuclear antigen to detect diseases. Topics addressed include substrate and fixative variations, fluorescence-labeled conjugates, reference intervals, test results, and criteria for classification of systemic lupus erythematosus.

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Contents

Foreword

Tests for the detection of antinuclear antibodies are helpful in the evaluation of several systemic rheumatic diseases, such as systemic lupus erythematosus (SLE), discoid lupus erythematosus, mixed connective tissue diseases (MCTD), systemic sclerosis, Sjögren's syndrome, polymyositis, dermatomyositis, and rheumatoid arthritis. Identification of autoantibodies has proven to be useful in the diagnosis, management, and treatment of these diseases.

In developing this guideline, the area committee defined quality assurance as the practice that encompassses all procedures and activities directed toward ensuring that a specified quality of product is achieved and maintained. The area committee believes that this guideline addresses some of the critical issues related to IF-ANA testing, including: criteria for the immunofluorescence ANA test (Section 3); substrate and fixative variations (Section 4); fluorescence-labeled conjugates (Section 5); microscope optics (Section 6); semiquantitation of results (Section 7); establishment of reference intervals (Section 8); reporting of test results (Section 9); reference sera for ANA tests (Section 10); ANA-negative SLE (Section 11); revised criteria for the classification of SLE (Section 12); and special considerations for the use of other laboratory tests for the detection of ANA (Section 14).

The area committee acknowledges the help and input of the Standards Committee of the Association of Medical Laboratory Immunologists (AMLI) chaired by Lynn Burek, PhD, of Johns Hopkins University. Gerald Miller, PhD, has written a detailed draft of the AMLI document, and many of the suggestions found in the draft have been incorporated into this guideline.

Universal Precautions

Because it is often impossible to know which might be infectious, all patient blood specimens are to be treated with "universal precautions." Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention. NCCLS document, M29-T2, *Protection of Laboratory Workers from Infectious Disease Transmitted by Blood, Body Fluids, and Tissue—Second Edition; Tentative Guideline*, deals specifically with all aspects of this issue.

Key Words

Autoantibodies, antinuclear antibodies, indirect immunofluorescence, nuclear antigen, systemic lupus erythematosus (SLE), quality assurance.

Quality Assurance for the Indirect Immunofluorescence Test for Autoantibodies to Nuclear Antigen (IF-ANA); Approved Guideline

1 Introduction

The rheumatic diseases are characterized by the presence of one or more autoantibodies that react with components of the nucleus, cytoplasm, or surface of cells. The rheumatic diseases listed below vary with the type of autoantibodies and the extent and severity of lesions in the various organ systems.[1-6]

- Systemic lupus erythematosus (SLE).
- Discoid lupus erythematosus (DLE).
- Drug-induced lupus erythematosus (LE).
- Mixed connective tissue disease (MCTD).
- Sjögren's syndrome.
- Scleroderma/CREST (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly elangiectasia) syndrome.
- Rheumatoid arthritis.
- Dermatomyositis and polymyositis.
- Other connective tissue disease syndromes that have been poorly defined as to clinical category. Includes syndromes associated with infectious diseases (such as Lyme disease), tumors, and drug reactions.

Over the past 10 years, there has been a progressive characterization of the immunochemical and molecular nature of various auto-antigens. An increased number of antigen–antibody systems associated with specific diseases have been identified. The terms “autoantibodies to nuclear antigens” or “antinuclear antibodies” (ANAs) have gained widespread use as generic descriptions of a group of autoantibodies. Several features of ANAs and their relationship to the rheumatic diseases have been reported.[1-6] Some of the ANAs have been used as diagnostic markers. Such ANAs include antinative DNA and anti-Sm in SLE, and anti-Scl-70 in diffuse scleroderma with lung disease; anticentromere in CREST (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia); and anti-tRNA synthetases in dermatomyositis and polymyositis. Other ANAs are also found in several of the other diseases, such as hepatic disorders, tumors, vasculititis, etc., and can differ markedly in prevalence from the systemic rheumatic diseases. Such ANAs include anti-histones in SLE and drug-induced lupus; anti-U1 ribonucleoprotein (RNP) in SLE and MCTD; and anti-SS-A/Ro and anti-SS-B/La in SLE and Sjögren's syndrome.

2 Scope

The ANAs are associated with many immunologic disorders; however, they are the essential hallmark of systemic rheumatic diseases.

The significance of ANAs is as follows:

- Useful for screening and diagnostic evaluation of systemic rheumatic diseases. A negative test result is helpful in ruling out the possibility of SLE.
- Some of these diseases have distinct profiles of ANA. Significant changes in the levels of certain specific ANA, such as antibodies to Ds-DNA, are useful in following the causes of the diseases and their responses to therapy. Titers of IF-ANA tests do not necessarily correlate with severity of disease or response to therapy.
- ANAs can be useful as experimental reagents in the isolation of nuclear antigens, especially nonhistone antigens or basic studies in cell biology.

Indirect immunofluorescence and immunoenzyme tests are commonly used for ANA screening because these procedures are practical, sensitive, primary antigen–antibody reactions. However, the standardization of the indirect immunofluorescence antibody tests (IF-ANA) has been difficult.[7-9]