

Systemic Sclerosis Antibodies

Systemic sclerosis (SSc), also called scleroderma, is a chronic autoimmune disorder characterized by fibrosis of the skin and various organs.^{1,2} Early diagnosis and classification are important so that patients can be evaluated for organ involvement and/or damage.³ However, because SSc is a heterogeneous disease, clinical presentation and disease course vary, and manifestations may overlap with those of other rheumatic disorders, all of which can complicate diagnosis.^{1,3,4} The initial testing strategy includes CBC with platelet count and automated differential and nuclear antibody (ANA) by IFA, IgG. Confirmatory or secondary testing should be performed based on ANA IFA patterns (centromere, nucleolar, and speckled patterns), clinical presentation, and/or ethnicity.

Disease Overview

Prevalence

0.3-2.8/100,000 worldwide¹

Age of Onset

20-50 years of age⁵

Sex

M<F, 1:3¹

Diagnostic Issues

Autoimmune connective tissue diseases may present with similar features, particularly early in disease, making diagnosis difficult. The following considerations may assist in determining a diagnosis of SSc:

- ANA IFA patterns may help define diagnostic pathways
 - Most patients with SSc will have either⁴:
 - Centromere antibodies
 - Scl-70 antibodies
 - RNA polymerase III antibodies
 - These three antibody tests are required for the initial evaluation of SSc although the use of other autoantibody markers may improve diagnostic sensitivity for disease
- The presence of SSc-specific antibodies may help predict disease phenotypes, which include:
 - CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome: antibodies against centromere are most common³
 - Diffuse cutaneous SSc: antibodies against Scl-70 and RNA polymerase III most common
- Antibody patterns may differ by ethnicity⁶
 - Antibodies against U3-RNP are more common in African Americans
 - Th/To autoantibodies are more common in Caucasians with limited cutaneous SSc

Tests to Consider

Comprehensive Systemic Sclerosis Panel 3000480

Method: Qualitative Immunoblot/Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Multiplex Bead Assay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

- Indicated when suspicion for SSc is high and patient presents with features of overlap syndrome
- Individual tests in panel may be ordered separately. (See [Related Tests](#).)

Criteria Systemic Sclerosis Panel 3000479

Method: Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Multiplex Bead Assay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

- Indicated for patients with distinct features of SSc
- Negative results do not rule out SSc; if test is negative and suspicion for SSc is high, consider testing for U3 RNP (fibrillarin), PM/Scl-100, U1RNP, Th/Tho, or other connective tissue disease autoantibodies based on patient's clinical presentation

Test Interpretation

Clinical Sensitivity⁶

- ANA by IFA for SSc: 90-95%
- Individual SSc-specific marker: may vary based on ethnicity

Results

- ANA patterns (including centromere) are reported
- If positive, pattern and titers are reported

Limitations

- Negative antibody test result does not exclude SSc (5-10% of patients with SSc are ANA IFA negative)^{2,6}
- Panel does not include Th/To

References

1. Knobler R, Moinzadeh P, Hunzelmann N, et al. [European Dermatology Forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, Part 1: localized scleroderma, systemic sclerosis and overlap syndromes](#). J Eur Acad Dermatol Venereol. 2017;31(9):1401-1424. PubMed
2. Salazar GA, Assassi S, Wigley F, et al. [Antinuclear antibody-negative systemic sclerosis](#). Semin Arthritis Rheum. 2015;44(6):680-686. PubMed
3. Tartar DM, Chung L, Fiorentino DF. [Clinical significance of autoantibodies in dermatomyositis and systemic sclerosis](#). Clin Dermatol. 2018;36(4):508-524. PubMed
4. van den Hoogen F, Khanna D, Fransen J, et al. [2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative](#). Ann Rheum Dis. 2013;72(11):1747-1755. PubMed
5. Alba MA, Velasco C, Simeón CP, et al. [Early- versus late-onset systemic sclerosis: differences in clinical presentation and outcome in 1037 patients](#). Medicine (Baltimore). 2014; 93 (2): 73-81. PubMed
6. Nandiwada SL, Peterson LK, Mayes MD, et al. [Ethnic Differences in Autoantibody Diversity and Hierarchy: More Clues from a US Cohort of Patients with Systemic Sclerosis](#). J Rheumatol. 2016; 43 (10): 1816-1824. PubMed

Related Information

[Systemic Sclerosis - Scleroderma](#)

Related Tests

[Antinuclear Antibody \(ANA\) with HEp-2 Substrate, IgG by IFA 3000082](#)

Method: Semi-Quantitative Indirect Fluorescent Antibody

[Antinuclear Antibody \(ANA\) with HEp-2 Substrate, IgG by IFA with Reflex by Pattern 3000601](#)

Method: Semi-Quantitative Indirect Fluorescent Antibody/Qualitative Enzyme-Linked Immunosorbent Assay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay/Semi-Quantitative Multiplex Bead Assay/Qualitative Immunoblot

[Centromere Antibody, IgG 0050714](#)

Method: Semi-Quantitative Multiplex Bead Assay

[Connective Tissue Disease First Line Panel with Reflex 3002463](#)

Method: Qualitative Enzyme-Linked Immunosorbent Assay/Semi-Quantitative Indirect Fluorescent Antibody (IFA)/Semi-Quantitative Multiplex Bead Assay

Connective Tissue Diseases Profile 0051668

Method: Semi-Quantitative Multiplex Bead Assay

Fibrillarin (U3 RNP) Antibody, IgG 2012173

Method: Qualitative Immunoblot

Extended Myositis Panel 3001781

Method: Qualitative Immunoprecipitation/Semi-Quantitative Multiplex Bead Assay/Qualitative Immunoblot

PM/Scl-100 Antibody, IgG by Immunoblot 2003040

Method: Qualitative Immunoblot

RNA Polymerase III Antibody, IgG 2001601

Method: Semi-Quantitative Enzyme-Linked Immunosorbent Assay

Smith/RNP (ENA) Antibody, IgG 0050470

Method: Semi-Quantitative Multiplex Bead Assay

Scleroderma (Scl-70) (ENA) Antibody, IgG 0050599

Method: Semi-Quantitative Multiplex Bead Assay

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology, 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
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