Systemic Sclerosis Antibodies

**Indications for Ordering**

Comprehensive evaluation of systemic sclerosis (SSc)

**Test Description**

Panel includes
- Scleroderma (Scl-70) (ENA) Antibody, IgG (antitopoisomerase)
  - Semiquantitative multiplex bead assay
- RNP (U1) (Ribonucleic Protein) (ENA) Antibody, IgG
  - Semiquantitative multiplex bead assay
- Nuclear Antibody (ANA) by IFA, IgG
  - Semiquantitative indirect fluorescent antibody (IFA)
  - Reports centromere pattern
- Fibrillarin (U3 RNP) Antibody, IgG
  - Qualitative immunoblot
- PM/Scl-100 Antibody, IgG by Immunoblot
  - Qualitative immunoblot
- RNA Polymerase III Antibody, IgG
  - Semiquantitative enzyme-linked immunosorbent assay (ELISA)

**Tests to Consider**

Typical testing strategy

Initial testing
- CBC with platelet count and automated differential
- Nuclear antibody (ANA) by IFA, IgG
  - Confirmatory or secondary testing based on one or more of the following
    - ANA IFA patterns with three main patterns observed (centromere, nucleolar, and speckled patterns)
    - Clinical presentation
    - Ethnicity

Primary tests

**Systemic Sclerosis Comprehensive Panel 2013325**
- Indicated when suspicion for SSc is high and patient presents with features of overlap syndrome
- Individual tests in panel (may also be ordered separately)
  - Scleroderma (Scl-70) (ENA) Antibody, IgG 0050599
  - RNP (U1) (Ribonucleic Protein) (ENA) Antibody, IgG 0050470
  - Nuclear Antibody (ANA) by IFA, IgG 0050639
  - Fibrillarin (U3 RNP) Antibody, IgG 2012173
  - PM/Scl-100 Antibody, IgG by Immunoblot 2003040
  - RNA Polymerase III Antibody, IgG 2001601

**Disease Overview**

**Incidence** – 3-20/million
**Age of onset** – peak onset 20-30 years
**Sex** – M<F, 1:3-8
**Ethnicity** – overall slight increase in prevalence for African Americans compared to Caucasians
- 10-fold increase in Choctaw Indians
Symptoms

- Dermatologic
  - Digital ulcers
  - Hair loss
  - Sclerodactyly
  - Abnormal nailfold capillaries
  - Raynaud phenomenon
  - Skin thickening
  - Telangiectasia
- Gastrointestinal
  - Gastroparesis/constipation
  - Esophageal dysmotility
  - Gastroesophageal reflux disease
  - Malabsorption
- Pulmonary
  - Pulmonary hypertension leading to interstitial fibrosis
- Musculoskeletal
  - Arthralgias/myalgias
  - Arthritis
  - Myopathy (usually proximal)
- Cardiovascular
  - Conduction abnormalities (eg, arrhythmias)
  - Myocardial fibrosis
  - Pericarditis
  - Valvular abnormalities
- Otorhinolaryngologic
  - Sicca syndrome
- Renal
  - Glomerulonephritis
  - Scleroderma renal crisis

Diagnostic issues

- Autoimmune connective tissue diseases may present with similar features, particularly early in disease, making diagnosis difficult
- ANA IFA patterns may help define diagnostic pathways
  - Most patients with SSc will have at least one of the following antibodies, and ordering tests for only these three antibodies is adequate for initial evaluation (van den Hoogen, 2013)
    - Centromere
    - Scl-70
    - RNA polymerase III
- The presence of SSc-specific antibodies may help predict disease phenotype
  - Calcinosi, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia (CREST) syndrome
  - Antibodies against centromere are most common
  - Diffuse cutaneous SSc
  - Antibodies against Scl-70 and RNA polymerase III are most common
- Antibody patterns may differ by ethnicity
  - Testing for less commonly associated SSc antibodies (eg, U3-RNP, PM/Scl, and Th/To) may be appropriate when results for antibodies commonly associated with SSc are negative.
  - Antibodies against U3-RNP are most common in African Americans
  - Th/To and PM/Scl are more common in Caucasians with limited SSc

Test Interpretation

Clinical sensitivity

- Sensitivity for ANA by IFA for SSc ranges from 90-95%
- Sensitivity for individual SSc-specific marker is dependent on ethnicity

Results

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

Limitations

- Negative antibody test result does not exclude SSc
  - 5-10% of SSc patients are ANA IFA negative
- Panel does not include Th/To

Reference