

Sjögren Syndrome

Diagnosis

Indications for Testing

- Dry eyes and mouth

Criteria for Diagnosis

- International consensus criteria
Criteria for Diagnosing Sjögren Syndrome

American-European Consensus Criteria for Sjögren Syndrome

- I. Ocular symptoms (≥ 1 present)
 - Symptoms of dry eyes for ≥ 3 months
 - Foreign body sensation in the eyes
 - Use of artificial tears ≥ 3 per day
- II. Oral symptoms (≥ 1 present)
 - Symptoms of dry mouth for at least 3 months
 - Recurrent or persistently swollen salivary glands
 - Need for liquids to swallow dry foods
- III. Ocular signs (≥ 1 present)
 - Abnormal Schirmer test (without anesthesia; ≤ 5 mm/5 minutes)
 - Positive vital dye staining of the eye surface
- IV. Histopathology
 - Lip biopsy showing focal lymphocytic sialoadenitis (focus score ≥ 1 per 4 mm²)
- V. Oral signs (at least one present)
 - Unstimulated whole salivary flow (≤ 1.5 ml/15 minutes)
 - Abnormal parotid sialography
 - Abnormal salivary scintigraphy
- VI. Autoantibodies (at least one present)
 - Anti-SSA (Ro) or anti-SSB (La)

Primary Sjögren syndrome diagnosis – (a) any 4 of the 6 criteria (must include either IV or VI); or (b) any 3 of the 4 objective criteria (III, IV, V, VI)

Secondary Sjögren syndrome diagnosis in patients with another well-defined major connective tissue disease – the presence of one symptom (I or II) plus 2 of the 3 objective criteria (III, IV and V) is indicative of Sjögren

Laboratory Testing

- Nonspecific tests – not specific for Sjögren syndrome; results may be seen in other connective tissue diseases
 - ESR/CRP – frequently elevated
 - Immunoglobulins – marked hypergammaglobulinemia (IgG>IgA>IgM)
 - Total protein – elevated
 - CBC – usually normal
 - IgM rheumatoid factor may be positive
- Antibody testing
 - Initial testing – ANA followed by extractable nuclear antibody (ENA) if positive
 - SS antibodies – although not specific for Sjögren syndrome, antibodies are relatively sensitive; may be useful to order panel screening for [connective tissue diseases](#) if Sjögren is not high probability

- Strong association between SSA antibodies and [vasculitis](#) in Sjögren syndrome
- Several studies identify SSB antibodies as serological marker for SS-sicca complex
 - SSB antibodies detected in approximately 60% of SS-sicca complex patients

Histology

- Labial gland biopsy – predominate lymphocytic infiltration
 - Should contain >50 lymphocytes with normal appearing acini per 4 mm² of glandular tissue
 - Sjögren syndrome focus score = number of lymphocyte aggregates x 4 ÷ area of salivary gland parenchyma
 - Focus score ≥1 considered diagnostic

Other Testing

- Objective ocular involvement – Schirmer test or Rose bengal staining
- Objective salivary gland involvement – sialography, scintigraphy or sialometry

Differential Diagnosis

- Multisystemic symptoms
 - Other connective tissue disease with overlap features
 - [Mixed connective tissue disease \(MCTD\)](#)
 - [Scleroderma](#) – systemic sclerosis
 - [Rheumatoid arthritis](#)
 - [Lymphoma \(B or T-cell\)](#)
 - [Vasculitis](#)
 - Chronic infection
 - [Endocarditis](#)
 - [HIV](#)
- Xerostomia
 - Drug-induced
 - [Sarcoidosis](#)
 - [Hepatitis C \(HCV\)](#)
 - [HIV](#)
 - [Amyloidosis](#)
 - [Diabetes mellitus](#)
 - [Head and neck radiation](#)
 - [Depression](#)
- Xerophthalmia
 - [Allergic conjunctivitis](#)
 - [Sarcoidosis](#)
 - [Rosacea](#)
 - [Blepharitis](#)
- Dysphagia
 - [Gastroesophageal reflux disease \(GERD\)](#)
 - [Gastritis](#)
 - [Gastroesophageal cancer](#)
 - [Achalasia](#)
- Neurologic symptoms
 - [Multiple sclerosis](#)

- Diabetes mellitus
- Vasculitis
- Sarcoidosis
- Musculoskeletal symptoms
 - Rheumatoid arthritis
 - Fibromyalgia
 - Polymyositis
 - Other connective tissue diseases
 - Osteoarthritis

Clinical Background

Sjögren syndrome is a slowly progressive autoimmune disease characterized by lymphocytic infiltration of exocrine glands resulting in dry eyes and dry mouth.

Epidemiology

- Prevalence – 2-4,000,000 persons in U.S.
 - Second most common autoimmune disease
- Age – peak is 40-60 years
- Sex – M<F, 1:9

Risk Factors

- Genetic predisposition (multigenetic factors)
 - Family history of Sjögren syndrome

Pathophysiology

- Mononuclear infiltrate with loss of ductal cells and relative preservation of acinar cells in secretory glands
- Leads to loss of secretory capacity of the gland
- Infiltration of cells may also be systemic, causing multi-organ disease

Clinical Presentation

- Head, eyes, ears, nose and throat (HEENT)
 - Dry eye (xerophthalmia, keratoconjunctivitis sicca)
 - Dry mouth (xerostomia) – increased incidence of dental caries
 - Enlargement of salivary glands
- Musculoskeletal – arthritis, arthralgias, myalgias
- Dermatologic – palpable purpura, cryoglobulinemia, Raynaud phenomena, alopecia
- Endocrine – autoimmune thyroiditis
- Neurologic – peripheral neuropathy, cranial neuropathies
- Pulmonary – interstitial pneumonitis, tracheobronchial sicca
- Complications
 - 20- to 40-fold increased risk of lymphoma, mostly mucosally associated lymphoid tumors (MALT)
 - Often associated with other connective tissue diseases (termed secondary Sjögren syndrome) – usually develops ~10 years after initial onset of primary connective tissue disease)
 - Rheumatoid arthritis (RA)
 - Systemic lupus erythematosus (SLE)
 - Primary biliary cirrhosis (PBC)
 - Autoimmune thyroid disease (thyroiditis)

Treatment

- Xerophthalmia – artificial tears, topical cyclosporine
- Xerostomia – pilocarpine or cevimeline derivatives

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
<p>Anti-Nuclear Antibodies (ANA), IgG by ELISA with Reflex to ANA, IgG by IFA 0050080</p> <p>Method: Qualitative Enzyme-Linked Immunosorbent Assay/Semi-Quantitative Indirect Fluorescent Antibody</p>	<p>First-line test for connective tissue disease screening</p> <p>All ELISA results reported as Detected are further tested by IFA</p> <p>ANA ELISA screen is designed to detect antibodies against dsDNA, histone, SS-A (Ro), SS-B (La), Smith, snRNP/Sm, Scl-70, Jo-1, centromere, and an extract of lysed HEp-2 cells</p>	<p>Low titer ANA common with advancing age; certain drugs may also cause low titer ANA</p> <p>ANA ELISA assays have been reported to have lower sensitivities for antibodies associated with nucleolar and specked ANA-IFA patterns</p>	<p>Recommend cutaneous direct immunofluorescence testing of active edge of new lesion (lesional biopsy) if dermatologic manifestations are present</p>
<p>Anti-Nuclear Antibody (ANA), IgG by ELISA with Reflexes to ANA by IFA and to dsDNA, RNP, Smith, SSA, and SSB Antibodies 0050317</p> <p>Method: Qualitative Enzyme-Linked Immunosorbent Assay/Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Multiplex Bead Assay</p>	<p>First-line test for connective tissue disease screening</p> <p>If ELISA screen is positive, then IFA using HEp-2 substrate will be added; if confirmed by IFA, titer and pattern will be reported and testing for dsDNA antibody and ENA antibodies will be added</p>		
<p>Extractable Nuclear Antigen Antibodies (RNP, Smith, SSA, & SSB) 0050652</p> <p>Method: Semi-Quantitative Multiplex Bead Assay</p>	<p>First-line test for connective tissue disease screening</p>		
<p>Sedimentation Rate, Westergren (ESR) 0040325</p> <p>Method: Visual Identification</p>	<p>Non-specific testing</p> <p>Often elevated in Sjögren syndrome</p>		

C-Reactive Protein 0050180 Method: Quantitative Immunoturbidimetry	Non-specific testing Often elevated in Sjögren syndrome		
Immunoglobulins (IgA, IgG, IgM), Quantitative 0050630 Method: Quantitative Nephelometry	Non-specific testing Includes IgA, IgG, IgM		
Protein, Total, Serum or Plasma 0020029 Method: Quantitative Spectrophotometry	Non-specific testing Often elevated in Sjögren syndrome		
CBC with Platelet Count and Automated Differential 0040003 Method: Automated Cell Count/Differential	Non-specific testing Evaluate white blood cell count		

Additional Tests Available

Test Name and Number	Comments
Connective Tissue Diseases Profile 0051668 Method: Semi-Quantitative Multiplex Bead Assay	Aid in identifying specific connective tissue disease Panel consists of Smith (ENA), RNP, SSA, SSB, Jo-1, RPP, centromere and Scl-70 antibodies
Extractable Nuclear Antigen Antibodies (RNP, Smith, Scleroderma, SSA, & SSB) 0050653 Method: Semi-Quantitative Multiplex Bead Assay	Clarify pattern result from ANA Assay may help differentiate among mixed connective tissue disease, rheumatoid arthritis, scleroderma, Sjögren syndrome and systemic lupus erythematosus
SSA (Ro) (ENA) Antibody, IgG 0050691 Method: Semi-Quantitative Multiplex Bead Assay	Order as secondary screen based on results of ANA test
SSB (La) (ENA) Antibody, IgG 0050692 Method: Semi-Quantitative Multiplex Bead Assay	Order as secondary screen based on results of ANA test

General References

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Reviewed by

Tebo, Anne E., PhD. Assistant Medical Director, Immunology at ARUP Laboratories; Assistant Professor of Pathology (Clinical), University of Utah

Diagnostic Algorithm(s)

PDF algorithm(s) available at www.arupconsult.com.

Connective Tissue Disease Testing Algorithm

Related Content

Connective Tissue Diseases

Cryoglobulinemia

Inflammatory Myopathies

Mixed Connective Tissue Disease - MCTD

Scleroderma - Systemic Sclerosis

Systemic Lupus Erythematosus - SLE

Vasculitis - ANCA

Wegener Granulomatosis

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