

## Sjögren's Syndrome — Diagnosis and Treatment

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**Sjogren's syndrome is a systemic chronic inflammatory disease that is characterized by infiltrative lymphocytic inflammation of the exocrine organs. Sjogren's syndrome is more common in women. Most patients are in their 50s to 60 years of age. Patients present with sicca symptoms which include xerophthalmia, xerostomia, and parotid gland enlargement.**



### Classification Criteria for the Diagnosis of Sjogren's Syndrome

Like other rheumatological disorders, Sjogren's syndrome is a diagnosis that is made after balancing the patient's presentation and findings with pre-set criteria to make the diagnosis an objective one. There are currently two classification sets of criteria available for clinicians for the diagnosis of Sjogren's Syndrome.

#### American-European Consensus Group Classification (AECG Criteria)

AECG criteria for the classification of Sjogren's syndrome have the advantage of allowing the diagnosis of Sjogren's syndrome in patients who **do not present with sicca symptoms**. The diagnosis of Sjogren's syndrome can be made if the patient has a positive minor salivary gland biopsy findings and positive anti-SSA or anti-SSB antibody

results.

**PLUS at least three of the following minor criteria:**

Ocular symptoms which include:

- Dry eyes for more than 3 months
- Foreign body sensation in the eyes
- Need for artificial tear use for more than 3 times a day

Oral symptoms include:

- Including the feeling of dry mouth for >3 months
- Swollen salivary glands
- Frequent use of liquids to aid in swallowing

Ocular signs such as:

- Positive Schirmer test (< 5 mm in 5 minutes)
- Positive vital dye testing

Oral signs such as:

- Abnormal salivary scintigraphy findings
- Abnormal parotid scintigraphy
- The unstimulated salivary flow below 1.5 mL in 15 minutes

Positive autoantibodies such as:

- Anti SSA (Ro)
- Anti SSB (La)

Patients who meet the above mentioned diagnostic criteria who do not have other connective tissue disorders are diagnosed with **primary Sjogren's syndrome**. Those who have a dry eye or mouth in addition to one more criterion of the above who also have a history of connective tissue disease are diagnosed with **secondary Sjogren's syndrome**.

AECG also put exclusion criteria that make the diagnosis of Sjogren's syndrome obsolete.

**AECG exclusion criteria include any of the following:**

- Hepatitis C
- Prior lymphoma
- [Sarcoidosis](#)
- Graft versus host disease
- Acquired immunodeficiency syndrome
- History of head and/or neck irradiation
- History of use of anticholinergic drugs

## American College of Rheumatology Classification Criteria for Sjogren's Syndrome

In 2012, the American College of Rheumatology formulated new diagnostic criteria for the diagnosis of Sjogren's syndrome. **The diagnosis of Sjogren's syndrome can be confirmed if two of the following are present:**

- Positive serum anti-SSA and/or anti-SSB antibodies

- Positive rheumatoid factor plus antinuclear antibody titer of at least 1:320
- Ocular staining score of at least 3
- The presence of focal lymphocytic infiltrates on labial salivary gland biopsy

The issue with these diagnostic criteria is that they cannot differentiate between primary and secondary Sjogren's syndrome.

## Epidemiology of Sjogren's Syndrome

Sjogren's syndrome is a very common rheumatologic disorder. In fact, recent epidemiological studies have shown that Sjogren's syndrome is the **second most common rheumatologic disorder** after [systemic lupus erythematosus](#) in the United States.

The estimated prevalence of Sjogren's syndrome in the general population is around 0.1 to 4%. This high variability in the reported prevalence among different epidemiological studies can be explained by the fact that the AECG diagnostic criteria, which are more commonly used than the American College of Rheumatology Criteria, take into account some subjective symptoms such as eye or mouth dryness.

Sjogren's syndrome has been reported to have an equal prevalence and natural history in all ethnic groups. The female-to-male ratio of Sjogren's syndrome is reported to be 9 to 1. Sjogren's syndrome typically affects women aged between 50 and 60 years.

Sjogren's syndrome carries a good prognosis. The prognosis of Sjogren's syndrome and the morbidity or mortality of the disease is largely dependent on the co-presence of other connective tissue disorders such as systemic lupus erythematosus. The risk of [non-Hodgkin lymphoma](#) is 18.9 times higher in patients with Sjogren's syndrome compared to the general population.

## Prognosis

Patients developing disorders related to Sjögren syndrome have a relatively good prognosis as seen with other closely related disorders such as lymphoma.

Of note is that primary Sjögren syndrome has been associated with a lower risk of cardiovascular events like myocardial infarction and stroke thus better survival rates.

## Morbidity and mortality

Morbidity from the disease arises from dysfunction of the involved exocrine organs, which are gradually infiltrated with lymphocytes.

Mortality has been associated with other disorders related to the disease such as primary biliary cirrhosis.

**The most important risk factors for the development of lymphoma in a patient with Sjogren's syndrome are tabulated below:**

- Regional or generalized lymphadenopathy
- Hepatosplenomegaly
- Presence of leukopenia
- Renal insufficiency
- Development of a monoclonal gammopathy
- Rheumatoid factor positivity

- Significant salivary gland enlargement
- Anti-SSA and anti-SSB positivity

Pregnant women with Sjogren’s syndrome might experience worsening of [pulmonary hypertension](#). Moreover, the risk of spontaneous abortion appears to be higher in pregnant women with Sjogren’s syndrome. The risk of congenital heart block in the offspring is related to the positivity of anti-SSA antibodies.

## Clinical Presentation of Sjogren’s Syndrome

The main symptoms of Sjogren’s syndrome include **xerophthalmia (dry eyes) and xerostomia (dry mouth)**. This is often associated with bilateral parotid gland swelling. Peri-epithelial infiltrative processes and extraepithelial extra-glandular involvement are the two most common types of extra-glandular involvement in Sjogren’s syndrome.

<b>Peri-epithelial infiltrative processes</b>	<ul style="list-style-type: none"> <li>• Interstitial nephritis</li> <li>• Liver involvement               <ul style="list-style-type: none"> <li>• Bronchiolitis</li> </ul> </li> </ul>
<b>Extraepithelial extra-glandular involvement</b>	<ul style="list-style-type: none"> <li>• Palpable purpura</li> <li>• Glomerulonephritis</li> <li>• <a href="#">Peripheral neuropathy</a></li> </ul>

These manifestations are associated with B-cell hyperreactivity, hypergammaglobulinemia, and the formation of immune complexes.

Dryness of the eyes presents with eye redness, itchiness, and pain. Patients might complain of foreign-body sensation. This is often described as a sandy sensation.

### Symptoms related to mouth dryness include:

- Inability to eat dry food
- Tongue sticking to the roof of the mouth
- Drinking large amounts of water at night
- Difficulty speaking for long periods
- Development of hoarseness
- Increased incidence of dental caries
- Development of oral candidiasis

Patients with Sjogren’s syndrome might also develop skin dryness, eyelid dermatitis, pruritus, or erythema annular. Dry cough due to the dryness of the tracheobronchial mucosa can be seen in patients with Sjogren’s syndrome. The risk of [interstitial lung disease](#) is higher in patients with Sjogren’s syndrome. Patients can also develop recurrent bronchitis, pneumonitis, or infectious pneumonia.

### The main neurologic manifestations of Sjogren’s syndrome are:

- [Seizures](#)
- Myelopathy
- Optic neuropathy
- Cognitive dysfunction
- Encephalopathy

Neurologic involvement is reported to occur in about 8% of patients with Sjogren’s syndrome. Subclinical sensory, motor or sensorimotor peripheral neuropathy is reported to be present in up to 50% of the patients with Sjogren’s syndrome.

# Schirmer Test in Sjogren's Syndrome

The Schirmer test is performed by **applying a bent piece of Whatman number 41 filter paper in the lower conjunctiva**. This needs to be done without anesthesia, hence it is expected to be very irritating to the eye. The amount of tearing is recorded.

Normal wetting in Schirmer test is defined as greater than 15 mm after 5 minutes of application. A definitive positive result is defined as less than 5 mm of wetting after 5 minutes of application.

## Diagnostic Workup for Sjogren's Syndrome

Before we talk about the more specific laboratory tests available for the diagnosis of Sjogren's syndrome, we shall discuss the general approach to a patient who is suspected to have Sjogren's syndrome.

**The following laboratory findings are commonly seen in patients with Sjogren's syndrome, however, none of them are specific:**

- Elevated serum erythrocyte sedimentation rate
- Leukopenia - associated with an increased risk of lymphoma
- Anemia
- Eosinophilia
- Hypergammaglobulinemia - associated with an increased risk of lymphoma
- Presence of antinuclear antibodies such as anti-Ro and anti-La
- Presence of rheumatoid factor
- Presence of anti-alpha-fodrin antibody - especially in juvenile Sjogren's syndrome
- Positive anti-SSA or anti-SSB

Staining is used to confirm the absence of a mucin protective layer in the eyes due to eye dryness. A stain such as rose Bengal, lissamine, or fluorescein is applied to the conjunctiva and cornea. If there is epithelial damage due to dryness, this can be easily visualized with a slit-lamp examination after the application of one of the previously mentioned stains.

Sialography and scintigraphy are helpful in the evaluation of the salivary glands in patients with Sjogren's syndrome. Sialography is helpful in evaluating the patency of the salivary gland ducts and in excluding strictures, whereas, scintigraphy is useful in the evaluation of the rate of saliva production which is expected to be diminished in Sjogren's syndrome.

The golden-standard to confirm the diagnosis of Sjogren's syndrome nowadays is a minor [salivary gland biopsy](#). Because the currently available treatments for Sjogren's syndrome are against the symptoms of the disease, the confirmation of the diagnosis with an invasive procedure such as a biopsy is rarely clinically indicated.

**If a biopsy is performed, the following findings confirm the diagnosis of Sjogren's syndrome:**

- Focal aggregates of lymphocytes
- CD4+ T cells predominance
- Focal aggregates are seen in all salivary glands
- Presence of 10% CD5+ B cells in the population of lymphocytes

The presence of more than 1 focus of lymphocytes aggregates per 4 mm<sup>2</sup> has a 95% specificity and 81% sensitivity for the diagnosis of Sjogren's syndrome.

## Complications related to Sjögren syndrome

The condition may lead to the development of the following:

- Infection of the parotid gland, that may cause unilateral worsening of symptoms, tenderness, warmth, and erythema. The incriminated organisms are staphylococcal, streptococcal, or pneumococcal species.
- The disease increases the chance of developing disorders associated with Sjögren syndrome, such as [systemic lupus erythematosus](#) (SLE), [rheumatoid arthritis](#) (RA)
- Development of parotid tumors, which depicts an unusually hard or unilateral parotid enlargement.
- Development of pseudolymphomas and non-[Hodgkin B-cell lymphomas](#).
- Dry mouth and eyes may lead to dental cavities and vision problems.
- It may also cause generalized inflammation of the body organs leading to states such as pneumonia or hepatitis.

## Treatment of Sjogren's Syndrome

Patients with Sjogren's syndrome receive symptomatic treatment as there is currently **no curative treatment for Sjogren's syndrome**. Patients who report skin and vaginal dryness are treated with creams such as Eucerin, and skin lotions. Vaginal estrogen creams might be used in postmenopausal women. Acetaminophen and nonsteroidal anti-inflammatory drugs are helpful in patients complaining of arthritis or joint pain.

Objective measurement of tearing parameters including tear film stability, tear osmolarity, and the degree of ocular surface damage needs to be performed before starting treatment. Patient's education is essential for the successful treatment of dry eyes in Sjogren's syndrome.

Symptoms	Treatment
<ul style="list-style-type: none"><li>• Mild symptoms</li><li>• No corneal damage</li></ul>	Artificial tears that need to be applied liberally.
<ul style="list-style-type: none"><li>• Moderate to severe symptoms</li><li>• Mild corneal or conjunctival staining</li></ul>	Unpreserved tears or gels, night-time ointments, topical steroids, cyclosporine A, and possible secretagogues.
<ul style="list-style-type: none"><li>• Severe symptoms</li><li>• Marked corneal damage</li></ul>	Serum tears, temporary plugging of the lacrimal puncta, and perhaps tetracyclines.
<ul style="list-style-type: none"><li>• Extremely severe symptoms</li><li>• Corneal erosions, or conjunctival scarring</li></ul>	Systemic anti-inflammatory therapy with acetylcysteine, topical vitamin A, and permanent punctual occlusion.

## References

Medscape: <https://emedicine.medscape.com/article/332125>

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