Primary Care Reports
The Practical, Peer-Reviewed Journal for Primary Care and Family Physicians
Volume 18, Number 8 / August 2012 www.ahcmedia.com

Authors:

Amal Mehta, MD, MBA,
Rheumatology Fellow, Loma Linda University Medical Center, Loma Linda, CA

Keith Colburn, MD,
Professor of Medicine, Chief of Rheumatology, Loma Linda University and Loma Linda VA Medical Center, Loma Linda, CA

Peer Reviewer:

Matthew E. Fink, MD,
Professor and Chairman, Department of Neurology, Weill Cornell Medical College, New York, NY

Statement of Financial Disclosure

To reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, Dr. Mehta (author), Dr. Colburn (author), Dr. Fink (peer reviewer), Dr. Wise (editor), Ms. Coplin (executive editor), and Ms. Kimball (managing editor) report no financial relationships relevant to this field of study.

AHC Media

An Update on Sjogren's Syndrome

Introduction

Sjogren's syndrome is an autoimmune condition that leads to chronic inflammation with salivary and lacrimal gland dysfunction. The diagnosis of Sjogren's often is delayed by several years because the initial presenting symptoms can be non-specific. However, some manifestations of Sjogren's may be life threatening, including brain damage and cancer. It is very important for the primary care physician to recognize the early signs and symptoms and to initiate the appropriate workup and treatment in coordination with consulting specialists to prevent further morbidity and mortality.

Epidemiology

Sjogren's syndrome is divided into two subclasses, primary and secondary Sjogren's. Primary Sjogren's refers to an autoimmune condition of chronic inflammation with salivary and lacrimal gland dysfunction without another underlying autoimmune condition.[1] Secondary Sjogren's is associated with autoimmune conditions, most commonly rheumatoid arthritis and systemic lupus erythematosus (SLE).[1,2] It is estimated that 25% of patients with rheumatoid arthritis and SLE have secondary Sjogren's.[1] The symptoms of Sjogren's and a secondary underlying autoimmune condition may overlap, which can make the diagnosis of secondary Sjogren's challenging. The prevalence of Sjogren's is estimated between 0.5% and 0.6% and it affects approximately 4 million people in the United States. The gender distribution is predominantly female, with a female to male ratio of 9:1. The mean age of onset is between 45 and 55 years of age. There is an equal distribution in the prevalence of primary and secondary Sjogren's.[1,2]

Pathology

The etiology of Sjogren's is unclear; however, there have been some reports of an association of this disease with specific HLA-DR and HLA-DQ alleles, but only in patients who are SS-A and SS-B antibody positive.[2] A biopsy of the minor salivary and lacrimal glands reveals periductal focal lymphocytic infiltrates (*See Figures 1 and 2*). The severity of inflammation is determined by a scoring system called the "focus score." The pathologist will count the number of inflammatory infiltrates of at least 50 cells in 4 mm squared of gland surface unit. A focus score > 1 per 4 mm squared is significant.[3]

Immunohistology reveals that 75% of the infiltrating cells are T lymphocytes, mainly CD45RO memory helper T cells, and 10% are B cells that are usually found within clusters of T lymphocytes.[4] Cell activating factor (BAFF) promotes maturation and survival of B cells. Elevated levels of BAFF have been found in the serum of Sjogren's patients and correlate with the levels

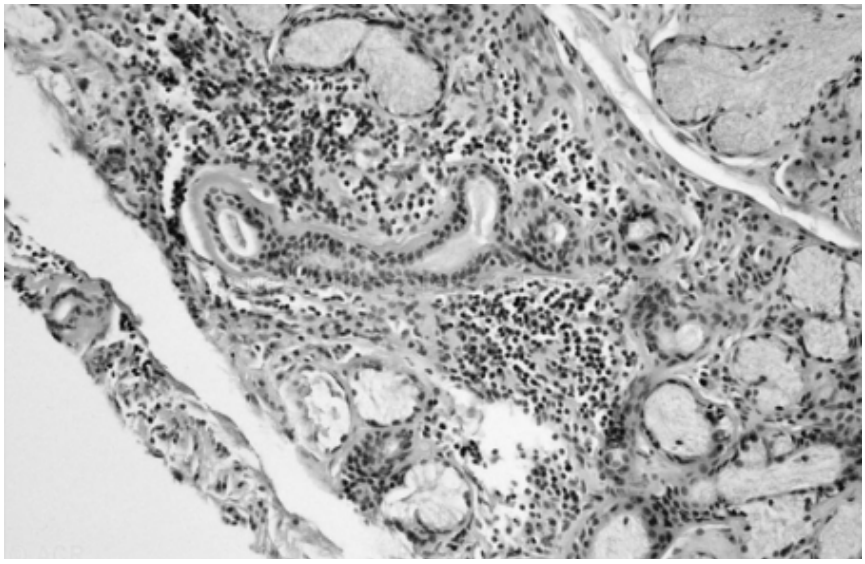
Executive Summary

Sjogren's syndrome is an autoimmune condition that leads to chronic inflammation with salivary and lacrimal gland dysfunction with two subclasses, primary and secondary.

- Mikulicz reported the index patient in 1892 describing a farmer with bilateral parotid and lacrimal gland enlargement with round cell infiltration. In 1933, the Swedish ophthalmologist Henrik Sjogren introduced the term keratoconjuntivitis sicca to describe the clinical and histologic characteristics of 19 women with dry mouth and dry eyes.
- Sjogren's affects an estimated 4 million people in the United States with a predominantly female to male distribution of 9:1 and a mean age of onset between 45 and 55 years of age.
- Salivary gland enlargement occurs in 30-50% of patients. The glands are firm, diffusely enlarged, and non-tender.
- Patients with primary Sjogren's have 40 times the risk of developing lymphoma compared to the general population.
- Systemic manifestations of Sjogren's include arthralgia, myalgias, fever, and easy fatigability.
- The primary care physician needs to be aware that the average time between a patient's first symptom and diagnosis is 6.5 years.
- Treatment typically includes comanagement with an ophthalmologist and dentist. The development of chronic erythrematous candidiasis typically requires antifungal therapy and extraglandular manifestations may require glucocorticoids and immunosuppressants.

of circulating autoantibodies.[1] Some researchers propose a viral mechanism that either includes chronic inflammation or provides an antigen that triggers autoimmunity.[1] Suggested viruses include Epstein-Barr virus (EBV), coxsackie, hepatitis C virus (HCV), human T-lymphotropic virus Type I, and human immunodeficiency virus (HIV). EBV DNA has been identified in the major and minor salivary gland tissue of Sjogren's patients and coxsackie RNA has been found in the minor salivary glands of primary but not secondary Sjogren's patients.[1]

Figure 1: Lip biopsy shows two lymphocytic foci adjacent to normal appearing mucinous acini typical of minor salivary gland abnormalities in Sjogren's Syndrome.



Source: © 2012 American College of Rheumatology. Used with permission.

Clinical Presentation

Patients with Sjogren's syndrome can present with a variety of clinical manifestations due to the inflammatory nature of the disease, but the two most common complaints are dry eyes and dry mouth. A prospective cohort of 400 patients found that 98% had xerostomia and 93% had xerophthalmia.[5] Keratoconjunctivitis sicca results from decreased tear production and changes in the tear film, which leads to repeated dehydration of the ocular surface epithelium and keratinization.[1] Characteristic symptoms include a foreign body sensation in the eye, pain, burning, inability to tear, and photophobia. The use of a tear substitute more than three times per day, even in the absence of xerophthalmia, fulfills the dry eye component of the diagnostic criteria. Patients with xerophthalmia have a higher risk of *Staphylococcus aureus* eye infections; immunosuppressant

medications are commonly used in the management of Sjogren's, so early detection and treatment of ocular infections is important.[1]

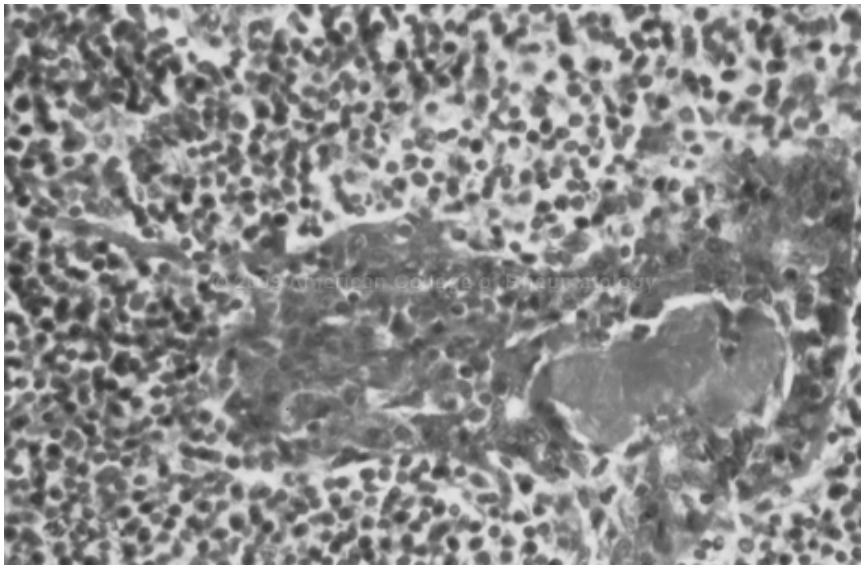
Chronic inflammation of the salivary glands leads to decreased saliva production and changes in the oral flora of the mouth. Patients complain of dry mouth, have difficulty chewing or swallowing dry food, and often take frequent sips of water due to the xerostomia.[1,2] The patient also may complain of a change in taste and a burning sensation in the mouth. Clinically, the examining physician should look for an absence of salivary pooling at the mouth floor, fissuring and redness of the tongue, and cavities in unusual places (*See Figures 3 and 4*). Patients with Sjogren's develop cavities at the neck of the teeth next to the gingiva, cusp tips of posterior teeth, or incisal edges of anterior teeth.[6]

Because of the dryness, these patients may develop hoarseness, recurrent bronchitis, and pneumonia. Exocrine gland dysfunction also may produce a loss of pancreatic function and hypochlorhydria.[7] Dermal and vaginal dryness also occur.

Salivary gland enlargement occurs in 30-50% of patients with Sjogren's, and the glands are firm, diffuse, and non-tender (*See Figure 5*). At least 20-30% of patients have bilateral enlargements of the parotid or submandibular glands (*See Figure 6*).

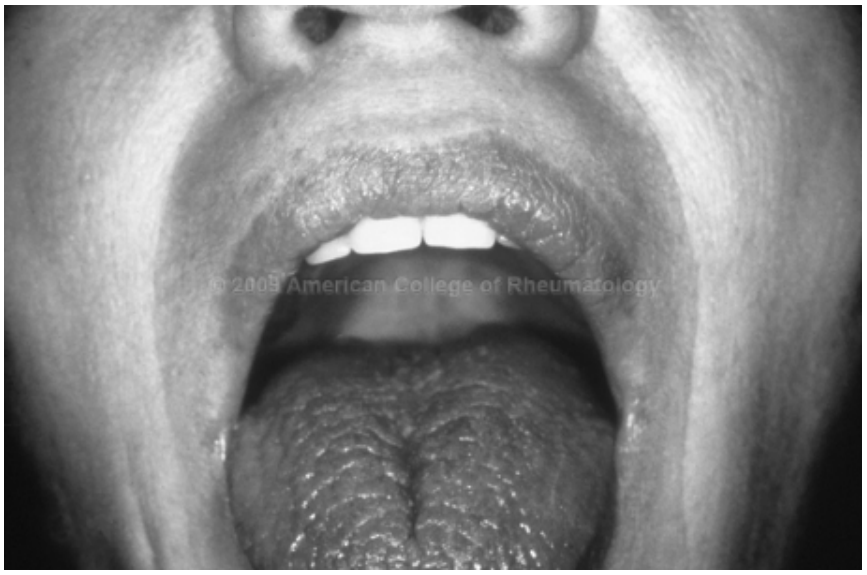
Patients with primary Sjogren's have 40 times the risk of developing lymphoma when compared to the general population.[5] Tumors are usually lymphoepithelial lesions due to a benign reactive process; however, they can transform into mucosa-associated lymphoid tissue (MALT) lymphoma (*See Figure 7*). Patients with B symptoms — such as fever, weight loss greater than 10% of body weight in 6 months, and night sweats — are at a higher risk for developing lymphoma and should be monitored closely.[8] The 5-year survival of appropriately treated MALT lymphoma is 85-95% and the 10-year survival is > 75%.[8] Systemic manifestations of Sjogren's include arthralgias, myalgias, fever, and easy fatigability. Arthritis that appears and acts like rheumatoid arthritis and that has erosions occurs in about half of patients with Sjogren's. It can develop into Jaccoud's arthritis like that in SLE and rheumatic fever.[7]

Figure 2: Parotid gland parenchyma has been replaced by lymphocytes. The lumen of the salivary ductile in the center of the field is occluded by an eosinophilic deposit of thickened secretion.



Source: © 2012 American College of Rheumatology. Used with permission.

Figure 3: Dryness of the mouth and tongue from a lack of salivary secretion causing a deep red tongue

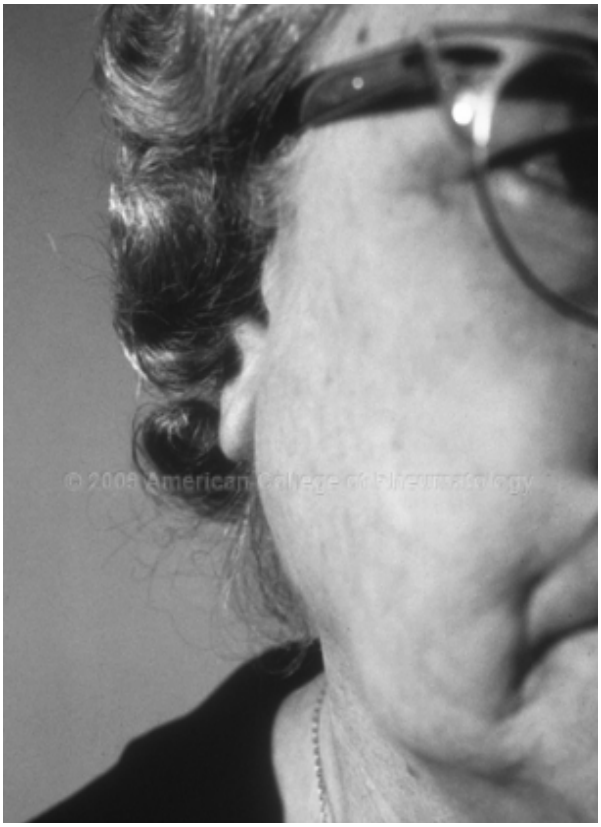


Source: © 2012 American College of Rheumatology. Used with permission.

Figure 4: Salivary hypofunction causing extensive fissuring of the tongue

Source: © 2012 American College of Rheumatology. Used with permission.

Figure 5: Unilateral parotid enlargement in a patient with Sjogren's syndrome



Source: © 2012 American College of Rheumatology. Used with permission.

Patients with Sjogren's syndrome may develop other extraglandular manifestations, such as Raynaud's syndrome, autoimmune thyroiditis, distal renal tubular acidosis (RTA), autoimmune hepatitis, primary biliary cirrhosis, pulmonary disease (chronic diffuse interstitial infiltrates, restrictive pattern demonstrated on pulmonary function tests [PFTs], pulmonary alveolitis, and later fibrosis), genitourinary symptoms (vaginal dryness, increased frequency of endometriosis, menorrhagia, metrorhagia), cutaneous vasculitis (usually small vessel lesions with a leukocytoclastic vasculitis and occasionally cerebral vasculitis), and peripheral nerve dysfunction.

Laboratory Tests

There are no definitive lab tests for Sjogren's; however, laboratory tests can be suggestive of Sjogren's. Patients may have elevated inflammatory markers including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), positive SS-A/SS-B antibodies, positive antinuclear antibody (ANA), and hypocomplementemia orcryoglobulinemia. A multicenter report of 400 patients with primary Sjogren's reported finding the following positive tests:[2]

- anti-Ro(ssA) — 40%
- anti-La(ssB) — 26%
- antinuclear antibody — 74%
- rheumatoid factor (RF) — 38%
- anemia — 20%
- leukopenia — 16%
- thrombocytopenia — 13%
- hypocomplementemia — 24%.

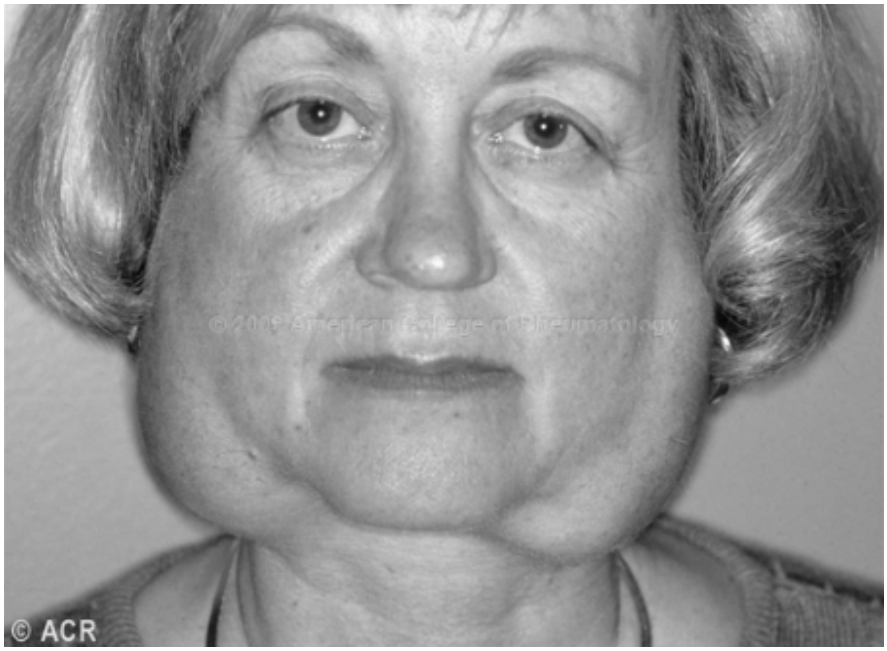
It is important to yearly monitor a rheumatoid factor, serum IGM, cryoglobulin level, and C4 levels in patients with Sjogren's syndrome,

because decreased levels of one or all may herald the occurrence of a lymphoma. A number of diseases are associated with Sjogren's Syndrome including some other autoimmune diseases (*See Table 1*).

Diagnosis

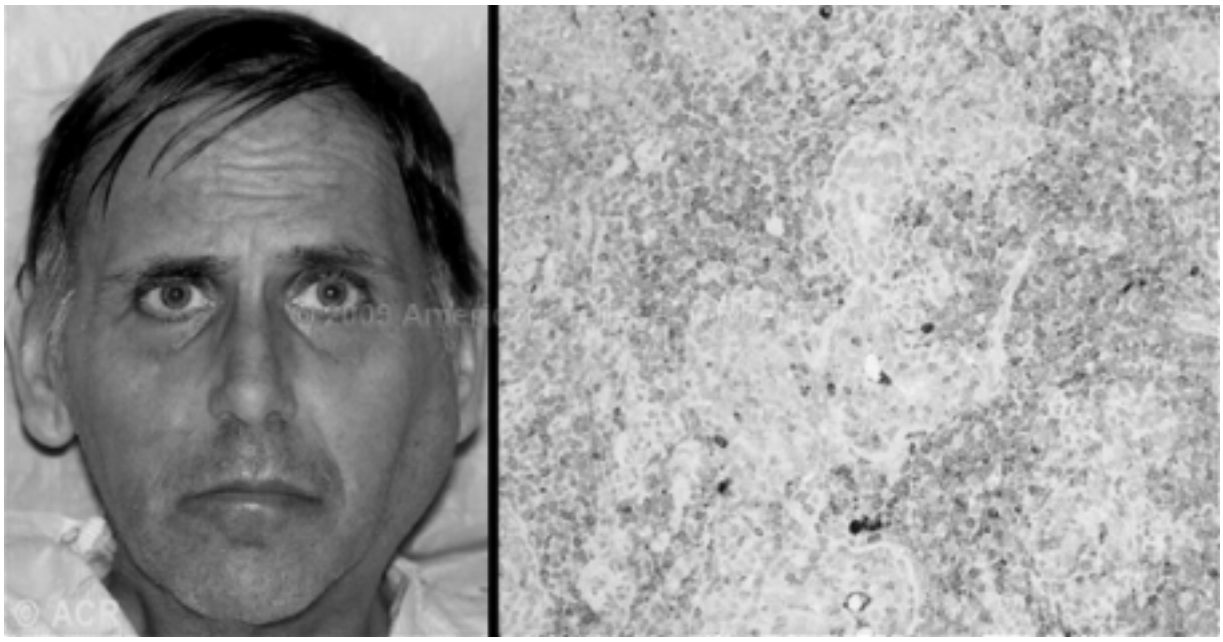
The diagnosis of Sjogren's syndrome often is delayed because the initial presenting symptoms can be nonspecific. A survey of 3000 patients with Sjogren's reported that the average time between a patient's first symptoms and diagnosis was 6.5 years.[2] More than 10 classification criteria have been developed, but the most widely used is the European Community Preliminary Criteria, which also is the least restrictive and diagnoses five times as many people as the most restrictive criteria.[1] Several revisions to the European Community Preliminary Criteria have been made. The most current is the American-European Consensus (*See Table 2*).

Figure 6: Marked bilateral parotid enlargement in a patient with Sjogren's syndrome



Source: © 2012 American College of Rheumatology. Used with permission.

Figure 7: 48-year-old man with Sjogren's syndrome with a large left parotid mass. On biopsy, B-cell lymphoma of MALT type was identified. Microscopic section of parotid biopsy, stained with immunoperoxidase for kappa light chains (brown-stained cells), showed monoclonal population of B cells, confirming the diagnosis.[8]



Source: © 2012 American College of Rheumatology. Used with permission.

Table 1: Disease Associations with Sjogren's Syndrome (Secondary Sjogren's)

- Scleroderma
- Systemic lupus erythematosus
- Rheumatoid arthritis
- Polyarteritis nodosa
- Mixed cryoglobulinemia
- Undifferentiated connective tissue disease (mixed connective tissue disease)
- Primary biliary cirrhosis
- Polymyositis/dermatomyositis
- Thyroiditis
- Chronic hepatitis C
- Fibromyalgia syndrome
- Lymphoma
- Waldenstrom's macroglobulinemia

The three tests for keratoconjunctivitis sicca are Schirmer's test, Rose Bengal, and tear breakup time. The Schirmer's test involves placing a piece of filter paper in the lateral third of the lower eyelid. The patient then closes his eye and the amount of wetting on the paper is measured. More than 10 mm of moisture on the filter paper in 5 minutes is normal. Less than 5 mm is definitely abnormal (*See Figure 8*). The Rose Bengal measures damage to the conjunctival and corneal epithelial cells by staining damaged tissue with Rose Bengal solution.[9,10,11] A slit lamp is needed to score the staining so this test is primarily performed by ophthalmologists (*See Figure 9*). The tear break-up time measures the

Table 2: American-European Consensus Classification Criteria for Sjogren's Syndrome

I. Ocular symptoms: A positive response to at least one of the following questions:

- Have you had daily, persistent, troublesome dry eyes for more than 3 months?
- Do you have a recurrent sensation of sand or gravel in the eyes?
- Do you use tear substitutes more than three times per day?

II. Oral symptoms: A positive response to at least one of the following questions:

- Have you had a daily feeling of dry mouth for more than 3 months?
- Have you had recurrently or persistently swollen salivary glands as an adult?
- Do you frequently drink liquids to aid in swallowing dry food?

III. Ocular signs: Objective evidence of ocular involvement defined as a positive result for at least one of the following two tests:

- Schirmer's test, performed without anaesthesia (< 5mm in 5 minutes)
- Rose Bengal score or other ocular dry score (> 4 according to van Bijsterveld's scoring system)

IV. Histopathology: In minor salivary glands (obtained through normal appearing mucosa) focal lymphocytic sialoadenitis, evaluated by an expert histopathologist, with a focus score > 1, defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4 square mm of glandular tissue

V. Salivary gland involvement: Objective evidence of salivary gland involvement defined by a positive result for at least one of the following diagnostic tests:

- Unstimulated whole salivary flow (<1.5 ml in 15 minutes)
- Parotid sialography showing the presence of diffuse sialectasias (punctuate, cavitary or destructive pattern), without evidence of obstruction in the major ducts
- Salivary scintigraphy showing delayed uptake, reduced concentration, and/or delayed excretion of tracer

VI. Autoantibodies: Presences in the serum of the following autoantibodies:

- Antibodies to Ro (SSA) or La (SSB) antigens, or both

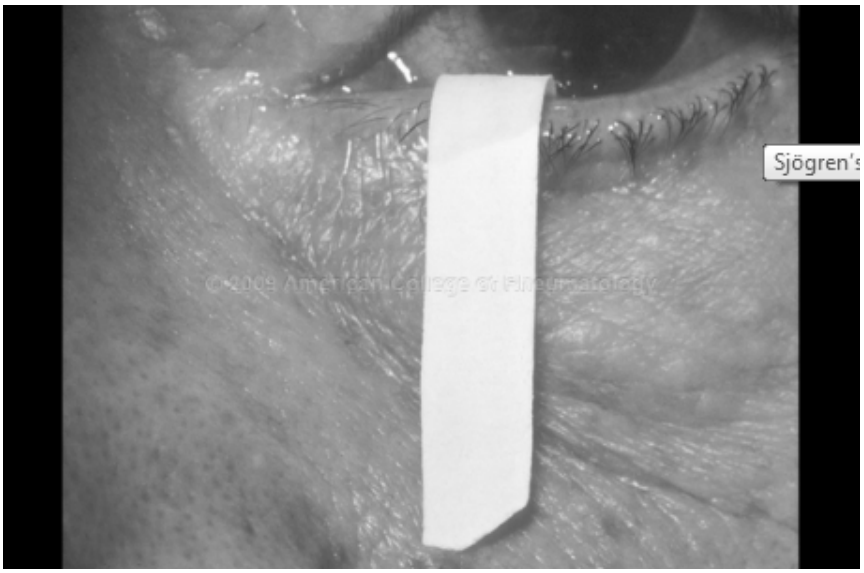
stability of the tear film. Fluorescein drops are added to the eye and the tear clearance is measured. Patients with Sjogren's have disturbances in the tear film and they have rapid clearance of tears. A clearance time of > 10 seconds is normal, 5-10 seconds is marginal, and < 5 seconds is abnormal.[10,11]

There are four tests to quantify xerostomia, salivary gland scintigraphy, parotid sialography, whole sialometry, and the Saxon test. Salivary scintigraphy measures the function of the major salivary glands. A very low uptake is specific but not sensitive for Sjogren's.[12] Parotid gland sialography is rarely performed in the United States and involves cannulating the major salivary gland ducts and adding a contrast material to aid in visualization. Studies report that salivary scintigraphy correlates better with parotid function.[13] Whole sialometry measures the volume of unstimulated saliva production in 15 minutes. Greater than 1.5 ml of saliva is normal. The Saxon test also measures the amount of saliva produced but also measures the amount of stimulated saliva production. The patient is given a sponge to chew on for 2 minutes and the weight of the sponge prior and post chewing is measured. An increase in weight of at least 2.75 g is considered normal.[14] It is important to note that these tests for xerostomia are primarily done for research purposes.

If clinical and serologic evidence is not sufficient to make the diagnosis, labial salivary gland biopsy can be performed. It is important for the surgeon to obtain the biopsy from the lower lip that is macroscopically normal and obtain at least four lobules of salivary tissue.[1,2]

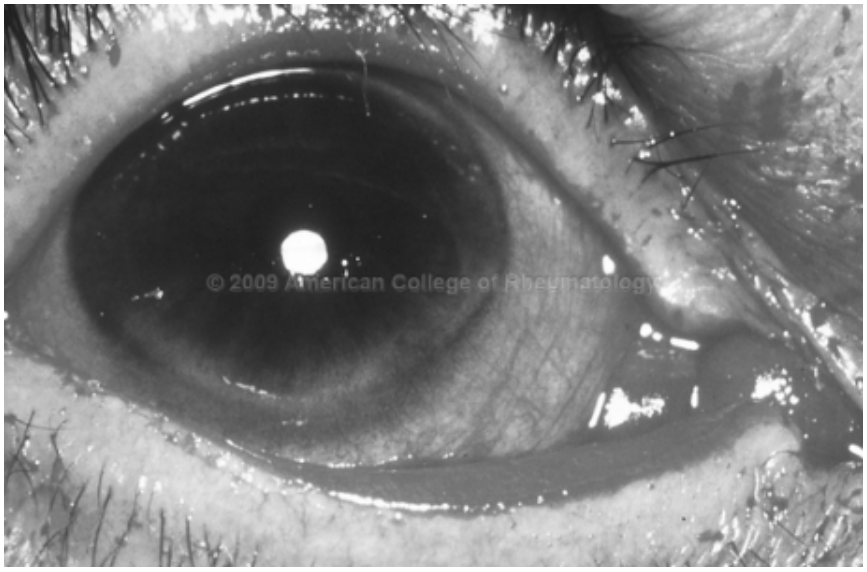
The nonspecific nature of Sjogren's allows for many mimicking diseases. A differential diagnosis for dry eyes should include anticholingeric medications, chronic conjunctivitis, neurologic diseases that impair blinking such as Bell's palsy, and diseases that infiltrate the

Figure 8: Schirmer's test: The filter paper strip is placed at the junction of the eyelid margin. After 5 minutes, 15 mm of paper should be moistened if tear production is normal, as shown here. Persons over the age of 40 may moisten between 10 mm and 15 mm. Patients with Sjogren's syndrome typically have less than 5 mm of moistening.



Source: © 2012 American College of Rheumatology. Used with permission.

Figure 9: Reddish-purple discolorations are seen in the lower portion of the cornea and conjunctiva. These changes are typical of keratoconjunctivitis sicca when the eye is stained with Rose Bengal dye; they are the result of decreased tear formation and represent corneal abrasions.



Source: © 2012 American College of Rheumatology. Used with permission.

Table 3: Conditions Causing Enlarged Salivary Glands

- Viral infections
- Sarcoidosis
- Diabetes mellitus
- Hyperlipoproteinemia
- Cirrhosis of the liver
- Chronic pancreatitis
- Acromegaly
- Idiopathic parotitis in children
- Neoplasms of salivary glands*
- Bacterial infections*
- Sialadenitis*
- Salivary duct stones*

*usually unilateral

lacrimal glands such as sarcoidosis, amyloidosis, and lymphoma.[1,2] The differential diagnosis for dry mouth should include anticholinergic medications, sialadenitis, viral infections such as HIV and HCV, and irradiation.[1,2]

If a patient has unilateral parotid swelling you should rule out infection, stones, and malignancy. The differential diagnosis of bilateral parotid swelling includes acute viral infections such as EBV, mumps, coxsackie, and chronic viral infections such as HCV, HIV, and tuberculosis. Other causes of bilateral parotid swelling include sarcoidosis, malnutrition, alcoholism, bulimia, acromegaly, and diabetes.[1,2] (*See Table 3.*)

Treatment

The treatment for ocular symptoms depends on the severity of symptoms and is often comanaged with an ophthalmologist. For mild keratoconjunctivitis sicca, artificial tear drops during the day and preservative-free ointments at night are the treatments of choice. For advanced disease, patients may benefit from systemic cholinergics, such as pilocarpine 5 mg TID to QID or cevimeline 30 mg TID.[1,2] It is advisable to start the patient on a low dose and slowly titrate up to minimize side effects. Cyclosporine 0.05% ophthalmic solution also can be beneficial, but it is important to evaluate for underlying eye infections before starting cyclosporine eye drops.[2,15] Aside from treating dry mouth symptoms, early detection and treatment of oral caries by a dentist is critical because many patients with salivary hypofunction cannot wear dentures. Dentists will use various fluoride preparations, make dietary recommendations, and use antibiotics to control oral flora. There are commercially available tests that monitor the level of caries causing bacteria.[6] Fluoride is used for remineralization of early cavity-causing lesions and also inhibits demineralization and may inhibit plaque bacteria.[6] Several over-the-counter synthetic saliva preparations are available and sugar-free lozenges for salivary stimulations are effective techniques for managing xerostomia.[1,2,6] Systemic cholinergics (pilocarpine and cevimeline) are also beneficial.[1,2] About 33% of patients with Sjogren's suffer from chronic erythematous candidiasis. Clinically, there is an absence of filiform papillae and symmetric mucosal erythema. If the patient produces an adequate amount of saliva, which is observable as salivary pooling at the mouth floor, then fluconazole 100 mg daily for 2 to 4 weeks is the recommended regimen.[2,15] If the patient does not produce an adequate amount of saliva, systemic antifungal agents will not reach the infected region so topical antifungals are the preferred treatment.[1,2] All commercially available topical antifungal preparations contain sucrose, which is contraindicated in Sjogren's, so the patient will have to be referred to a specialty pharmacy for a sugar-free preparation.[1,6]

The treatment of extraglandular manifestations depends on the manifestation and severity. Arthralgias and arthritis can be treated with non-steroidal anti-inflammatory drugs, hydroxychloroquine, and methotrexate.[1,2] Severe extraglandular manifestations, such as vasculitis, CNS disease, cardiopulmonary disease, and glomerulonephritis, may require glucocorticoids and strong systemic immunosuppressants, such as mycophenolate mofetil, cyclophosphamide, or rituximab.[1,2] Treatment with immunosuppressant agents should be administered under the guidance of a rheumatologist, if possible, largely to judge the effect of the medication and the early presence of potentially serious side effects.

Conclusion

Sjogren's syndrome is an autoimmune condition that leads to chronic inflammation and dysfunction of the salivary and lacrimal glands. Sjogren's syndrome is a systemic condition and extraglandular manifestations are common. The nonspecific nature of the disease often results in delays in the diagnosis. The management is typically multidisciplinary and requires primary care physicians, rheumatologists, ophthalmologists, and dentists to work together closely.

Table 4: Patient Information about Sjogren's Syndrome

What is Sjögren's Syndrome?

Sjögren's syndrome is an autoimmune disorder in which immune cells attack and destroy the glands that produce tears and saliva. Sjögren's syndrome is also associated with rheumatic disorders such as rheumatoid arthritis. The hallmark symptoms of the disorder are dry mouth and dry eyes. In addition, Sjogren's syndrome may cause skin, nose, and vaginal dryness, and may affect other organs of the body including the kidneys, blood vessels, lungs, liver, pancreas, and brain.

Sjögren's syndrome affects 1-4 million people in the United States. Most people are more than 40 years old at the time of diagnosis. Women are nine times more likely to have Sjögren's syndrome than men.

Is there any treatment?

There is no known cure for Sjögren's syndrome nor is there a specific treatment to restore gland secretion. Treatment is generally symptomatic and supportive. Moisture replacement therapies may ease the symptoms of dryness. Nonsteroidal anti-inflammatory drugs may be used to treat musculoskeletal symptoms. For individuals with severe complications, corticosteroids or immunosuppressive drugs may be prescribed.

What is the prognosis?

Sjögren's syndrome can damage vital organs of the body with symptoms that may remain stable, worsen, or go into remission. Some people may experience only the mild symptoms of dry eyes and mouth, while others go through cycles of good health followed by severe disease. Many patients are able to treat problems symptomatically. Others are forced to cope with blurred vision, constant eye discomfort, recurrent mouth infections, swollen parotid glands, hoarseness, and difficulty in swallowing and eating. Debilitating fatigue and joint pain can seriously impair quality of life.

What research is being done?

The goals of research on disorders such as Sjögren's syndrome focus on increasing knowledge and understanding of the disorder, improving diagnostic techniques, and finding ways to treat, prevent, and cure the disease.

Resources

National Organization for Rare Disorders (NORD)
55 Kenosia Avenue, Danbury, CT 06810
orphan@rarediseases.org
http://www.rarediseases.org
Tel: 203-744-0100

National Eye Institute (NEI)
31 Center Drive, Rm. 6A32 MSC 2510
Bethesda, MD 20892-2510
2020@nei.nih.gov
http://www.nei.nih.gov
Tel: 301-496-5248

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
31 Center Dr., Rm. 4C02 MSC 2350
Bethesda, MD 20892-2350
NIAMSinfo@mail.nih.gov
http://www.niams.nih.gov
Tel: 301-496-8190 or 877-22-NIAMS (226-4267)

National Institute of Dental and Craniofacial Research (NIDCR)
31 Center Drive, Room 5B-55
Bethesda, MD 20892
nidcrinfo@mail.nih.gov
http://www.nidcr.nih.gov
Tel: 301-496-4261

Sjogren's Syndrome Foundation
6707 Democracy Blvd., Suite 325, Bethesda, MD 20817
tms@sjogrens.org
http://www.sjogrens.org
Tel: 800-4-SJOGREN (475-6473)

Arthritis Foundation
P.O. Box 7669
Atlanta, GA 30357
help@arthritis.org
http://www.arthritis.org
Tel: 800-283-7800, 404-872-7100, or 404-965-7888

Source: National Institues of Health. National Institute of Neurological DIsorders and Stroke. NINDS Sjogren's Syndrome Information Page. Available at: http://www.ninds.nih.gov/disorders/sjogrens/sjogrens.htm. Accessed July 20, 2012.

References

1. Klippel J, et al. Sjogren's Syndrome. *Primer on the Rheumatic Diseases.* New York: Springer. 2008; 389-396.
2. Moutsopoulos H, et al. Sjogren's Syndrome. *Harrison's Rheumatology.* New York: McGraw-Hill. 2010; 124-128.
3. Daniels TE, Whitcher JP. Association of patterns of labial salivary gland inflammation with keratoconjunctivitis sicca. Analysis of 618 patients with suspected Sjogren's syndrome. *Arthritis Rheum* 1994;37:869-877.
4. Adamson TC 3rd, et al. Immunohistological analysis of lymphoid infiltrates in primary Sjogren's syndrome using monoclonal antibodies. *J Immunol* 1983;130:203-208.
5. Kruszka P, O'Brian R. Diagnosis and management of Sjogren syndrome. *Am Fam Physician* 2009;79:465-470. Available at: http://www.aafp.org/afp/2009/0315/p465.html. Accessed July 8, 2012.
6. Wu AJ. Optimizing dry mouth treatment for individuals with Sjogren's syndrome. *Rheum Dis Clin North Am* 2008;34:1001-1010.
7. Tzioufas AG, et al. Sjogren Syndrome. In: Eds. Hochberg MC, et al. *Rheumatology.* 5th Edition. Philadelphia, PA: Mosby/Elsevier. 2011;1339-1350.
8. Voulgarelis M, Moutsopoulos HM. Mucosa-associated lymphoid tissue lymphoma in Sjogren's syndrome: Risks, management, and prognosis. *Rheum Dis Clin North Am* 2008;34:921-933.
9. Afonso AA, et al. Correlation of tear fluoresceine clearance and Schirmer test scores with ocular irritation symptoms. *Ophthalmology* 1999; 106:803-810.
10. Van Bijsterveld. Diagnostic tests in the Sicca syndrome. *Arch Ophthalmol* 1969;82:10-14.
11. Kassan SS, Moutsopoulos H. Clinical manifestations and early diagnosis of Sjogren's syndrome. *Arch Intern Med* 2004;162:1275-1284.
12. Hermann GA, et al, Scintigraphic features of chronic sialadenitis and Sjogren's syndrome: A comparison. *Nucl Med Commun* 1999; 20:1123-1132.
13. Aung W, et al. Sjogren's syndrome: Comparison of assessments with quantitative salivary gland scintigraphy and contrast sialography. *J Nucl Med* 2000;41:257-262.
14. Kohler PF, Winter ME. A quantitative test for xerostomia. The Saxon test, an oral equivalent of the Schirmer test, *Arthritis Rheum* 1985;28:1128-1132.
15. Self SE. Autoantibody testing for autoimmune disease. *Clin Chest Med* 2010;31:415-422.

Primary Care Reports CME Objectives

Upon completion of this activity, participants should be able to:

1. Summarize recent, significant studies related to the practice of primary care medicine;
2. Evaluate the credibility of published data and recommendations related to primary care medicine;
3. Discuss the advantages and disadvantages of new diagnostic and therapeutic procedures in the primary care setting.

CME Instructions

To earn credit for this activity, please follow these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME questions

1. Lymphoma occurs in about 1-5% of patients with Sjogren's syndrome. To screen for lymphoma in these patients it is most important to:
   a. conduct yearly PET scans.
   b. conduct yearly chest x-rays.
   c. conduct yearly serum C4, cryoglobulins, rheumatoid factors, and IgM tests.
   d. every three months do an SPEP, UPEP, and ESR.
   e. have the patient self-examine for lymph nodes in the neck, axillary, and groin areas monthly.
2. Sjogren's syndrome is often associated with all the diseases mentioned below ***except***:
   a. fibromyalgia.
   b. scleroderma.
   c. Waldenstrom' macroglobulinemia.
   d. pseudogout.
   e. rheumatoid arthritis.
3. The most common antibody found in the serum of patients with Sjogren's syndrome is:
   a. ANA.
   b. anti-SSA antibodies.
   c. anti-SSB antibodies.
   d. rheumatoid factor.
   e. anti-uRNP antibodies.
4. Which medication does not help or is ***not*** usually used in the treatment of Sjogren's syndrome?
   a. Cyclosporin eye drops 2 drops bid/each eye
   b. Pilocarpine 5 mg tid
   c. Cevilamine 30 mg tid
   d. Rituximab 375 mg/meter squared weekly times 3 weeks
   e. Prednisone 10-15 mg daily
5. Extraglandular manifestations of Sjogren's syndrome do ***not*** include which of the following?
   a. Muscle weakness
   b. Glomerulonephritis
   c. CNS vasculitis
   d. Arthritis
   e. Hyperparathyroidism
6. Which one of the following manifestations of salivary gland swelling is usually unilateral?
   a. Sarcoidosis
   b. Diabetes mellitus
   c. Sialadenitis
   d. Acromegaly
   e. Viral infections
7. The incidence of lymphoma in patients with Sjogren's Syndrome is how many times the incidence in the general population?
   a. 3 times
   b. 10 times
   c. 20 times
   d. 40 times
   e. 100 times

In Future Issues: Managing Non-Cancer Related Chronic Pain without Opioids

Primary Care Reports™ (ISSN 1040-2497) is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Executive Editor: Leslie Coplin
Managing Editor: Neill Kimball
Senior Vice President/Group Publisher: Donald R. Johnston

GST Registration No.: R128870672

Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to Primary Care Reports, P.O. Box 105109, Atlanta, GA 30348.

Back issues: $26. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Multiple copy prices: One to nine additional copies, $314 each; 10 or more additional copies, $279 each.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail:
customerservice@ahcmedia.com

Editorial E-Mail:
leslie.coplin@ahcmedia.com

World Wide Web page:
http://www.ahcmedia.com

Subscription Prices

1 year *with* free AMA Category 1/Prescribed credits: $369

Add $17.95 for shipping & handling

(Student/Resident rate $170

Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.

All prices U.S. only.
U.S. possessions and Canada, add $30 plus applicable GST. Other international orders, add $30.

Accreditation

AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this educational activity for a maximum of 36 *AMA PRA Category 1 Credits™*. Each issue has been designated for a maximum of 2.30 *AMA PRA Category 1 Credits™*. Physicians should claim only credit commensurate with the extent of their participation in the activity.

This Enduring Material activity, *Primary Care Reports,* has been reviewed and is acceptable for up to 27 Prescribed credit(s) by the American Academy of Family Physicians. AAFP accreditation begins January 1, 2012. Term of approval is for one year from this date with the option of yearly renewal. Each issue is approved for 2.25 Prescribed credits. Physicians should claim only the credit commensurate with the extent of their participation in the activity. The AAFP invites comments on any activity that has been approved for AAFP CME credit. Please forward your comments on the quality of this activity to cmecomment@aafp.org.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

This CME activity is intended for primary care and family practice physicians. It is in effect for 24 months from the date of the publication.

AHC Media