

Sjögren's Syndrome: Stacking the Deck for Improved Outcomes

By Ronale Tucker Rhodes, MS

It is still unknown what causes this chronic autoimmune disease that affects so many people, but with growing awareness surrounding the disease, increased research is revealing new clues and more effective treatment options.

DESPITE THE HIGH

incidence of Sjögren's syndrome, the disease was not well known until 2011, when world champion tennis player Venus Williams revealed she had been diagnosed with it, forcing her to withdraw from the U.S. Open. Suddenly, Sjögren's went from obscurity to limelight, creating awareness not only on this particular autoimmune disease but on the growing prevalence of autoimmunity in general.

The symptoms of Sjögren's were first observed in 1930 by Dr. Henrik Sjögren, an ophthalmologist in Jönköping, Sweden, after a patient presented with low secretions from the lacrimal and salivary glands.

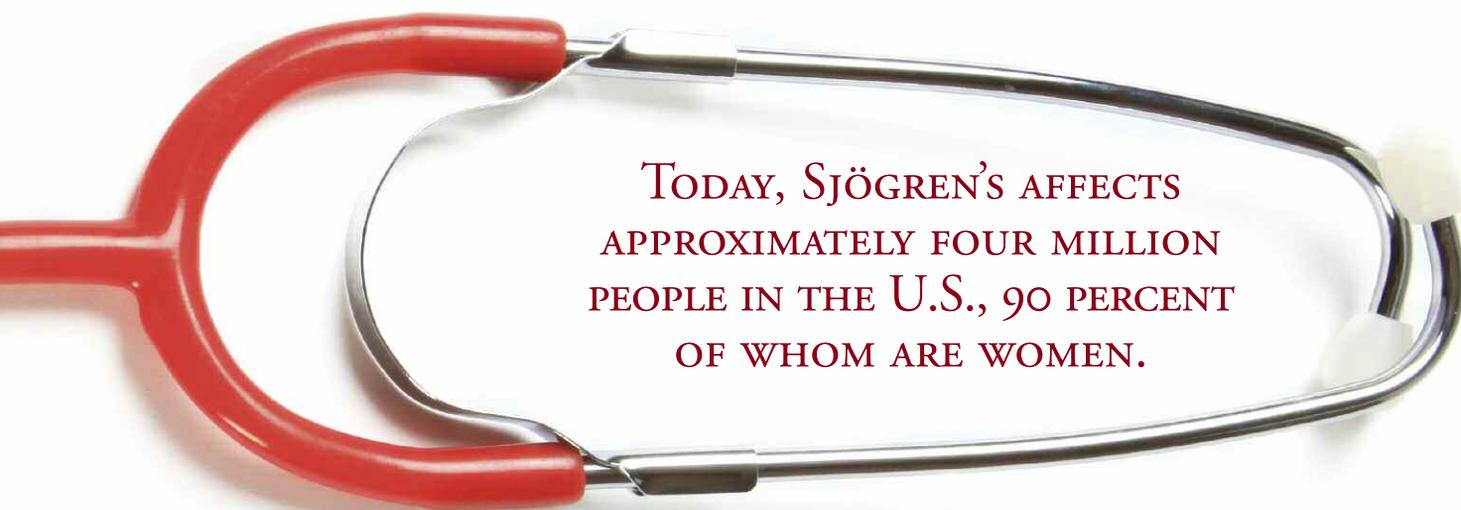
Dr. Sjögren published his doctoral thesis in 1933 describing 19 females with these symptoms, which caused

dry eyes (keratoconjunctivitis), for which he coined the term keratoconjunctivitis sicca. But, his thesis was not well-received until he published a paper in 1951 that described 80 patients with keratoconjunctivitis sicca, 50 of whom also had arthritis. This led to an international interest in the condition, which began to be identified as Sjögren's syndrome.¹

Today, Sjögren's affects approximately four million people in the U.S., 90 percent of whom are women.² And, while anyone can develop Sjögren's at any age, it is extremely rare in children, and most people are older than 40 at the time of diagnosis.^{3,4}

tooth decay (and eventual loss of teeth), persistent dry cough, problems chewing, loss of sense of taste, mouth sores or pain, problems swallowing, hoarseness, difficulty speaking, swollen salivary glands and recurring oral thrush. Symptoms associated with dry eye include a sensation that there is something in the eye, tired eyes, itchy eyes, mucus discharge from the eyes, photophobia, stinging or burning eyes, and swollen and/or irritated eyelids.^{4,5}

There also are symptoms that occur when other glands are inflamed, although these are less common. For instance, the lining of the breathing passages can become inflamed causing lung



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What Is Sjögren's?

Sjögren's is a chronic autoimmune disease that occurs when the white blood cells attack the saliva and tear glands, leading to dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca). In some women, the gland responsible for keeping the vagina moist is also affected, resulting in vaginal dryness. The attack on the glands takes place in association with lymphocytic infiltration of the glands, an inflammatory process that eventually severely damages or destroys the glands.^{1,5}

The syndrome is characterized as either primary or secondary Sjögren's. In primary Sjögren's, the disease doesn't develop as a result of another condition, while with secondary Sjögren's, it results because of or alongside another connective tissue disease such as lupus or rheumatoid arthritis.⁵

Symptoms of Sjögren's

Sjögren's is a systemic disease that affects the entire body. In addition to dry eyes and dry mouth, there are many other symptoms that may occur. Symptoms associated with dry mouth include

infections, and the vaginal glands can become inflamed causing pain during intercourse or recurrent vaginal dryness.⁶

In individuals whose immune system also attacks other parts of the body, symptoms can include general tiredness; aching muscles; inflammation, stiffness and pain in the joints; peripheral neuropathy; Raynaud's phenomenon; and vasculitis.^{4,5}

Symptoms vary among individuals; they can remain steady, worsen or, uncommonly, go into remission. Some people experience mild discomfort, while others suffer debilitating symptoms that impair their functioning.²

Causes of Sjögren's

It's unknown what causes Sjögren's, but it's believed that primary Sjögren's occurs due to a combination of environmental and genetic factors. For instance, genes can make some people more susceptible to having an abnormal immune system. And, an environmental factor such as hepatitis C viral infection or Epstein-Barr virus can trigger the immune system to not work properly. Since Sjögren's is diagnosed most commonly during

the age when menopause occurs, some experts believe that falling levels of estrogen might disrupt the immune system. Secondary Sjögren's, on the other hand, develops when another autoimmune condition progresses.⁵

Diagnosing Sjögren's

Because symptoms of Sjögren's often mimic other conditions or occur as a result of some medications, the disease is often overlooked or misdiagnosed, which is why it takes, on average, 3.9 years to diagnose.^{2,5} This lengthy delay can impede early treatment for Sjögren's and result in years of needless discomfort and even irreversible organ damage.

Ophthalmologists typically administer two tests to diagnose Sjögren's: the Rose Bengal test in which a nontoxic dye is dropped onto the surface of the eyes to measure the state and function of tear glands; and the Schirmer test in which strips of blotting paper are placed under the eyelid to analyze how much liquid the eye is producing.

Other tests include a lip biopsy, blood tests to determine if there are SSA and SSB (anti-Ro and anti-La, respectively) antibodies that show up in about 60 percent of Sjögren's patients, salivary flow rate to determine if the salivary glands are working properly, sialogram X-ray to determine how much saliva flows into a patient's mouth, salivary scintigraphy to measure salivary gland function, chest X-ray to determine if there is lung inflammation, and a urine sample to determine whether the kidneys have been affected.⁵

In 2013, the U.S. Food and Drug Administration approved a new lab test for early detection of Sjögren's. Developed by Immco Diagnostics and marketed by its partner, Nicox, Sjö combines three proprietary biomarkers — SP-1 (salivary gland protein-1), CA-6 (carbonic anhydrase-6) and PSP (parotid secretory protein) — with traditional markers (antinuclear antibodies [ANA], Ro, La and Rf [rheumatoid factor]). The proprietary markers — discovered by researchers at the University of Buffalo and Immco Diagnostics — are likely to be present early in the disease, allowing for faster and more accurate diagnosis. "The practitioner will be able to write the order for the patient to go to a local lab," said Nicox Director of Marketing Jason Menzo. "Forty-eight hours later, the practitioner will receive the results. Alternatively, the practitioner may use a lancet to take a sample, then overnight the sample to the Immco laboratory to avoid sending the patient out."^{7,8}

Most Sjögren's centers around the world diagnose Sjögren's based on the American-European criteria published in 2002 in the *Annals of Rheumatic Diseases* (Table 1). Originally designed to define patients for research studies, the criteria outline several different parameters, including key symptoms, objective tests for

dry eyes and dry mouth and tests for autoimmunity. Based on these criteria, the diagnosis of primary Sjögren's (dry eyes and dry mouth in a patient with no pre-existing history of connective tissue disease) requires the fulfillment of four out of six criteria. One of those criteria must be either anti-SSA/SSB positivity or a positive lip biopsy. Diagnosis of secondary Sjögren's (dry eyes and dry mouth in a patient with another pre-existing connective tissue disease) requires one dryness symptom plus two out of three objectives (numbers 3 through 5). Diagnosis of Sjögren's in a patient with no sicca symptoms (dryness of the eyes, mouth or other body parts) can be made if three of four objective criteria are fulfilled (numbers 3 through 6).⁹

In 2012, the Sjögren's International Collaborative Clinical Alliance (SICCA) released new classification criteria, the first that are based solely on objective clinical tests. The SICCA criteria stipulate that to be classified as Sjögren's, research participants must be positive for at least two of three objective diagnostic tests: anti-SSA/SSB blood test that results in 1) positive serum levels of either the SSA and/or SSB antibody and/or 2) positive serum levels of the rheumatoid factor antibody and elevated antinuclear antibody titers; a score of three or more on the ocular surface staining test, which measures the dissipation rate of a specialized dye that is applied to the tear film that bathes the surface of the eye; and a positive salivary gland biopsy.¹⁰

Complications of Sjögren's

Sjögren's is often associated with other complications. Some less serious complications are dental cavities and eye damage. More common associations are autoimmune thyroiditis (Hashimoto's), which can lead to abnormal thyroid levels, gastroesophageal reflux disease, which can cause difficulty swallowing and heartburn, and pulmonary infections. Biliary cirrhosis, an autoimmune disease of the liver that leads to scarring of the liver tissue, is a rare and serious disease association with Sjögren's, as are kidney failure and vasculitis. Last, a small percentage of Sjögren's patients develop lymphoma; however, this normally occurs only after many years with the illness.^{4,6}

Treating Sjögren's

There is no one specific medication to treat Sjögren's. Instead, the goal is to relieve symptoms mostly through topical therapy. However, physicians do prescribe some medications, including pilocarpine (Salagen) and cevimeline (Evxac) to increase the production of saliva and, sometimes, tears. These are typically used when systemic therapy is needed or local therapy isn't successful.¹¹ Other drugs may include hydroxychloroquine (Plaquenil), a drug designed to treat malaria, and methotrexate, which suppresses the



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Table 1. American-European Summary of Sjögren’s Syndrome Classification Criteria

1. Ocular symptoms (any 1 of 3)
Dry eyes >3 months Tear use >3x/day Foreign body sensation in eyes
2. Oral symptoms (1 of 3)
Dry mouth >3 months Swollen salivary glands Need liquids to swallow
3. Ocular signs (1 of 2)
Unanesthetized Schirmer’s <5mm/5 min (both eyes) Positive vital dye staining (rose bengal fluorescein, lissamine green)
4. Oral signs (1 of 3)
Abnormal salivary gland scan Abnormal parotid sialography Abnormal unstimulated salivary flow (<0.1ml/min)
5. Positive lip biopsy
Focal lymphatic sialadenitis (focus score >1/4mm)
6. Positive anti-SSA and/or SSB antibodies

Exclusions: hepatitis C, graft vs. host disease, use of drying medications, etc.

immune system. Rituximab has shown promise in treating patients with severe extraglandular manifestations of Sjögren’s such as vasculitis, cryoglobulinemia and peripheral neuropathy.^{12,13}

A surgical procedure known as punctal occlusion can be performed, which places small plugs near drainage ducts to help seal them and keep tears in the eyes. However, this is generally only recommended if all else fails.⁵

In some instances, intravenous immune globulin (IVIG) has been prescribed to treat Sjögren’s neuropathy. Unfortunately, data to support its use in primary Sjögren’s that was not caused by vasculitis are limited. One recent study, though, showed that it may be useful. In the study, modified rankin scores (MRS), which designate the degree of disability on the basis of symptoms and a global assessment by the care provider, improved in eight out of 19 patients with primary Sjögren’s presumed non-necrotizing vasculitic neuropathy with a mean age of 60 who had been treated with IVIG. “In 10 patients, the MRS was stable, and in one patient, the MRS worsened. According to clinician assessment, all patients with sensorimotor, nonataxic sensory neuropathy

and conduction block improved; however, of the nine patients with ataxic neuropathy, only two improved, four worsened and three remained stable. Ten of 13 patients who were treated with steroids were able to lower their doses, presumably as a result of the effects of IVIG. Only one patient discontinued IVIG because of an adverse effect (nausea), and no severe adverse effects such as thrombosis or renal failure were observed.”¹⁴

Living with Sjögren’s

Sjögren’s is not usually life-threatening, but it can be very life-altering. Individuals can ease their symptoms of Sjögren’s by sipping water throughout the day, chewing sugarless gum, avoiding medicines that cause mouth dryness, avoiding alcohol and using mouth rinses to replace minerals in their teeth.⁴ Other over-the-counter remedies include non-steroidal anti-inflammatory drugs such as ibuprofen to ease joint and muscle pains, saliva substitutes, drugs to help their salivary glands make more saliva, skin creams to ease dry skin, vaginal lubricants and moisture chamber spectacles (special glasses that wrap around the eyes to keep moisture in).^{4,5,11}

Patients newly diagnosed with Sjögren’s may find it helpful to view a video titled “Sjögren’s Syndrome: A Place to Begin” produced by the Sjögren’s Syndrome Foundation.²

Improving Sjögren’s Outcomes

A good deal of research is being conducted to improve the outcomes for Sjögren’s patients by identifying its possible causes for earlier diagnosis and developing new and more effective treatments.

In 2010, a group of Swedish researchers discovered that individuals with Sjögren’s have “skewed B cell maturation after receiving the H1N1 flu vaccine, resulting in higher amounts of vaccine-specific antibodies that may be related to inflammation ... [and] may reveal some links between B cells and autoimmune problems in Sjögren’s syndrome.”

Researchers at the National Institutes of Health are studying ways to diagnose Sjögren’s earlier by biopsying salivary glands of Sjögren’s patients to identify microRNAs (genes) that may be related to the disease. In fact, gene therapy is one of the more promising areas of research. A group of Dutch researchers have found that using B cell-targeting gene therapy to treat the salivary glands of mice reduced autoimmune-related inflammation, suggesting that gene therapy may help people with Sjögren’s.

Most of the new drug development is coming from Asia. Mizoribine (Bredinin) is an immunosuppressant drug designed to quiet an overactive immune system, although it is only available in Japan and China at this time. Mycophenolate sodium (Myfortic) is another immunosuppressant already in use as a treatment to prevent organ rejection in transplant recipients, but

it is being studied in a number of autoimmune, arthritis-related diseases, including Sjögren's. Nizatidine (Tazac, Axid) is an oral H2 blocker drug used commonly to treat excess stomach acid and is also being studied in Sjögren's as a way to treat oral dryness. Rebamipide (Mucosta) is a mucosal protective agent in Phase II trials in the U.S. for treating dry eye and mouth.

Researchers also are trying to develop artificial or regenerated salivary glands using tissue engineering, gene therapy-like techniques and stem cell methods.¹⁵

Awareness about Sjögren's syndrome has increased significantly since tennis star Venus Williams brought the disease to the public eye in 2011. But, much more needs to be learned. The Sjögren's Syndrome Foundation has taken a leading role in moving the field of Sjögren's forward by raising millions of dollars to fund research. Recently, it launched an initiative to improve the quality of care for Sjögren's patients by developing clinical practice guidelines for assessment and management of the systemic manifestations, dry eye and dry mouth that occur due to the disease.¹⁶ ■

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References

1. Wikipedia. Sjögren's Syndrome. Accessed at en.wikipedia.org/wiki/Sjögren%27s_syndrome.
2. Sjögren's Syndrome Foundation. About Sjögren's Syndrome. Accessed at www.sjogrens.org/home/about-sjogrens-syndrome.
3. Mayo Clinic. Sjögren's Syndrome Definition. Accessed at www.mayoclinic.org/diseases-conditions/sjogrens-syndrome/basics/definition/CON-20020275.
4. ADAM. Medical Encyclopedia. Sjögren Syndrome. Accessed at www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001491.
5. Medical News Today. What Is Sjögren's Syndrome? What Causes Sjögren's Syndrome? Accessed at www.medicalnewstoday.com/articles/233747.php.
6. Shiel, WC. Sjögren's Syndrome. MedicineNet.com. Accessed at www.medicinenet.com/sjogrens_syndrome/page2.htm.
7. Epstein, JM. Blood Test for Early Detection of Sjögren's Syndrome Now Available. Boston Foundation for Sight, Aug. 1, 2013. Accessed at blog.bostonsight.org/index.php/2013/08/blood-test-for-early-detection-of-sjogrens-syndrome-now-available.
8. Bailey, GM. Nicox Partners with Immco Diagnostics to Market Sjögren's Syndrome Test. *Optometry Times*, June 24, 2013. Accessed at optometrytimes.modernmedicine.com/optometrytimes/content/tags/immco/nicox-partners-immco-diagnostics-market-sj-gren-s-syndrome-test.
9. Vivino, FB. How Do You Diagnose Sjögren's Syndrome? Sjögren's World (reprint of Sjögren's Syndrome Foundation *The Moisture Seekers Newsletter*, April 2005). Accessed at www.sjogrensworld.org/how_do_you_diagnose.htm.
10. National Institutes of Health. New Classification Criteria Released for Research on Sjögren's Syndrome. Accessed at nidcr.nih.gov/Research/ResearchResults/NewsReleases/CurrentNewsReleases/SICCAREgistry.htm.
11. Pema, K. Sjögren Syndrome Medical Treatment. eMedicineHealth.com. Accessed at www.emedicinehealth.com/sjogren_syndrome/page8_em.htm#medical_treatment.
12. Miller, AV. Sjögren Syndrome Medication Summary. Medscape. Accessed at emedicine.medscape.com/article/332125-medication.
13. Sjögren's Syndrome Treatments and Drugs. Mayo Clinic. Accessed at www.mayoclinic.org/diseases-conditions/sjogrens-syndrome/basics/treatment/con-20020275.
14. Rist, S, Sellam, J, Hachulla, E, et al. IVIg for Sjögren Neuropathy: Worth the Price? *Arthritis Care Research* (Hoboken), 2011;63: 1339-1344. Accessed at www.medscape.com/viewarticle/751384.
15. Bernstein, S. Sjögren's Syndrome Treatment Research. Arthritis Foundation. Accessed at www.arthritisday.org/about-arthritis/types-of-arthritis/sjogrens-syndrome/treatment-plan/treatment-for-sjogrens-syndrome.php.
16. Sjögren's Syndrome Foundation. Scientific Initiatives. Accessed at www.sjogrens.org/home/research-programs/scientific-initiatives.

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