

Sjögren's Syndrome

Approximately 4 million Americans suffer from Sjögren's syndrome, which was first identified in 1933 by the Swedish ophthalmologist Henrik Sjögren. About 90 percent of victims are women with a mean age of 50, although Sjögren's can strike any age group, even children (Talal N 1987).

The main symptoms of Sjögren's are chronic dryness of the eyes and mouth, but it is also associated with dryness in external genitalia, the ear, and the nose and throat area. There may also be decreased secretions in the gastrointestinal tract.

Sjögren's is an autoimmune disorder. The symptoms associated with Sjögren's are caused by the infiltration of immune-system cells, usually B and T lymphocytes, into the glands responsible for secreting fluid. The disease can occur alone (primary Sjögren's) or in conjunction with other autoimmune diseases (secondary Sjögren's). Sjögren's has been associated with rheumatoid arthritis, systemic lupus erythematosus, scleroderma, and other connective tissue diseases (Talal N 1987). It has also been associated with autoimmune disorders in the thymus gland. Studies have shown that patients with Sjögren's may also suffer from thyroid disorders (Lazarus MN et al 2005).

Traditional treatment relies on cholinergics, or drugs that stimulate the parasympathetic nervous system, but they can have significant side effects. Nutritional therapy focuses on essential fatty acids, which have been shown to modulate the immune system. Lifestyle changes are also a valuable therapeutic tool.

Although the disease rarely shortens a patient's life span, Sjögren's can have devastating effects. Ocular (eye) dryness can lead to chronic keratoconjunctivitis and corneal ulcers; oral dryness can result in severe and chronic dental decay, fissures, infections, and difficulty in speaking and swallowing. The disease is often accompanied by depression, fatigue, and fever. Elevated liver enzymes occur in 25 percent of patients; liver enlargement in 33 percent; Raynaud's syndrome in 20 percent; fibromyalgia in 55 percent; and lymphoma in less than 5 percent (Carsons S 1998).

Oral symptoms of Sjögren's syndrome include reduced saliva; a dry, sticky mouth; and difficulty in chewing and swallowing. The decreased quantity of saliva makes the oral cavity more acidic, and the lowered pH, along with the reduction in the number of antibacterial enzymes normally present in human saliva, makes tooth decay a significant problem. Dental caries is considered a potential marker for the disease (Lynge Pedersen AM et al 2005). Dry mouth can also affect speech, taste, and tolerance to dental prostheses.

Chronic dryness of the eye causes inflammatory reactions (Badouin C 2001), leaving a feeling of grittiness in the eye and intolerance to light. The roughened surface of the eye caused by the dryness causes light to scatter, resulting in blurred vision. Dry eye also renders eyes more sensitive to irritants and more susceptible to infections, which can result in corneal ulcerations if left untreated. Eyelid dermatitis may be another manifestation of primary Sjögren's syndrome.

Other symptoms associated with Sjögren's include the following:

- Nasal dryness, nosebleeds, congestion, and impaired taste and smell, as well as more serious conditions, such as bronchitis and pneumonia, caused by damage to mucous glands in the nose
- Dryness in the eustachian tubes, which can lead to a clogged feeling in the ear and impaired hearing
- Itchy, dry skin
- Vaginal dryness
- Nutritional malabsorption, caused by affected mucous lining of the stomach
- Pancreatitis

Individuals with Sjögren's may develop neurological problems, such as impaired memory and reduced concentration (Sjögren's Syndrome Foundation). A French study linked the onset of facial palsy involving cranial nerves to Sjögren's (Rousso E et al 2005).

Because it progresses slowly, Sjögren's syndrome is frequently misdiagnosed and left untreated (Derk CT et al 2004). The symptoms of primary Sjögren's syndrome—dryness, fatigue, pain, head and neck complaints, hoarseness, or hearing loss—can also occur as a result of medication use, anxiety and depression, or normal aging (Mahoney EJ 2003; Mariette X 2002). In a Chinese study, the average time between onset of symptoms and establishment of diagnosis was 7.8 years, indicating most cases were either wrongly diagnosed or neglected (Zhang NZ 1993).

Sjögren's is diagnosed on the basis of the presence of specific autoantibodies and the presence of symptoms. During diagnosis, the physician will ask questions to determine if a patient is suffering from dry eyes or mouth and will test the functioning of salivary and ocular glands. In addition, tests could be conducted to detect antibodies to Ro/SS-A or La/SS-B antigens. Researchers have also discovered increased levels of the antibody interleukin-18, an immunoregulatory and proinflammatory cytokine in patients with Sjögren's (Bombardieri M et al 2004). This cytokine interferes with acetylcholine, the messenger chemical that triggers saliva production.

SJÖGREN'S: AN AUTOIMMUNE DISEASE

Like other autoimmune diseases, Sjögren's syndrome results from the immune system mistakenly attacking healthy tissue. The autoimmune response is not fully understood and may have multiple causes, including mimicry molecules, immature T cells, and leaky gut syndrome. Mimicry molecules excite the immune system to attack molecules they resemble. Immature T cells are those that have not been "trained" long enough in the thymus and cannot properly differentiate between harmful antigens and healthy tissues. Finally, leaky gut syndrome, characterized by an overly permeable intestinal wall, can arouse an allergic response by releasing large molecules into the bloodstream. In general, allergic reactions were found to be more common in people with Sjögren's syndrome (Tishler M et al 1998).

When healthy tissues such as excretion glands are attacked because of an autoimmune response, they become clogged with circulating immune complexes (Brito-Zeron P et al 2005). These large molecules are formed by the combination of an antibody and an antigen. When they lodge in the salivary and lachrymal glands (produce tears), they block these glands from supplying their watery and mucosal secretions.

Some researchers think that the underlying cause of autoimmune disorders like Sjögren's may be a flawed T cell response. T cells are lymphocytes that are "trained" in the thymus gland for their role in the immune system. However, if T cells are not "schooled" long enough in the thymus before being released, they tend to behave erratically, attacking healthy tissue.

Patients with Sjögren's show significant defects in T cell immunity (Gerli R 1989). Japanese researchers found that estrogen deficiency contributes to this dysfunctional T cell response (Ishimaru N et al 1999).

Depression, which is associated with Sjögren's (Stevenson HA et al 2004), can trigger the production of cytokines that interfere with salivary and lachrymal gland production.

PHARMACEUTICAL TREATMENT OF SJÖGREN'S

Few pharmaceutical treatments have shown efficacy for Sjögren's syndrome. The most common regimen includes drugs known as cholinergics as well as interferon-alpha (Venables PJ 2004). Cholinergics activate the parasympathetic system by mimicking acetylcholine, a neurotransmitter that stimulates the lachrymal and salivary glands. Two cholinergics are prescribed more frequently than any others:

- **Pilocarpine.** The cholinergic pilocarpine has been shown to reduce the symptoms of xerostomia (dry eye). It can cause gastrointestinal upset (Nusair S 1999).
- **Cevimeline.** The cholinergic cevimeline, taken at 30 mg three times daily, seems to be well tolerated and to provide substantive relief of dry eye. Twice that dosage was associated with an increase in the occurrence of adverse events, particularly gastrointestinal tract disorders. Cevimeline taken over prolonged periods or in too high doses can cause drowsiness, excessive sweating, and interference with night vision, as well as more serious side effects (Fife RS et al 2002).

Interferon has also been used in the treatment of Sjögren's. Among patients with primary Sjögren's syndrome, interferon has been shown to improve salivary output and decrease complaints of xerostomia without causing significant adverse medical events (Yamada S2005).

ESSENTIAL FATTY ACIDS: SUPPORTING HEALTHY GLANDS

Traditional drugs offer considerable potency in dealing with Sjögren's syndrome, but side effects make them a mixed blessing. In addition, pharmacological approaches target symptoms without addressing underlying causes or related health issues. Nutritional support may be successful, not only in mitigating the side effects of drugs, but in lowering dosages as well.

Essential fatty acids (EFAs) and eicosanoids, short-lived "messenger" hormones derived from EFAs, have been implicated in the abnormal function of salivary and lachrymal glands. Measurements in Sjögren's syndrome patients have shown that EFA deficiencies are present (Oxholm P et al 1998), and controlled clinical trials of supplementation with EFAs, including gamma-linolenic acid (GLA), have yielded positive results (Horrobin DF 1984).

Omega-3 and omega-6 fatty acids (EFAs) have been shown to alleviate symptoms of autoimmune disease by supporting the immune system and reducing inflammation (Harbige LS 1998; Horrobin DF 1984; Horrobin DF 1986; Oxholm P et al 1986). EFAs accomplish this in several ways:

- Determining whether genes are expressed
- Producing eicosanoids and cytokines
- Activating antioxidant enzymes

Cytokines. Cytokines are intercellular messenger chemicals that can be pro- or anti-inflammatory. Essential fatty acids support production of anti-inflammatory cytokines (Harbige LS 1998).

GLA. GLA is important to the production of the anti-inflammatory prostaglandin E1 (PGE1). Evening primrose oil, which is rich in GLA, may correct immunologic defects, halt atrophy of salivary and lachrymal glands, and increase the beneficial PGE1. Direct supplementation with GLA has resulted in clinical improvement in Sjögren's syndrome, scleroderma, and other conditions including high blood pressure and high cholesterol (Horrobin DF 1981).

SJÖGREN'S AND HORMONE DEFICIENCIES

Restoring dehydroepiandrosterone (DHEA) levels modulates immune and inflammatory responses. Women with primary Sjögren's show decreased serum concentration of DHEA and an increased cortisol/DHEA ratio (Valtysdottir ST et al 2001). Because most people over age 35 are deficient in DHEA, Life Extension believes that patients with Sjögren's should have their DHEA levels tested and if necessary supplement with this vital hormone. Retesting is recommended three to six weeks after therapy is initiated to ascertain if optimal DHEA levels have been obtained.

Sjögren's syndrome has also been linked to estrogen deficiencies in menopausal women (Hayashi Y et al 2004). While no human studies have been conducted on the value of estrogen restoration therapy among Sjögren's patients, Life Extension believes that women over 35 should have a complete hormone profile performed and correct any hormonal deficiencies. Women with hormone-dependent cancers, however, are generally advised against hormone restoration with estrogen. Hormone restoration might be especially important among Sjögren's patients who suffer from a disease that is associated with hormonal deficiencies, even if the mechanism is incompletely understood.

THYMUS EXTRACT

There is evidence that thymus extracts can improve the functioning and numbers of T cells and stimulate conversion of immature T6 cells (thymocytes) into non-dedicated T3 cells (Kouttab NM et al 1989; Wilson JL 1999). Thymomimetic drugs, such as levamisole and isoprinosine, stimulate the thymus and may be beneficial to T cell development (Hadden JW et al 1989). Because immature T cells have been implicated in Sjögren's syndrome, Life Extension believes that thymus extract may help reduce the severity of symptoms associated with the disease.

DIGESTIVE SUPPORT

The amino acid L-glutamine heals the intestinal lining and improves its mucosal structure (Klimberg VS et al 1990). Beneficial intestinal bacteria, such as *Lactobacillus acidophilus* and *Bifidobacterium bifidus*, and fructooligosaccharides, a form of sugar that can enhance beneficial bacteria, provide gastrointestinal tract support by increasing the gut population of healthy microflora.

EXERCISE

Exercise has also been shown to be anti-inflammatory, stimulating the production of anti-inflammatory cytokines and inhibiting pro-inflammatory cytokines (Petersen AM 2005). The Journal of the American Medical Association has reported that psychological stress disrupts the network of signals linking the nervous, endocrine, and immune systems and that stress reduction can significantly affect cellular immune response (Glaser R et al 1999). A variety of exercise methods will supply symptomatic relief.

AVOIDING DRY EYE

- Tear substitutes are efficient in mild to moderate cases of dry eye, although some may increase patients' complaints because of the preservatives they contain. Preservatives can be avoided by using monodose disposable packaging or brands that are preservative-free (Baudouin C 2004). Recent research suggests that topical cyclosporine is a promising possibility in treating dry eye (Kujawa A et al 2004).
- Studies have demonstrated that calcium carbonate in a petroleum base relieved dry eye when applied to the lower eyelid (Tsubota K et al 1999).
- For mild to moderate dry eye, slow-melting lubricating pellets, available by prescription and inserted into the lower pocket of

- the eyelid twice daily, will bring relief. Lubricating ointments are best used at night as they tend to blur vision during the day.
- Moisture-chamber eyeglasses will help preserve tear volume by minimizing airflow over the surface of the eye.
- Closing the tear ducts by using collagen or silicone plugs can increase tear volume by reducing drainage. The collagen plugs are absorbed; silicone plugs are easily removed. The lower tear ducts (punta) are sealed first; a determination is then made about sealing the upper punta. If permanent closure seems warranted, electrocautery or argon laser can permanently close the punta (Carsons S 1998)
- Avoiding dust, fumes, and excessive makeup, especially around the margin of the eyelid, may also help.

DENTAL CARIES: PROTECTING YOUR TEETH

- Brush frequently, both before and after meals, using an electric toothbrush. Floss and irrigate the teeth (using a Waterpik® or other tool) frequently. Among Sjögren's patients, oral hygiene is crucial in combating tooth decay. See a dentist regularly to monitor tooth decay and loss of enamel.
- Use a pH-balanced mouthwash to lower acidity. Try 1/4 teaspoon of baking soda dissolved in 1/4 cup of warm water. Alcohol-free goldenseal (*H. canadensis*) can be used as an antibacterial mouthwash. Dissolve 30 drops in 2 oz water and swish the solution about in the mouth.
- Avoid sugary foods. Bacteria produce acid for 20 minutes whenever sugar is ingested. Avoid acidic foods, including citrus fruits.
- Drink non-acidic bottled water (Wu AJ 2003).
- Use a straw to protect the mouth when drinking soft drinks and other acidic beverages.
- Avoid abrasive toothpastes that can harm already compromised tooth enamel. Certain toothpastes (e.g., Biotene) have been specially formulated for individuals with dry mouth.

FIGHTING ORAL DRYNESS

- Drink plenty of water to replace the lost moisture in the oral cavity. (Remember to avoid acidic beverages like tomato and orange juice.)
- A sugarless candy or sugar-free chewing gum kept in the mouth can stimulate saliva flow. Xylitol, a sugar substitute used in candy and gum, is thought by some to inhibit dental caries. Never sleep with anything in the mouth. Many health food stores carry rice- or barley-sweetened candies.
- Avoid caffeine, which is diuretic.
- Oral interferon-alpha in lozenge form, available by prescription, will significantly increase saliva flow (Ship JA et al 1999)

Goldenseal (*H. canadensis*) can help compensate for lower levels of antibacterial enzymes in the saliva. Swish with 30 drops goldenseal dissolved in 2 oz warm water, as suggested under "Dental Caries: Protecting Your Teeth," above.

PROTECTING YOUR NOSE AND THROAT

- Use a humidifier to keep the air moist.
- Breathe through the nose rather than the mouth; a soft cervical collar will inhibit open-mouth breathing at night by supporting the jaw. Keep your bedroom cool (Carsons S 1998).
- A mixture of saline and aloe can relieve dry nasal membranes and nosebleeds and is gentle enough for repeated use.

SKIN AND VAGINAL DRYNESS

- Avoid antibacterial and abrasive soaps; use soaps with added oils or moisturizers and moisturize the skin after bathing.

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Sjögren's therapy attempts to reduce the symptoms associated with the disease and help secretory glands excrete more fluid. Sjögren's patients are also advised to avoid drugs that decrease the function of salivary and tear glands, including diuretics, antihypertensives, and antidepressants.

Sjögren's patients should consult with a physician before launching a self-care program aimed at alleviating their condition. While prescription drugs are available, they are associated with side effects that can reduce the quality of life. Life Extension's comprehensive Sjögren's recommendations include:

- EPA and DHA:** 700 mg EPA and 500 mg DHA twice daily with food.
- GLA:** 285 mg one or two times daily with food.

- **Life Flora:** An intestinal bacteria to assist with digestion
- **Thymic Immune Factors.** Follow directions on label.
- **L-glutamine:** 500 mg daily.
- **DHEA:** Blood testing is recommended before DHEA therapy begins to establish a baseline; then a starting dose of 15 mg to 75 mg may be recommended. Retesting is recommended three to six weeks afterward to ensure youthful levels.
- **Goldenseal (H. canadensis):** Follow directions on label.

SJÖGREN'S SYNDROME SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

GLA

- Consult your doctor before taking GLA if you take warfarin (Coumadin). Taking GLA with warfarin may increase the risk of bleeding.
- Discontinue using GLA 2 weeks before any surgical procedure.
- GLA can cause gastrointestinal symptoms such as nausea and diarrhea.

Goldenseal

- When taken for an extended period of time, goldenseal may cause digestive problems, constipation, nervous excitement, hallucinations, and delirium.
- Do not take goldenseal for more than 3 weeks in a row. Wait at least 2 weeks before resuming use of goldenseal.

For more information see the Safety Appendix

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