1. Sjögren's Syndrome

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Summary

Sjögren's syndrome is a chronic disorder of unknown cause characterized by a particular form of dry mouth and dry eyes. This loss of tears and saliva may result in characteristic changes in the eyes (called aqueous tear deficiency or keratoconjunctivitis sicca) and in the mouth with deterioration of the teeth, increased oral infection, difficulty in swallowing, and painful mouth. There are many different causes for dry eyes and dry mouth. When they occur as a result of an "autoimmune" process, the condition is called Sjögren's syndrome, which usually occurs in middle-aged women and has prevalence in about 1 in 500 persons.

Patients may also have inflammation of the joints (arthritis), muscles (myositis), nerves (neuropathy), thyroid (thyroiditis), kidneys (nephritis), or other areas of the body. Also, patients may have severe fatigue and disruption of their sleep pattern. Also, the blood of Sjögren's patients may contain antibodies directed against normal cellular substances such as nuclear antigens and immunoglobulins. Therefore, this disease is termed an "autoimmune" disorder to denote the apparent reaction of the immune system against the patient's own tissues. The trigger for this process remains unknown but may be a virus.

Diagnosis is based on clinical examination of the eyes and mouth. Specific blood tests and a biopsy of the minor salivary gland (taken from the inside of the lower lip) help confirm the diagnosis. Sjögren's syndrome is not fatal. However, attention must be paid to preventing the complications due to dry mouth (such as rampant caries) and to dry eyes (corneal erosions and infections), as well as treatment of other organ systems involved as a consequence of the disease.

The risk for passing this disease on to family members is extremely low. There is a slightly increased incidence of autoimmune diseases in siblings and children. Pregnant women should notify their obstetricians and pediatricians, since maternal autoantibodies may cross the placenta and cause problems for the infant.

The Symptoms of Sjögren's Syndrome

Dry eyes and dry mouth result from lack of secretion by the lacrimal (tear) glands and salivary (parotid, sublingual and submandibular) glands. In the eye, this condition is called "aqueous tear deficiency" since the "water" secretion into the tears is diminished.

Historically, Mikulicz first reported these symptoms in 1898 so this condition was called "Mikulicz syndrome." It is more commonly named for Henrik Sjögren (pronounced sho-gren), a Swedish ophthalmologist, who reported the association of severe dry eyes [keratoconjunctivitis sicca (KCS)], dry mouth and rheumatoid arthritis in 1933. Later, it was recognized that patients might have dry eyes and dry mouth but no rheumatoid arthritis. Thus, the distinction was made as primary Sjögren's syndrome (SS) (1° SS with no associated rheumatoid arthritis) and secondary Sjögren's syndrome (2° SS, where associated rheumatoid arthritis is present). 1° SS and 2° SS both occur predominantly in middle-aged women, although they may be present in either sex at any age.

There is no "standard" criteria for diagnosis of Sjögren's syndrome at different medical centers. Although the diagnostic tests for dry eyes are well standardized, the definition for the "oral" component of Sjögren's syndrome remains controversial. This has resulted in confusion in the medical literature and in clinical practice. We favor a stringent criteria for diagnosis of Sjögren's syndrome in order to identify a group of patients with objective evidence of keratoconjunctivitis sicca and a systemic autoimmune process. These are listed in Table 1. Other groups use less stringent criteria for diagnosis and label many different conditions associated with dryness as Sjögren's syndrome. Therefore, we sometimes disagree with a previous diagnosis of Sjögren's syndrome. This discrepancy reflects an honest difference of opinion among rheumatologist who use different criteria for diagnosis.

Eye symptoms in Sjögren's patients usually include dryness and a "gritty" sensation in the eyes, often associated with pain or sensitivity to light (photophobia). The white part of the eye (conjunctiva) may be red and previous eye infections may have occurred. These symptoms result from a decreased production of tears that normally lubricate and protect the eye. To determine the amount of tear production, a strip of sterile filter paper is inserted under the lower eyelid and the amount of wetting in 5 minutes is recorded; normal values usually exceed 8 mm per 5 minutes, but even normal levels may decrease with age. This is called the Schirmer I tear test. If this measurement is low, the Schirmer II test is performed by stimulating the nasolacrimal gland reflex by inserting a Q-tip into the nose. To assess the effects of diminished tears on the eye, a small drop of fluorescein dye or rose bengal dye are carefully put inside the lower eyelid. Areas that are dry briefly retain this dye. The region between the eyelids, the exposure region, is particularly susceptible to drying since this area is only partially covered by the eyelids and is subject to more rapid evaporation. When the dryness has been prolonged and severe, corneal erosions can develop.

Dry mouth results from decreased salivary gland function. Under normal conditions, a low level of saliva is produced continuously to lubricate the mouth and is called "basal" or "resting" salivary secretion. When stimulation by taste, chewing, or smell occurs, the level of salivary flow is increased and is called "stimulated" secretion. The level of salivary flow is controlled by the brain and the signals are carried to the glands by nerves called "cholinergic" and "sympathetic" fibers. Thus, it is possible to have a normal number of salivary gland cells but to still have a dry mouth because the nerves are not giving the "on" signal to the glands. This is one reason why certain drugs (especially antidepressant medication as well as over-the-counter decongestant remedies) cause dry mouth and dry eyes; this side effect is due to their unwanted ability to inhibit the "cholinergic" nerve fibers that innervate the glands. In Sjögren's syndrome, it is likely that the mouth and eye dryness results both from destruction of the salivary glands and from interruption of nerve signals that control secretion. In the early stages of Sjögren's syndrome, patients experience maximum dryness between meals and during the night due to a diminished "basal" secretion, but are still able to eat dry food without difficulty. As the "dryness" syndrome progresses, more fluid is required to eat and swallow.

The diminished salivary flow also predisposes to periodontal disease and oral yeast infections such as Candida. This is because saliva contains important substances that combat these infections. Most saliva is normally made by the parotid, sublingual and submandibular glands, but minor salivary glands located inside the lips also contribute. In some patients, the infiltration of lymphocytes into the parotid or submandibular glands causes pain and swelling. The saliva made in the parotid glands enters the mouth by a small opening (called Stensen's duct) adjacent to the upper molars on each side of the cheek. To accurately measure parotid flow rate, a plastic suction cup is placed over the opening of the duct that leads from the gland into the mouth. These measurements allow us to determine whether the gland can respond to stimulation (i.e., that the secretory response apparatus is intact), and whether there is infection in the gland since pus may exude from this duct.

There are many causes of decreased flow of saliva. To determine the extent of salivary gland destruction associated with oral dryness, a biopsy may be taken from the lower lip. This biopsy is important since it shows how many (if any) salivary glands remain and reveals the type of inflammatory infiltrate present.

Although Sjögren's syndrome characteristically affects the eyes and the mouth, other parts of the body may also be affected. Joint and muscle pain are frequently present. In some cases, this is due to rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) or SLE-like diseases. These diagnoses are confirmed by blood tests and x-rays of the joint. However, in some cases, the muscle and joint pain is due to Sjögren's.

Fatigue is another common symptom. It is important to rule out hypothyroidism (which may develop in up to 20% of Sjögren's syndrome patients), anemia (due to decreased production of blood cells as well as blood loss from taking medicines such as aspirin, Advil or Naproxen for the joint pains), and poor sleeping patterns (especially due to frequent trips to the bathroom at night because of large oral fluid intake during the day). Decrease in memory and concentration sometimes occurs and may be due to the release of inflammatory substances by the immune system. They can also occur due to disrupted sleep pattern. Skin rashes, lung inflammation, swollen lymph nodes, and other symptoms also occur; these are listed in Table 3.

What Causes Sjögren's Syndrome

Salivary glands that produce saliva exist in "grape-like" clusters. There are no or few lymphocytes in the normal salivary gland but are present in Sjögren's syndrome. Lymphocytes are part of the immune

system that normally protect us from infection and tumors. When they appear to attack our own tissues (as in Sjögren's syndrome, systemic lupus, or in rheumatoid arthritis), the term "autoimmunity" is used. Lymphocytes originate in the bone marrow. Two types of lymphocytes, termed "T cells" and "B cells" are responsible for mediating immune reactions. The T cells migrate from the bone marrow to the thymus (thus the term T cell) where they mature and then exit into their peripheral circulation. B cells migrate to particular regions in the lymph nodes where they mature; in birds, where this process was first studied, the site of maturation is the Bursa of Fabricius (thus the term, B cell). B cells make antibodies, while T cells regulate this production. "T-helper" cells promote antibody formation and "T-suppressor" cells inhibit the B cells. Other T cells can directly kill viral-infected and cancer-transformed cells (the so-called T-cytotoxic cells). The entire lymphoid system is precisely regulated, largely by messenger molecules that instruct cells to "turn on" or "turn off." Autoimmunity, the excessive reaction against one's own tissues, then results from a failure of the normal regulation of T cells and B cells. This may be due either to an excessive production of helper signals or a failure to respond to suppressor signals. As a consequence, lymphocytes infiltrate the tissues and attack normal cellular structures.

The initial trigger that sets off the autoimmune events remains unknown. Circumstantial evidence suggests that a virus is involved. One possible candidate is the Epstein-Barr virus (EBV), which causes infectious mononucleosis, a condition characterized by swollen salivary glands, joint aches and fatigue. Virtually all adults have been infected with EBV by age 20 years. After the initial infection, this virus normally resides in the salivary glands for life but causes no problems. We and others have speculated that this virus (or a closely-related virus) may trigger an autoimmune response in genetically susceptible individuals. It needs to be emphasized that there is no direct proof that EBV plays a significant role in Sjögren's syndrome. This is simply one hypothesis and experiments are currently in progress to determine its potential role. Also, Sjögren's syndrome is different from the "chronic fatigue syndrome" or the "chronic EBV syndrome." Patients with Sjögren's syndrome have characteristic abnormalities in the blood tests and salivary gland biopsies that are absent in other syndromes.

It is thought that an as yet unknown infectious agent damages the salivary gland and attracts the "immune" lymphocytes into the salivary gland. These lymphocytes release specific autoantibodies such as rheumatoid factor (RF) and antinuclear antibodies; antibodies are directed against proteins termed Sjögren's-associated antigens A and B (or SS-A and SS-B). These antibodies can enter the bloodstream and are measured in the blood tests that we obtain to confirm the diagnosis of Sjögren's syndrome. Additional T cells enter the gland and the damage is perpetuated. Under normal circumstances, a class of cells called "suppressor cells" turn off the inflammatory process. The continued destruction of the gland represents the abnormal balance of excessive action of T-helper cells and deficient action of T-suppressor cells.

There has been a great deal of research to determine hereditary factors associated with Sjögren's syndrome. To summarize these complicated studies, hereditary factors are important. Particular genes (such as human leukocyte antigen or HLA genes) are inherited in the same manner from parents as are genes for hair color or eye color; that is, one gene from each parent. The HLA genes are important in controlling the immune response and many current research studies are trying to determine exactly how they perform this task. A specific gene named HLA-DR3 is found in high frequency in Caucasian patients with primary Sjögren's syndrome. In different ethnic backgrounds, different HLA genes are associated with Sjögren's. In addition to HLA, at least four other genes are involved. Although the relative frequency of Sjögren's or lupus is slightly increased in family members of Sjögren's syndrome patients, the specific risk that children or siblings will get these diseases remains very low (<10%). In addition to genetic factors, environmental factors also play a role. It has been proposed that viral infection represents the "other factor," and that Sjögren's syndrome disease results when a genetically susceptible individual (possessing HLA-DR3) is exposed to a certain virus or viruses.

Other Causes of Dry Eyes and Dry Mouth

The production of tears and saliva involves a complicated series of steps. A baseline level of salivation and tear production occurs automatically (just as we breathe and our intestines have motility) without conscious thought about these functions. Thus, the nerves that control these functions are termed the "autonomic" (or "automatic") nervous system. However, additional factors may increase or decrease the signals in tear flow and saliva flow. As Pavlov demonstrated about 100 years ago, dogs can be taught to increase salivation in response to a variety of sounds. Humans start to salivate at the thought or smell of food. Thus, the cognitive areas of the brain can send signals to glands through a series of nerves. Certain drugs can act on the brain to decrease tear and saliva flow and leads to increase symptoms of dryness. One example is tricyclic antidepressants (Elavil or Pamelor) or muscle relaxing agents (such as Flexeril) that influence the metabolism of certain specific brain cells as well as salivary and lacrimal glands. A different class of medications called monoamine oxidase (known as MAO) inhibitors also give severe dryness. Thus, the patient needs to be aware that many drugs, including anti-seizure

medications, blood pressure medications, muscle relaxants, and heart medications, lead to increased dryness by affecting different target molecules within the body.

The tear film contains several different components in addition to the "water" part of the tears. Of importance, substances called lipids are made by glands in the eye including the meibomian glands in the eyelids. This lipid stabilizes the tear film and helps retard evaporation. When these lipid-producing glands become inflamed, the corneal surface of the eye becomes inflamed, leading to "blepharitis." The loss of lipid production (that retards the evaporation of the aqueous tears) will further exacerbate the dry eye symptoms and the appearance of the keratoconjunctivitis sicca.

Increased Dryness Is a Side Effect of Other Disease

Several disease processes other than Sjögren's influence these brain centers for "autonomic" control of tears and saliva. For example, patients with multiple sclerosis and diabetes may have dryness of the eyes and mouth as a result of the disease process within the brain that also may affect other sensory and motor functions.

In addition to problems with the neural activation of the glands, other medical conditions can cause the glands to be dry or to become enlarged (Table 2). The goal of the physical examination and laboratory studies is to determine the precise cause for the dryness and swelling.

Of particular importance, some patients have a poorly understood group of symptoms called fibrositis or fibromyalgia. These patients have fatigue, memory loss, aching muscles and, occasionally, depression. They very frequently have dryness of the eyes and mouth. Since minor salivary gland biopsies of these patients have the glands with an intact appearance, we deduce that the cause of dryness must involve the generation of signals for the gland at the level of the central nervous system (brain) or in the peripheral nerves that carry these signals to the glands. These symptoms may be very disabling, but it is important to distinguish them from Sjögren's syndrome (an autoimmune process that destroys the gland) since the therapeutic approach is different.

Approaches to Treatment

At the present time, no therapies are available to "cure" the underlying causes of Sjögren's syndrome. Therefore, therapies are directed at improving symptoms, preventing the complications (such as dental caries, oral candida, or corneal damage) and preventing disease progression. In patients with autoimmune attack on the glands (i.e., Sjögren's syndrome), there may also be autoimmune attack on the joints (arthritis), muscles (myositis), thyroid (thyroiditis), lung (pneumonitis), kidney (nephritis), or other tissues that require specific treatment (Table 3). Also, there is a slightly increased risk of developing lymphoma (a tumor of the lymph nodes), so careful attention is paid to persistent swelling of these structures. Because of the complexity of decisions regarding the evaluation and treatment of extraglandular features of Sjögren's syndrome, this outline will only deal with the glandular (lacrimal/salivary) problems that are frequently encountered.

The Dry Mouth

Clinical management of the dry mouth is a very difficult problem. Some commercial products that may be helpful are listed in Table 4. In addition to chronic dryness, the patients have troublesome intraoral soft tissue problems that include rampant dental caries and difficulty with dentures due to dryness. Painful mouth lesions can result from Candida (yeast) infections of the lips (angular cheilitis) that are more frequent in dry mouth patients. The mouth frequently exhibits macular erythema (redness) on the hard palate and other areas of the oral mucosa. These lesions result from a chronic erythematous form of candidiasis.

Before any treatment program is started, it is important to identify contributing factors such as mouth breathing (due to congested nose), heavy smoking, stress, depression, and drugs that have anticholinergic side effects. The most frequently implicated drugs are the phenothiazines, tricyclic antidepressants, antispasmodic, anti-Parkinsonian, and decongestant medications (described in more detail below). Home remedies, some herbal remedies (including Chinese herbs) and nonprescription medications may possess anticholinergic side effects even though the patients may not recognize these agents as "drugs."

Dental prophylaxis by their dentists is supplemented by frequent use of dental floss, toothbrush or "Waterpik" device. Several toothpastes and mouth rinses have been developed for the patient with dry

mouth. For example, Biotene, “Dental Care,” and Retardent toothpastes are designed for the dry mouth patient (Table 4). These toothpastes lack detergents (such as lauryl sulfate) that are frequently present in many commercial toothpastes and that can irritate dry mucosal membranes. Biotene contains an enzyme important in preventing oral bacterial infections and gingivitis. This enzyme supplement is also present in an oral gel (Oral Balance) that is used to help provide salivary flow at night. “Dental Care” toothpaste contains sodium bicarbonate as a cleaning agent, while Retardent toothpaste uses a chlorine dioxide-based agent to decrease harmful mouth bacteria. These oral products do not contain alcohol as their liquid preservative (such as found in Listerine), which can be drying and irritating and do not result in staining of tooth enamel that can accompany the use of Peridex. Sugarless chewing gum and sugarless lemon drops are helpful in some cases. Use dental floss where possible. Special tooth brushes are often helpful in cleaning between the teeth. Use only a small amount of toothpaste and start on the biting surfaces, then work down to the gums.

A variety of saliva substitutes are available (Table 4). These differ in their flavoring agents and preservatives. MouthCote contains a substance called “mucins,” which are glycoproteins that help lubricate the mouth and thus last a little longer than “water-based” lubricants. Salivant spray has the theoretical advantage of containing no preservatives since these agents may be responsible for topical irritation in some patients. After administration of these sprays, parotid flow rates are increased for 7-8 minutes in Sjögren’s patients. However, the patients’ sense of “dry mouth” may be decreased for up to several hours.

Treatment with a 0.4% stannous fluoride has been suggested to enhance dental remineralization of damaged tooth surfaces. Neutral fluoride preparations are often better tolerated than acidic fluoride preparations that are often prescribed by dentists. In patients with severe dental demineralization, special dental “trays” are made for direct application of the fluoride.

Recent studies have reported increased salivary flow rates after administration of certain drugs such as pilocarpine or neostigmine as either a mouthwash or as a systemic medication. A commercial preparation of pilocarpine (Salagen) has recently been approved by the Food and Drug Administration (FDA) for dryness of the mouth in patients with prior radiation therapy; however, it is also useful in some patients with dry eyes and mouth due to Sjögren’s. Patients with asthma or irregular heart beat should not take pilocarpine since it may provoke a flare of the lung or heart symptoms.

Another approach to dryness is to help break up the thick, sticky secretions. Agents that contain iodides include 10% saturated solution of potassium iodide (SSKI) or organidin (both tablets and liquid). Other agents have properties similar to cough syrups (guanephesin) such as Humabid. Bromhexine, a cough syrup available in Europe, is currently under study in the United States. It is further discussed below. Varying degrees of success have been noted with these treatments. Our experience and that reported at the National Institutes of Health indicates that medications may help some patients with relatively early or mild dry mouth (xerostomia) but not patients with severe xerostomia.

Research at the University of California in San Francisco found that many of the symptoms of painful mouth and burning tongue were due to a chronic Candida (yeast) infection and could be improved by treatment with Nystatin or chlortrimazole tablets. These tablets (also called troches or pastilles) are sucked like a “life-saver” (once or twice a day) and suppress yeast in the mouth that secrete toxins and cause a painful mouth. The clinical improvement may not be apparent for at least 3-4 weeks, so be patient. Treatment of this problem is particularly difficult in a patient with dentures, since the denture must be concurrently treated with the mucosa. Perhaps the most effective treatment for the mouth is the use of Nystatin vaginal suppositories slowly dissolved in the mouth with sips of water twice daily for about 1 month. Although the vaginal suppositories have a bitter taste, other oral forms of antifungal therapy contain a high level of sugar to improve taste and contribute to dental decay. Chlortrimazole vaginal tablets are also available and may be used in the same manner.

The dentures must be carefully cleaned with a toothbrush before soaking overnight in benzalkonium chloride (for example, a 1/200 dilution of surgical scrub solution [Zephiran]). Nystatin powder should be applied to the fitting surfaces of the dentures before reinserting.

The Dry Eyes

The treatment of dry eyes is not only symptomatic but also designed to prevent infection or scarring of the cornea. Patients with Sjögren’s syndrome generally suffer from a deficiency in the “water” component of tears and are referred to as “aqueous tear deficient.” However, the tear film also contains lipids and mucins that help maintain the stability of the tear film. If these glands become inflamed (a condition called blepharitis, described above), then the residual aqueous tear film will not spread evenly

or will evaporate too quickly. Thus, the status of the lipid-producing glands in the eyelids (called meibomian glands) must be considered and treated in order to obtain maximal efficient use of the residual aqueous tears (or artificial tears).

The administration of artificial tears (designed to replace the diminished aqueous or "water" component of tears in Sjögren's patients) gives considerable relief to most patients, but disabling symptoms may persist in some patients. The choice of artificial tears (Table 4) in an individual patient is based on several variables. First, does the eye drop feel comfortable immediately upon instillation into the eye? In some cases, burning may be due to the preservative, and you may wish to try an artificial tear with a different preservative. Several types of artificial tears are preservative-free (Table 4). In patients who require the frequent use of artificial tears, it has been suggested that "preserved" tears not be used more than four times per day to prevent the problems associated with "preservative buildup." In this situation, the use of a "preserved tear" can be alternated with a "preservative-free" tear. It is important to remember that all artificial tears are not the same and that the patient may have to "educate" the local pharmacist who may substitute if sometimes he does not have the requested artificial tear in stock. We ask patients to try several different preparations sequentially in order to identify those that seem most tolerable.

The second point in evaluating an artificial tear preparation is "Do the drops last long enough?" If the artificial tears are beneficial but the symptoms return relatively soon (i.e., in 1-2 hours), then an artificial tear that is thicker or more viscous might be tried. If the tear preparations still do not last long enough, closing the tear drainage ducts (punctual occlusion) should be considered. The "puncta" are small openings at the inner corners of the eyelids. Under normal conditions, the tears use these "drains" to exit the eye. Thus, narrowing these puncta (on a temporary basis by inserting small plugs or on a permanent basis by sealing them with an electric cautery probe on an outpatient basis) will mean that artificial tears will remain for a longer period of time in the eye.

Third, what is the relative expense and convenience of the artificial tear? Unpreserved artificial tears are packaged in very small quantities, so their cost is relatively high. Some companies provide artificial tears to severe dry eye patients at "wholesale" cost. It does not hurt to ask your ophthalmologist if he/she can help you get artificial tears at a lower cost.

Fourth, some patients may benefit from Lacriserts. These are slow-release artificial tears that dissolve slowly and provide a protective tear film. However, some patients may note increased ocular irritation after inserting these pellets or excessive blurring, leading them to discontinue this medication.

Fifth, visual problems may wax and wane, particularly in association with the seasons when dry winds are prevalent. When patients can identify exacerbating problems, increased frequency of artificial tear application should be started before symptoms develop in the hope of preventing objective eye findings. The use of humidifiers at night, wraparound sunglasses, and even goggles (sold at ski shops) are often helpful. Sudden worsening of ocular symptoms should always suggest possible ocular infection. In patients with associated diseases such as rheumatoid arthritis, other causes of eye pain such as "scleral" lesions or vasculitis lesions also must be considered.

Sixth, do the artificial tears that previously worked currently seem inadequate? Failure to achieve adequate results with an artificial tear may be due to several causes. As noted above, the change in environment (i.e., Santa Ana wind conditions or being in a low humidity site such as an airplane or a department store) or medications (such as cold remedies) may cause a previously effective treatment regimen to be inadequate. Also, patients may progress from mild eye dryness or more severe dryness if the Sjögren's syndrome leads to more destruction of lacrimal glands.

Finally, other causes for persistent or increased eye symptoms must be considered. Corneal abrasions (a scratch on the surface of the eye is more common dry eye patients) or infection of the eye (often associated with a new type of pus-like discharge) may cause sudden worsening and must be promptly treated. Also, irritation of the glands in the eyelid may occur and is called "blepharitis." This cause should be suspected when swelling and redness of the eyelid occur. This may be due to a low-grade infection or sometimes due to irritative effects of preservatives in artificial tears or ointments. One part of the treatment for blepharitis is to keep the eyelids clean using "baby shampoo" or a special product called "eyelid scrub." In some patients with blepharitis, infection of the meibomian glands (in the eyelids) may require treatment with a low dose of antibiotic (such as tetracycline or doxycycline) for several weeks.

In addition to artificial tears during the day, lubricating ointments at night also play an important role in the treatment of dry eyes. Since ointments usually cause significant blurring of vision they are generally

used at bedtime. Sometimes the blurring persists in the morning and can be minimized by using only about 1/8-inch of the ointment at bedtime. It is a common mistake to use too much lubricant at bedtime. In some cases, it is useful first to put in the artificial tears at bedtime; then "seal the moisture in" with the application of the ointment. There are several different brands of ocular ointment (Table 4). As with artificial tears, they differ in their composition and preservatives. Thus, patients may tolerate some brands better than others.

A European study suggested that bromhexine (Bisolvon), a synthetic alkaloid derivative originally used as a mucolytic agent in cough remedies, may have slight beneficial effects in increasing lacrimal and salivary gland function. Doses of at least 48 mg/day were required since no benefit was reported at lower doses. This medication is not commercially available in the U.S. but is available in Mexico (sold as Bisolvon) and in Europe. Multicenter trials are in progress to determine whether the benefits will be significant enough to justify the expense and the large number of tablets per day.

In theory, soft contact lenses might help spread the tear film over the eye or prevent evaporation of tears. Some types of contact lenses absorb tear fluid as a way to maintain their rigidity and thus further diminish the amount of tears available to protect the eye. Also, great care must be taken to avoid infections and prevent damage to the cornea in dry eye patients who wear contact lenses. Rarely, a partial tarsorrhaphy (sewing the lateral portion of the eyelids together) may be required.

Nasal Dryness, Sinusitis, and Upper Airway Dryness

Many Sjögren's patients complain of nasal dryness and have symptoms of sinusitis with postnasal drip. In our experience, Sjögren's patients do not get a higher frequency of sinusitis infections than other individuals. However, they tend to last longer and have a higher chance of persisting longer with "postnasal" drip and cough, or developing into a bronchitis or pneumonia. These complications occur because of decreased secretion of glands lining the nasopharynx, leading to crusting of mucous secretions that block the airways and predispose to infection.

Our initial approach is to provide increased moisture to this region by use of normal saline sprays (Ocean) and humidifiers at night (Table 5). Also, "lavaging" the sinuses (i.e., rinsing them out with a mild solution of salt water) after loosening the secretions with a humidifier is often very useful in breaking the cycle of repeated sinus and upper respiratory tract infections. "Ocean" spray is simply a brand name for a solution of salt water that helps restore humidity to the nose. It is simple to make your own salt water spray by adding one teaspoon salt to one quart of deionized water and boiling to fully dissolve the salt. The Ocean spray container can then be refilled with homemade salt water. There are many different types of cool mist humidifiers that vary in size and cost. We recommend the small portable units (choose one that is silent and easy to clean/refill), and not the large humidifier units that are built into the house's furnace/air conditioning systems. The large room units may become contaminated with yeast or fungus that can subsequently lead to "allergic"-type reactions. This problem has not been encountered with the small portable units where the water is changed daily. In areas where the water is "hard" (i.e., contains large amounts of calcium and other salts), "distilled" water (similar to that used for irons) may be less irritating than water from the tap.

In patients with persistent or recurrent sinus blockage, it is important to keep the nose open since breathing through the mouth is a frequent cause of increased dry mouth and the problems described above. In addition to the Ocean spray, it may be beneficial to learn to "lavage" the sinuses to remove the dry, crusted secretions. This is easily performed by the patient using an irrigation syringe (similar to the syringe used for basting a turkey) or a Waterpik (set for the lowest pressure delivery level). In patients with persistent sinus symptoms, it is also useful to obtain a "nasal smear" to determine if allergic factors (indicated by presence of eosinophils on the smear) are playing a factor. Topical nasal sprays (such as Beconase Nasal AQ, Nasalide, or Flonase) may be helpful in these patients, especially after lavaging (Table 5).

In the setting of sinusitis, it is always important to notice if the color of secretions change from clear to dark green; the latter situation may indicate the occurrence of bacterial infection and necessitate treatment with antibiotics. The diagnosis of sinusitis is confirmed by sinus x-ray with air-fluid levels and purulent sinus drainage. When symptoms of sinus infection are persistent despite the above treatment measures, the possibility of an "abscess" within the sinus must be considered and this may require surgical drainage. In order to determine if the sinus infection requires this treatment, a CAT scan of the sinuses is performed. The radiologist can perform a "limited" CAT scan at a much lower cost than a full CAT scan. If an abscess is detected, it may be necessary for an ENT specialist to establish sinus drainage, obtain definitive cultures and treat with a specific antibiotic.

Skin Dryness

Dry skin and lips are common complaints in Sjögren's syndrome. Topical treatments with creams and lotions (Table 6) are often helpful. Creams are distinguished from lotions by being "greasier" than lotions, which often contain oil/water mixtures. Creams and ointments are preferred since they better "seal" in necessary moisture. In general, we suggest applying the creams after a shower or bath while the skin is still moist. Alternatively, the cream can be applied to dry skin directly after moistening with a damp cloth. Cosmetics such as lipstick can be applied 5-10 minutes later. Cracking at the angles of the cheek (cheilitis) is often due to Candida infection and will not effectively heal until a topical cream (such as Spectazole or Loprox) is applied (Table 6). For oral yeast (white patches inside cheeks) oral chlortrimazole troches (such as Nystatin Troches or Mycelex Pastilles) are very helpful. Unfortunately, both of these preparations contain a certain amount of sugar that can further exacerbate dental problems. The vaginal suppository (Nystatin vaginal tablets or Gynelotrimen) does not contain any sugar but has a slightly bitter taste. The oral troches or vaginal suppositories (that are used orally and sucked) must be used for at least 4-6 weeks for the oral yeast infection to be obliterated and the normal oral lining to be regenerated.

Gynecologic Issues

Vaginal dryness often leads to painful intercourse (dyspareunia). It is important to be reassured that this does not occur in all Sjögren's patients, even those with severe mouth and eye dryness. A gynecologic exam is useful to rule out other causes of painful intercourse and other causes of vaginal dryness. When it does occur as part of Sjögren's syndrome, the spouse needs to be reassured that this is a "physiological" problem and not related to a failure of sexual arousal. Sterile lubricants such as KY jelly or Surgilube are helpful. The Sjögren's patient currently has many more options regarding safe and effective vaginal lubrication than every before. Lubricants such as Maxilube and Astroglide have slightly different characteristics when compared with KY jelly or Surgilube and yet share the common characteristics of being water-soluble and nonirritating. This also holds true for the new non-hormonal vaginal moisturizer Replens which may be used unassociated with intercourse.

For those patients who do not like the gel-type lubricants, there is now available Lubrin vaginal inserts. Added to this, a new once-a-week vaginal lubricant called Vagikote is currently in clinical trials. Finding the right preparation for a specific individual is often a matter of trial and error inasmuch as satisfaction with each lubricant is a matter of personal preference. The patient needs to be frank with her physician regarding her satisfaction or dissatisfaction with a particular preparation. The external use of preparations containing petrolatum or oils which "seal in" moisture, such as vaseline or cocoa butter, may lead to maceration of the vaginal lining and are to be avoided.

Vaginal dryness in perimenopausal or postmenopausal women is often related to vaginal atrophy because of declining estrogen levels and therefore responds to vaginal estrogen creams. Cortisone creams are not beneficial in this situation. If vaginal yeast infection occurs, prompt treatment with clotrimazole cream or suppositories (Gynelotrimin) is effective and safe. On the external vulvar surface, dryness may be treated with lubricating creams as you would other skin surfaces (see section on skin dryness). Several patients have reported considerable satisfaction with the use of a thin film of vitamin E oil used on the vulva once or twice a day.

An issue of concern to female Sjögren's patients has been whether or not estrogen replacement therapy at the time of menopause is harmful to their condition. With regards to estrogen replacement in general, the clinical evidence is now fully convincing that blocking osteoporosis and reducing cardiovascular mortality while improving quality of life by eliminating hot flashes and hormone-related vaginal dryness, makes properly monitored estrogen replacement therapy an overwhelmingly attractive management strategy. Earlier investigators were concerned that estrogen might have a negative influence on Sjögren's based on animal studies. At Scripps Clinic, we have not seen any deterioration of Sjögren's syndrome related to either estrogen replacement therapy or low estrogen forms of oral contraceptives. Because of this, we encourage adequate estrogen replacement for the properly screened postmenopausal Sjögren's patient.

Many women with Sjögren's syndrome are interested in the risks of pregnancy and risks to the baby. Obstetrical authorities report slightly higher rates of recurrent fetal death and congenital heart block in those pregnancies complicated by maternal autoimmune disease. In rare patients, fetal loss has been associated with presence of the antibodies called "antiphospholipid antibodies," "lupus anticoagulant" and anticardiolipin antibodies. Congenital heart block is an abnormality of the rate or rhythm of the fetal or infant heart. Certain autoantibodies, such as an antibody called "anti-SS-A," have been associated with congenital heart block in the newborn. These autoantibodies may be present in patients with

systemic lupus erythematosus and with Sjögren's syndrome, as well as in patients with no apparent disease. However, it is important to reassure patients planning families that the vast majority of patients with Sjögren's syndrome have babies with no congenital abnormalities. Thus, we encourage family planning to be conducted without this being a major consideration. Nevertheless, it is important for patients anticipating pregnancy (or those with multiple prior miscarriages) to have screening blood tests and that their pregnancies require supervision by obstetricians experienced in handling patients with autoimmune diseases. A team approach combining both rheumatology and obstetrics can be used to optimize the outcome for both mother and baby.

Myalgias and Arthralgias

Physicians frequently use terms like arthralgia and arthritis. The former term means that the joint aches and the latter term means "inflammation" as indicated by the presence of heat, redness and swelling. In a similar sense, myalgia refers to aching of the muscle and myositis to actual muscle inflammation. Finally, neuralgia refers to "nerve pain" while neuritis or neuropathy refers to inflammation of the nerve.

The distinction between arthralgias and arthritis can often be made on clinical examination. However, more sensitive tests including x-rays or bone scans may be required. In the case of muscles, blood tests and, occasionally, electrical stimulation tests [called electromyography (EMG) and nerve conduction velocity] are useful.

In some patients, inflammation of the nerves may produce symptoms of pain. The nerves may be affected at many different sites. If inflammation of the brain is suspected, procedures such as an EEG (brain wave study) or MRI (magnetic resonance imaging) may be required. In our experience, brain inflammation is uncommon but has been reported in higher frequency at another medical center. There may be inflammation of peripheral nerves (those that have exited from the spinal cord). The involvement of the nerves can cause weakness or numbness. The EMG and nerve conduction study may be required for diagnosis in this situation.

Also, it is important to remember that many other common problems result in nerve, muscle or joint pain. For example, a pinched nerve at the level of the spine may cause numbness and weakness in an arm or leg. A torn cartilage in the knee or a degenerated disc in the back may lend to joint pain or muscle spasms. These common problems are not due to Sjögren's syndrome. Too often, patients and their physicians may not look for "the obvious" causes of symptoms and simply blame the problem on Sjögren's syndrome. This delays the institution of the correct therapy for the problem.

Fatigue

Fatigue is probably the most common complaint in patients with Sjögren's syndrome. Fatigue may have many causes, including those related directly and indirectly to the Sjögren's syndrome. Two types of fatigue should be considered. The first type is late morning or early afternoon fatigue. In this case, the patient arises with adequate energy but simply "runs out of gas." This type of fatigue suggests an inflammatory or metabolic process. Patients describe this type of fatigue as "flu-like" symptoms, and it results from an active immune system liberating specific hormones of inflammation called interleukins. To help determine whether fatigue is due to active inflammation, blood tests called "sedimentation rate" or "C-reactive protein" are ordered by your physician, since these tests are usually elevated by the same interleukins that cause fatigue.

A second type of fatigue is "morning fatigue," where the patient arises in the morning and does not feel that he/she has obtained an adequate night's sleep. This is also quite common in Sjögren's syndrome and may exist in addition to "inflammatory" fatigue. For example, patients may have inadequate sleep due to joint or muscle pain. Also, Sjögren's patients often drink a great deal of liquid during the day because of dry mouth and throat. Then at night, the patient may be awakened three or four times to urinate. This disrupts the sleep pattern and leads to morning fatigue. When this is the case, it is best to treat the symptoms directly and better sleep should follow. For example, humidifiers and oral lubricants (i.e., saliva substitutes) at night might be beneficial. Nonetheless, there may be periods when one doesn't sleep well, and it is important not to allow certain negative sleep habits to become ingrained. All persons, especially those with a tendency to poor sleep or daytime fatigue should adhere to the following general suggestions for good sleep:

1. Maintain a regular and consistent wake-up time. Do not oversleep or spend excessive amounts of time in bed.

2. If unable to sleep, it is better to get up and do something else that is quiet, restful, and enjoyable, such as reading, knitting, or doing a puzzle. Do not lay in bed and try too hard to sleep.
3. A steady daily amount of exercise probably deepens sleep.
4. Stress reduction techniques such as meditation, biofeedback, or progressive relaxation are encouraged.
5. Caffeine should be avoided after lunch, and alcohol should be avoided after dinner. In some people, even one cup of coffee or one alcoholic beverage is enough to disturb sleep.
6. The bedroom should be quiet, dark, and comfortable. During the daytime, exposure to sunlight for even one hour at a regular time can strengthen circadian rhythms and improve the quality of sleep. Especially in San Diego, get outside for your lunch hour or take a walk after dinner.

Sometimes following good sleep habits is not enough to improve the sense of daytime fatigue and poor sleep. If this is the case, a specific evaluation for sleep disorders can be done. Certain people may have a higher risk of physiologic sleep disorders. In our experience, patients with Sjögren's frequently have sleep disturbance due to nocturnal myoclonus (a spontaneous muscle cramping) that occurs at night and disrupts the amount of time spent in "restful" sleep. Some patients respond to quinine and vitamin E at bedtime. Other patients require a medication such as Klonopin (clonazepam), a member of a drug family called benzodiazepines (that includes Valium and Ativan). These drugs have the ability to prevent muscle spasms and were first developed to prevent muscle rigidity associated with seizures. Thus, patients who look up Klonopin are surprised to see that it was first approved for children with seizures. This is because Klonopin reduces severe muscle spasms, a life-threatening part of seizures in children. However, Klonopin is used in much lower doses to reduce the muscle spasms associated with nocturnal myoclonus. Like its parent compound Valium, Klonopin also has "anti-anxiety" activity and has other uses in addition to nocturnal myoclonus. Other medications such as Elavil (amitriptyline) or Pamelor (nortriptyline) are commonly prescribed for sleep disorders but are generally not well tolerated by Sjögren's patients due to their side effect of increased dryness.

Finally, sleep disruption can occur due to sleep apnea. Sleep apnea is suspected in patients who snore loudly or awake at night gasping for breath. Patients with recent weight gain (often due to corticosteroids) may develop sleep apnea. This problem requires the expertise of a sleep center for evaluation and treatment.

Depression in Sjögren's Syndrome

Depression can present in many forms, including difficulty concentrating, poor appetite, or a sleep disorder. The precise role of inflammation and hormone imbalances associated with Sjögren's syndrome as a contributing factor to depression remains unclear, but certainly depression is caused in part by chemical alterations in the brain. Stress, poor sleep, and chronic illness can all contribute to depression. When antidepressant medications are used to help regulate sleep patterns and treat fatigue, drugs lacking anticholinergic side effects are preferred. As mentioned earlier, certain antidepressants such as tricyclics (Elavil and Pamelor) and monoamine oxidase (MAO) inhibitors may greatly increase dryness and should be avoided. A second class of antidepressants with less dryness include trazodone (Desyrel); newer members of this family include Serzone. A third class of antidepressant drugs are called serotonin re-uptake inhibitors (SSRI). These include Prozac, Paxil, Zoloft, Luvox and Effexor. The incidence of increased dryness (and other side effects including sleep disruption) appears variable among different patients and a careful diary by the patient may help the physician in the selection of the correct drug.

Patient Support Groups

The increasing recognition of Sjögren's syndrome has led to the recent formation of patient support groups. One group, called the Sjögren's Syndrome Foundation, puts out a monthly newsletter, "The Moisture Seekers," and has local chapters in many cities including San Diego (local contact persons are listed in each issue of "The Moisture Seekers"). Another group, the National Sjögren's Syndrome Association, publishes a different newsletter, the "Sjögren's Digest," and has chapters including the Los Angeles area, Arizona, Minnesota and Florida. Both newsletters contain informative articles and therapeutic hints for patients.

Although we recommend these newsletters as a source of patient information, we wish to caution you that some of the material may be controversial and may conflict with our opinions. Nevertheless, we strongly believe that patients should have access to all points of view (including those opposed to ours) and we are happy to discuss our reasons for/against any specific suggestions. Just do not take everything that is in a newsletter (or that we say) as "gospel." Similarly, the periodic meetings of patient

support groups are a potential source of helpful information and emotional support. However, they also may be a source of misinformation. So approach patient support groups with an open mind as if you were competitively shopping for an important item. Whether you belong to a support group or not, it is important to surround yourself with people who believe in “wellness” behavior rather than with individuals who are chronic complainers.

Role of the Diet and Nutrition

Patients frequently ask about the role of diet either in causing their disease or in their treatment. No definite answers are known, but environmental agents (perhaps even food antigens) may play a role.

One of the best examples of diet-related autoimmune disease is celiac sprue, where autoimmune reaction against gliadin (a wheat-derived product) plays an important role. At a molecular level, the gliadin resembles a viral-encoded protein and thus the body mounts an “antiviral” response every time it encounters this food antigen. It is possible that other foods may provoke and adversely activate the immune system by mechanisms that we do not understand. It would be helpful if we had reliable methods to detect specific “food allergies” in patients. Despite two decades of trying to develop such tests, there are still no reliable methods. However, some unscrupulous individuals advertize special blood tests for “food allergy.” These tests have not been shown to have merit and circulating antibodies against specific food antigens have not been demonstrated in Sjögren’s syndrome. We do recommend that patients avoid candy and products containing sugar, which may cause dental cavities and increased gingival disease.

Recent interest has centered around the possible role of fatty acids that are precursors of prostaglandins and/or leukotrienes, which play an important role in the inflammatory response. One preliminary report suggests a deficiency of prostaglandin E1 (a derivative of fatty acids) in Sjögren’s patients that were treated with dietary supplements of fatty acids. Recent studies in rheumatoid arthritis have shown that mild subjective improvement and minor degrees of improvement in joint swelling could be achieved by taking fish oil tablets containing particular fatty acids known as omega-3 polyunsaturated fatty acids. It is too early to give these fatty acids any recommendation in Sjögren’s syndrome since this “medication” actually increased arthritis when fed to rats.

Little information is available on the beneficial role of vitamin or mineral supplements in Sjögren’s syndrome. Certainly, a daily multi-vitamin seems justified, particularly since dietary food intake is often altered due to tooth loss/gingival disease. The beneficial value of neutral fluoride for tooth enamel was described above. Although severe vitamin A deficiency can cause dry eyes, the clinical features of this dry eye syndrome are different from those in Sjögren’s syndrome. Further, serum vitamin A levels are normal in Sjögren’s patients and excessive intake of this vitamin can cause fatal liver damage. Based on reports that zinc was helpful in reducing stomatitis in patients after head and neck irradiation, we tried zinc sulfate (220 mg/day) without significant improvement in most cases. However, double-blind studies on large numbers of patients will be required before the role of vitamins and dietary factors can be adequately assessed. We have suggested daily yogurt (especially low fat) since this has had a beneficial response in decreasing oral Candida infections and thus decreasing mouth discomfort.

Heartburn and Esophageal Motility in Sjögren’s Syndrome

Saliva normally plays a major role in neutralizing gastric acidity. Thus, symptoms of “heartburn” or “hiatal hernia” are common in Sjögren’s syndrome. Gastric hyperacidity can be partly overcome by the use of antacids (such as Mylanta II or Maalox II) after meals and at bedtime. Also, elevation of the head of the bed on 1- to 2-inch wood blocks provides a way to reduce the gastric acid from washing back into the esophagus at night. In some patients with severe problems of “heartburn,” the medicine sucralfate (Carafate slurry) has been helpful. This medicine was designed to “coat” the esophagus and stomach of patients with ulcer disease. However, sucralfate coating of the stomach might interfere with the absorption of certain other medications so be certain to check this possible drug interaction with your physician and pharmacist. For heartburn, two types of medications decrease the gastric production of acid. The first type are called “H2 blockers” and include Tagamet, Pepcid, and Zantac; several of these have recently become available over the counter. A second type of medication is Prilosec, which inhibits the secretion of acid, still requires a prescription. Finally, some patients have decreased motility of the esophagus and may benefit from a medicine called cisapride (Propulsid). However, these medications are relatively expensive and may cause other side effects.

Since saliva normally helps during swallowing pills, it is important to recognize that pills can become stuck to “dry” walls of the esophagus and cause painful erosions. For example, iron supplement pills are large in size and uncoated tablets may get stuck in the esophagus, leading to pain and a choking

sensation. Also, certain time release preparations tend to adhere to the esophagus in the absence of sufficient saliva. To minimize these problems, coated tablets are preferred (when available) and medication should be taken with lots of water while sitting in the upright position (rather than lying down just after taking the pills).

Medications in Treatment of Sjögren's Syndrome

The key question for the physician is whether there is evidence of an active inflammatory process. Again, the history, exam and blood tests help provide the physician with objective evidence to guide therapy. The simplest anti-inflammatory agent is aspirin. To minimize stomach upset, enteric-coated forms are preferable (Table 7). Other forms of aspirin-like drugs (Disalcid or Trilisate) have fewer gastric side effects but require prescriptions. The most common anti-inflammatory drugs are called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have become very popular during the last decade for treatment of headache, joint and muscle pains. Although these medicines are considered as a single group (i.e., Clinoril, Naproxen, Indocin, Voltaren, Ansaid, Daypro, Relafen and others) (Table 7), individual patients may have good response to one drug and no response (or even toxicity) to another drug. Ibuprofen (Advil, Nuprin) is available over the counter and thus less expensive, while others such as Indocin, Clinoril and Voltaren have generic equivalents. Indocin is available as a suppository, which may be an advantage in patients where oral medicines lead to stomach upset. Voltaren is enteric-coated, and Naproxen will soon also be available in this form. Ansaid has been shown in one dental study to decrease periodontal disease by decreasing the inflammatory response in the gums.

Steroids (prednisone or Medrol) are stronger drugs that work very effectively to decrease the inflammatory response. Unfortunately, these drugs have many side effects when taken for prolonged periods, including diabetes, hypertension, osteoporosis, cataracts and increased risk of infections. However, steroids work rapidly and must be used in certain situations. Attempts to taper the dose of steroids should be pursued to avoid the side effects.

Disease-Modifying Anti-Rheumatic Drugs called (DMARDs) were first developed for rheumatoid arthritis and systemic lupus erythematosus, but are also frequently used in Sjögren's syndrome. One class are called "antimalarial" drugs since chloroquine was first developed for malaria and later found to have benefit in patients with autoimmune diseases. Since chloroquine at high doses was associated with side effects involving the eye, Plaquenil (hydroxychloroquine) was subsequently developed. When taken at the proper dose, Plaquenil has an extremely good safety record, although there remains a remote possibility (probably less than 1/1000) of significant build-up in the eye. At present, we recommend eye checks (generally every 6 months) so that the medicine can be discontinued if there is any significant ocular side effect. We have found Plaquenil to be beneficial in selected patients with evidence of an active, persistent inflammation. Other disease-modifying agents (imuran, methotrexate, and cyclosporin A) are much stronger drugs and require careful monitoring of their side effects. Our overall approach to medications is that it is best to avoid them if possible since all medications have risks. However, in certain situations, the damage to the body by the immune system is sufficiently great that the relative risks of these medications is justified.

Similarly, it is important to recognize that certain medications may cause increased dryness as a side effect (Table 8). If you are receiving these medications, you might discuss the possibility of changing to a less drying drug.

In these days of computer codes being required for insurance reimbursement (Table 9), we have listed several codes that are required for ordering a diagnostic test. If your insurance does not accept the initial diagnosis code, ask if the procedure is covered by Table 9.

Particular Needs of the Sjögren's Patient at the Time of Surgery

We recommend that patients bring their own medicines (including artificial tears, lubricants, and saliva substitutes) to the hospital. The patient may use their own medicines (if approved by their physician) and this saves not only money but time in dispensing the same medications from the pharmacy. Some special needs of the patient with Sjögren's syndrome are listed in Table 10.

Certain medications (especially aspirin or NSAIDs) may alter the normal blood clotting mechanisms and need to be stopped prior to surgery. In general, aspirin needs to be stopped approximately 6 days prior to major surgery, while nonsteroidal anti-inflammatory drugs (including Motrin and other over-the-counter analgesics such as Advil) approximately 48 hours prior to surgery.

Even if you are not undergoing surgery, it is always a good idea to carry a written list of your current medicines, their doses, and any drug allergies you might have. Nothing is more annoying for the physician (and dangerous to the patient) than trying to identify the name of “some small white pill” that the patient can’t quite remember in the stress of medical evaluation.

In summary, Sjögren’s syndrome is an autoimmune disease of unknown cause that results in decreased salivary and lacrimal gland function. Also, extraglandular symptoms are frequently present and may occasionally overshadow the complaints of dry eyes and mouth. Although there is no cure, significant symptomatic improvement can be achieved and many serious complications can be avoided by recognition and early treatment of the glandular and extraglandular manifestations of Sjögren’s syndrome. Research is currently focusing on the cause of Sjögren’s syndrome and new methods are being developed to control the “autoimmune” phenomena responsible for Sjögren’s. In an era of increasing health maintenance organizations (HMO’s) and the need for diagnosis codes, it is often necessary for the patient to help their physician or dentist by informing them of currently accepted diagnosis codes. A partial listing of several useful codes is provided in Table 9.

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Table 1. Criteria for Diagnosis of Primary and Secondary Sjögren’s Syndrome

I. Primary Sjögren’s Syndrome
   - A. Symptoms and objective signs of ocular dryness
     1. Schirmer I test <8 mm wetting per 5 minutes
     2. Positive rose bengal or fluorescein staining of cornea and conjunctiva to demonstrate keratoconjunctivitis sicca
   - B. Symptoms and objective signs of dry mouth
     1. Decreased parotid flow rate using Lashley cups or other methods
     2. Abnormal biopsy of minor salivary gland (focus score of 32 based on average of 4 evaluable glands)
   - C. Evidence of a systemic autoimmune disorder
     1. Elevated rheumatoid factor 31:320

2. Elevated antinuclear antibody 31:320
3. Presence of anti-SS-A (Ro) or anti-SS-B (La) antibodies

II. Secondary Sjögren's Syndrome
Characteristic signs and symptoms of SS (described above) plus clinical features sufficient to allow a diagnosis of rheumatoid arthritis, systemic lupus erythematosus, polymyositis, or scleroderma

III. Exclusions
Sarcoidosis, preexistent lymphoma, acquired immunodeficiency disease, hepatitis C and other known causes of keratitis sicca or salivary gland enlargement

Table 2. Causes of Keratitis and Salivary Gland Enlargement Other Than Sjögren's Syndrome

Keratitis Salivary Gland Enlargement

1. Mucous membrane pemphigoid 1. Sarcoidosis, amyloidosis
2. Sarcoidosis 2. Bacterial (including gonococci)
3. Infections: virus (adenovirus, syphilis) and viral infections (herpes, vaccinia), bacteria (infectious mononucleosis, tuberculosis, histoplasmosis, leprosy and actinomycosis)
4. Trauma (e.g., from contact lens) and environmental irritants, iodide, lead, or copper hypersensitivity including chemical burns, exposure to ultraviolet lights
5. Hyperlipemic states, especially or roentgenograms types IV and V. Neuropathy including neurotropic
6. Tumors (usually unilateral) keratitis [e.g., damage to fifth including cysts (Warthin tumor), cranial nerve and familial dysepithelial (adenoma, adenocarautonomia (Riley-Day syndrome) lymphoma, and mixed
7. Hypovitaminosis A
8. Erythema multiforme (Stevens- Johnson syndrome)
9. Excessive alcohol consumption
10. Human immunodeficiency virus (HIV)
11. Hepatitis C

Table 3. Extraglandular Manifestations in Patients With Sjögren's Syndrome

- Respiratory Chronic bronchitis secondary to dryness of upper and lower airway with mucus plugging
- Lymphocytic interstitial pneumonitis
- Pseudolymphoma with nodular infiltrates
- Pleural effusions
- Pulmonary hypertension, especially with associated scleroderma
- Gastrointestinal Dysphagia associated with xerostomia
- Atrophic gastritis
- Liver disease including biliary cirrhosis and sclerosing cholangitis
- Skin and mucous Candida–oral and vaginal membranes
- Hyperglobulinemic purpura
- Raynaud's phenomenon
- Vasculitis
- Thyroiditis
- Peripheral neuropathy involvement of hands and/or feet
- Mononeuritis multiplex
- Myositis
- Hematologic -neutropenia, anemia, thrombocytopenia
- Pseudolymphoma
- Lymphadenopathy
- Lymphoma and myeloma
- Renal Tubular-interstitial nephritis (TIN)
- Glomerulonephritis, in absence of antibodies to DNA
- Mixed cryoglobulinemia
- Amyloidosis
- Obstructive nephropathy due to enlarged periaortic lymph nodes

Table 4. Commercial Preparations of Artificial Tears and Saliva

All products in each category are not equivalent to each other

A. Mouth Preparations
Biotene Toothpaste; Laclede Labs; none
Retardent Toothpaste; Rowpar; none
Dental Care Toothpaste; Arm & Hammer; none
Oral Balance Gel; Laclede Labs; none
Biotene Mouth Rinse; Laclede Labs; none
Retardex Mouth Rinse; Rowpar; none

B. Artificial Saliva
MouthKote; Parnell; none
Saliment; Ferring; Parahydroxybenzoate
Xero-Lube; Scherer; Paraben
Saliva Substitute; Roxane; Paraben
Salivart; Westport; none

C. Artificial Tears
Cellufresh; Allergan; none
Biontears; CIBA; none
Liquifilm; Allergan; Chlorobutanol
Tears Plus; Allergan; Chlorobutanol
Liquifilm Forte; Allergan; Thimerosal
Hypotears; IOLAB benzalkonium chloride
Hypotears PF; IOLAB; none
Tears Naturale II; Alcon; Polyquad
Adsorbotear; Alcon; Thimerosal
Murocel Tears; Bausch & Lomb; Methylparaben

D. Ocular Ointments
Refresh PM; Allergan; none
HypoTears Ointment; IOLAB; none
Duolube Ointment; Bausch & Lomb; none
Duratears Ointment; Alcon; Methylparaben
Lacrilube; Allergan; Chlorobutanol

E. Blepharitis
Baby shampoo; Johnson & Johnson
I-Scrub; Cooper
EV Lid Cleaner; Eagle Vision
Ocusoft Scrub; Ocusoft

Table 5. Sinusitis

1. Humidifier (i.e., Cool Mist Vaporizer)
2. Ocean spray (salt water) to irrigate sinuses. Can make solution by dissolving 1 teaspoon salt in 1 quart distilled water.
3. Lavage of nasal passages with saline
    1. Basting syringe
    2. Waterpik — smooth the end of applicator and set at lowest setting
4. Decongestants
    1. Claritin, Seldane, Hismanal
5. Antibiotics
    1. Bactrin DS,· Augmentin (if sulfa allergy)
    2. Doxycline (especially for blepharitis)
6. In some cases, topical steroid sprays (use after lavage and Ocean Spray)
    1. Nasalid spray, Beconase Nasal AQ spray
    2. Vanconase spray, Flonase
7. Mucolytics
    1. Alkalol (used in lavage fluid)
    2. Humabid (Guaifenesin)
    3. Bromhexine (Bisolvon)
    4. Organidin (contains iodide)
    5. Saturated Solution Potassium Iodide (SSKI)
8. Multivalent flu vaccines

Table 6. Treatment For Skin and Mucous Membrane Manifestations

Skin Creams[*] *and Anti-Candida Medications for the Mouth*

Eucerin Lotrimin Cream[*], external
Moisturel Micatin cream[*], external
Ticreme Naftin cream, external
Aquaderm Spectazole cream, external
Complex 15 Loprox cream, external
Neutrogena Chlortrimazole cream, external
Gynelotrimen cream[*], external
Skin Lotions[*] Nystatin Oral Troche[*]
Mycelex troches[*]
Keri lotion Gynelotrimen vaginal suppositories[*]
Carmol
Lubriderm Vaginal Lubricants and Anti-Candida[*]
Nutraderm
Lac Hydrin Five Surgilube
Lacticare KY Jelly
Maxilube

Soaps and Shampoos[*] *Gyne-Moisture*

Astroglide
Purpose Feminase
Dove Topical estrogens (postmenopausal)
Alpha Keri bar Gynelotrimen vaginal suppositories or Aveenobar cream

Topical Steroids Sunscreens

0.5%Hydrocortisone[*]
Any sunscreen greater than SPF 15 with Lacticare HC (2.5% HC)
UVA and UVB blockers
Mid-strength corticosteroids Solbar 50 (Kenalog, Aristocort)–not for use on the face
Photoplex (UVB plus UVA blockers)

* Over the counter

Table 7. Systemic Medications for Treating Autoimmune Diseases

Anti-Inflammatory

Salicytes:
Aspirin (enteric-coated preferred)*
Disalcid, Trilisate

NSAIDs:
Ibuprofen (Advil, Nuprin)*
Clinoril (generic), less renal side effect
Indocin (available as suppository)
Voltaren (enteric-coated)
Ansaid (studies in periodontal disease)
Lodine, Daypro, Relafan (lower GI side effects)
Celebrex and Vioxx (very low GI side effects)

Steroids (Prednisone, Medrol, Decadron)

Disease-Modifying

Chloroquine
Plaquenil (hydroxychloroquine)
Imuran (azathioprine)
Methotrexate
Cytoxan (cyclophosphamide)
Cyclosporin A (sandimmune)

Table 8. Drugs Associated With Decreased Salivary Secretion and Increased Oral Dryness

I. Blood Pressure Medications

A. a-blockers (clonidine)
B. b-blockers (Inderal)
C. Combined ab-blockers (Labetolol)

II. Antidepressants
A. Amitriptyline (Elavil)
B. Nortriptyline (Pamelor)

III. Muscle Spasm
A. Flexeril
B. Robaxin
C. Baclofen

IV. Urologic Drugs
A. Ditropan
B. Yohimbe

V. Cardiac
A. Norpace

VI. Parkinson's
A. Sinemet

VII. Decongestants
A. Chlortrimeton
B. Pseudofed (pseudoephredine)
C. Many other over-the-counter preparations

Table 9. ICD-9-CM Code Assignments for Sjögren's Syndrome, Manifestations, Symptoms and Related Disorders

710.2 Sicca syndrome (Primary Sjögren's syndrome)
714.0 Rheumatoid Arthritis
710.0 Systemic Lupus Erythematous
710.1 Systemic sclerosis (scleroderma)
710.3 Dermatomyositis
710.4 Polymyositis
357.1 Polyneuropathy in collagen vascular disease
517.8 Lung involvement in diseases classified elsewhere
112.0 Candidiasis of mouth (thrush)
112.84 Candidial esophagitis
202.8 Lymphoma, malignant (non-Hodgkin's)
273.0 Polyclonal hypergammaglobulinemia
285.9 Anemia, unspecified
373.0x Blepharitis, unspecified
443.0 Raynaud's syndrome
447.6 Arteritis, unspecified
521.0 Dental caries
523.4 Chronic periodontitis
530.81 Esophageal reflux
571.49 Other chronic (active) hepatitis
571.5 Cirrhosis of liver without alcohol (cryogenic)
571.6 Biliary cirrhosis
595.1 Chronic interstitial cystitis
135.3 Dyspareunia
729.1 Myalgia and Myositis, unspecified (Fibromyalgia)
375.15 Tear film insufficiency (Dry eye syndrome)
370.33 Keratoconjunctivitis sicca, not specified as Sjögren's [excludes diagnosed Sjögren's syndrome]
527.1 Hypertrophy of salivary glands
527.7 Disturbance of salivary secretion (Xerostomia)
719.4x Pain in joint (requires fifth digit for site)
780.7 Malaise and fatigue
785.6 Enlargement of lymph nodes
797.2 Dysphagia
790.1 Elevated sedimentation rate

Table 10: Special Needs of the Sjögren's Syndrome Patient at the Time of Surgery

I. Preoperative Period
- Stop aspirin 1 week prior to surgery.
- Stop NSAIDs 3 days prior to surgery.

- Do not stop steroids.
- Notify anesthesiologist about specific problems with teeth, dentures, eyes, neck, sinuses, and lungs since this may affect the way intubation is performed.

II. Day of Surgery
- Take all medications with you to hospital in their bottles.
- Be sure to ask anesthesiologist to use an ocular ointment (such as Refresh PM) during surgery and in post-op recovery room.
- If receiving steroids, make sure these are taken on day of surgery either orally or through the IV. In some cases, a higher dose is required.
- All right to use artificial salivas (such as MouthCote) to keep mouth moist on the day of surgery when "NPO" (nothing per mouth).
- Ask anesthesiologist to use humidified oxygen in operating room and post-op.

III. Post-Operative Days
- Watch for yeast infections if receiving antibiotics.
- Use of artificial tears and salivas.
- Use of artificial salivas.

2. Sjögren's Syndrome :Dental Role in Providing Relief

James J. Sciubba, DMD, PhD and Erwin D. Mandel, DDS

Introduction

Sjögren's syndrome is an autoimmune disease in which sensitized lymphocytes selectively seek, infiltrate and destroy exocrine glandular tissue, including salivary glands. Lacrimal glands are also affected and, as a result, the sicca complex is clinically characterized by depressed levels of tear and saliva production.

Sjögren's syndrome is estimated to affect more than one million people in the United States. It is seen predominantly in middle-aged and elderly women, with females being affected 10 times more frequently than males.

Clinical Findings

Primary Sjögren's syndrome consists of dry eyes and dry mouth. These same symptoms are seen in secondary Sjögren's syndrome, along with an associated extraglandular connective tissue disease, such as rheumatoid arthritis or systemic lupus erythematosus. To establish the diagnosis of primary Sjögren's, it is essential to perform a lip biopsy to confirm that immune cells within the minor salivary gland tissue are causing the dry mouth. Additionally, it is necessary to demonstrate antinuclear antibodies in blood to specific tissue antigens (Ro/SS-A or La/SS-B).

To establish the diagnosis of secondary Sjögren's syndrome, definite dry eyes and dry mouth and/or a lip biopsy must be obtained in addition to serologic evidence of an accompanying connective tissue disease, usually rheumatoid arthritis. From a serological perspective, primary Sjögren's syndrome patients will often have a particular type of gene known as HLA-B8-DR3, while secondary Sjögren's syndrome will often show the genetic subtype of HLA-DR4 if the patient has rheumatoid arthritis.

It is thought that genetic factors render an individual susceptible for triggering of the autoimmune reaction, which to date remains poorly understood. Some experts believe that these genetic factors, plus infectious agents, may be responsible for generating the autoimmune attack on all exocrine glands in a manner similar to that noted in diabetes or thyroiditis. In these latter cases, glandular tissue is destroyed by activated lymphocytes mentioned above in the presence of auto-antibodies. Candidates for infectious

agents have been mentioned in the past. They include the Epstein-Barr virus; and more recently, a retroviral etiology has been suggested.

Differential Diagnosis

Since the most common cause of xerostomia is medication, the differential diagnosis must include, in addition to Sjögren's syndrome, use of certain drugs or medications. These include a long list of anticholinergics, antidepressants, anorectics, antipsychotics, sedatives, antihistamines, antihypertensive agents and diuretics. The clinician must carefully review current use of prescription and non-prescription medications before proceeding further. Patients who have received therapeutic radiation to the head and neck, including the major salivary glands, for diseases such as lymphoma or carcinoma are certain to have variable levels of xerostomia.

Organic diseases as well as autoimmune ones should be considered. These include the HIV complex, diabetes mellitus, hypertension, cystic fibrosis and dehyrdration secondary to impaired water intake. Diarrhea, renal disease and osmotic diuresis should also be included in the differential diagnosis. Psychogenic factors, in particular depression, can produce xerostomia as can decreased mastication due to limited intake of liquids or soft foods. (Table 1).

Table 1. Differential Diagnosis of Xerostomia

- medications
- irradiation to head and neck region
- depression
- organic diseases (autoimmune diabetes, hypertension, dehydration)
- soft diet and decreased mastication

Diagnosis of Sjögren's syndrome involves clinical tests and development of criteria for diagnosis. (Table 2). Several attempts to better define such components have been made over the years. Xerostomia is a likely clinical diagnosis if patients present with signs or symptoms over the dorsum of the tongue, such as atrophy or cobblestone surface changes. If such changes are present along with salivary gland enlargement, a reduction in salivary flow greater than 50 percent, and positive or so-called abnormal findings in salivary gland biopsy material, the diagnosis can be safely stated. The addition of reduced lacrimal flow rate, as measured by a Schirmer tear test, and punctate or filamentary keratitis establishes the diagnosis.

While these criteria are rather objective, the diagnosis of Sjögren's syndrome may be strongly suspected during the initial history and physical examination of the patient. Patients will often relate difficulty, if not an inability, to swallow a dry bolus of food, the so-called "cracker sign." Patients will likewise complain of a sandy or gritty sensation of the eyes, often accompanied by burning. Further oral signs include burning of the oral mucosa in some patients, oral mucosal erythema, stickiness of the oral mucosa, parotid gland enlargement or induration (hardening of the tissues) and the presence of focal sialoadenitis (inflammation of a salivary gland) upon analysis of a minor salivary gland biopsy.

Table 2. Methods of Evaluating Salivary Status

- sialometry
- sialography
- sialochemistry (99m Tc)
- imaging (ultrasound, CT, MRI)
- labial biopsy

In assessing salivary gland enlargement, in particular of the parotid glands, the clinician must determine if the swelling is unilateral or bilateral. If the former, the clinician should suspect potential salivary gland neoplasia or bacterial infection. When bilateral, lymphoma, granulomatous diseases such as sarcoidosis or tuberculosis, recurrent parotitis of childhood and sialadenosis, must be considered along with the benign lymphoepithelial lesion that usually accompanies Sjögren's syndrome.

With sialadenosis, the clinician must rule out potential underlying factors, including diabetes mellitus, hepatic cirrhosis, anorexia/bulimia, hypolipoproteinemia and chronic pancreatitis.

Symptoms associated with xerostomia include difficulty with speech, inability to chew and swallow dry food, a burning or tingling sensation of the oral tissues, in particular the tongue and an increase in dental caries. Bacterial sialoadenitis is often a common sequela of advanced and chronic xerostomia. Patients will often have difficulty coping with prosthetic appliances. Reduction in self-cleansing can result in increased plaque retention with a resultant increase in the incidence of periodontal disease as well as rates of disease progression.

The fundamental nature of Sjögren's syndrome and the accompanying xerostomia produce symptoms and signs centered exclusively on the diminution of saliva. The output of protective salivary constituents is altered significantly, thus setting the stage for alterations in the oral environment or ecology and the disease processes and breakdown that occur later. One such change in the microbial flora is colonization of the oral cavity by coliforms and Staphylococcus aureus. This shift appears to be common regardless of the etiology of xerostomia, that is, whether it is related to Sjögren's syndrome, radiation therapy or medication-induced dryness. Other changes in the oral microflora include an increase in Streptococcus mutans and Candida albicans levels. This, in turn, is responsible for the heightened incidence of caries and candidiasis, respectively.

Clinical Considerations

The impact of chronic xerostomia on the patient and on the dental practitioner can be devastating. The patient must be educated relative to Sjögren's syndrome, its general course and the fact that it is essentially incurable. At the same time, the practitioner should encourage the patient by indicating that the disease effects are manageable and with his/her cooperation the symptoms can be reduced and irreversible damage prevented.

An individual treatment plan must be devised for each patient to prevent new as well as recurrent dental caries. Daily fluoride mouth rinses are critical as is dietary modification–including discontinuing sugar-containing foods and beverages between meals–scrupulous daily oral hygiene, and routine and frequent dental examinations and treatment.

In patients with severe xerostomia, it is often necessary to use custom-made, soft acrylic trays or stents in conjunction with therapeutic-strength fluoride gels in an effort to help prevent rampant caries. Additionally, daily use of remineralizing solutions have proven helpful in that the earliest phases of tooth destruction can be altered and in many cases reversed, provided the carious lesion is in an incipient phase where sufficient enamel matrix may remain for remineralization to occur.

The presence of oral candidiasis is often under appreciated and unfortunately quite problematic in approximately one-third of patients with Sjögren's syndrome. Atrophic or erythematosus candidiasis will often have associated burning symptomatology with predisposition to ulceration. Less common, but by no means unusual, is pseudomembranous candidiasis, or so-called thrush. With thrush, curd-like aggregates of fungal colonies may be widely dispersed over the nonkeratonized mucosa and may be easily dislodged from the surface with gentle pressure.

Management of candidiasis involves the use of topically effective anti-fungal medications, which are generally sufficient. In more resistant or difficult circumstances, systemic anti-fungal drugs taken orally, such as ketoconazole and, more, recently, fluconazole, may be indicated. In individuals wearing partial or complete dentures, scrupulous hygiene and removal at bedtime, coupled with anti-fungal medications, are usually effective in controlling or eliminating fungal infection.

Salivary substitutes are currently available commercially and without prescriptions. Such substitutes fail to uniformly and completely suffice for natural saliva, yet they appear to be more effective than plain water and can provide relief for some patients. More recently, gel-based preparations have been introduced as well as salivary substitutes containing glycoproteins. These tend to more closely mimic natural saliva. Patients must be cautioned regarding chronic use of citric acid-containing drops. These could prove harmful in a short period of time in that tooth demineralization in the presence of relative dryness may quickly result.

Salivary stimulation by gustatory and/or masticatory means is the more common method for encouraging salivary flow. Use of sugarless chewing gum5 and sugarless hard candies often suffices for management of mild-to-moderate levels of xerostomia. Pharmacological intervention using pilocarpine

can be effective in increasing salivary production is some patients.6 A single dose of pilocarpine can often produce approximately one to two hours of improved salivary flow in individuals with some level of residual salivary function. Side effects, however, must be monitored. These include sweating, gastrointestinal discomfort and cardiovascular complications in individuals with hypertension.

Finally, a recently developed electrical stimulation device claims to produce improved salivary function in individuals with xerostomia. While results have not been uniform, this device clearly would require functional residual salivary tissue in order to be effective. A recent report7 underscores lack of sufficient data relative to evaluation of long-term clinical effectiveness of this modality of salivary stimulation and, equally importantly, to identify those who would benefit from this approach.

Conclusions

While the causes for xerostomia are multiple, individuals with Sjögren's syndrome tend to present with consistent and long-term xerostomia, which carries with it significant dental and oral complications. Both hard tissues and soft tissues can be affected with increase in the rates of caries and periodontal disease as well as oral mucosal discomfort and other factors that can severely affect quality of life. The dentist must be aware of this particular disease, its oral manifestations and their management.

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3. Problems Associated With the Dry Mouth of Sjögren Syndrome

Jason M. Tanzer, DMD, PhD

Among the most prominent and troublesome features of Sjögren's syndrome is xerostomia, a sense of dry mouth. While sensing dryness, patients seem as much to sense lack of lubrication in the mouth, as though the mucous membranes of the lips, cheeks and tongue fail to smoothly slide over the surfaces of the palate and teeth. Some patients tolerate this discomfort and both they and their health care providers often dismiss it as "growing older". In the early stages of Sjögren's syndrome it can be difficult to actually measure, under ordinary clinical conditions, a decrease of saliva flow for individual patients. Only later in the course of Sjögren's does it become relatively easy for the clinician to document the dryness, by the dental mirror sticking to the cheeks or by making actual measurements of the rate of saliva flow upon standardized stimulation of secretion. The problem is further confused by the typically oscillating character of Sjögren's, with periods of improvement and of worsening. When the patient is

persistently and measurably dry, therefore, it is clear that Sjögren's is relatively advanced and that a lot of salivary gland functional deficit (manifested as decreased flow rate of saliva) has already occurred.

Problems of Dry Mouth

Commonly, it is not until this state that the patient first presents to the dental health care provider and a tentative differential diagnosis–a list of possible explanations of a troublesome dry mouth symptom–is formulated. (If the patient had a predominance of eye complaints or joint complaints, they might have gone first to their ophthalmologist, rheumatologist, or primary care physician to seek diagnosis and help.)

Mouth complaints are usually voiced to the dentist, in the following way: "My mouth is dry; it hurts, sometimes it burns; I can't speak; I can't chew; I can't swallow my food without drinking at the same time; the corners of my mouth are red and sore; and my teeth are rotting (breaking, cracking, or decaying, or my fillings are falling out)." If the patient has already lost many teeth, the complaint often is that "I can't tolerate my dentures."

These complaints reflect at least two kinds of interrelated problems: 1) lack of flow and lubrication by saliva, with apparent loss of body defense molecules and buffers contained in saliva, and loss of the flushing of food and bacteria from the mouth; 2) infections (colonization) of the mucous membranes of the mouth by yeast and of the tooth surfaces by bacteria which become strongly decay-causing when the mouth is dry.

This article is addressed to the issue of the discomfort of the mouth and yeast infections, their diagnosis and management. It centers on the topic of oral mucositis, inflammation of the mucous membranes of the mouth.

Oral Mucositis

It is not totally clear why patients with dry mouths develop oral mucositis and variable sensations of soreness. There is, however, no evidence that different microorganisms live on the mucous membranes or teeth of Sjögren's patients than in non-Sjögren's patients. Some subtle ecological shifts may occur, however, because of the compromise of the host (patient) in the form of decreased amount of saliva flow, and decreased delivery of anti-yeast molecules to the oral environment. Indeed, it appears that yeast (usually an organism called Candida albicans) may increase in the mouth in this opportune time.

Fundamental to the management of dry mouth and its associated discomfort is frequent sips or sprays of water, or use of diet soda or other sugar-free drinks, to keep the mucosa hydrated. Fruit juices contain sugars and are a real risk for tooth decay complications, as is sugar-containing soda. Use of alcohol or mouth rinses containing alcohol is contraindicated because alcohol dries and damages the mucous membranes.

In some diseases Candida infections of the mouth present as a thick white membrane-like layer of yeast (also called fungi) on the mucosa. This plaque of yeast peels away upon gentle rubbing to reveal a very red/raw underlying tissue. The condition is known as "thrush" or pseudomembranous candidiasis. It is not typical of Sjögren's, although it can occur. Rather, in Sjögren's the mucosa more frequently appears slightly reddened (erythematous) and with a thin, fragile, parchment-like surface which has partially lost its typical surface features (atrophy). This is called erythematous or atrophic candidiasis. A frequent finding in a dry mouth is the partial or total disappearance of certain types of papillae of the tongue. Fissuring of the tongue is also common.

Unfortunately, these signs can be confusing and cannot, by themselves, be taken as diagnostic of Sjögren's syndrome. A large variety of medications also induce dryness and, depending on the constancy of that dryness, mucosal changes. Some other diseases can affect the salivary glands. Also, changes of the mucosal surface, of the tongue especially, can result from other phenomena, some of which are essentially normal. A high percentage of normal people have what has been called a geographic tongue. Clearly, the oral mucosa needs to be looked at by trained eyes, and the best ones to critically look, undoubtedly, are those of the dentist, who looks and works in mouths every day.

Virtually all humans have some Candida in the mouth; they are normal inhabitants. They are found in higher numbers between upper removable dentures and the palate, especially when the denture is worn at night and when it is not carefully cleaned or disinfected. But Candida numbers appear to increase in Sjögren's and the host's tissues seem intolerant to them. In addition, the corners of the lips, and

sometimes the entire surface of the lips become colonized by them and become inflamed, conditions called angular cheilitis (or perleche) and cheilitis, respectively. Scraping or scrubbing of the mucosal surfaces that evidence erythema with atrophy and examination of the scrapings microscopically or after culture on special diagnostic media reveals the presence of Candida. This, coupled with the complaint of soreness or burning of the mouth operationally give the diagnosis of Candida mucositis and justify anti-Candida treatment. A positive laboratory report for yeast alone, without evidence of chronic erythematous/atrophic mucositis, does not justify the diagnosis of Candida mucositis and treatment with an anti-yeast antibiotic.

Before discussing antibiotic treatment, it needs to be stated that a significant number of people who do not have Sjögren's syndrome have a phenomenon called burning mouth syndrome, also referred to by a lot of other names. Some of these patients have oral yeast infections; but most have neither erythematous/atrophic mucosal changes nor do they appear to have a mucosal yeast infection. Importantly, it is the minority of burning mouth syndrome patients who also have Sjögren's.

It also needs to be recognized that a variety of medications and conditions foster yeast infections of mucous membranes, with or without concurrent Sjögren's syndrome. For example, prolonged use of an antibiotic for a bacterial infection, especially one like tetracycline which inhibits the growth of a wide spectrum of bacteria but which does not inhibit growth of yeast, reduces the natural competition between yeast and bacteria in the mouth. Consequently, yeast on the mouth, throat, or genital mucous membranes have a special opportunity to flourish and "opportunistic" yeast infections are commonplace during antibiotic treatment. They almost always subside when the antibiotic is discontinued. The other common conditions in which yeast flourish on mucous membranes involve compromise of the immune (body defense) systems of the host–for example, as seen in poorly-controlled diabetes, in use of prednisone or other steroids, in use of medications used to control severe immunologic states such as graft rejection, and in AIDS. (People with yeast infections of mucous membranes who have Sjögren's shouldn't conclude that they have AIDS!)

There are some reasonable guidelines which can be suggested for the use of anti-yeast antibiotics in Sjögren's. Nonetheless, patients shouldn't be making diagnostic and treatment decisions themselves, for several reasons, but especially because the guidelines described below are not appropriate for those situations in which yeast infections occur in the bloodstream, which are life-threatening situations requiring different anti-yeast medications. A health care professional should be consulted to determine the necessary treatment.

Anti-Yeast Medications

The most established and probably the least expensive of the anti-yeast medications appropriate for the treatment of oral Candida mucositis are nystatin and clotrimazole. There are potential pitfalls in their use, but some sense can be made of the way they seem best prescribed.

First, both nystatin and clotrimazole are remarkably safe, with almost no adverse drug interactions. One needs to be assured of normal liver function before taking clotrimazole. Both drugs need to be used for a long period of time in order to have reasonable certainty of suppression of the yeast infection. Because the underlying problem of oral dryness and associated compromise of the host does not change as a result of using anti-yeast medication, the patient is likely to relapse, to have another oral yeast infection in the future. However, often patients unwisely stop using medications as soon as they begin to feel better. This frequently leads to early relapse. On/off self-medication is unwise and counterproductive.

A goal in the delivery of anti-yeast medications is to keep the drug at the affected site, in this case the mouth's mucosal surfaces, for a long time with each dose. A swishand-swallow anti-yeast mouth rinse makes limited sense. Similarly, the use of special anti-yeast medications that get into the bloodstream and are relatively toxic also makes little sense, except in cases of life-threatening yeast infection of the blood. Even if anti-yeast medications were secreted into saliva from the bloodstream, they wouldn't likely work in Sjögren's patients whose salivary glands are not working properly. Therefore, there is little doubt that topical treatment using a suckable dose delivery form is likely to be the best.

Neither nystatin nor clotrimazole taste good. This leads to a significant problem for patients who have teeth. Manufacturers want to mask the flavor of these drugs. They do it with sucrose or glucose, common, inexpensive, and generally safe sugars. However, both of them promote tooth decay, the other big oral problem for Sjögren's patients. For example, nystatin syrup is a 50% solution of sucrose containing nystatin. Furthermore, using a syrup hastens the swallowing of the medication. This puts it where it usually isn't needed, in the stomach. Nystatin pastilles are sucrose hard candies containing

nystatin. Clotrimazole is compounded into a suckable troche with glucose. (There would be tremendous virtue in having pleasant tasting sugar-free anti-yeast troches for Sjögren's sufferers.) As an alternative approach, the patient could be sucking on Nystatin Vaginal, a form of nystatin made without sugar, and originally made for the control of vaginal candidiasis. It doesn't taste great, but I have only once had a patient who refused to use it. Patients don't complain of the nystatin taste very much and there is no reason to have philosophical problems with oral use of something called Nystatin Vaginal.

However, to use either of the now readily available, suckable sugar-containing products without the simultaneous use of intensive topical fluoride gel therapy to inhibit tooth decay is to invite worsening of what may already be a bad tooth decay problem in the setting of the chronic oral candidiasis of Sjögren's patients. The patient needs a dentist to integrate the prescription fluoride gel and to manage the diet so as to minimize the risk for tooth decay, as well as to establish the diagnosis of oral Candida mucositis and the management of anti-yeast therapy.

Of course, if the patient no longer has her/his own natural teeth, this concern about sucking on hard candy is irrelevant. It should be remembered that Sjögren's patients have compromised salivary flow. As such, anything they put in their mouths remains there for a long time because it can't be washed away rapidly by saliva. This is good with respect to delivering an anti-yeast medication where the goal is to keep the medication in contact with the oral mucosa for a long time, but it is bad when the thing put in the mouth is sugar which is fermentable to acid by the oral bacteria that live on the teeth. This is why using candy or other sweets by a Sjögren's patient and the resultant aggressive tooth decay often become the biggest oral problems in Sjögren's.

It is the nature of yeast infections that they are not quickly suppressed. In one good study, to achieve reliable suppression of oral yeasts nystatin needed to be used twice daily for 60 days in the form of a lozenge. Typically, clotrimazole is used for 14 days, 5 times a day. In the case of Sjögren's patients, the dwell time can be especially long, a virtue, because not much saliva may be available to dissolve the troche. If it doesn't dissolve at all, however, it can't work, and occasional tiny sips of water may be needed.

If the troches are chewed on, their benefit is diminished because the medicine is cleared from the mouth too fast. Should the patient wear a removable denture, it needs to be removed during the time when the troche is being sucked to allow the anti-yeast antibiotic access to all of the Candida-infected sites in the mouth. But the denture itself also has to be disinfected, otherwise it will just recontaminate the mucous membranes that the patient has been trying to treat. There are two good ways to do this. The first step in both is to soak the denture in ordinary denture cleaner that can be bought in any drugstore or supermarket and to clean it carefully and completely with a soft toothbrush. (If tartar has accumulated on the denture, help from the dentist will be required to remove it.) Then, after thoroughly rinsing away the denture cleaner, the denture has to be soaked in disinfectant which kills yeast. A good one is Zephiran chloride, diluted 1 part to 750 parts with water, soaked for at least 1 hr. This has to be gotten from a drugstore. An alternative in those cases where there are no metal parts to the removable denture is diluted bleach, diluted 1 part per 100 parts of water, about 1 teaspoonful per cup of water. The denture should not be soaked for more than 1 hr. (Longer soaking in bleach or use of higher concentrations of bleach could change the color of the denture. Use of bleach on the metal parts of a denture may corrode them.) After disinfection, the dentures have to be thoroughly rinsed in water before putting them back into the mouth. Dentures should not be worn at night. They should be soaked during that time in ordinary supermarket-available denture cleaner.

Angular cheilitis represents an infection by bacteria and yeast of the tissue folds at the corners of the mouth. It is worse in patients who have lost their natural teeth and either have no dentures or whose dentures do not hold the mouth open sufficiently. As a result, the creases where the upper and lower lips meet are exaggerated, and the area is maintained moist from the mouth (even in Sjögren's patients) and from the lip itself when a break in the mucous membrane or skin occurs there. Some topical ointments, such as Mycology II, can help suppress this problem. These contain nystatin and a low dose of a steroid which reduces the local inflammation. While an anti-yeast ointment would seem adequate, the inclusion of the steroid seems to be helpful. The ointment is applied after meals.

Treatment of Candida-associated angular cheilitis will usually be unsuccessful in the long run unless the oral Candida mucositis is also suppressed and dentures are disinfected, otherwise the mouth contents simply reinfect the lips. Dry, cracking lips need to be cared for with ordinary lip balms or vaseline. If they are colonized by yeast, they first need to be treated with an anticandidal. Long-term successful management of the problem also requires that the patient's occlusion ("bite") be maintained either by adequate repair of existing teeth or by making adequate dentures.

Difficult Choices

Over the years I have seen a number of situations in which patients with the problem of a dry, sore/burning mouth have made bad choices for themselves, or their physicians or dentists have made bad choices, and have faced treatment dilemmas. Among them–advice to suck on hard candies; placement of topical or ingested tetracycline; use, in certain ways, of some medications that make the mouth drier. Often, patients must use a variety of other medications for problems other than Sjögren's. A few examples follow which should help the reader focus on this issue.

Benadryl (diphenhydramine) is an antihistamine, commonly used for hay fever. It is also a mild topical anesthetic, and when used in a mouth rinse, it is effective in transiently palliating sore or burning mouth symptoms. For this purpose it is usually formulated in a 1 to 1 mixture with either kaopectate or Maalox. It is intended to be spit out. The kaopectate coats the oral mucosa, so it also tends to be soothing and keeps Benadryl around in the mouth for awhile. However, it makes no sense for a sore mouth Sjögren's patient to be swallowing Benadryl, because it is an antihistamine. Like other antihistamines, when absorbed into the bloodstream from the gastrointestinal tract, it powerfully inhibits salivary secretion. Ask any hay fever sufferer who uses antihistamines whether they get a dry mouth. The thing that a Sjögren's patient surely doesn't need is more oral dryness.

Unfortunately, many important medications have the undesired side effect of reducing the flow of saliva. For the Sjögren's patient, they further dry the mouth. Some are used for regulating high blood pressure, controlling chronic diarrhea, helping with emotional problems, or controlling allergies to dust and pollen. There literally are over one hundred medications that can cause dryness. It is very important that patients inform their dentists of the use of all medications so that, where possible, ones that have diminished salivation-inhibiting properties can be tried. Obviously, this will require close consultation between the dentist, internist, psychiatrist or other relevant health care provider. However, patients should not on their own stop taking medications which are prescribed for them when they learn that they have Sjögren's. Similarly, they should inform all of their health care providers that they have Sjögren's syndrome.

Fluocinolone and triamcinolone are steroids which can be very useful as topical rinses, ointments, and creams. They can alleviate a lot of discomfort. But they carry some risks. Long-term use on surfaces, for example, make those surface membranes, either skin or mucosa, atrophic, i.e., less structured, more fragile, and less resistant to infection. Indeed, one of the several risks of long-term use of steroids is increased risk of various infections, including yeast infections.

One musn't be too dogmatic. For example, infection and inflammation of the eyelids is rather common among Sjögren's patients. It is often effectively treated by ophthalmologists with systemic (taken internally) tetracycline. But this treatment fosters Candida mucositis. It is, therefore, important for the dentist and the ophthalmologist to be in communication, to be monitoring the mouth and eye problems, and to adjust treatment in accordance with the status of oral Candida mucositis and/or eyelid bacterial infection. Therapy can be adjusted and it may be necessary to simultaneously use both tetracycline and an anti-yeast topical in the mouth.

It is clear that patients with sore or burning mouths are intolerant to acidic foods (fruit juice, tomatoes, salad dressings) and to alcohol. They have to adjust their diets. While it is theoretically a good strategy to put patients onto chlorhexidine mouthrinse (a good and safe antiseptic) to control oral yeast infections and to suppress dental plaque, the only chlorhexidine rinse available in the U.S. (Peridex) contains alcohol. It is the rare Sjögren's patient who can tolerate it. Additionally, almost all of the fluoride mouth rinses which can be purchased without a prescription in the supermarket or drugstore contain substantial amounts of alcohol and will increase mouth discomfort. It is better to use an alcohol-free fluoride gel which is a more potent tooth decay inhibitor than fluoride-containing (or fluoride-free) mouth rinses.

In summary, the sore mouth of Sjögren's, if established to be associated with yeast infection, probably will resolve with adequate anti-yeast treatment. It can be suppressed and palliated (made less troublesome, if not cured) with topical agents. The patient must be aware of the risk of tooth decay, potentially an even more frustrating and surely a more expensive problem. The management of the sore mouth (or tooth decay) problems must not be seen in isolation but must be an aspect of the comprehensive care of the Sjögren's syndrome patient.

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Laboratory Medicine, School of Medicine, University of Connecticut Health Center, Farmington, CT. This article was published in the July/August 1994 issue of The Moisture Seekers â Newsletter.

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Source:Sjögren's Syndrome Foundation, Inc.
333 North Broadway
Jericho, NY 11753

Table 1. Prevalence of Signs and Symptoms in Sjögren's Syndrome

Sign or symptom	% of patients
Xerostomia	90
Xerophthalmia	69
Dysphonia	59
Nocturnal fluid ingestion	45
Dysphagia	43
Cheilosis	43
Dysgeusia	33
Xeroderma	31
Xeromycteria	28
Raynaud's phenomenon	28
Tongue and mouth burning	26
Weight loss	22
Vaginitis sicca	19
Difficulty eating dry foods	17
Parotid swelling	16

From Vivino, FB, Huan CH: Arthritis Rheum 1993.2
Based on a total of 58 patients.

Table 2. Subjective Oral Dryness Symptoms

Symptom	Percent of Patients
Difficulties eating dry foods	52
Dry lips	66
Dryness of the tongue	52
Sensitivity to acids	52
Sensitivity to spicy foods (hot)	48
Pain/swelling of salivary glands	38
Altered bitter taste	24

Coughing episodes	29
Voice disturbances	38
Taking drug associated with infection[†]	19

[†]Glucocorticosteroid and immunosuppressant.
Data were collected with a questionnaire completed by the patient.

Adapted from the *Journal of Rheumatology* 1998; 25:5

4. Pilocarpine Tablets for the Treatment of Dry Mouth and Dry Eye Symptoms in Patients With Sjögren's Syndrome

Introduction

Sjögren's Syndrome (SS) is a chronic, autoimmune, rheumatic disorder characterized by lymphocyte-mediated destruction of exocrine glands and internal organ involvement that occur in association with autoantibody production or as a complication of a preexisting connective tissue disorder. Over time, progressive infiltration of lacrimal and salivary glands by mononuclear cells leads to diminished secretions, with resultant xerostomia (dry mouth) and xerophthalmia (dry eyes) being the most prevalent symptoms.

Morbidity from salivary and lacrimal gland hypofunction results from alteration of mucosal and ocular surfaces and breakdown of the normal host barriers to infection. In addition to significant discomfort from dryness, untreated dry mouth and dry eyes may also lead to complications, including stomatopyrosis (burning mouth), oral ulcers, malnutrition, weight loss, oral candidiasis, bacterial sialoadenitis, sleep disruption, accelerated dental caries, periodontal disease, corneal ulceration or perforation, and bacterial conjunctivitis. Use of currently available treatments, including tear and saliva substitutes, provides transient relief at best and often fails to prevent complications. In addition, patients often find these over-the-counter remedies costly, ineffective, inconvenient, or irritating.

Pilocarpine is a naturally occurring compound derived from the South American shrub Pilocarpus jaborandi. This plant alkaloid is a cholinergic parasympathomimetic agonist that binds to muscarinic-M3 receptors and can cause pharmacological smooth muscle contraction in humans and stimulation of various exocrine glands. Pilocarpine hydrochloride (Salagen) tablets are currently indicated for the treatment of radiation-induced dry mouth. In two previous multicenter, double-blind, placebo-controlled trials, use of pilocarpine tablets provided significant relief to patients with radiation-induced dry mouth. In these two studies, use of pilocarpine tablets significantly improved symptoms of intraoral dryness, oral discomfort, and dysphonia and patients' global assessment of dry mouth as well as reduced the need for administration of oral comfort agents, such as artificial saliva, water, and hard candy. Patients treated with pilocarpine tablets also demonstrated a statistically significant increase in saliva production, measured as either whole-mouth or parotid salivary flow. It is through this mechanism that cholinergic stimulation of residual-functioning exocrine glandular tissue in patients with SS could potentially alleviate symptoms of dry mouth, dry eyes, or other symptoms associated with SS. Therefore, the present study was undertaken to investigate the efficacy and safety of pilocarpine tablets for the treatment of symptoms associated with dry mouth and dry eyes in patients with SS.

Clinical Trial

After providing written informed consent, 373 patients with primary or secondary SS and clinically significant dry mouth and dry eyes were randomized to receive 2.5-mg pilocarpine, 5-mg pilocarpine, or placebo tablets 4 times daily for 12 weeks. Symptoms were assessed by questionnaires with visual analog scales or categorical checkboxes. Whole-mouth salivary flow rates were measured.

Saliva is a chemically complex fluid containing several organic and inorganic components, all of which play an essential role in maintaining oral health. Saliva is not only required to preserve the dentition and mucosal surfaces but also to facilitate digestion, phonation, mastication, deglutition, and gustation. Therefore, the oral consequences of salivary gland hypofunction extend beyond those of a dry mouth. Common oral symptoms in SS can also include dysphonia, dysphagia, stomatopyrosis (burning mouth), dysgeusia (altered taste), oral ulcers, and sleep disruption caused by nocturnal fluid ingestion. Attempts to treat these symptoms with replacement therapy using artificial salivas and oral lubricants have been largely unsuccessful, and patient satisfaction and compliance have been low.

For the treatment of symptoms associated with dry eyes in primary and secondary SS, there is a plethora of artificial tear and lubricant preparations available. However, the frequency with which they must be applied suggests the need for novel therapeutic interventions. Ultimately, tear preservation by punctual occlusion or cautery is the last resort to solve this problem. To date, no artificial tear or saliva preparation has successfully duplicated the physicochemical properties of the body's own fluids well enough to provide a comparable degree of benefit.

The medicinal properties of pilocarpine, including its ability to stimulate salivation, have been recognized for many centuries by the Tupi Indian tribe of northern Brazil, who named this indigenous shrub "jaborandi," or the "slobber-mouth plant." In 1888, a British physician described a 65-year-old woman with xerostomia and xerophthalmia who responded symptomatically to treatment with tincture of jaborandi, administered orally and subcutaneously.

Results

The benefit of pilocarpine tablets for treatment of symptoms of dry mouth from various causes, including SS, has been previously suggested in smaller studies and case reports. Data from the present multicenter trial indicate that the use of 5-mg pilocarpine tablets administered 4 times daily (20 mg/d) provides significant symptomatic relief of dry mouth cased by SS and significantly increases saliva production in measurable quantities. Regular use of pilocarpine tablets at this dosage significantly improves other specific symptoms of salivary gland hypofunction in patients with SS, such as oral discomfort, nocturnal fluid ingestion, and the need for saliva substitutes. Some benefit for dysphonia may also occur, as evidenced by the trend toward statistically significant improvement in the 5-mg pilocarpine group for this symptom.

Although the data show that pilocarpine-induced stimulation of salivary flow occurred within 30 minutes of ingestion of the first dose and was maintained through week 12, the onset of subjective benefit for various symptoms took 6 to 12 weeks. Because dry mouth develops rather insidiously in most patients with SS, it is not unreasonable to expect that improvement or reversal of symptoms after treatment would be delayed. This observations suggest that a patient's symptoms on a given day may reflect not only the quantity of saliva but also the cumulative effect of chronic tissue dehydration. For this reason, it seems that a prolonged treatment course with pilocarpine tablets (e.g., 6-12 weeks) should be recommended to patients to allow sufficient time for symptomatic benefits to occur. In this study, the most dramatic response occurred in patients who took 5-mg pilocarpine tablets 4 times daily. Although salivary flow rates were measured during only the first 90 minutes of the dosing interval, results of previous studies in healthy participants indicate that the pilocarpine effect on flow rates lasts 3 to 5 hours. Optimal therapeutic benefit can therefore be best achieved through a 4-times-daily dosing regimen.

In conclusion, the administration of 5-mg pilocarpine tablets 4 times daily (20 mg/d in divided doses) produced significant benefits for the symptomatic treatment of dryness associated with SS that clearly outweighed adverse effects and risks in this 12-week study. Patients experienced improvement in dryness of the nose, skin, and vagina and the ability to expectorate. Treatment success with pilocarpine will most likely depend on existence of residual exocrine gland function. In SS, this may vary in different organs and cannot always be predicted based on the duration of symptoms. As data from the present study suggest, use of pilocarpine tablets offers a wide range of potential therapeutic effects for patients with SS. Therefore, at the present time, almost any patient with SS with some degree of exocrine gland function could potentially benefit from this treatment depending on therapeutic goals. As with other patient groups with rheumatic conditions, early diagnosis and treatment offer the best hope for a good outcome.

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Source: Archives of Internal Medicine, Volume 159, January 25, 1999.

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5. Sjögren's Syndrome: Patient Information

Sjögren's Syndrome

Sjögren's syndrome is a chronic (lifelong) disorder that causes dry eyes and a dry mouth. It is named after the Swedish eye doctor, Dr. Henrik Sjögren, who first described it.

Sjögren's syndrome can occur in two ways: primary and secondary. Both forms affect roughly an equal number of people.

Primary Sjögren's syndrome occurs by itself and is not associated with other diseases. Secondary Sjögren's syndrome occurs with rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus ("lupus"), polymyositis, and some forms of scleroderma. Rheumatic diseases are conditions that affect joints, bones, muscles, skin, and sometimes other organs.

In Sjögren's syndrome, changes occur in the immune system–the body's defense against disease. In Sjögren's, the immune system lacks the usual controls. This causes white blood cells to invade glands in the body that produce moisture, such as the tear and salivary glands, and the Bartholins glands in the vagina. They can destroy the glands and cause them to stop producing moisture.

Sjögren's syndrome can also cause problems in other parts of the body, including the joints, lungs, muscles, kidneys, nerves, thyroid gland, liver, pancreas, stomach, and brain.

The causes of this condition are not known. There is some evidence that viral infections, heredity, and hormones may in some way contribute to Sjögren's syndrome.

Sjögren's syndrome can affect people of any race and any age. It usually affects women. It affects more than one million people in the U.S.

Symptoms

In people with no other health problems, the most common early symptom is the onset of severe dry mouth and eyes. In people with rheumatoid arthritis or related conditions, dry eyes and mouth develop more slowly. In this case, Sjögren's may be difficult to diagnose.

Sjögren's syndrome affects everyone differently. You may not have every symptom listed here, and you may have only minor problems with those you do have. The symptoms may seem worse at some times than at others.

Symptoms include:

- Dry mouth
  The mouth normally contains saliva, which aids chewing and swallowing. In people with Sjögren's syndrome, the amount of saliva is much less. This makes chewing, swallowing, and speaking difficult. It may also cause a decreased sense of taste.
- Dry eyes
  Your eyes may feel dry, "gritty," or "sandy." They may burn and look red. A thick substance may accumulate in the inner corner of your eyes while you sleep. Your eyes may be more sensitive to sunlight. If not properly treated, Sjögren's syndrome can lead to ulcers of the cornea (the clear covering of the eyeball). On rare occasions, this can cause blindness.
- Swollen salivary glands
  There are three sets of glands that produce saliva. They're located under your tongue, in the

cheeks in front of your ears, and in the back of your mouth. They may feel swollen and tender. This may occur along with a fever. This affects about one-half of people with the disorder.

- Dental cavities
  This is a common problem that results from a dry mouth. Saliva fights bacteria and defends against cavities. Because you have decreased saliva, your teeth may develop cavities more easily.
- Dry nose, throat, and lungs
  This may make your throat feel dry and tickly. You may have a dry cough, hoarseness, a decreased sense of smell, and nosebleeds. It can also lead to pneumonia, bronchitis, and ear problems.
- Dryness of the vagina
  This can cause painful intercourse for women with Sjögren's syndrome.
- Fatigue
  Fatigue is a common complaint. You may get easily exhausted and feel tired and worn out.
- Other problems
  Sjögren's syndrome can affect other parts of the body, such as blood vessels, the nervous system, muscles, skin, and other organs. This can lead to muscle weakness, confusion and memory problems, dry skin, and feelings of numbness and tingling. Sjögren's syndrome can also affect the liver and pancreas. When it does, there is a greater chance for developing cancer of the lymph tissue. Although this is unusual, it is one reason why medical exams and continued follow-up are important.

Diagnosis

Your doctor may do several things to find out if you have Sjögren's syndrome. This includes:

- Physical examination
  Your doctor will ask you to describe your symptoms, and will look for other symptoms, such as red, itchy eyes; swollen salivary glands; a dry, cracked tongue; and enlarged lymph glands in your neck.
- Blood tests
  Tests for specific blood markers can determine if you have Sjögren's syndrome. However, not everyone with Sjögren's has these markers.
- Schirmer test
  This helps determine how dry your eyes may be. It involves placing a small piece of filter paper under the lower eyelid to measure the amount of tears your eyes produce.
- Slit-lamp examination
  This is a more accurate way to find out if your eyes are dry. In this test, the doctor puts a drop of dye into your eye and examines the eye with a special instrument called a slit lamp. The dye will stain dry or eroded areas of the eye. This test is often done by an ophthalmologist (eye doctor}.
- Lip biopsy
  In this test, the doctor removes a few salivary glands from inside your lip. The tissue is examined under a microscope. The appearance of the tissue helps determine if you have Sjögren's syndrome.
- Salivary function tests
  These measure the actual amount of saliva you produce, to help determine if you have Sjögren's.
- Urine tests
  These may be done to test your kidney function.
- Chest X-ray
  This can help detect changes in your lungs.

As yet, there is no cure for Sjögren's syndrome. But proper treatment can help relieve symptoms so you can live a comfortable and productive life.

Treatment

The main goal of treatment is to relieve discomfort and lessen the effects of the dryness. Since Sjögren's syndrome affects everyone differently, your treatment plan will be based on your specific needs.

Your treatment may include different ways to relieve your symptoms, such as those listed below. If you have arthritis or another condition, you will also want to follow specific treatment for that condition.

See your family doctor and your dentist regularly. Since Sjögren's syndrome can affect many parts of the body, regular checkups can help detect and prevent future problems. You may also need regular check ups with an arthritis specialist and an eye specialist.

For dry mouth:

- Sip fluids throughout the day.
- Use sugar-free gum or candies to stimulate saliva production.
- Try saliva substitutes or mouth coating products. They may be useful in some people, and are available without a prescription.

To prevent dental cavities:

- Have frequent dental checkups.
- Use mouth rinses that contain fluoride.
- Brush and floss your teeth regularly.
- Use sugar-free products.

For dry eyes:

- Use artificial tears or eye drops to help relieve the discomfort of dry eyes. Use preservative-free products, if you apply the drops more than four times per day.
- Try lubricating ointments or small, long-acting pellets for overnight or long-lasting relief.
- Your ophthalmologist may recommend a simple operation that blocks tear drainage from your eye.

For dry skin:

- Use moisturizing lotions for sensitive skin.
- Avoid drafts from air conditioners, heaters and radiators, when possible.
- Use a humidifier in your house and at work.

For vaginal dryness:

- Use lubricants made specifically to help vaginal dryness. Do not use petroleum jelly.

Medications

Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) help reduce joint swelling and stiffness, as well as muscle aches. If you have serious complications, your doctor may recommend stronger medicines.

Exercise

Mild exercise, such as walking or swimming, can help keep joints and muscles flexible. Exercise may also protect against further joint damage.

A note about pregnancy: A certain blood marker often found in women with Sjögren's syndrome can, very rarely, be associated with heart problems in newborn babies. If you're a woman with Sjögren's syndrome who is planning to become pregnant, see your doctor about testing for this marker. If it is present, ask your doctor whether pregnancy is advisable. If you do become pregnant, you and your doctor can work out the best plan to manage the situation.

Sjögren's syndrome is generally not life-threatening. The outlook for people with this condition is usually good. Dryness, however, may last for the rest of your life. By using artificial moisture and practicing good oral hygiene, you can help prevent serious problems.

If you have Sjögren's syndrome and a rheumatic disease, make sure you follow your doctor's complete treatment program.

Support and More Information

Contact your local chapter of the Arthritis Foundation for more information about Sjögren's syndrome. The following booklets may be useful:

- Coping with Pain
- Coping with Stress
- Exercise and Your Arthritis
- Rheumatoid Arthritis
- Scleroderma
- Systemic Lupus Erythematosus

The National Sjögren's Syndrome Association is an international, nonprofit, all-volunteer organization dedicated to providing educational information to patients and health professionals worldwide. Sponsors support groups and national and regional conferences. Publishes a national newsletter ("The Sjögren's Digest"), a quarterly collection of articles ("Patient Education Series,") and a patient guide ("Learning to Live with Sjögren's Syndrome").

National Sjögren's Syndrome Association
3201 West Evans Drive
Phoenix, AZ 85023
1-800-395-NSSA (6772)

The Sjögren's Syndrome Foundation is an international organization that provides materials, educational programs, and support groups throughout the U.S. and abroad. Publishes "Sjögren's Syndrome Handbook: An Authoritative Guide for Patients" and a monthly "Moisture Seekers Newsletter".

Sjögren's Syndrome Foundation
366 North Broadway, Suite PH-W2
Jericho, NY 11753
1-800-475-6473

6. Sjögren's Syndrome Glossary

Immunologic Terms

Adenopathy Swelling of lymph nodes (glands). In Sjögren' syndrome, this usually occurs in the neck and jaw region.

Antigen(s) A substance that induces the formation of antibodies. This antigen-antibody reaction forms the basis of immunity.

Apoptosis A form of programmed cell death, in which the cell and its DNA both fragment.

Autoimmunity Autoimmune disease is a state where the body inappropriately produces antibody against its own tissues. In autoimmunity, the antigens (see above) are components of one's own body.

Connective Tissue Disease A disorder marked by inflammation of the connective tissue (joints, skin, muscles) in multiple areas. In most instances, connective tissues diseases are associated with autoimmunity. Fifty percent of Sjögren's patients have connective tissue disorders.

Corticosteroids (syn. Steroids, Cortisone) Natural adrenal gland hormones that have powerful anti-inflammatory activity and are often used in the treatment of severe inflammation affecting vital organs. The multiple side effects of corticosteroids should markedly curtail their use in mild disorders.

Erythema A medical term for a red color usually associated with increased blood flow to an inflamed area, often the skin.

Fibrosing Alveolitis (syn. Pulmonary Fibrosis) Thickening and stiffening of lung tissue caused by inflammation in areas of the lung.

Immunoglobulins (syn. Gamma Globulins) The protein fraction of serum responsible for antibody activity. Measurement of serum immunoglobulin levels can serve as a guide to disease activity in some patients with Sjögren's syndrome.

Immunosuppressive Agents (Drugs) A class of drugs that interfere with the function of cells that compose the immune system (see lymphocytes). Corticosteroids are immunosuppressive. Drugs used in the chemotherapy of malignant disease and in the prevention of transplant rejection are generally immunosuppressive and occasionally are used to treat severe autoimmune disease.

Interstitial Nephritis Inflammation of the connective tissue of the kidney usually resulting in mild kidney disease characterized by frequent urination. Interstitial nephritis may be associated with Sjögren's syndrome.

Lymphoma A severe proliferation (increase) in abnormal (malignant) lymphocytes manifested as cancer of the lymph glands. Although exceedingly rare, lymphoma may occur as a complication of severe Sjögren's syndrome.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) Chemical derivatives of aspirin (acetyl salicylic acid) that generally cause less side effects (heartburn), contain no cortisone, and are used to treat joint pains that occur in rheumatoid arthritis and other connective tissue disorders. Examples are ibuprofen (Motrin) indomethacin (Indocin), sulindac (Clinoril) and prioxicam (Feldene).

Petechia A small, pinpoint, non-raised perfectly round, purplish red spot caused by intradermal or submucosal hemorrhaging, that later turns blue or yellow.

Polymyositis A connective tissue disorder characterized by muscle pain and weakness secondary to inflammation.

Purpura A condition characterized by the presence of confluent (running together) petechiae or confluent ecchymosis over any part of the body.

Raynaud's Phenomenon Painful blanching of the fingertips on exposure to cold. This may be seen alone, or in association with a connective tissue disease.

Salicylates Aspirin-like drugs (see non-steroidal anti-inflammatory drugs above).

Scleroderma A connective tissue disorder characterized by thickening and hardening of the skin. Sometimes internal organs (intestines, kidneys) are affected, causing bowel irregularity and high blood pressure.

Scleroderma A connective tissue disorder characterized by thickening and hardening of the skin. Sometimes internal organs (intestines, kidneys) are affected, causing bowel irregularity and high blood pressure.

Sjögren's Syndrome A symptom complex of dry eyes, mouth and other mucous membranes associated with inflammation in the salivary glands. It can occur alone (50%) or in association with a connective tissue disease.

Sjögren's Antibodies Abnormal antibodies found in the sera (blood) of Sjögren's patients. These antibodies (Anti-SS-A/Ro and Anti-SS-B-/LA) can be helpful in the diagnosis of Sjögren's.

Systemic Any process that involves multiple organ systems throughout the body.

Ophthalmic Terms

Artificial Tears The mainstay of the treatment of dry eye is tear supplementation. Various types of over-the-counter (OTC) preparations are available.

Conjunctiva The membrane that lines the eyelids and covers the anterior portion of the eyeball.

Cornea A clear “watch crystal” like structure covering the pupil and iris (colored portion of the eye). Composed of a number of vital layers, all of which are functionally important. The surface layer or epithelium is covered by tears that lubricate and protect the surface.

Fluorescein Stain A dye used to test for dry eye. This dye stains areas of the eye surface in which cells have been lost.

KCS (Keratoconjunctivitis Sicca) Also referred to as dry eye. If associated with either a dry mouth or rheumatoid arthritis, the condition is then referred to as Sjögren's syndrome. Patients frequently complain of burning, irritation or a dry, “gritty” sensation.

Lacrimal Glands Two types of glands produce the essential fluid. Smaller (accessory) glands are found in the eyelid tissue and produce “minute to minute” tear needs. Large amounts of tears can be produced by the main lacrimal glands located inside the bony tissue surrounding the eye.

Meibomian Glands Fat producing glands found in the eyelids that produce an essential component of tears.

Mucolytic Agents Medication that tends to dissolve mucous. Dry eye patients with excess mucous discharge may benefit from use if other tear film enhancing drops are less than adequately effective.

Puncta Small openings in the eyelids that normally drain tears. Patients with severe dry eye may benefit from punctal closure that allows maximal tear preservation.

Rose Begal Staining Rose bengal is a dye that stains abnormal or sick cells on the surface of the eye. This diagnostic dye allows the ophthalmologist to follow the treatment of dry eye.

Schirmer Test The standard objective test to diagnose dry eye. Small pieces of filter paper are placed between the lower eyelid and the eyeball and soak tears for five minutes. The value obtained is a rough estimation of tear production in relative terms. Lower values are consistent with dry eye. It is important to emphasize that no single test can be considered diagnostic unless the condition is severe.

Xerostomic (Dry Mouth) Terms

Dysphagia Difficulty swallowing. In Sjögren’s syndrome, this may be due to several causes: decreased saliva, infiltration of the glands at the esophageal mucosa, esophageal webbing and abnormal webbing.

Ecchymosis A purplish patch caused by oozing of blood into the skin; ecchymoses differ from petechia only in size.

Epistaxis Nosebleed, hemorrhaging from the nose, that may be caused by dryness to the nasal mucous membrane in Sjögren's syndrome.

Esophagus A tube or connection with muscular walls allowing passage of food from the pharynx (end of the mouth) to the stomach.

Lip biopsy Incision of approximately two (2) centimeters on the inside surface of the lower lip and excision of some of the minor salivary glands for microscopic examination and analysis.

Otitis Inflammation of the ear, that may be marked by pain, fever, abnormalities of hearing, deafness, tinnitus and vertigo. In Sjögren’s syndrome, blockage at Eustachian tubes due to infection can lead to conduction deafness and chronic otitis.

Palate Biopsy A punch biopsy near the junction of the hard and soft palates to sample the minor salivary glands in that region.

Parotid Gland Flow An empirical, quantitative measure of the amount of saliva produced over a certain period of time. Normal parotid gland flow rate is 1.5ml/min. In Sjögren's syndrome, flow rate is approximately 0.5ml/min. with diminution of flow rate correlating inversely with severity of disease.

Radionuclide Studies The technique where radioactive substances such as human serum albumin is injected into an organ. A gamma scintillation camera coupled with a digital computer system and cathode ray display can read the radioactive emissions. Areas of perfusion will show marked radiographic emissions, areas of obstruction will show no activity.

Sialography Demonstration of the salivary ducts by means of the injection of substances opaque to x-rays. Radiologically sensitive dye is placed into the duct system serving to outline the ductal system clearly.

Xerostomia Dryness of the mouth caused by the arresting of normal salivary secretion; occurs in diabetes, drug therapy, radiation therapy, etc.

Source: Sjögren's Syndrome Foundation, Inc.

Appendix A

List of Products Frequently Used by People with Sjögren's Syndrome

PRODUCTS FOR DRY EYE

ARTIFICIAL TEAR PREPARATIONS: PRESERVATIVE-FREE*

Trade Name (single unit dose)	Distributor / Mfr.
Bion Tears	Alcon
Celluvisc	Allergan
Hypo Tears PF	Ciba Vision Ophthalmics
Moisture Eyes-Preservative Free	Bausch & Lomb
Nature's Tears	Rugby
Refresh; Refresh Plus	Allergan
Tears Natural Free	Alcon
Thera Tears ATF Formula	Advanced Vision Research

Trade Name (multidose bottle)	Distributor / Mfr.
GenTea)	Ciba Vision Ophthalmics
Refresh Tears	Allergan

Note regarding preservatives: Members of the Foundation's Medical Advisory Board often advise those who repeatedly use artificial tear preparations to avoid products that contain preservatives and to

use only those labeled "preservative-free." Consult your physician to determine whether the use of preservative-free products is necessary for your condition. Commonly used preservatives in artificial (ear preparations include chlorobutanol, benzalkonium and thimerosal. Read labels carefully; preservative-free and preserved products often have similar names, e.g. *HypoTears* (containing preservative) and *HypoTears PF* (Preservative-free).

ARTIFICIAL TEAR INSERT – PRESERVATIVE – FREE

Trade Name	Comments	Distributor /Mfr.
Lacrisert (Rx)	Water soluble insert	Merck

TEAR DUCT (PUNCTAL) PLUGS

Trade Name	Comments	Distributor /Mfr.
Collage Implant (Rx)	collagen	Lacrimedics
Herrick Lacrimal Plug (Rx)	silicone	Lacrimedics
Punctum Plugs (Rx)	silicone	Eagle Vision
Temporary Punctal / Canalicular Collagen Implants (Rx)	collagen	Eagle Vision

OCULAR LUBRICANTS - PRESERVATIVE-FREE

Trade Name (multidose bottle)	Distributor / Mfr.
Lanolin-Free	
Hypo Tears (ointment)	Ciba Vision Ophthalmics
Moisture Eyes PM (ointment)	Bausch & Lomb
OcuCoat PR (drops)	Storz / Lederle Ophthalmic Pharmaceuticals
Puralube (ointment)	Fougera
Tears Renewed (ointment)	Akom
Containing Lanolin	
Artificial Tears (ointment)	Rugby
Akwa-Tears (ointment)	Akorn
Duratears Naturale (ointment)	Alcon
Refresh PM (ointment)	Allergan

OPHTHALMIC SOLUTIONS

Trade Name	Comments	Distributor /Mfr.
LIVING WATER Eye Lotion	eye wash, irrigating solution to cleanse the eye	La Jolla Diagnostics. Inc.

PREPARATIONS FOR SPECIAL EYE CONDITIONS

Trade Name	Drug Class	Indication	Distributor /Mfr.
Acular (Rx)	NSA1D (anti-	seasonal allergic	Allergan

	inflammatory)	conjunctivitis	
Livostin (Rx)	antihistamine	seasonal allergic conjunctivitis	Ciba Vision Ophthalmics
Alomide (Rx)	mast cell stabilizer	treatment of ocular disorders including vernal conjunctivitis, keratitis and keratoconjunctivitis	Alcon
Muro 128	hypertonic sodium chloride	corneal edema	Bausch & Lomb
AK-NaCl	pulsed water stream	corneal edema	Akorn

MOISTURE SHIELDS FOR THE EYE

Trade Name	**Component**	**Comments**	**Distributor /Mfr.**
Flat Eye Shields	clear self-adhesive shields	may be used to keep moisture in overnight or during the day	Eagle Vision, Inc.
Moist Eye Moisture Panels	soft, pliable, clear panels	can be fined to the sides of most eye wear to create a moisture chamber	Eagle Vision, Inc.
NITEYE	clear plastic bubble	attaches over the eye area	Best Health, Inc.

EYELID CLEANSERS

Trade Name	**Component**	**Comments**	**Distributor /Mfr.**
I-Scrub	Sterile eyelid cleanser	lotion	Spectra
Lid Wipes-SPF	Sterile eyelid cleanser	moistened pads	Akorn
OcuClenz	Sterile eyelid cleanser	lotion	Storz / Lederle Ophthalmic Pharm.
OCuSOFT	Sterile eyelid cleanser	lid scrub lotion and pads	Cynacon / OCuSOFT

PRODUCTS FOR DRY MOUTH AND THROAT

ORAL MOISTURIZERS

Trade Name	**Comments**	**Distributor /Mfr.**
Entertainer's Secret (spray)	replaces mucosal coating of the nostrils, throal and larynx; apply via the mouth or nose	KLI Corp.
Moi-Stir (spray, swabs); Moi-Stir 10 (solution)		Kingswood Lab
Mouthhkote (spray)		Scandiphann, Inc.
Optimoist (solution and spray)	does not cause demineralization	Colgate Oral Pharmaceuticals
Oral Balance (gel)	soothes and protects mouth and gums	Laclede Professional Products

Orex (spray)		Young Dental
Salivart (spray)	pressurized container	Gebauer Company

SPECIAL TOOTHPASTES & MOUTHWASHES

Trade Name	Comments	Distributor /Mfr.
Biotene Toothpaste, Squigle Toothpaste	toothpaste for dry mouth	Laclede Professional Products, Squigle, Inc.
Toothpastes: Aquafresh For Kids, Crest For Kids, Colgate Jr., Oral B	mild flavored toothpaste	Smith Kline Beecham.Procter & Gamble, Colgate Oral Pharmaceuticals. Oral B Laboratories
Act For Kids (rinse)	alcohol-free, decay-preventing	Johnson & Johnson
Alkalol	mouth rinse and nasal douche	The Alkalol Co.
Biotene Mouthwash	mouth rinse; alcohol-free	Laclede Professional Products
Saline Solution	as a mouth rinse; breaks up thick mucus	

PRODUCTS & DEVICES FOR CLEANING TEETH

Trade Name	Product Type	Attributes	Distributor /Mfr.
Glide Colgate Total Floss	dental floss	non-shredding	W. L. Gore & Associates, Inc. Colgate Oral Pharmaceuticals
Oral B Ultrafloss	dental floss	interlocking network of spongy nylon that adapts to spaces between teeth	Qral-B Laboratories
Plaque Removers e.g., Interplak, Rota-Dent, Oral B, Gingibrush	electric toothbrushes	for those unable to properly brush with regular toothbrushes	
Proxabrushes: Py-Co-Twin; Oral B	interdental brushes	for cleaning between teeth, particularly when unable to floss	John 0. Butler Co. Block Drug Co
Waterpik Oral Irrigator	pulsed water stream	removes particles from gums & teeth	Teledyne

PREPARATIONS TO PROTECT AND/OR REMINERALIZE TEETH

Trade Name	Comments	Distributor /Mfr.
Fluoride Gels/Liquids: Gel-Kam Homecare (Rx) gel Gel-Tin (Rx) liquid Omnii gel PreviDent Brush-On (Rx) gel, PreviDent 5000 Plusv Revive (Rx) gel	 helps protect tooth enamel; brush on or use with dental trays remineralizing gel	 Scherer Young Dental Mfg. Omnii International Colgate Oral Pharmaceuticals Dental Resources Inc.

PRODUCTS & DEVICES THAT STIMULATE SALIVARY FLOW

Trade Name	Product Type	Comments	Distributor /Mfr.
Biotene. Carefree, Extra, Trident, Xylifresh	sugarless chewing gums	various sweeteners: aspartame, hydrogenated glucose syrup, mannitol, saccharin, sorbitol and xylitol	Laclede Professional Products; Nabisco Foods, Inc., Wm Wrigley Jr. Co., Warmer Lambert, Leaf Specialty Products
Salix SST	sugarless tablets	citrus-flavored	Scandinavian Natural Products, Inc
Salagen (Rx)	pilocarpine tablets	for treatment of dry mouth from Sjogren's syndrome and from radiation induced dry mouth in head & neck cancer patients	MGI Pharma, Inc.
Salitron (Rx)	electrical stimulator	limited to patients-who respond to trial stimulation in doctor's office	Biosonics , Inc.

*For some, sucking on fruit pits (peaches, cherries, nectarines), dried fruit slices or sugarless candies stimulates salivary flow

PRODUCTS TO SOOTHE LIPS

Trade Name (single unit dose)	Distributor / Mfr.
Blistex Up	Warner Lambert
Boric Acid Ointment	various brands
Borofax	Burroughs Wellcome
Lip Medex	Blistex
Orabase Up Healer	Colgate Oral Pharmaceuticals
Petroleum Jelly	various brands

PRODUCTS FOR DRY NOSE

Trade Name	Comments	Distributor /Mfr.
Afrin Saline Mist, Ayr, Nasal, Na-Zone, Ocean, Pretz, Saline X	saline nasal sprays; helps prevent nosebleeds; moisturizes nasal mucosal tissue; spray bottle	Schering-Plough, B.F. Ascher & Co., Winthrop, Snuva, Fleming & Co, Parnell, Muro Pharm.
Saline Solution		various brands
Ayr Gel	contains aloe; moisturizes nasal mucosal tissue	B.F. Ascher & Co.

Note: Physicians often recommend that petroleum-based products should be used sparingly, if at all, in the nose to avoid the risk of chemical pneumonia. Consult your physician to determine whether this risk applies to you.

PRODUCTS FOR DRY SKIN

Trade Name	Comments	Distributor /Mfr.

Carmol •20- 20% Urea	for rough, dry skin	Syntex Laboratories
Dorm-Apply™ Moisturizing Lotion		Snuva,Inc.
Dermal Therapy – Heel Care - 25% Urea	moisturizes and softens hard, dry callused heels and feet	Bayer Corporation
Dermal Therapy - Finger Care - 20% Urea	moisturizes and softens callused fingertips, nails and cuticles	Bayer Corporation
Ultra Mide 25 - 25% Urea	for extra dry skin	Baker-Cummins

PRODUCTS FOR VAGINAL DRYNESS

Trade Name	**Comments**	**Distributor /Mfr.**
Astroglide	provides light lubrication	Biofilm, Inc.
Maxilube Personal Lubricant	thick lubricant	Mission
Lubrin Vaginal Inserts	unscented, colorless pre-coital suppositories; prolonged lubrication Upscher-Smith	
Gyne-Moistrin	vaginal lubricant & moisturizing gel	Schering-Plough
Replens	unit dose filled applicator	Warner Lambert
Feminease	moisturizing and lubricating cream	Parnell Pharmaceuticals
Estrace Vaginal Cream (Rx)		Mead Johnson
Premarin Vaginal Cream (Rx)		Wyeth-Ayerst
Vitamin E Oil, Cream, Capsules	topical application to labia; capsules must be pierced, but are least expensive form	various brands

The products included in this listing are those reported to be most frequently used by our members, or are newly developed products. There are, of course, many other products that may be of help to Sjögren's syndrome patients. Also, new products are constantly being developed about which we may not have been informed.

Whether a product is or is not listed in no way reflects on its efficacy. This listing is intended to be informative and does not represent an endorsement by the Sjögren's Syndrome Foundation.

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Manufacturers' Index

Advanced Vision Research
7 Alfred Street, Suite 330
Woburn.MA 01801
800-5-RX-TEAR

Akorn Inc.
100 Akorn Drive

CIBA Vision Ophthalmics
P.O. Box 100024
Duluth.GA 30136
800 845-6585

Colgate Oral Pharmaceuticals
One Colgate Way

Mead Johnson
2400 W. Lloyd Expressway
Evansville, IN 47721
812426-6000

Merck Sharp & Dohme
PO Box 4
West Point, PA 19486

Schering-Plough Health Care
110 Alien Road
Liberty Corner, NJ 07938
908 604-1640

Smith Kline Bcecham
PO Box 1467

Abita Springs, LA 70420
800-535-7155

Alcon Laboratories 6201 South Freeway Ft.Worth.
TX 76134
817-293-0450

Alkalol Co., The P.O. Box 964 Taunton, MA 02780
508-823-3257

Allergan
2525 Dupont Drive Irvine,CA92713
800-347-4500

B.F. Ascher & Co. P.O. Box 717 Shawnee Mission, KS 66201
913 888-1880

Baker-Cummins Dermatologicals
1950 Swarthmorc Avenue
PO Box 3009 Lakewood, NJ 08865
800-735-2315

Bausch & Lomb, Inc. 1400 N. Goodman Street
Rochester, NY 14692
800-828-6974

Best Health, Inc. 855-3 St. John's Bluff Rd. Ste H Jacksonville, FL 32225
1-800-823-7828

Biofilm, Inc. 3121 Scott Street Vista, CA 92083
800-848-5900

Biosonics Inc. 260 New York Drive Fort Washington, PA
800-547-4357 19034

Blistex, Inc. 1800 Swift Drive Oak Brook, IL 60521
708-571-2870

Block Drug Co. Canton, MA 02021
800 225-3756

Dental Resources Inc. 530 River Street Delano, MN 800328-1276

Eagle Vision, Inc. 6263 Poplar Avenue Memphis, TN 38119
800-222-7584

Fleming & Co. 1600 Fenpark Drive Fenton, MO 63026
314-343-8200

E. Fougera & Co. 60 Baylis Road Melville, NY 11747
800-645-9833

Gebauer Co. 9410 St. Catherine Avenue
Cleveland, OH 44104
800-321-9348

W. L. Gore & Associates, Inc. 1500 North 4th Street Flagstaff, AZ 86004
602-526-3030

Johnson & Johnson 1 Johnson & Johnson Plaza
New Brunswick, NJ 08933
908-524-0400

KLI Corp. 1119 3rd Avenue SW Carmel, IN 46032
317-846-7452

Laclede Professional Products
15011 Staff Court Gardena, CA
90248 800-922-5856

La Jolla Diagnostics, Inc.
7777 Fay Avenue Ste. 160
La Jolla, CA 92037
800-454-6790

Leaf Specialty Products 500 North Field Drive
215661-5000

Mission Pharmacal Co. 1325E. Durango P.O. Box 1676 San Antonio, TX 78210
800-531-3333

Muro Pharmaceuticals 890 East Street Tewksbury, MA 01876
800 225-0974

Nabisco Foods, Inc. P.O Box 41 Winston-Salem,NC 27102
910741-2020

OCuSOFT Inc. PO Box 429 Richmond, TX 77406
800-233-5469

Omnii International PO Box 100 Gravette, AR 72736
800-643-3639

Oral-B Laboratories 1 Lagoon Drive Redwood City, CA 94065
415 598-5000

Procter & Gamble P.O. Box 171 Cincinnati, OH 45201
513983-1100

Rhone-Poulenc Rorer Pharm. Inc. 500 Arcola Road P. 0. Box 1200 Collegeville, PA 19426
215454-8000

Rugby Labs, Inc. 20 Nassau Avenue Rockville Centre, NY 11570
800-645-2158

Scandipharm, Inc. 22 Inverness Center Pkwy Ste 310 Birmingham, AL 35242
205-991-8085

Scandinavian Naturals 12 North 7th Street Perkasie, PA
Pittsburgh, PA 15230
412928-1000

Snuva,Inc.
Medical Innovators 715 South Boulevard Oak Park, IL 60302
708-848-4783

Spectra Pharmaceuticals, Inc Hanover Business Park 155 Webster Street Hanover, MA 02339
800-225-2578

Squigle, Inc. 105 Forrest Ave. Suite 4 Narberth, PA 19072
1-877-718-0718

Storz/Lederle Ophthalmic
Ph Div. American Cyanamid Co One Cyanamid Plaza Wayne, NJ 07470
800-533-3753

Syntex Laboratories 3401 Hillview Avenue Palo Alto, CA 94303
415-855-5050

Teledyne
1730 E. Prospect Rd Ft. Collins, CO 80525
303 484-1352

Upsher-Smith Labs, Inc. 14905 23rd Avenue N. Minneapolis, MN 55447
800-328-3344

Wamer Lambert 201 Tabor Rd. Morris Plains, NJ 07950
800 223-0432

William Wrigley Jr. Co. 410 N. Michigan Avenue Chicago, IL 60611
312 879-0400

W yeth-Ayerst PO Box 8299 Philadelphia, PA 19101
215 688-4400

Young Dental Mfg. 13705 Shoreline Court Maryland Hts, MO

257 Cornelison Avneue
Jersey City, NJ 0730
800-365-6500

Burroughs-Wellcome Research
3030 Cornwallis Road
Triangle Park, NC 27709
800-722-9292

John 0. Butler Co.
4635 W. Foster Avenue
Chicago, IL 60630
312-777-4000

Lake Forest, IL 60045
708-735-7819

MGI Pharma
Ste 300 E. Opus Center
9900 Bren Road East
Minnetonka, MN 55343
800-562-5580

800-288-2844

Scherer Labs, Inc.
315 Gilmer Ferry Road
Ball Ground, GA 30107
800-527-0222

63043
314344-0010