

Sjögren's Syndrome

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Abstract

Saliva is an essential body fluid. It is important in maintaining oral health, taste acuity, mastication, deglutition and digestion, oral flora regulation, oral cleansing, voice acuity, and speech articulation. Saliva is composed largely of water but also contains minerals, electrolytes, buffers, enzymes, growth factors, cytokines, immunoglobulins, proteins and metabolic waste products, with the concentrations and compositions of these components varying by individual. Many systemic disorders can affect salivary function, greatly compromising oral health. One such disorder is Sjögren's Syndrome (SS), an autoimmune exocrinopathy characterized by oral and ocular dryness with or without impairment of other organ systems. SS can cause substantial serologic autoimmune reactivity and in some instances is associated with other connective-tissue autoimmune disorders, such as rheumatoid arthritis, scleroderma, or systemic lupus erythematosus. SS increases the risk for developing malignant non-Hodgkin's lymphoma. Treatment of this syndrome consists of a combination of multiple agents, depending on the degree of symptomatology: cholinergic agonists, artificial salivary substitutes, nonsteroidal anti-inflammatory agents, antirheumatic drugs, and biologic agents. This article describes saliva and salivary function, the pathogenesis of SS, the current treatment of xerostomia, and quality of life issues related to salivary dysfunction.

The Salivary Glands and Saliva

There are three pairs of major salivary glands that produce 90% of salivary secretions: the parotids, the submandibulars, and the sublinguals (see

Figure 1). There are numerous minor salivary glands in the lining of the upper aerodigestive tract and the respiratory system. The paired major salivary glands have a basic anatomic structure that features acini with a specialized row of myoepithelial cells and a ductal system (Dawes, 1987; Percival, Challacombe, & Marsh 1994). The acinar cells are the secretory end pieces and are responsible for the initial transport of fluid into the glandular ductal system (Fox & Eversole, 2001). The parotid glands consist of mainly serous acinar cells, which are highly radiosensitive, and secrete mainly under stimulation (e.g., gustatory, mastication). The submandibular glands consist of both mixed mucous and serous cells, whereas the sublingual glands consist mainly of mucinous cells, which are highly radio-resistant. Resting saliva is mainly provided by the submandibular glands. The glands combined produce up to 1.5 liters of saliva a day. The ductal cells of each gland form a branching system that moves saliva into the respective glandular duct within the oral cavity (Dawes, 1987; Percival, et al. 1994; Fox & Eversole, 2001).

Saliva is a complex body fluid composed of 92% to 98% water, and an incredible array of immunoglobulins, proteins, enzymes, small organic molecules, and other components that protect, repair, and moisturize the oral cavity and destroy bacteria, viruses, and fungi (Percival, et al. 1994). The average daily output of saliva in healthy humans is 1000 to 1500 ml. The major salivary glands produce up to 90% of salivary secretions (Mercadante, Calderone, & Villari, 2000). The parotid glands compose between 52% and 70% of the salivary constituent upon stimulation (i.e., gustatory, masticatory) [Dawes, 1987; Percival, et al. 1994; Fox, et al. 2001; Chambers, Toth, Martin, Fleming, & Lemon, 1995]. The majority of the salivary flow from the parotid gland, however, is only present during mastication and occurs less than 1 hour a day. More importantly, most of the protective function of the saliva is attributable to

the effect of the submandibular glands. The submandibular glands contribute between 70% to 82% to the balance of resting whole saliva (Dawes, 1987; Percival, et al. 1994; Fox, et al. 2001; Chambers et al. 1995).

The role of saliva in maintaining oral homeostasis is underappreciated and has not been fully researched. Saliva protects and lubricates the oral cavity and serves as an antibacterial, antiviral, and antifungal agent (Chambers et al., 1995). Saliva is also an important facilitator of eating, particularly the early breakdown of food as well as taste acuity, and articulation. Clinically, when the salivary gland is operating in a deficient mode ("hypo" function), observable effects include difficulty speaking, difficulty chewing, difficulty swallowing, and impaired ability to taste. Other results of salivary gland hypofunction are increased incidence of caries and periodontal disease with the presence of opportunistic organisms. The increased incidence of caries is caused by an increase in caries-forming organisms, which flourish in an acidic environment; therefore, even minimally functioning salivary glands can maintain an increase in the pH of the saliva and decrease the harmful effects of caries-forming organisms (Dawes, 1987; Percival, et al. 1994; Fox, et al. 2001; Chambers et al. 1995). Any increase in saliva, no matter how small, with concomitant increases in the production of salivary constituents may benefit patients with xerostomia.

The volume of salivary secretion may be decreased by a number of disease processes and other factors. Xerostomia is defined as the perception of dry mouth and is estimated to affect 22% to 26% of the general population (Peterson, 2000). It reportedly occurs more commonly in the elderly (Chambers, 2003) and in patients with advanced cancer (29% to 77%) (Peterson, 2000). Xerostomia has also been associated with some immunotherapy (Davies & Singer, 2001), chemotherapy (Narhi, 1994; Schiodt, 1992), and radiation treatment involving the major sali-

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vary glands (Sreebny, Valdini, & Yu, 1989).

Sjögren's Syndrome

SS is a common autoimmune disease that affects the eyes, the oral cavity, and the mucosal membranes of the body through a process in which mononuclear inflammatory cells invade the lacrimal and salivary glands (Jabs, 2001; Carsons, 2001). It is estimated that 1% of the population is affected by this syndrome which is generally chronic in nature (Jabs, 2001). In the United States, a reported two to four million people have SS, and one million have sought medical attention (Jabs, 2001; Carsons, 2001). SS predominantly affects people 30 to 55 years of age, and the female to male ratio is 9:1 (Carsons, 2001). It can occur independently of other morbidities (primary Sjögren's syndrome) or it can be associated with autoimmune Connective tissue disorders such as rheumatoid arthritis and lupus erythematosus (secondary Sjögren's syndrome) (Carsons, 2001; Fox, 1994). In some instances, primary SS may be associated with organ-specific autoimmune conditions such as thyroiditis and primary biliary

cirrhosis (Carsons, 2001; Anaya & Talal, 1997; Fox, 1994). Of the one million diagnosed cases in the US, the distribution between primary and secondary Sjögren's is about 50:50.

SS was named for the Swedish ophthalmologist Henry Sjögren who, in the early 1900s, classified this condition as an autoimmune disorder characterized by dry eyes and dry mouth (Sjögren, 1940). Since that time, there has been significant research to evaluate the effects of SS. More recently, the term "autoimmune exocrinopathies" was adopted to describe the primary pathologic process of SS (Carsons 2001; Vivino & Orlin, 2000; Libby 1998; Anaya et al., 1997; Bloch, Buchanan, Wohl, & Bunim, 1956; Fox 1994; Friedlander 1992; Prause 1989; Rhodus & Schuh, 1991; Fox et al 1995; Willis, Folberg, Krachmer, & Holland, 1987; Crystal 2002; Fox et al., 1998). In this disease, a lymphocytic inflammatory process invades salivary glands and lacrimal glands. In normal salivary glands there are zero to several lymphocytes (Carsons, 2001). On the contrary, in patients with SS, lymphocytic infiltration is found in major salivary gland

tissues (Fox et al., 1995). The target tissues in SS are the exocrine glands, that secrete into the upper aerodigestive tract, resulting in compromised function. There is a cumulative effect from this process and, as the patient ages, the disease results in increasingly poor quality of life.

There are three distinct diagnostic criteria for SS (Jabs 2001; Carsons 2001). The first is dryness, which manifests as xerophthalmia and xerostomia. The second is a positive antinuclear antibody (ANA) test. Hematology tests can distinguish two subclassifications of SS, Sjögren's associated antigens A and B (SSA and SS-B autoantibodies) respectively (Carsons 2001; Fox et al., 1995; Fox et al., 1998). The third diagnostic criteria is an abnormal lip biopsy showing a focal aggregation or accumulation of mononuclear lymphatic cells identified within a minor salivary gland (Carsons, 2001). There has been a considerable amount of research evaluating the hereditary factors associated with SS; specifically, genes such as human leukocyte antigen or HLA genes

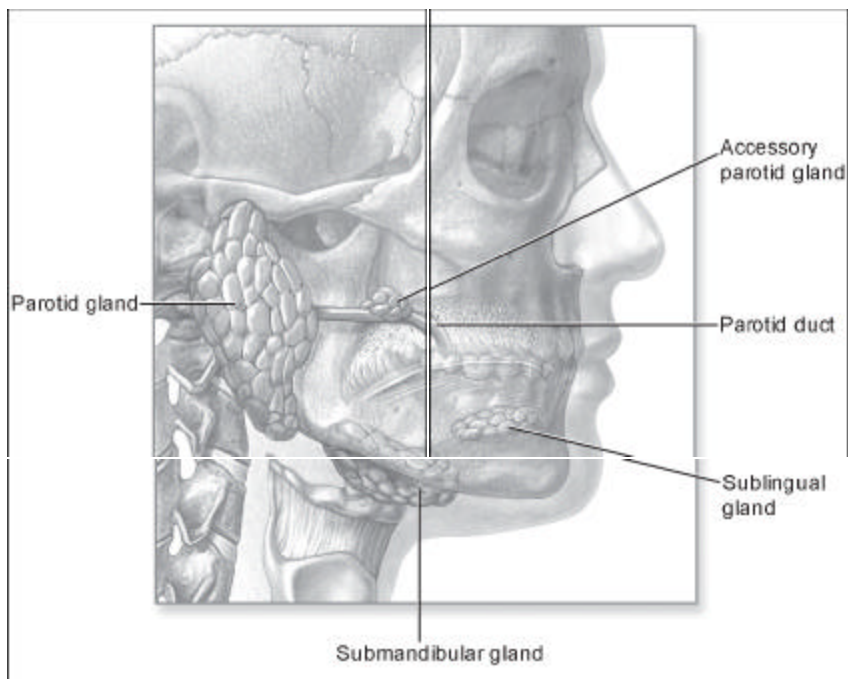


Figure 1: Major Salivary Glands. (Photograph purchased from A.D.A.M., Inc. Atlanta, GA.)

inherited from parents (Fox, 1995). SS is an inflammatory infiltration that develops over time, so the scarring effect is not as evident with this disease as it is in radiation-induced fibrosis (Carsons, 2001). SS may be caused by apoptosis (programmed cell death) that precedes the inflammatory events or it could be initiated by viral infection (e.g., Epstein Barr, Hepatitis C) (Carsons 2001; Fox RI 1995; Fox et al., 1998). Most researchers agree that the exocrine tissue in patients with SS demonstrates inflammatory infiltration (Jabs 2001; Carsons 2001). This infiltration is from lymphocytes, monocytes, and plasma cells which leads to exocrinopathy that worsens over time. The replacement of normal glandular tissue results in exocrine gland dysfunction.

Ocular Manifestations

Ocular manifestations of SS include a dry gritty feeling or foreign body sensation in the eyes (Carsons 2001; Vivino et al., 2000; Friedlander 1992; Prause 1989; Willis et al., 1987; Crystal 2002). Irritation and photophobia are frequently reported, particularly at nighttime. These patients may also have intraocular hypertension. They have a diminished Schirmer's strip reading, and slit lamp examinations show a hypotear effect (Fox 1995; Willis et al., 1987; Crystal 2002). There is mucosal threading and there are also multiple irritations with conjunctivitis (Carsons, 2001). Patients with SS may also experience pruritis of their periorbital skin and eyes resulting in rubbing and irritation. As SS progresses, ocular fluid will decrease, leading to various chronic manifestations.

Oral Manifestations

Oral manifestations of SS are characterized by swollen salivary glands, specifically, parotid or submandibular gland swelling, and a parched sensation in the oral cavity and throat (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997; Bloch et al, 1956; Fox 1994; Friedlander 1992; Prause 1989; Rhodus et al., 1991; Fox RI et al., 1995; Willis et al., 1987; Crystal 2002; Fox et al., 1998). Some patients may appear to have a mumps-like presentation in the parotid region. Chewing and swallowing become difficult without increased liquids. SS pa-

tients have a higher incidence of fungal infections (e.g., oral candidiasis) resulting from oral dryness and the resultant acidic environment with odynophagia and angular cheilitis. Multiple periodontal complications can occur as sequelae of xerostomia (e.g., gingivitis, erythema of oral mucosa, loss of papillary anatomy on the dorsal tongue) (Fox et al., 2001; Carsons 2001; Fox et al., 1998). This deteriorating effect can result in bony infection with resultant dental hypersensitivity. Cariesforming and periodontal organisms (e.g., *Streptococcus mutans*, *Lactobacillus*) increase in the oral cavity as the xerostomic state worsens (Chambers et al., 1995). Patients with xerostomia will benefit remarkably from using an anticaries preventive regimen and increasing salivary flow with locally applied and systemic pharmacotherapies.

Prosthetic rehabilitation of edentulous or partially edentulous patients with SS can be highly complicated, as tissues are easily damaged due to the xerostomic state. Removable prostheses can be frictionally irritating to dry tissues leading to morbid complications, e.g., soft tissue necrosis, oral pain, and fungal infection. Use of denture adhesives can further irritate tissues and lead to oral complications. In addition, the adhesive can act as a harbor for fungal colonization with deleterious effects on the underlying tissues.

Systemic Manifestations

Systemic manifestations of SS can be problematic (Carsons 2001; Fox RI et al., 1995; Fox et al., 1998). There are significant musculoskeletal complications (e.g., myalgias, arthralgias); therefore, rheumatologists should be actively involved in treating SS patients who present with rheumatoid arthritis or a confirmed rheumatoid factor (Jabs 2001; Carsons 2001; Anaya et al., 1997; Fox et al., 1998). As expected, the most common skin manifestation is dryness with resultant rash, pruritis, purpura, vasculitis, or Raynaud's phenomenon (Carsons 2001; Crystal 2002). Other extraglandular effects can include xerotrachea, vasculitis, and lymphocytic infiltration of the parenchymal tissue of the pulmonary system (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997). A significant

number of SS patients have problems with chronic coughing (Libby, 1998). In addition, patients who have been diagnosed with either primary or secondary SS have a significant potential for developing lymphoma (e.g., B-cell lymphoma), Waldenström's macroglobulinemia, or neurologic disease (e.g., cranial neuropathy such as trigeminal neuralgia) (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997).

Diagnosis

In diagnosing SS, it is most important to determine whether the patient has primary or secondary SS. Therapeutic modalities should be based on clinical presentation, laboratory testing, and formulating a differential diagnosis (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997). In the initial workup, dryness of the oral cavity and eyes should be objectively assessed. Evaluation of salivary flow is also an essential part of the oral assessment of patients suspected of having SS. In this workup, sialometry is performed, to evaluate unstimulated and stimulated flow rates. Patients with unstimulated whole saliva flow rates of less than 0.5 ml per 5 minutes or stimulated (gustatory or masticatory) whole saliva rates of less than 0.5 ml per 1 minute are considered xerostomic (Fox et al., 2001). A number of blood and urine tests can be performed, particularly to evaluate autoantibodies, antinuclear antibodies, and rheumatoid factor (Fox et al., 2001). Ocular assessment includes a Schirmer's test in which filter paper is placed under the lower eyelid, and tearing is measured over a 5-minute period (Vivino et al., 2000; Friedlander 1992; Prause 1989; Crystal 2002). Less than five mm of tearing is considered a hypofunctional state. If this test is positive, then the next level of testing is the slit lamp examination and evaluation of corneal topography.

Diagnostic imaging (e.g., magnetic resonance imaging and computed tomography) has been added to the testing regimen along with scintigraphy to evaluate the effect of SS on the parotid glands (Fox et al., 2001). A magnetic resonance scan can image the anatomy of salivary gland tissues with accuracy. A technetium scintigraphy is beneficial

in determining dysfunctional glandular tissue. In this procedure technetium ^{99m}Tc is introduced intravenously and its uptake is timed (Fox et al., 2001). ^{99m}Tc has a rapid uptake into exocrine glands, particularly the submandibular and parotid glands, in healthy individuals. In contrast, in patients with SS, ^{99m}Tc uptake is delayed, and the release of the tracer into the oral cavity may not be noted. This test will show the overall effect and the homogeneity of the rapid uptake of the radioisotope into the glands and will thus correlate to the observed flow rate (Carsons 2001). Another method of testing oral secretions is through a sialogram, where iodine-containing contrast material is introduced directly into the ductal system (such as the Stenson's duct) by cannulation, and the flow is visualized by cephalometric radiographs (Fox et al., 2001). In this test, the contrast material has uptake into the branching ductal system. Normal or abnormal distribution of secretions through the main excretory duct and ductules is demonstrated, including any disruption caused by a tumor or punctate sialiectasis as can occur in patients with SS.

Lip biopsy, which identifies minor salivary gland abnormality, is the former standard technique for diagnosing SS (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997). A small punch biopsy is used to remove minor glandular tissue. If the pathology assessment is positive for SS, the specimen will have a focus of mononuclear cell aggregation. Hematologic assessment is a newer diagnostic tool for confirming SS and includes routine chemistries, blood counts, urinalysis, and specific rheumatoid factor and anti-nuclear antibody tests to reveal any autoimmune disease (Carsons 2001; Fox et al., 1998). More specific serologic markers of SS autoimmunity are tests for the SS-A/Ro and SS-B/La autoantibodies, which are found in 60% and 40% of patients, respectively (Fox et al., 2001; Carsons 2001). Patients with SS often have elevated levels of the IgG, IgM, and IgA immunoglobulin subtypes (Fox et al., 2001).

Quality of Life

The hallmark characteristics of SS can adversely impact a patient's quality

of life. A delay in diagnosing SS may have a significant physical, psychological, and economic impact on the affected person. Xerostomia can produce serious negative effects on the patient with SS, affecting dietary habits, nutritional status, speech, taste, tolerance to dental prostheses, and increases susceptibility to dental caries and fungal activity. Xerophthalmia can further reduce quality of life.

Medical treatments along with patient education can reduce discomfort and prevent potential health problems in patients with SS. A knowledgeable and skilled healthcare team can enhance the quality of life of a patient with SS by decreasing the patient's stress level, providing pain and comfort management, avoiding habits that can worsen the symptoms of SS, and ultimately treating or preventing the principal and secondary complications of the disease process (Petruzzi et al., 2003). Scheduling and monitoring clinical and laboratory tests on patients with SS on a routine basis optimizes early treatment of incidental findings and reduces complications.

Treatment

In general, treatment for SS requires a multidisciplinary approach that involves a primary care physician, rheumatologist, ophthalmologist, and oral medicine specialist (Carsons 2001; Crystal 2002). This approach is indicated due to the multiple feature of the disease that present special management challenges, particularly joint disorders, myalgias, and fatigue. Fatigue is by far one of the most complicated complaints of patients with SS, particularly the elderly patients (Jabs 2001; Carsons 2001). More severe features, such as vasculitis, require immunosuppressive medication to preserve organ function.

The goal of treatment for SS should be preservation or replacement of moisture and systemic palliation of symptoms (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997). Most patients will require tear and salivary supplementation (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997). Administration of substantial amounts of artificial salivary substitutes in conjunction with other protocols, such as with

cholinergic agonists, produce good results for these patients (Jabs 2001; Carsons 2001). For xerophthalmia, punctal occlusion may be accomplished by inserting a collagen or silicone plug into the inferior lacrimal ducts resulting in pooling tears and adding ocular moisture (Willis et al., 1987; Crystal 2002). Salivary stimulation from sialogogue therapy with pilocarpine or cevimeline is highly indicated in patients with SS (Mercadante et al., 2000; Peterson 2000; Chambers 2003; Davies et al., 2001; Narhi 1994; Schiodt 1992; Sreebny et al., 1989). In addition to the moisture replacement therapy, systemic therapies for palliation of musculoskeletal and pulmonary complications may be necessary (e.g., antiinflammatory, corticosteroid, or cytotoxic agents).

Antiarthralgia and fibromyalgia medications can be introduced to treat rheumatology symptoms. Additionally, corticosteroids or immunosuppressive medications are used to treat the myalgias (Carsons 2001; Sjogren 1940; Vivino et al., 2000; Libby 1998; Anaya et al., 1997; Bloch et al., 1956; Fox 1994).

Xerostomia: Pharmacologic Options

Current therapies for the pharmacologic management of xerostomia include the use of prescription fluoride agents to maintain optimal oral hygiene, antimicrobials to prevent dental caries and oral infection, saliva substitutes to relieve dryness, and sialogogues to stimulate saliva production from remaining intact salivary gland tissues (Table 1) (Fox et al., 2001; Chambers et al., 1995; Carsons 2001; Fox et al., 1998). Proper oral care in patients with SS is essential, with use of topical 0.4% stannous fluoride gel once daily to minimize dental caries (Chambers et al., 1995). Oral antimicrobial agents may also be beneficial to prevent oral infection. Chlorhexidine gluconate, for example, provides broad-spectrum activity *in vitro* against gram-positive, gram-negative, and fungal pathogens and binds well to oral surfaces, minimizing gastrointestinal absorption (Chambers et al., 1995). However, the alcohol in some chlorhexidine solutions may exacerbate xerostomia; therefore, an aqueous-based

Table 1: Xerostomia: Pharmacologic Options

	Product	Manufacturer
Saliva Substitutes	Oral Balance®	Laclede Research Labs Gardena, CA
	Salivart®	Gebauer Company Cleveland, OH
	MouthKote®	Parnell Pharmaceuticals Larkspur, CA
	Saliva Substitute®	Roxane Laboratories Columbus, OH
	MoistPlus®	Medical Warehouse Stormville, NY
Cholinergic agonists	Evxac® (Cevimeline HCl)	Daiichi Pharmaceuticals Montvale, NJ
	Salagen® (Pilocarpine HCl)	MGI Pharma Minnetonka, MN
Fluoride	Gel Kam® (0.4% SnF)	Colgate Oral Pharmaceuticals Canton, MA
	Prevident Gel® (1.1% NaF)	Colgate Oral Pharmaceuticals Canton, MA
	NeutraCare® (1.1% NaF)	Oral-B Laboratories Belmont, CA
	Prevident 5000 plus® dentifrice	Colgate Oral Pharmaceuticals Canton, MA

solution may be beneficial (Chambers et al., 1995; Schubert et al., 1999).

Saliva substitutes containing hydroxyethyl-, hydroxypropyl-, or carboxymethylcellulose may be beneficial as palliative agents to relieve the discomfort of xerostomia by temporarily wetting the oral mucosa (Rhodus & Schuh, 1991). One recent study investigated the use of a xanthan gum-based saliva substitute. Patients report similar improvement with the xanthan gum-based saliva substitute and placebo (of similar composition, without xanthan gum), but with a trend toward increased improvement in speech and sensory problems with the xanthan gum agent (Jellema et al., 2001). Other new saliva substitutes (moisturizing gels), with enzyme and protein components (i.e., glucose oxidase and lactoperoxidase) that claim antibacterial effectiveness (reducing caries forming and fungal organisms) and increased oral moisture,

are under study (Rhodus et al., 1991; Chambers 2003).

For patients with residual salivary gland function, cholinergic agonists may produce symptomatic improvement (Mercadante et al., 2000; Peterson 2000; Chambers 2003; Davies et al., 2001; Narhi 1994; Schiodt 1992; Sreebny et al., 1989). Pilocarpine (Salagen®) is a widely used systemic sialagogue approved by the Food and Drug Administration for treatment of SS. Pilocarpine functions primarily as a muscarinic-cholinergic agonist with mild adrenergic activity. Muscarinic agonists in sufficient doses can increase secretion of exocrine glands, such as salivary and sweat glands, and the tone of smooth muscle in the gastrointestinal and urinary tracts. Studies have shown oral pilocarpine to have efficacy in patients with SS, radiation-induced xerostomia, and opioid-induced xerostomia, as well as increasing salivary flow and restoring

salivary composition in those with graft-versus-host disease, resulting from allogeneic bone marrow transplantation (Mercadante et al., 2000; Leek et al., 2002; Fox et al., 1986; Chambers et al., 1997; Chambers et al., 1997; Chambers et al., 1997). The recommended oral dose of pilocarpine for the initiation of treatment is 5 mg TID with titration up to 10 mg TID. The incidence of the most common adverse events (e.g., excessive sweating, rhinitis) increases with dose.

LeVeque and colleagues (LeVeque et al., 1993) conducted a randomized, placebo-controlled, dose-escalation study of pilocarpine and Johnson and colleagues (Johnson et al., 1993) conducted a three-arm randomized, placebo-controlled trial (placebo, pilocarpine 5 mg TID, and pilocarpine 10 mg TID). In both studies, significantly more pilocarpine-treated patients than placebo recipients reported improvement in xerostomia. In addition, LeVeque and

colleagues found that treatment with pilocarpine led to a significant decrease in the use of oral comfort agents such as artificial saliva, hard candies, and water. In a randomized crossover study of pilocarpine mouthwash versus mucin-based artificial saliva, Davies and Singer (Davies et al., 1994) found a mean change in the xerostomia score after three months of 22.5% improvement with pilocarpine and 15.2% with artificial saliva.

Cevimeline (Evoxac®) is a newer Food and Drug Administration-approved muscarinic agonist that has been used in treating xerostomia associated with Sjögren's syndrome (Atkinson et al., 2001; Al-Hashimi 2001). Cevimeline has shown efficacy in animal studies in increasing saliva secretions after radiation of the head and neck (Iga et al., 1998). It is currently under study for use in patients with head and neck cancer who have radiation- and graft-versus-host-disease-induced xerostomia. A randomized, double-blind, placebo-controlled study was conducted using cevimeline in patients with SS, and the majority of the subjects on active drug had a global improvement in dry mouth symptoms. The effects of cevimeline at 15 mg TID (45 mg/day) and 30 mg TID (90 mg/day) were compared with those of placebo, finding statistically significant global improvement in the symptoms of dry mouth ($P = .0004$) for the 30-mg TID group compared with placebo. Salivary flow rates increased at both doses of cevimeline compared with the placebo (Petroni et al., 2002). The incidence of serious adverse events was low in all treatment groups. The most common drug-related adverse events were excessive sweating, nausea, rhinitis, and diarrhea (Evoxac Capsules: Physician's Desk Reference, 58th ed, 2004, 1182). The recommended dose of cevimeline is 30 mg taken three times daily.

Pilocarpine and cevimeline are contraindicated in patients with uncontrolled asthma, acute iritis, narrow-angle glaucoma, or known sensitivity to cholinergic agonists. It should be used with caution in patients with asthma, known hypersensitivity, chronic bronchitis, chronic obstructive pulmonary disease, miosis, or cardiovascular disease (Evoxac Capsules: Physician's Desk Refer-

ence, 58th ed, 2004, 1182; Wiseman et al., 1995). Cholinergic agonists can potentially alter cardiac conduction, heart rate, increase airway resistance and bronchial secretions, as well as decrease visual acuity.

Patient Education

There are many resources for learning about the chronic autoimmune disorder SS. One excellent resource is the Sjögren's Syndrome Foundation. The mission of the Foundation is to broaden public awareness about this disease and to educate health care professionals and patients with SS about characteristics and current treatment paradigms for the disease. The Foundation distributes pamphlets about SS by mail upon request. Information regarding the pathophysiology and current treatment recommendations for this disease are available at the foundation's website www.sjogrens.org. The foundation's monthly newsletter, "The Moisture Seekers," is also available upon request.

Conclusion

- ? Saliva is a complex bodily fluid that has multiple properties: protective, digestive, lubricatory, remineralizing, and facilitates speech, eating, and swallowing.
- ? SS is a chronic autoimmune multi-system disorder with degeneration of mucous-secreting glands.
- ? The two hallmark characteristics of SS are xerostomia and xerophthalmia.
- ? The majority of patients with SS are female, Caucasian, and middle-aged.
- ? The systemic manifestations of SS include rash, Raynaud's phenomenon, fatigue, and nerve and muscle pain.
- ? Patients with SS have lymphocytic infiltration in major salivary gland tissues.
- ? The pathogenesis of SS is multifactorial: immunological, genetic, hormonal, and possibly infectious.
- ? The treatment for SS requires a multidisciplinary approach that involves multiple specialists aimed at providing comfort and preventing progression of disease.

- ? Nurses are instrumental as part of the healthcare team in providing supportive care to patients with SS.
- ? Future strategy in treating SS will be targeted at systemic treatment with improved immunomodulating and COX-2 inhibitor medications, time-released cholinergic agonist medications improving salivary function, and vision correction with laser technology.

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