Managing xerostomia and salivary gland hypofunction

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Background. Xerostomia, also known as “dry mouth,” is a common but frequently overlooked condition that is typically associated with salivary gland hypofunction, which is the objective measurement of reduced salivary flow. Patients with dry mouth exhibit symptoms of variable severity that are commonly attributed to medication use, chronic disease and medical treatment, such as radiotherapy to the head and neck region. Chronic xerostomia significantly increases the risk of experiencing dental caries, demineralization, tooth sensitivity, candidiasis and other oral diseases that may affect quality of life negatively. This article presents a multidisciplinary approach to the clinical management of xerostomia, consistent with the findings of published systematic reviews on this key clinical issue.

Conclusions and Practice Implications. Initial evaluation of patients with dry mouth should include a detailed health history to facilitate early detection and identify underlying causes. Comprehensive evaluation, diagnostic testing and periodic assessment of salivary flow, followed by corrective actions, may help prevent significant oral disease. A systematic approach to xerostomia management can facilitate interdisciplinary patient care, including collaboration with physicians regarding systemic conditions and medication usage. Comprehensive management of xerostomia and hyposalivation should emphasize patient education and lifestyle modifications. It also should focus on various palliative and preventive measures, including pharmacological treatment with salivary stimulants, topical fluoride interventions and the use of sugar-free chewing gum to relieve dry-mouth symptoms and improve the patient’s quality of life.

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Authors and acknowledgements

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Xerostomia, the subjective sensation of dry mouth, is a frequent complaint and the most common symptom of salivary gland hypofunction (SGH). Factors that contribute to dry mouth include systemic disease and medical therapies such as medication or radiation treatment.  

Although xerostomia often is a manifestation of impaired salivary gland function, it can occur with or without a noticeable decrease in saliva production. In most circumstances, xerostomia is accompanied by SGH, which reflects an objective, measurable decrease in salivary flow (hyposalivation). Symptoms of dry mouth may range from mild oral discomfort to significant oral disease that can compromise patients’ health, dietary intake and quality of life.

Identifying and treating the underlying causes of dry mouth are essential to providing optimal oral health care. Effective prevention and early detection and treatment of oral problems associated with dry mouth require aggressive management by both dentist and patient. This article presents a practical, evidence-guided approach to managing xerostomia and SGH for use in the treatment of patients with salivary dysfunction.

FUNCTIONS OF SALIVA

In addition to its role in digestion, saliva serves several protective functions, including cleansing the oral cavity, facilitating oral processing and swallowing of food, protecting oral tissues against physical and microbial insults, maintaining a neutral pH and preventing tooth demineralization.

The antimicrobial properties of saliva are due to a wide variety of immune and non-immune salivary proteins that inhibit the adherence and growth of viruses and bacteria. Salivary proteins and mucins contribute to the lubrication and coating of oral tissues, protecting the oral mucosa from chemical, microbial and physical injuries. Saliva provides lubrication and moisture to facilitate speech and taste. Dissolution of substances in saliva allows for stimulation of taste receptors on the tongue. Significant loss of salivary gland function is associated with altered taste sensation (dysgeusia).
ETIOLOGY

Systemic diseases. Table 1 presents medical conditions that may cause dry mouth. An estimated 4 million people in the United States have Sjögren syndrome (SS), an autoimmune disease commonly associated with hyposalivation. SS is a chronic inflammatory disease characterized by lymphocytic infiltration of the salivary and lacrimal glands, resulting in xerostomia and dry eyes (xerophthalmia). Approximately 90 percent of those with SS are women, and patients often experience associated symptoms such as fatigue, joint pain and neuropathy.

Table 1. Medical conditions associated with xerostomia*

<table>
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<tr>
<th>Condition</th>
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<tr>
<td>Autoimmune and inflammatory conditions (such as Sjögren syndrome or primary biliary cirrhosis)</td>
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<td>Graft-versus-host disease</td>
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<td>Immunoglobulin G4–related sclerosing disease</td>
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<td>Degenerative disease (amyloidosis)</td>
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<td>Granulomatous disease (sarcoidosis)</td>
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<tr>
<td>Infections: human immunodeficiency virus/AIDS, hepatitis C</td>
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<tr>
<td>Salivary gland aplasia or agenesis</td>
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<td>Lymphoma</td>
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* Sources: Scully, Al-Hashimi and Navazesh and Kumar.

Individuals with diabetes commonly complain of dry mouth, and moderate to severe xerostomia is reported by 30 to 40 percent of patients with human immunodeficiency virus (HIV), with increasing prevalence based on age and duration of HIV positivity.

Side effects of medical treatment. Salivary gland damage is the most common adverse effect associated with radiation therapy to the head and neck region. Salivary flow decreases rapidly during the first week of treatment, followed by fibrosis of the salivary glands and permanent loss of secretory capacity, thus dramatically diminishing quality of life. The degree of damage is dependent on the
volume of tissue irradiated and the total dose administered. Patients undergoing chemotherapy also may experience transient xerostomia.6

Medication. The use of systemic medications is one of the most frequently reported causes of xerostomia.1,10,12,20-22 More than 500 drugs are known to cause oral dryness, including many of the most commonly prescribed classes of medications (Table 2).10,21,23

Table 2. Medications frequently associated with xerostomia†

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<tr>
<td>• Anticholinergic drugs</td>
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<td>• Antihistamines</td>
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<tr>
<td>• Antihypertensive agents: angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, α- and β-adrenergic blockers, diuretics</td>
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<tr>
<td>• Opioids</td>
<td></td>
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<td>• Psychotropic agents: antidepressants, antipsychotics</td>
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<td>• Skeletal muscle relaxants</td>
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* Sources: Scully,10 Elsevier/Gold Standard21 and Neville and colleagues.23
† None of the medications listed in Table 2 is known to damage the salivary glands.

The vast majority of medications do not damage the salivary glands, but the likelihood of decreased unstimulated salivary flow rates increases in the presence of numerous diseases and medications. Although patients receiving multiple xerostomic medications tend to have more severe dry-mouth symptoms,22,23 the effects of xerostomic medications on patients can be highly variable.24 Patients with salivary gland hypofunction are more susceptible to the xerogenic side effects of medications than patients with normal salivary gland function.

Over-the-counter medications associated with xerostomia include those used to treat allergic conditions, congestion, motion sickness and diarrhea. Some medications, such as those prescribed for overactive bladder disease, irritable bowel syndrome and Parkinson disease, are used specifically for
their anticholinergic properties. These medications directly inhibit salivary flow and often are associated with dry-mouth symptoms.10,25-27

**Physiologic or psychogenic causes.** Dehydration, mouth-breathing and neurological or psychological disorders (such as depression or anxiety) may add to the perception of oral dryness.10,28,29 Affective (mood) disorders may affect the autonomic nervous system, and patients with such conditions may experience xerostomia.10,30-32 The degree of hydration affects salivary flow substantially. In one study, investigators found that dehydration as a result of abstaining from food and liquids for 24 hours reduced unstimulated parotid salivary flow by approximately 90 percent.28 Given the increased prevalence of dehydration in older adults, it is important to assess fluid status in these patients.

**SIGNS AND SYMPTOMS**

Table 3 presents clinical signs and symptoms of hyposalivation. Salivary gland hypofunction can disrupt homeostasis of the oral cavity, may increase susceptibility to oral infection and dental disease, and can compromise quality of life.7,33

Table 3. Clinical signs and symptoms of hyposalivation.

<table>
<thead>
<tr>
<th>TEETH</th>
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<tbody>
<tr>
<td>• Increased incidence of tooth decay (cervical and incisal)</td>
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<td>• Enamel demineralization (chalky spots at the cervical regions of</td>
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<tr>
<td>the teeth)</td>
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<tr>
<td>• Enamel erosion and attrition</td>
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<td>• Increased plaque accumulation</td>
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<td>• Increased tooth hypersensitivity</td>
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<td><strong>ORAL MUCOSA</strong></td>
<td></td>
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<tr>
<td>• Mucositis</td>
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<tr>
<td>• Mucosal desquamation</td>
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<tr>
<td>• Atrophic mucosa</td>
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<td>• Allergic or contact stomatitis and lichenoid lesions (mostly</td>
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<tr>
<td>opposing metal restorations)</td>
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<tr>
<td>• Recurrent oral candidiasis</td>
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<td>• Traumatic ulcerations on the lateral border of the tongue, the</td>
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<td>buccal mucosa or both</td>
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<td>• Painful or burning mouth (intolerance to spicy, sour or salty</td>
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<td>food and drinks)</td>
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<tr>
<td>• Nonspecific gingival inflammation and generalized oral erythema</td>
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### Table 3 (cont.). Clinical signs and symptoms of hyposalivation.

<table>
<thead>
<tr>
<th>TONGUE</th>
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<tbody>
<tr>
<td>• Dryness, fissuring, lobulation</td>
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<tr>
<td>• Atrophy</td>
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<tr>
<td>• Erythema</td>
</tr>
<tr>
<td>• Loss of papillae</td>
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<tr>
<td>• Crenulations on tongue (scalloped borders)</td>
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<table>
<thead>
<tr>
<th>LIPS</th>
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</thead>
<tbody>
<tr>
<td>• Dryness, chapping</td>
</tr>
<tr>
<td>• Peeling</td>
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<tr>
<td>• Fissuring</td>
</tr>
<tr>
<td>• Angular cheilitis</td>
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<th>MAJOR SALIVARY GLANDS</th>
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<tr>
<td>• Poor salivary output</td>
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<tr>
<td>• Frothy saliva</td>
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<td>• Absent or reduced salivary pooling</td>
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<tr>
<td>• Swelling or enlargement of salivary glands</td>
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<tr>
<td>• Recurrent sialadenitis affecting major salivary glands (parotid or submandibular)</td>
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<th>ORAL CAVITY</th>
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<tbody>
<tr>
<td>• Oral allergic or contact reactions</td>
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<tr>
<td>• Halitosis</td>
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<tr>
<td>• Difficulty talking, chewing or swallowing (dysphagia)</td>
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<td>• Plaque accumulation</td>
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<tr>
<td>• Reduced oral clearance</td>
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<tr>
<td>• Altered taste sensation (dysgeusia)</td>
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<tr>
<td>• Food retention and debris on the teeth, tongue or along gingival margins</td>
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<th>OTHER</th>
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<tr>
<td>• Nutritional deficiencies (manifested as dehydration, weight loss, increased thirst, or changes in food and drink preferences)</td>
</tr>
<tr>
<td>• Dry eye accompanied by dry mouth (Sjögren syndrome)</td>
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</table>

Patients with dry mouth often have atrophic and erythematous oral mucosa, loss of papillae on the tongue\textsuperscript{34} and lips that peel and crack. Traumatic lesions may be visible on the buccal mucosa and the lateral borders of the tongue. Dentures may become loose, causing painful ulcerations.\textsuperscript{35} Patients also may describe the need to sip fluids, especially when eating, or may need to drink water when awakened from sleep.\textsuperscript{22,36}
Cervical or root surface caries and candidiasis often are observed in patients with xerostomia. These patients may demonstrate enlargement of the major salivary glands, as well as salivary gland infection. Inspection and palpation of specific salivary glands may reveal swelling, discomfort, a cloudy or purulent discharge (pus), or a complete absence of clinically evident secretions.

**DIAGNOSIS**

**History and examination.** Appropriate evaluation and patient assessment, including a comprehensive medical and dental history, are essential for diagnosing SGH. A positive response to any of the following questions has been associated with reduced saliva, even in patients who have not expressed complaints of xerostomia:

- Does the amount of saliva in your mouth seem to be too little?
- Does your mouth feel dry when eating a meal?
- Do you sip liquids to aid in swallowing dry food?
- Do you have difficulty swallowing?

A comprehensive head and neck examination—both extraoral and intraoral—is important in identifying the presence or absence of pooled saliva, as well as in providing an initial assessment of the quantity and quality of saliva. The clinician should inspect and palpate major salivary glands to identify masses, swelling or tenderness.

**Diagnostic tests. Salivary flow measurement.** Whole saliva is relatively easy to collect in a clinical setting. Although there is only limited evidence regarding the effectiveness of clinical assessment of oral dryness, periodic evaluation of the salivary flow rate provides a tool for monitoring salivary gland function and dry-mouth symptoms.

Unstimulated whole saliva often is collected by means of the draining or drooling method, in which a patient’s head is tilted forward and pooled saliva is collected into a sterile container. An unstimulated whole saliva flow rate of less than 0.1 milliliter per minute is suggestive of significant SGH. Stimulated whole saliva is collected by challenging the glands through mastication, such as chewing paraffin wax, or through gustatory stimulation using citric acid, followed by expectoration into a
collection tube. Stimulated whole saliva flow rates below 0.7 mL/min are within the lower range of output and suggest salivary hypofunction.43,44

**Blood tests.** Laboratory studies (e.g., complete blood count test) may be useful when xerostomia is suspected to be related to systemic disease. Autoantibody screening may be helpful when xerostomia is also associated with xerophthalmia, a characteristic of Sjögren syndrome, including serologic results positive for serum antinuclear antibody, rheumatoid factor or the antibodies anti-SS-A (anti-Ro) or anti-SS-B (anti-La).45,46

**Biopsy.** Minor salivary gland biopsy is a useful diagnostic tool for identifying underlying pathological changes associated with salivary gland dysfunction, especially when the clinician is attempting to identify the underlying etiology of salivary dysfunction as it relates to systemic diseases. Histologic changes are one of the diagnostic criteria used in the diagnosis of Sjögren syndrome; tissue samples are graded according to the level of inflammation within the salivary gland.47 The biopsy also is important in determining whether salivary gland dysfunction is caused by diseases such as amyloidosis,48,49 sarcoidosis50 and other conditions (Table 110-12).

**Candida smear or culture.** In most individuals, *Candida albicans* is part of the normal oral flora, but patients with xerostomia often exhibit recurrent oral candidiasis.51,52 A Candida smear or culture may be useful in confirming the presence of candidiasis and the need for antifungal therapy.

**MANAGEMENT**

Treatment planning to alleviate dry-mouth symptoms should be tailored to the individual patient. A multidisciplinary model of care for xerostomia and SGH should include the following components:

- patient education—a patient-centered process emphasizing daily oral hygiene, regular dental visits, use of topical fluoride, tobacco-use cessation counseling and other interventions;
- management of systemic conditions and medication use in consultation with the patient’s physician, oncologist or other health care provider;
• preventive measures to reduce oral disease and associated complications;

• pharmacologic treatment with salivary stimulants (sialogogues); and

• for patients who cannot tolerate sialogogues, palliative measures to improve salivary output may be considered, such as using sugar-free salivary stimulants (e.g., chewing gum).

**Patient education.** Patients should receive detailed information about the potential causes of dry mouth and the potential sequelae of impaired salivary secretion, including dental caries, candidiasis and mucosal complications. Preventive oral health care should be strongly emphasized, along with oral hygiene instruction stressing the importance of effective plaque removal and of regular dental visits to promote oral health. A meticulous oral hygiene regimen is recommended, including twice-daily tooth-brushing, regular use of floss or another interdental cleaner and use of alcohol-free mouthrinse. Patients can also be encouraged to consult online resources (Box) for further information on xerostomia and SGH.

**BOX**

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<th>Patient resources on xerostomia.</th>
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**Managing systemic conditions and medication use.** Consultation with the patient’s primary care provider or specialist may be considered in cases where hyposalivation is suspected to be due to underlying systemic disease or medical treatment (Tables 110-12 and 210,21,23). Patients with dry mouth, dry eyes and salivary gland enlargement should be evaluated for Sjögren syndrome, as these
individuals have a 16-fold increased risk of lymphoma compared with the general population.\textsuperscript{53,54} Prompt diagnosis allows for recognition of comorbid diseases, and encourages aggressive management of ocular and intraoral complications. Dentists must also be aware of prescription and over-the-counter medications associated with dry mouth to discuss dose modification or possible drug alternatives with physicians.

Clinicians also should recognize that most patients with head and neck cancer receive intensity-modulated radiotherapy, which involves using computer-generated information to establish the distribution of radiation that conforms to the patient’s tumor yet minimizes the dose delivered to surrounding tissues. Intensity-modulated radiotherapy significantly reduces radiation to major salivary glands, thereby helping to maintain adequate salivary flow and enhancing quality of life.\textsuperscript{6,55}

**Preventive measures to reduce oral disease.** Preventive oral health care is essential for optimal care of patients with hyposalivation, who commonly require more frequent visits to the dentist (typically every three to six months).\textsuperscript{56,57} Management of secondary infections (e.g., candidiasis) is often required concurrently with attempts to address xerostomia and SGH.

Tobacco use is associated with dry mouth\textsuperscript{7} and ideally should be minimized or discontinued altogether. Assessment of tobacco use is important for comprehensive treatment planning, early recognition of oral mucosal changes, and integration of tobacco-use cessation counseling, including pharmacotherapies.\textsuperscript{58}

Maintaining adequate hydration is also important for patients with dry mouth, who often find temporary relief by frequently sipping water, sucking on ice or using a humidifier during sleep.\textsuperscript{10,36}

**Caries prevention and control.** Patients with salivary gland hypofunction are at high risk of experiencing dental erosion,\textsuperscript{59} demineralization and dental caries,\textsuperscript{60} which often affect coronal tooth structure around existing restorations and exposed root surfaces. Diminished salivary gland function should be considered part of a comprehensive caries risk assessment for all patients, particularly
those at high risk who likely will benefit from a more aggressive approach to caries management and prevention.\textsuperscript{56}

Salivary hypofunction is highlighted by quantitative and qualitative changes in oral secretions, culminating in the possibility of reduced buffering capacity and antibacterial activity, altered dental pellicle formation, reduced amounts of bioavailable calcium and phosphate, and a lack of oral clearance that places the dentition at increased caries risk.\textsuperscript{56,61} The presence of an acidic oral environment caused by a highly acidogenic microflora and dietary choices, including more acidic foods or drinks, may present a significant caries challenge.

Patients with SGH may benefit from pH neutralization strategies when buffering capacity is in question. These strategies may include traditional methods such as stimulating saliva by using sugar-free gum or candies, as well as pharmacotherapies.\textsuperscript{56}

Although regular use of over-the-counter fluoride dentifrices effectively reduces caries, products containing higher concentrations of fluoride often are recommended for patients with SGH who are at high risk of experiencing dry mouth.\textsuperscript{56,62} Prescription-strength fluoride dentifrices and gels designed for daily use in high-risk patients commonly contain 1.1 percent sodium fluoride, and generally are well tolerated in patients with increased dentinal sensitivity.\textsuperscript{63} Fluoride gels can be applied with a toothbrush or delivered in trays to maximize surface exposure.

In-office fluoride therapy is generally applied in the form of a gel or varnish. The daily use of 1.1 percent neutral sodium fluoride toothpaste or gel (contains 0.5 percent fluoride ion), or at least weekly use of 0.2 percent neutral sodium fluoride mouthrinse (contains 0.09 percent fluoride ion), combined with the application of 5 percent neutral sodium fluoride varnish (contains 2.26 percent fluoride ion) at least every six months, is recommended for at-risk patients of all ages.\textsuperscript{64,65} Professional office treatments, home-use fluoride products, dental sealants and dietary counseling are considered the first line of defense in caries prevention.
In 2011, the Council on Scientific Affairs (CSA) published its first evidence-based clinical recommendations on non-fluoride caries preventive agents. In these recommendations, a CSA expert panel concluded that “[i]n children aged 5-16 years, supervised consumption of chewing gum sweetened with sucrose-free polyol (xylitol-only or polyol combinations) for 10 to 20 minutes after meals marginally reduces the incidence of caries.” In addition, regarding the use of xylitol lozenges or hard candies, a majority of the CSA expert panelists recommended that at-risk children ages 5 and above consume from 5 to 8 grams of xylitol per day, divided into 2 or 3 doses after meals.

Candidiasis prevention and control. Candidiasis is a common mucosal infection in patients with salivary hypofunction. Topical therapy with nystatin or clotrimazole (available in suspensions, powders, creams, ointments, lozenges or pastilles) may provide effective treatment for many patients who have uncomplicated oral candidiasis without esophageal involvement. Commercially available nystatin suspensions have a high sucrose content and should be used with care or avoided in dentate patients with dry mouth. Patients with dry mouth may find lozenges and pastilles difficult to dissolve and irritating to the oral mucosa.

Systemic antifungal agents for the treatment of candidiasis include fluconazole and itraconazole. The clinician must take care to treat not only the oral cavity but also any removable dental appliance, including nightguards, to avoid reinfection. Antifungal therapy, topical or systemic, generally is prescribed for seven to 14 days.

Pharmacotherapy with salivary stimulants. Stimulation of salivary output can be achieved using pharmacological agents known as “sialogogues.” Currently, pilocarpine and cevimeline are approved by the U.S. Food and Drug Administration for treating dry mouth that is due primarily to SS or radiation therapy. Pilocarpine and cevimeline hydrochloride are cholinergic, parasympathetic agonists, and both are well-tolerated medications.

The recommended dosage for pilocarpine is 5 milligrams four times per day, and the dosage for cevimeline is 30 mg three times per day. Response to these medications may vary based on the
amount of healthy acinar cells within the salivary glands. Patients with extensive salivary gland
damage, such as those with radiation-induced SGH, may not respond as well as do patients with less
severe damage. The use of cevimeline and pilocarpine is contraindicated in patients with
hypersensitivity, narrow-angle glaucoma and uncontrolled asthma, and these agents should be used
with caution in patients using β-blockers.

Ophthalmic formulations of muscarinic agonists may cause visual blurring, especially at night. Patients
using cevimeline or pilocarpine should be advised to exercise caution or refrain from driving at night or
performing hazardous activities in reduced lighting.

The adverse effects associated with cevimeline and pilocarpine are similar, primarily sweating, nausea
and rhinitis.44,72 Other, less common adverse effects with both medications include headache, sinusitis,
and diarrhea, but the incidence of these adverse effects is not appreciably different from that seen in
patients treated with placebo. It is advisable to consult the medication package insert for additional
adverse effects with less frequent occurrence.

**Palliative care.** The high prevalence of xerostomia among the general population has generated a
market for numerous over-the-counter products for dry mouth, including oral patches, rinses, lozenges,
toothpastes, sprays, gels, and chewing gums.

Despite the wide array of topical dry-mouth formulations, there is no clear consensus as to the most
efficacious ingredients or products for alleviating oral dryness. Authors of a 2011 Cochrane review of
topical therapies for managing dry mouth concluded that “there is no strong evidence that any topical
therapy is effective for relieving the symptom of dry mouth.”73 The same Cochrane review did find that
oxygenated glycerol triester saliva substitute spray was more efficacious than an electrolyte spray.73

Patients should be aware that because of the dynamic nature of the oral cavity, salivary substitutes are
removed from the mouth during swallowing, which shortens their duration of effect. Also, salivary
substitutes do not provide the protective functions of saliva.
Use of sugar-free gum. Mastication stimulates the production of saliva. Several studies on topical dry-mouth products have found that patients with residual salivary function preferred chewing gum over other interventions. Authors of a 2010 systematic review reported that the use of salivary stimulants, including sugar-free chewing gum, in patients with residual salivary function appeared to be more helpful than using salivary substitutes. However, there is insufficient evidence to prove chewing gum is superior to other interventions in alleviating dry mouth symptoms.

Alternative treatment. Four systematic reviews have considered acupuncture administered to patients with xerostomia following radiation therapy for cancer of the head and neck region. Two of the systematic reviews found only limited evidence of improved salivary flow or reduced xerostomia-related symptoms; the other two systematic reviews did not find sufficient, high-quality evidence to evaluate acupuncture’s safety or efficacy in managing xerostomia. Researchers are currently evaluating gene therapy and transplantation in human salivary glands, which has shown potential in improving salivary secretion.

CONCLUSION
Dentists are often challenged when diagnosing and treating patients with xerostomia and salivary gland hypofunction, which can have potentially devastating effects on the oral cavity. Early detection, comprehensive evaluation and diagnostic testing may prevent significant oral disease and lead to multidisciplinary care that includes collaboration with physicians.

Patient education, management of systemic conditions associated with salivary dysfunction and implementation of preventive measures to reduce oral disease are critical components of patient care. An evidence-guided approach to xerostomia management should focus on providing suitable interventions to relieve dry mouth symptoms, reduce oral complications, and improve quality of life.
REFERENCES


