36. Therapy of Oral and Cutaneous Dryness Manifestations in Sjögren's Syndrome

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36.1. Background

Sjögren's syndrome (SjS) is characterized by dry eyes and dry mouth. This chapter will concentrate on the treatment of dry mouth and other mucosal surfaces, particularly skin and vaginal tissues.

The importance of oral dryness extends far beyond simple difficulty in eating certain foods or increased frequency/expense of dental problems. Women, who are disproportionately affected by this disorder compared with men, socialize around eating. The inability to eat the same foods with family and friends impact on their overall quality of life, as measured by the "Oral Health Quality/Assessment Scales" [1, 2].

Women increasingly engage in "working" breakfast, ~~lunch~~ lunch, and dinner meetings, as well as the need to give oral presentations. All of these activities are profoundly impacted by dry mouth and difficulty with talking due to oral dryness. For example, it may be necessary to pause for a sip of water every few sentences in order to be able to spend hours on the phone or give public presentations. Tooth loss leads to expensive and often painful dental restorations, but also may alter the nutritional intake, as the patient is unable to chew or swallow particular foods.

A first step in the effective management of SjS is the recognition of medications with drying ~~anti-cholinergic~~ anticholinergic side effects. These include blood pressure medications, sleeping aids, anti-convulsant medications, and drugs designed to treat symptoms of neuropathy. Indeed, more than 40% of prescription medications are listed to have ~~anti-cholinergic~~ anticholinergic side effects [3].

The use of ~~anti-cholinergic~~ anticholinergic medications at bedtime may play a large role in sleep disturbances and the accompanying symptoms of fatigue often associated with SjS. The interruption of sleep due to dryness may result from a vicious cycle of drinking more water and resulting polyuria that leads to morning fatigue. Thus, patients might be encouraged to drink less water after dinner and use oral lubricants and lip balm to soothe dry lips, in order to avoid sleep disruption due to need for urination.

The treatment of dryness symptoms remains unsatisfactory, due in part to the poor correlation of patient symptoms of oral discomfort with objective measurement of salivary flow rates [4]. There is a general misconception that dryness results from the destruction of the salivary glands, when only about 50% of the acini/ductal cells are destroyed in patients with severe dryness. This points out the importance of the inflammatory process on the neural innervation and post-neural salivary gland function induced by local production of cytokines and metalloproteinases. Stimulated saliva production correlates most closely with markers of inflammation [5].

However, symptoms of dry mouth (like dry eyes) are dependent on a "functional circuit" in which afferent nerves from the mucosal surface travel to the midbrain ~~(salvatory~~ (salivatory nucleus) [6]. The

midbrain also receives input from higher cortical regions [7] that mediate including taste, smell, hearing, and anxiety. Careful studies of the fifth cranial nerve's sensory afferents ~~localizes~~ localize the problem to the level of the gasserian ganglia rather than the trigeminal ganglia [8].

The discrepancy between signs and symptoms of dry mouth is extremely important clinically. It is most apparent in those patients with "burning mouth" syndrome, where severe symptoms are not accompanied by objective evidence of oral dryness on exam or a dramatic decrease in the flow salivary flow rate by scanning technique [9–13]. This emphasizes the role of the central nervous system (central sensitization) or localized neuropathy in the generation of symptoms and how the patient perceives the severity of "dryness."

Patients with clinical depression, anxiety, neuropathy, Alzheimer's disease (even in the presence of drooling), and multiple sclerosis frequently have complaints of dryness [14, 15]. This indicates the importance of cortical influence and cholinergic white matter (cholinergic) outflow tracts.

The first line of treatment for dry mouth includes topical agents to lubricate and facilitate swallowing and talking, as well as lip balms to moisturize and soothe the lips. In addition, over the past 20 years, a variety of mechanical and electrical devices placed in the mouth have been shown to stimulate basal saliva flow [16, 17]. For the past 20 years, a variety of electrical devices (such as the Salitron) have been approved by FDA but have not proven ~~cost effective~~ cost-effective [18]. However, these devices do establish the role of mechanical stimulation in stimulation of saliva. As such, patients need to recognize the importance of mechanical stimulation in saliva stimulation and the importance of brushing their tongue and buccal mucosa when brushing their teeth, as well as frequent use of sugar-free lozenges.

In addition, other sicca symptoms include dryness of the skin (xerosis), nasal dryness, and vaginal dryness [19]. The need to keep the nasal passages clear and moist will prevent mouth breathing, particularly at night, when the basal secretory rate is diminished. The role of smell is closely linked to gustatory stimulation [20].

36.2. General Approach to Dry Mouth

36.2.1. Oral Hygiene and Self-Care by the Patient

Approaches to clinical management of oral sicca symptoms are generally the same for primary or secondary SjS. The quality of information available from resources on the Internet or from patient support groups varies widely.

Current recommendations by the American Dental Association [21–23] include:

- Use of dental floss after EACH meal, AND fluoride – either as toothpaste or a mouth rinse daily.
  - Carrying portable toothbrush and fluoride toothpaste is a very worthwhile practice for patients with SjS.
- Avoidance of sucrose, carbonated beverages, juices, and water with "sweetener" additives.
- Avoidance of oral irritants (e.g., coffee, alcohol, and nicotine).
- Maintenance of good hydration by taking regular sips of water and drinking sugar-free liquids (see "Fluids" below).
- Use of toothpastes specifically designed for dry mouth, which lack detergents (such as sodium laurel sulfate, which is the foaming agent in most toothpastes). These substances, present in many types of toothpaste, can irritate dry mouths.

Some fluoride-containing toothpastes may lead to brown discoloration of the teeth. Many of these “dry mouth” toothpastes are widely advertised, but have not been carefully studied in terms of their outcome for dental caries or tooth loss.

- One commercially available toothpaste (Biotene®) was found to give improved symptomatic relief in SjS patients, although no change in the microbacterial composition of the biofilm was noted [24, 25].

We strongly encourage our patients to use toothbrushes with features that improve effectiveness, such as ~~inter-dental~~ interdental brushes (for cleaning between teeth) and electric toothbrushes. Table 3 shows suggestions for dental products that are helpful to patients with SjS.

A number of basic measures are used to prevent as well as treat dry mouth in those with SjS. The published evidence supporting these measures consists largely of clinical experience and small case series [25]. Several older double-blind studies in SjS patients demonstrated that the addition of mucins or lactoperoxidase to carboxymethylcellulose (CMC) was superior to CMC alone [24, 26]. A small single-blinded study using a commercially available product (Oral Balance®) also showed symptomatic benefit [24].

The following measures for prevention of dryness, stimulation of secretions, dental prophylaxis, and attention to complications should be used in all patients with dry mouth due to SjS, regardless of symptom severity:

1. Avoidance of drying medications that may worsen oral dryness, especially those with ~~anti-cholinergic~~ anticholinergic side effects. These include over-the-counter antihistamines, cold and sleep ~~remedies;~~remedies.
2. Avoidance of smoking and ~~alcohol;~~alcohol.
3. Maintenance of open nasal passages to avoid mouth breathing (see ‘Nasal Dryness’ ~~below);~~below).
4. Use of room cold humidifiers, particularly at night, in areas that are dry or ~~windy;~~windy.
5. Stimulation of salivary secretions, using sugar-free salivary stimulants (e.g., chewing gums and ~~lozenges);~~lozenges).
6. Careful chewing of food before swallowing (see ‘Topical Stimulation of Salivary Flow’ ~~below);~~below).
7. Meticulous oral hygiene and regular dental care, and avoidance of pre-processed “soft” foods that may be high in sugar content (see ‘Basic Dental Care’ below and ‘Prevention of Dental Caries’ below).
8. Recognition of oral candidiasis that may mimic or exacerbate dry mouth symptoms (see ‘Oral Candidiasis’ below).

Various solutions – ranging from water to forms of artificial saliva – can be used to replace oral secretions. We suggest frequent sips of water, because of convenience, low cost, and efficacy. The water does not have to be swallowed, but can be rinsed around the mouth and expectorated. Although water provides temporary moisture, it does not provide the lubricating properties that are characteristic of the mucin/water mixtures that constitute normal saliva.

Patients should be aware that excessive water sipping might actually reduce the mucus film in the mouth and increase symptoms. If water consumption is excessive, especially in the evening, nocturia can occur, resulting in sleep disturbance that may worsen fatigue, cognitive difficulties, and pain that some patients experience.

We advise patients to avoid acidic beverages, which may adversely affect dental enamel. Examples of common beverages and their relative acidity include:

- Carbonated waters have high acidity
- “Energy drinks” are usually acidic
- Flavored waters are often acidic
- Cola drinks pH 2.6 (Black Cherry soda: highest acidity and sugar)
- Tea, herbal pH 3.2
- Coffee pH 5.0
- Tea, black pH 5.7–7.0
- Water from tap pH 7.0 (neutral)

The maintenance of pH in the oral cavity is highly important [27]. When the pH in the oral cavity is stable, there is a decrease in the amount of demineralization that takes place. Further, the pH of the oral cavity affects the ~~micro flora~~microflora [28], the ~~biofilm~~biofilm, and the ability of bacteria to adhere to the dental enamel [29]. The pH and buffer capacity in the parotid saliva of individuals with SjS are much lower when compared with those in normal control individuals. The buffer systems responsible for the human saliva-buffering capacity include bicarbonate, phosphate, and protein. Even a minor drop in pH can result in dental caries or damage to the teeth by erosion [30, 31].

36.3. Additional Dental Needs of the SjS Patient

36.3.1. Background

At most medical centers and for rheumatologists in practice, communication with dentists and specialists in Oral Medicine is quite limited. However, rheumatologists need to be familiar with the terminology used by Oral Medicine in order to read the relevant literature published on SjS, and to advise patients regarding particular dental procedures that may influence their medical status. Radiation therapists have developed a close working relationship with Oral Medicine to prevent and treat oral complications, but similar interactions for rheumatologists are uncommon. Therefore, we will review basic terminology and approaches as a background to specific discussions listed below.

Tables 36.1 and 36.2 present a series of items that the rheumatologist may need to understand in order to communicate effectively with the dentist. These items include:

- The contents of saliva
- Biofilm
- Dental plaque and accelerated caries
- Structure of dental enamel and its dissolution based on low pH
- Role of fluoride in maintaining oral health
- Dental restorations, including veneers
- Whitening or bleaching agents for cosmetic dentistry

Patients may require:

- Additional visits for their oral hygiene, ranging from every 3 to 6 ~~months;~~months
- Topical fluoride treatment after their dental ~~cleaning;~~cleaning
- Use of a stronger fluoride applied by dental trays used at ~~night;~~night
- Use of calcifying agents such as MI ~~paste;~~paste

- Topical antibiotics to retard gum ~~recession.~~recession

In individuals with SjS, there is an increase in dental caries (usually root and incisal caries), appearing as destruction around the necks of the teeth and even on the labial and incisal surfaces [32].

Dental plaque, consisting of more than 500 species of bacteria in a mature state, is a complex biofilm of microbes that adheres to the surfaces of teeth and provides a reservoir for oral microbial pathogens [33]. Streptococci account for approximately 20% of the total number of oral bacteria, and they are predominantly the first colonizers of freshly cleaned enamel surface. These bacteria are also the primary causative agents of biofilm formation and dental caries.

The bacteria normally are dislodged and expelled from the tooth surfaces and oral cavity by the mechanical forces of salivary flow and tongue movement [34]. The alteration of bacterial flora occurs with dryness due to causes other than SjS, including anxiety or medications [14].

SjS, as well as other conditions including xerostomia associated with aging, also increases a person's likelihood of contracting opportunistic infections such as oral candidiasis and the proliferation of cariogenic microorganisms [35].

A study demonstrated that persons with primary SjS were reported to have higher numbers of cariogenic and acidophilic microorganisms in comparison with those found in control individuals [36].

Another comprehensive study, carried out with interviews and clinical oral examinations of 53 persons with primary SjS and 53 age-matched control individuals, found that those with primary SjS had more teeth extracted, more problems with their teeth in their lifetime, and higher dental expenses, compared with the control group.

In a separate study [37], the number of decayed, missing, or filled teeth was higher in both the younger and older groups of persons with primary SjS, compared with the normal control individuals. The young persons had, on average, seven teeth missing, compared with two missing in the control individuals. Those with primary SjS had more frequent dental visits compared with control individuals.

Even with excellent oral hygiene, individuals with SjS have elevated levels of dental caries, along with the loss of many teeth early in the disease. Pedersen et al. [36] reported that persons, who brushed their teeth with toothpaste containing fluoride and visited their dentist more frequently, still had higher numbers of missing, filled, and decayed teeth, along with a higher gingival index.

Fluoride is an extremely important element in the prevention of dental caries [32, 38–42]. However, certain regions do not maintain fluoridation in the water supply; patients living in these areas are at particular risk. In addition, the increasing use of non-fluoridated bottled water in place of fluoridated tap water is having a profound effect in decreasing fluoride exposure for many patients.

Topical fluoride promotes remineralization of teeth by the development of a crystalline protective veneer at the site of demineralization and inhibition of bacterial metabolism and acid production. Fluoride may be applied in various forms, depending on the severity of disease, including mouth rinses, fluoride gels applied at home in custom-fitted trays, and by dental office-based application of fluoride varnish [32, 38–42].

Chemoprophylaxis – Several approaches may be taken in an effort to reduce oral bacterial flora, including the use of chlorhexidine (CHX), a topical antimicrobial agent, and products containing baking

soda, ~~bicarbonate~~ bicarbonate, or xylitol (see below) [32, 43–45]. In addition, CHX has an antifungal affect that may also benefit patients with SjS. CHX may also be used to soak dentures overnight. Dentures may be a source of bacterial infection as well as recurrent candida infection, and patients should not wear dentures overnight.

Polyol ~~sweeteners~~ sweeteners, such as xylitol and sorbitol that are not fermentable by acid-producing bacteria, are of low cariogenic or noncariogenic potential; they may prevent or limit demineralization and promote the remineralization process. Xylitol may be a useful adjunct to other anti-caries treatments, but should not be considered in patients with SjS as a substitute for fluoride or other well-established interventions [46, 47].

Patients with SjS may have more difficulty wearing dentures because of the decreased moisture in the mouth. No ~~adequately-controlled~~ adequately controlled clinical trials have addressed this question. In general, dentures cannot replicate the efficiency and comfort of natural teeth.

There are scattered case reports regarding the ability of patients with SjS to handle dental implants, although the often-poor status of oral tissues and bone loss in SjS patients may cause difficulty. The majority of reports for SjS patients appear favorable, but do not provide long-term follow-up [48, 49]. Decisions regarding use of implants in a given patient with SjS should be made on an individual basis, and the limited evidence should be acknowledged.

The safety of home products for whitening or brightening of teeth in patients with dry mouth and salivary gland dysfunction has not been studied. However, the use of such products should be avoided, since there may be increased risk from the acidity of some over-the-counter products designed for use in patients with normal salivary flow and content.

If professionally applied whitening processes are considered, the use of a rematerializing solution containing calcium phosphate and a fluoride treatment may be beneficial in conjunction with a bleaching treatment. Such procedures should only be performed after consultation by the patient with their dry mouth dentist.

36.4. Particular Oral Needs of the SjS Patient to ~~bc~~ Be Assessed by the Rheumatologist

The particular needs for evaluation and treatment in SjS patients by the rheumatologist are summarized in Table 36.3. These include:

- Recognition of oral candidiasis, particularly under ~~dentures;~~dentures
- Need for secretagogue ~~therapy;~~therapy
- Recognition of “burning mouth syndrome” out of proportion to objective ~~dryness;~~dryness
- Recognition of medications with ~~anti-cholinergic~~ anticholinergic medications (often from other ~~physicians).~~physicians)

The response to therapy may be evaluated by ongoing assessment for common clinical signs of dry mouth. These include:

- Difficulty with swallowing or speech due to ~~dryness;~~dryness
- Absence of a pool of saliva on the floor of the ~~mouth;~~mouth
- “Lipstick sign” (spreading of the patient’s lipstick onto ~~teeth);~~teeth)
- “Sticking” of a gloved finger to the ~~mucosa;~~mucosa
- Frequent occurrence of erythematous ~~candida;~~candida

- Atrophic glossitis (or lack of papilla) on the ~~tongue,~~tongue
- Dental caries at the gingival margin, especially of the mandibular ~~incisors,~~incisors
- Dry, cracked ~~lips.~~lips

36.5. Use of Secretagogues

In patients who do not respond adequately to the basic measures described above, and those who continue to have signs or symptoms of dry mouth despite the measures noted above, we suggest additional measures, including the use of muscarinic agonists such as sialogogues.

Use of a systemic ~~sialogue~~ sialogogue (administered orally) is indicated in patients with more than very mild salivary dysfunction, who do not achieve sufficient salivary excretion with topical stimulants such as those described above. Two muscarinic agonists, pilocarpine and cevimeline, increase salivary flow and improve symptoms of dry mouth [22, 50–57]. Pilocarpine and cevimeline are most effective in SjS patients with early disease and thus greater residual excretory capacity. A double-blind trial has recently been reported for a buccal insert that releases pilocarpine [58] and the early promising results have not yet been confirmed [59].

Their use of cholinergic secretagogues may sometimes be limited by poor tolerance, largely due to cholinergic side effects including undesirable increased/excessive perspiration. Although very uncommon, patients should also be cautioned about driving at night or performing hazardous activities in reduced lighting, because they may experience altered visual acuity or impaired depth perception.

Pilocarpine, a muscarinic agonist that stimulates predominantly muscarinic M3 receptors, can significantly increase aqueous secretions in patients with residual salivary gland function. The usual dose is 5 mg three or four times/day. It is most effective when taken four times/day because of its short duration of action. We thus suggest that patients try to take the medication four times daily if they do not receive adequate symptomatic relief with three times daily dosing. Side effects, including sweating, abdominal pain, flushing, or increased urination, may limit its use. In some patients with unacceptable levels of side effects at the full dose, a reduced dose of 2.5–3.75 mg three times daily, or 5 mg twice daily may still provide benefit.

In addition to effects upon xerostomia, pilocarpine may improve symptoms of ocular dryness, although without any objective change in tear production.

In the largest randomized trial that demonstrated the benefit of pilocarpine, 357 patients were randomly assigned to receive either pilocarpine (5 or 2.5 mg every 6 h) or placebo for 12 weeks. The following findings were observed:

- A significantly greater proportion of patients receiving pilocarpine (5 mg), compared with those who received placebo, experienced improvement in global assessments of symptoms of both dry mouth and dry eye (61% vs. 31%, and 42% vs. 26%, respectively).
- There was no difference in benefit found between pilocarpine 2.5 mg every 6 h and placebo.
- Sweating and increased urinary frequency were both more common with pilocarpine 5 mg compared with placebo (43% vs. 7% and 10% vs. 2%, respectively).
- No serious adverse events occurred, and only 3% of patients taking pilocarpine 5 mg withdrew from the study due to drug-related adverse events.
- The overall withdrawal rate did not differ between the three groups (6–7%).

There are no published studies that have examined the long-term efficacy of pilocarpine in patients with SjS.

Due to the potential for pilocarpine to stimulate the muscarinic M2 receptor, theoretical cardiac or lung (asthmatic complications) might occur, and therefore, patients with these historical features were excluded from clinical trials of pilocarpine or cevimeline [22, 50, 60–64]. However, clinical practice with these agents in patients with radiation xerostomia (who frequently have a long history of smoking and cardiac disease) has not shown this to be a clinically significant problem [55].

Cevimeline is taken three times a day (optimally about half an hour before meals), and can be taken up to four times a day (including an additional tablet at bedtime to help with nocturnal dryness).

- Cevimeline has a longer half-life in serum, and longer occupancy on receptor, which correlates with patient salivation profile [55].
- Pilocarpine is taken four times a day, and the patients typically experience a brief "spurt" of saliva due to its relatively short half-life in the sera.

The two drugs have not been compared directly. Issues that determine choice principally include cost to the patient, convenience, individual clinical response, and tolerance of adverse effects.

The choice between pilocarpine (Salagen®) and cevimeline (Evoxac®) is largely determined by individual factors, since both appear similarly effective. However, it has been the experience of several SjS centers that the longer half-life of cevimeline leads to improved tolerance and lower side effects.

Some patients do not respond sufficiently well to the muscarinic agonists to justify continued use, especially when cholinergic side effects are present. However, in those with an inadequate response, it is important to examine the patient carefully to rule out oral candidiasis, which may be responsible for a lack of symptomatic improvement with use of a secretagogue. The examination should include removal of upper dentures and determining if signs such as angular cheilitis are present.

When initiating therapy with these ~~agents…~~agents:

- We suggest gradually increasing the dose and taking it about 30 min before meals.
- We increase the dose gradually (starting once/day for a week).
- We add a proton pump inhibitor if needed to avoid gastric bloating and sudden onset of sweating.
- We suggest a trial of at least ~~3 months~~ 3-months duration if the medication is tolerated, since the response is frequently delayed.
- If patients do not tolerate one preparation, they may try the other preparation.

Major side effects of cevimeline include excessive sweating, nausea, rhinitis, diarrhea, and visual disturbances. Use of lower doses in patients with poor tolerance of the full dose has been reported. Efficacy in lower dosing is obtained by dissolving the desired fraction of a ~~30 mg~~ 30-mg capsule's contents in water, or to employ a "rinse-and-spit" regimen (also called "cevimeline gargle") to minimize systemic absorption [64].

In randomized placebo-controlled trials, cevimeline significantly increases salivary flow and ~~patient~~ patient's "oral quality of life" [65]. The efficacy of cevimeline was illustrated in a study that randomly assigned 197 patients with either primary or secondary ~~SjS,~~ SjS to cevimeline or placebo [66]. The following outcomes were observed:

- Patients' global assessments of dryness were improved significantly more often by cevimeline 30

mg three times daily than by TID doses of 15 mg or placebo (65%, 32%, and 35%, respectively).

- The most common adverse events seen more often with the drug (30 or 15 mg TID) than placebo were nausea (21% and 12% vs. 7%), increased sweating (18% and 5% vs. ~~1%)~~ 1%), and diarrhea (16% and 14% vs. 7%).
- Withdrawal from the study for adverse events was more common in patients on cevimeline (30 or 15 mg TID) compared with placebo (16.1% and 13.8% vs. 4.3%, respectively).
- Serious adverse events were seen in <3% of patients, and were not more common with cevimeline.

Drugs that inhibit cytochrome CYP2D6 and CYP3A3 also inhibit the metabolism of cevimeline. Individuals who are known to be deficient in these cytochrome isoenzymes should use cevimeline with caution.

36.5.1. Other Cholinergic Agonists

Bethanechol and pyridostigmine are cholinergic agonist agents that are approved in the USA for use in urinary retention and myasthenia gravis, respectively, but not for SjS. They have mixed muscarinic and nicotinic activity, and are used much less often for SjS because of greater adverse effects ~~compared~~ (compared with pilocarpine and cevimeline). However, they have been shown to provide palliative care of radiation xerostomia in small double-blind studies [67–69].

Amofostine is an agent that may provide protection of the salivary glands during radiation therapy [70], but was not as effective as pilocarpine in patients with xerostomia after radiation or SjS [71].

Bromhexine (a mucolytic agent) also showed palliative response in radiation xerostomia, and had been suggested for symptomatic treatment in SjS [72–74]. However, this agent has now been withdrawn from the market although it exhibited a good safety profile [75]. These agents have theoretical benefit, but they have not been subject to controlled clinical trials to demonstrate efficacy in SjS. Anecdotal trials of these agents in SjS, as well as amofostine, have been disappointing in our clinic particularly in relation to their cost.

36.5.2. Additional Topical Treatments

- Topical interferon alpha [76]. Although oral interferon alpha was promising in early studies, results were far less encouraging in a subsequent larger well-designed study [77–79]. Further studies will be needed before this medication can be recommended in this setting. However, the use of interferon alpha in patients with hepatitis C and sicca symptoms has exacerbated their dryness ~~complaints;~~complaints.
- Acupuncture and herbal teas [80] that may result in qualitative changes in saliva as well as increased flow in some patients ~~[81]~~[81].
- Anhydrous crystalline maltose to stimulate masticatory and gustatory response ~~[82],~~[82].
- Anetholetrithione which exhibited modest benefit in ~~a~~ an initial small ~~double-blind~~ double-blind trial [83], but subsequent larger trials were not ~~reported~~reported.

36.5.3. Systemic Therapy

36.5.3.1. TNF-Alpha Blockers

Short-term studies with infliximab, a TNF-blocker, showed significant improvements in SjS symptoms

in an initial open trial [84]. However, randomized, ~~double-blind,~~ double-blind, placebo-controlled studies showed no indication of increased efficiency in persons treated with infliximab [85]. Randomized, double-blind, placebo-controlled studies with etanercept also showed no reduction of sicca symptoms in SjS [86–88].

Rituximab, known for its tolerability, is an anti-CD20 antibody that is effective in persons with various autoimmune diseases. Several small controlled studies have shown a mild increase in saliva flow in a subset of patients with early disease [89–91]. Salivary biopsies from treated patients have also shown decreases in lymphocytic infiltrates [92, 93].

Epratuzumab, directed against the B-cell epitope CD22, appears to function by modulation of B-cells than by depletion of these cells from the circulation [94]. Steinfeld et al. presented preliminary results in the treatment of primary SjS including increased salivary flow in the ~~drug-treated~~ drug-treated cohort. The study consisted of 16 Caucasian individuals, two of whom discontinued due to complications. However, ten persons reported adverse events, which included acute infusion, dental abscess, transient ischemic attack with secondary seizure, and osteoporotic fracture. Non-serious adverse events included headache, paresthesia, and acute infusion reaction, which resolved quickly [94].

Recently, a monoclonal anti-BAFF antibody (belimumab) has shown promising results in SLE leading to FDA approval. Trials of belimumab are just beginning [95, 96].

36.6. Oral Candidiasis

Oral candidiasis, a common complication of SjS, occurs in more than ~~one-third~~ one-third of patients [97–99]. Symptoms include a painful mouth, sometimes with a burning sensation, and sensitivity to spicy or acidic foods. Oral candidiasis is particularly frequent following antibiotic treatment or the use of glucocorticoids (see “Clinical Manifestations of Oropharyngeal and Esophageal Candidiasis”).

Oral candidiasis is one of the most common oral infections. In 1980, an inverse relationship between salivary flow rates and the level of Candida infection was described [100]. Persons with SjS have also been reported to have *Candida albicans* more frequently than the general population at a given salivary flow rate, indicating a role for qualitative anti-candida factors such as lysozyme content in saliva [101, 102].

Findings in SjS patients with oral candidiasis include:

- Diffuse or patchy erythema, and (less often), white patches on the mucosal surfaces.
- The tongue, buccal mucosa, palate, ~~lips~~ lips, and the corners of the lips may be affected.
- There may be loss of tongue papillae.
- Angular cheilitis and atrophic changes of the buccal mucosa are common manifestations in SjS.

In patients with SjS and oral candidiasis, several particular factors require consideration. Because most antifungal preparations for oral use contain sugar to improve taste, such agents should not be used immediately before bed without following with a thorough tooth brushing.

An alternative oral ~~“off-label”~~ “off-label” approach preferred by some experts is use of topical Nystatin Vaginal tablets (100,000 units/tablet) sucked on like a lozenge three to four times/day for 7–10 days. These tablets do not contain fermentable carbohydrate in the carrier.

- We initially treat with ~~clotrimazol~~ clotrimazole (200 mg/day) for 5 days, and treat angular cheilitis using topical ~~clotrimazol~~ clotrimazole cream.

- We advise use of a compounded oral mouth rinse of the type recommended by radiation therapists for mucositis.
  - The rinse should be used for 2 min (rinse plus gargle) three times/day for 2–3 weeks.
  - These rinses are known by various names, such as “Stanford Mouth Rinse” or “Miracle Mouthwash.”
  - We use a mixture containing:
    - Mylanta (aluminum hydroxide/magnesium hydroxide) 240 mL (as a ~~vehicle),~~vehicle)
    - Diphenhydramine 20 ~~mL,~~mL
    - Nystatin 20 ~~mL, and~~mL
    - Doxycycline 20 ~~mL.~~mL
  - The components can be ordered separately and mixed by the patient.
  - Variations of this mouth rinse may contain viscous lidocaine, low-dose glucocorticoids, or brompheniramine/pseudoephedrine elixir.
  - Several mouth rinses used by radiation therapists may also be helpful, ~~as may:~~such as:
    - A homemade remedy of 12 tsp. salt and 1/2 tsp. baking soda in 8 oz ~~water,~~water
    - A wound rinse with aloe vera ~~extract, and~~extract
    - Carafate suspension as a rinse used twice per ~~day.~~day

There is some concern in patients with severe salivary dysfunction that insufficient local (salivary) levels of medication may be reached with use of systemic medications. Thus, in dry mouth patients who do not respond adequately to systemic medications within 7–10 days, switching to a topical oral antifungal is suggested.

In patients with more persistent oral fungal disease, we recommend the use of nystatin vaginal troches (100,000 units) that are sucked on daily with water sweetened with an artificial sweetener (to improve the taste). Treatment twice daily for up to 4–6 weeks may be required.

- Alternatives include:
  - Miconazole oral gel (sugar-free, 24 mg/mL = 20 mg/g), 5–10 mL four times/day, held in the mouth before ~~swallowing; and~~swallowing
  - Amphotericin lozenges (10 mg) four times ~~daily.~~daily

36.7. Treatment and Management of Cutaneous Manifestations

36.7.1. Treatment of Dry Skin in SjS Is Similar to Managing Xerosis in Other Conditions

1. The patient should moisturize the skin with a fragrance-free cream moisturizer once or twice a day. Moisturizing is performed immediately after bathing or showering, while the skin is still damp, to prevent further evaporation from the skin.
   Sometimes in cases of extreme dryness, an ointment is suggested, for its barrier and protective properties (such as petrolatum jelly or Aquaphor®).
   If ointment is used, then application should be onto damp skin, as the ointment itself does not contain water. Excess greasiness can be blotted with a towel.
   Sometimes a moisturizing cream with ~~beta~~beta- or ~~alpha hydroxy~~alpha-hydroxy acid, or urea, can add extra moisture, but in cases of cracks in the skin, these will sting and ~~irritate~~irritate.
2. Excessive, long, hot showers or baths should be avoided, in addition to heavily fragranced

cleansers.

3. Cleansing of the skin: The usual recommendation is to cleanse with a moisturizing soap such as Dove® fragrance-free bar, or a soap-free cleanser such as Cetaphil® gentle cleanser or Aquanil® cleanser.
   If the xerosis leads to pruritis, then safe anti-pruritic topical treatments are recommended.
4. Over-the-counter lotions containing menthol, camphor (Sarna Anti-Itch Lotion®), 2% lidocaine (Neutrogena Norwegian Formula Soothing Relief Anti-Itch Moisturizer®), and pramoxine (Aveeno Anti-Itch Concentrated Lotion®) are readily available.
5. Oral antihistamines should be used with caution because of their anticholinergic effects. Fexofenidine (Allegra) does not cross the blood-brain barrier and may have slightly less dryness as a side effect. Over-the-counter sleeping medications that contain hydroxyzine (Atarax) or diphenhydramine (Benadryl) are very drying, and may contribute to sleep disturbance.
6. Topical corticosteroids: We generally do not like to use topical corticosteroids, especially the ultra-potent ones, but even the mid-potency ones – for more than a couple of weeks at a time. In the case of inflammatory skin findings, local treatment with potent topical steroids can augment systemic treatments.
   Sometimes topical corticosteroids are used for pruritus, but their use should be limited due to long-term side effects such as skin atrophy, tachyphylaxis, and absorption.
7. We always suggest constant daily sun protection for patients with autoimmune conditions. Because the wavelength of light causing sun sensitivity in autoimmune conditions may not be in the UVB spectrum (290–320 nm), patients should use a broad-spectrum sunscreen.
   - SPF factors refer to UVB protection only, so patients cannot count on simply the SPF factor.
   - Most sunscreens available now have added UVA protection (290–320 nm), commonly from chemical ~~UVA-absorbing~~ UVA-absorbing compounds, such as Parsol 1789 (avobenzone).
8. We prefer physical sun blocks, since wavelengths outside of both UVB and UVA may affect the patient with autoimmune disease.
   - Physical sun blocks contain titanium dioxide or zinc oxide, which reflect rays.
   - One commonly available sun block is Neutrogena Sensitive Skin Sun Block SPF-30®, which uses purely titanium dioxide as its active ingredient.
9. The most effective protection is sun-protective clothing, since it will not wear off as sunscreens do. This includes hats, sun glasses, UV-protective lip balm, long-sleeved shirts (some clothing is sun-repellent).
   Obviously, avoiding excess sun contact altogether is prudent, such as trying to stay indoors during the intense sunlight hours of 10 a.m. to 2–4 p.m.
10. ~~Mucous-promoting~~ Mucous-promoting compounds. Study of the tear film and saliva has shown that SjS symptoms are more than the simple absence of aqueous secretions. In particular, the lubricating film contains a series of mucins and proteins in an emulsified gel. A lipid layer prevents subsequent evaporation. As many of the extraglandular symptoms of SjS may result from decreased lubrication, such as chronic upper airway dryness or vaginal dryness, these agents may part of future treatments. Agents that are currently in trial (particularly for oral and ocular) include:
    (a) Diquafosol, an agonist of the P2Y2 receptor that stimulates net chloride transfer from the serosal to the mucosal side of epithelial membranes [103, 104].
    (b) 15-S Hete, an ~~arachadonic~~ arachidonic acid metabolite, acts as a mucin secretagogue and has been shown to stimulate mucin I production [105].
    (c) Rebamide [106], ecabet sodium ~~[107]~~ [107], and gefarnate [108] have been used in Japan as gastroprotective agents because of their mucus secretary action.

36.7.2. Vaginal Dryness

A gynecologic examination is useful to rule out other causes of painful intercourse and other causes of vaginal dryness.

Sexual considerations: When vaginal dryness does occur as part of SjS, the spouse or partner needs to be reassured that this is a "physiological" problem, and not related to a failure of sexual arousal. Psychological fear of discomfort may further exacerbate the problem. Sterile lubricants such as Astroglide®, KY Brand® jelly or Surgilube® are helpful (and should be liberally applied to both partners for maximal comfort) [109, 110].

- Despite liberal application of lubrication to the female, if the partner's penis is not well lubricated, the female SjS patient will likely experience discomfort during and after intercourse.

Lubricants such as Maxilube® and Astroglide® have slightly different characteristics when compared with KY Brand® jelly or Surgilube®, and yet, share the common characteristics of being water-soluble and non-irritating. 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.~~inserts are now available.

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 physician also needs to assure the female SjS patient that her male partner should also be sensitive to her needs, and actively participate in preparations to help maximize sexual satisfaction for both partners.

The external use of preparations containing petrolatum or oils that "seal in" moisture, such as Vaseline® or cocoa butter, as well as "scented" or "flavored" preparations may lead to maceration and irritation of the sensitive and fragile vaginal mucosal lining, and are to be avoided.

Vaginal dryness in ~~peri-menopausal~~ perimenopausal or ~~post-menopausal~~ postmenopausal women is often related to vaginal atrophy because of declining estrogen levels, and therefore may respond to vaginal topical estrogen creams such as Estrace® (if tolerated without irritation). Cortisone creams are not beneficial in this situation.

If vaginal yeast infection occurs, prompt treatment with clotrimazole topical cream, vaginal suppositories (Gynelotrimin®), or p.o. gluconazole 150 mg is safe and effective. Oral gluconazole's benefit is that it can be started earlier in the day, rather than waiting until bedtime to use cream or suppository. With yeast infection, prompt treatment is essential to avoid rapid escalation of the infection during the day, along with higher level of discomfort for the patient.

On the external vulvar surface, dryness may be treated with lubricating creams, as 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 [111] used on the vulva once or twice a day.

An issue of concern to female SjS patients has been whether or not estrogen/hormone replacement therapy (HRT) at the time of menopause is harmful to their condition [112]. With ~~regards~~ regard to estrogen replacement in general, the clinical evidence is controversial whether the risks of blocking osteoporosis and reducing cardiovascular mortality adequately offset the small increase in risk in breast cancer.

It is also worth noting that the subset of women who had previous hysterectomy/ovariectomy was not found to have increased risk of breast cancer on receiving estrogen replacement [113].

Of importance, some women feel that estrogen replacement improves their quality of life, in terms of mood elevation and by reducing hot flashes and hormone-related vaginal dryness [114–116]. Part of this improvement may relate to the interconversion of hormones to include DHEA, which appears to have beneficial effects on local mucosal surfaces [117] as well as affect [118].

Earlier investigators were concerned that estrogen might have a negative influence on SjS or SLE based on animal studies. At our clinic, we have not seen any deterioration of ~~SjS-related~~ SjS 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 SjS patient who feels that it improves their quality of life. Although the data has not been formally collected in SjS, there have been extensive trials on the use of oral contraceptives and estrogen replacement in SLE patients [114, 115, 119]. These studies have indicated safety in terms of breast cancer and disease activity. However, caution with regard to blood clot risk remains, particularly in the patient with circulating anti-coagulants or a past history of thromboembolic disease.

Nonetheless, estrogens would not be the agent of choice to deal with either ~~post-menopausal~~ postmenopausal osteoporosis or elevated lipid profiles. Other therapeutic alternatives for osteoporosis (alendronate, Fosamax®, and residronate, Actonel®) and other agents for lowering cholesterol (such as statins) are now available, and estrogens are now not the agents of choice for these medical issues.

36.7.3. Special Precautions at the Time of Surgery

SjS patients have particularly unique needs at the time of surgery. Patients with ocular dryness are at increased risk for corneal abrasions in operating rooms (generally have low-humidity environments), and particularly in the ~~post-operative~~ postoperative recovery room, where non-humidified oxygen is blown across their face at a time when they are still too groggy to have adequate blink reflex.

Therefore, we have recommended application of an ocular ointment or gel prior to surgery.

Patients are subject to severe dryness of the mouth as a consequence of their disease but are told to be “NPO” for at least 12 h before surgery (and often longer if they are a later operative case in the day). We have found that patients can safely use their oral mouth sprays for comfort ~~pre-operatively,~~ preoperatively, while not having the risk of gastric contents and aspiration during anesthesia. If possible, patients should request from their surgeons that they be placed in an early slot in the OR schedule.

The anesthesiologist will need to take special precautions with oral intubations, as these patients have “fragile” teeth and often have expensive dental reconstructions and restorations including implants.

Therefore, it is important for the patient to make certain that a “heads-up” note is recorded in – or better yet – on the front – of the chart.

Patients with SjS often have very dry upper airways and minimal use of ~~anti-cholinergic~~ anticholinergic agents to control tracheal secretions. The tenacious mucus secretions may predispose to mucus inspissations and ~~post-operative~~ postoperative obstructions. The use of humidified oxygen and mucolytics may help minimize this process.

Although anesthesiologists and surgeons are familiar with precautions regarding NSAIDs and bleeding risk, they are often less familiar with the relatively long duration of agents such as the new biologic agents. Although most of the literature about increased rate of infection after joint replacements deal with TNF inhibitors, it is likely that similar caveats will apply to additional biologic agents as they become available.

Finally, steroid coverage for "stress" levels may be required in patients on chronic steroids. Also, oral candida is quite common in the ~~post-operative~~ postoperative patient who has been on steroids and recent antibiotic therapy.

Patients should also be permitted to have their eye and mouth moisturizers and other appropriate remedies at bedside if hospitalized.

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Tables:

Table 36.1
Saliva content and stimulation in normal individuals

Saliva functions
• Saliva also breaks down food caught in the teeth, protecting them from bacteria that cause decay. Furthermore, saliva lubricates and protects the teeth, the tongue, and the tender tissues inside the mouth.
• Saliva also plays an important role in tasting food, by trapping thiols produced from odorless food compounds by anaerobic bacteria living in the mouth. Saliva secretes ~~Gustin~~ gustin hormone which is thought to play a role in the development of taste buds.
Stimulation of saliva
• The production of saliva is stimulated both by the sympathetic ~~nervous system~~ and ~~the parasympathetic.~~parasympathetic nervous systems.
• The saliva stimulated by sympathetic innervation is thicker, and saliva stimulated parasympathetically is more watery.
• Parasympathetic stimulation leads to acetylcholine (ACh) release onto the salivary acinar cells. ACh binds to muscarinic receptors and causes an increased intracellular calcium ion concentration (through the IP3/DAG second messenger system). Increased calcium causes vesicles within the cells to fuse with the apical cell ~~membrane~~ membrane, leading to secretion formation.

• ACh also causes the salivary gland to release kallikrein, an enzyme that converts kininogen to lysyl-bradykinin. Lysyl-bradykinin acts ~~upons~~ upon blood vessels and capillaries of the salivary gland to generate vasodilation and increased capillary permeability respectively. The resulting increased blood flow to the acinar allows production of more saliva.
• Lastly, both parasympathetic and sympathetic nervous ~~stimulation~~ stimulations can lead to myoepithelium contraction which causes the expulsion of secretions from the secretory acinus into the ducts and eventually to the oral cavity.
Contents of saliva
Electrolytes:
• 2–21 mmol/L sodium (lower than blood plasma)
• 10–36 mmol/L potassium (higher than plasma)
• 1.2–2.8 mmol/L calcium (similar to plasma)
• 0.08–0.5 mmol/L magnesium
• 5–40 mmol/L chloride (lower than plasma)
• 25 mmol/L bicarbonate (higher than plasma)
• 1.4–39 mmol/L phosphate
• Iodine (mmol/L usually higher than plasma, but dependent variable according to dietary iodine intake)
• Mucus in saliva mainly consists of mucopolysaccharides and glycoproteins
• Antibacterial compounds (thiocyanate, hydrogen peroxide, and secretory immunoglobulin A)
• Epidermal growth factor or EGF
• Various enzymes. There are three major enzymes found in saliva
• α-amylase (EC3.2.1.1). Amylase starts the digestion of starch and lipase fat before the food is even swallowed
• It has a pH optima of 7.4
• Antimicrobial enzymes that kill bacteria
– Lysozyme
– Salivary lactoperoxidase
– Lactoferrin
– Immunoglobulin A
– Proline-rich proteins (function in enamel formation, Ca_2+-binding, microbe ~~killing~~ killing, and lubrication)
• Minor enzymes include:
– ~~salivary~~ Salivary acid phosphatases A + B, *N*-acetylmuramoyl-*L*-alanine amidase
– NAD(P)H dehydrogenase (quinone), superoxide dismutase, glutathione transferase, class 3

aldehyde dehydrogenase, glucose-6-phosphate isomerase, and tissue kallikrein (function unknown)
• Cells: Possibly as much as 8 million human and 500 million bacterial cells per mL. The presence of bacterial products (small organic acids, amines, and thiols) causes saliva to sometimes exhibit foul odor
• Opiorphin, a newly researched pain-killing substance found in human saliva

Table 36.2
Terminology of oral medicine

Oral biofilm
A biofilm is an aggregate of microorganisms in which cells adhere to each other and/or to oral surfaces. They play a key role in dental decay and oral candidiasis.
Biofilms have been found to be involved in a wide variety of microbial infections in the ~~body,~~ body: by one ~~estimate~~ estimate, 80% of all infections including dental decay and oral candidiasis. Biofilms also are important in other mucus membranes where they influence local vaginal immunity, ocular infections, sinus and upper respiratory tract infections found more frequently in SS patients. In addition to the lubricating and antibacterial properties, these secretions may influence extracellular polymeric substance (EPS) involved in cellular recognition of specific or ~~non-specific~~ nonspecific attachment sites on a surface such as dental enamel, or mucosal membranes.
Dental plaque
Dental plaque is the material that adheres to the teeth and consists of bacterial cells (mainly *Streptococcus mutans* and *Streptococcus sanguinis*), salivary ~~polymers~~ polymers, and bacterial extracellular products. Plaque is a biofilm on the surfaces of the teeth. This accumulation of microorganisms ~~subject~~ subjects the teeth and gingival tissues to high concentrations of bacterial metabolites which results in dental disease.
Tooth enamel
The high mineral content of enamel, which makes this tissue the hardest in the human body, also makes it susceptible to a demineralization process which often occurs as dental caries. In SS patients, the lack of saliva leads to poor mechanical removal of bacteria, alteration of the biofilm, and a lowering of the oral pH due to the decreased volume of alkaline secretion and proteins with buffering capacity.
Sugars from candies, soft drinks, and even fruit juices play a significant role in tooth decay, and consequently in enamel destruction. The mouth contains a great number and variety of bacteria, and when sucrose, the most common of sugars, coats the surface of the mouth, some intraoral bacteria interact with it and form lactic acid, which decreases the pH in the mouth. Then, the hydroxylapatite crystals of enamel demineralize, allowing for greater bacterial invasion deeper into the tooth. The most important bacterium involved with tooth decay is *Streptococcus mutans*, but the number and type of bacteria varies with the progress of tooth destruction.
Oral hygiene and fluoride
Considering the vulnerability of enamel to demineralization and the daily menace of sugar ~~ingestion~~ ingestion, prevention of tooth decay is the best way to maintain the health of teeth in SS patients. Naturally occurring calcium fluoride is not the same as sodium fluoride, a byproduct of the fertilizer industry and the fluoride that is added to drinking water. The recommended dosage of fluoride in drinking water depends on air temperature; in the ~~USA~~ USA, it ranges from 0.7 to 1.2 mg/L. Fluoride catalyzes the diffusion of calcium and phosphate into the tooth surface, which in turn remineralizes the crystalline structures in a dental cavity. The remineralized tooth surfaces contain fluoridated ~~hydroxyapatite~~ hydroxylapatite and fluorapatite, which resist acid attack much better than the original tooth did. Thus, despite fluoridation's detractors, most dental health care professionals and organizations agree that the inclusion of fluoride in public water has been one of the most effective

methods of decreasing the prevalence of tooth decay.
Dental veneer in cosmetic dentistry
Veneers were invented initially for Hollywood actors to alter the appearance of actors' teeth. At the time, they fell off in a very short time as they were held on by denture adhesive. Today, with improved cements and bonding agents, they typically last 10–30 years.
Veneers are an important tool for the cosmetic dentist. A dentist may use one veneer to restore a single tooth that may have been fractured or discolored, or multiple teeth to create a "Hollywood" type of makeover. Many people have small teeth resulting in spaces that may not be easily closed by orthodontics.
A problem with cosmetic dentistry in SS patients is that areas of underlying decay are no longer visible for detection or accessible to dental care and thus may progress more rapidly to tooth loss.
Tooth whitening or dental bleaching
Dental bleaching, also known as *tooth whitening*, is a common procedure in general dentistry but most especially in the field of cosmetic dentistry. A child's deciduous teeth are generally whiter than the adult teeth that follow. As a person ~~ages~~ ages, the adult teeth often become darker due to changes in the mineral structure of the tooth, as the enamel becomes less porous. Teeth can also become stained by bacterial pigments, ~~foodstuffs~~ foodstuffs, and tobacco.
There are many methods to whiten teeth: bleaching strips, bleaching pen, bleaching gel, laser bleaching, and natural bleaching. Oxidizing agents such as hydrogen peroxide or carbamide peroxide are used to lighten the shade of the tooth. The oxidizing agent penetrates the porosities in the rod-like crystal structure of enamel and oxidizes interprismatic stain deposits; over a period of time, the dentin layer, lying underneath the enamel, is also bleached. Power or light-accelerated bleaching, sometimes colloquially referred to as laser bleaching, uses light energy to accelerate the process of bleaching in a dental office. Different types of energy can be used in this procedure, with the most common being halogen, LED, or plasma arc.
Although tooth bleaching may be safely done in SS patients in a dentist's office, it should not be done by non-dental individuals who increasingly offer their services at shopping center mall kiosks, spas, salons, or other similar places. In these sites, the "amateurs" greatly accelerate the laser bleaching to save time and this may result in damage to the dental surface and gingival damage.
Even in the dentist's office for the SS patient, it may be necessary to use lesser quantities of lightening agents or to perform on alternate days (rather than on a single day). Even when these ~~precauations~~ precautions are taken, side effects of dental bleaching may include ~~hcmical~~ chemical burns from gel bleaching (if a high-concentration oxidizing agent contacts unprotected tissues, which may bleach or discolor mucous membranes), sensitive ~~teeth~~ teeth. It is worth advising patients who ask that nearly half the initial change in color provided by an intensive ~~in- office~~ in-office treatment (i.e., ~~1 h~~ 1-h treatment in a dentist's chair) may be lost in 7 days. Rebound tooth sensitivity is experienced due to a dehydration of the tooth.
Certain tooth whitening "tooth pastes" have an overall low pH, which can put enamel at risk for decay or destruction by demineralization. Consequently, care should be taken and risk evaluated when choosing a product which is very acidic. Also, tooth whiteners in toothpastes work through a mechanical action. They have mild abrasives which aid in the removal of stain but also may weaken dental enamel.

Table 36.3
Specific precautions for the oral hygiene of the ~~Sjogren's~~ Sjögren's patient

(a) Recognition that a dry mouth is not necessarily a painful mouth. There is a poor correlation between painful mouth and saliva flow. The development of a painful mouth should initiate a search for other causes such as oral yeast infection or a local neuropathy (called burning mouth syndrome).

(b) Dry mouth patients are more difficult to maintain without additional home care protocols. Dental flossing after meals and mechanical stimulation, such as using a soft toothbrush to stimulate the tongue and buccal mucosa at frequent ~~intervals~~ intervals, is useful.

(c) The use of a power toothbrush at home significantly improves brushing efficiency, and requires half the pressure of hand brushing to reduce trauma and overall wear and tear. There are a variety of shapes and sizes of interdental brushes that function as floss alternatives. Another option is a WaterPik, now called WaterFlosser.

(d) Tooth sensitivity may be a problem, and a mild desensitizing toothpaste like Biotene for Sensitive teeth or Pronamel ~~utilize~~ utilizes a different detergent than in most other toothpastes.

Toothpastes should be recommended to enhance the patient's plaque management program. The new Biotene BPF formula ~~contain~~ contains two extra enzymes that break up attached plaque and reduce buildup and inflammation.

Casein derivatives and lactoperoxidase have been shown to be beneficial in radiation xerostomia.

(e) Frequent breaks during the day for use of ~~sugar free~~ sugar-free (as opposed to low sugar) mints or lozenges mechanically stimulate saliva. Also, frequent dental hygiene after meals (or between meals) to remove food debris. A variety of lubricating ~~mouthrinses~~ mouth rinses and sprays may be used to facilitate eating and dental hygiene.

(f) Super dry patients will have a more difficult time tolerating any products with a strong mint flavor. Some patients ~~can't~~ cannot even tolerate the bland flavor of Oral Balance ~~(GSK)~~ (GSK); so another product like Align Pharma's Numoisyn Liquid or even the mucositis treatment, Xclair, may be necessary.

Xclair is a cream, indicated for the management of radiation-induced dermatitis and stomatitis, including relief and management of the most common signs and symptoms such as pruritus, erythema, ~~burning~~ burning, and pain. Xclair is presented in an airless tube containing ~~50 mL~~ 50-mL cream. Xclair acts by adhering to the injured tissue to ~~moisturise~~ moisturize and reduce the sensitivity of inflamed tissue. It is a hydrolipidic wound dressing, and contains the hydrating, ~~barrier-forming~~ barrier-forming, and ~~moisturising~~ moisturizing ingredient sodium hyaluronate, which may ~~favour~~ favor tissue hydration and therefore benefit the healing process. To improve the wound environment and therefore mitigate this common skin reaction to radiotherapy, it also contains additional

(g) For dental hygiene ~~procedures~~ procedures, the use of a ~~low power~~ low-power ultrasonic scaler to debride or deep scale can significantly reduce the risks of tissue trauma. Soft polishing cups that occilate, rather than spin, create less heat and ~~don't~~ do not scuff up tender gum tissues.

(h) Bonding, cements, and crown margins are subject to acid attack, which is more prevalent when there ~~isn't~~ is not adequate salivary output to rinse away food particles or dilute acids.

(i) There is no contraindication to tooth whitening for the average ~~Sjogren's~~ Sjögren's patient. Products should be approved by the American Dental Association to confirm that their testing was done in a scientific manner, and should be buffered pH as much as possible. Directions must be followed exactly since each product may have different exposure times or intervals to obtain optimal results with the less ~~side-effects.~~side effects.

(j) Implants, while expensive, do provide an alternative when tooth loss has been unavoidable. According to Yale's Dr. Frazio at a recent California Dental Association meeting, the only contraindications would be smoking, or the lack of commitment on the part of the patient to do what it takes to maintain the health of the implants. The medical ~~work up~~ workup should focus on any condition or medications that would compromise the healing process.

Implants in SS patients remain at the "state of an art" stage since there is no clear standard for the timing of different stages in the implant process (i.e., when the posts are uncovered and the implant ~~inserted)~~ inserted), and thus experience with SS patients should be carefully researched by the patient prior to this expensive procedure.

progressive dental decay and enamel loss.
Several products that have been used in radiation xerostomia and have been used in SS patients in our clinic
(a) MI paste and MI paste plus Recalcitrant
(b) Xclair for oral mucositis
MI Paste contains the active ingredient RECALDENT™ (CPP-ACP), a special milk-derived phosphopeptide that binds calcium and phosphate to tooth surfaces, ~~plaque~~ plaque, and surrounding soft tissue. *MI Paste* is a water-based, sugar-free ~~crèam~~ cream that is applied directly to the tooth surface or oral ~~cavity *also*~~cavity. *Also improves* fluoride uptake as well as soothing sensitive surfaces – making patient compliance easier.
MI Paste Plus is similar to *MI Paste*, but is enhanced with a form of fluoride (900 ppm) to further promote remineralization and protect teeth from caries development. Since the fluoride acts in conjunction with RECALDENT™ (CPP-ACP), it is reported more effective than fluoride alone. Patients are instructed to apply a pea-sized amount to their teeth every 4 h. The minerals not only provide the necessary building blocks for the remineralization that maintains the status quo, but also binds with acids to neutralize the oral pH, reducing the patient's risk of further tooth loss.
Caphasol is an orally available agent suggested to retard calcium loss.

Table 36.4
Vaginal dryness and dyspareunia in the SS patient

• Insertional dyspareunia
– Lubrication difficulties
Lack of knowledge of sexual response
Lack of arousal
Postmenopausal atrophy
– Vulvitis – infectious or irritative
– Vaginitis – infectious or irritative
– Vaginismus
– Psychological concerns
• Pain in a specific area of vulva or vagina
– Hymenal ring difficulty
– Old scars, lesions, abscesses, gland enlargement
– Vulvitis – infectious or irritative
– Vaginitis – infectious or irritative
• Pain with deep penetration
– Masses or uterine enlargement
– Endometriosis
– Adhesions

– Vaginismus
– Condyloma accuminata
– Psychological concerns