

Oral and General Health - Exploring the Connection

Research Review August 2011

Dry Mouth (Xerostomia): Diagnosis, Causes, Complications and Treatment

DENTAL PROFESSIONAL VERSION

The research for this Report was generously supported with funding from Delta Dental Plans Association (DDPA) and performed by Wenche S. Borgnakke DDS MPH PhD, George W. Taylor DMD MPH DrPH, Patricia F. Anderson MILS, and M. Carol Shannon MA MPH at the University of Michigan. ©DDPA 2010.

Oral and General Health – Exploring the Connection

Research Review August 2011

**Dry Mouth (Xerostomia):
Diagnosis, Causes, Complications and Treatment**

DENTAL PROFESSIONAL VERSION

Contents

I	EXECUTIVE SUMMARY	3
II	INTRODUCTION	4
	1. Saliva in Health and Disease	4
	2. Definition of Xerostomia	5
	3. Prevalence of Xerostomia	6
	a) Severity of Xerostomia: The Xerostomia Inventory (XI)	6
	b) Changes in Xerostomia over Time	7
	4. Age and Xerostomia	5
	5. Sex and Xerostomia	8
III	CAUSES OF XEROSTOMIA	8
	1. Primary causes	8
	a) Primary Sjögren’s Syndrome	8
	2. Secondary causes	9
	a) Xerogenic Medications	10
	b) Radiation Treatment for Head and Neck Cancer	11
IV	COMPLICATIONS OF XEROSTOMIA	12
	1. Dental Caries and Periodontal Disease	12
	2. Oral Mucositis & Candidiasis	13
	3. Dental Erosion	13
V	MANAGEMENT OF XEROSTOMIA	14
	1. Palliative Management	14
	2. Salivary Secretion Stimulating Treatment	16
	a) Saliva Stimulating Medications	16
	b) Non-Medication Salivary Stimulation	16
	3. Non-Saliva Stimulating Medications	17
VI	ADDITIONAL INFORMATION SOURCES ON XEROSTOMIA	17
VII	SALIVARY DIAGNOSTICS	18
VIII	BIBLIOGRAPHY	19

I. EXECUTIVE SUMMARY

Xerostomia is defined as the subjective perception of oral dryness and is often accompanied with **hyposalivation**, but not always. **Dry mouth** refers to either xerostomia or hyposalivation or both. Dry mouth is an important condition that significantly decreases the quality of life for 20 to 30% of the United States adult population with around 40% among seniors. Treatment and palliative management of dry mouth with its potentially serious subsequent complications require compassion, patience, creativity, and collaboration among the oral and medical health care providers, as well as high degree of cooperation and compliance from the patient.

Certain patients with hyposalivation may benefit from administration of medications that stimulate salivary output, such as pilocarpine or cevimeline. Xerostomia can be alleviated by using saliva substitutes in spray, gel, or liquid form, as well as stimulatory sugarless candies or chewing gum. For management of mucositis and the oral diseases caries and periodontitis, alcohol free mouth rinses should be used. In general, alcohol-free and bland oral care products, such as children's toothpaste, are better tolerated in patients with dry mouth and oral mucosal inflammation than conventional products. Patients with significant hyposalivation should be closely monitored for the development of dental caries, which can be prevented by the daily use of 1.1% sodium fluoride dentifrice or gel. Meticulous oral hygiene and basic oral care are important to reduce the bacterial load in the oral cavity and thereby the risk for periodontitis and other local infections. A "clean mouth" also decreases halitosis and promotes overall comfort.

Identification and management of the xerostomia patient present a welcome opportunity to practice dental and medical health care according to today's novel paradigm in which collaboration among health care providers is essential for delivery of timely and optimal health care to improve the health, daily function and quality of life for their mutual patients.

II. INTRODUCTION

Xerostomia is a common condition that can significantly diminish the quality of life for the patient¹. A comprehensive review of the current evidence in the scientific literature regarding xerostomia and its causes, consequences, and treatment options has been conducted and is summarized in this report. The majority of the practical information is also provided in easy to view tables. For example, questions used by researchers to allocate study subjects to the xerostomia group are displayed as inspiration for questions to ask patients in order to diagnose dry mouth. More emphasis is allocated to describing conditions that may not be so well known as opposed to providing details regarding the causes and pathology of caries and periodontal diseases, the major oral diseases caused or exacerbated by xerostomia.

Researchers conducted a comprehensive online MEDLINE search of PubMed for articles related to xerostomia in collaboration with information experts. Researchers also searched the authoritative Cochrane Collaboration for systematic reviews. These searches were enhanced by hand-searching of recent tables of contents in relevant journals and following leads in bibliographies in publications. In selecting evidence for description in this report, most emphasis was placed on recent publications, according to the mandate for this report. Additional citations were added in the form of original research reports, reviews, guidelines and online citations. By online searching, reviewers identified relevant professional associations and other resources helpful for dental practitioners.

Main concepts and conclusions are shown in **bold** text. Also, individual studies are described in subsections named *Examples of Evidence* and experimental and novel research is mentioned in *Research Frontiers*. These subsections are set in italic text and single line format for immediate identification.

The aim of this report is to summarize the current state of the evidence in the scientific literature regarding dry mouth. It is not the goal to write guidelines for practicing dentists. This report is intended as a resource for dental practitioners in gaining knowledge and understanding of current evidence regarding diagnosis, causes, complications and treatment of mouth dryness in order to better manage patients with this condition. In many cases, such management will be in close collaboration with the patients' medical care providers.

1. Saliva in Health and Disease

Saliva is essential for proper sense of taste, initial digestion and chewing, swallowing, maintenance of healthy gingival tissues and teeth, voice and speech, articulation and denture retention. Saliva helps prevent potentially severe problems of the hard and soft tissues of the oral cavity, as it plays important roles in removing food debris and remineralization of enamel/tooth structure, as well as

maintenance of the integrity of the oral mucosa. It also provides a first defense against chemical, mechanical, and infectious attacks, and acts as a general lubricant for all oral functions. Its mechanical cleansing action is enhanced by constituent antimicrobial agents (e.g., thiocyanate, lysozyme, immunoglobulins). Additionally, its buffering properties maintain oral pH.

Research Frontiers: The composition of saliva reflects the oral and general health status to such a degree that several components can be used for screening and diagnostic purposes, examples of which are described further in section VII Salivary Diagnostics (page 15).

2. Definition of Xerostomia

Dry mouth (xerostomia) is defined for the public by the National Institute of Dental and Craniofacial Research-National Institutes of Health (NIDCR) as the condition of not having enough saliva to keep the mouth moist². However, **xerostomia** is the medical term for **subjective experience of mouth dryness (symptom)**³⁻⁷, which may or may not be associated with objectively measured **hyposalivation (reduction in salivary secretion) (sign)**. This is an important distinction to keep in mind, and it is not obvious from the NIDCR definition. The term **dry mouth** is used in the literature to mean **either xerostomia or hyposalivation, or both**, so it is imperative to pay attention to the context in which the term is used³.

Saliva is produced in four major glands or groups of glands with their respective estimated flow rate of resting whole saliva of 0.4 mL/min) distributed as follows: Submandibular (65%~0.26 mL/min), parotid (20%~0.08 mL/min), sublingual (8%~0.03 mL/min) and minor salivary glands (7%~0.03 mL/min)³. When measuring saliva production during stimulation with for instance acidic liquid dripped onto the tongue, the normal stimulated flow rate of whole saliva varies between 1 and 2 mL/min³. So in health, humans are able to increase saliva secretion 2.5 to 5 times when needed (stimulated) compared to during alert rest. Most researchers use cutoff points between 0.5 and 0.7 mL/min stimulated saliva output for diagnosing objectively assessed xerostomia.

Example of Evidence: Large variability in salivary flow rates within and between individuals has been reported, which has impaired the establishment of standard values. Among 36 healthy males and females (18 young, ages 20-38; 18 older, ages 60-77) salivary flow rates varied 27-44% during a 6 hour period, suggesting that a 45% range in salivary flow rates could be considered normal salivary variation, and values below 45% of normal levels could be used to define salivary hypofunction⁸.

Some patients experience a feeling of oral dryness despite seemingly normal, objectively measured, levels of saliva secretion^{4-6,9}, whereas others do not complain about dry mouth despite objectively diagnosed hyposalivation^{4-5,10}.

Examples of Evidence: In case-control studies of menopausal women, the stimulated whole saliva flow rate and concentrations of ions of magnesium, chloride, sodium, and potassium, as well as total protein concentrations were not different in those experiencing and those not experiencing oral dryness. However, oral dryness feeling and its severity seemed to be positively associated with

salivary content of calcium¹¹⁻¹², parathyroid hormone¹¹, cortisol¹³, and progesterone¹⁴, but was negatively associated with levels of 17 β -estradiol¹⁵.

3. Prevalence of Xerostomia

Xerostomia is measured by self-report. It is probably safe to estimate that 20 – 30% of the U. S. adult population experiences dry mouth³ and therefore, **it is likely that the dental care practitioner will encounter patients suffering from dry mouth on a regular basis**¹⁶.

Because of the often serious adverse health consequences of xerostomia with its diminishing quality of life, it is of paramount importance that general dental and medical health care practitioners are aware of the possibility their patients might suffer from xerostomia. They must be prepared to identify and treat -- or refer for further evaluation and treatment-- such cases, even for those who do not seek care for or complain about dry mouth symptoms. Studies have shown that **dry mouth is usually not among the primary complaints patients present with, but if asked, they will agree they experience dry mouth**. In many cases, dentists are the first to notice signs of serious systemic diseases, such as Sjögren's Syndrome, an example of dental professionals having an important role in diagnosing, treating, and referring patients suffering from xerostomia. For guidance in exploring the possible diagnosis of xerostomia, please see examples of questions to ask patients displayed in Tables 1A-E (page 23) and common symptoms and signs in Table 2 (page 24).

Examples of Evidence: 1) Prevalence in Populations: Studies from all continents, except for Africa, have reported prevalences ranging from 13% in family dental practice¹⁷ to 63% among hospitalized patients. A representative study of the Hungarian population, showed that one-third of the adult population suffers from xerostomia⁵. Studies in the US are scarce. However, among those 65 years and older, one study reported a prevalence of 17.2% among 2,482 non-institutionalized in Maryland¹⁸ and another 39% in 600 Floridians¹⁹. 2) Racial Difference: No differences in salivary flow was found between 65-84 year old whites and blacks¹⁸.

a) Severity of Xerostomia: The Xerostomia Inventory (XI)

The Xerostomia Inventory (XI) is an 11-item scale designed to measure the severity of xerostomia, expressed as one number. The items are displayed in Table 1B (page 23). Several studies have used this scale in different populations^{1,11,13,15,20-26}. The XI was found to be correlated with quality of life as assessed by the 14-item version of the Oral Health Impact Profile (OHIP) scale¹. A study over 2 months concluded that a difference in XI score of 6 scale points was clinically meaningful²⁵, and it was demonstrated that in patients who were about to undergo radiotherapy for head/neck cancer, there was an increase in xerostomia two months later.

b) Changes in Xerostomia over Time

Few longitudinal studies are published. In the Baltimore Longitudinal Study of Aging (National Institute on Aging, National Institutes of Health) there was no overall longitudinal effect of time on

stimulated parotid flow rates among 396 healthy 21 – 96 years old women over a 17-year period²⁷. Also, there were no significant changes in salivary flow rates over a 1-year period among 39 adults aged 54-90 years for whole or parotid unstimulated saliva nor for stimulated parotid saliva²⁸. South Australians (aged 60+) underwent an interview and dental examination at baseline (N=1,205), and these assessments were repeated 2, 5 (n=669) and 11 years (n=246) afterward with xerostomia assessed at 5 and 11 years. While the overall prevalence of xerostomia increased during the observation period, there was considerable instability, with one-quarter of the cohort changing their xerostomia status²³.

4. Age and Xerostomia

Saliva production varies between individuals and within individuals. More older people suffer from dry mouth. However, xerostomia is either 1) a direct effect of various chronic, slowly developing, cumulative diseases and conditions whose prevalence increases in older age groups or 2) an indirect consequence of therapy for those ailments, especially the extensive use of xerogenic medications.

Increasing age alone does not cause dry mouth. **Increasing age does not by itself cause hyposalivation.**

Examples of Evidence: An Israeli team applied a novel method to measure salivary viscoelasticity by relaxation times and studied salivary distribution and lubrication and found that submandibular and sublingual salivary viscoelasticity was significantly higher than that of parotid saliva, especially during stimulation²⁹. In addition, an age-related reduction of 62% in flow rate was demonstrated, accompanied by an increase in both relaxation time (by 54%) and protein content (by 48%). Increased salivary viscoelasticity results in compromised salivary flow and lubrication properties, which “may render the oral cavities of the elderly and other xerostomic persons more vulnerable”²⁹.

On the other hand, in a large study (N=3,313) of Swedes who were asked: “Does your mouth usually feel dry?”, there was no age-related pattern for the 20-60-year olds who were not taking xerogenic medications, of whom 10% to 14% of men and 11% to 20% of women answered affirmative⁹. At ages 70 and 80 years, 28% men and 20% women versus 21% men and 39% women, respectively, answered yes. So there was not a consistent, linear increase in prevalence of xerostomia by age.

In another Swedish study over a period of 15 years of over 6,000 citizens born in 1942 who responded every five years from the ages of 50 to 65, there was an almost linear increase in prevalence in xerostomia from 6% at age 50 to 15% among 65-year olds³⁰. However, logistic regression analyses showed that only impaired health and smoking were significantly associated with daytime xerostomia, whereas age was not significant.

Among 315 Brazilian, independently living individuals aged 60 and over, the prevalence of xerostomia was 25%³¹. Table 1C (page 23) displays the xerostomia definition used. However, the mean values for unstimulated and stimulated salivary flow were 0.20 mL/min and 1.08 mL/min, the former about half of normal flow, but the latter within normal range. In a Michigan study of individuals between 54 and 90 years of age had an average flow of unstimulated saliva of 0.26 mL/min, but with the older (over 70 years) having higher output than those younger¹⁰. A British study among 1,103 patients in general dental practices concluded that medications usage is a better predictor for xerostomia than either age or sex¹⁷. There is acinar (secretory) cell atrophy with

aging³²⁻³³. However, in healthy, non-medicated elders there is no decrement in salivary output³⁴, supporting a hypothesis that a secretory reserve exists to preserve function in normal aging³⁵.

5. Sex and Xerostomia

In several research reports, feeling of dry mouth consistently is experienced by 25% to 50% more women than men^{17,26}, regardless of age and intake of xerogenic medications⁹. However, other studies report women to have higher salivary output^{3,10}. Oral discomfort is found in many menopausal women in addition to more general climacteric complaints. Yet, hormone replacement therapy (HRT) does not necessarily prevent or help women with oral symptoms. White 65-84 year old women were found to have more xerostomia than black women in Maryland¹⁸. **Women tend to suffer from xerostomia more often than men**, although the evidence is mixed.

Research Frontiers: Future gene profiling could identify women who may or may not benefit from HRT with regard to oral symptoms³⁶.

III CAUSES OF XEROSTOMIA

Dry mouth can be caused by a multitude of factors that may result in salivary hyposecretion, some on a temporary, but most, unfortunately, on a permanent basis. An overview of common causes of xerostomia is provided in Table 3 (page 25).

1. Primary causes

Primary or direct causes of dry mouth are conditions that directly affect the salivary glands and cause decreased salivary production and outputs³⁷. These conditions include: Primary Sjögren's Syndrome; salivary gland conditions; endocrine conditions, such as type 1 and type 2 as well as gestational diabetes; thyroid disease; adrenal conditions; Parkinson's Disease; renal or hepatic deficiencies.

Research Frontiers: A novel finding measured diminished salivary flow rates in patients with periodontitis. The authors concluded that "Periodontitis induces an increase in the output of proteins, including mucin and amylase, thereby enhancing the protective potential of saliva, but this is accompanied by a decrease in flow rate"³⁸. Interestingly, this study was able to demonstrate a dose response relationship between salivary secretion and severity of periodontal disease: The salivary flow rate steadily diminished from 1.03mL/min in periodontal health to 0.85mL/min in severe periodontitis, with severity of periodontitis determined by modified CDC/AAP Workgroup's case definitions³⁹.

a) Primary Sjögren's Syndrome

Primary Sjögren's Syndrome (PSS) is the most common xerogenic disease in the United States with over a million inhabitants thought to be affected. The condition is named after the Swedish ophthalmologist, Henrik Samuel Conrad Sjögren (1899 – 1986). PSS is an autoimmune disease characterized by inflammation of the exocrine glands and may occur independently or in association with other diseases such as rheumatoid arthritis or lupus. A minimally invasive technique of minor salivary gland biopsy of the lower lip can aid in the diagnosis⁴⁰. The secretory hypofunction causes

dryness of mucosal surfaces, most noticeable of the mouth and eyes. Nine of ten patients are women, typically postmenopausal⁴¹.

The first large-scale study to compare the oral health of 1,502 PSS sufferers in the United States to 606 age- and sex-matched healthy controls was published in 2008⁴². Almost all cases (96%) experienced oral problems, which were the initial symptoms in more than half the PSS patients. Dry mouth-associated signs and symptoms were common and severe. Oral dryness was significantly associated with reduced quality of life, including poorer general health and social functioning, as well as greater fatigue. Cases had 2 -3 times more dental decay or severe periodontal disease than controls and had 65% more dental visits associated with 2.7 times greater costs.

Awareness and recognition of hyposalivation are essential in order to help patients minimize dryness symptoms, to institute preventive measures and to limit oral complications⁴³. The dental professional has the opportunity to ask every patient if he or she is experiencing dry mouth, please see Tables 1A-1E (page 23) for examples of question to pose and Table 4A-4B (page 17-28) for explorative tasks for the clinician. In particular, complaints of dryness while eating, or difficulty swallowing dry foods, or the necessity of using liquids to ease swallowing are important clues that salivary function may be impaired. As part of a routine oral examination, the dental professional should examine the oral cavity carefully for signs of salivary gland dysfunction. Findings such as an increase in caries activity, mucosal alterations, infection, or salivary gland enlargement may indicate salivary dysfunction. Evaluation should be conducted proactively at each patient visit. Early recognition will minimize damage and allow appropriate management to begin. Although the salivary dysfunction may be irreversible, preventive measures and conservative treatments can avoid or limit mucosal breakdown, infections, and permanent damage to teeth. Adequate symptomatic relief is possible with local palliative and systemic measures in many patients. Appropriate management of symptoms and attempts to increase salivary output may help patients feel more comfortable and improve their quality of life.

Research Frontiers: Currently, mostly palliative management is available⁴⁴, but gene therapy has the potential for inserting molecules such as cytokines that could modulate inflammation in salivary glands to slow or prevent their destruction in Sjögren's Syndrome. Also, the capacity to produce molecules that enhance saliva production by residual salivary gland cells might be introduced by gene transfer. Eventually, development of artificial salivary glands may have application in patients who have lost all functional salivary glands due to radiation treatment or Sjögren's syndrome.

2. Secondary causes

Secondary or indirect causes of xerostomia are conditions of which hyposalivation or a feeling of oral dryness are side effects. The most prevalent of these indirect causes is use of xerogenic medications, including cytotoxic chemotherapeutic anti-cancer agents. Modest reduction in salivary

gland secretions rates have also been reported in children during leukemia treatment⁴⁵⁻⁴⁷. Many individuals suffer simultaneously from several xerogenic factors, such as 1) use of some of hundreds of **nonprescription and prescription drugs**; 2) **autoimmune disorders**, such as rheumatoid disorders and scleroderma⁴⁸, or immune deficiency HIV infection, especially in advanced stages⁴⁹⁻⁵⁵; 3) **endocrine disorders**, such as diabetes^{10,31} and thyroid and adrenal gland diseases; 4) **Parkinson's disease**; 5) **graft versus host disease (GVHD)** following allogeneic^{20,56-60} or autologous hematopoietic stem cell transplantation⁶¹⁻⁶² or either type⁶³, and renal or hepatic deficiencies; 6) **malnutrition**; 7) **chronic or neurogenic pain**; 8) **stress or nervousness**; 9) **smoking tobacco and cannabis**⁶⁴⁻⁶⁵, or 10) **recreational drugs** such as methamphetamine⁶⁶⁻⁶⁹; 11) drinking **alcohol or caffeine-containing fluids**; as well as 12) **sleeping with open mouth or mouth breathing** at any time, such as during nasal congestion, 13) **breathing polluted air**, and 14) using **inhalers**. Finally, dry mouth is a common side effect of several 15) **iatrogenic procedures and regimens**, such as anesthesia, NPO (nothing by mouth), intubation/ventilator-assisted breathing, mechanical oral suctioning, and intravenous feeding.

a) Xerogenic Medications

Xerogenic drugs are the most important cause of xerostomia, with cholinergic antidiuretics, antihistamines, and antidepressants most dominant. **Medications (estimated to exceed 400) from all major drug groups have the potential to cause dry mouth**, even daily aspirin²³, hormones, and iron supplements. Use of inhalants also contributes to oral dryness. Medications taken alone may not cause xerostomia, whereas polypharmacy, i.e. the use of multiple medications, could. Furthermore, some medications do not cause dry mouth if taken for a few years, but can if taken for several years. Thus, reactions to drugs are individualized to such a high degree that it is impossible to reliably predict whether a given patient will experience the side effect dry mouth. Consequently, there is no direct dose-response relationship between medication and occurrence or intensity of xerostomia. Therefore, no list of xerogenic drugs is displayed in this report. Such overviews may be found in several of the resources listed in Table 6A-6B (pages 33-36). The first item listed, namely the book titled "Dry Mouth, the Malevolent Symptom: a Clinical Guide", supplies an online list of names of hundreds of drugs capable of causing xerostomia that can be accessed using a code word found in the book³.

It is important for the clinician to collect accurate information on a patient's use of drugs, both those prescribed and those purchased over the counter. Our team has developed and used in several clinical studies forms for recording information on medication usage. A generic version that can be edited and used by practitioners is shown in Figure 1 (page 37).

In order to prevent or diminish dry mouth symptoms, it might suffice to simply change the dosage to multiple smaller dosages instead of one, large dose, provided the therapeutic level is maintained. For a patient with uncontrolled type 2 diabetes, it might suffice to attain glycemic control (using modifications of diet, exercise, and possibly oral anti-diabetic medication or insulin), which potentially eliminates the hypo-salivation. Also, exercise can have the same effect on depression as psychopharmaca⁷⁰⁻⁷¹.

Adjusting and fine-tuning a patient's medication regimen may require considerable patience, creativity, and collaboration among health care personnel, and of course, the patient has to cooperate and closely comply with any revised drug regimen. However, such efforts can significantly increase the patient's quality of life, especially in combination with the use of additional remedies for oral dryness, examples of which are displayed in Table 5A-5C (pages 29-32).

Examples of Evidence: Among 3,313 Swedes, the average prevalence of dry mouth was statistically, significantly greater among medicated than non-medicated subjects, namely 32.1% versus 16.9%⁹. There was also a strong association between xerostomia and polypharmacy.

b) Radiation Treatment for Head and Neck Cancer

As the sixth most common cancer in the developed world, squamous cell carcinoma of the head and neck affects about 45,000 people in the United States⁷². Many of these tumors have disfiguring effects on the mouth, lips and face, and they also can disrupt a person's ability to eat and swallow. Even more troubling is that about half the people diagnosed with this type of cancer die within five years, a statistic that has not changed much the past three decades⁷². The predominant causes are tobacco smoking and excessive alcohol consumption. Additionally, human papilloma virus is recognized as a factor in development of oral squamous cell carcinoma⁷³⁻⁷⁴. Head and neck cancers (HNC) include cancer of the lip, oral cavity, oropharynx, hypopharynx, nasopharynx, the glottis larynx, and the supraglottic larynx. HNC also comprises tumors of the ethmoid and maxillary sinuses and the salivary glands. However, cancers of the thyroid are not considered to be HNC.

For head and neck cancer (HNC) patients, it is pivotal to assist the patient in avoiding as much damage to the salivary glands as possible in order to minimize the permanently decreased quality of life caused by hyposalivation⁷⁵. Advanced radiotherapy planning approaches may be particularly important for parotid sparing in radiochemotherapy because of cisplatin-related increased radiosensitivity of glands⁷⁶. For instance, it is possible to use a virtual simulation, 3-dimensional-conformal-radiotherapy-technique in which the relative toxicity of radiation to the surrounding normal tissues is reduced, allowing a higher dose of radiation to be delivered to the tumor than conventional techniques would allow⁷⁷. Excellent management of even advanced oropharyngeal cancer can be obtained using parotid⁷⁸ and submandibular gland⁷⁹ sparing intensity modulated radiotherapy (IMRT) that decreases radiation doses to normal structures without compromising the

doses to the target⁸⁰. The IMRT technique is currently undergoing further improvement⁸¹. Several reports published the last few years concern effects of and comparisons between various radiotherapeutic techniques in HNC patients related to preservation of salivary glands^{76-77, 82-109} and in treatment of cervical lymph node metastases from cancers of unknown origin¹¹⁰.

Radiation treatment of non-head and neck cancer lesions does not directly cause oral complications. They are consequences of the accompanying dry mouth due to stress and nervousness, as well as to chemotherapeutic medication and psychopharmaca prescribed for anxiety, depression, or insomnia. Dental clinicians should manage hyposalivation issues in HNC radiation as they would any other patient with dry mouth, except in collaboration with the oncology team.

Decisions regarding inclusion of elective nodes also should take into consideration the need for preserving as much salivary gland tissue as possible. Unfortunately, it is not yet standard practice by oncologic teams to be acutely aware of and take into consideration the importance of preserving salivary glands of any magnitude. Therefore, dental care providers can play a critical role in ensuring salvation of salivary glands by communicating with the patients' oncology team.

IV COMPLICATIONS OF XEROSTOMIA

In the absence of saliva in amounts sufficient for its debriding, antimicrobial, re-mineralizing, and lubricating functions in health, several oral diseases and conditions will readily develop. These include caries (especially root caries), periodontal diseases, Candidiasis (thrush), oral mucositis, enamel erosion, (subjective) halitosis¹¹¹⁻¹¹², and possibly osteonecrosis. Patients also can experience trouble speaking, chewing, and swallowing (dysphagia).

1. Dental Caries and Periodontal Disease

Apart from being more pronounced throughout the entire dentition in the absence of cleansing saliva and meticulous oral hygiene and care in xerostomia patients, the two most prevalent oral infectious diseases, caries and periodontal disease, are mostly pathologically identical to the manifestations in patients with normal salivation. More root caries as well as caries at unusual surfaces, such as the buccal surfaces of incisors, is often seen in xerostomia. Dental patients abusing *methamphetamine* (3,4-Methylenedioxymethamphetamine, also known as "Ecstasy", and as "E", "X", "Thizz" and "XTC") can present with severe xerostomia, rampant caries ("*Meth Mouth*"), excessive tooth wear, and poor oral hygiene⁶⁶⁻⁶⁹. Oral rehabilitation of patients using methamphetamine can be challenging.

Research Frontiers: In a study of non-smoking Sjögren's Syndrome (SS) patients, a novel technique has been applied that utilized periodontal capillaroscopy to investigate the features of microcirculation, recording visibility, course, tortuosity (being tortuous or twisted, having many turns), as well as the possible presence of microhemorrhage, the average caliber of the capillary loops, and the number of visible capillary loops per square millimeter¹¹³. The study showed evident

alterations to the capillaries and a typical conformation of the interdental papilla microcirculation. Observed were a reduced caliber of capillaries as well as a greater number and tortuosity of capillary loops. Such capillary alterations contribute to decreased gingival microcirculation and therefore possibly to diminished healing and anti-inflammatory capacity.

2. Oral mucositis & Candidiasis

Acute oral mucositis (“stomatitis”) has emerged as a common, dose-limiting toxicity that often causes delays and interruptions of radiation therapy of head and neck cancer^{59,86,94,106,114-125} with subsequent increased treatment duration and costs. Symptoms include patchy or confluent oral mucositis and severe pain, especially on swallowing, that dictates the need for nasogastric tube feeding and narcotic medicines¹²⁶. Dentists can play a role in managing this condition on consultation with the oncology team.

In 2009, the National Comprehensive Cancer Network (NCCN) published guidelines for prevention and treatment of cancer-related infections of the mouth, such as necrotizing ulcerations, Candidiasis (thrush), and vesicular lesions with fungi¹²⁷ (Table 6A, page 33-35)..

Management of non-radiation-related oral mucositis and Candidiasis is described in detail in a previous report in this series: “Oral Health of Non-Head & Neck Cancer Patients”.

Salt-water rinses and bioadherent oral gel are relatively inexpensive and nontoxic agents for managing xerostomia-related mucositis¹²⁸. Saliva substitutes can provide symptomatic relief from symptoms of hyposalivation, and clinical experience suggests that physician-prescribed pilocarpine is a worthwhile drug option for stimulating saliva production¹²⁸.

Research Frontiers: High-dose enteral glutamine did not reduce the incidence nor severity of oral mucositis in pediatric oncology patients when given alongside chemotherapy¹²⁹. An instrument named Children's International Mucositis Evaluation Scale (ChIMES) has been developed and tested¹³⁰⁻¹³¹ as a standard to use among pediatric patients. A different study applied another measuring instrument, the Oral Mucositis Assessment Scale (OMAS), and concluded that laser technology can be used as a novel form of both prevention and treatment of the oral mucositis¹³².

3. Dental Erosion

Any condition that involves vomiting or regurgitation of stomach contents back to the oral cavity can cause xerostomia and enamel erosion due to the acidity of the stomach contents. Of greatest importance to reestablishing oral homeostatis following any acid attack on enamel is the saliva. Salivary flow rate, composition, and buffering capacity are important biological factors influencing erosive tooth wear. In decreased salivary secretion, dental erosion will be therefore be facilitated¹³³. A description follows of causes of repeated vomiting, apart from the occasional bouts of bacterial or viral infections.

Causes of vomiting: Gastrointestinal disorders (peptic ulcers, hiatus hernia, intestinal obstruction, gastroenteritis, food allergies); nausea in pregnancy (“morning sickness”); metabolic and endocrine disorders (diabetes mellitus, renal failure, hyperthyroidism, adrenal insufficiency); neurological and central nervous system disorders (migraine headaches; vertigo, such as that

associated with the inner ear disorder Ménière's disease, and intracranial neoplasms); psychogenic vomiting syndrome; chronic alcoholism or binge drinking; side-effect of drugs (central emetic [a medicine that induces nausea and vomiting] side effects, secondary effects due to gastric irritation), and eating disorders, such as "bulimic" or "vomiting" anorexia nervosa using purging (self-induced vomiting and/or laxative abuse) and bulimia nervosa (repeated episodes of binge-eating and purging). Gastro-esophageal reflux disease (GERD) can also cause dry mouth and enamel erosion, as acidic stomach content repeatedly leaks back through the esophagus to the oral cavity¹³⁴. GERD is usually caused by permanent or transient changes in the barrier between the stomach and the esophagus, including abnormal relaxation of the lower esophageal sphincter, impaired expulsion of gastric reflux from the esophagus, or a hiatal hernia, a condition in which part of the stomach moves above the diaphragm. The most prominent symptom is heartburn. Obesity, cigarette smoking, pregnancy, and possibly alcohol intake increases the risk of GERD, as does use of several commonly used medications, such as anticholinergics (e.g., for seasickness), beta-blockers for hypertension or heart disease, calcium channel blockers for hypertension, bronchodilators for asthma, dopamine-active drugs for Parkinson's disease, progestin for abnormal menstrual bleeding or birth control, sedatives for insomnia or anxiety, and tricyclic antidepressants. Ruminant Syndrome is a behavioral disorder consisting of daily, effortless regurgitation of undigested food within minutes of starting or completing a meal. The food is either held in the mouth or re-chewed and then re-swallowed or expectorated. This condition is exhibited in 6 to 10% of mentally challenged institutionalized patients and 20% of people with bulimia, adults with normal intelligence. Erosion may present in different locations of the dentition depending of the retention/chewing pattern¹³⁵.

Acidic soft drinks are an increasing source of dental erosion¹³⁶ as is excessive intake of white wine¹³⁷.

By being aware of the possibility of underlying conditions, dental health care providers can assist their patients in diminishing the sequelae by recommending frequent oral rinses with water immediately after oral presence of acidic content, the regular use of fluoride, sleeping in a semi-reclined position, and referral to medical care providers for possible adjustment of medications and possibly amelioration or termination of the underlying conditions.

V MANAGEMENT OF XEROSTOMIA

Unfortunately, treatment regimens to cure dry mouth are scant, except in a few cases, such as xerostomia being caused by uncontrolled diabetes, which can be cured by bringing diabetes under control. Examples of treatments are provided in Table 5 (pages 29) and summarized in the following.

1. Palliative Management

Most remedies available for patients with dry mouth are palliative in nature^{6, 44, 138} and aim to avoid or alleviate discomfort and pain as well as to prevent complications of xerostomia. Table 5 (pages 29-32) displays remedies to consider for recommendation to patients with dry mouth.

Of great importance is collaboration and mutual consultation between all the patients' pertinent medical and dental care providers. Since the majority of cases of xerostomia are caused by xerogenic medications, it is important to discuss possible prescription of alternative drugs with less desiccative side effects. Also, for mental health, decreasing dosage of psychopharmaca could for example be attained by adding an exercise regimen that could consist of simply walking outside.

Patients should be acutely aware of the importance of proper *hydration* and should frequently sip water or sugar free, neutral (non-acidic) liquids, such as salt-free broth. They should avoid any caffeine-containing drinks, such as tea, coffee, and several soft drinks. Sugar free popsicles and Jell-O might be soothing. They also would benefit from sipping appropriate liquids during meals, as that will facilitate chewing, initiation of swallowing, and swallowing. It may also improve the taste of food. Alcohol and smoking should be avoided to prevent further drying out of the oral cavity. Xerostomia can be ameliorated by using *saliva substitutes* in liquid, spray, or gel form. Sugarless (citrus, cinnamon, or mint-flavored) hard candies can be soothing and stimulate any capability to produce saliva, as can chewing gum that in dentate individuals preferably should list xylitol as the first, most abundant, ingredient. There is evidence that xylitol has antibacterial properties that alter the oral ecology¹³⁹. Special *denture adhesives* for individuals with xerostomia also may provide some retention aid for removable dentures.

In general, *alcohol-free mouth rinses* and *bland oral care products*, such as *children's toothpaste*, are better tolerated in patients with dry mouth than conventional products. A *humidifier* might also help adjust air moisture content to a comfortable level, especially at night during sleep when any residual salivary secretion is physiologically decreased.

Patients with significant xerostomia should be closely monitored for the development of dental caries, which may be prevented by the daily use of *1.1% sodium fluoride (NaF) dentifrice* or *gel*. A study evaluated the use of *calcium phosphate supersaturated remineralizing rinse* in tandem with 1.1% NaF for daily use in patients at high risk for caries due to xerostomia¹⁴⁰. Compliant patients experienced a significant increase in reversals of caries, and a significant decrease in net coronal and root surface caries increment, suggesting that long-term compliance with the daily supersaturated rinse was protective against caries progression in a high-risk population.

Periodontal diseases may be prevented by using an *alcohol-free, bactericidal mouth rinse*, such as *chlorhexidine*.

Professional *oral hygiene* procedures and instructions in home care as well as diligent and meticulous oral self-care are crucial to reduce the bacterial load in the oral cavity and thus the risk for halitosis and oral infection with its subsequent inflammation. Oral care is also important for the patient's general comfort.

Managing patients with xerostomia presents an opportunity to practice dentistry according to the new paradigm in which the close relationship between oral and systemic condition is acknowledged: In order to ensure optimal health for mutual patients, the entire team of medical and dental care providers should closely collaborate and continuously consult each other to explore, select, and provide the best possible treatment options.

2. Salivary Secretion Stimulating Treatment

In cases in which some salivary glands remain functional, various forms for stimulation of the secretory tissue may be attempted to increase the salivary output:

a) Saliva Stimulating Medications

Any agent that has the ability to influence salivary glands to increase production of saliva is termed a *secretagogue*. Some patients who do not have certain cardiac and several other conditions may benefit from the administration of two drugs that are approved by the U.S. Food and Drug Administration (FDA) for treatment of dry mouth, namely *pilocarpine* and *cevimeline*³. Both are secretagogues, but their side effects include sweating, flushing, and urinary urgency, which may be dehydrating. Medications that increase saliva secretion are usually effective only a few hours after intake and therefore need to be taken frequently. Pilocarpine (5 mg q.i.d. to 10 mg t.i.d.) has shown effect even when given during radiation therapy¹⁴¹, and cevimeline (30 mg t.i.d.) is an alternative¹⁴². A systematic review from July 2010 of 37 reports on treatment of Primary Sjögren's Syndrome¹⁴² reported pilocarpine to be associated with improvements in dry mouth in 3 trials and cevimeline in two. However, a subgroup of patients with Secondary Sjögren's Syndrome did not respond to pilocarpine stimulation¹⁴³.

Prescription of any secretagogue drugs should always occur in close collaboration with medical care providers, if not directly by the physicians, due to the magnitude of contraindications.

Research Frontiers: The American Society of Clinical Oncology's 2008 clinical practice guideline update on the use of chemotherapy and radiation therapy protectants recommended that use of amifostine may be considered to decrease acute and late xerostomia with fractionated radiation therapy alone for head and neck cancer¹⁴⁴. However, a systematic review on reports on the effects of the drug on salivary glands in radioactive iodine-treated differentiated thyroid cancer identified only two reports. Both failed to demonstrate any effect of amifostine over acid-stimulating agents to increase salivary secretion¹⁴⁵. So until more evidence becomes available, prevention of xerostomia and mucositis with amifostine is controversial¹²⁸. In a 30-week longitudinal study of women with Sjögren's Syndrome published in 2010, daily doses of 400 mg hydroxychloroquine were found to increase unstimulated, but not stimulated, salivary flow rate¹⁴⁶. Hydroxychloroquine is classified as an anti-malarial medication and is also used to decrease inflammation in systemic lupus erythematosus as well as rheumatoid arthritis and Sjögren's Syndrome (all rheumatic disorders).

b) Non-Medication Salivary Stimulation

Patients irradiated in the head and neck region often suffer from severe dry mouth and for alleviation use *acidic saliva stimulating products*, which may cause erosion of teeth¹⁴⁷⁻¹⁴⁸.

Research Frontiers: Saliva flow rates increased significantly (15-fold) when sucking Xerodent lozenges with or without fluoride¹⁴⁸. Both types were found to be non-erosive, however, for additional caries protection the fluoride variant is preferable¹⁴⁸.

Modified acidic candy with calcium has reduced erosive potential and could therefore be used as a saliva secretory stimulant for relief of dry mouth¹⁴⁷. Eating lemon-lime sorbet just prior to lunch successfully increased saliva production and food intake among elders with drug-induced dry mouth residing in a nursing home¹⁴⁹.

Massaging the salivary glands, in particular the parotid, is shown to be helpful as part of a mouth exercise program¹⁵⁰.

Acupuncture: In November 2010, a systematic review of effects of acupuncture in irradiation-induced xerostomia in 61 articles left only three reports sufficiently similar to be included in the review¹⁵¹. Improvement in xerostomia occurred in all three trials. A narrative review from October 2010 identified a potential role for acupuncture in xerostomia¹⁵². Current evidence is insufficient to recommend this intervention, but it is sufficient to justify further studies¹⁵³. Since acupuncture is safe with minimal side-effects and is reported to be clinically effective in some patients^{21, 24, 153-162}, health professionals should be open to explore the use of acupuncture for management of their cancer patients with xerostomia.

Mouth Exercises: A unique study reported positive results in the intervention group after a 3 month oral function promotion program for independently living Japanese¹⁵⁰, which included facial muscle and tongue exercises as well as salivary gland massage. Indeed, the salivary flow rate increased; tongue coating scores decreased as did the organoleptic score of oral malodor. The amount of food debris in the oral cavity decreased, and the tongue dryness also improved.

3. Non-Saliva Stimulating Medications

A 2010 systematic review concluded that *melatonin* may have beneficial effects in certain oral pathologies, including periodontal diseases, herpes viral infections and Candida, local inflammatory processes, xerostomia, oral ulcers and oral cancer mostly due to its anti-inflammatory properties in alleviating oxidative stress¹⁶³.

Research Frontiers: In the current quest for new treatment for patients with compromised oral health often seen in patients with xerostomia, it was found that the tooth-bleaching agent 10 % carbamide peroxide (CP) applied in a custom-fitted tray has positive effects on plaque, gingival health, and caries and may thus hold great promise for patients with dry mouth¹⁶⁴. CP may reduce caries by elevating the pH level above that at which carious lesions progress, in addition to debriding the teeth and improving gingival health.

Palifermin (a recombinant human keratinocyte growth factor; DeltaN23-KGF) is important for healing. It was the first agent to received FDA approval to stimulate the proliferation and differentiation of mucosal epithelium to reduce the severity and duration of oral mucositis in patients receiving myelotoxic therapies requiring hematopoietic cell support¹⁴⁴. Palifermin has been used successfully in a study in patients receiving concurrent chemoradiotherapy for advanced head and neck squamous cell carcinoma¹⁶⁵. Palifermin appeared to reduce mucositis, dysphagia, and xerostomia during hyperfractionated radiotherapy (n = 40), but not during standard radiation therapy (n = 59) while not altering tumor response or survival. The conclusion was that 10 once-weekly doses of palifermin at 60 microg/kg were well tolerated¹⁶⁵. Palifermin is used to prevent¹⁶⁶ or decrease severe oral mucositis¹⁴⁴ in the setting of hematopoietic stem cell transplantation and oral cryotherapy used in conjunction with bolus 5-FU, melphalan, or edatrexate¹⁶⁶.

VI ADDITIONAL INFORMATION SOURCES ON XEROSTOMIA

Various publications and online resources are listed in Table 6A (pages 33-35) for health care providers and Table 6B (page 36) for patients. One highly relevant publication is to be especially recommended, namely “*Dry Mouth, the Malevolent Symptom: A Clinical Guide*”. This comprehensive book published in late 2010 was edited by the leading world experts on xerostomia

through several decades, Leo M. Sreebny and Arjan Vissink. Please, see Table 6A (page 33) for more detail, including purchasing information.

VII SALIVARY DIAGNOSTICS

A report on saliva-related conditions would not be complete without a brief mention of additional attributes and uses of saliva. For the past two decades, salivary diagnostic approaches have been developed to monitor oral diseases such as *periodontal diseases* and to assess *caries risk*¹⁶⁷. The mapped salivary proteome, or “dictionary”, of proteins present in human saliva, is currently available online⁷². Salivary diagnostics is a dynamic and emerging field utilizing nanotechnology and molecular diagnostics to aid in the diagnosis of oral and systemic diseases¹⁶⁸.

The avenue of saliva diagnostics incorporating *transcriptomic, proteomic, and metabolomic findings* will enable utilizing salivary molecular analytes in *cancer*¹⁶⁷, such as *oral squamous cell cancer*¹⁶⁹, the aggressive cancer of the *mobile part of the tongue*¹⁷⁰, and detection and follow-up of cancer of the *salivary glands* themselves¹⁷¹, as well as cancers located remotely from the mouth¹⁷², such as *breast cancer*¹⁷²⁻¹⁷⁴. *Capillary electrophoresis mass spectrometry-based saliva metabolomics also have identified oral, breast, and pancreatic cancer-specific profiles*^{174a}.

Elevated *glucose levels in parotid saliva* ≥ 2 hours after food intake can indicate *impaired glucose tolerance* or manifest *diabetes mellitus (DM)*¹⁷⁵; salivary glucose levels may serve as a simple, quick, and economical measure of autonomic *neuropathy* in DM¹⁷⁶; and type 2 DM could be detected and monitored via proteomic identification of salivary biomarkers¹⁷⁷ or by infrared saliva spectroscopy¹⁷⁸. *Mid-infrared spectroscopy* has identified salivary *periodontitis-specific molecular markers*¹⁷⁹; *fatty acids*¹⁷⁵ and *three periodontal pathogens*¹⁸⁰ have been used as diagnostics for *chronic periodontitis*; and *combinations of salivary biomarkers* provide highly accurate predictions of *periodontal disease category*¹⁸¹. Saliva may also be a clinical tool for *bile acid testing*¹⁸². Non-invasive molecular analysis of *fetal DNA* is the diagnostic goal of prenatal medicine and it is hypothesized that saliva might contain such DNA¹⁶⁸. Salivary diagnostics can also detect *drug abuse*, such as *ecstasy*⁶⁹. Furthermore, the salivary gland secretes proteins and hormones and is a sophisticated bioreactor that may be used to *deliver drugs, genes, proteins or other molecules to the bloodstream*.

In summary, the composition of saliva is likely to be unique to each individual. Saliva provides a window into the entire body through its content of various substances stemming from conditions in health and disease anywhere in the human organism, reflecting emotional, endocrinal, nutritional, metabolic, and genetic variations.

Miniaturization of detection devices (probes) will facilitate salivary diagnostics to be used for minimally interventional, pain-free, chairside diagnosis, treatment, and monitoring of a host of oral and systemic conditions, including home-use to alert patients to consult their health professionals at the earliest sign of disease. The vast majority (87.7%) of a representative sample of U.S. general dentists (N=1,945) is ready and willing to collect saliva samples for detection and follow-up of systemic disease¹⁸³, and almost all (96.4%) will refer patients to their physician counterparts for consultation and further follow-up. A new era of practicing dentistry and medicine according to a novel, collaborative paradigm is here.

VIII BIBLIOGRAPHY

1. Willumsen T, Fjaera B, Eide H. Oral health-related quality of life in patients receiving home-care nursing: associations with aspects of dental status and xerostomia. *Gerodontology* 2009.
2. National Institute of Dental and Craniofacial Research-National Institutes of Health. Dry mouth (xerostomia); 2010.
3. Sreebny LM, Vissink A, editors. Dry mouth, the malevolent symptom: a clinical guide. Singapore: Wiley-Blackwell. 268 pp.; 2010.
4. Ship JA, Fox PC, Baum BJ. How much saliva is enough? 'Normal' function defined. *J Am Dent Assoc* 1991;122(3):63-9.
5. Marton K, Madlena M, Banoczy J, Varga G, Fejerdy P, Sreebny LM, et al. Unstimulated whole saliva flow rate in relation to sicca symptoms in Hungary. *Oral diseases* 2008;14(5):472-77.
6. Glore RJ, Spiteri-Staines K, Paleri V. A patient with dry mouth. *Clin Otolaryngol* 2009;34(4):358-63.
7. von Bultzingslowen I, Sollecito TP, Fox PC, Daniels T, Jonsson R, Lockhart PB, et al. Salivary dysfunction associated with systemic diseases: systematic review and clinical management recommendations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103 Suppl:S57 e1-15.
8. Ghezzi EM, Lange LA, Ship JA. Determination of variation of stimulated salivary flow rates. *J Dent Res* 2000;79(11):1874-8.
9. Nederfors T, Isaksson R, Mornstad H, Dahlof C. Prevalence of perceived symptoms of dry mouth in an adult Swedish population--relation to age, sex and pharmacotherapy. *Community Dent Oral Epidemiol* 1997;25(3):211-6.
10. Chavez EM, Taylor GW, Borrell LN, Ship JA. Salivary function and glycemic control in older persons with diabetes. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89(3):305-11.
11. Agha-Hosseini F, Mirzaii-Dizgah I, Mansourian A, Zabihi-Akhtechi G. Serum and stimulated whole saliva parathyroid hormone in menopausal women with oral dry feeling. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics* 2009;107(6):806-10.
12. Agha-Hosseini F, Mirzaii-Dizgah I, Moghaddam PP, Akrad ZT. Stimulated whole salivary flow rate and composition in menopausal women with oral dryness feeling. *Oral diseases* 2007;13(3):320-23.
13. Agha-Hosseini F, Mirzaii-Dizgah I, Mirjalili N. Relationship of stimulated whole saliva cortisol level with the severity of a feeling of dry mouth in menopausal women. *Gerodontology* 2010.
14. Mirzaii-Dizgah I, Agha-Hosseini F. Stimulated and unstimulated saliva progesterone in menopausal women with oral dryness feeling. *Clin Oral Investig* 2010.
15. Agha-Hosseini F, Mirzaii-Dizgah I, Mansourian A, Khayamzadeh M. Relationship of stimulated saliva 17beta-estradiol and oral dryness feeling in menopause. *Maturitas* 2009;62(2):197-99.
16. Guggenheimer J, Moore PA. Xerostomia: etiology, recognition and treatment. *J Am Dent Assoc* 2003;134(1):61-9; quiz 118-9.
17. Field EA, Fear S, Higham SM, Ireland RS, Rostron J, Willetts RM, et al. Age and medication are significant risk factors for xerostomia in an English population, attending general dental practice. *Gerodontology* 2001;18(1):21-4.
18. Hochberg MC, Tielsch J, Munoz B, Bandeen-Roche K, West SK, Schein OD. Prevalence of symptoms of dry mouth and their relationship to saliva production in community dwelling elderly: the SEE project. *Salisbury Eye Evaluation. J Rheumatol* 1998;25(3):486-91.
19. Gilbert GH, Heft MW, Duncan RP. Mouth dryness as reported by older Floridians. *Community Dent Oral Epidemiol* 1993;21(6):390-7.
20. Brand HS, Bots CP, Raber-Durlacher JE. Xerostomia and chronic oral complications among patients treated with haematopoietic stem cell transplantation. *Br Dent J* 2009;207(9):E17; discussion 428-9.
21. Garcia MK, Chiang JS, Cohen L, Liu M, Palmer JL, Rosenthal DI, et al. Acupuncture for radiation-induced xerostomia in patients with cancer: a pilot study. *Head Neck* 2009;31(10):1360-8.

22. Leung KC, McMillan AS, Wong MC, Leung WK, Mok MY, Lau CS. The efficacy of cevimeline hydrochloride in the treatment of xerostomia in Sjogren's syndrome in southern Chinese patients: a randomised double-blind, placebo-controlled crossover study. *Clin Rheumatol* 2008;27(4):429-36.
23. Thomson WM, Chalmers JM, John Spencer A, Slade GD, Carter KD. A longitudinal study of medication exposure and xerostomia among older people. *Gerodontology* 2006;23(4):205-13.
24. Pfister DG, Cassileth BR, Deng GE, Yeung KS, Lee JS, Garrity D, et al. Acupuncture for pain and dysfunction after neck dissection: results of a randomized controlled trial. *J Clin Oncol* 2010;28(15):2565-70.
25. Thomson WM. Measuring change in dry-mouth symptoms over time using the Xerostomia Inventory. *Gerodontology* 2007;24(1):30-35.
26. Thomson WM, Chalmers JM, Spencer AJ, Slade GD. Medication and dry mouth: findings from a cohort study of older people. *J Public Health Dent* 2000;60(1):12-20.
27. Ghezzi EM, Wagner-Lange LA, Schork MA, Metter EJ, Baum BJ, Streckfus CF, et al. Longitudinal influence of age, menopause, hormone replacement therapy, and other medications on parotid flow rates in healthy women. *J Gerontol A Biol Sci Med Sci* 2000;55(1):M34-42.
28. Chavez EM, Borrell LN, Taylor GW, Ship JA. A longitudinal analysis of salivary flow in control subjects and older adults with type 2 diabetes. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;91(2):166-73.
29. Zussman E, Yarin AL, Nagler RM. Age- and flow-dependency of salivary viscoelasticity. *Journal of dental research* 2007;86(3):281-85.
30. Johansson AK, Johansson A, Unell L, Ekback G, Ordell S, Carlsson GE. A 15-yr longitudinal study of xerostomia in a Swedish population of 50-yr-old subjects. *European journal of oral sciences* 2009;117(1):13-19.
31. Borges BC, Fulco GM, Souza AJ, de Lima KC. Xerostomia and hyposalivation: a preliminary report of their prevalence and associated factors in Brazilian elderly diabetic patients. *Oral Health & Preventive Dentistry* 2010;8(2):153-58.
32. Scott J, Flower EA, Burns J. A quantitative study of histological changes in the human parotid gland occurring with adult age. *J Oral Pathol* 1987;16(10):505-10.
33. Drummond JR, Newton JP, Abel RW. Tomographic measurements of age changes in the human parotid gland. *Gerodontology* 1995;12(1):26-30.
34. Ship JA, Pillemer SR, Baum BJ. Xerostomia and the geriatric patient. *J Am Geriatr Soc* 2002;50(3):535-43.
35. Ghezzi EM, Ship JA. Aging and secretory reserve capacity of major salivary glands. *J Dent Res* 2003;82(10):844-8.
36. Meurman JH, Tarkkila L, Tiitinen A. The menopause and oral health. *Maturitas* 2009;63(1):56-62.
37. Thomas BL, Brown JE, McGurk M. Salivary gland disease. *Front Oral Biol* 2010;14:129-46.
38. Sanchez GA, Miozza V, Delgado A, Busch L. Determination of salivary levels of mucin and amylase in chronic periodontitis patients. *J Periodontal Res* 2011;46(2):221-7.
39. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *Journal of Periodontology* 2007;78(7 Suppl):1387-99.
40. Teppo H, Revonta M. A follow-up study of minimally invasive lip biopsy in the diagnosis of Sjogren's syndrome. *Clinical rheumatology* 2007;26(7):1099-103.
41. National Institutes of Health: National Institute of Dental and Craniofacial Research National Institutes of Health. Sjögren's Syndrome Clinic.
42. Fox PC, Bowman SJ, Segal B, Vivino FB, Murukutla N, Choueiri K, et al. Oral involvement in primary Sjogren syndrome. *Journal of the American Dental Association* 2008;139(12):1592-601.
43. Fox PC. Xerostomia: recognition and management. *Dent Assist* 2008;77(5):18, 20, 44-8; quiz 50-1.
44. Lalla RV, Sonis ST, Peterson DE. Management of oral mucositis in patients who have cancer. *Dental Clinics of North America* 2008;52(1):61-77.

45. Karolewska E, Konopka T, Pupek M, Chybicka A, Mendak M. Antibacterial potential of saliva in children with leukemia. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics* 2008;105(6):739-44.
46. Wahlin YB. Salivary secretion rate, yeast cells, and oral candidiasis in patients with acute leukemia. *Oral Surg Oral Med Oral Pathol* 1991;71(6):689-95.
47. Mansson-Rahemtulla B, Techanitiswad T, Rahemtulla F, McMillan TO, Bradley EL, Wahlin YB. Analyses of salivary components in leukemia patients receiving chemotherapy. *Oral Surg Oral Med Oral Pathol* 1992;73(1):35-46.
48. Vincent C, Agard C, Barbarot S, N'Guyen J M, Planchon B, Durant C, et al. Orofacial manifestations of systemic sclerosis: A study of 30 consecutive patients. [French]. *Rev Stomatol Chir Maxillofac* 2010;111(3):128-34.
49. Nittayananta W, Chanowanna N, Jealae S, Nauntofte B, Stoltze K. Hyposalivation, xerostomia and oral health status of HIV-infected subjects in Thailand before HAART era. *J Oral Pathol Med* 2010;39(1):28-34.
50. Navazesh M, Mulligan R, Karim R, Mack WJ, Ram S, Seirawan H, et al. Effect of HAART on salivary gland function in the Women's Interagency HIV Study (WIHS). *Oral Dis* 2009;15(1):52-60.
51. Jainkittivong A, Lin AL, Johnson DA, Langlais RP, Yeh CK. Salivary secretion, mucin concentrations and *Candida* carriage in HIV-infected patients. *Oral Dis* 2009;15(3):229-34.
52. Cavasin Filho JC, Giovani EM. Xerostomy, dental caries and periodontal disease in HIV+ patients. *Braz J Infect Dis* 2009;13(1):13-7.
53. Moura MD, Senna MI, Madureira DF, Fonseca LM, Mesquita RA. Oral adverse effects due to the use of Nevirapine. *J Contemp Dent Pract* 2008;9(1):84-90.
54. Gennaro S, Naidoo S, Berthold P. Oral health & HIV/AIDS. *MCN Am J Matern Child Nurs* 2008;33(1):50-7.
55. Engeland CG, Jang P, Alves M, Marucha PT, Califano J. HIV infection and tooth loss. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;105(3):321-6.
56. Coracin FL, Pizzigatti Correa ME, Camargo EE, Peterson DE, de Oliveira Santos A, Vigorito AC, et al. Major salivary gland damage in allogeneic hematopoietic progenitor cell transplantation assessed by scintigraphic methods. *Bone marrow transplantation* 2006;37(10):955-9.
57. Epstein JB, Raber-Drulacher JE, Wilkins A, Chavarria MG, Myint H. Advances in hematologic stem cell transplant: an update for oral health care providers. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107(3):301-12.
58. Pereira CM, de Almeida OP, Correa ME, Costa FF, de Souza CA, Barjas-Castro ML. Detection of human herpesvirus 6 in patients with oral chronic graft-vs-host disease following allogeneic progenitor cell transplantation. *Oral Diseases* 2007;13(3):329-34.
59. Defabianis P, Braida S, Guagnano R. 180-day screening study for predicting the risk factors for developing acute oral Graft-versus-Host disease in paediatric patients subjected to allogeneic haematopoietic stem cells transplantation. *Eur J Paediatr Dent* 2010;11(1):31-4.
60. Ohbayashi Y, Imataki O, Ohnishi H, Iwasaki A, Ogawa T, Inagaki N, et al. Multivariate analysis of factors influencing oral mucositis in allogeneic hematopoietic stem cell transplantation. *Annals of Hematology* 2008;87(10):837-45.
61. Larsen J, Nordstrom G, Ljungman P, Gardulf A. Factors associated with poor general health after stem-cell transplantation. *Supportive Care in Cancer* 2007;15(7):849-57.
62. Majhail NS, Ness KK, Burns LJ, Sun CL, Carter A, Francisco L, et al. Late effects in survivors of Hodgkin and non-Hodgkin lymphoma treated with autologous hematopoietic cell transplantation: a report from the bone marrow transplant survivor study. *Biology of Blood & Marrow Transplantation* 2007;13(10):1153-59.
63. Ozturk M, Komurcu S, Kilic S, Ozet A, Arpaci F, Ozturk B, et al. Self-reported experience of mucositis in cancer patients who underwent conditioning regimen and stem cell transplantation. *Support Care Cancer* 2009;17(10):1295-9.

64. Versteeg PA, Slot DE, van der Velden U, van der Weijden GA. Effect of cannabis usage on the oral environment: a review. *Int J Dent Hyg* 2008;6(4):315-20.
65. Schulz-Katterbach M, Imfeld T, Imfeld C. Cannabis and caries--does regular cannabis use increase the risk of caries in cigarette smokers? *Schweiz Monatsschr Zahnmed* 2009;119(6):576-83.
66. Turkyilmaz I. Oral manifestations of "meth mouth": a case report. *J Contemp Dent Pract* 2010;11(1):E073-80.
67. Hamamoto DT, Rhodus NL. Methamphetamine abuse and dentistry. *Oral Dis* 2009;15(1):27-37.
68. Heng CK, Badner VM, Schiop LA. Meth mouth. *N Y State Dent J* 2008;74(5):50-1.
69. Brand HS, Dun SN, Nieuw Amerongen AV. Ecstasy (MDMA) and oral health. *Br Dent J* 2008;204(2):77-81.
70. Hoffman BM, Babyak MA, Craighead WE, Sherwood A, Doraiswamy PM, Coons MJ, et al. Exercise and Pharmacotherapy in Patients With Major Depression: One-Year Follow-Up of the SMILE Study. *Psychosom Med* 2010.
71. Pakkala I, Read S, Leinonen R, Hirvensalo M, Lintunen T, Rantanen T. The effects of physical activity counseling on mood among 75- to 81-year-old people: a randomized controlled trial. *Prev Med* 2008;46(5):412-8.
72. National Institute of Dental and Craniofacial Research: National Institutes of Health. NIDCR strategic plan 2009-2013.
73. Cameron JE, Hagensee ME. Oral HPV complications in HIV-infected patients. [Review] [43 refs]. *Current HIV/AIDS Reports* 2008;5(3):126-31.
74. Syrjanen S. Human papillomavirus (HPV) in head and neck cancer. *J Clin Virol* 2005;32 Suppl 1:S59-66.
75. Henson BS, Inglehart MR, Eisbruch A, Ship JA. Preserved salivary output and xerostomia-related quality of life in head and neck cancer patients receiving parotid-sparing radiotherapy. *Oral Oncol* 2001;37(1):84-93.
76. Hey J, Setz J, Gerlach R, Vordermark D, Gernhardt CR, Kuhnt T. Effect of Cisplatin on parotid gland function in concomitant radiochemotherapy. *International journal of radiation oncology, biology, physics* 2009;75(5):1475-80.
77. Hey J, Setz J, Gerlach R, Janich M, Sehlleier S, Schaller HG, et al. Parotid-gland-sparing 3D conformal radiotherapy in patients with bilateral radiotherapy of the head and neck region--results in clinical practice. *Oral Oncol* 2009;45(2):e11-7.
78. Ingle CJ, Yip K, Caskie V, Dyson C, Ford A, Scrase CD. Intensity modulated radiotherapy (IMRT) in the management of locally advanced oropharyngeal squamous cell carcinomata (SCC): disease control and functional outcome using the therapy outcome measure (TOM) score--report from a single U.K. institution. *Head Neck Oncol* 2010;2:28.
79. Murdoch-Kinch CA, Kim HM, Vineberg KA, Ship JA, Eisbruch A. Dose-effect relationships for the submandibular salivary glands and implications for their sparing by intensity modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2008;72(2):373-82.
80. Platteaux N, Dirix P, Dejaeger E, Nuyts S. Dysphagia in head and neck cancer patients treated with chemoradiotherapy. *Dysphagia* 2010;25(2):139-52.
81. van Holten MJ, Roesink JM, Terhaard CH, Braam PM. New insights in the vascular supply of the human parotid gland - consequences for parotid gland-sparing irradiation. *Head Neck* 2010;32(7):837-43.
82. Ahmed M, Hansen VN, Harrington KJ, Nutting CM. Reducing the risk of xerostomia and mandibular osteoradionecrosis: the potential benefits of intensity modulated radiotherapy in advanced oral cavity carcinoma. *Med Dosim* 2009;34(3):217-24.
83. Al-Nawas B, Al-Nawas K, Kunkel M, Grotz KA. Quantifying radioxerostomia: salivary flow rate, examiner's score, and quality of life questionnaire. *Strahlentherapie und Onkologie* 2006;182(6):336-41.
84. Dijkema T, Terhaard CH, Roesink JM, Braam PM, van Gils CH, Moerland MA, et al. Large cohort dose-volume response analysis of parotid gland function after radiotherapy: intensity-modulated versus conventional radiotherapy. *Int J Radiat Oncol Biol Phys* 2008;72(4):1101-9.
85. Dirix P, Nuyts S. Evidence-based organ-sparing radiotherapy in head and neck cancer. *Lancet Oncol* 2010;11(1):85-91.

86. Dirix P, Vanstraelen B, Jorissen M, Vander Poorten V, Nuyts S. Intensity-modulated radiotherapy for sinonasal cancer: improved outcome compared to conventional radiotherapy. *Int J Radiat Oncol Biol Phys* 2010;78(4):998-1004.
87. Houweling AC, Dijkema T, Roesink JM, Terhaard CH, Raaijmakers CP. Sparing the contralateral submandibular gland in oropharyngeal cancer patients: a planning study. *Radiother Oncol* 2008;89(1):64-70.
88. Houweling AC, van den Berg CA, Roesink JM, Terhaard CH, Raaijmakers CP. Magnetic resonance imaging at 3.0T for submandibular gland sparing radiotherapy. *Radiother Oncol* 2010;97(2):239-43.
89. Huang K, Xia P, Chuang C, Weinberg V, Glastonbury CM, Eisele DW, et al. Intensity-modulated chemoradiation for treatment of stage III and IV oropharyngeal carcinoma: the University of California-San Francisco experience. *Cancer* 2008;113(3):497-507.
90. Jellema AP, Slotman BJ, Doornaert P, Leemans CR, Langendijk JA. Unilateral versus bilateral irradiation in squamous cell head and neck cancer in relation to patient-rated xerostomia and sticky saliva. *Radiotherapy & Oncology* 2007;85(1):83-89.
91. Jensen SB, Pedersen AM, Vissink A, Andersen E, Brown CG, Davies AN, et al. A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life. *Support Care Cancer* 2010;18(8):1039-60.
92. Kam MK, Leung SF, Zee B, Chau RM, Suen JJ, Mo F, et al. Prospective randomized study of intensity-modulated radiotherapy on salivary gland function in early-stage nasopharyngeal carcinoma patients. *Journal of Clinical Oncology* 2007;25(31):4873-79.
93. Kan T, Kodani K, Michimoto K, Fujii S, Ogawa T. Radiation-induced damage to microstructure of parotid gland: evaluation using high-resolution magnetic resonance imaging. *Int J Radiat Oncol Biol Phys* 2010;77(4):1030-8.
94. Kong L, Zhang YW, Hu CS, Guo Y. Neoadjuvant chemotherapy followed by concurrent chemoradiation for locally advanced nasopharyngeal carcinoma. *Chin J Cancer* 2010;29(5):551-5.
95. Koukourakis MI, Tsoutsou PG, Karpouzis A, Tsiarkatsi M, Karapantzios I, Daniilidis V, et al. Radiochemotherapy with cetuximab, cisplatin, and amifostine for locally advanced head and neck cancer: a feasibility study. *Int J Radiat Oncol Biol Phys* 2010;77(1):9-15.
96. Li Y, Taylor JM, Ten Haken RK, Eisbruch A. The impact of dose on parotid salivary recovery in head and neck cancer patients treated with radiation therapy. *International journal of radiation oncology, biology, physics* 2007;67(3):660-69.
97. Liu WS, Lee SP, Lee JK, Su MC, Chen GD, Lee HS, et al. Factors influencing the parotid function in nasopharyngeal carcinoma treated with parotid-sparing radiotherapy. *Japanese journal of clinical oncology* 2006;36(10):626-31.
98. Ng MK, Porceddu SV, Milner AD, Corry J, Hornby C, Hope G, et al. Parotid-sparing radiotherapy: does it really reduce xerostomia? *Clinical Oncology (Royal College of Radiologists)* 2005;17(8):610-17.
99. Pehlivan B, Luthi F, Matzinger O, Betz M, Dragusanu D, Bulling S, et al. Feasibility and efficacy of accelerated weekly concomitant boost postoperative radiation therapy combined with concomitant chemotherapy in patients with locally advanced head and neck cancer. *Ann Surg Oncol* 2009;16(5):1337-43.
100. Pow EH, Kwong DL, McMillan AS, Wong MC, Sham JS, Leung LH, et al. Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report on a randomized controlled clinical trial. *International journal of radiation oncology, biology, physics* 2006;66(4):981-91.
101. Rades D, Stoeckl M, Meyners T, Bohlen G, Nadrowitz R, Dunst J, et al. Evaluation of prognostic factors and two radiation techniques in patients treated with surgery followed by radio(chemo)therapy or definitive radio(chemo)therapy for locally advanced head-and-neck cancer. *Strahlenther Onkol* 2008;184(4):198-205.
102. Rusthoven KE, Raben D, Ballonoff A, Kane M, Song JI, Chen C. Effect of radiation techniques in treatment of oropharynx cancer. *Laryngoscope* 2008;118(4):635-9.

103. Rusthoven KE, Raben D, Schneider C, Witt R, Sammons S, Raben A. Freedom from local and regional failure of contralateral neck with ipsilateral neck radiotherapy for node-positive tonsil cancer: results of a prospective management approach. *Int J Radiat Oncol Biol Phys* 2009;74(5):1365-70.
104. Saarilahti K, Kouri M, Collan J, Kangasmaki A, Atula T, Joensuu H, et al. Sparing of the submandibular glands by intensity modulated radiotherapy in the treatment of head and neck cancer. *Radiotherapy & Oncology* 2006;78(3):270-75.
105. Seung S, Bae J, Solhjem M, Bader S, Gannett D, Hansen EK, et al. Intensity-modulated radiotherapy for head-and-neck cancer in the community setting. *Int J Radiat Oncol Biol Phys* 2008;72(4):1075-81.
106. Thariat J, Bolle S, Demizu Y, Marcy PY, Hu Y, Santini J, et al. New techniques in radiation therapy for head and neck cancer: IMRT, CyberKnife, protons, and carbon ions, Improved effectiveness and safety? Impact on survival? *Anticancer Drugs* 2010.
107. van de Water TA, Lomax AJ, Bijl HP, de Jong ME, Schilstra C, Hug EB, et al. Potential Benefits of Scanned Intensity-Modulated Proton Therapy Versus Advanced Photon Therapy with Regard to Sparing of the Salivary Glands in Oropharyngeal Cancer. *Int J Radiat Oncol Biol Phys* 2010.
108. Vergeer MR, Doornaert PA, Rietveld DH, Leemans CR, Slotman BJ, Langendijk JA. Intensity-modulated radiotherapy reduces radiation-induced morbidity and improves health-related quality of life: results of a nonrandomized prospective study using a standardized follow-up program. *Int J Radiat Oncol Biol Phys* 2009;74(1):1-8.
109. Wada A, Uchida N, Yokokawa M, Yoshizako T, Kitagaki H. Radiation-induced xerostomia: objective evaluation of salivary gland injury using MR sialography. *AJNR Am J Neuroradiol* 2009;30(1):53-8.
110. Madani I, Vakaet L, Bonte K, Boterberg T, De Neve W. Intensity-modulated radiotherapy for cervical lymph node metastases from unknown primary cancer. *Int J Radiat Oncol Biol Phys* 2008;71(4):1158-66.
111. Cortelli JR, Barbosa MD, Westphal MA. Halitosis: a review of associated factors and therapeutic approach. *Braz Oral Res* 2008;22 Suppl 1:44-54.
112. Pratibha PK, Bhat KM, Bhat GS. Oral malodor: a review of the literature. *J Dent Hyg* 2006;80(3):8.
113. Scardina GA, Ruggieri A, Messina P. Periodontal disease and sjogren syndrome: a possible correlation? *Angiology* 2010;61(3):289-93.
114. Schoenfeld JD, Sher DJ, Norris CM, Jr., Haddad RI, Posner MR, Balboni TA, et al. Salivary Gland Tumors Treated With Adjuvant Intensity-Modulated Radiotherapy With or Without Concurrent Chemotherapy. *Int J Radiat Oncol Biol Phys* 2010.
115. Sun HB, Gao XJ, Deng J, Li NY, Lu HJ. Progress of oral sequelae during head-neck radiotherapy. *Chin J Dent Res* 2010;13(1):51-5.
116. Lambertz CK, Gruell J, Robenstein V, Mueller-Funaiole V, Cummings K, Knapp V. NO SToPS: Reducing treatment breaks during chemoradiation for head and neck cancer. *Clin J Oncol Nurs* 2010;14(5):585-93.
117. Farrington M, Cullen L, Dawson C. Assessment of oral mucositis in adult and pediatric oncology patients: an evidence-based approach. *ORL Head Neck Nurs* 2010;28(3):8-15.
118. Goel A, Tripathi A, Chand P, Singh SV, Pant MC, Nagar A. Use of positioning stents in lingual carcinoma patients subjected to radiotherapy. *Int J Prosthodont* 2010;23(5):450-2.
119. Moon SH, Jung YS, Ryu JS, Choi SW, Park JY, Yun T, et al. Outcomes of Postoperative Simultaneous Modulated Accelerated Radiotherapy for Head-and-Neck Squamous Cell Carcinoma. *Int J Radiat Oncol Biol Phys* 2010.
120. Saavedra MM, Henriquez-Hernandez LA, Lara PC, Pinar B, Rodriguez-Gallego C, Lloret M. Amifostine modulates radio-induced apoptosis of peripheral blood lymphocytes in head and neck cancer patients. *J Radiat Res (Tokyo)* 2010;51(5):603-7.
121. Deng Z, Kiyuna A, Hasegawa M, Nakasone I, Hosokawa A, Suzuki M. Oral candidiasis in patients receiving radiation therapy for head and neck cancer. *Otolaryngol Head Neck Surg* 2010;143(2):242-7.
122. Buntzel J, Riesenbeck D, Glatzel M, Berndt-Skorcka R, Riedel T, Mucke R, et al. Limited effects of selenium substitution in the prevention of radiation-associated toxicities. results of a randomized study in head and neck cancer patients. *Anticancer Res* 2010;30(5):1829-32.

123. Chitapanarux I, Lorvidhaya V, Tharavichitkul E, Mayurasakorn S, Sittitrai P, Pattarasakulchai T, et al. A phase II study of docetaxel and carboplatin with concurrent radiation therapy for locally advanced head and neck cancer. *Auris Nasus Larynx* 2010.
124. Glenny AM, Gibson F, Auld E, Coulson S, Clarkson JE, Craig JV, et al. The development of evidence-based guidelines on mouth care for children, teenagers and young adults treated for cancer. *Eur J Cancer* 2010;46(8):1399-412.
125. de Castro G, Jr., Guindalini RS. Supportive care in head and neck oncology. *Curr Opin Oncol* 2010;22(3):221-5.
126. Janssens GO, Terhaard CH, Doornaert PA, Bijl HP, van den Ende P, Chin A, et al. Acute Toxicity Profile and Compliance to Accelerated Radiotherapy Plus Carbogen and Nicotinamide for Clinical Stage T2-4 Laryngeal Cancer: Results of a Phase III Randomized Trial. *Int J Radiat Oncol Biol Phys* 2011.
127. National Comprehensive Cancer Network. Prevention and Treatment of Cancer-Related Infections. 107 pp. Version 2 ed; 2009.
128. Scarpace SL, Brodzik FA, Mehdi S, Belgam R. Treatment of head and neck cancers: issues for clinical pharmacists. *Pharmacotherapy* 2009;29(5):578-92.
129. Ward E, Smith M, Henderson M, Reid U, Lewis I, Kinsey S, et al. The effect of high-dose enteral glutamine on the incidence and severity of mucositis in paediatric oncology patients. *European Journal of Clinical Nutrition* 2009;63(1):134-40.
130. Tomlinson D, Gibson F, Treister N, Baggott C, Judd P, Hendershot E, et al. Designing an oral mucositis assessment instrument for use in children: generating items using a nominal group technique. *Supportive Care in Cancer* 2009;17(5):555-62.
131. Tomlinson D, Gibson F, Treister N, Baggott C, Judd P, Hendershot E, et al. Understandability, content validity, and overall acceptability of the Children's International Mucositis Evaluation Scale (ChIMES): child and parent reporting. *Journal of Pediatric Hematology/Oncology* 2009;31(6):416-23.
132. Khouri VY, Stracieri AB, Rodrigues MC, Moraes DA, Pieroni F, Simoes BP, et al. Use of therapeutic laser for prevention and treatment of oral mucositis. *Brazilian Dental Journal* 2009;20(3):215-20.
133. Zero DT, Lussi A. Erosion--chemical and biological factors of importance to the dental practitioner. *Int Dent J* 2005;55(4 Suppl 1):285-90.
134. Di Fede O, Di Liberto C, Occhipinti G, Vigneri S, Lo Russo L, Fedele S, et al. Oral manifestations in patients with gastro-oesophageal reflux disease: a single-center case-control study. *Journal of Oral Pathology & Medicine* 2008;37(6):336-40.
135. Zero DT. Etiology of dental erosion--extrinsic factors. *Eur J Oral Sci* 1996;104(2 (Pt 2)):162-77.
136. Magalhaes AC, Wiegand A, Rios D, Honorio HM, Buzalaf MA. Insights into preventive measures for dental erosion. *J Appl Oral Sci* 2009;17(2):75-86.
137. Chehal HK, Pate DH, Cohen DM, Bhattacharyya I. Dental erosion due to excessive wine consumption. *Gen Dent* 2009;57(5):519-23.
138. Visvanathan V, Nix P. Managing the patient presenting with xerostomia: a review. *Int J Clin Pract* 2010;64(3):404-7.
139. Twetman S. Treatment protocols: nonfluoride management of the caries disease process and available diagnostics. *Dent Clin North Am* 2010;54(3):527-40.
140. Singh ML, Papas AS. Long-term clinical observation of dental caries in salivary hypofunction patients using a supersaturated calcium-phosphate remineralizing rinse. *J Clin Dent* 2009;20(3):87-92.
141. Burlage FR, Roesink JM, Kampinga HH, Coppes RP, Terhaard C, Langendijk JA, et al. Protection of salivary function by concomitant pilocarpine during radiotherapy: a double-blind, randomized, placebo-controlled study. *Int J Radiat Oncol Biol Phys* 2008;70(1):14-22.
142. Ramos-Casals M, Tzioufas AG, Stone JH, Siso A, Bosch X. Treatment of primary Sjogren syndrome: a systematic review. *JAMA* 2010;304(4):452-60.
143. Jorkjend L, Bergenholtz A, Johansson AK, Johansson A. Effect of Pilocarpine on impaired salivary secretion in patients with Sjogren's syndrome. *Swed Dent J* 2008;32(2):49-56.

144. Hensley ML, Hagerty KL, Kewalramani T, Green DM, Meropol NJ, Wasserman TH, et al. American Society of Clinical Oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants. *J Clin Oncol* 2009;27(1):127-45.
145. Ma C, Xie J, Jiang Z, Wang G, Zuo S. Does amifostine have radioprotective effects on salivary glands in high-dose radioactive iodine-treated differentiated thyroid cancer. *Eur J Nucl Med Mol Imaging* 2010;37(9):1778-85.
146. Cankaya H, Alpoz E, Karabulut G, Guneri P, Boyacioglu H, Kabasakal Y. Effects of hydroxychloroquine on salivary flow rates and oral complaints of Sjogren patients: a prospective sample study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;110(1):62-7.
147. Jensdottir T, Buchwald C, Nauntofte B, Hansen HS, Bardow A. Erosive potential of calcium-modified acidic candies in irradiated dry mouth patients. *Oral Health Prev Dent* 2010;8(2):173-8.
148. Lajer C, Buchwald C, Nauntofte B, Specht L, Bardow A, Jensdottir T. Erosive potential of saliva stimulating tablets with and without fluoride in irradiated head and neck cancer patients. *Radiother Oncol* 2009;93(3):534-8.
149. Crogan NL. Managing xerostomia in nursing homes: pilot testing of the Sorbet Increases Salivation intervention. *J Am Med Dir Assoc* 2011;12(3):212-6.
150. Hakuta C, Mori C, Ueno M, Shinada K, Kawaguchi Y. Evaluation of an oral function promotion programme for the independent elderly in Japan. *Gerodontology* 2009;26(4):250-8.
151. O'Sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review. *Acupunct Med* 2010.
152. O'Regan D, Filshie J. Acupuncture and cancer. *Auton Neurosci* 2010;157(1-2):96-100.
153. Wong RK, Sagar SM, Chen BJ, Yi GY, Cook R. Phase II Randomized Trial of Acupuncture-Like Transcutaneous Electrical Nerve Stimulation to Prevent Radiation-Induced Xerostomia in Head and Neck Cancer Patients. *J Soc Integr Oncol* 2010;8(2):35-42.
154. Braga FP, Sugaya NN, Hirota SK, Weinfeld I, Magalhaes MH, Migliari DA. The effect of acupuncture on salivary flow rates in patients with radiation-induced xerostomia. *Minerva Stomatol* 2008;57(7-8):343-8.
155. Cho JH, Chung WK, Kang W, Choi SM, Cho CK, Son CG. Manual acupuncture improved quality of life in cancer patients with radiation-induced xerostomia. *J Altern Complement Med* 2008;14(5):523-6.
156. Deng G, Hou BL, Holodny AI, Cassileth BR. Functional magnetic resonance imaging (fMRI) changes and saliva production associated with acupuncture at LI-2 acupuncture point: a randomized controlled study. *BMC Complement Altern Med* 2008;8:37.
157. Jensen SB, Pedersen AM, Vissink A, Andersen E, Brown CG, Davies AN, et al. A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: management strategies and economic impact. *Support Care Cancer* 2010;18(8):1061-79.
158. Meidell L, Holritz Rasmussen B. Acupuncture as an optional treatment for hospice patients with xerostomia: an intervention study. *Int J Palliat Nurs* 2009;15(1):12-20.
159. Pinkowish MD. Acupressure and acupuncture for side effects of radiotherapy. *CA Cancer J Clin* 2009;59(5):277-80.
160. Simcock R, Fallowfield L, Jenkins V. Group acupuncture to relieve radiation induced xerostomia: a feasibility study. *Acupunct Med* 2009;27(3):109-13.
161. Standish LJ, Kozak L, Congdon S. Acupuncture is underutilized in hospice and palliative medicine. *Am J Hosp Palliat Care* 2008;25(4):298-308.
162. Weidong L, Posner MR, Wayne P, Rosenthal DS, Haddad RI. Acupuncture for dysphagia after chemoradiation therapy in head and neck cancer: a case series report. *Integr Cancer Ther* 2010;9(3):284-90.
163. Gomez-Moreno G, Guardia J, Ferrera MJ, Cutando A, Reiter RJ. Melatonin in diseases of the oral cavity. *Oral Dis* 2010;16(3):242-7.
164. Lazarchik DA, Haywood VB. Use of tray-applied 10 percent carbamide peroxide gels for improving oral health in patients with special-care needs. *J Am Dent Assoc* 2010;141(6):639-46.

165. Brizel DM, Murphy BA, Rosenthal DI, Pandya KJ, Gluck S, Brizel HE, et al. Phase II study of palifermin and concurrent chemoradiation in head and neck squamous cell carcinoma. *J Clin Oncol* 2008;26(15):2489-96.
166. Bensinger W, Schubert M, Ang KK, Brizel D, Brown E, Eilers JG, et al. NCCN Task Force Report. prevention and management of mucositis in cancer care. *Journal of the National Comprehensive Cancer Network* 2008;6(1).
167. Spielmann N, Wong D. Saliva: diagnostics and therapeutic perspectives. *Oral Dis* 2010.
168. Malamud D. Saliva as a diagnostic fluid. *Dent Clin North Am* 2011;55(1):159-78.
169. Brinkmann O, Kastratovic DA, Dimitrijevic MV, Konstantinovic VS, Jelovac DB, Antic J, et al. Oral squamous cell carcinoma detection by salivary biomarkers in a Serbian population. *Oral Oncol* 2010.
170. Bello IO, Soini Y, Salo T. Prognostic evaluation of oral tongue cancer: means, markers and perspectives (II). *Oral Oncol* 2010;46(9):636-43.
171. Bierz M, Minarowski L, Wozniak L, Chojnowska S, Knas M, Szajda S, et al. The activity of selected glycosidases in salivary gland tumors. *Folia Histochem Cytobiol* 2010;48(3):471-4.
172. Bigler LR, Streckfus CF, Dubinsky WP. Salivary biomarkers for the detection of malignant tumors that are remote from the oral cavity. *Clin Lab Med* 2009;29(1):71-85.
173. Streckfus C, Bigler L. The use of soluble, salivary c-erbB-2 for the detection and post-operative follow-up of breast cancer in women: the results of a five-year translational research study. *Adv Dent Res* 2005;18(1):17-24.
174. Streckfus CF, Brown RE, Bull JM. Proteomics, morphoproteomics, saliva and breast cancer: an emerging approach to guide the delivery of individualised thermal therapy, thermochemotherapy and monitor therapy response. *Int J Hyperthermia* 2010;26(7):649-61.
- 174a. Sugimoto M, Wong DT, Hirayama A, Soga T, Tomita M. Capillary electrophoresis mass spectrometry-based saliva metabolomics identified oral, breast and pancreatic cancer-specific profiles. *Metabolomics* 2010;6(1):78-95.
175. Ferrando R, Szponar B, Sanchez A, Larsson L, Valero-Guillen PL. 3-Hydroxy fatty acids in saliva as diagnostic markers in chronic periodontitis. *J Microbiol Methods* 2005;62(3):285-91.
176. Marchetti P, Tognarelli M, Giannarelli R, Grossi C, Picaro L, di Carlo A, et al. Decreased salivary glucose secretory rate: usefulness for detection of diabetic patients with autonomic neuropathy. *Diabetes Res Clin Pract* 1989;7(3):181-6.
177. Rao PV, Reddy AP, Lu X, Dasari S, Krishnaprasad A, Biggs E, et al. Proteomic identification of salivary biomarkers of type-2 diabetes. *J Proteome Res* 2009;8(1):239-45.
178. Scott DA, Renaud DE, Krishnasamy S, Meric P, Buduneli N, Cetinkalp S, et al. Diabetes-related molecular signatures in infrared spectra of human saliva. *Diabetol Metab Syndr*. 2010/07/16 ed; 2010 July 14. p. 48.
179. Xiang XM, Liu KZ, Man A, Ghiabi E, Cholakis A, Scott DA. Periodontitis-specific molecular signatures in gingival crevicular fluid. *Journal of Periodontal Research* 2010;45(3):345-52.
180. Saygun I, Nizam N, Keskiner I, Bal V, Kubar A, Acikel C, et al. Salivary infectious agents and periodontal disease status. *J Periodontal Res* 2011;46(2):235-39.
181. Ramseier CA, Kinney JS, Herr AE, Braun T, Sugai JV, Shelburne CA, et al. Identification of pathogen and host-response markers correlated with periodontal disease. *J Periodontol* 2009;80(3):436-46.
182. Higashi T, Shibayama Y, Ichikawa T, Ito K, Toyo'oka T, Shimada K, et al. Salivary chenodeoxycholic acid and its glycine-conjugate: their determination method using LC-MS/MS and variation of their concentrations with increased saliva flow rate. *Steroids* 2010;75(4-5):338-45.
183. Greenberg BL, Glick M, Frantsve-Hawley J, Kantor ML. Dentists' attitudes toward chairside screening for medical conditions. *J Am Dent Assoc* 2010;141(1):52-62.

IX APPENDIX: TABLES 1 – 6 & FIGURE 1

Table 1A-1E	Examples of Questions to Ask Patients to Diagnose Xerostomia	23
Table 2	Assessment of Symptoms and Signs to Diagnose Xerostomia	24
Table 3	Direct and Indirect Causes of Xerostomia	25
Table 4A	Tasks for Dental Professional and Recommendations for All Xerostomia Patients	27
Table 4B	Tasks for Dental Professional and Recommendations to Patients by Cause of Xerostomia	28
Table 5	Remedies to Possibly Recommend to Xerostomia Patients	29
Table 5A	Medicinal Stimulation of Saliva Secretion	29
Table 5B	Prevention of Caries and Periodontal Disease	30
Table 5B1	Therapeutic Mouth Rinses to USE	30
Table 5B2	Therapeutic Mouth Rinses to NOT Use Due to Alcohol Content	31
Table 5B3	Anti-Cariogenic Non-Mouthwash Products	31
Table 5C	Palliative Remedies to Increase Comfort	32
Table 6	Additional Informational Resources	33
Table 6A	Resources for Health Care Providers	33
Table 6B	Online Resources for Patients	36
Figure 1	Medication Usage Form	37

DISCLAIMER:

The authors have no financial or other interest in any of the companies or products mentioned in this report. All examples are included for informational purposes only.

PLEASE NOTE:

- 1) For the reader's convenience, the website addresses displayed in all tables are hyperlinks and can therefore be accessed directly from this report when reading it online by holding down the "Ctrl" key while clicking on the underlined (blue-colored) text.
- 2) The numbers in parenthesis in the tables refer to citations listed in the bibliography.

Table 1. Examples of Questions to Ask Patients to Diagnose Xerostomia

Table 1A. Scale of Questions Used to Allocate Study Participants to Xerostomia Group ^{11,13-15}			
Item#	Question	Response	
1	Does your mouth feel dry when eating a meal?	Yes	No
2	Do you have difficulties swallowing any foods?	Yes	No
3	Do you need to sip liquids to aid in swallowing dry foods?	Yes	No
4	Does the amount of saliva in your mouth seem to be reduced most of the time?	Yes	No
5	Does your mouth feel dry at night or on awakening?	Yes	No
6	Does your mouth feel dry during the daytime?	Yes	No
7	Do you chew gum or use candy to relieve oral dryness?	Yes	No
8	Do you usually wake up thirsty at night?	Yes	No
9	Do you have problems in tasting food?	Yes	No
10	Does your tongue burn?	Yes	No

Table 1B: The Xerostomia Inventory (“XI”) ^{1,11,13,15,20-26}						
Item#	Complaint	Never	Hardly Ever	Occasionally	Fairly Often	Very Often
1	I sip liquids to help swallow food.	1	2	3	4	5
2	My mouth feels dry when eating a meal.	1	2	3	4	5
3	I get up at night to drink.	1	2	3	4	5
4	My mouth feels dry.	1	2	3	4	5
5	I have difficulty in eating dry foods.	1	2	3	4	5
6	I suck sweets or cough lollies to relieve dry mouth.	1	2	3	4	5
7	I have difficulties swallowing certain foods.	1	2	3	4	5
8	The skin of my face feels dry.	1	2	3	4	5
9	My eyes feel dry.	1	2	3	4	5
10	My lips feel dry.	1	2	3	4	5
11	The inside of my nose feels dry.	1	2	3	4	5

Table 1C. “Yes” Responses to Both Questions Used to Allocate Study Participants to Xerostomia Group ³¹			
Item#	Question	Response	
1	Do you have a constant sensation of dry mouth?	Yes	No
2	Do you feel the need to ingest liquids during meals?	Yes	No

Table 1D. “Yes” Response to 1 Question Used to Determine that Study Participant had Xerostomia ⁹			
Item#	Question	Response	
1	Does your mouth usually feel dry?	Yes	No

Table 1E. Self-Assessment to Diagnose Xerostomia: “Do you suffer from dry mouth? Find out:”*			
Item#	Question	Response	
1	Does your mouth usually feel dry?	Yes	No
2	Do you have difficulty with swallowing?	Yes	No
3	Do you have trouble with tasting foods?	Yes	No
4	Is your mouth sensitive to acidic, salty or spicy foods?	Yes	No
5	Do you have recurring dental decay problems?	Yes	No

Table 2. Assessment of Symptoms and Signs to Diagnose Xerostomia

Action	Subjective Symptoms & Complaints	Objective Examination for Signs
Assess the Patient for Symptoms and Signs of Xerostomia:		
Ask & Clinically Examine:	<ul style="list-style-type: none"> • Dry mouth in the morning/at night • Cheeks sticking to teeth or dentures • Retention problems with dentures • Removable dentures cause irritation/pain • Don't use removable dentures • Trouble chewing • Trouble initiating swallowing/swallowing • Need to sip water/liquid "all the time" • Always have glass of water at bedside • Burning sensation in mouth/tongue • Heartburn • Avoidance of certain foods (sticky, dry, spicy, pungent) 	<ul style="list-style-type: none"> • Dental mirror sticks to mucosal surfaces or tongue • Saliva does not pool in sublingual area • Patient has trouble speaking/ articulating • Mucositis (oral soft tissues dry, red, inflamed, tongue fissured) • Increase in number or extent of carious lesions • Changes in caries presentation, such as incisal, cuspal, and root caries • Enamel erosion • Enlarged salivary glands • Eyes dry, red, inflamed (Sjögren's Syndrome)
Update Medical History; Probe for:	<ul style="list-style-type: none"> • Cancer & its treatment • Autoimmune or endocrine diseases* • Bulimia & Other Eating Disorders • Alcohol & drug abuse 	<p>*<u>Autoimmune or endocrine diseases:</u></p> <ul style="list-style-type: none"> • Sjögren's Syndrome • diabetes (frequent urination, thirst) • rheumatoid arthritis
Record ALL medications (+/- Prescription, OTC, vitamins, supplements):	<ul style="list-style-type: none"> • Patient should bring ALL medications in original packaging • Use special form to record medication name, dosage, frequency, and start/end date • Please, see sample form: Figure 1 	<ul style="list-style-type: none"> • Allergic reactions • Drug interactions • <u>Consult medical care provider:</u> <ul style="list-style-type: none"> ○ Discontinuation or substitution with potentially less xerogenic medication <ul style="list-style-type: none"> ▪ NOTE: Substitution with exercise (54a,54b) ○ More frequent, but smaller dosages
Assess the Patient for Sequelae of Xerostomia:		
Caries	<ul style="list-style-type: none"> • Toothache • Sensitivity to heat, cold, acid, sweet 	<ul style="list-style-type: none"> • Especially secondary and root caries, especially in older or head and neck cancer radiation-treated individuals
Periodontal diseases	<ul style="list-style-type: none"> • Bleeding gingiva during tooth brushing • Sensitivity to heat, cold, sour, sweet 	<ul style="list-style-type: none"> • Gingivitis • Periodontal pockets • Exposed root surfaces
Candidiasis	<ul style="list-style-type: none"> • Pain or "itching" in mouth, especially the roof of the mouth 	<ul style="list-style-type: none"> • Check all soft tissue, incl. palate, cheeks, sublingual mucosa
Oral Mucositis	<ul style="list-style-type: none"> • Pain in soft tissues in oral cavity, especially when eating or drinking • Food avoidance (spicy, tangy) 	<ul style="list-style-type: none"> • Check all soft tissue, incl. palate, cheeks, sublingual mucosa

Enamel Erosion	<ul style="list-style-type: none"> • Sensitivity to heat, cold, acid, sweet • Decreased occlusal height 	<ul style="list-style-type: none"> • Thinning of enamel, mostly lingual and occlusal; transparent; yellow dentin might shine through • Decreased occlusal bite height • <i>Probe for eating disorders or alcohol abuse</i> • Rhagades: [Candida] infected fissures radiating from corners of mouth
Halitosis	<ul style="list-style-type: none"> • Bad taste, feeling of bad breath 	<ul style="list-style-type: none"> • Malodor
Dysgeusia	<ul style="list-style-type: none"> • Altered sense of taste 	<ul style="list-style-type: none"> • Ask about any changes in sense of taste

Table 3. Direct and Indirect Causes of Xerostomia

Direct Causes:	Comments
Sjogren's Syndrome	<ul style="list-style-type: none"> • Autoimmune disorder in which salivary and lacrimal glands are damaged by inflammation • Dryness of eyes • Swelling of salivary glands • Affects 9 times more women
Lupus	<ul style="list-style-type: none"> • Systemic lupus erythematosus (SLE) is a chronic, inflammatory autoimmune disorder that may affect the skin, joints, kidneys, heart, lungs, vasculatures, brain, and mouth
Scleroderma	<ul style="list-style-type: none"> • Scleroderma is a widespread connective tissue disease that involves changes in the skin, blood vessels, muscles, and internal organs.
Mixed Connective Disease	<ul style="list-style-type: none"> • Diffuse scleroderma can overlap with other autoimmune diseases, including systemic lupus erythematosus and polymyositis. In such cases, the disorder is referred to as "mixed connective disease".
Diabetes Mellitus (DM)	<ul style="list-style-type: none"> • Type 1 (insulin-dependent), Type 2, gestational/pregnancy • Uncontrolled diabetes can cause hyposalivation, which recedes upon controlling DM
Ageing	<ul style="list-style-type: none"> • Chronic conditions manifest with increasing age • Age per se is not causing xerostomia, although evidence is ambiguous
Female Sex	<ul style="list-style-type: none"> • Controversial role; ambiguous evidence • More women have xerostomia due to living longer and having Sjögren's Syndrome
Indirect Causes:	Comments
Xerogenic medications/ Polypharmacy	<ul style="list-style-type: none"> • All major drug groups can cause hyposalivation, including psychopharmaca/ antidepressants antihistamines, diuretics & antihypertensive medication
Cancer treatment	<ul style="list-style-type: none"> • Chemotherapeutic medications • Radiation of oral or head and neck cancer damaging salivary glands • Stress & anxiety can cause dry mouth in all cancer patients regardless of neoplasm location
Asthma, other mostly pulmonary diseases	<ul style="list-style-type: none"> • Inhaled medications common • Inhaling drugs cause desiccating air flow
Periodontitis	<ul style="list-style-type: none"> • Severity of periodontitis is related to salivary flow rate in a dose-response manner³⁸: Periodontitis induces an increase in the output of proteins, including mucin and amylase, thereby enhancing the protective potential of saliva, but flow rate is decreased • Papillary capillaries are altered in Sjogren's Syndrome causing decreased gingival microcirculation and therefore possibly to diminished healing and anti-inflammatory capacity¹¹³
Gastro-esophageal reflux disease (GERD)	<ul style="list-style-type: none"> • Acidic content from stomach can cause dry mouth and enamel erosion¹³⁴

Table 3. Direct and Indirect Causes of Xerostomia, continued

Bulimia Other disorders that include vomiting	<ul style="list-style-type: none"> • Acidic content from stomach can cause dry mouth and erosion, as well as increased caries activity due to softening of enamel
Nervousness/stress/anxiety	<ul style="list-style-type: none"> • Psychological stress causes dry mouth
Alcohol use/abuse	<ul style="list-style-type: none"> • Alcohol is a desiccant • Acidic stomach content in vomiting is xerogenic
Smoking	<ul style="list-style-type: none"> • Smoking of tobacco products & recreational drugs dries out oral mucosa
Drug abuse	<ul style="list-style-type: none"> • Poor oral hygiene • Rampant caries (“Meth mouth” in methamphetamine use)⁶⁷ • Excessive tooth wear⁶⁷ • The most important factor in treating the oral effects of abuse of methamphetamine or other drugs is for the patient to stop using the drug. Continued abuse will make it difficult to increase salivary flow and hinder the patient's ability to improve nutrition and oral hygiene. • Local anesthetics with vasoconstrictors should be used with care in patients using methamphetamine because they may result in cardiac dysrhythmias, myocardial infarction, and cerebrovascular events
Mouth Breathing Sleeping with open mouth/Snoring	<ul style="list-style-type: none"> • Air movement through mouth dries out oral mucosa
Rinsing with mouthwashes containing alcohol	<ul style="list-style-type: none"> • Alcohol is a desiccant
Breathing polluted air (dust, fumes, smoke, dirt, other irritants)	<ul style="list-style-type: none"> • Particles in air may cause oral dryness
Breathing dry (heated) air	<ul style="list-style-type: none"> • Air movement through mouth dries out oral mucosa, especially when air is dry
Avoidance of liquid intake	<ul style="list-style-type: none"> • Aversion to bathroom visits due to mobility difficulties, lack of thirst, or in order to prevent sleep interruption
<u>Iatrogenic side effects of medical procedures:</u> <ul style="list-style-type: none"> • anesthesia • NPO (nothing by mouth) • Intubation/ventilator-assisted breathing • mechanical oral suctioning • intravenous feeding 	<ul style="list-style-type: none"> • Can dry out the mouth severely, increasing the oral cavity’s vulnerability to infection and inflammation or accumulation of debris and plaque, causing such complications as microbial infections and inability to talk or eat

Table 4A. Tasks for Dental Professional & Recommendations for All Xerostomia Patients

Cause(s) of Xerostomia:	Actions by Dental Care Provider	Recommendations to Patients
<p>ANY:</p>	<p><u>For ALL Patients:</u></p> <ul style="list-style-type: none"> • Conduct careful medical history • Carefully record ALL medications (type, dosage, frequency, start date)* • Inquire regarding compliance with medicine regimen prescribed • Conduct thorough oral examinations and keep in mind all possible underlying causes deducted from any source, such as: <ul style="list-style-type: none"> ▪ Casual conversation with patient ▪ Medical history ▪ Medication use ▪ Oral signs (please see Table 1) ▪ Callus formation on back of hand/knuckles caused by upper incisors while provoking vomiting in eating disorder ▪ Practitioner’s experience, imagination & creativity 	<p><u>For All Patients with Xerostomia:</u></p> <ul style="list-style-type: none"> • Proper oral hygiene • Do not brush teeth immediately upon wakening when thin surface layer of enamel is slightly softened due to acidic activity and lack of liquid intake during sleep • Sip water frequently • Rinse mouth with plain water after eating & drinking liquids other than water • Anti-caries mouth rinse without alcohol • Anti-caries xylitol-containing products • Anti-periodontal-bacterial mouth rinse without alcohol • Avoid alcoholic and caffeinated beverages • Discontinue tobacco smoking, if available by attending smoking cessation sessions offered by dental office • Know possible consequences of smoking • Use a humidifier at night • Use salivary flow stimulants: sugarless gum, hard candy, or lozenges • Use palliative saliva substitutes, such as: <ul style="list-style-type: none"> ▪ Liquids ▪ Gels ▪ Sprays

*Please, see Figure 1.

Table 4B. Tasks for Dental Professional & Recommendations to Patients by Cause of Xerostomia

Cause of Xerostomia:	Actions by Dental Care Provider	Recommendations to Patients
Sjögren's Syndrome:	<ul style="list-style-type: none"> • Discuss with medical care provider prescription of salivary stimulating medication in eligible patients, such as: <ul style="list-style-type: none"> ▪ Pilocarpine ▪ Cevimeline ▪ Amifostine ▪ Hydroxychloroquine* 	<ul style="list-style-type: none"> • Please, see Table 5A • Understand possible side effects, such as sweating that may lead to dehydration *Not a recommended practice, only one new study showing increased salivary flow in Sjögren's Syndrome¹⁴⁶. Hydroxychloro-quine is classified as an anti-malarial medication and is also used to decrease inflammation in systemic lupus erythematosus as well as rheumatoid arthritis and Sjögren's Syndrome, all rheumatic disorders
Xerogenic Medications & Polypharmacy:	<ul style="list-style-type: none"> • Consult with physician for assessment of alternative medications and possible reduction of number or dosage/frequency of medications • Psychopharmaca may at least partially be substituted by other therapy, such as talking or walking (psychotherapy & exercise) 	<ul style="list-style-type: none"> • Urge to participate in medication selection, adaptation, and revision • Urge to be aware exactly which drug is taken for which ailment • Urge to consider being willing to discontinue any drugs in consultation with physician • Urge to comply with any medication regimen
Cancer Treatment:		
Chemotherapy	<ul style="list-style-type: none"> • Consult with physician for assessment of alternative medications and possible reduction of number or dosage/frequency of oral or injected medications 	<ul style="list-style-type: none"> • Urge to participate in treatment selection, adaptation, and revision • Urge to comply with any treatment regimen
Radiation Therapy of Non-Head and Neck Cancer (NHNC)	<ul style="list-style-type: none"> • Consult with physician for assessment of alternative methods to attempt to decrease intensity of xerostomia 	<ul style="list-style-type: none"> • Urge to participate in treatment selection, adaptation, and revision • Urge to comply with any treatment regimen
Radiation Therapy of Head and Neck Cancer (HNC)	<ul style="list-style-type: none"> • Consult with physician for consideration of alternative methods to spare as much salivary gland tissue as possible • Discuss with patient the pros and cons of radiation therapy and compare frankly to only palliative treatment in the light of expected life span and quality of life 	<ul style="list-style-type: none"> • Urge to participate in treatment selection, adaptation, and revision • Urge to comply with any treatment regimen • Urge to carefully consider options, choices • Urge to be as realistic as possible

Table 5. Remedies to Possibly Recommend to Xerostomia Patients

Medium Recommendation	Action Substance Medium Type	Brand Names (Examples)	Comments
Table 5A. Medicinal Stimulation of Saliva Secretion <i>in Consultation with Medical Care Provider:</i>			
Pilocarpine Hydrochloride	<ul style="list-style-type: none"> Affects the nervous system to increase saliva secretion Drug class: cholinergic agonists <u>Cancer Treatment:</u> 10 mg 3 times/day <u>Sjogren's Syndrome:</u> <ul style="list-style-type: none"> 10 mg 4 times/day Take without food FDA pregnancy category C: Unknown whether harmful to unborn or breast-feeding baby 	Salagen® 5mg & 7.5mg tablets	<ul style="list-style-type: none"> http://www.eisai.com/pdf_files/201370-B%20Salagen%20Outsert.pdf Manufactured by: 201370 Patheon Inc., Ontario, L5N 7K9. Manufactured for: Eisai Inc., Woodcliff Lake, NJ 07677. Many drug interactions Consult with medical care provider before prescribing Salagen® Some patients may benefit Contraindicated in heart disease The side effect of sweating may cause dehydration and worsen dry mouth condition¹⁴² Some benefit in 1 to 2 weeks; may take up to 3 months for full effect
Cevimeline	30 mg t.i.d.	Evoxac®	<ul style="list-style-type: none"> Some patients may benefit¹⁴² Many drug interactions, see: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0000452
Amifostine	<p>500 mg of amifostine in single-use vial for reconstitution for injection</p> <p>Selective cyto-protective agent used to help reduce certain toxicities associated with cancer chemotherapy and radiotherapy.</p>	Ethylol®	<ul style="list-style-type: none"> Manufactured by: MedImmune Pharma B.V. 6545 CG Nijmegen The Netherlands http://www.medimmune.com/ Distributor: Ben Venue, Inc. Bedford, Ohio 44146; Product information: 1 877 633 4411 U.S. Patents 5,424,471;5,591,731;5,994,409 Recommended by 2008 clinical practice guidelines of American Society of Clinical to consider for decreasing acute & late xerostomia with fractionated radiation therapy alone for head and neck cancer¹⁴⁴ http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/020221s0241bl.pdf
Hydroxychloroquine	400 mg/day	Plaquenil® Dolquine® Quensyl®	Not a standard practice; only one new study demonstrated increased salivary flow in Sjogren's Syndrome ¹⁴⁶
Apple acid Sodium fluoride Xylitol	<p>Lozenge</p> <p><u>Taste:</u></p> <ul style="list-style-type: none"> Licorice Orange 	Xerodent® 30 & 90 lozenges	<ul style="list-style-type: none"> http://www.actavis.dk/dk/products/Xerodent.htm Not available in the U.S., but in Denmark, Norway, Sweden, Finland, Great Britain Apple acid stimulates saliva production Fluoride strengthens enamel Xylitol inhibits bacterial growth & enhances re-mineralization

Table 5. Remedies to Possibly Recommend to Xerostomia Patients, continued

Table 5B. Prevention of Caries and Periodontal Disease:			
Proper (immaculate) home oral hygiene regimen with professional intensive preventive care and monitoring	<ul style="list-style-type: none"> • Extra soft toothbrush • Toothpaste formulated for dry mouth • Children's (mild) toothpaste • Dental floss without strong flavor • Disclosing agents 	<ul style="list-style-type: none"> • Biotene Dry Mouth Toothpaste • Biotene Sensitive Toothpaste • Biotene PBF Toothpaste • Any children's toothpaste 	<ul style="list-style-type: none"> • Biotene by Glaxo Smith Kline; http://www.biotene.com/Products/Toothpaste.aspx; • Low-foam toothpastes without sodium lauryl sulfate
10 % carbamide peroxide <u>Also called:</u> <ul style="list-style-type: none"> • urea peroxide • urea hydrogen peroxide • percarbamide 	<ul style="list-style-type: none"> • Tooth-bleaching agent applied in a custom-fitted tray • Oxidizer • 3% hydrogen peroxide equivalent • FDA pregnancy category C:Unknown whether harmful to unborn or breast-feeding baby 	<ul style="list-style-type: none"> • Dr. Collins All White Bleaching System • NUPRO® White Gold Take Home Carbamide Peroxide (Dentsply) • White & Brite™ whitener (3M-ESPE) 	<ul style="list-style-type: none"> • One study found the tooth-bleaching agent 10 % carbamide peroxide has positive effects on plaque, gingival health & caries (elevates pH) and may thus hold great promise for patients with dry mouth ¹⁶⁴ • Peroxide is the active ingredient • http://www.dentsply.com/default.aspx?pageid=757 • http://solutions.3m.com/wps/portal/3M/en_US/3M-ESPE-NA/dental-professionals/products/category/whitening/white-brite/
1.5% hydrogen peroxide mouth rinse	Antiseptic	None	<ul style="list-style-type: none"> • Mix OTC standard 3% solution with water (50/50 mix) • Might be as effective as 10 % carbamide peroxide tooth whiteners
2.5 mg chlorhexidine gluconate	Strip for pocket depth ≥5 mm Bacteriocidal	Periochip® Biodegradable chip made of hydrolyzed gelatin	<ul style="list-style-type: none"> • Manufactured by Perio Products Ltd., Jerusalem, Israel • http://www.dexcel.com/DrugsIL/Recipe/periochip/Int • Distributed by Dexcel Pharma Technologies Inc., Edison, N.J. • Approved by the FDA in May 1998

Table 5B1. Therapeutic Mouth Rinses to USE (Listed by Active Ingredient):

Fixed combination of essential oils: <ul style="list-style-type: none"> • thymol 0.064% • eucalyptol 0.092% • methyl salicylate 0.060 % • menthol 0.042 % 	Antibacterial (Not Antiseptic)	LISTERINE® ZERO™ Alcohol free	<ul style="list-style-type: none"> • http://www.listerine.com/product-zero.jsp • Johnson & Johnson Healthcare Products Division of McNEIL-PPC, Inc.
0.05% sodium fluoride (0.02% w/v fluoride ion)	Caries preventive Bacteriostatic	ACT® Fluoride Rinse: <ul style="list-style-type: none"> ○ Mint (green) ○ Cinnamon (red) ○ Kids (blue) ○ Bubblegum Blowout (pink) <ul style="list-style-type: none"> • Alcohol free • Highest fluoride 	Sanofi Aventis: <ul style="list-style-type: none"> • http://www.actfluoride.com/mint-fluoride-rinse.html; • Product selection: http://www.actfluoride.com/productcomparison.html • Use only for children ≥6 years. • Supervise children 6-12 years: Parents

		<p>concentration in rinse form available without prescription</p> <ul style="list-style-type: none"> • Exact dosage meter (10ml) built into bottle • American Dental Association Seal of Acceptance 	<p>Resource Center: http://www.actfluoride.com/parents/index.html 8 part education pamphlets (pdf): http://www.actfluoride.com/professional/patiented.html</p>
0.12% chlorhexidine gluconate	<ul style="list-style-type: none"> • Antiseptic: <ul style="list-style-type: none"> ○ bactericidal ○ bacteriostatic 	None (Naturally alcohol free)	<ul style="list-style-type: none"> • Effective on both Gram-positive & Gram-negative bacteria • ~Neutral: pH range 5-7
1.5% hydrogen peroxide mouth rinse	Antiseptic	None (Naturally alcohol free)	Mix standard 3% solution with water: 1/1 mix = 50%/50% mix

Table 5B2. Therapeutic Mouth Rinses to NOT USE Due to Alcohol Content (Listed by Active Ingredient):

<p>0.12% chlorhexidine gluconate + 11.6% alcohol</p> <p><i>Prescription only(Rx)</i></p>	<ul style="list-style-type: none"> • Antiseptic: <ul style="list-style-type: none"> ○ bactericidal ○ bacteriostatic • ~Neutral: pH range 5-7 • Effective on Gram-positive & Gram-negative bacteria 	<p>1)Peridex™: Chlorhexidine Gluconate 0.12% Oral Rinse (Rx) by 3M-ESPE</p> <p>2)Perichlor (Rx) by Pharmascience (?% alcohol)</p> <p>3)Periogard Oral Rinse (Rx) by Colgate</p>	<p>1)http://solutions.3m.com/wps/portal/3M/en_US/3M-ESPE-NA/dental-professionals/products/category/preventive/peridex/</p> <p>2)http://www.pharmascience.com/Applications/Details.aspx?ProductID=185</p> <p>3)http://www.colgate.com/app/Colgate/US/OC/Products/FromTheDentist/PerioGardAntimicrobial.cvsp</p>
<p>Fixed combination of essential oils:</p> <ul style="list-style-type: none"> • thymol 0.064% • eucalyptol 0.092% • methyl salicylate 0.060 % • menthol 0.042 % <p>+ 21.6% alcohol</p>	Antibacterial (Not Antiseptic)	<p>All* LISTERINE® products, except for LISTERINE® ZERO™</p> <p>*Including:</p> <p>1)LISTERINE® TOTAL™</p> <p>2)LISTERINE® POCKETMIST</p> <p>3)LISTERINE® POCKET-PAKS®</p>	<ul style="list-style-type: none"> • http://www.listerine.com/product-zero.jsp • Johnson & Johnson Healthcare Products Division of McNEIL-PPC, Inc. • 1)A additional anti-carries affect; marketed since 11/30/2009 • 2)Spray in small bottle • 3)Instantly dissolving” strips
<p>1) 0.05% sodium fluoride (NaF)(0.02% fluoride ion) x1/day</p> <p>+ 11% alcohol</p> <p>2)0.02% NaF x 2/day (0.009% fluoride ion)</p>	Anti-carries Antibacterial (Not Antiseptic)	<p>ACT Restoring™ Mouthwash “</p> <p>ACT TOTAL CARE</p>	<p>Sanofi Aventis:http://www.actfluoride.com/ Professional Resource Center: http://www.actfluoride.com/professional/alcohol.html</p>

Table 5B3. Anti-Cariogenic Non-Mouthwash Products (Should Preferably Contain Xylitol as First Ingredient):

Sugarless chewing gum with 30% xylitol (=first ingredient)	<ul style="list-style-type: none"> • Salivary stimulant • Anti-bacterial • Remineralization enhancer 	<p>Wrigley’s Extra Menthol sugar free gum</p> <ul style="list-style-type: none"> • Not sold in the US 	<p>Wrigley Scandinavia AB, Box 1616, S-183 16 Täby, Sweden; infosw@wrigley.com; tel.: +46 (0)8 544 760</p>
Sugarless chewing gum with xylitol as first ingredient	Salivary stimulant, anti-bacterial, remineralization enhancer	Xylifresh	<p>Leaf International, Oosterhout, The Netherlands; http://www.leaf.eu/brands/xylifresh.html Sweetened with 100 percent Xylitol</p>

Spray	Moisturizer	Biotene Moisturizing Mouth Spray	Biotene by Glaxo Smith Kline; http://www.biotene.com/Products/Spray.aspx
-------	-------------	----------------------------------	--

Table 5C. Palliative Remedies to Increase Comfort:

Water	Moisturizer		
Sugarless chewing gum	Salivary stimulant Apple mint flavor	Biotene Dry Mouth Gum Biotene PBF Gum	GlaxoSmithKline: http://www.biotene.com/Products/Gum.aspx
Lozenges	Salivary stimulant	SalivaSure™ lozenges (formerly called Salix)	Scandinavian Formulas, Perkasio, PA: http://www.naturalypure.com/DryMouthRelief.htm
Saliva substitute: Moistens, cleans, dissolves mucin	Neutral, supersaturated Ca(2+)/PO(4)(3-), Use also in xerostomia	Caphosol® 2 min.x 4-10/day in cancer treatment	EUSAPharma (USA), Inc. Tel.: (215) 867-4900 http://www.caphosol.com/
Saliva substitute	Saliva substitute Moisturizer	Glandosane®	Fresenius Kabi, Ltd, D-61352 Bad Homburg, Germany T +49 (0) 6172 608-0 http://www2.fresenius-kabi.com/internet/kabi/gb/fkintpub.nsf/Content/Product+Features+Glandosane
Gel	Moisturizer/Lubricant Anti-bacterial (not antiseptic)	Biotene Oral Balance Gel	Biotene by Glaxo Smith Kline; http://www.biotene.com/Products/Gel.aspx
Liquid	Moisturizer/Lubricant Anti-bacterial (not antiseptic)	Biotene Oral Balance Liquid	Biotene by Glaxo Smith Kline; http://www.biotene.com/Products/Liquid.aspx
Liquid	Moisturizer/Lubricant Glycerin-based Mild mint flavor	Oasis Mouthwash 1 oz. for ≥30 seconds Not intended to be swallowed	Oasis Consumer Healthcare LLC, Cleveland, OH 44115 http://www.oasisdrymouth.com/Pages/Products.aspx
Spray	Moisturizer/Lubricant Anti-bacterial (not antiseptic)	Biotene Moisturizing Mouth Spray	Biotene by Glaxo Smith Kline; http://www.biotene.com/Products/Spray.aspx
Spray	Moisturizer Aqueous solution with predominant electrolytes present in saliva	Moi-Stir® Oral Spray	Kingswood Laboratories, Inc., 10375 Hague Rd, Indianapolis, IN 46256 Tel.: 317-849-9513/ 800-968-7772 http://www.kingswood-labs.com/moistir.html
Spray	Saliva substitute Moisturizer Xylitol-sweetened	MouthKote Dry Mouth Spray	Parnell Pharmaceuticals, Inc., 1525 San Francisco Blvd., San Rafael, CA 94901 Tel.: 800-457-4276/415-256-1800 http://www.parnellpharm.com/mouthkote.htm
Spray	Moisturizer/Lubricant Glycerin-based	Oasis Mouth Spray ≤60 sprays/day Can be swallowed	Oasis Consumer Healthcare LLC, Cleveland, OH 44115 http://www.oasisdrymouth.com/Pages/Products.aspx

Humidifier	Moisturizer	Any	At night if air is dry
Sleep w/mouth closed	Avoid dehydration	n/a	Air stream is a desiccant
Avoid alcohol	Avoid dehydration	Any	Alcohol is a desiccant
Avoid dry, sticky, spicy, or salty foods	Avoid pain & irritation	Any	Also avoids food adherence to oral tissues & problems chewing/swallowing
Do not smoke	Avoid dehydration	Any tobacco, etc.	Smoke is a desiccant

Table 6. Additional Informational Resources

Table 6A. Resources for Health Care Providers	
<p>Sreebny L, Vissink A, editors. “Dry mouth, the malevolent symptom: a clinical guide”. Singapore: Wiley-Blackwell; 2010. 268 pp. ISBN: 978-0-8138-1623-4; Paperback For purchase: http://www.wiley.com/WileyCDA/WileyTitle/productCd-0813816238.html (\$74.99) “Xerostomia, more commonly called dry mouth, affects an estimated 20% of adults worldwide and can severely diminish one’s quality of life. <i>Dry Mouth, the Malevolent Symptom: A Clinical Guide</i> (“<i>Dry Mouth</i>”) relies on evidence-based research to provide an introductory primer on oral dryness and the modalities available to treat it. The book describes the varied etiology of the disease, but emphasizes clinical protocols and step-by-step procedures for diagnosis and treatment planning. <i>Dry Mouth</i> is a user-friendly manual guiding clinicians through identifying and managing this common condition. Causes including radiotherapy, chemotherapy, systemic diseases, polypharmacy, and the natural progression of aging are discussed in conjunction with the clinical symptoms and signs associated with each one. Multiple avenues for treatment are presented, highlighting salivary stimulation and supplementation techniques, pharmacologic aids, and critically required oral therapy. Although intended primarily for the professions that treat those affected by xerostomia, <i>Dry Mouth</i> may also be of interest to sufferers of this condition”. <i>Please note: All illustrations from this publication as well as supplementary information may be accessed online by using a code word found in the book.</i></p>	
<p>Jensen SB, Pedersen AM, Vissink A, Andersen E, Brown CG, Davies AN, et al. “A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: management strategies and economic impact”. <i>Support Care Cancer</i>. 2010 Aug;18(8):1061-79.</p>	
<p>Jensen SB, Pedersen AM, Vissink A, Andersen E, Brown CG, Davies AN, et al. “A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life”. <i>Support Care Cancer</i>. 2010 Aug;18(8):1039-60.</p>	
<p>“Drug Facts and Comparisons”, Wolters Kluwer, St. Louis, MO, 2008</p>	
<p>“Drug Information Handbook for Dentistry”, LexiComp, Hudson (Cleveland), OH, 2008</p>	
<p>“Physician’s Desk Reference”, Medical Economics Co., Des Moines, IA, 2008</p>	
<p>“U.S. Pharmacopeia”, Micromedex, Englewood, CO, 2008</p>	
<p>“Merck Manuals”: Generic and trade (brand) names for drugs: http://www.merckmanuals.com/professional/drugnames-index/generic/a.html</p>	
American College of Rheumatology (ACR)	<p>“Arthritis and Rheumatic and Musculoskeletal Diseases”: http://www.rheumatology.org/</p>
American Dental Association	<p>“Dry Mouth”:http://www.ada.org/3014.aspx?currentTab=1 <i>“There is no professional/clinical information on this topic”</i></p>
American Dental Association: ADA® Center for Evidence-Based Dentistry™	<p>Evidence-Based Reviews: http://ebd.ada.org/SearchResult.aspx?Search=xero</p>
Dental Healthcare Professional Journal Database	<p>http://www.nature.com/vital/journal/v6/n2/full/vital944.html (requires free subscription)</p>

Head and Neck Cancer Alliance (formerly known as The Yul Brynner Head and Neck Cancer Foundation)	“Oral, Head and Neck Cancer Awareness Week”: http://campaign.r20.constantcontact.com/render?llr=or5oj5cab&v=001J8BvtJGIt7vjdd3QIXjNcpDaaV8yKuE_T0HU-BcHLxIAE8z-NXB8z1F7hS7ammRsUq6BpMx2VPNFnOdquRfIVi2lDc2K1mRDsJlI0FxSTam4hhAXVRiXo4XWBaDRHdYd
Head and Neck Cancer Alliance (formerly known as The Yul Brynner Head and Neck Cancer Foundation)	http://www.headandneck.org 50 Facts about Oral, Head and Neck Cancer: http://www.headandneck.org/atf/cf/%7B62182A04-09FB-47FA-80AB-94B692B89FF3%7D/50facts.doc

Table 6A. Resources for Health Care Providers, continued

International Academy of Oral Oncology (IAOO)	Official Journal: “Oral Oncology” http://www.elsevier.com/wps/find/journaldescription.cws_home/105/description#description
International Academy of Oral Oncology (IAOO)	Comprehensive list of URLs for Oral Cancer: http://www.homepages.ucl.ac.uk/~sfhvcms/iaoo/links.html
National Comprehensive Cancer Network (NCCN)	http://www.nccn.org/index.asp
National Comprehensive Cancer Network (NCCN) “NCCN is a not-for-profit alliance of 21 of the world’s leading cancer centers and is dedicated to improving the quality and effectiveness of care provided to patients with cancer.”	Clinical guidelines for health care providers: http://www.oralcancerfoundation.org/treatment/pdf/infections-NCCN.pdf & http://www.nccn.org/professionals/physician_gls/f_guidelines.asp (Free login required): Head and Neck Cancers: <ul style="list-style-type: none"> • Cancer of the Lip • Cancer of the Oral Cavity • Cancer of the Oropharynx • Cancer of the Hypopharynx • Cancer of the Nasopharynx • Cancer of the Glottic Larynx • Cancer of the Supraglottic Larynx • Ethmoid Sinus Tumors • Maxillary Sinus Tumors • Unresectable/Recurrent/Persistent Head and Neck Cancer • Occult Primary • Salivary Gland Tumors • Mucosal Melanoma
National Institute of Dental & Craniofacial Research (NIDCR), National Institutes of Health (NIH), USHHS	“Dry Mouth (Xerostomia)”: http://www.nidcr.nih.gov/OralHealth/Topics/DryMouth
National Institutes of Health (NIH), USHHS	“Dry Mouth” interactive textbook: http://symptomresearch.nih.gov/chapter_27/sec2/cpfs2pg1.htm
National Institutes of Health: National Library of Medicine	Scleroderma: http://www.nlm.nih.gov/medlineplus/ency/article/000429.htm
Oral Cancer Foundation (OCF)	http://www.oralcancerfoundation.org/searchresults.htm?cx=015422755131303034108%3Ao3fylifwmag&cof=FORID%3A11&q=bartlett#328
Oral Cancer Foundation (OCF)	“Prevention and Treatment of Cancer-Related Infections”, 41 pp: http://www.oralcancerfoundation.org/treatment/pdf/infections-

	NCCN.pdf
Oral Cancer Foundation (OCF)	“Xerostomia Information for Dentists”: http://www.oralcancerfoundation.org/dental/xerostomia.htm
Sjögren’s Syndrome Classification Criteria: American-European Consensus	http://ard.bmj.com/cgi/reprint/61/6/554 (requires free subscription)
Sjögren’s Syndrome Foundation:	http://www.sjogrens.org/
Sjögren’s Syndrome:	“Information for Healthcare Providers”: http://www.sjogrens.org/home/about-sjogrens-syndrome/healthcare-providers

Table 6A. Resources for Health Care Providers, continued

Sjögren’s Syndrome: Diagnosis Criteria	http://www.sjogrens.org/home/about-sjogrens-syndrome/healthcare-providers/diagnosis-criteria
Sjögren’s Syndrome Clinic National Institute of Dental and Craniofacial Research (NIDCR) Building 10, Room 1N113 10 Center Drive MSC 1190 Bethesda, MD 20892-1190 Tel: 301-435-8528	http://www.nidcr.nih.gov/Research/NIDCRLaboratories/MolecularPhysiology/SjogrensSyndrome/
Sjögren’s Syndrome Foundation, Inc. 6707 Democracy Blvd Suite 325 Bethesda, MD 20817 Tel: 1-800-475-6473	http://www.sjogrens.org/
The International Academy of Oral Oncology [IAOO]	http://www.homepages.ucl.ac.uk/~sfhvcms/iaoo/index.html
Wrigley Chewing Gum:	List of Xerogenic Drugs: http://www.drymouth.info/practitioner/SearchByClass.asp
Wrigley Chewing Gum: Information for Healthcare Providers	“Dry Mouth”: http://www.drymouth.info/practitioner/sources.asp#source

Table 6B. Online Resources for Patients	
American College of Rheumatology (ACR)	“Arthritis and Rheumatic and Musculoskeletal Diseases”: http://www.rheumatology.org/
American Dental Association	“Dry Mouth” http://www.ada.org/3014.aspx?currentTab=1
Head and Neck Cancer Alliance (formerly known as The Yul Brynner Head and Neck Cancer Foundation)	“Oral, Head and Neck Cancer Awareness Week”: http://campaign.r20.constantcontact.com/render?llr=or5oj5cab&v=001J8BvtJGIt7vjdd3QIXjNcpDaaV8yKuE_T0HU-BcHLxIAE8z-NXB8z1F7hS7ammRsUq6BpMx2VPNFnOdquRfVi2IDc2K1mRDsJlIOfxSTam4hhAXVRiXo4XWBaDRHdYd
Head and Neck Cancer Alliance (formerly known as The Yul Brynner Head and Neck Cancer Foundation)	http://www.headandneck.org: “50 Facts about Oral, Head and Neck Cancer”: http://www.headandneck.org/atf/cf/%7B62182A04-09FB-47FA-80AB-94B692B89FF3%7D/50facts.doc
National Comprehensive Cancer Network (NCCN)	“A website devoted to patients, caregivers, and their families http://www.nccn.com/
National Institutes of Health (NIH), U.S. Department of Health and Human Services	“Dry Mouth” interactive textbook: http://symptomresearch.nih.gov/chapter_27/sec2/cpfs2pg1.htm
Sjögren’s Syndrome Patients Support Site	“Living with Dryness”: http://www.livingwithdryness.com/
Sjögren's Syndrome Foundation, Inc. 6707 Democracy Blvd Suite 325 Bethesda, MD 20817 Tel: 1-800-475-6473	http://www.sjogrens.org/
Sreebny L, Vissink A, editors. <u>Dry Mouth, the Malevolent Symptom: a Clinical Guide</u> . Singapore: Wiley-Blackwell; 2010. 268 pp. ISBN: 978-0-8138-1623-4	Book: May be of interest to patients. For purchase: Paperback; \$74.99: http://www.wiley.com/WileyCDA/WileyTitle/productCd-0813816238.html
U.S. Department of Health and Human Services, National Institutes of Health (NIH), National Institute of Dental and Craniofacial Research (NIDCR)	“Dry Mouth”. 8pp pamphlet for patients: http://www.nidcr.nih.gov/NR/rdonlyres/A22079A5-8C4C-4E6D-80C1-D6A1D2EB07F8/0/DryMouth.pdf
Wrigley Chewing Gum: Information for Patients	“Dry Mouth”: http://www.drymouth.info/consumer/default.asp

Figure 1. Medication Usage Form (Please see comments on the following page)

NAME OF DENTAL PRACTICE
 STREET, CITY, ZIP CODE
 TELEPHONE NUMBERS

MEDICATIONS

Patient ID: _____ Date: _____ Reviewer: _____

1. Diabetes medication taken now or in the last 6 months? Yes No => Go to #2 Don't Know

Name of Diabetes Medication	Dosage		Frequency (times/day)	Start Date (MM/DD/YYYY)	End Date (MM/DD/YYYY)
	Amount	Unit (IU or mg)			

2. Non-Diabetes prescription medication taken now or in the last 6 months? Yes No => Go to #3 Don't Know

Name of Non-Diabetes Prescription Medication	Dosage		Frequency (times/day)	Start Date (MM/DD/YYYY)	End Date (MM/DD/YYYY)
	Amount	Unit (ml, mg, g)			

3. Non-prescription medication taken now or in the last 6 months..... Yes No => Go to #2 Don't Know

Name of Non-Prescription Medication (OTC, drops, vitamins, supplements, etc.)	Dosage		Frequency (times/day)	Start Date (MM/DD/YYYY)	End Date (MM/DD/YYYY)
	Amount	Unit (ml, mg, g)			

COMMENTS: _____

Comments to Fig. 1 Medication Usage Form (*Please see form on the previous page*)

It is often extraordinarily difficult to obtain a correct report of all drugs used, as many patients do not remember. Therefore, it is advisable to ask the patient to bring along all medication in their original packaging for a staff member to meticulously record all medicinal substances the patient is currently taking or has used the last six months or so. Skill is required in getting the patient to truthfully report their current use, which may be substantially different from that prescribed.

Such detailed information can be used for a number of purposes. Firstly, it gives the dental or medical practitioner an overview of the categories and multitude of drugs used. Secondly, this record is a helpful, indispensable tool in consultations among health care providers. Often, physicians who prescribe drugs for certain ailments do not have a complete overview of which medications a patient is using, so drug interactions might be identified in a comprehensive listing. Also, some drugs prescribed in the past might still be used after a substitute has been prescribed. In reviewing the record of medications, drugs might be identified that can be discontinued altogether, or substitute drugs may be tried. A meticulous, continuous record of medication changes with start and end dates is essential to adjust the drug regimen to reach the optimal combination of drugs for any given patient at any given time.