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THE SALIVARY SYSTEM

Leo M. Sreebny

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CRC Press, Inc.
Boca Raton, Florida

SCHOOL OF DENTAL MEDICINE

STATE UNIVERSITY OF NEW YORK @ STONY BROOK

STONY BROOK, N.Y. 11794-8702

February 3, 1988

Contributors
"THE SALIVARY SYSTEM"
CRC PRESS, Inc.
Boca Raton, FL.

Guido

Dear Colleague,

ברוך השם -- "Blessed be His name"

For those who are patient, all kinds of things can happen. Even, the publication of a book.

By now, you should have received your copy of "THE SALIVARY SYSTEM". My first reaction was one of relief. After all this waiting, it is finally out! The data, of course, are already out-of-date. But on the whole, I believe that it is a worthwhile addition to our field.

I sincerely thank you for your help. I hope, that this little volume will contribute, in its own special way, to the awareness and realization that the salivary system is as interesting and important to the fields of biology and medicine as other, more accepted, systems.

I hope to see you all in Montreal.

Sincerely yours,

Leo M. Sreebny

Chapter 9

XEROSTOMIA (DRY MOUTH)

Leo M. Sreebny and Guido Broich

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I. INTRODUCTION

Xerostomia is the subjective feeling of oral dryness. Although it may seriously affect the quality of life of those affected by this condition, it can hardly be categorized as a serious concern of the medical profession. Indeed, dry mouth is barely mentioned in standard textbooks of internal medicine. Due largely to exocrine gland dysfuntion, xerostomia may markedly affect the organs and tissues of the oral cavity. Moreover, it may be but one of several symptoms characterized by intense desiccation which affect exocrine gland supplied organs and tissues throughout the body. Though its cause may be variable, it is becoming increasingly evident that dry mouth is a symptom which is primarily associated with a number of systemic disorders, many of which are fatal, as well as with the use of over 400 drugs.

The objectives of this chapter are (1) to review our current knowledge of the pathogenesis of xerostomia, (2) to assess the sialometric findings in this condition, and (3) to present a rationale for its treatment.

II. EPIDEMIOLOGY

It is generally accepted that dry mouth is a common clinical complaint.[1-3] Moreover, it is widely believed that the condition is primarily found among the elderly.[4] Whereas these beliefs are supprted by anecdotal information and individual case reports, prevalence data, arrived at through rigorous scientific research, are sparse.

Estimates of the prevalence of xerostomia may be obtained from subjective data supplied by the patient, from data derived from clinical examinations of the mouth for signs of oral dryness, and from laboratory tests which directly measure the rate of flow of saliva. Ideally, these three techniques should be used in concert. Few studies, however, have pursued such a course.

Lamb[5] observed that only 1 in 1500 patients at the Glasgow Dental Hospital cited xerostomia as a primary complaint; however, when these patients were querried as to whether they experienced dry mouth as a regular symptom, 1 in 10 affirmed that they did.

Osterberg et al.[4] recently studied the oral condition of 1148 70-year-old people in Göteborg, Sweden. Positive responses to the question "Does your mouth feel distinctly dry?" were given by 16% of the men and 25% of the women. Most of the subjects regularly took prescribed medications. Among those who did not consume any drugs, about 10% complained of dry mouth. The flow rate of whole saliva was measured in a consecutive subsample of 110 drug-taking and nondrug-taking subjects. About 25% of the women and 7% of the men demonstrated low salivary flow rates (between 0.0 and 0.5 mℓ/min).

Partial estimates of the prevalence of dry mouth may be made by examining data from patients with diseases in which xerostomia is a frequent complaint. One such disease is rheumatoid arthritis. It has been estimated that the prevalence of rheumatoid arthritis in the U.S. is about 2%.[6] The symptom of xerostomia is found in about half of the patients who have this disease.[7] These data suggest that in rheumatoid arthritis alone, there are about 4 to 5 million people who suffer from xerostomia.

The data, though sparse, support the belief that xerostomia is a common complaint which

is particularly prevalent among the aged. What is needed, however, is a comprehensive study of the prevalence of dry mouth in a normal adult population.

A. Aging and Salivary Flow

Since xerostomia is often found in aged subjects, it is of more than passing interest to determine if aging per se, or some other factors associated with the aging process, affect the flow of saliva. It has been widely believed that salivary secretions diminish with age. A number of studies performed on whole saliva and on saliva obtained from the major and minor salivary glands tend to support this belief.[1,8-13] The decrease in the flow of "resting" parotid and whole saliva was, respectively, about 21 and 40%.[1,8,10] In the case of the submandibular glands, the decrease for unstimulated submandibular saliva was 78% and 61% for the stimulated secretion.[11] A decrease of 50% was noted in the stimulated labial minor salivary glands.[12] In addition to these sialometric investigations, morphometric analyses performed on postmortem specimens showed that there is a 44% age dependent decrease in the acinar volume of the labial salivary glands.[14]

In contrast to these findings, a number of investigators have recently shown that with the exception of postmenopausal women, age per se is not associated with a decrease in the flow of stimulated whole or resting and stimulated parotid saliva.[10,15-17]

Conflicting data thus exist regarding the relationship between aging and salivary flow. Some of the differences may reflect actual functional and morphologic changes in some glands. Others may be due to the differences in the methods used to collect the saliva or, especially in the earlier studies, to the fact that the health and the drug status of the subjects were not taken into account. None of the studies attempted to correlate the rates of flow of saliva with the patient's subjective impression of xerostomia. Even if there is a "normal" age-associated diminution in the secretion of saliva, it is questionable if the number of glands affected and the magnitude of the decrease in flow can actually cause the feeling of dry mouth (see Section III.A.2). There can be little doubt, however, that it may significantly contribute to the development of dry mouth.

III. DIAGNOSTIC TECHNIQUES EMPLOYED IN XEROSTOMIA

The tests which are employed to study patients suspected of having xerostomia are of two types. The first of these, sialometry, directly measures the flow of whole (mixed) saliva or saliva derived from the individual salivary glands. Other tests, not discussed herein due to space limitations, are employed to determine the causes of the feeling of oral dryness. These include: sialochemistry, sialography, salivary scintigraphy, computerized tomography (CT), and biopsy. These tests provide data which are primarily used to evaluate the structural integrity and the functional status of the acinar and ductal components of the salivary glands.

A. Sialometry

Several techniques are available to collect whole saliva or the secretions from the parotid, the submandibular/sublingual (SM/SL)* and the minor salivary glands. Whole saliva is a mixture of the secretions from the major and minor salivary glands. In addition to the salivary secretions, it contains bacteria, food debris, leukocytes, sloughed epithelial cells, and other particulate material. Because of the complex nature of this secretion, its use as an index of salivary gland dysfunction has fallen into disrepute. With respect to the mater of oral dryness, however, whole saliva is the secretion of choice. Since dry mouth is a multiglandular

* The secretions from the submandibular and the sublingual glands frequently enter the mouth via a common duct, thus making it impossible to distinguish their origin. In the discussion which follows, the secretions from these glands will be combined.

Table 1
NORMAL FLOW RATES: WHOLE AND GLAND-DERIVED SALIVA

Source	Unstimulated saliva	Stimulated saliva (2% citric acid)
Whole saliva	0.3—0.5 (mℓ/min)	1.0—3.0 (mℓ/min)
Parotid	0.04 (mℓ/min/gland)	0.70 (mℓ/min/gland)
SM/SL	0.15 (mℓ/min/gland)	0.60 (mℓ/min/gland)

condition wherein the overall flow of saliva is seriously impaired, the determination of the flow rate of unstimulated whole saliva is all that is needed to confirm its diagnosis.

Whole saliva may be obtained by allowing the fluid to drip passively into a graduated tube, by aspirating it from the floor of the mouth, or by requesting that the patient actively expectorate the accumulated secretions into a collecting vessel. Of these methods, the expectoratory technique is probably the most reliable.[18] Generally, the secretions from the parotid and the SM/SL glands are collected by the use of specially constructed devices which, respectively, fit over the orafices of Stenson's[19] or Wharton's duct.[20] Capillary tubes or filter paper are employed to collect saliva from the labial minor salivary glands.[3,11]

Although no standardized procedure has been adopted for the collection of saliva, it is geneally recognized that it should be obtained under rigidly controlled conditions. Most frequently, it is collected after an overnight fast or 2 hr following a meal. The tests should be conducted in a quiet area and a brief accomodation period should precede its collection.* Mechanical (paraffin) or gustatory agents (2% citric acid) are usually employed to stimulate the flow of saliva. The citric acid may be applied to the dorsum of the tongue with a cotton applicator at 30-sec intervals. Alternatively, 20 mℓ of a 2.5% citric acid solution may be held in the mouth for a period of 1 min.[21] Saliva is usually collected for 5 to 10 min. The amount secreted is determined by volumetric or gravimetric procedures. Results are generally expressed as mℓ/min or mg/min for whole saliva or mℓ/min/gland or mg/min/gland for a gland-derived saliva.

1. The Normal Flow Rate of Saliva

There are no universally accepted standards for the normal mean flow of whole or gland-derived saliva. The flow rates listed in Table 1 are consistent with the data obtained by the following investigators: Syrjanen,[7] Parvinen et al.,[15] Becks and Wainwright,[22,23] Dawes,[24] Ferguson,[25] Krasse,[26] Mandel and Wotman,[27] and Shannon.[28]

Recent studies on the flow from the SM/SL and the minor salivary glands, however, present strikingly different findings. Pedersen et al.,[11] utilizing a newly designed SM/SL collecting device, determined that the rate of flow of unstimulated saliva from the SM/SL glands was 0.06 mℓ/min/gland and 0.26 mℓ/min/gland for stimulated saliva. These values are appreciably less than those obtained by investigators who have employed the Schneyer-type SM/SL collecting device.

Only a few reports in the literature deal with the flow from the minor salivary glands. Schneyer et al.[29] demonstrated that 0.002 to 0.008 g of labial gland saliva was secreted over a 10 to 20 min interval. Dawes and Wood[30] estimated that the minor salivary glands contributed 7 to 8% of the total amount of saliva secreted daily, a volume of about 50 mℓ. Recent estimates of the rate of flow of saliva from the minor salivary glands[12] demonstrated that the mean rate of flow of stimulated saliva, obtained from the lower lip, was 0.0021 mℓ/min.

* Provisional estimates of salivary flow in suspected xerostomic patients can be peformed at any time or any place. The diminution in flow is often so great, it is well out of the normal range.

Table 2
RATES OF FLOW OF SALIVA IN XEROSTOMIC PATIENTS

Type of saliva	Xerostomia	Ref.
Whole, unstimulated	0.01—0.1[a]	8
	0.10[a]	34
Parotid, unstimulated	0.02[b]	35, 36
Parotid, stimulated[c]	0.18[b]	35
	0.1—0.6[b]	37
	<0.20[b]	4
	<0.20[b]	38
	<0.27[b]	39

[a] mℓ/min.
[b] mℓ/min/gland.
[c] Stimulus was 2% citric acid.

Table 3
ESTIMATED FLOW RATES OF UNSTIMULATED WHOLE SALIVA IF SELECT GLANDS ARE NONFUNCTIONAL

Gland function	mℓ/min[a]
Normal flow rate: all glands functional	0.40
If 1 parotid gland nonfunctional	0.36
If 2 parotid glands nonfunctional	0.32
If 1 SM/SL gland nonfunctional	0.25
If 2 SM/SL gland nonfunctional	0.10
If 1 parotid and 1 SM/SL glands nonfunctional	0.21
If 2 parotids and 1 SM/SL glands nonfunctional	0.17
If 1 parotid and 2 SM/SL glands nonfunctional	0.06
If 50% of all glands nonfunctional	0.20
If 75% of all glands nonfunctional	0.10

[a] Based on data shown in Table 1.

2. Flow Rates of Saliva in Xerostomia

As with normal flow rates, no standards have been established for xerostomia. Clearly, a spectrum of diminishing flow must accompany the transition from the normal functional state to dry mouth, but the "cut-off range" is not known. Given that normal flow rates vary widely among individuals, it should be expected that the flow rates at which the dry mouth is noted will also vary considerably. Some investigators[4,8] have observed a positive correlation between the perception of dryness and a reduction in the production of saliva. It is well known, however, that some patients who complain of xerostomia do not show evidence of decreased salivary flow. In others, the converse is true.[31-33] Some select flow rates for patients with dry mouth are shown in Table 2.

The data suggest that it is likely that the feeling of dry mouth would be present in individuals whose flow rates for unstimulated whole and stimulted parotid saliva are, respectively, in the range of 0.01 to 0.1 mℓ/min and 0.10 to 0.27 mℓ/min/gland.

It is of interest to compare the actual values for the flow rates of "resting" whole saliva in xerostomic patients with values obtained for normal subjects in which one or more glands are theoretically nonfunctional (Table 3).

These derived values show that only when both SM/SL glands or 50 to 75% of all of the

salivary glands are nonfunctional do the flow rates approach those seen among patients with xerostomia. They support the belief that extensive gland damage or dysfunction must be present before a patient would complain of dry mouth.

It is tempting to ponder the relationship between the sensation of oral dryness and the following salivary factors: (1) the type of saliva (resting vs. stimulated), (2) the character of the saliva (mucous vs. serous), and (3) the volume of saliva required to obviate the feeling of dry mouth. Unfortunately, little is known about these issues.

Osterberg et al.[4] and others[31,37] have observed that the subjective feeling of oral dryness was most closely correlated with the flow of unstimulated (resting), rather than stimulated, saliva. About 80% of resting whole saliva is composed of secretions from the mucous-secreting SM/SL and minor salivary glands. These secretions form the protective coating of the delicate membranes which line the mouth. The belief that the quality of the secretions, in this case the mucins rather than actual flow rate, may play a role in the genesis of xerostomia was first proposed by Mandel and Wotman.[27] Two pieces of evidence support this belief:

1. The secretions during sleep, albeit minimal, are primarily mucous in character. Yet, under normal circumstances, no feeling of dryness is present during sleep or in the early postwaking state.
2. The use of salivary substitutes, which, with but few exceptions, do not contain mucinous substances, do not appreciably reduce the feeling of dryness in patients with xerostomia.

Aside from the type and quality of the oral secretions, little is also known about how much saliva is necessary to obviate the feeling of dry mouth. Data from patiets indicate that xerostomia is noted when the flow rate of whole saliva approaches 0.1 mℓ/min. Two recent studies have determined that a small amount of residual saliva is normally present in the oral cavity (0.24 to 0.77 mℓ)[21,40] Schneyer[41] showed that about 0.002 to 0.008 g of labial (i.e., mucous) saliva was secreted over a 10-min period. The labial glands comprise about 1/40th of the total area occupied by the minor oral salivary glands.[42] Thus, at rest, about 0.08 to 0.32 g of minor gland saliva would be present in the mouth. These figures are in accord with the data obtained for residual saliva. They suggest that only minute amounts of largely mucous saliva are needed to adequately moisten the oral mucous membranes. This is further supported by the observation that the mucous membranes of xerostomic patients who are incapable of producing a readily measurable flow of saliva following citric acid stimulation often appear moist. The observations suggest that very little, most likely mucous-containing saliva, may prevent the feeling of xerostomia.

IV. DISEASES AND CONDITIONS WHICH CAUSE XEROSTOMIA

A. General Considerations

Before analyzing the various conditions and diseases which induce xerostomia, it is useful to consider some general phenomena which affect this relationship. Two terms, xerostomia and hyposalivation, are frequently used to refer to conditions in which there is a reduction in the flow of saliva. Whereas xerostomia connotes the subjective feeling of oral dryness resulting from a severe reduction in the rate of flow of saliva, hyposalivation refers to a less severe state. Conditions in which there is a gradual impairment of the function of salivary gland tissue initiate a series of events which, in all likelihood, progress from hyposalivation to xerostomia. A major shut-down of the secretory apparatus, as for example with drugs or neurogenic influences, may, on the other hand, rapidly lead to a feeling of oral dryness.

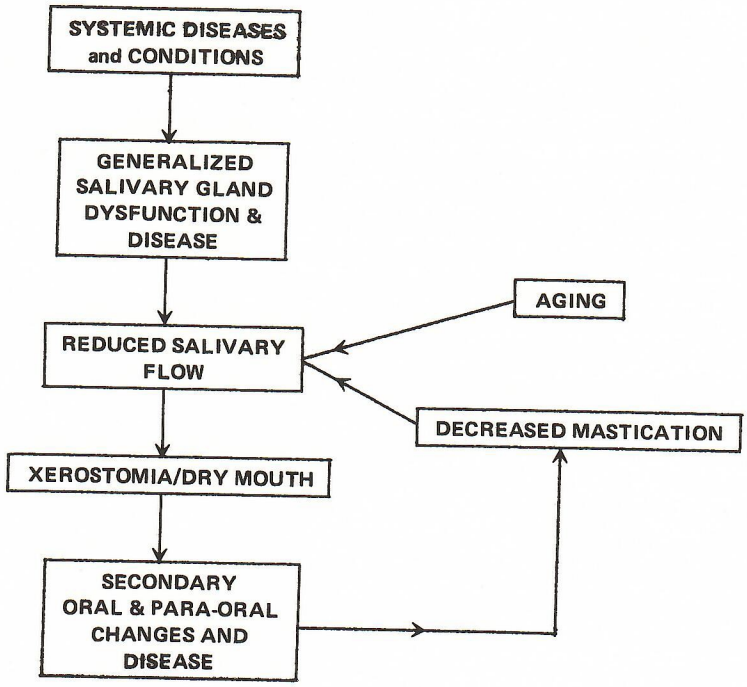

FIGURE 1. Xerostomia: causes and interrelations.

1. Salivary Flow: Disease Related Considerations

In and of itself, a reduction in salivary flow may be a trivial matter which may go completely unnoticed by the subject. However, if severe, as for example, when caused by serious, often morbid systemic disorders, and if it extends over months or years, it may cause considerable discomfort and anxiety. Moreover, it may initiate a series of events which lead to extensive oral and paraoral (salivary) changes and diseases. The complex relationship between reduced salivary flow and disease may be represented as in Figure 1.

A number of systemic conditions and decreased mastication may, via their affects on the salivary glands, induce a reduction in the flow of saliva. In some cases, the effects are temporary; in others, they tend to be permanent. The systemic disorders may be of an organic or functional nature. Prominent among the organic causes are autoimmune diseases, e.g., Sjogren's syndrome, irradiation and possibly depression, dehydration, and debilitation. Drugs and decreased mastication are examples of functional disorders.

The oral changes induced by the depression in flow may include (1) oral dryness, (2) an increase in dental caries, (3) swelling of the salivary glands, (4) atrophy of the oral mucosa, (5) burning sensations in the tongue and the appearance of fissures on its dorsal surface, (6) cheilosis and cheilitis, (7) an increase in oral infection, (8) difficulty with the solubilization of ingested substances leading to an impairment of taste and an inability to absorb lingually placed drugs, and (9) difficulty with swallowing and speech.[8,39,43,44] The reduced flow may also predispose the salivary glands to retrograde infection.[45] This may, on occasion, cause the formation of acute and chronic sialadenitis and perhaps, sialolithiasis.[46] Episodic attacks of these conditions may, in turn, induce even further reductions in flow; all in all, a viscious circle.

2. Salivary Flow: Anatomic and Physiologic Considerations

a. Site of Water Transport

The salivary glands are confluent acino-tubular structures which, in essence, are factories

that produce and transport saliva; 99% of the saliva is water. There is little if any transfer of water across the walls of the ducts.[47]

In xerostomia, the secretion of water is reduced. The source of the water is the blood; its principal sites of entry into the glands are the acini and the small, intercalated ducts. Various electrolytes are added to this primary fluid, and some subsequently removed, during its passage through the ductal labyrinth. The pivotal role played by the acini in the transfer of water is demonstrated by the fact that selective destruction of the acini, e.g., as a consequence of duct ligation or irradiation of the salivary glands, results in a decrease in the rate of flow of saliva, but no change in the concentration of its electrolytes.[47,48] Destruction of the striated and excretory ducts, but not the acini on the other hand, by the retrograde infusion of mercuric chloride into the ductal system, affects the concentration of electrolytes in saliva but not its rate of flow.[50] In some conditions, wherein the reduction in flow is rapidly induced, the flow, after a brief, often times embarassing period, usually returns to normal. This bespeaks of a depression in the rate of formation of saliva but not with a defect in the mechanisms by which water is handled by the gland. In other conditions, the underlying mechanisms might be affected.

b. Duct Specialization

The parotids are designed to transport a saliva which is mainly thin and watery; its ducts are short and comparatively thin. The paired submandibular gland, with its longer but wider duct, specializes in the passage of a more viscid, mucous type of saliva. In some disorders of the parotid gland, the affected gland may demonstrate signs of acinar atrophy, a narrowing of its ducts, and a metaplastic conversion of the cells which line them.[50] It is alleged that the presence of mucin in glands geared to the production of watery-like secretions may cause extensive damage to the entire acinotubular system.[45,52] The evidence to support this is, however, sparse.

3. Single vs. Multiple Gland Involvement

It has already been stated that a major shut-down of virtually the entire secretory apparatus is required before the patient would complain of dry mouth. Conditions which primarily affect single glands, such as neoplasms, calculi, trauma or duct strictures, can markedly reduce the secretion from the affected gland, but do not actually induce the feeling of oral dryness. Further, even patients with bilateral parotidectomies do not complain of dry mouth.[53] Implicit in these observations is the recognition that xerostomia is a multiglandular disease which is primarily caused by systemic, rather than local factors. Even in those comparatively rare cases where ''local'', or properly, ''regional'' conditions are the cause, as in patients who have received radiation therapy for oral cancer, many glands are affected.

4. Salivary Gland Swelling and Pain

Parotid gland swelling and pain may accompany the feeling of oral dryness. When present, the swelling may be bi- or unilateral. The presence of swelling and pain indicate that pathologic changes have occurred in the affected organ. Their absence, however, does not preclude the fact that salivary dysfunction may be present. Maynard[45] showed that in cases of unilateral chronic recurrent parotitis, the unaffected, as well as the clinically affected side, demonstrated decreases in the rate of flow of saliva.

Complete duct obstruction, for example in duct ligation, results in a transient retrograde enlargement of the gland, followed by acinar atrophy. Partial obstruction, on the other hand, may lead to episodic, recurrent swelling of the affected glands. Secondary infection may cause such swellings to become painful. Pain may be also be noted when the partially occluded glands are stimulated to secrete, for example, during eating.

B. Radiation-Induced Damage to the Salivary Glands

Xerostomia is a common complaint among patients who have received ionizing radiations for the treatment of radiosensitive neoplasms to the head and neck region. The severity of the condition depends on the daily radiation dose, the period of its administration, and the centrality of the salivary glands to the field of irradiation. Most irradiated patients receive between 5000 and 7000 rad. This is usually given over a 4- to 6-week-period, or 200 rad each visit.[54,55]

Early in the course of radiation, the patients frequently complain of dry mouth and pain, and exhibit signs of erythema and mucous plaque formation; oral ulcers appear after about 2 weeks.[56] Early histopathologic changes in the glands include inflammation, damage to the cellular organelles, and localized cell necrosis.[57] The acini are more affected than the ducts, serous acini more than the mucous acini.[58,59] In keeping with these observations, the parotid gland is more sensitive to the ionizing radiations than the submandibular gland; the sublingual gland is the least affected.[47,58,60,61] Ultimately, the glands undergo involution, atrophy, and fibrosis. The destruction is primaily irreversible.[58,60]

The complaint of dry mouth is almost invariably accompanied by a severe reduction in the flow of saliva.[55,56,58,60,62-64] After 1 week of radiotherapy, Dreizen et al.[63] and Shannon et al.[64] observed a 40% decline in the flow of stimulated and unstimulated whole saliva. By 6 weeks flow had fallen to between about 5 and 15% of normal.

Of particular interest are the reports by some investigators that irradiated patients complain of xerostomia and demonstrate signs of diminished salivary flow soon after the onset of their treatment. Frank et al.[60] observed a "drastic depression" of unstimulated whole saliva during the first day of treatment. Kashima et al.[58] noted that patients complained of dry mouth as early as 2 to 6 hr after irradiation. Eneroth et al.[62] studied the effect of fractionated radiotherapy on parotid gland function. The daily dose was 200 rad. Severe reductions in the flow of resting saliva were observed after 2 to 3 days. Shannon et al.[64] noted a 50% reduction in the flow rate of parotid saliva 24 hr after the first ^{60}Co treatment with 225 rad.

The profound reduction in the rate of flow of saliva in postirradiated patients is also accompanied by changes in the physical properties of saliva. In postirradiated patients the saliva becomes viscid, excessively foamy, and yellow to brown in color.[60]

The xerostomia seen in postirradiated patients can be accounted for by the extensive acinar destruction present in the affected glands. The physical transformation of the mixed saliva from one which is normally thin to one which is thick and mucinous is unexplained.

The extensive damage to the parenchyma of the salivary glands following irradiation has been reasonably well described; however, the mechanisms which initiate these tissue responses are not known. A recent study by Bodner et al.[65] sheds some light on this issue. These authors, in a study conducted on rats, demonstrated that parotid flow rates fell to 45% of the control values 3 days after irradiation with 2000 rad; however, when salivary gland cell preparations were studied in vitro, they functioned normally. These findings suggest that nerves or blood vessels, rather than the acini, are primarily affected by the ionizing radiation. If so, this may account for the observation in humans that there is such a marked decrease in the flow of saliva soon after irradiation is instituted. Morphologic damage to the parenchyma develops after days or weeks;[58,60] interference with the vascular or neural mechanisms which regulate the flow of saliva would have an almost immediate effect on the glands. Vascular changes are commonly seen within a few hours after the onset of radiation therapy; neural tissues, on the other hand, tend to be radioresistant to ionizing radiations.[54] Little is known about the effect of X-irradiation on salivary neuroreceptors.

C. Sjogren's Syndrome

Sjogren's syndrome is a chronic, multisystem, autoimmune disorder. The prominent features of this disease are (1) exocrine gland dysfunction, (2) multiple organ system ab-

normalities, and (3) serologic hyperreactivity. Two forms are held distinct: a primary form (PSS; "sicca complex"), characterized by xerophthalmia and xerostomia, and a secondary form (SSS), in which at least one of these two symptoms and a connective tissue disorder (mainly rheumatoid arthritis) are present. Other collagen diseases may substitute for rheumatoid arthritis in this syndrome. Prominent among these are lupus erythematosus, Raynaud's phenomenon, chronic hepatobiliary disease, polymyositis, and scleroderma.[66,67]

Besides rheumatoid arthritis, Sjogren's syndrome is considered to be the most common collagen disease.[66] The syndrome is more frequent in women than in men (9:1) and is most often found in patients over 40 years of age. Some cases may develop during childhood. About half of the cases are primary; the remainder are secondary.

1. Signs and Symptoms

The symptoms and signs of Sjogren's syndrome may be conveniently assigned to two groups: (1) those associated with hypofunction of the exocrine glands and (2) those associated with other organs and tissues. In its early stages, few signs and symptoms may be present; later, they increase in frequency.

a. Hypofunction of the Exocrine Glands

i. Oral Findings

The oral findings (Table 4) in Sjogren's syndrome are primarily due to a decrease in the function of the major and minor salivary glands. The most common oral complaint, found in over 90% of the patients, is xerostomia.[8,39,68,69] The amount of saliva is reduced, and that which is secreted appears thick and flocculent.[37,70] Salivary swelling is seen in over 80% of the cases and may precede the onset of dry mouth.[66] Other oral signs and symptoms are usually the result of extended periods of oral dryness. Prominent among these are fissuring of the tongue and an increase in the intake of water. The data suggest that most symptoms are more prevalent in PSS than SSS.

Tapper-Jones et al.[71] reported that Sjogren's patients with a positive rheumatoid factor, were more susceptible to infections by *Candida albicans*. This is of particular interest, since infection with *C. albicans* is an almost universal accompaniment of individuals with severe deficiencies in cell-mediated immunity.[72]

Many investigators, past and present, have shown that salivary gland enlargement is a prominent clinical feature of Sjogren's syndrome.[8,67,68,73] The swelling of the glands is particularly evident in patients with the primary form of the disease.[67,68] The parotid glands, perhaps because of their long and narrow ducts,[52] are more frequently affected than the submandibular glands; it is not clear whether uni- or bilateral swelling is more commonly seen. These findings are in sharp contrast to recent observations by Fox et al.,[3] who reported that they rarely observed salivary gland swelling in their patients. The reason for this disparity is not known.

ii. Findings in Other Exocrine Glands

In addition to the salivary glands, Sjogren's syndrome may involve the secretory glands of the eye, ear canal, nose, throat, and eustachian tube;[68,69,74,75] the vocal cords;[68,69] the exocrine glands of the alimentary tract, particularly the pancreas and the liver;[66,76,77] the mucous glands which line the bronchi;[78,79] the vaginal mucosa;[68,80] and the skin.[68]

b. Involvement of Other Organs and Tissues

Patients with Sjogren's syndrome may manifest a wide variety of systemic abnormalities. Some, such as joint symptoms, fever, and cutaneous eruptions may be due to the collagen diseases associated with SSS. Other signs and symptoms, however, appear to be unrelated to these connective tissue disorders. Included are changes which occur in the gastrointestinal tract, the pulmonary and cardiovascular system, and thyroid and neurological abnormalities.[66]

Table 4A
SJOGREN'S SYNDROME: PREVALENCE OF ORAL AND PARAORAL SIGNS AND SYMPTOMS

	PSS (%)	SSS (%)	Ref.
Xerostomia	96—100	83—97	8, 68, 69
Salivary gland enlargement	28—74 H[a]	16—88 H[b]	38, 68, 69
	6—82 E[c]	4—32 E	39, 67—69
Tongue, fissuring	53—70	27—96	8, 39, 70
Tongue, burning of	—	26	8
Oral soreness/irritation	52—59	31—74	8, 68, 69
Oral ulcers/fissures	24—78	36—56	39, 68, 69
Increase in dental caries	63	17—36	8, 39
Difficulty with full dentures	33	18—51	8, 39, 70
Decrease in taste acuity		52[d]	43
Difficulty with mastication	83	60	68
Difficulty with swallowing	—	6	8
Difficulty with speech	—	23	8
Increased fluid intake, with meals	41—91	42—57	68, 69
Increased fluid intake, between meals	76—78	23—35	68, 69

[a] H = history of enlargement.
[b] 88% value includes evidence of enlargement obtained from history and clinical examination.[8]
[c] E = enlargement on examination.
[d] Includes both PSS and SSS patients.[43]

Table 4B
REFERENCES AND SUBJECT CHARACTERISTICS

PSS			SSS			
N	Sex (%)	Age	N	Sex (%)	Age	Ref.
23	96 F	17—75	30	97 F	24—69	68
—	—	—	35	91 F	27—80	8
71	90 F	M = 63	94	88 F	M = 60	69
40	100 F	22—76	25	68 F	22—76	39
22	100 F	M = 56	21	90 F	M = 50	67
14	—	—	15	—	—	43

It has been shown that many of these systemic complications are more severe in patients with the primary form of Sjogren's syndrome.[67] Patients with Sjogren's syndrome are also at greater risk (40 times more) to develop malignant lymphomas.[81] This is in accord with the relationship which exists between immunologic deficiency states and diseases of the lymphoid system. This too is more common among those with the primary form of the disease.

2. Histopathologic Findings

The primary histopathologic finding in Sjogren's syndrome is the lymphoepithelial lesion. It is found in the salivary as well as other exocrine glands affected by the disease. In its mature form it is characterized by (1) acinar degeneration and atrophy, (2) lymphoreticular cell proliferation, and (3) ductal metaplasia and hyperplasia. These changes lead to the formation of myoepithelial islands.[82] The majority of the proliferating lymphocytes appear to be T cells.

Table 5
SJOGREN'S SYNDROME: SALIVARY FLOW RATES (SELECT STUDIES)

Disease	N	Sex	Age	Salivary flow: Source	Salivary flow: Type	Flow rate (mℓ/min)	Ref.
PSS	12	F	M = 62	Parotid	Stim	0.016	68
	40	F	22—76	Parotid	Stim	0.012	39
	32	F	41—60	Parotid	Stim	0.24[a]	1
		F	>61	Parotid	Stim	0.27[a]	1
		M	>61	Parotid	Stim	0.43[a]	1
	17	N/A	N/A	Parotid	Unstim	0.02	36
	17	N/A	N/A	Parotid	Stim	0.16	36
SSS	16	F	M = 49	Parotid	Stim	0.09	68
	13	M & F	N/A	Parotid	Unstim	0.14	35
	13	M & F	N/A	Parotid	Stim	0.18	35
	86	M	41—60	Parotid	Stim	0.93[a]	1
		F	41—60	Parotid	Stim	0.47[a]	1
		M	>61	Parotid	Stim	0.43[a]	1
		F	>61	Parotid	Stim	0.41[a]	1
SS/tns[b]	12	M & F	N/A	Parotid	Stim	0.17	89
	28	M & F	26—78	Parotid	Unstim	<0.02	90
	28	M & F	26—78	Parotid	Stim	<0.19	90
	15	14M; 1F	35—78	Parotid	Stim	0.10 (N = 6) 0.60 (N = 9)	37
PSS/SSS	12	N/A	N/A	Whole	Unstim	0.085	91
PSS	22	N/A	N/A	Whole	Unstim	0.11	34
SSS	12	N/A	N/A	While	Unstim	0.11	34

[a] Stimulant, 5% citric acid; stimulant in others, 2% citric acid.
[b] Sjogren's syndrome; type not specified.

Lymphoepithelial changes in salivary glands may also be observed in a number of other hyposecretory conditions. Among these are atrophic gastritis[83] and acute pancreatitis.[84] They are also seen in patients treated for hematologic disorders with bone marrow transplants.[85]

Of major clinical importance, since it allows for a ready access to biopsy material, is the observation that histopathologic changes similar to those observed in the major salivary glands may also be present in the minor glands. In an examination of the labial salivary glands in patients with Sjogren's syndrome, it was demonstrated that 70% of them exhibited the signs of focal chronic inflammation that are typical for this disease.[86] Moreover, there is good agreement, in postmortem data, with the findings present in the major salivary glands.[87] Labial gland biopsies from patients with PSS generally demonstrate more severe changes than those with SSS.[39,86,88]

3. Serologic and Immunologic Findings

Numerous serologic and immunologic abnormalities have been noted in the serum of patients with Sjogren's syndrome. Prominent among these are an elevated sedimentation rate, hypergammaglobulinemia, the rheumatoid factor and antibodies to acidic nuclear antigens [SS-A(Ro) and SS-B(La)]. It has also been shown that there is an increase in the level of alloantigens of the class II, HLA-Dw2 type in PSS; HLA-Dw4 is more commonly observed in SSS.[70]

4. Sialometry

A number of studies have been performed to measure the rate of flow of saliva in patients with Sjogren's syndrome. The results of some of these findings are shown in Table 5.

Most of the data show that in both PSS and SSS there is a striking reduction in the flow of both resting as well as stimulated parotid and whole saliva.

Of particular interest are the recent findings of Stuchell et al.[37] All of their patients (N = 15) complained of dry mouth and demonstrated a reduction in the flow of resting parotid saliva. Following stimulation with citric acid, however, nine of them secreted parotid saliva at rates which were equal to those found among normal individuals. Given that in Sjogren's syndrome there is a progressive destruction of glandular tissue, these data suggested that stimulated flow could be used as an index of the level of destruction of the acinar parenchyma.[37]

This belief is supported by the recent findings of Tsianos et al.[92] These investigators showed that in patients with a variety of autoimmune disorders, flow was not reduced in the early stages of these diseases. Significant reductions, however, were observed in the more advanced cases.

The presence of xerostomia and the markedly decreased flow of saliva in patients with Sjogren's syndrome are in accord with the histopathologic findings of acinar atrophy in this disease.

D. Depressive Illness

The ability of psychic stimuli to depress the flow of saliva has been known for a long time.[93] Classic examples of these are threat and fear, hypnotism, mental stress, transcendental mediation, and various personality traits.[94-97] Moreover, it has been alleged that xerostomia, as distinct from hyposalivation, is frequently found in nonmedicated patients who suffer from depressive illness.[98,99] The literature, however, is troublesome. In some studies, scant or no attention was given to the symptom of dry mouth or to the intake of drugs by the patients. In others, little evidence was provided as to whether they were affected by conditions other than depressive illness.

Davies and Gurland[100] and Bolwig and Rafaelsen[101] showed that the mean flow rate of unstimulated mixed saliva among patients with endogenous depression was about 0.3 g/min. The normal flow rate for resting saliva, expressed as g/min, is about 0.65.[100,101] The decrease in flow in depressed patients thus amounts to approximately 50% of the values found among normal subjects. Busfield et al.[102] noted that there was no correlation between the rate of flow of whole saliva and the feeling of dry mouth.

Depressive illness is often treated with tricyclic and other antidepressant drugs. Xerostomia is an unfortunate side effect of their use. Given the serious nature of depressive illness, it is unreasonable to suggest that these medicaments should not be prescribed to patients with this condition. Noncompliance with treatment, however, is found in about 25% of patients. Dry mouth is one of reasons cited for noncompliance. The development of drugs which do not induce xerostomia would clearly be desirable.

Unlike the patients with end-stage lymphoepithelial diseaes or postirradiation salivary dysfunction, depressive patients, when stimulated with weak acid or metacholine, demonstrate a significant increase in salivary flow. This supports the belief that functional, rather than organic, factors account for the reduced secretion.

E. Drugs

The existence of drugs which induce xerostomia have been known for a long time. Atropine, a member of the deadly nightshade family of shrubs, was purified by Mein[103] in 1831. Only recently, however, have drugs been definitively entered as an integral part of the equation of the causes of dry mouth. Bahn,[104] in a review of drugs listed in the *Physician's Desk Reference*, identified over 200 drugs which were listed as having xerostomic side effects. A recent survey[105] shows that this list has now grown to over 400 drugs. Many classes of drugs affect the flow of saliva. These are shown in Table 6.

Table 6
SELECT CLASSES OF DRUGS WHICH MAY INDUCE XEROSTOMIA

Anorectic drugs	Sedatives and hypnotics
Anticholinergics	Antihistamines
Antidepressants	Antiparkinsonism drugs
Antipsychotics	Antihypertensive agents
Diuretics	

1. Epidemiologic Surveys

Several epidemiologic studies have been conducted over the past few years to determine the prevalence of reduced salivary flow and xerostomia among medicated patients. Parvinen et al.[15] measured the flow of paraffin-stimulated whole saliva among 642 unmedicated and 463 medicated subjects 30 years of age and older. Significant reductions in flow (30 to 40%) were observed in the subjects who took antipsychotic drugs, tricyclic antidepressants, and antihypertensive agents. The observed flow rates were in the range of 1.1 to 1.3 mℓ/min. These are probably well above the level at which patients will complain of xerostomia. No assessment was made of the prevalence of the subjective feeling of xerostomia in these patients.

Osterberg et al.[4] observed that 16 to 25% of their elderly patients (N = 1148) complained of oral dryness; 58% of the men and 75% of the women regularly took prescribed medications. The prevalence of xerostomia was positively correlated with the consumption of anticholinergic drugs, antihistamines, sedatives, and hypnotics. They noted, moreover, that the prevalence of oral dryness increased with the number of drugs taken by the subjects.

Johnson et al.[38] examined the rate of flow of stimulated parotid saliva, the prevalence of dry mouth, and the intake of drugs among 154 chronically ill, long-term hospital patients. They reported that 43% of the patients had flow rates of <0.2 mℓ/min; 44% of these complained of almost constant xerostomia. Only the tricyclic antidepressants, especially in combination with diuretics, were positively associated with the symptoms of dry mouth.

In a preliminary report of 157 ''healthy'' elderly institutionalized patients, Baric and Handelman[106] observed that the mean flow rate of masticatory stimulated whole saliva was 0.39 mℓ/min. These depressed rates of secretion were primarily related to the intake of antipsychotics, antihypertensives, and antihistamines. The presence of dry mouth was positively correlated with the number of drugs taken by each patient and by the length of time they were on these drugs.

Little is known about the relationship between the intake of drugs, hyposalivation, and dry mouth in younger age groups. It is known that the consumption of mood elevating drugs and cocaine, a ''recreational drug'', is not uncommon among these people. These drugs exert antisialogogue effects.

2. Clinical Studies

A number of clinical investigations, in normal as well as diseased subjects, have studied the effect of select drugs on the flow of saliva. Some of these are listed in Table 7.

Drug-induced side effects are not a new problem. Indeed, it is likely that they have been known since the first herbal extracts were given to man. In determining the wisdom of the use of any drug, it is clear that one must weigh the magnitude, as well as the significance, of its side effects against its primary effectiveness in the treatment of the disease for which it has been prescribed. In cases where the drug is prescribed for short periods of time, it is probably of little concern to the attending physician or dentist. In other cases, for example, in chronic illness where drugs are prescribed for protracted periods of time, xerostomia is

Table 7
ANTISIALAGOGUES: SELECT CLASSES OF DRUGS

Drug class	Drug	Ref.
Anorectic	Amphetamine	107
Antineoplastic	^{131}I	108
Anticholinergic	Atropine	109
	Glycopyrrolate	109
	Phenglutarimid	110
	Scopolamine	111
	Methantheline	111
Antidepressant	Amitriptyline	112
	Amitriptyline	113
	Imipramine	31
	Nortriptyline	114
Antihypertensive	Clonidine	115
		116
Antiparkinsonism	Benztropine	117
Antipsychotic	Phenothiazines	118
	Phenothiazines	119
	Phenothiazines	120

of greater concern since it may impact on the willingness of the patient to take the medications and impinge on his or her quality of life. Some of the medicaments which are given for extended periods are prescribed for life-threatening situations. Condemning the cure where the side effect is, by comparison, small is of little help. Other drugs, however, are given to patients for less serious ailments. Examples of this may be found in the widespread, and perhaps, promiscuous use of drugs in weight reduction schemes and mood alterations. Clearly, attention should be paid to the complaint of dry mouth. Where possible, efforts should be made to substitute or eliminate those drugs which cause it.

Unlike in other xerostomia-related diseases, drug-induced xerostomia is rarely a consequence of irreversible damage to the salivary glands. Implicit in this statement is the recognition that the glands retain their ability, when stimulated, to produce saliva. Bertram et al.[114] demonstrated that nortriptyline, a tricyclic antidepressant, inhibited the flow of whole saliva in eight patients. The flow rates returned to their original level once the drug was discontinued. The reversible nature of drug-induced dry mouth forms the basis for therapeutic regimens designed to counter the effect of these medicaments (see section on therapy).

The iatrogenic, xerostomic side effects of many drugs are of particular concern to the elderly. They tend to take multiple medications and are often unaware of their purpose or action. Often, due to dry mouth, they will refuse to take the prescribed medications.[121] In addition, their diminished ability to withstand stress and their limited physiological reserve makes them particularly vulnerable to the noxious effects of these agents.[122] In a recent study, it was noted that almost 30% of 107 randomly selected elderly subjects took four or more drugs per day.[121] About one third of them had adverse reactions to these medications. Many drugs had the capacity to induce dry mouth.

The xerostomic effects of some of these drugs, e.g., the anticholinergic agents, is in all likelihood due to a direct effect on the salivary glands. The possibility of developing a less xerogenic, but equally active molecule, may be remote. With other drugs, however, their mechanism of action is not entirely clear. It is possible, for example, that a dichotomy exists between the xerostomic effects and the principal medical actions of the antihypertensive drugs or the mood-regulating agents. If such is the case, it may be possible to develop compounds which elicit low xerostomic side effects while at the same time preserving the effect for which they are primarily prescribed.

The awareness that many medicaments have the capacity to cause xerostomia has led several investigators to search for drugs which, though effective in the treatment of the condition for which they were prescribed, do not possess the noxious, mouth drying, side effects.[31,109,112,113,115,123]

F. The Effect of Decreased Mastication on the Salivary System

The secretory process in exocrine glands consists of the synthesis of materials for export, their storage within acinar cells, and their expulsion into the saliva. Ample evidence exists, though primarily from studies in animals, that mastication plays an important regulatory role in this process (see Chapter 7). Its effect on the glands is mediated through general somatic afferent nerves which are located in the oral mucosa and the periodontal membrane.[124]

A decrease in mastication, e.g., as induced by the provision of isocaloric liquid chow to rats normally raised on pelleted food, results in the following: (1) inhibition of gland growth,[125-127] (2) an obliteration of the diurnal cycle,[128] and (3) gland atrophy.[129,130] No such changes are observed in the pancreas.[130]

Saliva is also affected by changes in mastication. Hall et al.[131] demonstrated in man that the consumption of a liquid diet for a period of 1 week resulted in a 30% decrease in the flow of parotid saliva and a decrease in protein output. Parotid flow is also reduced in patients whose jaws were immobilized by intermaxillary fixation following orthognathic surgery.[132]

The import of these findings with respect to the prevalence xerostomia is not known. The physical consistency of the dietary in our ''fast-food'' society can hardly be characterized as requiring vigorous mastication. It is doubtful if the decreases in flow observed in the clinical studies cited above can actually induce dry mouth. They may, however, contribute to the pathogenesis of this condition. Moreover, patients with xerostomia may, because of their difficulty with mastication, demonstrate a preference for soft and liquid foods in their diet. This will tend to aggravate an already serious problem.

V. THE DIAGNOSIS OF XEROSTOMIA

Since xerostomia is a symptom of disease, a provisional diagnosis of dry mouth can be made if the patient complains of a feeling of oral dryness or of a lack of saliva. As noted, however, the subjective awareness of xerostomia is not always correlated with a diminution in the flow of saliva. Other procedures must therefore be employed to confirm its presence. Included among these are (1) the case history, to determine the presence of other symptoms which are frequently associated with this condition, (2) a clinical examination of the mouth and other organs for signs of dessication, and (3) sialometry. Moreover, since xerostomia is caused by systemic diseases and conditions, a thorough medical examination and select clinical tests are required to determine the factors which give rise to the feeling of oral dryness.

This topic will not be dealt with in this report. For a systematic presentation of the many factors which must be considered in the evaluation of the xerostomic patient, see the review by Fox et al.[3]

VI. THE TREATMENT OF XEROSTOMIA

The primary objective of the techniques used to treat xerostomia is to increase the flow of saliva or, where this is not possible, to keep the oral tissues moist and protected by other means. The success of these therapeutic measures is dependent, in the first instance, on the degree to which the salivary glands are able to respond to various stimuli. This response may be tested with a gustatory stimulant, 2% citric acid. This acid is normally able to evoke

a near-maximal flow of saliva. Failure to obtain flow with such a stimulus indicates that there is a virtual shut-down of the secretory apparatus. When flow is present, it indicates that the glands are able to respond to exogenous stimuli; the amount of saliva obtained is, in all likelihood, directly related to the viability of residual salivary gland tissue. (In some patients with xerostomia, the 2% citric acid solution may act as a severe irritant and cause pain. In these individuals, dilution of the acid may be helpful; in others, acidic solutions may have to be avoided. Mechanical stimuli may be employed.)

A. Therapeutic Measures: "Responders" to Citric Acid

General measures to promote salivation in those who respond to the citric acid test include the use of gustatory and mechanical stimuli and select drugs. Krasse[26] reports that the chewing of a piece of paraffin wax (about 1.5 g; three to five time a day) is an effective stimulus to secretion in xerostomic patients. He further recommends the use of acidulated calcium phosphate tablets.

Other stimulants may also be used. Among these are nonsugar-containing gums (masticatory stimulants) and sour tasting candies (gustatory stimulants). The latter should be used with caution, however, since the excessive use of "acidic" candies may lead to localized demineralization of the enamel and cementum of the teeth. To overcome this problem, we use a citric acid preparation which is saturated with $CaHPO_4$.[133] Its formula follows:

Citric acid	2.5 g
Aspartame	0.25 g
Water	100 mℓ
Calcium acid phosphate	To saturation

Note: This may be employed as a solution (20 mℓ, held in the mouth for 1 min, 3—5 times/day) or as a spray. In preliminary tests, slices of enamel were shaken for a period of 24 hr with the above solution. No evidence of surface or subsurface demineralization was observed. Control samples, without $CaHPO_4$ demonstrated "white lesions", cavitation, and other signs of demineralization.[134]

These therapeutic measures are generally used between meals to stimulate the flow of "resting" saliva. Since mastication stimulates the flow of saliva, the patients should, where possible, be encouraged to consume foods which require chewing. They may also be advised to increase the number of meals they consume daily. The use of alcoholic beverages and smoking, especially pipe smoking, should be discouraged since they probably contribute to the feeling of oral dryness.

B. Therapeutic Measures: "Nonresponders" to Citric Acid

For those in whom no flow of saliva is obtained following the use of citric acid, exogenous stimuli may be of little or no help.* In these subjects salivary substitutes may be employed to try to keep the oral tissues moist. The electrolyte composition of these solutions is generally similar to that found in saliva. None of them, however, contain the protective proteins and glycoproteins which are characteristic of this secretion. The composition of some of these is listed by Grad et al.[134]

Few controlled studies have tested the value of the saliva substitutes in the treatment of

* One should not dismiss the use of citric acid to stimulate flow in these subjects. It has been our experience that even though there is no measurable increase in the flow of saliva, a number of patients allege that their mouth feels moist.

dry mouth. Double-blind studies conducted by Klestov et al.[135] and Kaarela and Mutru[136] found that with one exception, the salivary substitutes tested, "VA-Oralube" and "Salisynt", were not significantly better than a placebo. The exception is an important one. Both investigations reported that the substitutes provided significant relief to nocturnal oral discomfort. Given the difficulty in treating this form of xerostomia, this observation is probably sufficient to warrant the testing and use of these agents.

C. The Use of Drugs to Stimulate the Flow of Saliva

Historically, the first agent employed to stimulate the flow of saliva was Jaborandi, the dried leaf that is the source of pilocarpine.[138] Recently, Fox et al.[139] studied the effect of this cholinomimetic alkaloid on six xerostomic patients whose salivary glands responded positively to the citric acid test. They reported that 6 mg tablets of pilocarpine could increase the production of saliva from the parotid and the SM/SL glands and could relieve the sensation of oral dryness for approximately 3 hr. No changes were observed in the blood pressure, heart rate, or electrocardiogram. Surprisingly, sustained-release pilocarpine was less effective in relieving dry mouth.[140]

This study suggests that pilocarpine can effectively stimulate the flow of saliva among patients who possess some viable salivary gland tissue. However, since such patients will need to use the drug over extended periods of time, perhaps for life, more extensive testing will be required before it can be routinely recommended.

A number of drugs other than pilocarpine have been used to treat xerostomia. Among these are bromhexine,[141,142] bethanchol chloride,[143] methacholine,[144] and trithrio-*p*-methoxyphenylpropene (Sulfalrem).[145,146] Although allegations have been made that they alleviate the symptoms of dry mouth, in only a few of the studies were the rates of flow of saliva actually measured.

D. Additional Techniques: Responders and Nonresponders

Particular attention should be given, in dentulous subjects, to the care of the teeth. Of primary concern is the rigorous control of dental plaque and dental caries. Professional dental care should be sought and dental prophylaxes should be performed about twice monthly.[26] Topical fluoride, as a gel or as a varnish, should be applied to the teeth; remineralizing agents can also be used.

Efforts may be made, through the use of room humidifiers, to provide moist air to individuals who suffer from dry mouth.[147] In some cases, the topical application of petroleum jelly to the lips is helpful.

E. The Treatment of Drug-Induced Xerostomia

The xerostomia which occurs as a result of the intake of medicaments is rarely a consequence of irreversible damage to the salivary glands. When stimulated, the glands produce saliva. The objectives of therapy in drug-induced dry mouth should be directed at the drugs themselves and at other means of increasing gland function.

Where appropriate, a number of approaches may be tried to modify the drug-intake patterns of patients. These include: (1) the elimination of some drugs or a reduction in their intake, (2) a change in the manner in which they are taken, and/or (3) substitution of one drug for another with less noxious side effects.[105] The appropriateness of any of these should be done in consultation with the original prescribers of the medications. Unfortunately, little is known about the mechanisms or the relative ability of most medicaments to induce xerostomia. Furthermore, patients respond differently to given pharmacologic agents; thus, therapy must be personalized.

Since the salivary glands in drug-induced xerostomia may be stimulated, even in the presence of antisialogogues, to secrete saliva,[143] gustatory and mechanical stimulants, like

those described in the preceding section, should be prescribed. Special attention, also as previously noted, should be given to care of the teeth.

Drug-induced xerostomic patients are usually middle-aged or elderly. Their quality of life has been seriously impaired by this condition and they are often beset with serious systemic disease and emotional problems. Moreover, because of their advancing age, they are the least able, because of physical, emotional, and financial constraints, to care for their health. Their dental ailments may seem, to some, to rate low on the list of health-related priorities. It is essential to realize, however, that the mouth is often a symbol of our health, and it plays a pivotal role in the intake of food as well as in chewing and swallowing. This, coupled sometimes with a concomitant impairment of the intestinal exocrine glands, can lead to severe problems in the overall assimilation of food.

The treatment of drug-induced dry mouth is difficult and oftentimes, empiric and palliative. In contrast to some of the other diseases and conditions which are associated with xerostomia, the drug-dependent form may be reversible. Success will depend, in part, on how well the health providers work together to unravel the pharmacologic dilemmas which may confront the patient. In many patients, it may be possible to alleviate the symptoms of dry mouth; in others, impossible.

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