

12. EFFECT OF XEROSTOMIA ON THE ORAL TISSUES

A.G. Bartley in the Medical Times and Gazette, 1868, has been reported³⁶⁶ as having given the first description of xerostomia as a patient's only symptom or complaint. Bartley quite adequately described the major changes affecting the oral mucosa and tongue, the patient's sipping of cold tea to relieve the dryness and the apparent lack of effect on the patient's health.

Prinz (1932)³⁶⁷ gave an accurate assessment of the effects of xerostomia on the oral tissues noting that the changes affected the oral mucosa, tongue and lips. Disturbances of deglutition and speech as well as the need for frequent sips of water and development of rampant dental caries were discussed. Xerostomia was considered to develop either suddenly or gradually over many months depending on its etiology.

The effects of xerostomia on the oral cavity can be predicted if the functions of saliva are recalled (vide supra: Functions of saliva, p. 49).

SYMPTOMS

Dryness of the mouth is expected to be a complaint of the patient suffering from xerostomia. However not every patient complaining of oral dryness can objectively be classified as showing signs of xerostomia¹⁵². Bertram (1967)³⁶⁸ used the term hyposalivation where patients had a subnormal flow rate of saliva (secretion 0.2 ml/15 min) which in his estimation was too high to be classified as xerostomia. The distinction is not of clinical value when the patient still seeks relief from subjective oral dryness.

Bertram (1967)³⁶⁸ reported that a few of his patients did not consider they had dry mouths even though they had low salivary

flow rates which caused symptoms of xerostomia in other patients. Conversely patients may have a subjective impression of a dry mouth when salivary flow appears normal and these patients are often classified as obsessional or in need of psychiatric help (vide supra: Psychogenic factors and reduced salivary flow, p. 108).

Patients' mouths may be dry at all times or only intermittently and xerostomia may be mild or severe with complaints ranging from stickiness to severe burning, dryness and pain^{84,153,216}. However this sensation has not been correlated with the ulceration and infection that may also present in xerostomia^{153,319,368}.

Complaints other than dryness associated with pronounced or complete lack of saliva include difficulty in eating and swallowing, increased fluid intake, difficulty with speech, alterations in taste sensation, pain, ulceration and irritation in the mouth and an increase in the incidence of dental caries as well as difficulty in wearing dentures.

Fluid intake in patients with xerostomia increases because they sip water while eating and throughout the day and night. Severely affected patients will avoid dry foods such as biscuits, bread and peanut butter because they find they cannot form a bolus and the food tends to stick to the mouth or teeth^{319,321,322,368}. Some patients reported losing the position of food in their mouths and testing showed that they had problems of oral stereognosis³²². Thus questioning patients on their pattern of eating including the avoidance of dry and occasionally spicy food will give an indication of the severity of their xerostomia.

Henkin, Talal and Larson (1972)³²² showed that taste loss may accompany a marked reduction in salivary flow. The loss of taste acuity occurred either at the time patients recognised persistent

xerostomia or more frequently within three years of the onset of dryness. Other studies^{321,368} have also associated loss or changes in taste sensation with xerostomia.

Oral dryness can affect speech by causing the lips, cheeks and tongue to stick together making conversation difficult. Hoarseness and deepening of the voice probably related to dryness of the pharynx and larynx have been noted in Sjögren's syndrome^{321,322}. These voice changes are unlikely to affect patients whose sicca symptoms are restricted to the mouth.

Block et al (1965)³¹⁹ noted that while fissuring or ulceration of the mouth and lips was frequently reported by patients, routine examination revealed few or only subtle mucosal abnormalities.

Dental symptoms in xerostomic dentate patients were related to an increase in the incidence of caries with recurrent failure of restorations^{153,317,319,321}. Denture wearers complain of discomfort and inability to keep dentures in the mouth for more than a short time. However less severely affected patients may be able to wear their dentures without problems^{84,369}. Saliva provides a lubrication of the denture/mucosal interface which reduces denture-related trauma. Movement of a denture base across a dry mucous membrane will cause discomfort and occasionally oral ulceration^{369,370}.

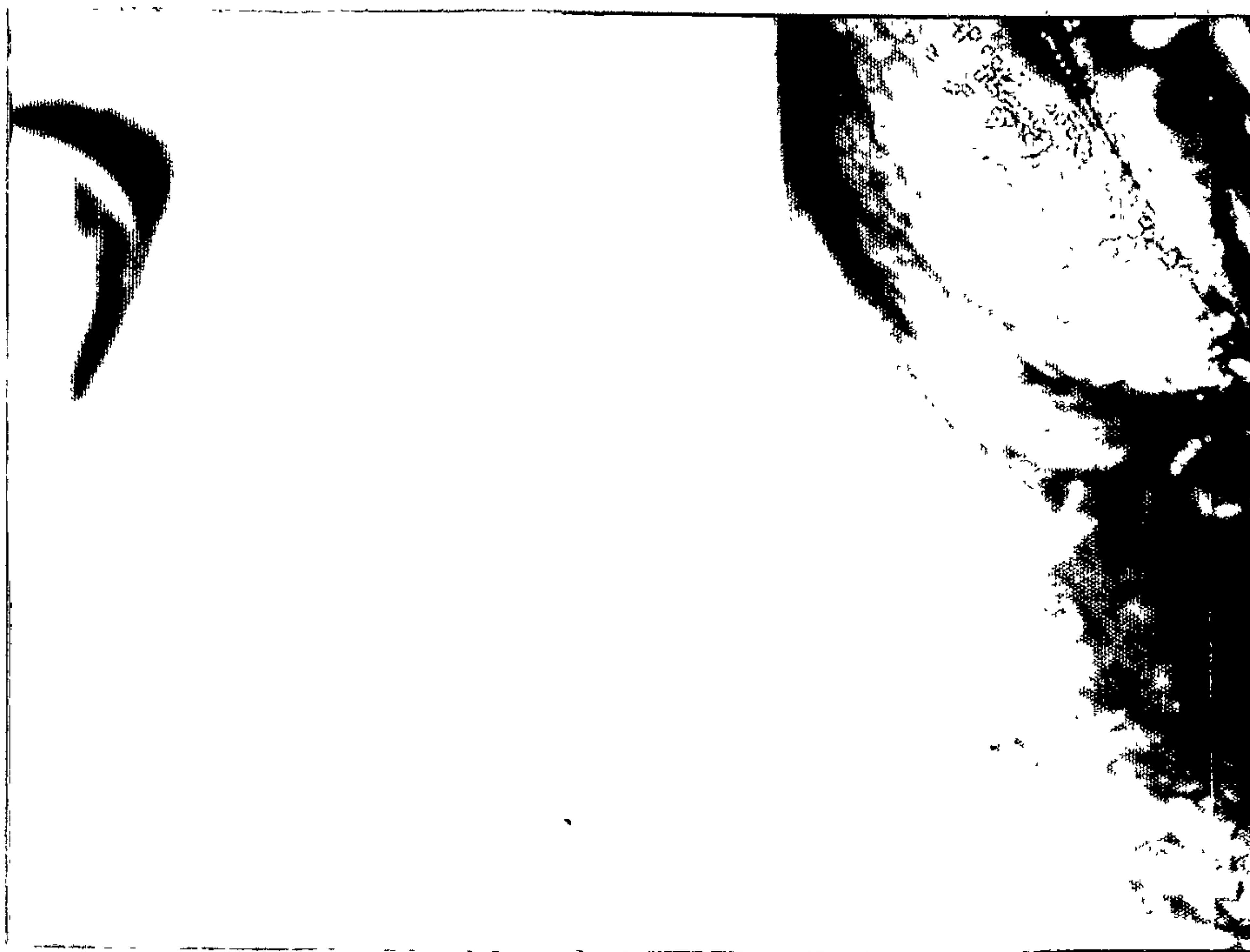
Pollock, Buch and Kalnins (1964)³⁷¹ noted poor denture fit and retention in 54 patients with oral dryness caused by phenothiazines or antidepressants. Prior to taking the medication denture fit was good and the subsequent denture problems were attributed to the lack of saliva. Kawazoe and Hamada's (1978)³⁷² investigations showed that either too little or too much saliva will cause a loss of maxillary denture retention.

SIGNS

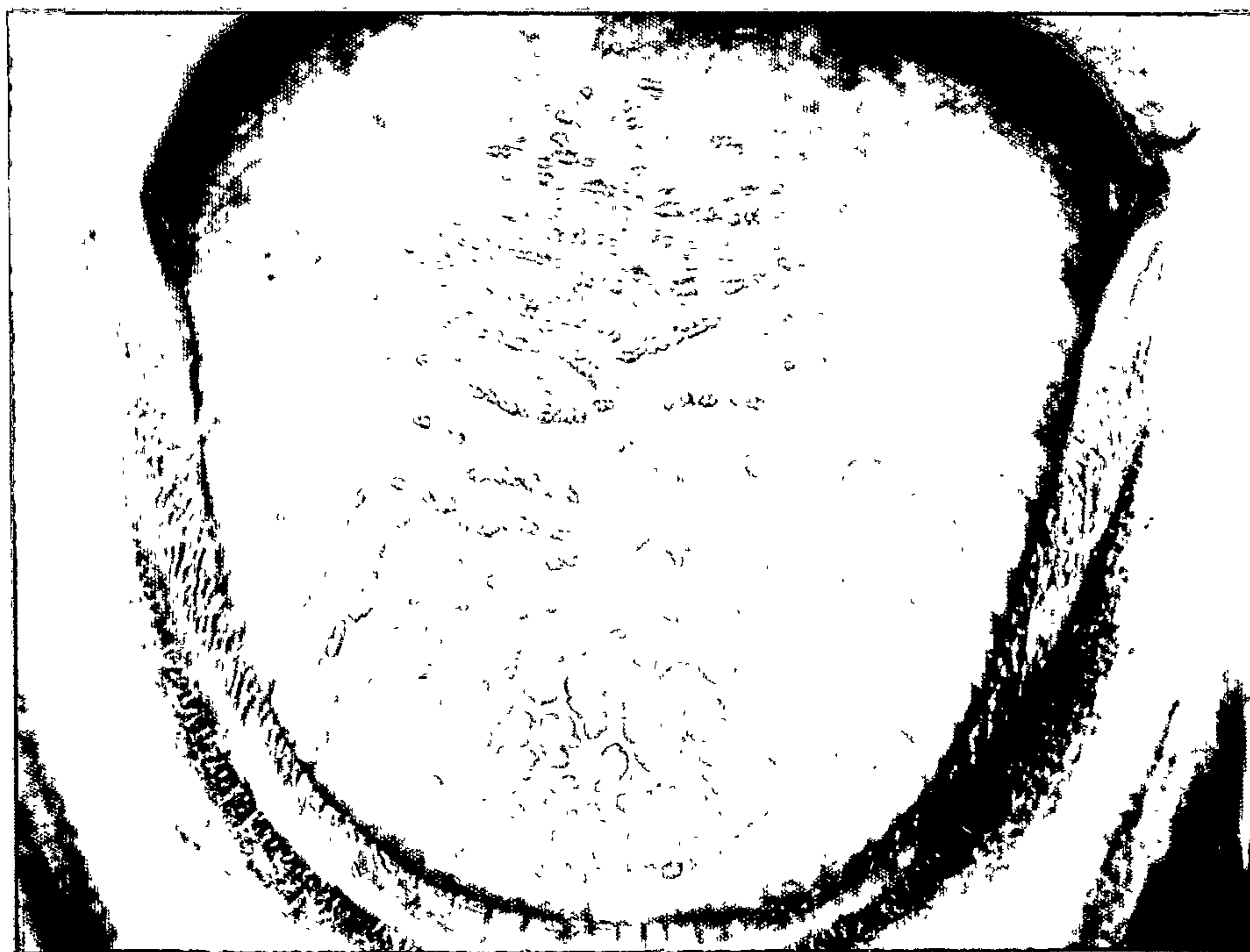
Xerostomia is an indication of some underlying disorder, usually systemic, which causes salivary gland dysfunction. Therefore the signs of xerostomia may be modified by the oral signs of a systemic illness^{153,216}. For example, iron deficiency and pernicious anaemia can cause distinct oral changes which are unrelated to xerostomia (vide supra: Oral changes in anaemia, p.203).

In health the oral mucosa is usually characterized by a moist shiny appearance and in patients with xerostomia the mucosa may appear normal and the salivary deficiency may be evident only because the saliva is mucoid, sticky, weblike, bubbly or frothy rather than thin and watery^{84,152,153}. The absence of a pool of saliva in the floor of the mouth indicates a moderate deficiency of saliva^{317,319}. A complete or nearly complete absence of saliva will give a dry, smooth, pale and semi-translucent appearance to the oral mucosa [see Plate 9] and prolonged dryness causes mucosal erythema, atrophy and fissuring. The mouth may be lined by an adherent exudate which is presumably a residue of mucoid salivary secretions undiluted by normal serous saliva^{84,153,319}. Severe xerostomia, where an examining finger or dental mirror sticks to the oral mucosa³¹⁹, probably only occurs where a systemic condition such as Sjögren's syndrome affects both major and minor salivary glands.

Mucosal ulceration has been reported in patients with xerostomia but trauma to dry and atrophic tissues, often from dentures, is the likely cause^{317,369}. An example of chemical trauma from a dentrifice causing oral desquamation was seen in a patient taking anticholinergic medication. It was concluded that a lack of saliva allowed concentration of the dentrifice in the patient's mouth which caused a chemical burn and sloughing of oral epithelium³⁷³.



- Plate 9. Appearance of the buccal mucosa in xerostomia.



- Plate 10. Dry and fissured lips and tongue. Note also loss of filiform papilla and residue of salivary mucus.

Spontaneous ulceration has been noticed in a patient with xerostomia but it could have been related to an unspecified systemic illness. Even in patients with Sjögren's syndrome mucosal ulceration is not a frequent complication^{317,319,322}.

In more severe xerostomia the lips may become dry and fissured with the appearance of a scaly crust [see Plate 10]. The angles of the mouth are also susceptible to fissuring and become friable^{84,319,368}. Faber (1943)²²⁷ observed angular cheilitis in all of his patients with xerostomia irrespective of the cause of dryness. He found this occurrence interesting because cheilitis is usually associated with excessive saliva in the folds at the angles of the mouth. Smith (1976)³⁷⁴ reviewed the etiology of angular cheilitis which included excessive folds at the angles of the mouth, candidal infection, nutritional disorders and anaemia. Dryness and fragility of labial tissue and increased susceptibility to candidal infection is the probable cause of angular cheilitis in xerostomic patients. Bertram (1967)³⁶⁸ reported that 5 of his patients with xerostomia had angular cheilitis. Two patients had poor dentures as a suggested cause while in the remaining 3 candidal infection as a result of xerostomia was implicated as a causative factor.

The tongue mucosa is subject to varying degrees of erythema, atrophy, fissuring and loss of papillae in response to a reduction in salivary flow^{153,317,322}. Bertram (1967)³⁶⁹ divided the tongue changes into first, second and third grade changes and found a good correlation ($p < 0.001$) between a decrease in salivary flow and an increase in the severity of tongue changes. Grade one represented slight erythema, perhaps slight fissuring and minimal atrophy of filiform papillae of the tip of the tongue. Grade two showed moderate erythema, fissuring, irregular papillary atrophy and possibly the

beginning of lobulation. Grade three changes were of pronounced erythema, total papillary atrophy and marked lobulation or deep fissuring. The grade three classification also included an erythemic smooth "lacquered" (or glazed) tongue. These lingual changes were observed in xerostomia from different causes but were most consistent in patients with Sjögren's syndrome [see Plates 11A and 11B]. Plate 10 shows a patient whose tongue represents grade two changes.

Oral candidiasis is frequently a complication of chronic xerostomia^{181,339}. The burning sensation of parts of or the entire oral mucosa frequently encountered in xerostomia may be related to candidiasis. Acute pseudomembranous candidiasis may accompany more severe xerostomia. Chronic atrophic candidiasis may be seen more frequently in denture wearers and others with less severe xerostomia^{321,371} [see Plates 12A and 12B]. Macfarlane and Mason (1974)³³⁹ suggested that the predisposition to candidal infection in patients with xerostomia could be caused by three factors:

- (i) Decrease in the quantity of inhibitory antibodies normally found in the saliva.
- (ii) Low salivary pH in patients with xerostomia - candida albicans is encouraged by low pH.
- (iii) Loss of the mechanical washing action of saliva which removes debris and bacteria from the mouth.

Llory, Damron and Frank (1971)³⁷⁵ also reported a decrease in salivary pH and the changes in the oral microflora in patients with low salivary flow following irradiation of their salivary glands.

Patients with chronic xerostomia because of a predisposition to candidal infection should be kept under periodic clinical and bacteriological review³³⁹. When oral candidiasis is detected then antifungal therapy involving the use of antifungal lozenges and

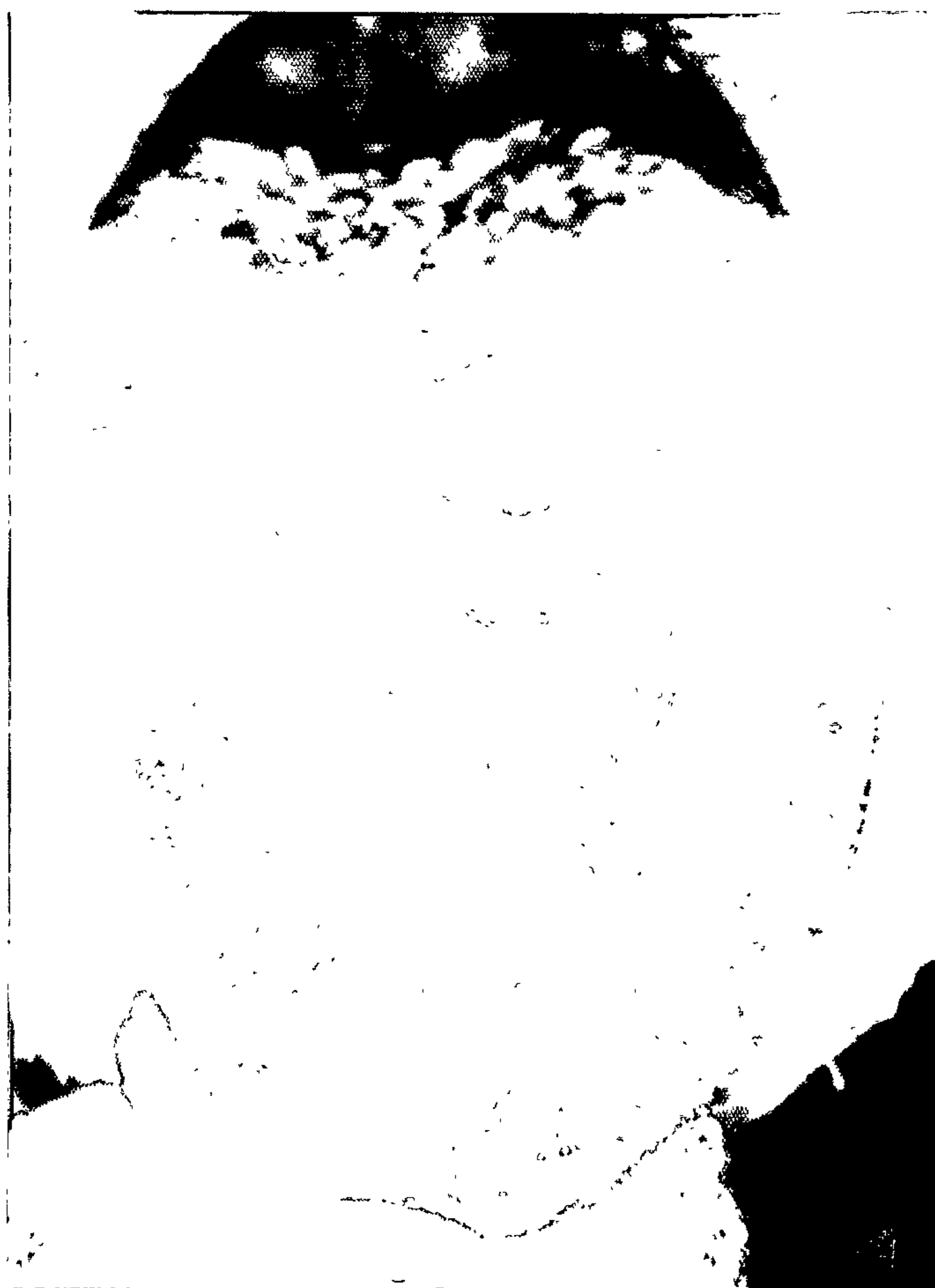


Plate 11A. Grade I changes in the tongue of a patient with Sjögren's syndrome. Some loss of filiform papilla and slight fissuring and lobulation are apparent.

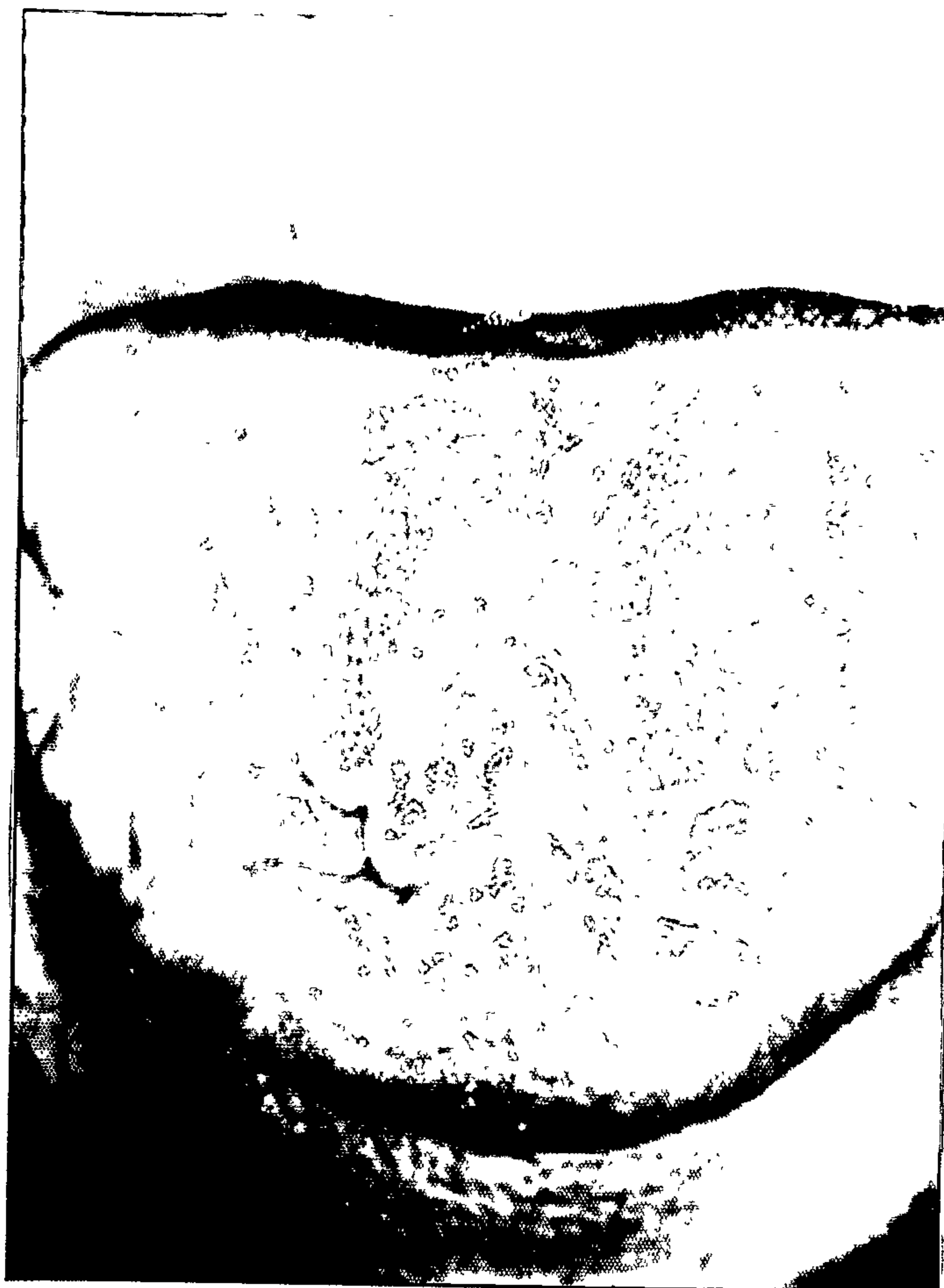


Plate 11B. Grade II changes in the tongue of a patient with Sjögren's syndrome. Lobulation and loss of filiform papilla are obvious.



Plate 12A. Acute pseudomembranous candidiasis in xerostomia.

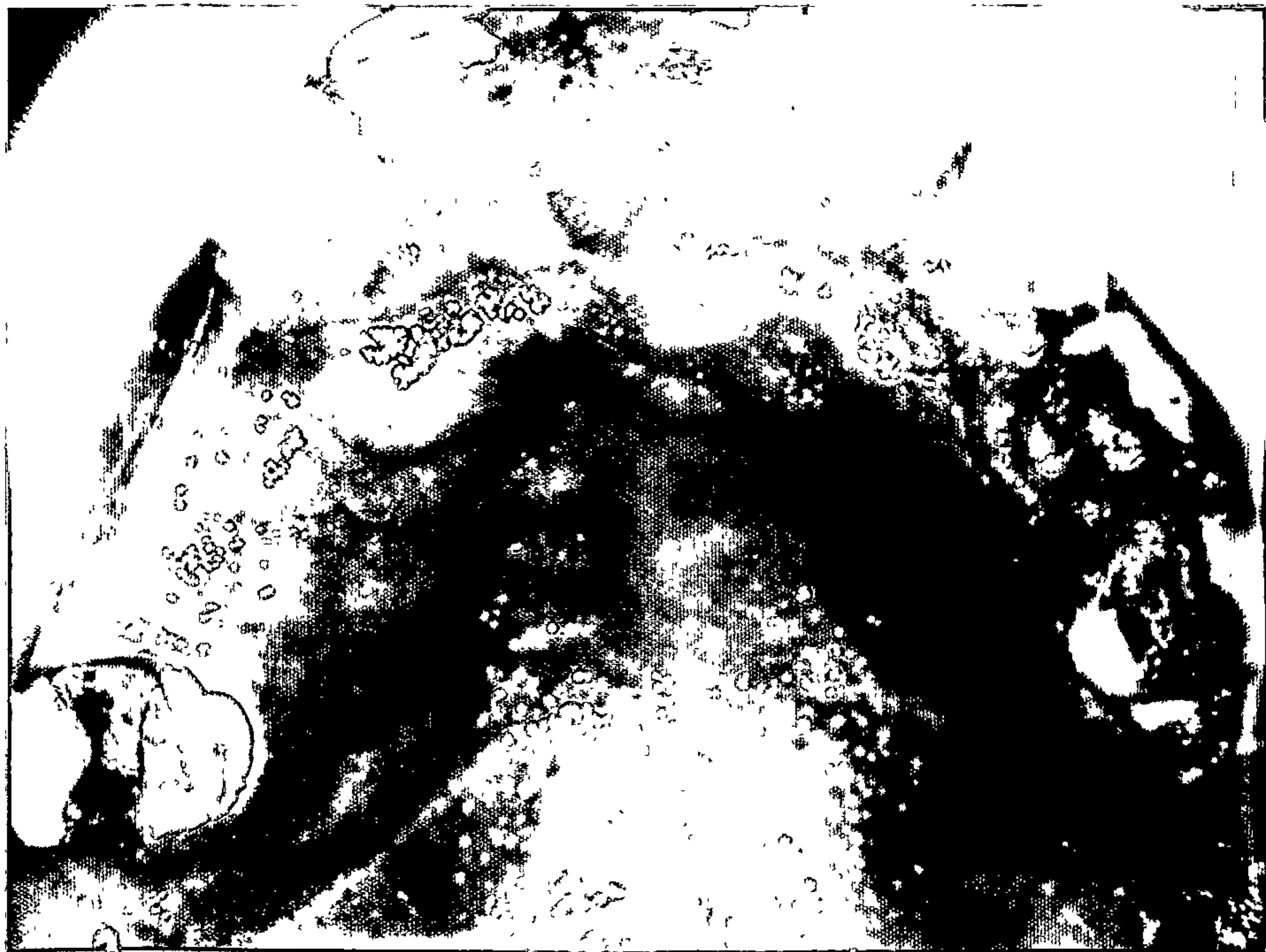


Plate 12B. Chronic atrophic candidiasis in xerostomia.

creams applied to the mouth and dentures for at least two weeks is necessary.

XEROSTOMIA AND DENTAL CARIES

The direct role of saliva in maintaining the integrity of the dental hard tissues has been discussed (vide supra: Saliva and the loss of tooth substance, p. 50). It seems reasonable to assume that a marked reduction or complete absence of salivary flow removes or reduces the protective role played by saliva in the resistance to dental caries. However the relationship between low salivary flow rate and increased caries experience in 'normal', non-xerostomic subjects is controversial³⁷⁶. The complexity of the caries process where bacterial, dietary, gingival, enamel and other factors have a varying influence makes it difficult to show the role of any single factor in causing decay³⁷⁷.

The importance of saliva as a natural defence against dental caries is most evident when salivary gland function is compromised to a degree sufficient to produce prolonged xerostomia. The association between xerostomia and the increased incidence of dental caries has been often observed in man over the past 90 years^{153,227,317,319,321,322,367,369}. Animal experiments also show a greatly increased caries activity as a result of blocking the secretion from the major salivary glands^{369,378}. Schwartz and Shaw (1955)³⁷⁹ showed that the removal of the major salivary glands on only one side of a rat's mouth resulted in an increase in the dental caries score on that side compared to the side not desalivated.

Clinically the relationship between xerostomia and dental caries has been most apparent in patients with irradiated salivary glands, aplasia of salivary glands and in Sjögren's syndrome³⁷⁸.

The time that it takes for the development of dental caries after the onset of xerostomia is likely to vary depending on factors such as the degree of reduction in salivary flow and individual susceptibility to caries. Frank et al (1965)¹⁸¹ reported the development of caries in a patient one month following 3000 r of cobalt 60 teletherapy which involved all major salivary glands. However more usually the increased incidence of caries will become apparent between 3 months and 6 months after the onset of xerostomia. Without careful oral hygiene and preventive dental therapy no patient is likely to remain caries free after the onset of severe chronic xerostomia^{378,380,381}.

Xerostomia precipitates adverse changes in the physical, bacterial, biochemical, immunological and dietary parameters that influence the rate of dental caries³⁷⁸.

The sparsity and low flow rate of saliva in xerostomia deprive the teeth of an important mechanical washing action (vide supra: The antibacterial action of saliva, p.53). All tooth surfaces in xerostomic patients tend to become vulnerable to dental caries^{181,192,381,382}.

Several recent publications^{339,375,378,380} have shown that a loss of saliva will cause alterations to the composition of the oral microflora. Pronounced population shifts in the oral bacteria result in an increase in the numbers of highly acid-tolerant bacteria and a decrease in the less acid-tolerant bacteria. Increases of streptococcus mutans, lactobacilli, yeasts, catalase-positive diphtheroids and total anaerobes are paralleled by significant decreases in streptococcus sanguis, neisseria, bacteriodes and fusobacteria^{375,378,380}. Dreizen and Brown (1976)³⁷⁸ noted that the peak increase in the numbers of streptococcus mutans coincided with the onset of clinically demonstrable caries. Factors such as a change

to a high sucrose diet and microbial antagonism also influences the change in the oral flora of xerostomic patients. A few strains of streptococcus mutans and several species of lactobacillus produce inhibitory substances that affect a broad range of oral commensals³⁷⁸,
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Biochemical changes may also influence the caries rate in xerostomic patients and these include a loss in the acid buffering action of saliva, a loss of water from saliva increasing its viscosity and decreasing its mechanical washing action and a decrease of salivary pH associated with low flow rates. Valentine, Anderson, and Bradnock (1978)³⁸³ confirmed that there was a significant ($p < 0.01$) association between salivary pH and the caries experience in 1,990 children with no significant difference in oral hygiene ($p > 0.05$). When the teeth are bathed in saliva calcium and phosphate ions are available to replace demineralized enamel (vide supra: Saliva and the loss of tooth substance, p. 50). Lack of saliva will deprive the teeth of this caries protective action.

Immunological changes resulting from a decrease in salivary flow involve secretory immunoglobulin A, salivary lysozyme, leukocytes, serum immunoglobulins and other antibacterial factors (vide supra: The antibacterial action of saliva, p. 53). Secretory antibodies to streptococcus mutans have been demonstrated in human secretions and these may give some protection against dental caries³⁸⁴.

The mean volume-based levels of salivary immunoglobulin A, immunoglobulin G and lysozyme are known to increase during the development of xerostomia in radiotherapy patients. However the increased concentration of immunoglobulins is offset by the great reduction in salivary flow ($> 93\%$)³⁷⁸.

Cole, Arnold, Rhodes et al (1977)³⁸⁴ reported that there

was a general trend for caries to develop in patients with immune dysfunction irrespective of the immunoglobulin class involved. Patients with immunoglobulin A deficiency showed a greater susceptibility to dental caries than control patients. It was stressed that levels of immunoglobulins may not reflect the degree of immunoprotection because quantity alone is not a reflection of functional antibody activity. Some patients appeared to compensate for immunoglobulin A deficiency by selective secretion of other immunoglobulins notably immunoglobulin M. These patients did not show any increased susceptibility to dental caries and their secretory immunoglobulin M showed activity against streptococcus mutans.

A decrease in other salivary antibacterial factors such as lactoferrin and thiocyanate ion may also increase the susceptibility to dental caries (vide supra: The antibacterial action of saliva, p. 53).

A change in the dietary habits of xerostomic patients will contribute to an increased incidence of dental caries by providing more substrate for cariogenic bacteria. Difficulty in eating leads to a preference for a liquid, soft, non-detergent diet rich in carbohydrate until the patient becomes accustomed to the xerostomia. Multiple small feedings are often instigated in an attempt to maintain protein and caloric balance. This dietary pattern is most evident in head and neck radiotherapy patients where an acute radiation mucositis and taste loss accompany the xerostomia^{378,381}. Taste loss may accompany xerostomia from other causes and this is likely to result in an increase in consumption of sweet cariogenic foods. The sucking of hard lollies or candy in an attempt to increase salivary flow in dentate patients with xerostomia should definitely be discouraged³⁸⁵.

The changes related to reduced salivary flow which result

in an increased incidence of dental caries can be summarized as:

- (i) loss of mechanical washing action.
- (ii) decreased salivary pH and decreased buffering capacity.
- (iii) increase in cariogenic oral micro-organisms and related dietary change.
- (iv) decrease in the immunological influence on oral micro-organisms.

PATTERN OF DENTAL CARIES

All of the tooth surfaces become equally vulnerable to dental caries in patients with very low salivary flow. Those with irreversible xerostomia, whatever its etiology, invariably develop rampant dental caries unless prompt preventive measures are taken to protect the teeth^{181,378,381}.

del Regato (1939)¹⁹² described the type of caries, which is now classically associated with a deficiency of saliva, as a decay of the necks of all the teeth [see Plate 13A]. The caries was seen to begin on the labial surface of the incisors and canines and then involve the molars. The lesions were initially superficial and extended around the cervical area of the teeth and eventually progressed towards complete amputation of the crown [see Plate 13B]. Sometimes a different type of lesion affected the teeth, predominantly the molars, where the entire tooth surface lost its brilliance and became grey and eventually black and then broke down under masticatory stress. Another form of caries observed was a "wearing away" of the incisal or occlusal surfaces of the teeth with or without cervical lesions.

Frank, Herdly and Phillipe (1965)¹⁸¹ observed the classic type of cervical caries noted by del Regato in post-radiotherapy patients. Caries involving all of the teeth with a marked brown-black

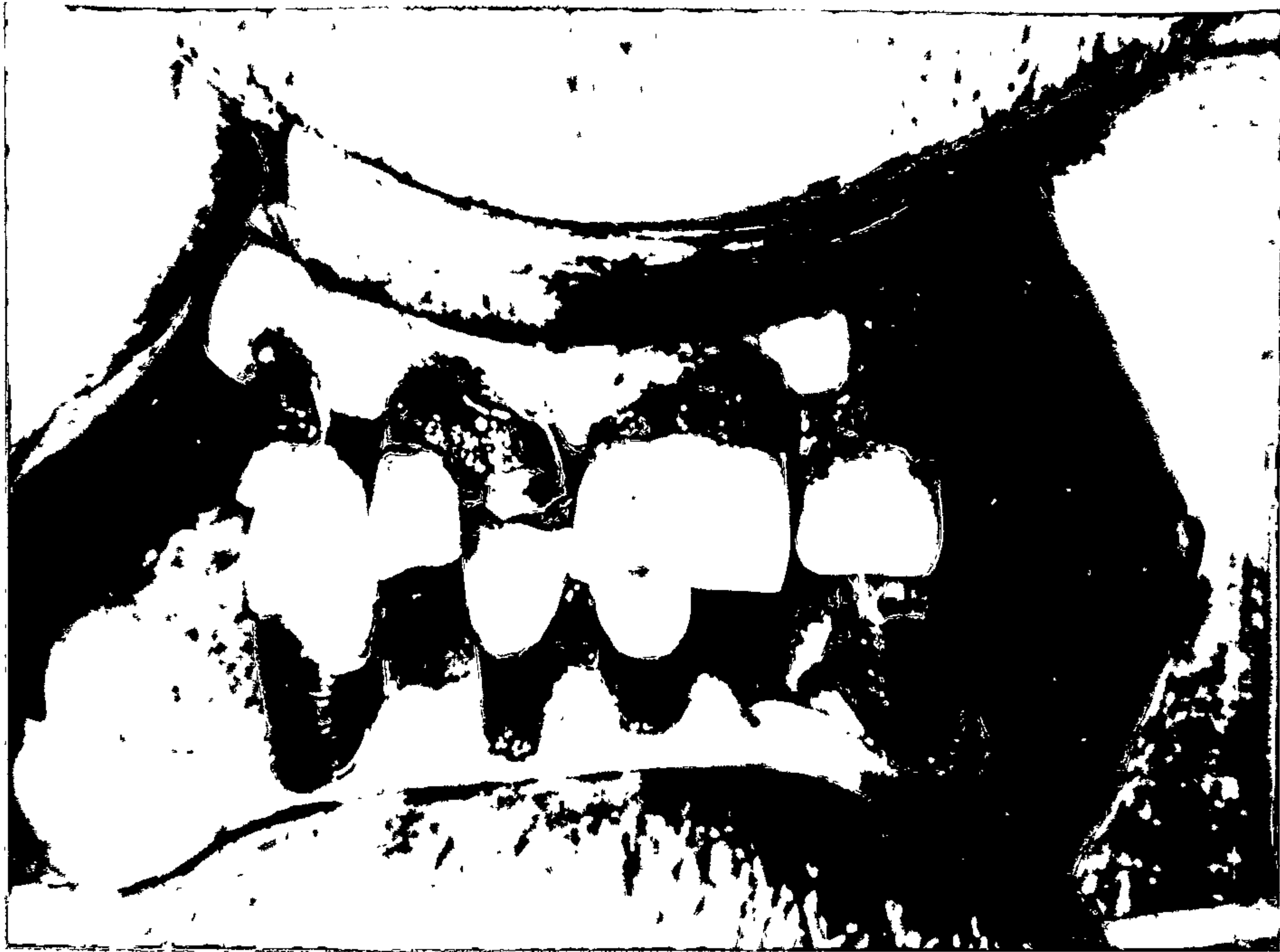


Plate 13A. Classic cervical caries in xerostomia



Plate 13B. "Amputation" of the clinical crowns of teeth in xerostomia.

Note that the patient wore a mandibular denture.

discolouration giving an ebony appearance was also noted [see Plate 14]. The most frequently encountered lesions were generalized and superficial lesions which appeared initially as fine diffuse and punctate defects. They occurred first on the buccal and then later on the palatal and lingual surfaces of the teeth and often only the incisal and occlusal surfaces were affected. Histologically the caries related to xerostomia was similar to the caries seen in the general population, the only difference being in the widespread nature of the lesions.

Karmiol and Walsh (1975)³⁸¹ described 5 radiotherapy patients who developed rampant caries similar to the patterns described above. They noted the widespread loss of tooth structure which involved the incisal edges and cusps as well as early caries involvement of the mandibular anterior teeth. Loss of the relative caries immunity of the lower anterior teeth was attributed to the loss of saliva from the nearby orifices of the submandibular and sublingual salivary glands that normally and constantly bathe the teeth in a fluid rich in calcium and phosphate ions. The clinical pattern of caries was described as a rapid generalized decalcification and loss of enamel followed by demineralization and softening of dentine. The difference between caries in xerostomia and ordinary smooth surface caries was considered to be that demineralization occurred much more extensively and considerably in advance of proteolysis and loss of the anatomic form of the dentine. This resulted in the dentine becoming rubbery without the large cavitary defects usually seen when caries progresses through to the dentine and breakdown of the crown occurred later than was to be expected when these lesions were first examined.

Thus the development of rampant dental caries following the onset of xerostomia seems to be related to accumulation of a large



Plate 14. Caries with an "ebony" appearance in a patient with xerostomia.

quantity of highly acidogenic plaque. The different clinical appearances of carious lesions probably results from variations in individual susceptibility including differences in oral hygiene, the severity of xerostomia, dietary changes and the physical, bacterial, biochemical and immunological factors discussed previously.

13. TREATMENT OF XEROSTOMIA

Xerostomia is a sign or symptom of an underlying disorder affecting the salivary glands and to determine the nature of this disorder a thorough history and examination of the patient is required. When the cause of the xerostomia can be found the definitive treatment may result in resolution of the dryness. However when the cause of the xerostomia cannot be diagnosed or when the salivary glands or their nerve supply are irreversibly damaged then only symptomatic treatment and preventive dental care remain useful.

An etiologic classification of xerostomia based on this review is presented in Table 6.

Symptomatic treatment of xerostomia in the past has been directed at providing the affected patient with a rinsing solution to keep the mouth moist. Many patients have carried containers of water with them to moisten their mouths when necessary. Indeed the patient who has only mild xerostomia may require no more than an occasional rinse with water to remain comfortable. Patients with severe xerostomia may find that it is difficult or inconvenient to carry or obtain the amount of water they require to keep their mouths moist throughout the day. Also, they need to spit out and not drink the bulk of the rinsing water or polyuria may be a problem (vide supra: Oral and salivary gland involvement, p. 224).

The advent of radiotherapy, with its adverse effects when involving the salivary glands, has emphasized the need for a substitute for saliva both during and after treatment. The ideal artificial saliva would have the following characteristics:

- (i) A small volume moistens and lubricates the mouth for a prolonged time (large quantities do not have to be carried).
- (ii) Pleasant or bland tasting.

TABLE 6

USUALLY REVERSIBLE XEROSTOMIA - SALIVARY GLANDS FUNCTIONAL

1. Mouthbreathing
2. Psychogenic - fear, nervousness, anxiety, depression.
3. Changes in body water and electrolyte balance - dehydration, endocrine disorders, haemorrhage, low cardiac output and oedema, renal failure.
4. Irradiation of major salivary glands - less than approximately 4000 r to 5000 r.
5. Obstruction to the secretion of saliva - salivary calculi and congenital absence of salivary ducts.
6. Sialadenitis - chronic, allergic and viral; Heerfordt's syndrome (sarcoidosis).
7. Drugs - CNS depressants, autonomic ganglion blockers, cholinergic blockers, adrenergic blockers, drugs affecting body water and electrolyte balance, antineoplastics.

USUALLY IRREVERSIBLE XEROSTOMIA - SALIVARY GLANDS NONFUNCTIONAL.

1. Irradiation of major salivary glands - greater than 4000 r to 5000 r.
2. Agenesis of salivary glands.
3. Sjögren's syndrome and sicca syndrome.
4. Neurological pathology - damage to salivary centres in the brain, dysfunction of central or peripheral secretory nerves.

Table 6. Classification of xerostomia

- (iii) Does not dry to a sticky or crusted residue.
- (iv) Cariostatic and bacteriostatic or maintains a normal ratio of oral commensals.
- (v) Remains stable.
- (vi) Low cost, readily available.

Dykes, Harris and Marston (1960)³⁸⁶ reported the use of a glycerin type of pastille containing gelatin, glycerin, sucrose, lemon essence, sodium benzoate, citric acid, amaranth solution and water; xerostomic patients used the pastilles on an ad lib basis. An objection must be made to the use of any medication containing sucrose to be used in the caries susceptible xerostomic patient.

Halpern and Freedman (1975)³⁸⁷ encouraged frequent use of sodium chloride and sodium bicarbonate mouthrinses which were prepared at home. This solution does not have a pleasant taste to recommend its frequent use.

Gravenmade, Roukema and Panders (1974)³⁸⁸ devised an artificial saliva made from bovine salivary glands obtained from an abattoirs which was then homogenized and centrifuged. The material was processed into freeze-dried white powder which could be made up fresh by the additon of 100 mg of powder to 10 ml of water. No solutions were kept for more than two days. To relieve their symptoms most patients used between 2 ml and 5 ml of the solution each day. One rinsing provided from between one and a half hours to four hours relief from dryness. Bacteriological cultures of the powdered salivary gland material showed an absence of significant bacterial contamination. Nevertheless bacterial contamination and a short shelf life could be a problem with a product from an animal source. Also fluoride was not added to the bovine saliva. The advantages of the solution were that it retained its effectiveness, only small quantities

were needed each day, it could be swallowed and did not accumulate in the mouth and it was pleasant tasting or tasteless.

Shannon, Trodahl and Starke (1978)³⁸⁹ recognised that there was potential for a remineralizing constituent to be added to a synthetic saliva for use by the high caries risk xerostomic patient. Their experiments showed that the addition of calcium, phosphate and fluoride ions to an artificial saliva called VA OraLube produced up to a 5.5% increase in the microhardness of human tooth enamel. Addition of fluoride ions alone or calcium and phosphate ions alone resulted in much reduced increases in enamel hardness (0.6% and 1.3% respectively).

Clinical trial of VA OraLube by 125 xerostomic patients over a four month period showed almost complete relief of intraoral soft tissue symptoms. Patients consistently noted that their mouths were much more comfortable and that they did not have to repeatedly sip water. Those that had complained of a dry sore throat also reported consistent relief. The duration of the beneficial effect varied from one hour to three hours between ad lib rinses. It was emphasized that this solution was not considered to be a substitute for oral hygiene measures and topical fluoride application in xerostomic patients. The composition and directions for preparing VA OraLube are as follows:

Potassium Chloride	2.498 g
Sodium Chloride	3.462 g
Magnesium Chloride	0.235 g
Calcium Chloride	0.665 g
Potassium hydrogen phosphate	3.213 g
Potassium dihydrogen phosphate	1.304 g
Methyl p-hydroxybenzoate	8.0 g

Flavouring	16.0	g
Wintergreen-Coriander spice 70% Sorbitol	171.0	g
Sodium carboxymethylcellulose	40.0	g
Sodium fluoride	17.68	g
FD and C Red 40 dye (2%)	1.0	ml
Water q.s. ad	4000.0	ml

Instructions:

Heat water to approximately 50°C and place in a blender.

Add all dry ingredients - mix at high setting for two minutes. Filter through loose glass wool prior to packing in four ounce soft plastic bottles.

Recently an artificial saliva Salube (Orapharm, Melbourne) has been advertised for use in relieving xerostomia. This product is apparently similar to the American VA OraLube and it also contains fluoride. Salube is packed in 25 ml and 200 ml dispenser bottles to be sold through chemists and dental supply houses³⁹⁰. If Salube is made this readily available it should prove valuable for the patient with irreversible xerostomia.

The frequency of use of artificial saliva will depend upon factors which vary for each patient. These factors include the severity of the xerostomia, the amount of talking, eating and mouth-breathing and also the degree to which the xerostomia discomforts the patient. When directions for the use of artificial saliva are to use as required it can be expected that patients will use less than 20 ml each day divided between one and eight rinses. Patients have found that artificial saliva is especially valuable at night for when intra-oral dryness awakens them a rinse with the solution enables them to resume sleeping comfortably. Patients can also be advised that rinsing with artificial saliva on retiring will help them in

going to sleep^{388,391,392}.

STIMULATION OF SALIVARY FLOW

Stimulation of salivation by sucking sweets, chewing gum and by taking parasympathomimetic drugs such as pilocarpine have been advised for the relief of xerostomia^{385,393}. These remedies will not help the patient suffering from irreversible xerostomia where salivary gland tissue is no longer functional. Sucking sweets and chewing sugared gum should not be advised for dentate patients with xerostomia because of their high susceptibility to dental caries. However sugarless chewing gum such as Orbit (Wrigley's Co.,) may be useful to stimulate salivation in patients taking antisialogenous medication, in patients who have received low doses of radiation to their salivary glands or in mouthbreathers.

Bruun and Givskov (1978)³⁹⁴ investigated the degree of release of fluoride from fluoride chewing gum. The composition of the gum included 0.1% sodium fluoride and mannitol but no sucrose. When the gum was chewed for ten minutes the salivary fluoride concentration remained above the pre-chewing level for approximately one hour. Shorter periods of chewing did not release as much of the fluoride from the gum and the elevation of fluoride in saliva did not last as long. The authors suggested the fluoride gum as both a salivary stimulant and a caries-preventive measure for patients with xerostomia. One disadvantage in using gum as a salivary stimulant is that prolonged chewing may cause fatigue and discomfort in facial and masticatory muscles.

Pilocarpine is a parasympathomimetic agent with the muscarinic effects of acetylcholine. This drug is most frequently used in ophthalmology as a miotic and for the treatment of glaucoma. Oral

doses of between 2.5 mg and 5 mg have been used to counteract the anticholinergic side effects of medications such as ganglion blockers³⁹⁵. The salivary stimulant action of pilocarpine has been noted previously (vide supra: A test of salivary gland function by assessing salivary flow rate, p.78). Prutting (1965)³⁹³ reported the use of pilocarpine for patients taking antidepressant medication as an antagonist to the anticholinergic side effects. Six patients with dryness of the mouth caused by antidepressant medication were reported to have been given relief by the use of between 2.5 mg and 5 mg of pilocarpine given orally 3 or 4 times daily. The only unpleasant effect of this drug was a slight increase in perspiration in one patient and this was overcome by a reduction of the dosage. In one case there was interference with the therapeutic action of antidepressant medication. One patient with xerostomia caused by nervousness was treated with pilocarpine but with only moderate success. Xerostomia caused by a "disturbance of the end-organs of the nerves supplying the salivary glands" has been reported to be relieved by administration of pilocarpine (vide supra: Xerostomia associated with neurological pathology, p.254).

Some of the more serious toxic effects of pilocarpine include increased bronchial secretion and bronchospasm, bradycardia and hypotension and eventually severe weakness, paralysis, convulsions and coma. There may also be paradoxical tachycardia and hypertension³⁹⁵. Thus patients with pulmonary disease, especially asthma and those with cardiac pathology should be carefully assessed before being given cholinergic drugs such as pilocarpine. Because pilocarpine increases gastrointestinal activity and secretions, it has been advised to restrict its use in patients with gastrointestinal acidity or irritability. The lethal dose of pilocarpine is not known but a 100 mg dose

is considered dangerous³⁹³.

Bethanechol chloride is a parasympathomimetic drug with actions and toxic effects similar to pilocarpine³⁹⁶. It has also been used with apparent success in the treatment of xerostomia in patients taking psychotropic medication³⁹⁷. Everett (1975)³⁹⁷ noted that because bethanechol chloride cannot cross the blood-brain barrier it must act as a peripheral cholinergic agent only. Therefore the drug cannot be expected to relieve the antisialogenous side effects of medication which arise centrally, such as high doses of anti-depressants.

Either pilocarpine or bethanechol chloride may be of use in the treatment of xerostomia caused by antidepressants or any other medication with anticholinergic side effects but the dangers of polypharmacy and toxic effects need to be carefully considered especially when xerostomia is a patient's sole anticholinergic side effect.

Drugs whose main therapeutic action is anticholinergic vide supra: Drugs blocking parasympathetic neuroeffectors, p.171) will most likely show reduced or abolished activity if cholinergic drugs are used concurrently. Thus the use of drugs such as pilocarpine and bethanechol chloride with drugs with a therapeutic anticholinergic action is contraindicated. The physician who prescribed the medication causing a patient's xerostomia should be consulted about the use of cholinergic drugs in treatment.

Bromhexine is a drug which has been used as an expectorant in treating chronic bronchitis. Its action is to reduce the viscosity of sputum and change the nature of bronchial secretion³⁹⁸. Because bromhexine appears to be of value in increasing lacrimal secretion in patients with Sjögren's syndrome it was hoped that salivary secretion would also increase. However crude estimations have suggested that

bromhexine has little or no effect on salivary gland secretion³⁹⁹.

PREVENTIVE AND RESTORATIVE ASPECTS OF TREATMENT

It is not the purpose of this treatise to detail the complete dental treatment of the patient with irreversible xerostomia but some important considerations will be discussed.

1. Xerostomia causes a change to a highly acidogenic plaque microflora at the expense of non-cariogenic micro-organisms regardless of any caries preventive program that is instituted. Therefore continual use of plaque disclosing dye, correct toothbrushing and flossing as well as applications of topical fluoride and restriction of dietary sucrose are necessary³⁷⁸. Dreizen and Brown (1976)³⁷⁸ compared the efficacy of three caries preventive programs namely plaque disclosing alone, plaque disclosing and 1% topical sodium fluoride gel 5 minutes each day, and plaque disclosing and fluoride gel combined with a sucrose restricted diet. Patients practicing all three preventive measures had the lowest incidence of caries measured by DMFT and DMFS scores. It was suggested that radiotherapy patients ideally should be commenced on a caries preventive regimen prior to their initial dose of radiation so that maximum anticaries benefit is achieved. Because of their high caries susceptibility patients with xerostomia should be given a dental examination more frequently than is usual.

2. Xerostomia predisposes a patient to oral candidal infections and the need for antifungal therapy may require periodic review (vide supra: Effect of xerostomia on the tissues, p.263).

3. Xerostomia allows the teeth to dry out and apparently they become more susceptible to fracture. Thus deflective occlusal contacts should be sought and eliminated to reduce the risk of tooth

damage. Also stress on abutment teeth should be reduced to a minimum and therefore bridge pontics should be made narrow and cantilevered pontics avoided. Large restorations should be made full coverage to prevent chipping or cracking of teeth⁴⁰⁰.

Full prostheses should be avoided in xerostomic patients where possible. If dentures are necessary then they should have no over extensions or occlusal discrepancies because movement of the denture base over a dry mucosa is certain to cause irritation. Artificial saliva or silicone oil applied to a denture base may allow it to be worn comfortably for prolonged periods of time. Soft denture bases may also be of value to the denture wearer with xerostomia⁴⁰¹.

4. Patients with rampant caries from a variety of causes including unrecognised or untreated xerostomia⁴⁰² may present for dental treatment. Hill and Levine (1978)⁴⁰³ reviewed the clinical management of rampant caries and presented the two aims of the initial treatment plan as follows:-

- (a) to introduce intensive procedures to control caries including advice about fluoride treatment, plaque control and diet.
- (b) to provide limited operative treatment to relieve pain and to minimize the risk of pulp involvement in symptomless teeth with established caries.

After this initial treatment the patient is then reviewed in from three months to four months and the result of caries control is assessed. If the result is considered satisfactory then complex treatments such as root canal therapy, crowns and partial dentures can be instigated. When caries control is unsuccessful but some patient motivation is evident, then the initial treatment plan can be

repeated. Where a patient lacks any interest in preserving his dentition then a basic service for the relief of pain leading to provision of dentures is all that can be achieved.

CONCLUSION

The adverse effects of xerostomia on the hard and soft tissues of the oral cavity and the causes of salivary gland dysfunction in which xerostomia may be a sign or a symptom have been reviewed.

In the presence of a severely dry mouth the diagnosis of reduced salivary flow is not difficult. However when the flow of saliva is only moderately reduced then the diagnosis may be complicated by the lack of obvious signs. The large variation in the physiological flow rate of saliva in different individuals must be considered in making quantitative assessments. In many instances the clinician has to rely on a thorough history, on symptoms and upon his experience in determining the degree of reduction in salivary flow.

While there are numerous possible causes of xerostomia three in particular, namely drug induced, radiotherapy and Sjögren's syndrome, are the most frequent. Drug therapy has become very significant in the treatment of disease but in many instances the therapy may produce relatively mild or even severe side effects. Although xerostomia may be considered a minor side effect of drug therapy it may cause serious oral disorders. Radiotherapy is used extensively in the treatment of radiosensitive head and neck malignancies. It has been stressed that the clinician should recognise and treat appropriately the serious complications associated with the xerostomia that may occur in patients treated by radiotherapy. Sjögren's syndrome causes xerostomia as a consequence of replacement of salivary gland tissue by lymphoid cells. The lymphoid infiltrate has been seen to undergo malignant transformation and it is important that the affected patient be kept under review.

For the patient with xerostomia caused by conditions which

cannot be treated definitively, then symptomatic treatment should be attempted. The dental surgeon can provide much relief for the patient with intractable xerostomia by treating and preventing candidal infection, reducing the rate of dental caries and by prescribing lubricating agents for the mouth and dentures if used.

The clinician who is aware of both the causes and consequences of xerostomia will be able to provide affected patients with appropriate relief from this distressing condition.

APPENDIX

DRUGS WITH XEROSTOMIA AS A REPORTED OR POTENTIAL SIDE EFFECT

NOTE: 1. Trade names are given first.

2. Brackets indicate main drug in medication responsible for xerostomia.

3. The main pharmacological action responsible for xerostomia is presented as follows:

AACH : Anticholinergic action

AACH-M : Anticholinergic specifically antimuscarinic

AGB : Autonomic ganglion blocker

CNS : Central nervous system depression or action

MAOI : Monamine oxidase inhibition

SYM : Sympathetic action

ALL SIAL : Allergic sialadenitis produced

WR SR : Water retention, sodium retention

DEH : Dehydration

ADH : Antidiuretic hormone-like action

4. Question marks indicate doubtful drugs or actions for inclusion.

ANTISPASMODICS - AACH-M

Alkabarb (belladonna)

Antrenyl (oxyphenonium bromide)

Atrobel (belladonna alkaloids)

Belladonna-Neutralon (belladonna alkaloids)

Bellatran (belladonna)

Buscopan (hyscine)

Cantil (mepenzolate)

ANTISPASMODICS - AACH-M (Continued)

Daricon (oxyphencyclimine)
 Donnabarbital (belladonna)
 Donnalex (hyoscamine, atropine)
 Donnatab (hyoscamine, atropine)
 Donnatal LA (hyoscamine, atropine)
 Eumydrin (atropine)
 Infacol syrup (dicyclomine))
) Large doses ?
 Kolantyl (dicyclomine))
 Librax (chlordiazepoxide)
 Merbentyl (dicyclomine) Large doses ?
 Nacton (poldine)
 Pamine (hyoscine)
 Pantheline (propantheline)
 Piptal (pipenzolate)
 Pro-Banthine (propantheline)
 Procyclomin (dicyclomine) Large doses ?
 Robinul (glycopyrrolate)
 Stelabid (isopropamide, trifluoperazine)
 Tyrimide (isopropamide)
 Valpin (octatropine)
 Visceralgin (tiemomium)

ANTIULCERANT - AACH-M

Monadral (pethienate)

CATHARTICS - DEH

Agarol (phenolphthalein)
 Agiolax (senna)

CATHARTICS - DEH (Continued)

Casevac (cascara)
 Coloxyl suppositories (bisacodyl)
 Coloxyl with Danthron (danthron)
 Dorbanate (danthron)
 Durolax (bisacodyl)
 Formulax (danthron)
 Petrolagar (phenolphthalein)
 Senokot (senna)
 Toilex (bisacodyl)
 Travad (sodium dihydrogen phosphate)
 Veracolate (cascara, phenolphthalein)

ANTIHYPERTENSIVES

Aldomet (methyldopa)	CNS
Ansolysen (pentolinium)	AGB
Catapres (clonidine)	CNS
Mevasine (mecamylamine)	AGB
Minipress (prazosin)	?
Perolysen (pempidine)	AGB

ANTIARRHYTHMICS - AACH

Norpace (disopyramide)
 Rythmodan (disopyramide)
 Persantin (disopyramide)

β -ADRENERGIC BLOCKING AGENTS - Non-selective β -adrenergic blockade

Aptin (alprenolol)

Betacard (alprenolol)

ANTIMIGRAINE PREPARATIONS

Dixirit (clonidine) CNS

Ergodryl (diphenhydramine) AACH

Sandomigran (pizotifen) ? AACH

ANALGESICS, ANTIPYRETICS - CNS

Morphalgin (morphine)

Mortha (morphine)

Omnopon-Scopolamine (hyoscine) AACH

Pethilorfan (pethidine)

Pethoid (pethidine)

SEDATIVES, HYPNOTICS

Bellegal (belladonna) AACH

? Dalmane (flurazepam) CNS

Mandrax (diphenhydramine) AACH

Tropinal (atropine, phenobarbitone) AACH, CNS

? Raporan (medazepam) CNS

ANTIPSYCHOTICS - CNS, AACH

Anatensol (fluphenazine)

Calmazine (trifluoperazine)

Compazine (prochlorperazine)

Dartalan (thiopropazate)

ANTIPSYCHOTICS - CNS, AACH (Continued)

Largactil (chlorpromazine)
 Melleril (thioridazine)
 Modecate (fluphenazine)
 Promacid (chlorpromazine)
 Protran (chlorpromazine)
 Sparine (promazine)
 Stelazine (trifluoperazine)
 Stemetil (prochlorperazine)
 Terfluzin (trifluoperazine)
 Trilafon (perphenazine)

ANTIDEPRESSANTS - AACH

Allegron (nortriptyline)
 Aventyl (nortriptyline)
 Concordin (protriptyline)
 Elavil (amitriptyline)
 Imiprin (imipramine)
 Insidon (opipramol)
 Iramil (imipramine)
 Laroxyl (amitriptyline)
 Marplan (isocarboxazid) MAOI
 Marsilid (iproniazid phosphate) MAOI
 Mutabon (amitriptyline, perphenazine)
 Nardil (phenelzine) MAOI
 Nortab (nortriptyline)
 Noveril (dibenzepin)
 Parnate (tranylcypromine) MAOI
 Parstelin (tranylcypromine, trifluoperazine) MAOI, AACH

ANTIDEPRESSANTS - AACH (Continued)

Pertofran (desipramine)
 Prothiaden (dothiepin)
 Quitaxon (doxepin)
 Saroten (amitriptyline)
 Sinequan (doxepin)
 Simipra (imipramine)
 Tofranil (imipramine)
 Triptil (protriptyline)
 Tryptanol (amitriptyline)

CNS STIMULANTS - SYM

Durophet (amphetamine)

ANTIPARKINSON AGENTS - AACH

Akineton (biperiden)	
Antadine (amantadine)	? Large doses > 200 mg
Anti Spas (benzhexol)	
Artane (benzhexol)	
Cogentin (benztropine)	
Disipal (orphenadrine)	Parasympatholytic
Kemadrin (procyclidine)	
Lysivane (ethopropazine)	Parasympatholytic
Pagitane Hydrochloride (cycimine)	
Sinemet (levodopa, carbidopa)	Dopamine ? - SYM
Symmetrel (amantadine)	? Large doses > 200 mg
Tremonil (methixene)	

ANTICONVULSANTS - AACH

Tegretol (carbamazepine)

ANTIEMETICS, ANTINAUSEANTS - AACH some also CNS

Adrumin (dimenhydrinate)

Anti-Naus (prochlorperazine) CNS

Avomine (promethazine) CNS

Benacine (diphenhydramine, hyoscine)

Compazine (prochlorperazine) CNS

Debendox (dicyclomine, doxylamine)

Decadol (dimenhydrinate)

Dramamine (dimenhydrinate)

Marzine (cyclizine)

Stemetil (prochlorperazine) CNS

Torecan (thiethylperazine) CNS

Travacalm (dimenhydrinate, hyoscine)

NON-STEROID ANTI-INFLAMMATORY AGENTS - ALL SIAL

Butazolidin (phenylbutazone)

Butalgin (phenylbutazone)

Butazone (phenylbutazone)

Buzon (phenylbutazone)

MUSCLE RELAXANTS - AACH

Norflex (orphenadrine)

Norgesic (orphenadrine)

DIURETICS - DEH and as indicated

Cardrase (ethoxzolamide)	+ Carbonic anhydrase inhibitor ?
Chlotride (chlorothiazide)	+ Sialadenitis
Diamox (acetazolamide)	+ Carbonic anhydrase inhibitor ?
Dichlotride (hydrochlorothiazide)	+ Sialadenitis
Diuret (chlorothiazide)	+ Sialadenitis
Diurone (chlorothiazide)	+ Sialadenitis
Doburil (cyclothiazide)	+ Sialadenitis
Dyazide (triamterene)	
Dytac (triamterene)	
Edecril (ethacrynic acid)	
Enduron (methyclothiazide)	
Esidrex (hydrochlorothiazide)	+ Sialadenitis
Frusid (frusemide)	
Lasix (frusemide)	
Lasix High Dose (frusemide)	
Midamor (amiloride)	
Moduretic (amiloride)	
Navidrex (cyclopenthiazide)	
Nefrolan (clorexolone)	
Neo Naclex (bendrofluazide)	
Osmitrol (mannitol)	
Uremide (frusemide)	
Urex (frusemide)	

ANTI-DIURETICS - ADH

Di Sipidin (posterior pituitary gland hormone)
Minirin (desmopressin)
Pitressin (anti-diuretic hormone)

ANTI-DIURETICS - ADH (Continued)

Vasopressin spray (anti-diuretic hormone)

PENICILLIN

Geopen Oral (carindacillin) Dehydration from diarrhoea ?

ANTIFUNGAL ANTIBIOTICS - DEH

Fulcin (griseovulvin)

Grisovin (griseovulvin)

OTHER ANTIBIOTICS

Choramol (chloramephenicol) ALL SIAL Anaemia ?

Chloromycetin (chloramphenicol) ALL SIAL Anaemia ?

Dalacin (clindamycin) DEH

ANTITUBERCULOTICS - MAOI

Inapasade (isoniazid)

Istinyl (isoniazid)

ANTIVIRAL AGENTS - AACH and ? Dopamine

Antadine (amantadine)

Symmetrel (amantadine)

APPETITE SUPPRESSANTS - SYM

Duromine (phentermine)

Pre-Sate 65 (chlorphentermine)

Sanorex (mazindol)

Tenuate (diethylpropion)

EXPECTORANTS, ANTITUSSIVES, MUCOLYTICS, DECONGESTANTS -

SYM and AACH unless indicated otherwise

Actifed (pseudoephedrine, triprolidine)	
Apracur (clemizole, ephedrine)	
Avil (pheniramine)	AACH
Benadryl (diphenhydramine)	AACH
Benatab (pseudoephedrine)	SYM
Benatuss (diphenhydramine, phenylephrine)	
Benyphed (diphenhydramine, phenylephrine)	
* Bisolvon (bromhexine)	Initial increase in secretions then decrease
Codral Cold Tab (pseudoephedrine)	SYM
Codral Linctus (pseudoephedrine)	SYM
Colfed (pseudoephedrine)	SYM
Demazine (dexchlorpheniramine, pseudoephedrine)	
Dicodid (hydrocodone)	As morphine
Dimetapp (brompheniramine, phenylephrine, phenylpropanolamine)	
Diophen (ephedrine, ethyl morphine)	SYM
Drixora (pseudoephedrine)	SYM
Eskornade (isopropamide, diphenylpyraline, phenylpropanolamine)	
Fabahistin Plus (mephedrolin, pseudoephedrine)	
Hycomine (homatropine, chlorpheniramine, phenylephrine)	
Neo-Diophen (norephedrine, ethylmorphine, atropine)	
Neo-Synephrine Cold Tab (phenylephrine)	SYM
Ni-Col (pseudoephedrine)	SYM
Orthoxicol (phenylpropanolamine)	SYM
Phensedyl (promethazine, ephedrine)	
Polaramine (dexchlorpheniramine)	AACH
Quiactin (doxylamine, ephedrine)	

EXPECTORANTS, ANTITUSSIVES, MUCOLYTICS, DECONGESTANTS -

SYM and AACH unless indicated otherwise (continued)

Sudafed (pseudoephedrine)	SYM
Sudelix (pseudoephedrine)	SYM
Synephricol (pseudoephedrine)	SYM
Thenfacol (pseudoephedrine, thenyldiamine)	
Ticarda (normethadone, oxyephedrine)	
Tixylic (promethazine, phenylpropanolamine)	
Triogesic (phenylpropanolamine)	SYM
Tusselix (pseudoephedrine)	SYM
Tussils (pseudoephedrine)	SYM
Valledrine (ephedrine)	SYM
Vallex (phenylpropanolamine)	SYM

BRONCHOSPASM RELAXANTS - SYM

Ephedronoctal (ephedrine, homatropine)	SYM, AACH
Nethaprin (phenylephrine, doxylamine)	SYM, AACH
Orthoxine (methoxyphenamine)	
Panasma (ephedrine)	
Priatan (ephedrine)	
Tedral (ephedrine)	

ANTI-HISTAMINES - AACH

Actidil (triprolidine)	
Alergicap (diphenhydramine)	
Allercur (demizole)	
Allergex (chlorpheniramine)	
Ancolan (meclozine)	
Antegan S-R (cyproheptadine)	

ANTI-HISTAMINES - AACH (Continued)

Anthisan (mepyramine)

Anti-Hist (diphenylpyraline)

Atarax (hydroxyzine)

Avil (pheniramine)

Banistyl (dimethothiazine)

Benadryl (diphenhydramine)

Chlor-Trimeton (chlorpheniramine)

Chlorcyclizine (chlorcyclizine)

Clistin (carbinoxamine)

Dilosyn (methdilazine)

Dimetane (brompheniramine)

Fabahistin (mebhydrolin)

Fenamine (pheniramine)

Fenostil (dimethindine)

Histalert (diphenylpyraline)

Histex (carbinoxamine)

Histryl (diphenylpyraline)

Meth-Zine (promethazine)

Periactin (cyproheptadine)

Phenergan (promethazine)

Piriton (chlorpheniramine)

Polaramine (dexchlorpheniramine)

Prothazine (promethazine)

Tacaryl (methdilazine)

Tavegyl (clemastine)

Teledrine (chlorpheniramine)

Triominic (pheniramine, mepyramine, phenylpropanolamine) SYM

Vallergan (trimeprazine)

ANTI-HISTAMINES - AACH (Continued)

Zadine (azatadine)

VACCINES, ANTISERA, ANTIVENOMS

Mumps-vax (live mumps virus)

Parotitis (occasional)

fever, dehydration

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2. Vide supra: Drugs and reduced salivary secretion, p.171.

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