Diseases of the Oral mucosa

DISEASES OF THE
ORAL MUCOSA

Diagnosis,
Management,
Therapy

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This book is affectionately dedicated

to

FRANCIS P. McCARTHY

Professor Emeritus of Oral Medicine
Tufts University School of Dental Medicine

Who for many years has been our teacher and guide

in the field of stomatology

Foreword

Diseases of the soft tissues of the mouth have, all too frequently, remained obscured in a twilight zone between dermatology and dentistry. They have often been investigated and classified by one group, without taking advantage of the skills and special knowledge of the other. In the interpretation of oral changes as reflections of systemic diseases, much of the literature in general medicine and nutrition contains confusing statements. These result from the lack of knowledge of most medical writers about the wide spectrum of changes which may affect the oral soft tissues and about the difficulty in recognizing delicate shades of differences between them.

No one over sixty will ever forget the way in which the old family doctor peered into a child's mouth and throat. This often was the principal part of the physical examination, particularly in the doctor's office. The results of it were awaited with great suspense by the small patient, because so much of the interpretation of the physical state and, even more important, the particular type of unpleasant treatment to be given, depended on it. The decision was often announced by little more than a kindly grunt, followed by dispensing of the medicine or by a few ciphers scratched on the prescription pad.

This reference to a method of oldtime medicine is not made in any disparaging fashion; I can attest to the remarkable ability of our medical grandfathers to arrive at very shrewd deductions on the basis of this simple examination. It sometimes resulted in quite an accurate diagnosis. But it was part of the art of medical practice which had serious shortcomings and inevitably faded away before the advances of more sophisticated methods of diagnosis. However, the science of medicine was slow to replace the art insofar as oral soft tissue diseases were concerned.

The writers of the present volume have special qualifications for a task well-accomplished. Dr. McCarthy, broadly trained in medicine and dermatology, was raised under the professional influence Dr. Francis P. McCarthy, his father, whose lifelong interest and competence in oral diagnosis is well-known. A thoroughgoing knowledge of dentistry and of oral histopathology has been added by Dr. Shklar. The result is a very complete summation of current knowledge of oral diseases. The documentation is adequate, and evidence of the author's wide personal experience shines throughout the book. They do not hesitate to express their own judicious opinions clearly and forcefully when they are in conflict with old or new cants and shibboleths.

Perhaps one of the greatest values of this volume is the way in which it points out gaps in knowledge in this special field. For example, the histologic diagnosis of oral lesions sometimes leaves much to be desired, except in the case of neoplastic lesions. Nevertheless, there should be no hesitancy in taking biopsies in any obscure mouth disease; it is a simple procedure, rarely involving any risk. Bullous lesions are often very difficult to differentiate if not accompanied by skin lesions, but further broad experience may enable pathologists to sharpen their criteria greatly. Further studies are needed on the bacterial and yeast flora of the mouth; except in occasional clear-cut infections, such studies are often uninformative with present methods.

To anyone familiar with the difficulties of obtaining adequate photographs of oral lesions, because of highlights and varying depths of focus, the generally superior level of the pictures in this volume is most welcome. The inclusion of many representative photomicrographs adds much.

In short, I would be greatly surprised if this excellent work did not find wide appeal among dentists and physicians, whether of generalist or specialist persuasion. The title of the volume does not, perhaps, do it full justice, because

the text includes descriptions of the systemic and dermatologic manifestations of a large number of diseases which regularly or occasionally produce oral lesions. There is much, also, about diseases and malformations of the teeth and facial bones. The authors have approached their subject with commendable breadth. The book should, also, serve as a stimulus to investigators in the field of oral pathology and physiology, of whom there are still too few.

Donald M. Pillsbury, M.D.
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Preface

There are several reasons that have prompted us to present a new treatise on oral mucous membrane disease at this time. In the past ten years there have been considerable advances in the field of stomatology on both diagnostic and therapeutic levels. In the departments of oral medicine and oral pathology at Tufts University School of Dental Medicine and through our associations with a variety of large teaching hospitals, we have had the opportunity of studying a very large number of cases of oral mucosal disease. We have also been engaged in extensive investigative work on oral mucous membrane and its reactions to local and systemic influences. Recent contributions in the field of stomatology can be listed under five main headings.

1. *Significant Advances in the Therapy of Oral Mucous Membrane Diseases.* Apart from the use of antibiotics in bacterial infections the most valuable new therapeutic agents have been the corticosteroid drugs and the antimycotic agents. The corticosteroids have completely revolutionized the management of oral mucosal diseases and it is only in recent years that definitive information is being acquired as to their optimal use, side effects and contraindications. The corticosteroids can effect spectacular therapeutic results in erythema multiforme, drug reactions, and severe trauma such as radiation burns. Oral lesions of pemphigus respond as the disease itself is controlled by systemic corticosteroids. Aphthous stomatitis has been shown to be helped with local application of corticosteroids in the form of ointment or local intralesional injection.

Among the antimycotic agents, mycostatin has been shown to be effective against monilia, and amphotericin B appears to be the first drug effective against such rare mycotic infections as mucormycosis.

Lesions of discoid lupus erythematosus have been shown to respond well to chloroquin.

In addition to drug therapy there have been advances in the treatment of invasive oral carcinoma by the use of megavoltage radiation therapy.

2. *Advances in Diagnostic Procedures.* These can be related to improvement in several diagnostic disciplines as well as the evolution of new technics.

(*a*) Advances in our knowledge of the histopathology of mucous membrane diseases has offered opportunities for the diagnosis of diseases such as pemphigus based on the findings of acantholysis in biopsy sections. Biopsy for the diagnosis of pemphigus lesions of oral mucosa is now routine. The histopathology of discoid lupus erythematosus, lichen planus and a variety of oral lesions has been further clarified in recent years.

(*b*) Oral cytology and smear technic has been shown of value in the diagnosis of pemphigus and viral disease such as herpetic stomatitis. Its role in the diagnosis of early mouth cancer is being explored and defined.

(*c*) Histochemistry is being utilized in the diagnosis of some diseases. The oral lesions of chronic discoid lupus erythematosus are well demonstrated on biopsy with the periodic acid-Schiff technic for acid mucopolysaccharides. This technic is now used routinely in our laboratory whenever a possibility of lupus erythematosus exists. Enzyme studies on fresh frozen tissue specimens have been of great interest in their suggestion of altered metabolic patterns in leukoplakia and in malignant neoplasms. Enzymes such as nonspecific esterase and succinic dehydrogenase show notable reduction in activity and these reactions may become useful as tests for early malignant lesions.

3. *Advances in our Understanding of the Etiology of Oral Disease.* The role of psychosomatic factors in the etiology of aphthous stomatitis and lichen planus is becoming well established so that a great deal of confusing information in the literature can now be under-

stood. The establishment of herpangina as a distinct oral disease of viral origin has reduced the confusion concerning the therapy and management of so-called 'strep throat' or 'septic sore throat.'

Extensive animal investigation has helped to clarify the etiology of such conditions as chronic periodontal disease (pyorrhea).

The reaction of oral mucosa to nutritional deficiency, radiation, hormonal disturbances, has also been studied in extensive animal experimentation. The hamster buccal pouch has offered an opportunity for the study of malignancy of mucosal tissue in an experimental animal. Epidermoid carcinoma can be produced routinely in this tissue by the application of chemical carcinogens such as dimethyl benzanthracene (DMBA), and the various stages of development of the lesion studied. Newer technics such as electron microscopy have been of great interest but have as yet not proven of value in the interpretation of oral mucosal diseases.

4. *Advances in Clinical Studies of Oral Mucosal Diseases.* Advances on a clinical level have been the establishment of certain distinct syndromes of oral and other mucosal or skin lesions. Among these are the Peutz-Jeghers correlation of oral melanosis and intestinal polyposis, the McCarthy-Shklar correlation of pyostomatitis vegetans and ulcerative colitis and a variety of other rare syndromes. Correlations of oral cancer with malignancy elsewhere in the gastrointestinal tract have been made and the reasonably common occurrence of multiple oral carcinomas has made follow-up of oral cancer therapy more stringent. The common occurrence of certain oral lesions in systemic diseases has led to further appreciation of the diagnostic importance of oral manifestations in systemic disease. The gingivitis seen in monocytic leukemia and the severe periodontal disease in diabetes has been described many years ago. However, the smooth atrophic tongue may be indicative of one of a large variety of systemic conditions including vitamin B deficiency, iron deficiency anemia, pernicicus anemia, sprue and the Plummer-Vinson syndrome.

5. *New Disease Patterns due to New Etiologic Agents.* The number of drugs in use today has increased markedly over the past few years and a large variety of oral lesions as a manifestation of drug reaction has been categorized. Oral mucosal reactions to various ingredients of prepared foodstuffs, mouthwashes, toothpastes, may also be expected as pharmaceutical firms vie with one another to introduce new ingredients into their products to render them more effective.

Much of this material in this book is presented to senior dental students as a course in oral medicine. The course was first presented at Tufts Dental School in 1926 by Professor Francis P. McCarthy and was the first established course in oral medicine to be presented at an American dental school.

There have been several fine treatises on oral medicine in the past. These include Butlin's 'Diseases of the Tongue,' Mikulicz and Kummel's 'Die Krankheiten des Mundes.'

Among current books on oral disease, none limit themselves to a discussion of diseases of oral mucosa. We felt that a need for this type of book existed, and felt that our extensive experience with oral mucosal lesions qualified us to present this material. Stomatology is of great importance to practitioners in both dentistry and medicine. We are in a position as physician and dentist respectively to place the subject in proper perspective for both professions.

Acknowledgements

We are greatly indebted to Francis McCarthy, M.D. for his guidance over the years in the subject of oral mucous membrane diseases. His vast experience has been passed on to us as well as to many generations of students. We hope that we are continuing in some small way his pioneer efforts in stomatology.

Dimitri Afonsky, D.D.S., Ph.D. kindly read the manuscript, offered many helpful suggestions, and permitted the use of Fig. -15 from his collection on nutritional research. Irving Meyer, D.M.D., D.Sc. (Med.) has permitted us to use many clinical photographs from his extensive and varied collections. Among these are Figs. 7-16, 3-13, 15-10, 24-4, 28-57, 29-11, 29-34, and 30-6.

M. Michael Cohen, D.M.D. has permitted us to use a number of clinical photographs of oral mucosal lesions in children. Among these are Figs. 3-2, 17-6, 23-6, and 28-40.

Clinical photographs were also kindly presented to us by Clodomiro Mora, D.D.S. (Fig. 8-18), James Springer, D.M.D. (Figs 14-4*B* and 31-3 and Plate 3-3), Leslie Milne, D.M.D. (Fig. 17-8), Sumner Kalman, D.M.D. (Fig. 30-9), Cleveland R. Denton, M.D. (Fig. 12-25 *A* and *B*).

Max Listgarten, D.D.S. permitted us to use some of his excellent electron microscopic studies of oral mucosa, (Figs. 1-6 and 1-7).

We wish to thank [illegible] Goodman who took many of the photomicrographs. Mel Mendelsohn took many of the photomicrographs and assisted greatly in the preparation of suitable black and white prints from our extensive collection of colour transparencies. Robert Ullrich executed the fine drawings.

We wish to express appropriate thanks to Miss Mary Peluso who typed the manuscript.

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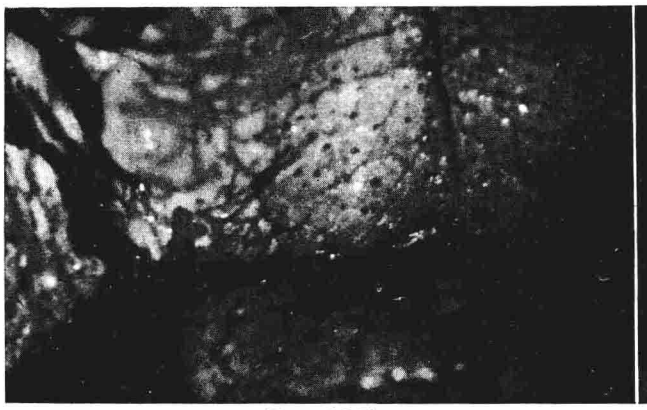

FIG. 12-7

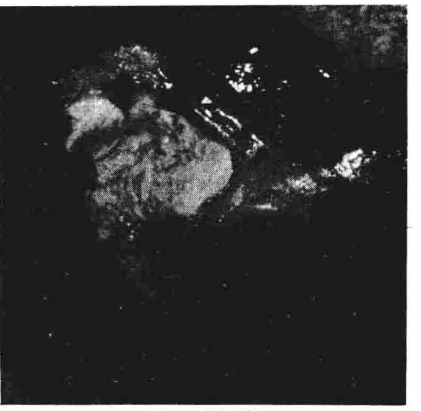

FIG. 12-8

FIG. 12-7. Extensive leukoplakial involvement of the entire oral mucosa in a forty-eight-year-old male, a habitual heavy smoker. The hard palate is severely involved as is the buccal mucosa. The pores on the palate represent the openings of the ducts of the palatal mucous glands.

FIG. 12-8. Solitary area of leukoplakia in an edentulous fifty-two-year-old male. Note the folded, wrinkled character of the thick plaquelike lesion.

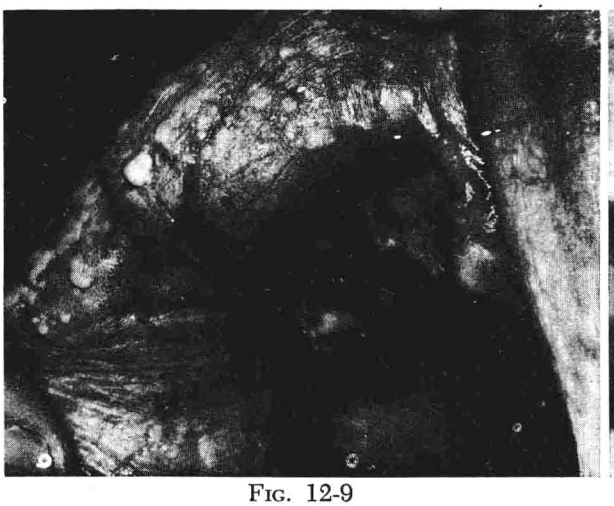

FIG. 12-9

FIG. 12-10

FIG. 12-9. Leukoplakia of the buccal mucosa in sixty-two-year-old male who was a heavy smoker for many years. Note the generalized involvement with localized excrescences. The edentulous maxillary alveolar mucosa presents leukoplakial involvement with areas of ulceration. Biopsy revealed extensive dyskeratosis.

FIG. 12-10. Extensive leukoplakial involvement of edentulous alveolar ridge mucosa. Biopsy revealed notable dyskeratosis.

and granular. Deep fissures and erosions are apparent, with areas in which the mucosa appears ulcerated. Occasionally warty proliferations are seen to arise in these lesions, giving a verrucous texture to the lesion. The color in these lesions may be brown in areas, although the bulk of the lesion is chalky or dull white. Malignant tumors often arise in this type of lesion and appear as an area of tissue proliferation (Figs. 12-13 to 12-15) or as a zone of increased induration.

Symptoms. The symptoms of leukoplakia are vague. Areas of slight involvement are usually asymptomatic and are discovered upon

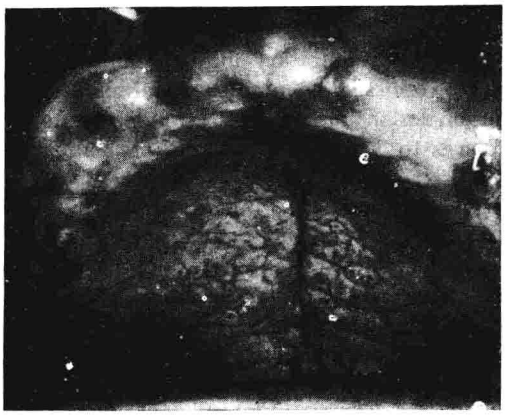

FIG. 12-11. Moderate palatal leukoplakia in an edentulous forty-year-old male (so-called "smoker's palate").

FIG. 12-12. Severe palatal leukoplakia. Note the thick plaques and the reddened areas representing the glandular duct openings.

FIG. 12-13

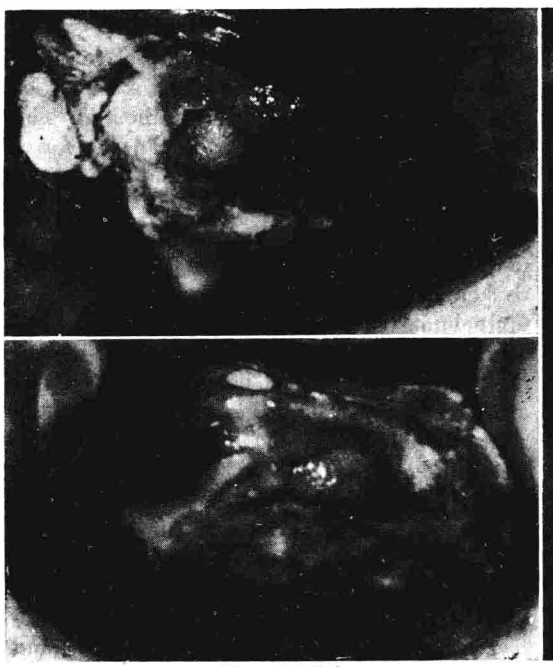

FIG. 12-15

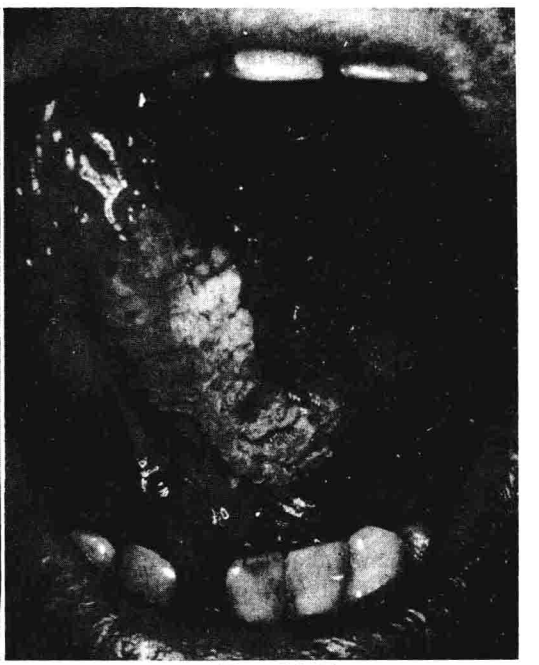

FIG. 12-14

FIG. 12-13. Extensive leukoplakia of the buccal and alveolar mucosa in a sixty-eight-year-old male, with development of carcinoma within the zone of leukoplakia.

FIG. 12-14. Leukoplakia of the ventral surface of the tongue with carcinoma directly adjacent and posterior to the leukoplakial lesion.

FIG. 12-15. Leukoplakia of palate, alveolar ridge mucosa, and mucobuccal fold area with carcinoma forming as a tumor mass.

routine dental or medical examination. In areas of moderate involvement there may be a slight itching or burning sensation, particularly in reference to the tongue. A sensation of dryness may also appear in diffuse involvement. In severe involvement the induration produces loss of normal tissue mobility, and this feature leads to obvious minor distress in relation to the tongue. The rough surface of these lesions also leads to such habits as rubbing the tongue over the leukoplakia area.

Histopathology

The microscopic features of oral leukoplakia show considerable variation. In general, the histopathologic picture may represent one of two reasonably well-defined groupings. In the first there may be various combinations of hyperkeratosis, parakeratosis, acanthosis; with minimal inflammatory infiltration into the underlying connective tissue, or notable inflammatory infiltration. In the second group there may be increased keratinization, but the characteristic feature is a dyskeratosis or an abnormal orientation of epithelial cells with increased chromaticity and obvious cellular atypism. This histopathologic picture is to be regarded as a definite premalignant lesion, is to be considered as carcinoma in situ, and is to be treated as such. The different patterns may be graded 1 to 4 following the terminology of McCarthy, with grade 4 representing the dyskeratotic lesions.

The severe clinical involvement may represent the dyskeratotic lesion microscopically, but this correlation does not hold consistently, and completely innocuous appearing clinical lesions may demonstrate dyskeratosis and early malignant alterations microscopically. For this reason all leukoplakial lesions must be biopsied, and a microscopic diagnosis must be correlated with the clinical lesion before an intelligent treatment plan can be formulated.

The microscopic picture of leukoplakia tends to show one of the following conditions:

Simple Hyperkeratosis. There is an increased width of the stratum corneum of the mucosal stratified squamous epithelium. This may appear either as a hyperkeratosis or as a parakeratosis. With the hyperkeratosis, there may be an accentuation of the stratum granulosum. Acanthosis and some extension of rete pegs may be apparent, particularly in lesions of the alveolar mucosa and tongue. Chronic inflammatory infiltration into the underlying connective tissue is minimal or absent. This type of lesion represents a simple keratotic response to some mild irritant or stimulant (Fig. 12-17).

Hyperkeratosis and Inflammation. In this reaction there is hyperkeratosis and often notable inflammatory infiltration into the underlying connective tissue (Figs. 12-16, 12-18). The infiltrate consists of lymphocytes, plasma cells, histiocytes, and scattered polymorphonuclear leukocytes. Dilated capillaries are often in evidence. There may be extension of rete pegs, and some hydropic degeneration may be seen in the stratum spinosum.

In lesions of the lower lip and hard palate (smoker's palate), there is an involvement of the palatal mucous glands characterized by acinar distention and ductal dilatation (Figs. 12-11, 12-12).

The degree of keratinization is variable. The stratum corneum may be as thick or thicker than the rest of the epithelium. The thickness of the keratin layer can be correlated with the white opacity and the raised appearance of the clinical lesion.

Hyperkeratosis and Dyskeratosis. In addition to a hyperkeratosis there is evidence of dyskeratosis or an abnormal orientation of the epithelium with cellular atypism. The width of the stratum corneum may be very great, or it may be minimal. The notable alterations are seen in the stratum germinativum and the stratum spinosum. There is a lack of cohesion between epithelial cells, and the tonofibrils appear well defined as the cells separate. The clear demarcation between the different zones is absent, and the deeper staining nuclei of the basal layer are no longer outlined. Large bizarre cell forms are in evidence. The nuclear-cytoplasmic ratio appears altered, and increased mitotic activity may be noted. The connective tissue is infiltrated with chronic inflammatory cells, and there is not the usual clear separation between epithelium and connective tissue at the basement membrane zone. The epithelium and connective tissue appear to blend into one another. However, there is no obvious invasion of the epithelium into connective tissue. This type of leukoplakia reaction will eventually give rise to a

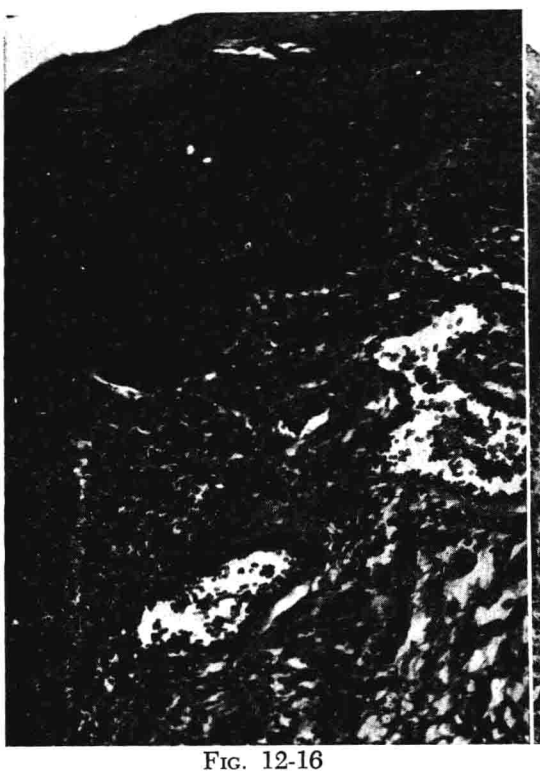

FIG. 12-16

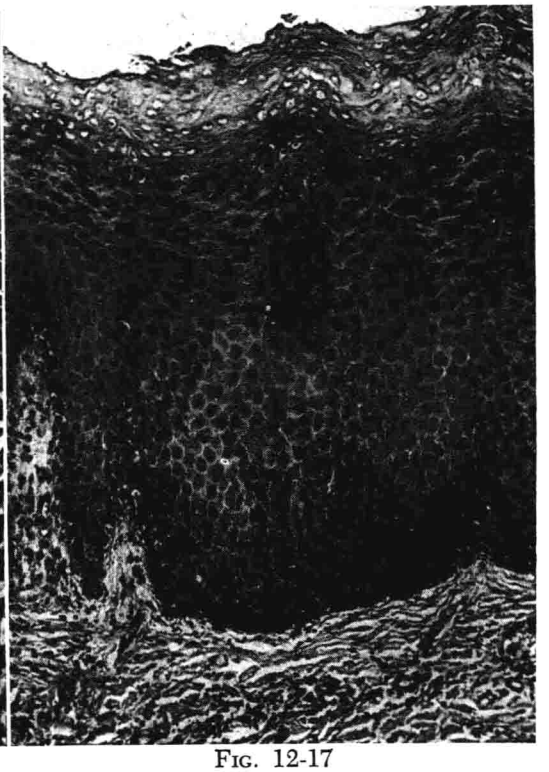

FIG. 12-17

FIG. 12-16. Leukoplakial lesion showing hyperkeratosis and notable inflammatory infiltration into the underlying connective tissue. Intense vascular engorgement is also evident.
FIG. 12-17. Hyperkeratosis.

frank epidermoid carcinoma (Fig. 12-19) and is to be considered a definite premalignant lesion or a carcinoma in situ.

Etiology

Several factors appear to be of importance in the cause of leukoplakia. Among local factors may be listed occlusal problems and chronic irritation. Occlusal problems would include a variety of conditions in which the buccal mucosa, tongue, or lower labial mucosa is constantly irritated by the teeth. Malocclusion is one important condition in reference to this problem. The maxillary and mandibular teeth do not meet in harmonious relationship at an even occlusal line, and the teeth may scrape along the buccal mucosal tissue in the act of mastication. Individual teeth out of alignment in the dental arch may impinge on the mucosa of the cheek and tongue.

Occlusal problems would also refer to occlusal traumatic habits. These may be of a neurotic type or may be a response to inadequate stimulation of the teeth because of malocclusion. Neurotic habits may cause severe irritation to the oral mucosa. Tongue or cheek biting, thrusting of the tongue against the teeth or against labial mucosa are common habit patterns.

Local irritation refers to traumatic influences such as ill-fitting dentures, overhanging crowns and fillings, and poor restorative dentistry in general. Ill-fitting, moving dentures are a source of severe irritation to mucosa, and the irritation is constant. Smoking is to be regarded as an irritant, presumably because of the drying effect on the mucosa, the products of combustion, and the heat. The heat would refer to the pipestem resting on the lower labial mucosa. Local irritation, including smoking, is to be regarded as the primary exciting cause of leukoplakia. These exciting factors presumably must act in a susceptible

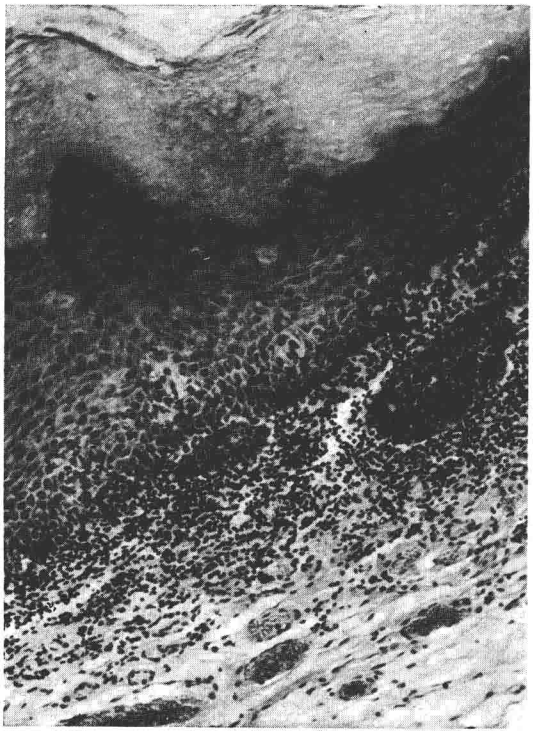

FIG. 12-18. Notable hyperkeratosis with some extension of rete pegs.

host, and heredity doubtless plays an important role in determining the individual's susceptibility or resistance to the development of leukoplakia. Systemic predisposing factors or conditioning factors may be hormonal alterations and nutritional deficiencies. Estrogen deficiency may determine the susceptibility of females at the menopause. Vitamin-A deficiency can produce a hyperkeratosis in experimental animals, but this reaction has not been adequately demonstrated in human beings, and therapy based on this assumption is not justified at present.

Continuous irritants such as heat and spicy foods may be a factor. Occasional individuals are able to drink extremely hot beverages (coffee), and the mucosa must react to protect itself against injury. Irritating mouthwashes may occasionally be implicated. Syphilis may be responsible for leukoplakial lesions of the tongue secondary to the atrophic glossitis of tertiary syphilis. The glossitis is apparently more highly susceptible to the action of local irritants in the mouth. Furthermore, many cases of glossitis develop into carcinoma. The number of syphilitic lesions of the oral mucosa is, however, negligible, and the importance of

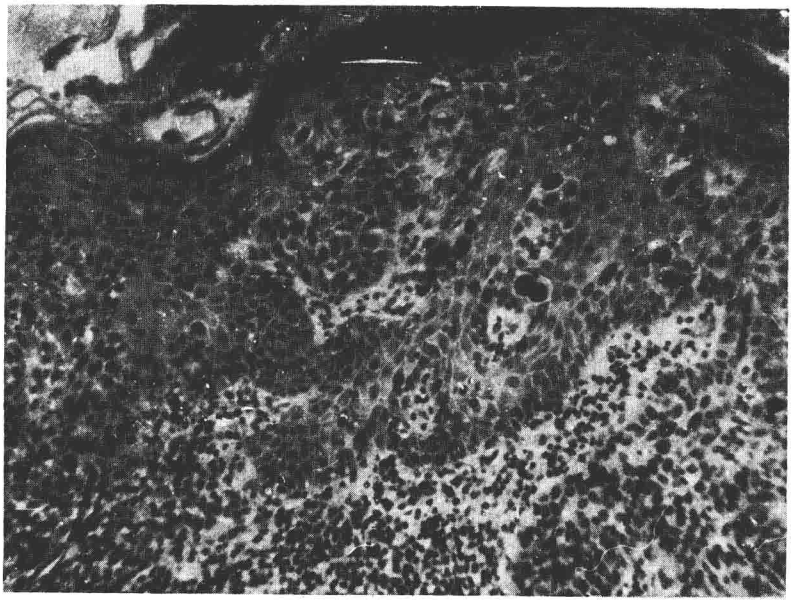

FIG. 12-19. Parakeratosis with notable dyskeratosis. The epithelial cells appear to lose cohesion; the epithelial–connective tissue boundary is indistinct. Large bizarre cells are in evidence with hyperchromatic nuclei. This lesion is to be considered carcinoma in situ.

syphilis as a causative factor in leukoplakia is to be minimized.

In summary, the causes of leukoplakia can be listed as follows. The systemic factors have not been adequately clarified at present.

Exciting (local)	*Predisposing (systemic)*
Local irritation	Heredity
Sharp, malposed teeth	Hormonal factors
Ill-fitting dentures	Estrogen deficiency
Poor restorations	Nutritional factors
Occlusal disharmony	
Occlusal habit	
Smoking	
Thermal factors	
Irritant foods, spices	
Irritant chemicals (Mouthwashes, etc.)	

Diagnosis

The diagnosis of leukoplakia is made on the basis of clinical observation. The grade or type of leukoplakia and the possibility of a premalignant lesion can be determined conclusively only on the basis of microscopic studies. The clinical picture may suggest a premalignant or dysplastic lesion, but only biopsy can confirm this. Often a small innocuous appearing area of leukoplakia may represent a premalignant or even a malignant lesion. Biopsy is imperative in cases of leukoplakia. In the diffuse type involving large areas of the mouth, two or multiple representative biopsy specimens may be desirable. In general, we feel that leukoplakial lesions do not alter microscopically except in rare cases. A simple hyperkeratotic lesion does not change into a dyskeratotic lesion. Presumably this type of change would require a cellular mutation rather than a simple hyperkeratotic response to some irritant. Therefore, therapy will be predicated upon the microscopic appearance of the lesion and the presence or absence of dyskeratotic changes.

Differential Diagnosis

Lichen Planus. Plaque-type lesions of lichen planus may resemble leukoplakia very closely. If the papular nature of the lichen planus lesions cannot be discerned, then biopsy may in some cases reveal the classic pattern of lichen planus. Lichen planus may present skin lesions. Leukoplakia is a localized lesion confined to the oral cavity.

Discoid Lupus Erythematosus. Chronic discoid lupus erythematosus may present oral lesions somewhat similar in appearance to the initial localized lesions of leukoplakia. Skin lesions are usually present in lupus, and a biopsy of the oral lesion will reveal a characteristic pattern of perivascular inflammatory infiltration and collagen degeneration as well as hyperkeratosis and hydropic degeneration of the stratum germinativum.

Edema (Leukedema). Occasionally edema of the buccal mucosa along the occlusal line of the teeth may present a white-gray appearance resembling the initial lesions of leukoplakia. Biopsy will reveal an absence of hyperkeratosis and considerable edema of epithelial cells, particularly in the stratum spinosum.

Carcinoma. An epidermoid carcinoma may resemble a lesion of leukoplakia, usually of the severe localized variety with induration. Biopsy will reveal the characteristic features of a malignant lesion.

Traumatic Lesions. Either chemical or thermal traumatic lesions may appear as a white raised area because of necrosis of the surface epithelium. This white surface slough can be easily wiped off with a sponge or wooden throat stick, leaving a raw ulcerated area.

Moniliasis. The lesions of acute moniliasis or thrush may present as white plaques and resemble leukoplakia superficially. These areas represent extensive overgrowth of *Monilia albicans*, and the mycotic organisms invade and destroy the epithelium. Smears will reveal the organisms either in spore or mycelial patterns. The monilial plaque areas are easily scraped off the mucosa, leaving an ulcerated zone.

Therapy and Management

Management of leukoplakia depends upon microscopic diagnosis.

If there is evidence of dyskeratosis or early malignant alterations, the lesion is to be considered as an early preinvasive epidermoid carcinoma. Current therapy would involve surgical removal of the lesion with a reason-

able margin of normal tissue. A "stripping" operation is preferred by many surgeons, and this procedure is acceptable since the lesion is not invasive and does not penetrate deeply into underlying connective tissue. Electrosurgery may be used as well. Radical surgery is not indicated for this type of lesion. Radiation is contraindicated. Its effectiveness in treating leukoplakia is questionable, and the possible complications in relation to mucosa and bone may be considerable. Following surgical therapy the patient must be warned against smoking and all oral irritation. Obviously he is a susceptible individual and will again develop leukoplakia or carcinoma if the mucosa is irritated.

If there is no evidence of dyskeratosis microscopically, the lesion may be considered a simple response to irritation of the oral mucosa. We are not justified in placing a premalignant connotation upon this type of lesion. Therefore, surgical removal is not necessary. All irritants should be removed if possible. Obvious dental irritants, sharp teeth, and ill-fitting appliances should be corrected. Smoking should be reduced. Cessation or even reduction of smoking often results in disappearance of the leukoplakial lesion.

Vitamin-A therapy, based on animal experimentation, has not proved of value, and keratotic lesions in human beings resulting from vitamin-A deficiency have not been demonstrated. Multivitamin supplements have not been found to be of value in the therapy of leukoplakial lesions. Estrogenic hormone may increase the resistance of the tissues to leukoplakial involvement in menopausal females; but this therapeutic approach is not suggested unless the lesions are particularly severe and widespread. The carcinogenic potentialities of estrogenic hormone indicate its use only in situations of sufficient gravity.

With regard to therapy, the removal of local irritants must be of primary importance. It is well known that a denture will protect the palatal mucosa from the development of leukoplakia by offering a physical barrier to the irritating smoke. For this reason there is no contraindication to placing a well-fitting denture over areas of palatal leukoplakia. In most cases the leukoplakia will regress, provided that it has been shown to be of the simple hyperkeratotic variety.

Hereditary Keratosis

White Sponge Nevus

In 1935 Cannon[23] described as "white sponge nevus of the oral mucosa" a diffuse grayish-white lesion of the oral mucosa. The cheeks, lips, lateral borders of the tongue, palate, gingiva, and floor of the mouth were characterized by a spongy whitish mucosa. Lesions of the labia, vagina, and rectum were also present and were essentially similar to the oral lesions. The lesions were described as being spongy and soft, asymptomatic, and present since birth. The oral lesions on microscopic examination revealed parakeratosis, dyskeratosis, and edema.

Similar cases have been reported since this initial report, and a variety of terms have been used. Congenital leukokeratosis was the term used by Ludy and Shirazy.[28] Congenital keratosis,[31] pachyderma oralis,[27] familial white folded hypertrophy of the mucous membranes,[25] white folded gingivostomatitis,[26] oral epithelial naevi[24] were terms used by others. Zegarelli et al.[34,35] have recently reviewed the 15 cases in the literature and reported on 8 additional cases. The disorder apparently may appear at birth, in infancy, or in childhood and reaches full severity at puberty. From the cases studied it appears that the condition is a hereditary or familial disturbance, reaching maximal severity at adolescence and not undergoing further alteration.

Clinical Manifestations. The lesions appear as gray-white spongy areas of involvement with fissures and folds. Superficially the lesions resemble initial diffuse leukoplakial involvement, but the lesions tend to be spongy and soft upon palpation. The lesions are usually seen in young patients, and the hereditary background is suggested by the involvement of siblings or parent and child. The entire oral mucosa tends to be involved, with the most obvious lesions on the buccal mucosa, floor of the mouth, and ventral surface of the tongue (Figs. 12-20, 12-22). The lesions are totally asymptomatic.

Histopathology. Microscopic examination of tissue from cases of hereditary keratosis reveals some acanthosis and edema or vacuolization of cells in the stratum spinosum. Parakeratosis is also commonly seen as a feature of