

Oral Mucous Membrane Lesions

Pathologic Features

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FROM A HISTOLOGICAL and embryological point of view, the mucosa of the oral cavity is similar to the skin, but it is subjected to a more complex and inconstant environment. The complex liquid medium of the saliva, coupled with a highly labile microbiological flora combines to produce unusual lesions of local origin and to modify decidedly the systemic and particularly the dermatological lesions that occur in the mouth.

HISTOLOGY

Anatomically there are three types of mucosa and all have distinct clinical and histological features: (1) Attached or masticatory mucosa, (2) free or thin mucosa and (3) dorsal mucosa of the tongue. The extent of the oral mucosa for the purpose of this paper is from the vermilion border of the lips posteriorly to the anterior tonsillar pillars and to the sulcus terminalis of the tongue. Some lesions may be found only on one of the three.

The attached or masticatory mucosa is found on the hard palate and it also forms the gingiva of the maxilla and the mandible. Both the epithelium and the lamina propria are thick and in the latter there are heavy interwoven collagen bundles which often fuse directly with periosteum. Only in the posterior part of the hard palate are minor salivary glands found. This mucosa is not easily displaced and it withstands trauma well.

The thin or free mucosa is found on the lips, buccal surfaces, soft palate, floor of the mouth and the ventral surface of the tongue. The epithelium is thin and normally exhibits no keratinization. The lamina propria contains loose collagen and many elastic fibers. Mucous glands are found in most areas, the greatest concentration being on the lips and soft palate. As this mucosa is flexible and resilient, it "escapes" from many physical irritants.

The dorsum of the tongue is a unique membrane because it possesses no submucosa and voluntary muscle attaches directly into the lamina propria. In addition, there are papillae (filliform, fungiform, circumvallate, foliate, and conical) which are sup-

• Lesions of the oral mucous membranes often present bizarre, clinical and histological patterns because of the salivary environment and the complex organization of the various membranes. Diagnosis of oral lesions depends primarily on tissue biopsy, which must be modified in some cases from the usual dermatological technique. Exfoliative cytology has become an important adjunct to biopsy. Congenital, keratotic, malignant and dermatological lesions are those which are most easily diagnosed by clinical as well as histopathological and cytological examination.

The first professional examination of an oral lesion is by far the most important because at this time the determination of the correct diagnostic procedure is made.

ported by primary ridges which radiate laterally and anteriorly from the midline. The papillae act as prehensile structures, aid in mastication and support many sensory structures.

DIAGNOSTIC METHODS: BIOPSY AND CYTOLOGY

The two most valuable diagnostic procedures for oral mucosal lesions are tissue biopsy and exfoliative cytology. Bacterial smears and cultures are of limited value because of the great variety of the oral flora.

Biopsy. The conventional scalpel is the ideal instrument and there is little need for punches and special tissue forceps. Because of the flexibility and vascularity of oral tissues, a special needle technique has proved very valuable. (Figure 1.) The tissue may be more firmly held and bleeding is easily controlled.

Cytology. This procedure is not a substitute for biopsy but a valuable adjunct as well as a screening tool. Chief indications for its use are: (1) Benign appearing lesions, (2) highly suspicious lesions when the condition of the patient contraindicates biopsy, and (3) postsurgical and postradiation observations in treated cancer patients. A moistened tongue blade, a spatula, or a swab will usually produce a good cellular smear. (Figure 2.)

CLINICAL AND PATHOLOGICAL CONDITIONS

Pathological entities of most consequence to physicians, especially dermatologists, are outlined

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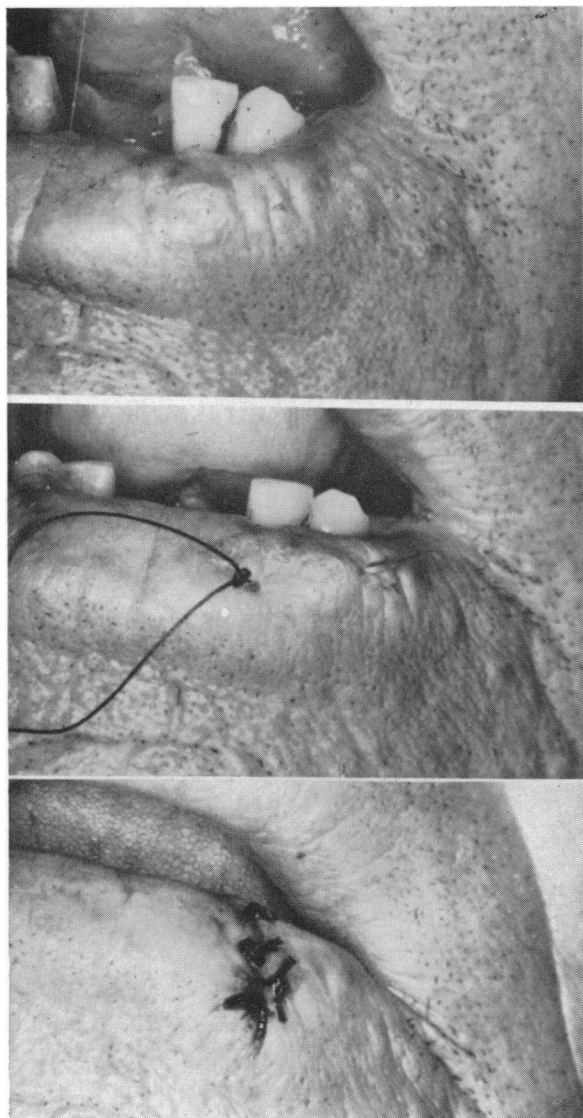


Figure 1.—Biopsy technique utilizing a needle. *Top*: Discrete, slightly indurated lesion of the dry mucosa of the lower left lip. *Middle*: A large curved needle has been placed well beneath the lesion with the entrance of the needle and its emission providing sufficient lateral margins. Because of the flexibility of the mucosa and the underlying muscle, the needle can be placed deep enough to provide a safe surgical margin. *Bottom*: Following excision the primary suture is drawn entirely through the lip and the two sides are accurately approximated. Auxiliary sutures are then placed. The lesion was an early squamous cell carcinoma.

below. (This series of lesions does not include many of the conditions diagnosed and treated most frequently by practicing dentists.)

Congenital and Hereditary Disturbances

There are many developmental defects which affect the oral mucous membrane that are of interest to dermatologists and other physicians. Most of these conditions have little clinical significance but

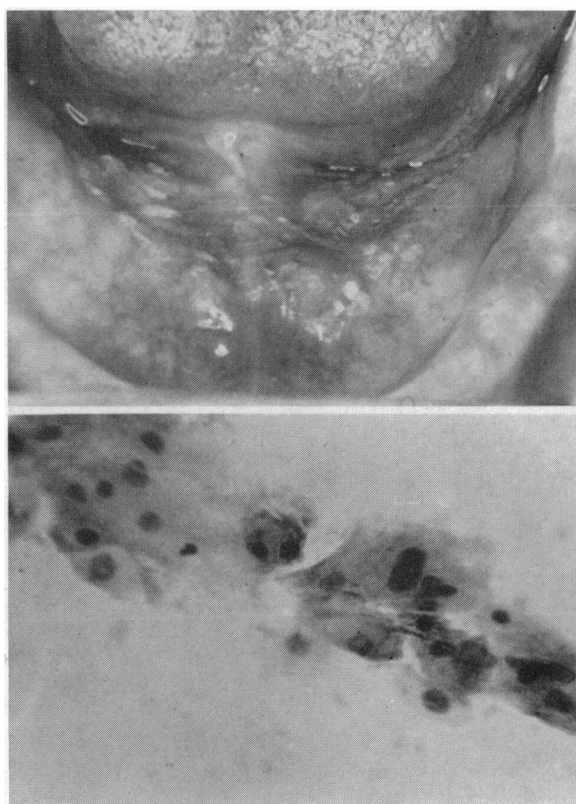


Figure 2.—Cytological evaluation of an atrophic keratotic lesion. The patient was a 60-year-old woman who was receiving an anticoagulant. Atrophic, somewhat fragmented keratosis of the floor of the mouth had been noted for approximately three months, since her remaining mandibular teeth were extracted. Cytological material was obtained from both sides of the midline with a small medicament spatula. This was spread on a glass slide and placed in fixative. The cytological smear ($\times 430$) demonstrates atypical squamous cells with a reduced nucleus-cytoplasm ratio, nuclear pleomorphism, and other features of a low-grade malignancy. Subsequent biopsy was performed in a hospital and confirmed the diagnosis of squamous cell carcinoma.

it is important to recognize the causes and to differentiate them from possibly more serious conditions.

1. *Pigmentation* (melanoplakia). Melanin pigmentation of the mucosa is commonly seen in Negroes and is frequently observed in Arabs, Indians, Greeks, and Italians. It most commonly affects the free mucosa and the facial surfaces of the gingiva. It seldom involves the interdental papillae or the palate, and on the tongue the pigment will occasionally involve the fungiform papillae. Hyperplastic lesions and healing wounds, particularly from periodontal surgical operations, are often devoid of pigment.

2. *Fordyce granules* (Fordyce disease, ectopic sebaceous glands). The teeth are homologous to the hair follicle, but they are not associated with sebaceous glands. Fordyce granules occur in about 82 per cent of the population. They are most commonly

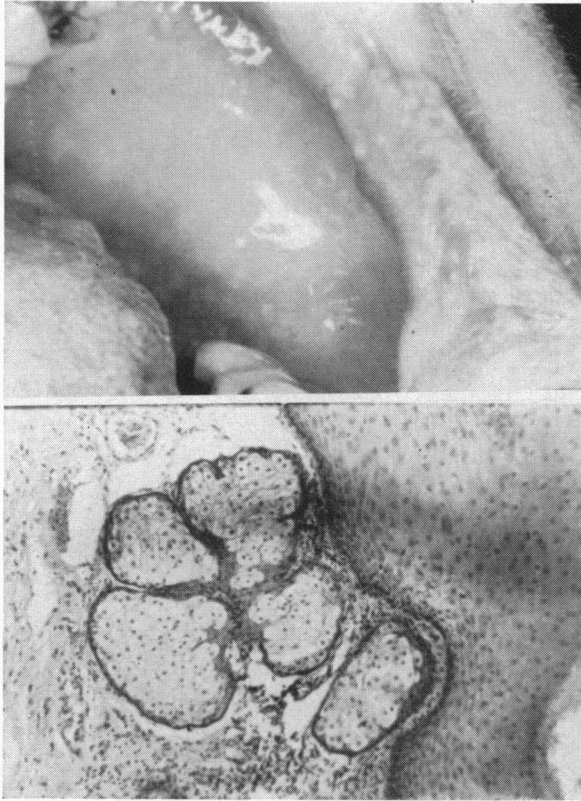


Figure 3.—Fordyce granules of the left cheek with involvement of the dry mucosa of the lower lip. *Top*: The greasy tan spots are most numerous in the occlusal-line area but many involve the upper and lower lip. *Below*: A photomicrograph ($\times 100$) of Fordyce granules which lie in the lamina propria and in the upper portions of the submucosa. These are a group of sebaceous glands which were present in a biopsy specimen of an inflammatory lesion of the buccal mucosa. A few of the inflammatory cells are observed.

seen in adults and the most frequent site is the buccal mucosa and the dry mucosa of the upper lip. The glands are static in size and very few are associated with ducts. These structures are often seen in the "cancer phobe." Tumors are extremely rare and lesions seldom become inflamed despite biting trauma. (See Figure 3.)

3. *White sponge nevus*. This apparently familial condition does not run a true hereditary pattern. It is more frequently seen in the buccal mucosa and in the vestibulae of the maxilla and the mandible. Histologically, there is a remarkably thickened stratum corneum in which keratinization is apparently incomplete and the cells are extremely edematous (Figure 4).

4. *Median Rhomboid Glossitis*. This is a so-called "tuberculum impar defect" and probably results from a failure of the posterior portion of the dorsal ectoderm to fuse in the midline. The clinical lesion is often smooth and devoid of papillae, which makes it appear more erythematous (Figure 5).

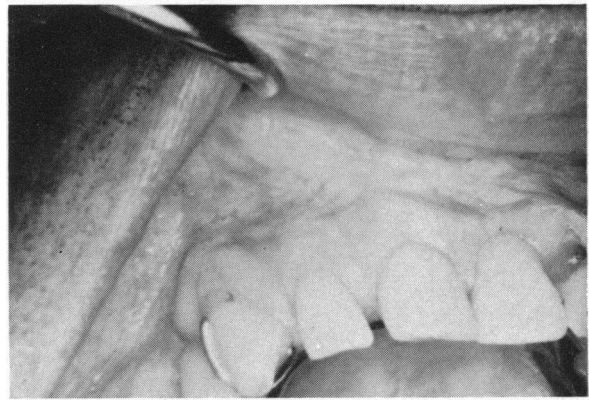


Figure 4.—White sponge nevus. The thin mucosa in this case of a 35-year-old white man shows a white, soft thickening. It is most prominent in the maxillary vestibule. One of the patient's two brothers and his maternal grandfather also had the condition. Biopsy confirmed the presence of a stratum corneum in which there was considerable thickening by parakeratosis with considerable edema in the stratum corneum.



Figure 5.—Median rhomboid glossitis. The patient, a 35-year-old white woman, first became aware of this lesion when it was noticed by her dentist. It was devoid of papillae, was somewhat reddened and nodular.

Keratotic Lesions

Although there are many special and unusual keratotic lesions, only the two main types, hyperplastic and atrophic, are of importance.

Hyperplastic. The hyperplastic keratotic lesions are known variously as leukoplakia, focal-keratosis, diffuse keratosis, keratosis simplex and pachyderma-*or*is. All of these terms have been used for generally similar conditions which are characterized by hyperkeratosis and acanthosis. Inflammatory involvement of the lamina propria is of apparently no significance in the outcome of the condition. Smoking, low grade frictional irritation, direct contact with tobacco, and hot and spicy foods are the most frequent etiological factors. Occasionally dyskeratotic lesions develop and these in turn may terminate in squamous cell carcinoma (Figure 6). Most of these conditions will regress following elimination of the local irritants.



Figure 6.—Keratosis, long-standing, with malignant change. The keratosis of the left lateral surface of the tongue had been present for many years with previous biopsies reporting only "diffuse keratosis." Here, localized induration has occurred in two areas and biopsy revealed early squamous cell carcinoma.

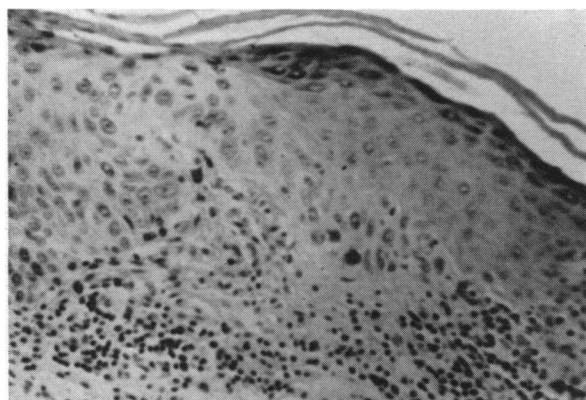


Figure 7.—Dyskeratotic leukoplakia. In the photomicrograph ($\times 100$) there is hyperchromatism, loss of polarity, and pleomorphism. However, the epithelium has not invaded the lamina propria and the basement membrane is intact. Clinically and histologically the hyperkeratosis is even and fairly regular.

Atrophic. Atrophy of the mucosa with keratinization is often described by the same diagnostic terms as the hyperplastic keratotic lesions. These lesions, however, present more of a clinical problem and are frequently associated with sudden dyskeratotic or outright malignant change. Vitamin A deficiency is a frequent factor, but in the floor of the mouth in postmenopausal women this keratosis is a frequent finding. Since the floor of the mouth is the only area of the oral mucosa in which malignant disease is seen as frequently in women as in men, this is an extremely important clinical consideration (see Figure 2). In addition, the Plummer-Vinson syndrome is seen in women, particularly of Scandinavian origin, who have a dry mucosa, irregular keratotic lesions and glossodynia. This syndrome frequently is associated with pharyngeal and oral malignancies.

Dyskeratotic Lesions

Dyskeratotic lesions are usually associated with



Figure 8.—Squamous cell carcinoma of the maxillary tuberosity. This lesion under a denture was treated for two months as a "denture infection" by a chiropractor. Biopsy revealed Grade II squamous cell carcinoma. Note the presence of keratinization and the rolled peripheral margin.

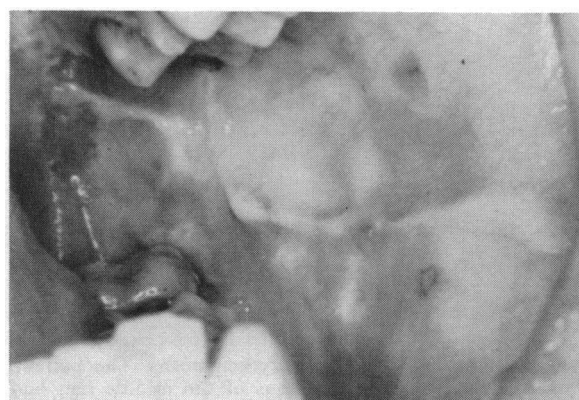


Figure 9.—Stevens-Johnson syndrome. All of the oral mucous membranes are edematous and in many areas large bullae are forming. Considerable ulceration has already occurred in the retromolar area. The patient also had penile lesions.

an increased stratum corneum, but on the free or thin mucosa dyskeratosis will often occur without hyperkeratosis. Dyskeratotic lesions are histologically almost identical to senile keratosis.

Leukoplakia is a term which is generally reserved for the dyskeratotic lesion when it is associated with keratinization. Since there has been considerable confusion surrounding this term, many oral pathologists today prefer to use the term *dyskeratotic leukoplakia* (see Figure 7).

Malignant Tumors

Cancer of the oral mucous membrane is most commonly squamous cell carcinoma. Basal cell carcinoma does not occur as such on the mucous membrane. Adenocarcinoma is predominately in the palate and arises from the minor salivary glands.

Oral lesions of squamous cell carcinoma are responsible for approximately 5 per cent of cancer

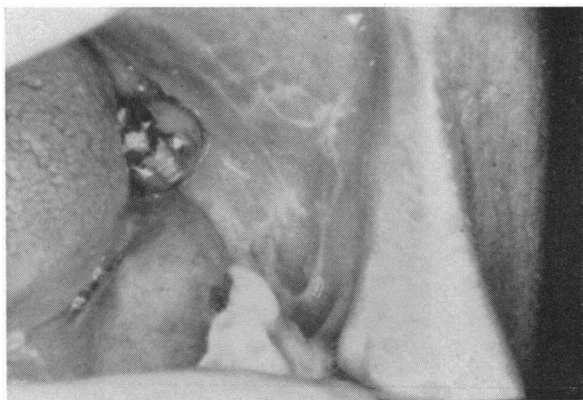


Figure 10.—Lichen planus of the buccal mucosa. The patient has involvement of both buccal mucosae, the soft palate, and the dorsum of the tongue. All of the lesions have a white lacy appearance without a definite pattern. Occasionally, there is erythema between the linear white areas.



Figure 11.—Discoid lupus erythematosus. The patient, an Hawaiian, had typical lesions of the middle face and lesions of the dry mucosa near the commissures. Biopsy of these areas shows typical mucosal lupus erythematosus. The patient also had lesions of the buccal mucosae near the retromolar area.

deaths and such lesions make up approximately 12 per cent of malignant lesions in all other parts of the body. Approximately 85 per cent of intra-oral carcinoma and 94 per cent of all malignant lesions of the lip occur in men. The average age at onset is 55 years. These lesions generally grow by direct extension and metastasis usually is to the cervical lymph nodes, not often to more distant sites. The more differentiated carcinomas are almost always associated with keratinization. (See Figure 8.) The more undifferentiated lesions are frequently not associated with keratinization.

Dermatological Lesions

There are a few skin diseases which frequently have associated with them mucosal changes that give a better clue to diagnosis than do the skin lesions themselves.

Stevens-Johnson Syndrome. This is one of the mucocutaneous-ocular syndromes. In most cases the oral lesions are the most severe and the most dis-



Figure 12.—Moniliasis (candidiasis). The patient received numerous antibiotics for recurrent kidney infections in the three months preceding this picture. A white-pearly lesion occurred previously. The infection responded to nystatin therapy.



Figure 13.—Geographic tongue (benign migratory glossitis). This fissured tongue contains typical white, linear lesions of geographic tongue. Because there is no remarkable coating of the tongue in this case, the lesions are not as dramatic as in some cases. This condition is most frequently seen in patients with fissured tongue and frequently the white linear areas are not observed because of the prominent fissuring. Very frequently the pain of fissured tongue is actually due to the presence of these lesions.

tinctive. Large bullae often leave extensive areas of ulceration which are more painful than lesions of pemphigus. Because of the oral lesions, patients often reach a severe nutritional crisis (see Figure 9).

Lichen Planus. This presents a distinctive linear keratotic lesion (Wickham's striae) which exhibits no pattern of local response to irritation. The buccal mucosa lesions are most distinctive but the lesions can occur in any area. On the gingiva the condition often becomes erosive and is called gingivitis (see Figure 10).

Discoid Lupus Erythematosus. The lower lip and the posterior buccal mucosa are the most common sites. The lesions appear as white, rimmed, erythematous patches (see Figure 11).

Moniliasis. Oral lesions are seldom associated with systemic moniliasis. The lesions occur most of-

ten following broad spectrum antibiotic therapy but the condition often develops in debilitated patients. The pearly white lesions are composed of the bulk of the epithelium expanded by edema and containing many of the organisms (see Figure 12).

Oral Dermatological Lesions

The only lesion in this category is a concomitant involvement of the epithelium and lamina propria called *geographic tongue* or *benign migratory glossitis*. Such lesions are often found on fissured rather than smooth tongues. They appear as linear zones of

whitish-gray edematous epithelium which sloughs slowly, producing a migratory lesion. (See Figure 13.) Histologically many bacteria invade the epithelium and considerable pain can result.

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REFERENCES

1. Bernier, Joseph L.: The Management of Oral Disease, 2nd ed., C. V. Mosby, St. Louis, 1959.
2. Lever, Walter F.: Histopathology of the Skin, 3rd ed., J. B. Lippincott, Philadelphia, 1961.
3. Tiecke, Richard W., Stuteville, Orion H., and Calandra, Joseph C.: Pathologic Physiology of Oral Disease, C. V. Mosby, St. Louis, 1959.

