

ORAL EPIDERMOID CARCINOMA

GENERAL CONSIDERATIONS AND ETIOLOGIC FACTORS

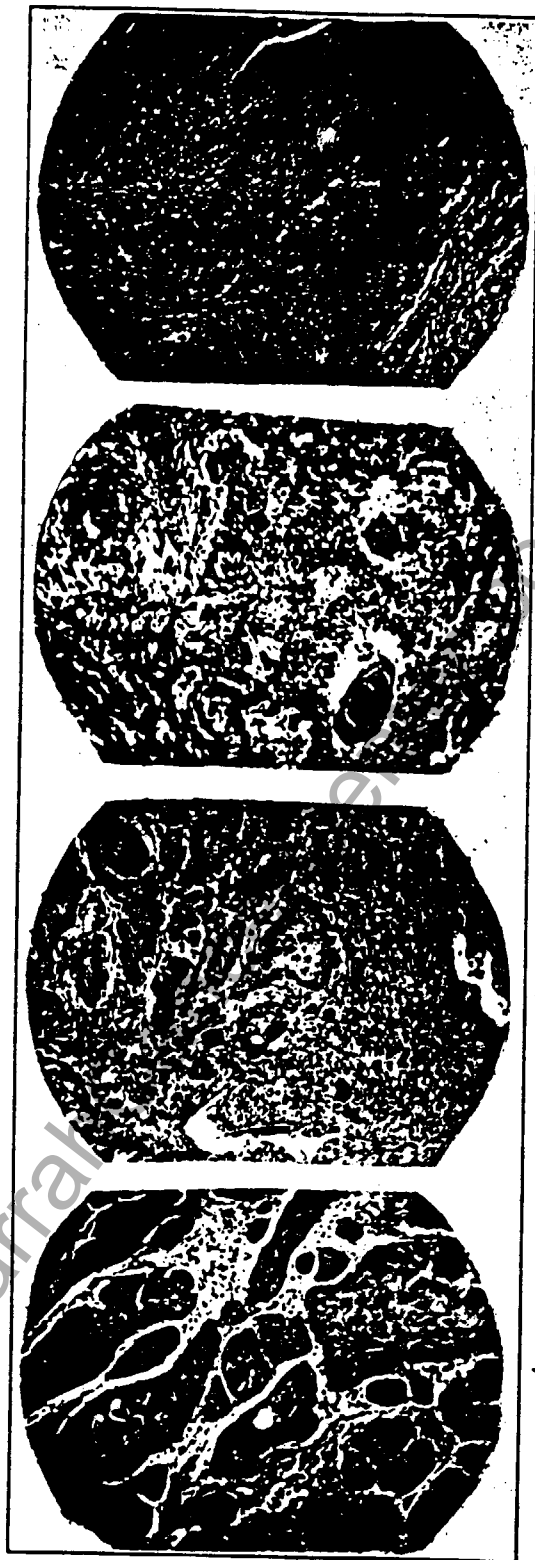
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THE aspects of cancer in and about the oral cavity are somewhat protean. To select properly the best treatment at the present time for the individual patient requires a triumvirate of knowledge—namely, of pathology, of radiology, and of surgery. Surgery, irradiation, or both, are our only weapons of attack. Whenever a cure seems probable or possible, the attack must be planned so as to encompass completely the anatomic as well as the pathologic necessities of the given case. When palliative treatment alone is considered possible, the method is selected which will give the patient the longest period of comfort with the least disability. The life history of the tumor is important in this consideration.

During the past two decades, very considerable addition has been made to our knowledge of epidermoid carcinoma of the tongue and oral cavity in general. The use and development of irradiation methods have markedly influenced ways of treatment. Broders' scheme (Fig. 1) of classification of epidermoid carcinoma in particular has served to emphasize the importance of studying the character of the disease as an aid in determining the prognosis. Pathologic studies along with observation of the irradiation response have been combined in recent attempts to recognize histologic criteria for grouping tumors according to their radiosensitivity. In some instances it has been found that the tumor most susceptible to surgical attack is least susceptible to irradiation and vice versa.

The importance of a more careful selection of the weapons for carcinoma destruction has become increasingly evident. The good therapist, therefore, has come to the realization that he must understand the pathology of the lesion, the possibilities that may be offered by surgical attack, the possibilities to be offered by irradiation treatment, and finally the possibilities to be offered by both surgery and irradiation.

NOTE.—A series of articles which will appear in continued form proposes to cover the field of malignancies as they are seen about the face, mouth, and jaws. This subject is an extremely important one especially to the dentist. Since it is impossible to give an adequate discussion of all phases of the subject in an article or two, it has been thought best to take up the subject in a continuous form and to cover it in its entirety. All efforts will be made to stress the various diagnostic features which are always of paramount importance to the man who has to make the original decision as to the type of lesion. Also an attempt will be made to discuss the pathogenesis and the pathology of the tumors of this region, and finally to take up the principles of irradiation and the surgical methods which one has to know in order to be able to treat the disease. An adequate number of illustrations will accompany these articles. An apology is offered for the triteness of the first article which takes up a discussion of some rather fundamental preliminaries which it seems best to cover in a preface, so to speak, to the more detailed regional discussion.



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 Fig. 1.—A, Epidermoid carcinoma showing a rather marked tendency toward adult cellular differentiation, Broders' Group 1; 75 to 100 per cent adult cellular differentiation.
 B, Epidermoid carcinoma, Broders' Group 2; 50 to 75 per cent adult cellular differentiation.
 C, Epidermoid carcinoma, Broders' Group 3; 25 to 50 per cent adult cellular differentiation.
 D, Epidermoid carcinoma, Broders' Group 4; 0 to 25 per cent adult cellular differentiation.

The pathologist and the surgeon have thus been given a new responsibility. By a study of the microscopic appearance and the clinical course, often the character of the tumor and its probable response to the various types of therapy can be to a certain extent foretold. The plan of treatment must often be altered in accordance with the clinical course, the stage of development, and the irradiation response of the lesion. (Fig. 2.)

Contrary to a somewhat general skepticism, epidermoid carcinoma in and about the face, mouth, and jaws has a relatively good prognosis when due consideration is given all phases of the picture, and when sound methods of attack are adequately employed. Good end-results of treatment of carcinoma in this region depend upon the complete eradication of all malignant cells within and about the local lesion and its tributary lymphatics. Fortunately, in the more adult squamous cell epitheliomas, the collarlike arrangement of lymphatics about the neck serves as a barrier which usually prevents metastasis below the clavicle. In balancing the factors for and against a given



Fig. 2.—Epidermoid carcinoma. Biopsy removed six weeks after radium application. The ulcerating lesion had healed. Shows some round cell infiltration, a moderate amount of hyalinization, and there is some evidence in the field of a few injured but possibly viable squamous carcinoma cells.

method, the same rules will not hold for both the local lesion and the embolically filled tributary lymphatics. Irradiation does not affect metastatic squamous cell carcinomas in the lymph nodes as favorably as it affects the local lesion. As a matter of fact, there is evidence that irradiation very rarely if ever cures adult metastatic squamous cell carcinomas when located in the lymph nodes. Moreover, regarding the treatment of local lesions, it should be mentioned that, when bone is involved, irradiation methods usually do not effect a cure unless bone necrosis is produced. Consequently, as a rule, an excision or a destructive procedure becomes the method of choice.

Irritants to the Oral Mucosa.—Those conditions which produce a chronic inflammatory reaction or cause a chronic inflammatory reaction to continue, practically all are associated with some increase in the incidence of cancer in the oral region. But a considerable amount of proof has now accumulated that conditions which will cause a malignant degeneration in one individual do not necessarily produce it in another. In other words, not only the irrita-

tive factor is important but also the susceptibility of the individual plays a part. As we have no yardstick for measuring either, a discussion of the exact position of the factors must necessarily be somewhat indefinite. In some instances not only the susceptibility factor but several irritative factors apparently contribute their part in the development of a malignant lesion.

Inclement Weather. On the face and the lip even inclement weather has a detrimental effect in many individuals. Cancer of the skin of the face is undoubtedly slightly more common in those leading an active outdoor life. One may mention the tendency of railroad firemen and engineers to show a higher incidence of cancer of the skin of the face. Some keratotic lesion generally precedes for a considerable period of time the appearance of an actual malignant degeneration. Besides the wind, the sunshine may tend to irritate the skin. Farmers seem to show an increased incidence of cancer of the lip. Their lips are often cracked and irritated by the rigorous outdoor life. New mentions the increased incidence of epithelioma of the lip in farmers when discussing the Mayo series.

Tobacco.—Tobacco also has some definite influence in the development of lip and oral cancer. It stimulates the epithelium, produces a chronic hyperemia, local erosions, edema, and lymphocytic infiltrations. In smoking, heat effects may be added. This is especially true in pipe smokers. Tobacco chewers are somewhat more prone to develop cancer where the quid is held against the cheek. Tobacco to a lesser extent affects the posterior tongue, the palate, tonsils, pharynx; and the effects of excessive amounts of tobacco smoke on the larynx have long been emphasized.

Statistics in regard to the part that tobacco plays in producing cancer of the oral mucosa must necessarily be rather indefinite. Tobacco is rather commonly used in lesser or greater amounts. The quantity used is probably an important factor in the development of malignant degeneration. Moreover, individuals who have never used tobacco also develop malignant changes probably due to the factor of susceptibility plus the various irritative factors.

Alcohol. Alcohol has been suggested as a factor. The fact that cancer of the mouth is eight times more frequent in men than in women contributed in the past to the idea that alcohol was of some importance. At present, however, it is thought that the effect of alcohol is ordinarily too temporary to be a factor of importance in increasing the incidence of buccal cancer.

Bacterial Irritation. No one can fail to be impressed with the uncleanness of the teeth in the average patient suffering from cancer of the buccal cavity. There is probably some relationship. Even normally the anterior half of the tongue is covered with papillae to which cling myriads of bacteria. Whether the uncleanness of the mouth somewhat characteristic of the patient with oral cancer is one of cause or of effect is difficult to say. Inflammatory conditions of the gums, such as pyorrhea, may eventually have an indirect relationship to mouth cancer on the basis of being a long-continued irritant. In some individuals the evident mouth infection is probably secondary. Any prolonged chronic irritation possibly increases the incidence of oral cancer in such individuals.

Tartar accumulation may over a long period of time promote a low grade inflammation of the gums. Carious, jagged teeth or poorly built dental appliances almost constantly rub and irritate various parts of the oral mucosa. Chronically inflamed tissue and ulcerations are thus developed which may ultimately undergo malignant degeneration in the susceptible.

Luetic Scars.—The scars of an old syphilitic infection—especially on the tongue—have been blamed for a certain percentage of epithelioma of this region. Fraser places the incidence of syphilis in cases of carcinoma of the tongue as a whole at 42.3 per cent and in carcinomas of the dorsum of the tongue at 78.3 per cent. In various series of malignancy of the mouth the percentage has been estimated from 4 to 90 per cent as having been preceded by luetic scars on the mouth (Meller 3.5 per cent, Fournier 92 per cent). Although undoubtedly the latter percentage is too high, Fraser states that syphilis often precedes leucoplakia and that 90 per cent of carcinoma of the dorsum is preceded by leucoplakia. This figure again is undoubtedly exaggerated. Most observers have found that in somewhat less than one third of oral cancer some evidence of leucoplakia is demonstrable. About 20 per cent of all leucoplakic lesions of the mouth in the series studied by Lund showed evidence of lues. When the patients without a Wassermann test were excluded, the percentage was 30 per cent. Lund found in 1,540 cases studied that the relationship of cancer to syphilis varies greatly according to location. In all locations except the tongue and cheek, the presence of a positive history of syphilis or positive Wassermann test is so low that the incidence may be assumed to be close to the normal incidence in the population, considering the average age and social status of patients having cancer of the mouth. The relationship of syphilis to cancer is much more important in the tongue, falling somewhere between 17 and 32 per cent (Lund).

Another interesting feature of Lund's study is that the pathologic index or grading of the cancers of the tongue developing in syphilitic lesions indicates a higher degree of malignancy than was noted in nonsyphilitic cases. No conclusions could be reached for other locations.

Probability of an Ulcerous Lesion of the Mouth Being Due to Syphilis in Those of Cancer Age. Of interest to the frequency of syphilis alone, when an ulcer in the mouth is found in an elderly individual and the question of diagnosis arises, are the observations of Lund from the Colles P. Huntington Hospital and the Massachusetts General Hospital. In 1,518 cases with ulcerous lesions of the mouth seen in a cancer clinic, only 9 were found in which the single diagnosis of syphilis of the mouth was made (Lund). These did not include leucoplakia. The locations were: tongue 4, tonsil 2, palate 2, and lip 1. The types of lesions were ulcerative gumma 6, gumma 1, multiple ulcers and fissures 1, glossitis 1. The sex incidence was male 6 and female 3.

Leucoplakia. The importance of leucoplakia as a precursor of malignant degeneration of the oral mucosa seems definitely established in all series of patients. (Fig. 3.)

Fournier and von Bergmann originally estimated that leucoplakia preceded in about 30 per cent of cancer of the buccal cavity. No evidence has been

presented to this day that would lead one to believe that these observers underestimated the importance of leucoplakia as a precursor of oral cancer. All leucoplakias should be destroyed if their diffuseness does not contraindicate such a radical procedure. In the latter case certainly careful and prolonged observation should be insisted upon, as the slightest tendency to ulceration usually means a malignant change.

Papillomas.—Papillomatous projections of the oral mucosa—especially if subjected to trauma or prolonged irritation—for one reason or another undoubtedly contribute to a certain share of buccal epithelioma. (Fig. 4.) Butlin



Fig. 3.—(High magnification.) Leucoplakia of the mouth showing the increased thickness of the epithelial layer. The epithelial cells show no tendency to infiltration.

states that all papillomas of the mouth should be removed without procrastination because of their tendency to undergo malignant change. An indolent crack near the base of such a lesion is especially likely to be an early malignant change.

Summary of Importance of Irritative Factors.—It can truthfully be said that in the neighborhood of 75 per cent of epidermoid carcinoma of the buccal cavity is preceded by some one of these precancerous factors, and conceivably if it were possible to eliminate adequately all such influences or destroy all such early lesions, the incidence of epithelioma of the oral cavity would be reduced very materially.

Precancerous Lesions.—Before discussing the fully developed malignant lesions of the oral cavity, it is well to say a word concerning the various precancerous lesions.

As the mouth cavity is examined commonly by both physician and dentist, each should be schooled in the recognition of the so-called precancerous lesions, first, because the dividing line between the precancerous and the early cancerous lesions is not always distinct clinically and, second, it is well established that epidermoid cancer often develops in unhealthy or abnormal epithelium. Certainly both avoidable prostration and uninformed advice and treatment do much to keep cancer of the tongue and oral cavity a most dreadful and fatal disease.



FIG. 4.—Section of a warty papilloma of the mouth. No absolute evidence of infiltration is seen.

One cannot overemphasize the importance of localized thickenings, indent cracks, papillary structures, as well as chronic ulcers, irritative appliances, and generally, uneven teeth.

Importance of Biopsy.—When in doubt of the diagnosis, excision followed by microscopic examination is a reliable procedure that must be insisted upon. When the lesion is evidently precancerous, the irritative factor should be eliminated especially in those individuals of the cancer age, and periodic observation should be advised. When the lesion is an early malignant degeneration, a great service has been done for the patient, for in such cases proper treatment offers a good chance of a permanent cure.

Importance of Early Diagnosis.—The importance of early diagnosis of buccal malignancies cannot be too definitely stressed. When one considers, on the one hand, the improbability of successful treatment in the late stages, the suffering of the victim, and the invariable outcome when treatment is unsuccessful, and, on the other hand, the long periods of no visible evidence or perhaps even the lasting obliteration of the disease that may follow proper treatment at an early date, the importance of early diagnosis and early treatment cannot be overestimated. Nowhere else, save on the skin, can precancerous or early cancerous lesions be so easily observed. Dentists especially may contribute to the reduction of cancer of the mouth, as most persons in this country of cancer age frequently consult their dentists. At that time their teeth are disintegrating or artificial bridges and teeth are being fitted.

Warning Against the Use of Local Irritants.—A point worth mentioning is the evil effects of the use of irritants upon cancerous growths. One of the most pernicious and prevalent is the use of silver nitrate or such applications. Many histories state that after such treatment rather indolent carcinomatous growths have been stimulated into more virulent activity. The questionable lesion should never be stimulated to a greater activity by the application of an irritant insufficient to destroy.

Incidence of Intraoral Cancer.—In 1929 (last available census), in the United States, about 120,000 persons died of cancer, of which about 4,000 died from intraoral cancer. Thus, it would appear that about 3 per cent of all cancer occurs in the intraoral region.

Incidence as to Site.—In 2,741 cases of intraoral cancer quoted by Quick in 1928 and seen at the Memorial Hospital, the following numbers as to site are of interest:

Lip	555
Tongue	473
Floor mouth	281
Mucosa of cheek	185
Superior maxilla	122
Antium	103
Inferior maxilla	119
Tonsil	318
Hard and soft palate	106
Pharynx	63
Intensive larynx	165
Extensive larynx and epiglottis	221

Fraser presented a diagram to illustrate the incidence as to site (Fig. 5).

Roughly it may be stated that of all buccal cancer proper, about 43 per cent appear on or in the region of the anterior two-thirds of the tongue, 20 per cent in the palatoglossal regions, 11 per cent in the gingivoglossal sulcus, and 10 per cent in the floor of the mouth.

Sex Incidence in Intraoral Cancer. Burnam in 165 cases had 128 of the male sex and 37 of the female sex. Piquantin (Ewing) estimated 17 per cent of intraoral cancer occurs in women. Roughly about 85 per cent of intraoral cancer appears in the male sex.

Age Incidence.—It is well known that epithelioma of the intraoral region is most common between the ages of forty and sixty years with the maximum number falling in the fifth decade. The maximum incidence per given number falls between the seventy-fifth and the eighty-fifth years. After the sixth decade the number of cases decreases on account of the progressive decrease in the number of individuals who are living after sixty years of age. The incidence on a percentage basis of those living, however, increases.

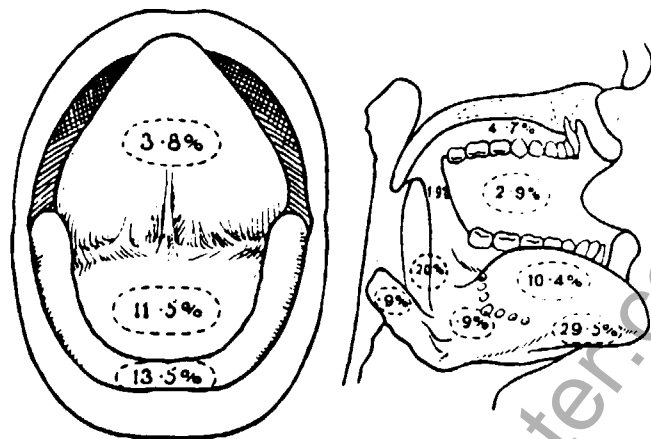


Fig. 5.—Diagram showing the incidence of carcinoma in the mouth in the various locations. (After Frazer.)



Fig. 6.—A, Original squamous cell carcinoma of the lip on the left side.

B, Squamous cell carcinoma on the left side was excised by a V-shaped excision, and the scar is shown in the photograph. It remained healed for two years, after which a second carcinoma developed in the corner of the mouth on the right side. It was mostly in the upper lip. The question arises in this case, however, whether this was a second carcinoma or whether it was a recurrence through the circle of lymphatics around the mouth. The microscopic pictures of the two lesions, however, were somewhat different; and, since the second lesion seemed to be mostly on the upper lip, it was considered to be a second carcinoma developing in the same individual.

C, Photograph of patient three months after interstitial irradiation of the second carcinoma.

Malignant Neoplasms in the Young.—In 301 malignant neoplasms of the oral cavity, Friedman and Rubenfeld (Bellevue Hospital) found 9 patients between the ages of one and twenty years. Three were spindle cell sarcomas

involving the floor of the mouth, cheek, and soft palate respectively. One was a lymphosarcoma of the antrum; 3 were epitheliomas of the nasopharynx and 2 of the tonsil. Of 16,565 malignant lesions seen at Memorial Hospital, Pack and LeFevre found 37 instances of malignant lesions in the upper respiratory passages in patients between the ages of seven and twenty years. In 6,670 autopsies at Johns Hopkins Hospital, Pearl and Bacon found 49 malignant tumors in children. Helmholtz found 56 in the intraoral region, and 4 of these were squamous cell carcinomas.

Second Buccal Cancer.—In regard to the incidence of a second buccal cancer in the same patient, Lund found in a series of 1,548 cases of buccal cancer that it is indicated that the development of a second carcinoma of the mouth is about 15 times as common as it would be if chance were the only factor (Fig. 6). He also found that the development of cancer in some other organ is about twice as common as it is in the population of the same age and sex.

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