LEUCOPLAKIA BUCCALIS

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The first time that the existence of this rare condition was brought to the notice of the writer was in 1898, when he was called upon to review, "The Atlas of Syphilis and Venereal Diseases," by Franz Mračeck.[1] In this Atlas, the following case was reported:

Case I.—*Leucoplakia buccalis, involving the hard palate, showing elevated, coalescent papules* (Fig. 2). R. S., twenty-one years old, prostitute, admitted November 16, 1896. The patient was first infected in 1893, and has since been treated nine times for syphilis. Most of the relapses consisted in papular eruptions on the genitals. The present attack first attracted the patient's notice two weeks ago.

On the hard palate, stretching from the fossa behind the incisors to the soft palate, is a coalescent group of mulberry-like proliferations of hard, yet elastic consistence, somewhat lighter in color than the slightly inflamed mucous membrane of the surrounding parts. The edges of the soft palate and uvula are slightly thickened and distorted as the result of a former attack of the disease, which even now betrays itself by an infiltration on the edge of the soft palate and uvula. The vibrations of the pillars of the fauces during phonation are sluggish and irregular. Concomitant symptoms are found in flat, glistening papules, as large as a bean, on the labia majora, and in a general glandular enlargement.

Treatment.—Inunctions. The specific infiltrations disappeared, the proliferations on the hard palate subsided, and the mobility of the pillars became almost normal.

In this particular case there was a definite history of syphilis, and the writer believed from the context that leucoplakia buccalis was really a syphilitic lesion appearing in the mouth in relatively rare instances.

Several years passed before another published case attracted the attention of the writer. This also was reported by a German authority,[2] and was summarized as follows:

Case II.—*Leucoplakia buccalis, involving the tongue. Associated with ulcerating papules* (Fig. 3). P. P., forty-nine years old. Has been treated as an outpatient. The patient says that four years ago she noticed fiery-red, isolated nodules in the tongue for the first time. Various remedies were tried, among them cauterization (with lunar caustic), which caused the nodules to disappear for a time, but they always recurred. A year ago they again appeared, and the patient underwent twenty inunctions, whereupon the eruption subsided. Two months ago the nodules began to develop again, and with them whitish, coalescent ulcers.

Present Condition.—The tongue is only slightly swollen; at the back the papillæ are still intact; the front is smooth and covered for the most part with a cloudy, whitish layer of epithelium. A discolored, slightly raised ulcer extends

[1] Atlas of Syphilis and the Venereal Diseases, by Franz Mračeck, of Vienna. W. B. Saunders, Philadelphia, 1898. Fig. 42-A, 1344–3819.

[2] Atlas of Syphilis and the Venereal Diseases, by Franz Mračeck, of Vienna. W. B. Saunders, Philadelphia, 1898. Fig. 41-B, 1343–3818.

across the tongue and along both margins, while a similar ulcer, as large as a pea, occupies the tip of the tongue a little to the left of the centre. The ulcers are slightly raised above the surface and surrounded by a sharply defined inflammatory border.

The submaxillary glands are hard and moderately swollen. Painful mastication.

After the patient had been treated for eight days, scar-formation began in the middle of the ulcer, which finally was converted into a whitish, epithelial hyperplasia.

In this case, also, there was a distinct history of syphilis, and in this case the syphilitic lesions of the mouth overshadowed the leucoplakia patches.

About the same time, in 1903, the following case was also noted: [3]

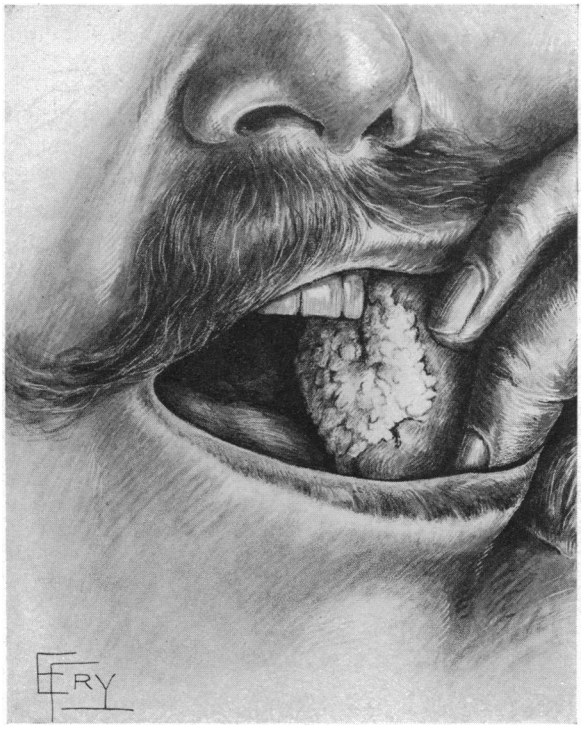

FIG. 1.—Leucoplakia of left cheek, Case IX.

Case III.—*Leucoplasia* (*Psoriasis*) *Linguæ* (Fig. 4). C. J., forty-nine years old. Under treatment for emphysema and pulmonary catarrh.

The patient has had various diseases. In 1872, he acquired a hard chancre, which was followed by eruptions on the skin and sores in the mouth. With the exception of local remedies and river-baths the patient did not undergo any treatment for his disease. Lunar caustic, gargles, and precipitate ointments were the local remedies he employed.

The patient was formerly a heavy smoker; he worked on a freight train and smoked a cigar, or a pipe, day and night. In 1891, he noticed for the first time whitish vesicles on the tongue, which bled when they were opened with a pin. The present condition of the tongue the patient says he has noticed for the last eighteen months. He is thin, but not cachectic.

Present Condition.—The tongue is not perceptibly swollen; but the patient can only protrude it a little and with difficulty. The surface is white, moderately thickened, and divided into irregular islands by shallow grooves. These grooves do not appear to be due to contracting scars, but rather to correspond to the normal furrows in the tongue. On the other hand, the islands appear slightly raised, owing to the thickening of the epithelium and to the moderate inflammation

[3] Atlas of Syphilis and the Venereal Diseases, by Franz Mračeck, of Vienna. W. B. Saunders, Philadelphia, 1898. Fig. 42-B.

which preceded their formation, described by the patient as "blisters." The tongue does not feel hard, and in its present condition is not painful. All delicate tactile sensibility is lost.

The chewing of highly seasoned food or sharp pieces of bread is apt to produce fissures, which, however, heal of their own accord in a few days. The epithelium of the buccal mucous membrane opposite the alveolar border is also somewhat cloudy, but not so thick as that of the tongue.

Submaxillary glands are not swollen. No demonstrable syphilitic symptoms.

The patient disappeared from observation, and the ultimate result is unknown.

In this case history it will be noted that the presence of syphilis could not be definitely shown. This exclusion in diagnosis was based upon the knowledge of syphilis as it then existed, but it must be remembered that at that time the *spirochæte pallida* had not been discovered, and the Wassermann test was unknown.

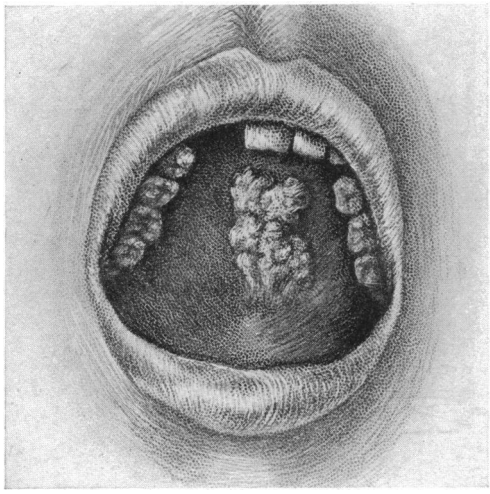

FIG. 2.—Leucoplakia of hard palate, Case I.

In 1909, the writer's interest in the subject of leucoplakia was again stimulated as a result of a study of a fatal case of thrush,[4] and the article by Mikulicz in his classical "Atlas der Krankheiten der Mundhöhle" gave much additional and valuable information in the matter of differential diagnosis of this condition, and of allied diseases, characterized by patches more or less snow white in appearance which appear in the buccal cavity of affected individuals. The illustration (Fig. 5) here shown is reproduced from the above-mentioned article.

In an attempt to review as far as possible all of the various articles in current medical literature, describing the condition of leucoplakia, it was found that such cases, while they are reported from time to time, are really of great relative rarity, and as lesions of this disease vary materially in different individuals, practically all of the cases available in medical literature are herewith collected for study and for comparison.

CASE IV.—*Leucoplakia of the tongue* (*Psoriasis Linguæ*).[5] H. R., a merchant, fifty years of age, living in Eastern Prussia, was very nervous as a child and subject to epilepsy. As a young man he had frequent outbreaks of boils. In 1857, he acquired a syphilitic chancre and was subjected to a course of anti-syphilitic treatment. Later he suffered repeatedly from tumors and eruptions which healed

[4] Thrush: A Clinical Study and Differential Diagnosis, by Henry P. de Forest, M.D., American Journal of Obstetrics, January, 1910.

[5] Atlas der Krankheiten der Mund und Rachenhöhle. J. Mikulicz und P. Michelson, Berlin, August Hirschwald, 1892, Plate XXXI. (Fig. 3.)

after using iodide of potash and mercurial preparations. Some years ago he had severe headaches, pressure in the eyes, and dimness of vision of the left eye. These symptoms disappeared after the use of iodide of potash. The same conditions redeveloped a year ago combined with loss of memory, sleeplessness, and complete inability for mental work. At this time the patient observed for the first time some painful spots in the left half of the tongue, while eating, speaking, or in any movement of the tongue. Examination with a mirror showed him some white spots on the dorsum of the tongue, which at that time had a well-marked border and gradually increased to the present extent.

In December, 1889, the patient came to the clinic of Doctor Mikulicz; his condition is shown by the illustration herewith presented. In the well-nourished, otherwise healthy patient, no other pathologic conditions could be detected. The urine showed no abnormalities and there was no evidence of an active syphilis. Upon the trunk and the extremities were a number of large and small pigmented scars for the most part quite superficial. On the dorsum of the tongue, as shown in the illustration, there existed an irregular network of broad and narrow snow-white streaks, enclosing small islands of mucous membrane, more or less ruddy in appearance. The entire tongue has a dull surface and as a result the diseased portion is easily distinguished from the adjacent normal mucous membrane. The borders between the normal and the milk white mucous membrane are indistinct. The affected portion is more sensitive to slight motion than to firm pressure. The greatest pain is felt on the border of the tongue. Palpation discloses no difference in the consistence of the various portions of the organ. The patient formerly smoked a great deal. He has been hard of hearing for twelve years.

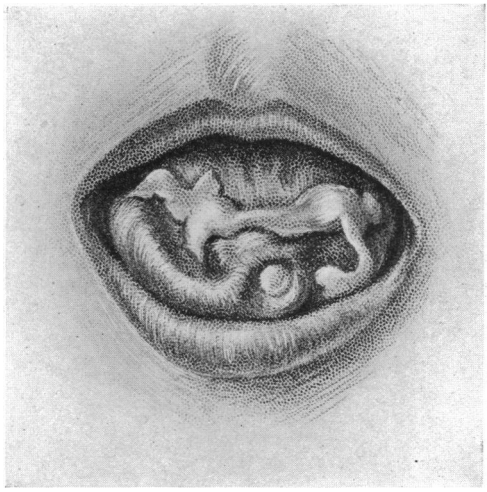

FIG. 3.—Leucoplakia of tongue, Case II.

Treatment.—Iodide of potassium and bromide of soda were given internally, one gram daily. Local treatment consisted of painting with a cocaine solution and with frequent cleansing of the mouth with a mild antiseptic. In the course of treatment of about two months, the appearances almost completely disappeared. The patient felt himself mentally and bodily quite restored to health. The condition would improve or grow worse from time to time and occasionally superficial excoriations would occur which were quite painful. These raw spots healed, as a rule, in the course of from one to two weeks. The healing was hastened by a daily penciling with blue vitriol. At the end of July, 1890, the local condition remained practically unchanged.

CASE V.—*Leucoplakia of the tongue* (*Psoriasis Linguæ*).[6] K. K., a merchant, sixty-two years old, otherwise healthy. For a number of years there slowly developed a series of white patches upon the dorsum of his tongue. At the beginning the patient had no distress and paid little attention to this condition. During the last

[6] Atlas der Krankheiten der Mund und Rachenhöhle. J. Mikulicz und P. Michelson. Berlin, August Hirschwald, 1892. Plate XXXI. (Fig. 2.)

two or three years he suffered from a more or less well-marked painful sensation in the left half of the tongue. Movement, or even firm pressure of the tongue, was not painful, but while speaking or eating with ordinary movements of the tongue, he noticed a painful spot in it. Frequently the pain began spontaneously, especially when the patient was alone. When in the company of others, as a rule, he forgot his distress. The patient is a well-marked hypochondriac, and when otherwise unemployed, thinks chiefly of his condition and imagines that it indicates all possible ailments. He has consulted numerous physicians; has tried various remedies and cures without permanent relief. Unfortunately there is no record in history of the case, whether he was syphilitic, or whether he smoked to excess.

On the 7th of February, 1889, he came to the Clinic of Doctor Mikulicz for the first time. He was well nourished, did not show his age, and showed no other pathologic changes. Upon the dorsum of the somewhat broadened tongue appeared the patches well shown in the illustrations. They are of milk-white color and are divided by numerous well-marked dark colored lines and streaks. The surface is dull and sharply differentiated from the neighboring normal epithelium. If the finger be passed lightly over the surface of the growth, the rough velvety surface of the affected portion of the mucous membrane is distinctly felt. On the more horny portions of the growth there is no especial difference to be felt in the consistence. Both sides of the tongue show light impressions of the outline of the teeth. This is accounted for by the fact that the patient believes that absolute immobility of his tongue is necessary for his comfort.

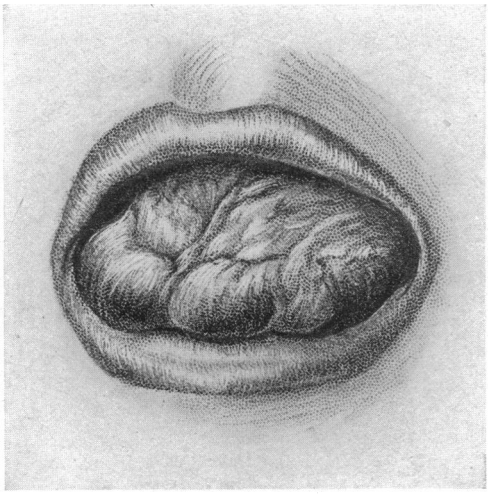

FIG. 4.—Leucoplakia of tongue, Case III.

The further course and treatment of the disease is not indicated.

CASE VI.—*Leucoplakia buccalis* (Fig. 5).[1] R. R., forty years old, a merchant in Russian Poland, acquired syphilis when sixteen years of age. Four years ago he observed for the first time white spots on the top of the tongue which gradually increased in circumference and later similar spots appeared upon the mucous membrane of the cheek and lower lip. At the beginning this patient had no distress. But in the last few years he experienced a sharp burning pain on the left border of the tongue which increased during speaking or chewing. Since that time the patient has developed a marked hypochondriac voice. All treatment, both local and systemic, including anti-syphilitic cures, have been of no assistance. The patient smokes strong cigarettes to excess (about fifty a day). He drinks brandy also to excess.

At the time of the preparation of the accompanying plate in March, 1890, he was a well-built, well-nourished man with little to be observed, aside from the changes in the mucous membrane of the mouth. There are no other evidences of syphilis. The patches in the mouth are snow-white, of a dull surface, rather thin, and showing the color of the mucous membrane through them. Some are large,

[1] Atlas der Krankheiten der Mund und Rachenhöhle. J. Mikulicz und P. Michelson, Berlin, August Hirschwald, 1892, Table XVI. (Fig. 1.)

some are small, and some are confluent. They are distributed irregularly upon both borders of the tongue and upon its dorsum. The portions of mucous membrane between the patches are hyperæmic. A discoloration, with poorly defined edges, exists upon the mucous membrane of the cheeks and lips, in an almost symmetrical form on both sides. This is most pronounced at the angle of the mouth where there is a well-marked centre with radiating streaks. There are a number of small millet-seed patches upon the mucous membrane of the lower lip. The left side of the tongue is sensitive to motion. In the remaining portions of the affected mucous membrane, sensation is diminished.

Treatment. — The patches were painted with cocaine and boroglycerine solution. Thermo-cautery was used thoroughly over the painful area on the side of the tongue. The ultimate outcome of this case is unknown.

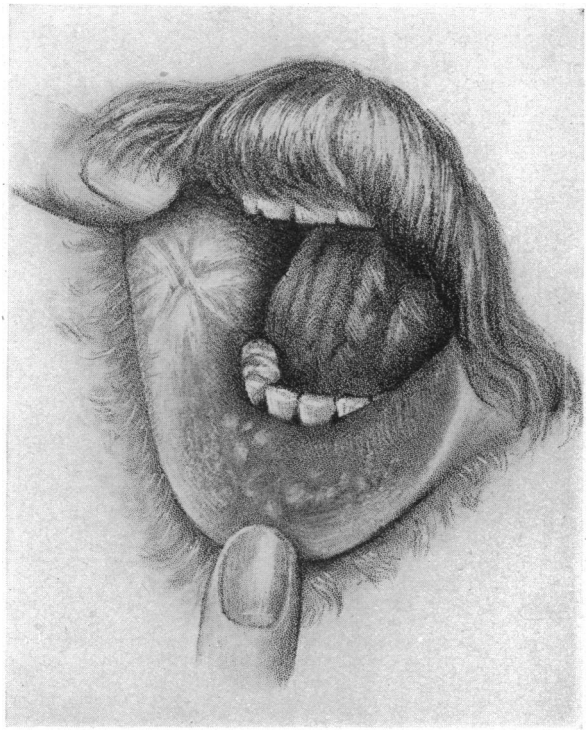

FIG. 5.—Leucoplakia of the right cheek, Case VI.

CASE VII.— *Epithelioma of the tongue with hair-like hypertrophied papillæ following a leucoplakia of the tongue; twenty years' standing* (Fig. 7).[8] K. S., sixty years old, a postmaster in Austrian Silesia. In good general health. He formerly smoked to excess, but denied the excessive use of alcohol. For the past twenty years the dorsum of the tongue has shown a number of white horny patches which caused no particular disturbance. Now and then he felt a moderate burning of the tongue. A few weeks ago a growth developed in the anterior portion of the left border of the tongue. This he believes was due to a sharp corner of a broken tooth. The growth gradually increased in size and finally reached its present condition. With this exception the patient complains of no other illness.

On the 14th of March, 1886, he entered the Clinic of Professor Billroth in Vienna. He was a powerful man in good condition for his years. On the tip of the tongue was a well-marked tumor represented in the illustration. It appears as an irregular nodular thickening of the tip of the tongue, ulcerated in several places. A considerable portion of the growth was covered with a milk-white layer of epithelium. Its most pronounced characteristic was the appearance of the tremendously increased growth of the papillæ of the tongue (5 to 15 mm. long)

[8] Atlas der Krankheiten der Mund und Rachenhöhle. J. Mikulicz und P. Michelson. Berlin, August Hirschwald, 1892, Plate XXXI. (Fig. 1.)

which surrounded like a white moustache the posterior and right border of the tumor. The larger portion of the dorsum of the tongue was covered by a thick milk-white, dull epithelial layer. The examining finger could feel a well-marked nodular tumor occupying the anterior third of the tongue in its central portion. The other portions of the mouth showed nothing abnormal; the glands were not enlarged.

On the 22nd of March, the diseased portion of the tongue was excised and the wound completely sutured. The healing was uneventful. The further fate of the patient is unknown.

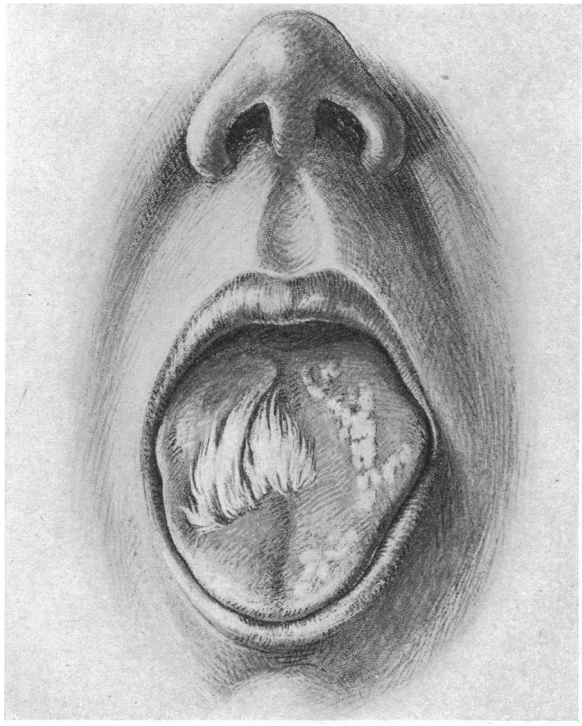

FIG. 6.—Leucoplakia oris (psoriasis linguæ, tylosis, ichthyosis buccalis), Case IV.

The microscopical examination showed a squamous-celled epithelioma. The elongated papillæ arose from a basal structure of connective tissue from one to two millimetres thick. The epithelial growth extended between the papillæ into the structure of the tongue itself. This illustration is taken from the records of Professor Billroth.

The series of illustrations thus far presented have been selected for the purpose of illustrating the various phases of the disease beginning with the milder type and ending with a more severe form, in which cancer is combined with leucoplakia. The ultimate outcome of this unfortunate combination is not necessarily fatal. In the case illustration, Fig. 8, a cancer of the left half of the tongue existed, combined with leucoplakia and bilateral cervical adenopathy. The cervical and buccal lesions were removed in two sittings. The small glands on the right side were unfortunately left in place. Fulguration, March 21, 1909. The patient was cured for nearly three years. The source of this case report is unknown, but it was obtained in recent medical literature.

A careful study of this series of cases, which, though not numerous, epitomize practically all of the cases that have been reported in current medical literature for the past thirty years, discloses certain facts which are worthy of more careful and detailed consideration.

Synonyms.—The disease itself, although it has been recognized and described by a number of writers, has never until recent years been given a

definite and well-recognized name. It has been variously described under the following titles:

Leucoplakia buccalis, psoriasis linguæ, tylosis oris, buccal keratosis, ichthyosis buccalis, plaques nacreés, chronic superficial glossitis, leukonia, raucherplaques, plaquesnarben, lingual psoriasis, epithelial white plaques of the tongue.

The present title of leucoplakia buccalis appears to have been first suggested by Merklen at the Congress of London in 1881, and was accepted by *Hillairet, Kaposi, Vidal Clément, Duncan Bulkley, Behrund* and *Wilson.* Two years later it was taken as the title of an article by Leloir, and since then it has been incorporated and accepted in current medical nomenclature. The other designations above mentioned have been proposed both before and after 1881, but have not been generally adopted. Each name represents an attempt on the part of the person proposing it to describe the salient feature and real nature of the disease. To enumerate them is to trace the history of the different opinions which have been expressed.

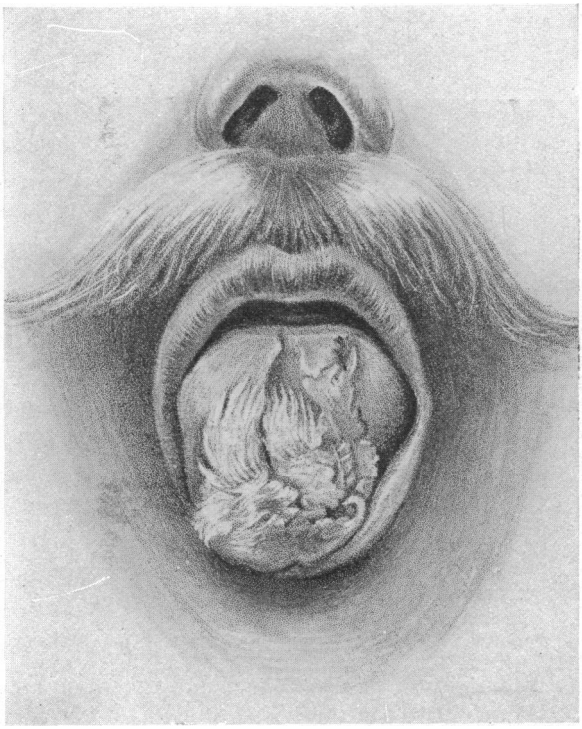

FIG. 7.—Leucoplakia of tongue with epithelioma, Case VII.

Schwimmer proposed the name of "White Plaques of the Mouth." This is mentioned for the sake of completeness, for it is merely a synonym of leucoplakia buccalis.

Definition.—Leucoplakia may be defined as a chronic and progressive affection of the mouth, characterized by the occurrence upon the mucous membrane of snow-white patches, sometimes circumscribed, sometimes diffused.

Historical Sketch.—Bazin, in 1868, in his "Leçon Clinique," described the disease under the name of "Lingual Psoriasis," and made a study of this condition which has remained classic. Without giving the name "Psoriasis" the exact meaning which really belongs to it, he believed it to be a constant accompaniment of arthritis. In 1878, Deboe in a thesis, and Mauriac in an

important article, without agreeing with the ideas of Bazin as to the nature of the disease used the term "Psoriasis," which gives a good idea of the general aspect of the lesion and is not ambiguous. The English school, impressed particularly by the hardness assumed by the mucous membrane, becoming as Hulke says, like kid leather, proposed the name of ichthyosis, which was adopted by Clark and by Morris, and has persisted up to the present time. Before this time, Clark had attempted to make London physicians accept the term, tylosis linguæ. This was rejected by the English, but was accepted by Ullmann of Germany, and by Lallier of France. This title has since been given up. Devergie, in 1876, without success, proposed the name of epithelial white plaques of the tongue. Recently Doyon and Besnier have been equally unsuccessful in regard to the terms, chronic epithelial glossitis, and buccal keratosis.

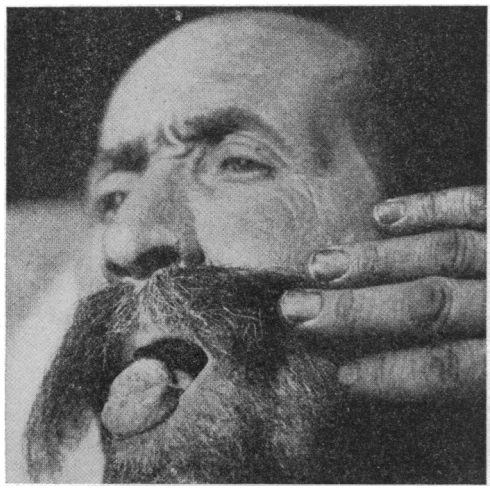

FIG. 8.—Cancer of the left half of the tongue, with leucoplakia and bilateral cervical adenopathy. Removal in two sittings of the cervical and buccal lesions. The small glands on the right side were left in place (unfortunately). Fulguration, March 21, 1909. Cured for nearly three years.

This disease which has been described under so many different names, and which we shall hereafter refer to as leucoplakia buccalis, has an obscure history. This is due, not only to the various terms under which it has been described and the dissimilar ideas expressed in regard to its pathogenesis, but also to the fact that it has a varied etiology, and under this name many inflammatory conditions of the tongue have been included which look alike but which are in reality totally different in character.

Etiology.—The etiology of this disease is in part still obscure. It is certain that the predisposition to abnormal tenderness and the lack of resistance of the mucous membrane may cause irritation of the oral cavity.

Leucoplakia buccalis is essentially a disease of adults. So far as age is concerned, it is most frequent in the fifth or sixth decade of life; it rarely occurs before the fortieth year. It is a rare occurrence in women (one to sixteen, according to Clark, and one to thirty-five, according to Leloir). According to Deboe, it exists only in men.

It is described by some writers as an occupational disease: "The White Plaques of Glass-Blowers." Still other writers have regarded it as a constitutional disturbance. Arthritis and a variety of herpes seem to play an important rôle in the causation of a number of cases. Anæmia, consumption, diabetes, or any disturbance of digestion may be factors in the etiology.

Leucoplakia has been noted in connection with special irritative conditions

of the digestive tract, such as dilatation of the stomach. In some instances it appears to have developed as a result of the irritation of the tongue, due to faulty dentition, or sharp corners of broken teeth. The habitual use of alcohol is an undoubted factor and so also is the use of highly spiced and irritating foods and condiments. Protracted medication with such drugs as the mercurials or the iodides are predisposing causes. So, also, is the habitual inhalation of smoke and dust.

The principal cause is undoubtedly the smoking of many and strong cigars or cigarettes, or the use of tobacco in short-stemmed pipes. The nicotine of tobacco is not the only cause, but the combustion products of the tobacco, such as carbonic acid gas, ammonia, creasote. All empyreumatic oils are especially irritating.

This fact accounts for the much greater preponderance of leucoplakia in men than in women, for it has been observed that in those countries where women also smoke to excess, leucoplakia occurs equally in both sexes.

Many writers have regarded this disease as habitually depending upon the former syphilitic affection, and therefore have described it as a symptom of syphilis. This view does not seem to be supported. The carefully compiled statistics of Erb and of Neisser show that in a large number of typical cases of leucoplakia, syphilis could be excluded. Especially convincing in this particular are the number of cases observed in which a patient who had suffered from long-standing leucoplakia had developed a primary syphilitic lesion with the secondary symptoms appearing in due time. If the disease of the mucous membrane were of specific origin, the patient would then be immune against a new syphilitic affection. The resistance of leucoplakia to ordinary anti-syphilitic treatment, also supports the belief that it is not due to this disease. If leucoplakia really exists, it is made worse by such treatment. Mercury appears to be without effect, though there is a slight filling of the mucous membrane as a result of its use, and there is no doubt that the long-continued use of mercury, of the iodides alone, or of both together, tends to irritate the mucous membrane, and possibly produce a variety of leucoplakia. That these growths do not go on to the thick and horny formation of other forms is because the injury caused by mercury is a transitory one. When it is no more needed its use is stopped, while smoking and drinking are, in many instances, continued throughout the entire life.

If, however, syphilis is not to be regarded as a direct cause of leucoplakia, there is no doubt that it is an important predisposing factor in the occurrence of this condition. Schoengarth published a list of all the hitherto reported cases of leucoplakia which he could collect; 65 per cent. show a syphilitic history. The great improvement made recently in the accurate diagnosis of syphilis by the Wassermann test will unquestionably do much to eliminate syphilis as a causative factor in many cases where its existence was formerly suspected but could neither be verified nor excluded. All authors have agreed that leucoplakia is an extremely rare occurrence in women, though syphilis, of course, occurs in practically the same number of women as in men.

Tobacco and syphilis must be regarded as the most important factors in etiology. Where syphilis exists it is probably true that less smoking is necessary to develop leucoplakia. Erb is right when he says that unless these two causes are present, leucoplakia is rarely found.

Symptomatology.—The symptoms of this disease are usually quite evident. There appear to be two fairly well marked clinical forms of leucoplakia. The *undeveloped form* and the *common form.*

The *undeveloped form* has been thoroughly studied by Benard. This usually occurs in patients suffering from gout or arthritis, and particularly in persons who are excessive smokers. Its beginning is very insidious. Its advance slow, almost imperceptible. It is accompanied by almost no disturbances. On examination of the mouth, particularly the tongue, a slight turgescence of the papillæ is noticed, accompanied by a hyperæmia of the mucous membrane. The normal furrows of the tongue are markedly accentuated. This is the so-called "Parquet" tongue, characteristic of gouty people; it may persist for years. Gradually the tongue becomes gray and then white. At this stage where hypertrophy of the papillæ is much more evident, each one of them is covered with thick epithelium, and examination shows that the pearly-white coloration is found only at the base of the interpapillary furrows. This intermediary stage may persist for months or years; finally a light desquamation takes place, small superficial ulcers are formed, and true fissures develop in place of the furrows. At all stages of this type of the disease, the treatment of the coexistent constitutional condition produces an amelioration of the local affection.

In the common form the symptoms are much more typical. There are often pronounced functional disturbances, stiffness of the tongue, difficulty of speech, mastication and swallowing. Later ulcers and fissures develop, finally accompanied by pain. Salivation and an occasional hemorrhage occur, due to tearing of the tissues underlying the base of the deep fissures. The lesions exist in very irregular patches. They are grayish-white, pure white or sometimes of a glistening irridescent white, suggesting mother of pearl (plaques nacrées, Fournier).

Clinically these areas appear as quite smooth, dry, milk-white patches, hence the name. The more recent layers of epithelial thickening are relatively thin, show a more rosy-red color, and are not sharply separated from the surrounding tissue. The affected spot appears as if the mucous membrane had been slightly touched with nitrate of silver, or lunar caustic. Through the thin whitish layer, the normal red of the mucous membrane is visible. The older masses appear as thick rinds and are of a pure white or bluish-white color. These masses are for the most part sharply differentiated from the adjacent mucous membrane, and there is frequently an inflamed red border surrounding them, less than 1 mm. wide. As time goes on these rinds become progressively thicker, and more like leather. They are markedly raised and as a result are easily torn free from the underlying tissue by mechanical means such as the teeth, the movements of the tongue or

hard particles of food. Fissures of the superficial tissues develop, extending deep into the tissue of the tongue itself. Slight hemorrhages occur from accidental causes, and the rinds then assume yellowish or brownish colors, which are transitory, for the white color reappears as soon as the blood is reabsorbed.

As a rule leucoplakia is limited to the anterior portion of the dorsum of the tongue, either at the tip, or upon its borders where are found patches, large or small, isolated or coalescent. The upper surface of the tongue as the result of this growth, presents a peculiar facetted appearance, though, as a rule, the outlines are quite irregular, especially when new growths are interposed between those of long standing.

Infrequently similar growths appear on the inner surface of the cheeks and lips. A characteristic growth often appears at the junction of the upper and lower lip where leucoplakial streaks may radiate from the angle of the mouth in a fan-like fashion. If the lips themselves are involved, the growth progressively diminishes toward the vermilion border. More rarely it attacks the hard and soft palate. The gums and alveolar processes are almost never involved.

Fissures appear most frequently upon the surface of the tongue itself, since this organ is most apt to be injured by mechanical means as a direct result of its mobility and function.

If the patches themselves are subjected to a microscopic examination, it is found that the pavement epithelial cells of the white patches are more or less enlarged and thickened, the submucosa is filled with lymphoid cells; the blood-vessels are increased, dilated and surrounded by a small-celled infiltration. When the growth has persisted for some time, a horny thickening of the superficial epithelia takes place, oftentimes accompanied by a marked increase in the size and length of the papillæ. In the lower layer of the epithelium there is a marked stratification of the cells and a sort of cup-like formation of the nuclei in the midst of this horny epithelial layer. A peculiar substance, eleidin, appears to be produced as a result of the horny changes in the epithelium.

The *pathological anatomy* of these growths was exhaustively studied by Leloir, who notes three successive phases of development.

First, the hyperkeratinization of the mucous membrane which becomes horny, hypertrophied, and shows a granular layer rich in creatin or eleidin. This layer then swells and becomes very large as a result of this thickening of the horny layer.

Second, the formation of ulcers, as the result of this excessive hardening. These take the form of fissures within the plaques themselves, and around their edges. These fissures extend completely through the mucous membrane as far as the papillæ and as a result cause inflammatory lesions, exfoliation, desquamation and infiltration. A pronounced change in the submucous glands may also develop.

Third, the last phase shows a thickening and hardening of the dura around

the plaques. Sclerotic atrophy of the blood-vessels with dis-association, compression and atrophy of the muscular fibres occur. In this stage the underlying tissues may be involved, disintegrate, and favor the invasion of agents leading to the formation of epitheliomata. Upon the edges of the organ, deep indurations may develop, sometimes very painful and accompanied by rapidly developing adenopathy. If the usual form of cancer of the tongue develops, it progresses with its usual malignity, though certain cases have been observed in which an early excision of the cancerous growth appears to have been followed by permanent cure. In the later and more marked development where cancerous changes do not occur, the papillæ form warty, spinous or shield-like prominences, still preserving their sharply marked outlines.

As a general rule there are found at this stage torn furrows, and gaping rhagades appear on the lips and on the tongue, that is in those parts where, as a result of their musculature, movements are most pronounced. These patches do not change into ulcers. Papillomatous growths on the borders or in the fissures of the patches are occasionally observed, not unlike a chicken's comb in appearance.

A similar discoloration of the epithelium has been observed upon the mucous membrane of the vulva of the uterus and even of the kidneys. In rare instances it has been observed in the skin eruptions of psoriasis and in lichen planus.

The subjective manifestations vary materially in different patients. In the greater number of cases in the early stage of the disease, there is almost no discomfort, and the trouble not infrequently is discovered only as a result of a feeling of an annoying burning of the mucous membrane of the mouth, or of the sensation that a foreign body is lying upon the surface of the tongue or cheeks which needs to be removed. An examination by the patient with a mirror is then made and the incipient leucoplakial patches are discovered. There may be great sensitiveness in speaking, eating, drinking or smoking. The use of spiced foods or of alcoholic drinks often causes especial irritation. In the later stages when the thickened and horny condition of the epithelium has developed, there may be but little distress except the discomfort complained of from the stiffness and difficulty in moving the tongue and lips, in chewing or in speaking. If the epithelium be distorted to a large extent by furrows, ulcerated fissures, pronounced excrescences or carcinomatous infiltrations, the affection may become very painful. In such cases hemorrhages often occur. The alteration in taste or in salivation is rarely observed unless the disease is extensively developed.

Diagnosis.—The detailed account of the lesions observed and the symptoms to which they give rise, described in the preceding section, should make the diagnosis of this disease a matter of comparative ease and certainty.

In view of the fact that syphilis has played such an important rôle in considerably more than half of all of the cases of leucoplakia which have been reported, the positive exclusion of this disease or confirmation of its existence should always be made by means of the Wassermann test.

If a man be suffering from syphilis, he often regards these patches as a manifestation of that disease. Other patients believe that cancer is about to develop. These two conditions are generally regarded by the laity with great apprehension, and therefore many patients with leucoplakia become hypochondriacs upon this subject. They magnify their symptoms of discomfort in the mouth and attribute to the disease much greater importance than really attaches to it. There is a real reason for anxiety, however, for in not a few cases in which leucoplakia was first observed an epithelioma of the tongue developed later, but it is not always easy to determine whether the cancerous growth took its origin in the leucoplakial patch or in some other local irritation of the organ. The same causes of irritation of the tongue and mucous membrane favor the development of this form of carcinoma quite as well as of leucoplakia itself. It would be quite erroneous to maintain that every case of leucoplakia ultimately terminates in carcinoma. Moderate degrees of leucoplakia are far more frequently seen than severe cases of the disease, and in many cases the condition remains stationary for years, even for decades. We must admit in view of the number of cases of leucoplakia which have been reported in which epitheliomata subsequently developed that this disease may be regarded as a predisposing factor in the formation of cancer of the tongue. The extreme degree of mental apprehension, hypochondriasis, or well-marked neurasthenia, which have been observed in severe cases of leucoplakia, should of themselves be regarded as important factors in an accurate diagnosis of this disease.

The illustrations selected show well the various stages of the disease in various localities of the oral cavity, and should greatly facilitate or confirm the diagnosis.

Differential Diagnosis.—Certain diseases of the mouth always give rise to white patches upon the mucous membrane. No one unfamiliar with the classical "Atlas of Mikulicz" can realize that an entire volume may well be devoted to the diseases of the mouth alone. Many of these diseases differ materially in their clinical appearance from the lesions of leucoplakia, but certain ones are to be borne in mind where any question of diagnosis arises.

In infancy, thrush, acute gonorrhœal stomatitis, Bednar's aphthæ (Bednar's plaques, ulcera pterygoidea palati) are most frequently observed. The age of the patient alone should serve to differentiate these conditions from leucoplakia, although thrush also occurs in adults.

In the adult, the three conditions most apt to be confused clinically with the disease under discussion are those of aphthous stomatitis and chronic recurrent aphthæ. The clinical history of these diseases is quite characteristic.

Acute papular glossitis, an extremely rare disease, more closely simulates leucoplakia buccalis so far as the pure white color is concerned than any other buccal affection, but the shape of the lesion with a depressed centre and a snow-white periphery easily serves to differentiate the two conditions. The article of the writer upon "Thrush," which has already been mentioned, gives further details of differential diagnosis.

Another disease in the adult with which leucoplakia may sometimes be confused is tuberculosis of the tongue. This disease is also extremely rare in the buccal cavity, but the possibility of its occurrence must always be borne in mind.

As a rule the form of tuberculosis which develops is of a non-malignant type and oftentimes, though chronic in its course, can be cured by the use of superficial thermo-cautery combined with the administration of iodide of potassium internally. The growth itself is not of the silvery white observed in leucoplakia, but has a greenish tint and tends to ulceration. A number of excellent illustrations of this condition may be found in the volume of Mikulicz already cited.

Miliary tuberculosis of the tongue may develop which resembles leucoplakia much more closely than the ulcerative form just mentioned.

It is also possible to confuse leucoplakia with lichen-ruber planus. In this growth there are occasionally found smaller and larger isolated or confluent white patches on the lips, cheeks, tongue, gums and soft palate which appear very similar to the leucoplakial growth. According to Touton, the group-like formation of the patches and the net-like streaks, as well as the formation of definite nodes and the simultaneous or shortly following affection of the outer skin, serves to distinguish them. The internal use of arsenic combined with the local application of corrosive sublimate rapidly cures the lichen planus, while leucoplakia is practically unaffected by this treatment.

Most important of all in the differential diagnosis is the fact that certain lesions of the papular form of syphilis which occur in the oral cavity sometimes closely simulate in general outline the growths of leucoplakia. The persistence of the patches in true leucoplakia is an especial characteristic; they remain for months at a time at one and the same place in spite of all treatment, whereas the syphilitic papules as well as benign growths remain for a much shorter period in any one place, and either extend their borders rapidly or heal. Although the leucoplakial patches never change into ulcers though fissures may sometimes develop, the syphilitic patches after a short time usually become superficial ulcers. The leucoplakial growths with the passage of time become steadily harder, more resistant, and finally, warty or horny; the syphilitic growths soon coalesce and become slightly coherent and soft. Syphilitic patches heal with relative promptness under general and local treatment without scars, whereas leucoplakia is rarely influenced by the use of mercury or iodine; in any event there always remains a depressed central scar.

To add to this confusion certain forms of syphilides, particularly of the large macular variety, show first a roseola which may disappear without leaving any appreciable change in the skin, or on the other hand, in rare instances, a slight, barely noticeable desquamation of the epidermis in the affected areas occurs after the disappearance of the eruption. More frequently the pigmentation disappears, so that the affected parts appear white and lead to the formation of cutaneous leukoplasia, though the pigment disappears in

the centre of the eruption it may be increased around its periphery. This is particularly the case in parts naturally rich in pigment, as the nape of the neck and the genital region. Occasionally the entire surface of the body is thickly covered with pale, non-pigmented, circular or oval spots. This so-called syphilitic leukoplasia is a more valuable sign than any other, as it may represent the remains of a cutaneous syphilide of very long standing and form a diagnostic point of the highest importance in doubtful cases of diseased organs.

The mucous membrane of the oral cavity is almost always involved during the secondary period of syphilis. Papular ulcers and fissures are constantly found. The alterations which are produced in the tertiary stage are known as *syphilitic pachydermata* or *psoriasis mucosæ oris;* they occur in the mucous membrane of the tongue, the cheeks, especially opposite the teeth, and in several other localities. The characteristic sign is a thickening of the mucous membrane with the formation of whitish patches consisting of several layers of proliferated epithelium almost as hard and horny as the skin.

There is scarcely an organ in the body in which syphilis deposits so many and such various pathologic products as in the tongue. The later stages of secondary syphilis are often marked by papular eruptions and ulcerations along the margin of the tongue and by extensive infiltrations on its surface. Among the tertiary forms some writers include so-called psoriasis or leucoplasia of the tongue. These facts have been so long observed in connection with syphilis and the terminology employed is so similar to that of leucoplakia, that there is little doubt that much confusion has occurred in the accurate diagnosis of these similar conditions of the mouth. In many instances there is no doubt that leucoplakia and syphilis have co-existed. In other cases leucoplakia has been regarded as a late syphilitic manifestation. At the present time this confusion can easily be avoided by the routine use of the Wassermann test in all cases of leucoplakia which come under observation.

The case herewith submitted of leucoplasia is taken from Mračeк.[9]

CASE VIII (Fig. 9).—*Leukoplasia of the neck. Papules on the genitalia.* A. B., eighteen years old, servant girl. Has never had a venereal disease. In the beginning of December, 1895, she began to be troubled with burning during micturition; at the same time several "pustules" developed on the outside of the labia majora, which burst after several days and healed over. There was also a painful swelling of the right inguinal glands, lasting several weeks and disappearing finally after rest in bed and the use of compresses. In February, 1896, she was troubled with pain in the throat, and for two weeks was unable to swallow solid food. These symptoms improved after gargling with alum. A few days afterward an erythematous eruption appeared on the throat, on the flexor surface of both elbows, and on both legs. Since the end of March the eruption has been brown. On May 23 she came under hospital treatment; up to that time she had not consulted a physician. Last coitus six months ago; last menstruation, April 29. Has never given birth, nor had an abortion.

Present Condition.—Eroded, œdematous papules on both large and small labia, especially on the right side; inguinal glands on both sides much enlarged; at the

[9] Atlas of Syphilis and the Venereal Diseases, by Franz Mračeк, Vienna. W. B. Saunders, Philadelphia, 1898.

anus the mark of an old papule. On the lower extremities a specific eruption in process of regeneration; intense leukoplasia of the neck; both tonsils enlarged and ulcerated.

Cured after twenty inunctions. (See Fig. 9.)

With this history it is little wonder that with the characteristic white spots on the body confusion in diagnosis could easily occur if similar white areas appeared in the buccal cavity.

Prognosis.—The course of leucoplakia is always a very chronic one; it may become limited in its growth within a few months, or may persist for ten, twenty or thirty years; indeed, throughout life. More frequently there are periods of activity, alternating with periods of quiescence and excess in smoking not infrequently causes a desquamation of the epithelial masses. Prognosis, except in cases where syphilis co-exists and mercury is of help, is very doubtful. Leucoplakia often occurs without material discomfort, and occasionally is cured spontaneously. On the other hand, a permanent cure is the exception. The prognosis therefore is dubious. According to Schuchardt, any chronic irritant affecting either the skin or mucous membrane by producing an increased vascularization of the tissue favors the formation of cancer. The presence of leucoplakial patches in the mouth, therefore, increases the liability to this unfortunate termination. Even if excision is of the cancerous growth performed at an early stage, recurrence is frequent. The occurrence of carcinomata in leucoplakia deposits, though it sometimes does happen, cannot be regarded as the rule.

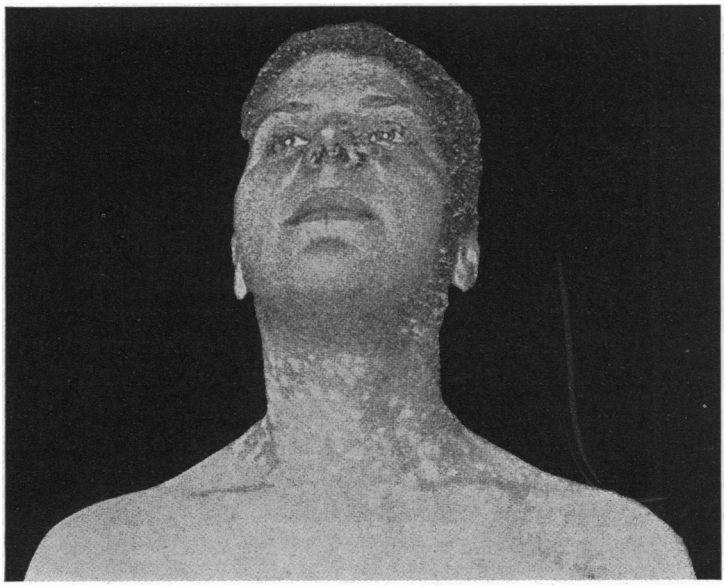

FIG. 9.—Leukoplasia of the neck. Papules on the genitalia, Case VIII.

It is possible that the treatment practiced and advocated by the writer and described later in this paper may materially affect the prognosis of this disease.

Treatment.—When the clinical history of a case of leucoplakia is carefully considered it is apparent that the prophylaxis is quite as important as the

administration of medicine or any local treatment which promises to relieve the condition.

The preventive treatment which should be at once begun is self-evident from the clinical history of the disease. The use of tobacco in all forms must be stopped. Most patients themselves observe that with the cessation of smoking their trouble is materially improved, and if they begin again it is made worse. It is a severe punishment for a confirmed smoker to give up this habit, particularly because of the appearance of an apparently harmless disease, so in most cases the best we can do is to limit the daily number of cigars or cigarettes, and to recommend the habitual use of a long cigar-holder. Short pipes must be prohibited. It must not be forgotten that tobacco juice is also a powerful irritant to mucous membranes so that chewing tobacco must also be forbidden. If possible, after a progressive diminution in the use of tobacco, its use in any form should be entirely discontinued.

The use of mercury must be excluded as well as any irritation of the mouth by acid, acrid or irritating foods, drinks or spices.

If the teeth are broken or decayed, pointed useless roots should be extracted and the cavities filled. In fact, all causes of irritation of the mucous membrane of the mouth are to be removed.

Dyspeptic disturbances, consumption and anæmia must all be cared for according to their respective needs. Anti-syphilitic treatment is not only unnecessary, but even harmful as Erb early maintained. This, of course, presupposes the fact that the existence of syphilis has been excluded by the Wassermann test.

Unfortunately the disease is very resistant to treatment, and as is usually the case in diseases of obscure etiology, many local applications have been recommended. In the milder cases, antiseptic and slightly astringent mouth-washes can be used to keep the mucous membrane in good condition and to allay the patient's apprehensions. Tincture of myrrh, tincture of nutgalls flavored with a drop or two of oil of peppermint, peroxide of hydrogen, and similar medications can be tried. No one of these should be continued too long as the taste of the patient varies materially from time to time. The treatment of single patches of leucoplakia in obstinate cases is best done by means of caustics. Pure lunar caustic, a 50 per cent. solution of nitrate of silver, a 5 per cent. solution of lactic acid gradually increased to 50 per cent., chromic acid solutions, and, more recently, concentrated preparations of peroxide of hydrogen, are all to be recommended. Salicylic acid is of value to aid in the dissolving and softening of the mucous membrane. A 2 per cent. solution of resorcin has been used. Rosenberg recommends the painting of the patches with pure balsam of Peru, allowing it to stay in the mouth for from three to five minutes.

Unfortunately in most cases, this entire list of medication proves to be of no value, and often this very lack of result confirms the patient in his belief that he has an incurable disease which will ultimately end in cancer. Many cases therefore give rise to a severe form of hypochondriasis, although, as a

rule, the patient suffers but little discomfort. If speaking, eating, and drinking are interfered with, mental disturbance is still more apt to occur.

Some writers advocate that as soon as the patches of leucoplakia develop to any extent, they should be thoroughly curetted away and the base cauterized with the thermocautery. Or the tip of the tongue can be firmly grasped in a bit of gauze and with a sharp scalpel the patch of leucoplakia can be shaved off exactly as the skin is removed for transplantation.

Rinsohoff gives preference to the procedure of decortication of the skin after first sprinkling the affected areas with crystals of permanganate of potash. After this procedure there is often left in place of the sensitive rind a soft insensitive scar. Such a procedure can hardly be necessary in patches of small size, but at any rate it prevents the later development of larger growths. The effect upon the patient's mental condition of the absolute removal of the growths by any of these procedures is usually a salutary one if the treatment be successful. On the other hand, if it be unsuccessful, these procedures only make the mental attitude of the patient worse. One is certainly justified in regarding the condition as harmless as long as the area of the lesion is not extensive.

The possibility of the ultimate development of an epithelioma should in all cases be stated to the patient, and if such a growth begins to develop, radical surgical procedures should be at once instituted.

This in its essentials indicates the line of treatment which has been pursued by many physicians at many times. The very fact that such a large number of remedies have been suggested indicates the little knowledge which we possess as to the true cause of the disease and the uncertainty of all forms of treatment that have been mentioned.

Personal Observations.—Up to the time that I prepared my article on "Thrush," the subject of leucoplakia to me had but an academic interest. No case of the disease had ever come under my observation, and in view of its extreme rarity, it seemed improbable that I should ever be called upon to care for a patient suffering from this disease. On June 9, 1911, however, there was referred to me by Dr. Francis J. Magilligan, of Brooklyn, a patient whose history was a typical one. The result of treatment, involving as it did certain phases of medication, never before used, so far as I am aware, quite surpassed all reasonable expectations.

CASE IX (Fig. 1).—J. O. S., a native of Ireland, sixty-three years of age, a former member of the Police Department of this city. Family history negative. His mother died in childbirth; his father, at the age of eighty-two.

Personal History.—He formerly chewed a package of tobacco a day, and he himself concluded that this caused the onset of his trouble. He stopped chewing tobacco six years ago. He has smoked since he was a small boy, using a pipe indoors and cigars outside. He was a total abstainer until twenty-four years of age; since then he has drunk beer and whiskey in moderation. He likes to have his food highly spiced. He is regular in his habits, was twenty-five years in the Police Department, and looks young for his age.

His present illness was first noted in 1894 when a snow-white patch appeared on the inside of his left cheek opposite the first molar tooth. This has grown

steadily forward until it is now an oval patch 6 cm. long and 3 cm. wide. This covers practically the entire inner surface of the left cheek. This patch is snow-white in color, is raised 0.5 cm. above the level of the adjacent mucous membrane and is crossed by numerous deep fissures extending well into the substance of the cheek. These fissures bleed freely upon examination or while chewing his food. The mass is composed of a large number of thick, pearly-white, glistening, hypertrophied papillæ closely overlying each other like an exaggerated piece of white velvet. It was not painful unless torn by some mechanical means. Its appearance when first seen was well shown by the accompanying sketch made at the time.

All forms of treatment appear to have been tried by the many physicians whom he has consulted during the seventeen years that this mass has been in existence. It was thoroughly burned with chromic acid by a prominent dermatologist; this caused much pain, but the growth continued. His former family physician burned it with nitric acid and gave him a red mouth wash to use. This had no effect, so a number of pieces were cut off with scissors and the base cauterized. At the end of a year of this treatment the condition was much worse than it was at the beginning. Thermo-cautery was used by another physician; this caused much pain, gave no improvement and the patient never returned for observation. A large number of mouth washes and various medications have been used—the formulas of these he does not know.

I first advised to discontinue the use of tobacco and alcohol entirely, have his teeth carefully cleansed and begin for the first time the habit of brushing them regularly each day. An alkaline mouth wash was advised for local cleanliness. Local application was made with pure carbolic acid over the patch, which after a moment or two was neutralized with pure alcohol. After a month of observation the growth appeared to be somewhat thinner in the centre and I had hopes that the prophylaxis and treatment which he had followed carefully would permanently relieve him.

Upon my return home from my summer vacation early in September, I found that for the preceding month, the patient had suffered much pain inside of the face, sometimes of great severity, and the area of growth was practically the same as when it was first seen.

It then occurred to me that inasmuch as leucoplakia is so frequently associated with syphilis, and though undoubtedly a different disease, closely resembles syphilis in some important particulars, it might be due to some organism similar in character to the spirochæte pallida or to some form of protozoa. If a large dose of arsenic administered intravenously would destroy the spirochæte, as it unquestionably does, possibly a similar treatment would have the same effect in this disease.

In order to be sure of the diagnosis and to exclude syphilis, the patient was referred to a reliable laboratory and the Wassermann test was made. Two tests were made by two different laboratories. In both instances the test was negative. Syphilis, therefore, could be excluded.

On the 14th of September, a full dose of salvarsan was administered in the median basilic vein of the left arm. Some difficulty was experienced in entering the vein with the needle for, because of the anæmic condition of the patient, the veins almost collapsed. He had a slight chill immediately after the injection; stimulation was given him and he was put to bed. Late in the afternoon he insisted upon returning home with his wife. The usual diarrhœa with some nausea, which frequently follows injections of 606, lasted for an hour or two, but by midnight his discomfort was at an end. He slept well that night for the first night in a month, and when seen four days later, stated that he had been entirely free from pain in his face ever since the injection was administered.

On the 23rd of September further increase in size of the growth had stopped and the edges had begun to separate noticeably from the underlying mucous membrane. The growth now appeared as if it could be lifted off from the surface of the cheek. This separation progressively continued, and on the 5th of October, he appeared before my clinic at the Post Graduate Medical College. No physician of the score or more who were present had ever seen a case of leucoplakia. This illustrates the rarity of the disease. By the end of October the growth had steadily separated from the periphery toward the centre, healing as the recession advanced, and early in November, when the patient was last seen, the leucoplakial growth had entirely disappeared and the mucous membrane lining the left cheek appeared to be in quite as healthy a condition as that of the right. He still suffered from anæmia, for which tonics and iron were being administered, but so far as the disease of his cheek was concerned, he was cured. He still remains cured. There has been no recurrence.

FIG. 10.—Leucoplakia at angle of mouth. Drawing from life. (Case X.)

So far as I can determine this is the first time in which 606 was administered for the cure of leucoplakia, and the results secured could certainly not be surpassed.

A year elapsed before I had an opportunity to see another case, but on May 21, 1912, a former patient reappeared.

CASE X (Fig. 10).—*Leucoplakia of right angle of mouth.* J. A. S., an American, twenty-nine years of age. His family history was negative. He has had no serious illness. He stated that he had a chancre eight years ago, but no secondary symptoms ever developed, and his family physician believes that the sore noted was probably herpetic or a chancroid. No evidence of syphilis could be detected; there was no adenopathy.

When first seen in 1911, he came for an operation for a tumor of the left spermatic cord. This was removed by operation and proved to be tubercular in character. He came to my office after a year's absence in order that I might observe the ultimate result of the operation. The scar could be with difficulty determined, and there was no secondary involvement of the neighboring parts.

The patient called my attention to the fact that on the right side of the mouth

there was a growth which had started during the previous year and which appeared to be extending. Examination showed this to be leucoplakial in character, of the typical fan-like arrangement of four or five striæ, 1 mm. in width, extending posteriorly from the angle of the mouth upon the right side. The central strips were 2 cm. in length. The lateral ones were not so long. No pain had been experienced, but it was an annoyance to him in speaking and he felt continually obliged to rub the growth with the tip of his tongue.

A Wassermann test was made but proved negative. With the experience of the former patient fresh in mind, no attempt was made at any local treatment, save the penciling over the mucous membrane once or twice a day with a solution of permanganate of potash and a mouth wash of three parts of alcohol, one part of glycerin and six parts of water. The usual full dose of salvarsan was administered. The growth progressively decreased in size and at the end of a month the mucous membrane of the buccal cavity was normal. No recurrence has taken place.

CONCLUSIONS

Leucoplakia buccalis then may be regarded as a chronic, slowly progressive disease over the buccal mucous membrane.

The etiology of the disease is unknown. Local irritants in the mouth are unquestionably factors in its production, but it is probable that it is a disease of parasitic origin. Just what the parasite is remains to be determined, but that it is similar in character to the known parasite which causes syphilis and to the unknown parasite which often leads to the production of epitheliomata in the same region, is probable. Whether this parasite resembles the spirochæte, whether it is a protozoal form similar to a plasmodium of malaria, of Texas fever, of sleeping sickness or of other diseases, is not known. At any rate, it seems probable that it may be destroyed by the same means now at our disposal which will destroy the spirochæte. The writer has used salvarsan in two cases of malaria in which the plasmodium was found before the injection. Both patients have never had a subsequent chill, all their malarial symptoms have disappeared, and health has been restored. Subsequent examinations of the blood failed to show plasmodia. In one instance of non-operable small round-celled sarcoma of the upper jaw, subsequent to an operation where the entire superior maxilla was removed and the diagnosis determined beyond all question in one of the best hospitals in the city, this remedy was also administered with excellent results. Pain was eliminated, and for at least a year no further progress of the disease took place. It seems probable that arsenic administered in this form may be safely and widely used in all forms of disease of parasitic origin, non-bacterial in character. The capsule surrounding most of the bacteria appears to prevent the destructive action of arsenic and thus prevents beneficial results from being secured by the injection.

It, of course, would be unwise to predict that all cases of leucoplakia can be as readily cured by this means as the two which have been recorded, but at any rate, it is safe to state that a new weapon has been found which will in some cases at least act efficiently as a cure for a disease notoriously resistant to all former methods of medication or of treatment.