A PECULIAR AFFECTION OF
THE MUCOUS MEMBRANE OF THE LIPS
AND ORAL CAVITY

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[Reprinted from the Journal of Cutaneous and Genito-Urinary Diseases
for November, 1896]
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(Illustrating Dr. Fordyce’s Article.)
Fig. 1.—Section through mucous membrane, showing thickened epithelial layer and stratified surface cells. Spencer ½ in. Projection ocular 2, Zeiss. × 100.

Fig. 2.—A more highly magnified view of a portion of Fig. 1, showing the peculiar change in the cell protoplasm. Spencer ½ in. Projection ocular 2, Zeiss. × 300.

Fig. 3.—A more highly magnified view of a portion of Fig. 2, showing the cell degeneration. Spencer ⅛ in. Projection ocular 2, Zeiss. × 800.

ILLUSTRATING DR. FORDYCE'S ARTICLE ON A PECULIAR AFFECTION OF THE LIPS.

(Photomicrographs by the Author.)
A PECULIAR AFFECTION OF THE MUCOUS MEMBRANE OF THE LIPS AND ORAL CAVITY.*

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In the autumn of 1895 I presented to the New York Dermatological Society† a physician who had consulted me for an affection of the mucous membrane of the lips and oral cavity. The patient's attention was first attracted to the condition about two years ago by a symmetrical fading of the vermillion border of the upper lip, extending from the corners of the mouth almost to the median line, leaving only a narrow margin free next to the skin and a wedge-shaped area in the center of the lip. The two patches were connected at the inferior median line, where the lips come in contact, by a segment of a circle, making three patches, all of uniform color, with well-defined borders and areas slightly elevated. When first noticed the color was but a shade lighter than normal; the appearance otherwise did not seem abnormal, but, by putting the tissues on the stretch, small, irregular, closely aggregated miliumlike bodies of a light yellow color just beneath the surface epithelium were plainly visible and completely covered the patches. (See colored plate.) While the borders appeared as well-defined lines, a chain of from one to three milium bodies could occasionally be seen in advance of the main patch, but not disconnected. The two sides have progressed sym-

* Read at the Twentieth Annual Meeting of the American Dermatological Association, September 8, 1896.
† Two hundred and forty-sixth regular meeting, October, 1895. Journal of Cutaneous and Genito-Urinary Diseases, January, 1896.
metrically. On the lower lip was a parallel line of similar bodies extending horizontally through the center. The patient is unable to state positively whether there has been any extension of the condition since it was first noticed; he is positive, however, that the color has become lighter within the past six months. This he thought might be due to the fact that the bodies have become more closely aggregated. The subjective symptoms have been very slight. The patient experiences at times a slight immobility of the upper lip, which he is inclined to attribute to a dryness just above a nerveless tooth. This feeling preceded the onset of the above condition by several years. Within the past year he has felt a slight burning and itching of the upper lip, accompanied by some stiffness, as though the lip was swollen. This is only an occasional feeling, and may be due to errors of diet. The patient does not use tobacco or alcohol. His family as well as his past history is negative, and he is in good health at present.

An examination of the mucous membrane of the mouth revealed a similar condition extending along the line of the closed teeth from the angle of the mouth backward to a point opposite the lost molar teeth. The lesions within the oral cavity were lighter in color and in places somewhat elevated and papillomatous in character.

On the lips the minute yellowish-white bodies imbedded in the mucous membrane suggested the ordinary milium seen on the face. An endeavor was made to remove them by incising the skin and picking them out with a needle. They were, however, found to be firmly adherent, and could with difficulty be detached from the surrounding tissue.

The lesions were rendered much less noticeable for a time by the use of the curette. When the superficial layer of the epithelium was scraped away, some of the bodies could be pressed out by the blunt edge of the instrument, but as a rule a portion of the discoloration remained, as if only the upper part of the affected tissue had been removed. When the epithelium was restored a marked improvement was noted in the appearance of the lips, but after a few weeks it became less perceptible, gradually assuming the same yellowish-white granular appearance that was present before interference.

Little information was obtained from the members of the society regarding the nature or treatment of this apparently unique affection. Dr. Elliot had observed a similar condition on the mucous surface of the prepuce, and Dr. Bulkley had seen similar lesions on the lips, which he had regarded as akin to milium.

After an examination of some microscopic sections which were
submitted to the members, Dr. Lustgarten agreed with me that the changes were chiefly confined to the epithelial cells, the protoplasm of the cells being apparently converted into a substance allied to keratohyalin, which under normal conditions does not exist in mucous membranes.

Dr. Lustgarten suggested the application of tincture of iodine to the implicated area, on the supposition that the affection was allied to one described by Baelz and Unna. Such applications were subsequently made by the patient, but without a favorable result.

After leaving New York my patient returned to his former home in the South, and wrote to me the following interesting communication:

"I found the same condition, for which I consulted you, in all the members of my family, from the youngest aged seventeen, to the oldest aged forty, including a paternal half sister aged fifty.

"I discovered it in nearly every case examined, existing as a few bodies confined to the lips, to an involvement of both lips and buccal mucous membranes, in individuals who were and in those who were not related. The younger the individual affected, the larger and more grouped were the bodies found to be, involving the inner surface of the upper lip when not found elsewhere. As the affected person grows older, and where there is a family predisposition, as it seems to be worse in some families, the bodies become more numerous, and, judging from their smaller size, undergo atrophy.

"It was not remarked before the age of puberty and existed regardless of sex.

"The same condition prevails, but to a lesser extent, in half the negroes examined. In a mulatto male of seventy years both lips and buccal mucous membranes were implicated. Near the angle of the mouth and extending half the distance backward the membrane presented a smooth opaque surface, somewhat thickened, with three deeply imbedded, slightly elevated papules about half the size of a split pea. Farther back was a pearly epithelial tumor of less size. (This diagnosis was apparently not confirmed by a microscopic examination.)

"He had suffered no annoyance from the affection, although he was accustomed to smoking, chewing, and the use of alcoholic stimulants.

"Some of the persons complain of fissures of their tongues which smart when irritating substances or acids are taken into the mouth.

"In most of the cases seborrhœal eczema was present at the same time."
On returning to his home in the West, he wrote me that the treatment by tincture of iodine had failed to produce any beneficial result. A slight scaly condition of the lips, which was worse in cold weather, had been aggravated by the local application.

"The curetted areas show as much of the epithelial change as elsewhere, but retain more of the normal vermilion color. I have seen a few cases in Oregon, but none so well marked as my own.

"I consulted a number of dentists as to whether they had observed instances of such a condition in the mouth, but received a negative reply to all my inquiries."

Since my attention has been called to the affection by the case of the doctor just reported, I have seen several instances of the same affection in a number of dispensary patients, and several dermatologists have stated to me that they have also observed the same changes on the lips and in the mouth.

I have noted the two following instances in which the mucous membrane lesions were associated with other pathological conditions:

H. P. B., aged forty-seven years. Alopecia and seborrhoeal eczema of the scalp, keratosis of the palms. Miliumlike bodies of lips and inner surface of cheeks presenting an almost identical appearance to the case previously reported. The patient was ignorant of the existence of the trouble, as it gave rise to no subjective sensations.

M. R., aged sixty-three years, smoker (pipe), syphilis twenty-five years ago.

In the center of the lower lip an indurated and slightly ulcerated nodule, probably a beginning epithelioma, was noted.

The mucous surface of the lower lip was slightly scaly, and the seat of a number of pale-yellow nodules; the upper lip and buccal mucous membrane were also involved.

No glandular enlargement was present.

The association of a probably beginning epithelioma with this epithelial cell change is suggestive, and should direct attention to the condition of the upper lip in the early stages of the malignant disease. On the skin we know of many pre-epitheliomatous changes in the epidermis, and it is possible that the changes described may bear some relationship to the cancerous process. In Paget's disease it is known that for many years changes exist in the cells of the epidermis, interfering with the normal formation of horny tissue and leading to malignant changes in the mammary-gland epithelium.
The infrequency of cancer of the upper lip may be explained on the theory that in smoking less pressure is exerted on this part, and consequently there is less danger of the changed epithelium being stimulated to proliferate.

*Microscopical Examination.*—I excised a small piece of tissue from the inner side of the cheek where the pathological condition was well marked and hardened it in absolute alcohol.

The sections were cut in the usual manner and stained in haematoxylin, methylene blue, acid fuchsin, and in other ways. They included the epithelial layer and a considerable portion of the tissue beneath. The entire epithelial layer was considerably thickened, being covered by a number of stratified cells containing flattened nuclei and approaching in character the stratum corneum of the epidermis (Fig. 1). The epithelial cell layer below was also found to be thickened, extending in branching processes within the connective tissue below. The lowermost cell layers were normal, readily taking the stain. With this exception, however, all the epithelial cells were the seat of a peculiar change which seemed to be confined almost exclusively to the protoplasm, their nuclei remaining in a normal condition. (Figs. 2 and 3.)

The change or degeneration in question is best seen by an examination of the photographs. (See plate.) The nuclei in some of the cells is surrounded by a clear space due to a retraction of the protoplasm which is broken up into irregular granules and fragments which have a bright glistening appearance, and were not at all stained by the coloring fluids used.

These granules are also seen in the upper stratified layer, but not so clearly as in the cells below.

The granules differed from keratohyalin in their larger size, irregular outline, and in not taking the staining reagents. Their chemical composition and their reaction to osmic acid were not tested.

It is my intention, however, to do so when an opportunity offers of excising tissue from another case.

It is possible that we have to do, as suggested by Dr. Lustgarten, with a cell change allied to that which takes place in the granular layer of the epidermis, leading to an imperfect cornification of the mucous membrane.

It seems more probable that some degenerative change of an unknown nature has taken place in the cell protoplasm, as indicated by the clear space about the nucleus, and by the breaking up of the cell contents into irregular masses.
The mucous glands were normal, their cells presenting no appearance like those in the epithelial covering.

There was also no evidence of an inflammatory process in the subepithelial tissue.

*Diagnosis.*—In considering the diagnosis of the affection, it could scarcely be confounded with leucokeratosis, which presents a uniform bluish-white discoloration of the mucous membrane and not the pale-yellow color seen in my patient. The granular look of the patches differs from the diffuse change which leucokeratosis presents. In 1890 Unna * described a chronic affection of the mucous membrane of the lips to which his attention was first called by Dr. Baelz, characterized by thickening, suppuration with crusting, and terminating after a variable duration in healing with scar formation.

Unna believed it to be an affection of the mucous glands.

He does not mention any changes in the epithelium that would tend to ally it to the affection under consideration.

Jamieson † has lately discussed some superficial affections of the red portions of the lips, reporting a case which clinically corresponds with Unna's description of Baelz's disease.

Jamieson's case affected a Russian Jew who had been addicted to excessive cigarette smoking. The disease began as a scaling spot which continued for two years, then the lip became swollen to double its normal size. In places it was granular, covered by crusts, and in other parts superficially cicatrized.

A careful microscopic examination was made by a pathologist to whom Dr. Jamieson submitted the specimen. He concluded that in its histological features it approached more the character of a mild superficial epithelioma than any other condition. The labial glands were not found in the specimen examined. Jamieson mentions the close resemblance which his case presented to one reported by Galloway ‡ under the name of Chronic Exfoliating Inflammation affecting the Lower Lip, in which the part was swollen, protruding, and covered by a brownish epithelial crust. The condition had lasted for fifteen years. The patient suffered with dyspepsia and also from seborrhoea of the face and scalp.

Both Jamieson's and Galloway's cases are probably examples of Baelz's disease, although Unna's description had evidently escaped their observation.

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† British Medical Journal, December 7, 1895.
‡ British Journal of Dermatology, 1895, p. 113.
Volkmann's cheilitis glandularis could hardly come under the list of affections for differential diagnosis, as it was claimed by that author to be an unmistakable affection of the muciparous glands attended by a thickening of the lip. In my case the glands were found to be normal and no inflammation was present.

Although the individual lesions, smaller than a mustard seed, resembled to some extent the milium bodies on the face, they were grouped in patches so close as to be scarcely distinguishable. Independent of a microscopic examination one could not well refer them to the obstructed ducts of the glands, as the lesions were too numerous to be accounted for in this way.

The clinical features of my own case are totally different from any of those referred to, and the histological appearances are so unlike anything that has come under my observation that I report the affection as an example of a mucous-membrane change, which, while apparently not uncommon, has hitherto escaped observation.