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EPITHELIAL CHANGES IN ORAL SUBMUCOUS FIBROSIS

by

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The reports available on oral submucous fibrosis describe the epithelial changes only briefly. Even so, the findings have been conflicting (see Table I). We therefore felt that it was worthwhile to undertake a detailed analysis of the oral epithelium in patients suffering from this condition.

The most frequently reported findings are thickening and acanthosis of the epithelium. Only two authors describe some atrophy of the epithelium. If the verbal descriptions are compared with the illustrations, a discrepancy is found. Neither *DeSa*'s Fig. 7 (1957) nor *Sirsat & Khanolkar*'s Fig. 1 (1957) exhibit a marked thickening of the epithelium as described in the texts. Most of the cases included in their series were from ear, nose and throat clinics. Hence adequate control material was not available for comparison. One of the present authors (J.J.P.) had the opportunity of studying the histologic sections in *Sirsat & Khanolkar*'s series. While some isolated areas in a few biopsies show epithelial hyperplasia, the bulk of the material shows an atrophic epithelium.

The exfoliative cytology of patients with submucous fibrosis

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Table I

Previously reported histologic changes in the epithelium in oral submucous fibrosis

Author	Number of cases examined histologically	Changes in epithelium
Lal (1953)	2	1. Normal epithelium 2. Flattening of rete pegs
Su (1954)	3	Acanthosis and parakeratosis
DeSa (1957)	?	Marked thickening and acanthosis
Sharan (1959)	8	Hypertrophy, occasionally areas of atrophy. Liquefaction in basal cell layer
Rao (1962)	? (palate) (cheek)	Epithelium normal, but somewhat atrophic
Sirsat & Khanolkar (1957)	40 (palate)	Marked thickening and acanthosis

has been studied by *Peters & Rijsinghani* (1956) who saw a marked pleomorphism in smears from the early stages of the disease. In more advanced cases, groups of cells showed very large nuclei. *Peters & Rijsinghani* emphasized that when cell atypia and degeneration are prominent, the interpretation becomes somewhat difficult.

MATERIAL AND METHODS

This study is based on 23 patients with oral submucous fibrosis. The clinical features of the disease in these patients are described in a previous paper (*Pindborg, Chawla, Srivastava, Gupta & Mehrotra,* 1964). A total of 34 biopsies were taken under local anesthesia. Most of these were punch biopsies. 29 came from the buccal mucosa, 3 from the lower lip, 1 from the palate, and 1 from the tongue. All biopsies were fixed in 10 % formalin, embedded in paraffin and cut in serial sections. The following staining methods were used: Hematoxylin-eosin, a modified Mal-

lory connective tissue stain (*Weinmann & Meyer* 1959), and periodic acid Schiff reagent with or without diastase pretreatment.

The sections were evaluated with regard to thickness of epithelium as judged by the width of the spinous cell layer, type of keratinization, histomorphologic changes in basal and spinous cell layer, precancerous and malignant changes.

FINDINGS

Thickness of epithelium

Thirty of 33 biopsies had en atrophic epithelium, Figs. 1—3. In some biopsies the number of cell rows was as low as 3—4. In

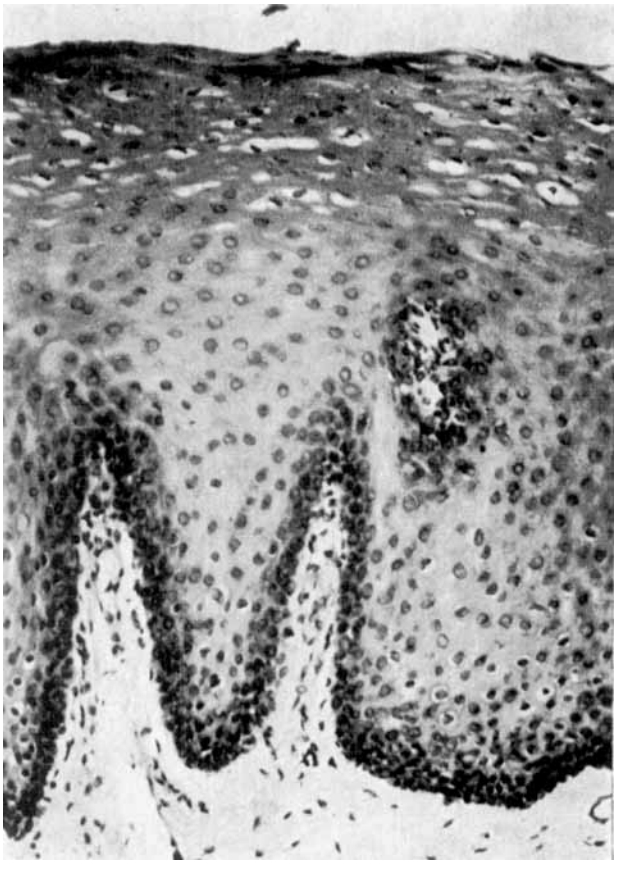

Fig. 1. Width of buccal epithelium in a normal 30-year-old male Indian. × 155.

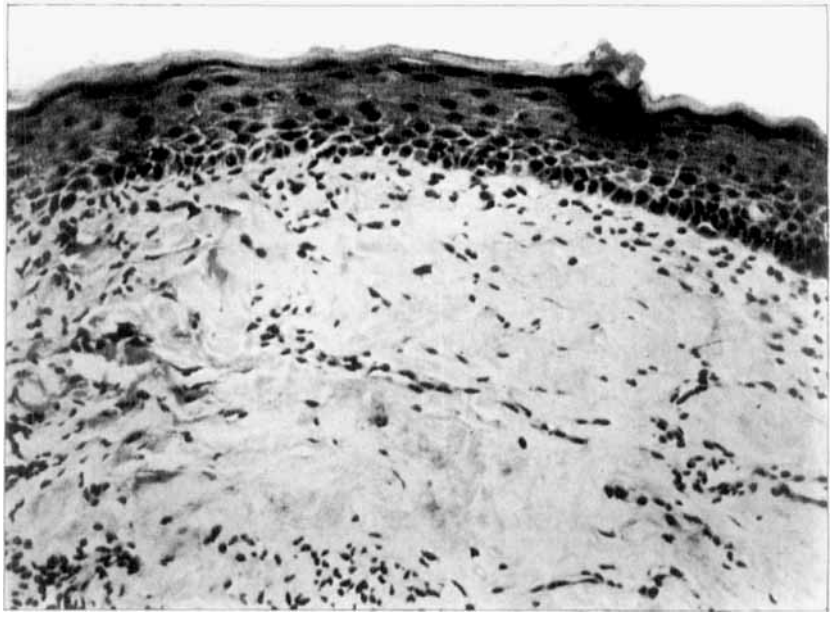

Fig. 2. Atrophy of buccal epithelium in a 50-year-old male Indian with oral submucous fibrosis. Note also the orthokeratosis. × 155.

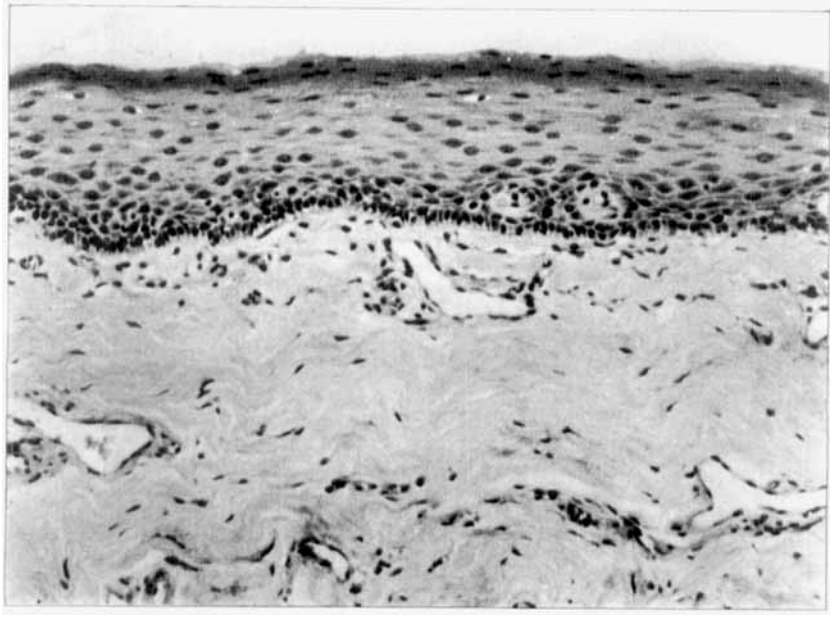

Fig. 3. Atrophy of buccal epithelium in a 60-year-old male Indian with oral submucous fibrosis. Note also the parakeratosis. × 155.

21 biopsies the epithelium was not only reduced in thickness, but the rete pegs had completely disappeared. In some instances the rete pegs were present, but reduced in width. In two biopsies the thickness of the epithelium was normal and in one case a hyperplasia was observed. This patient habitually kept chewed tobacco in the lower labial groove, a habit which sometimes leads to hyperplasia of the epithelium (*Pindborg, Srivastava & Gupta*, 1964).

Type of keratinization

Of 33 biopsies 15 had an unkeratinized surface, but 18 had undergone a keratinizing metaplasia. Ten of these were orthokeratotic, two hyperorthokeratotic, five parakeratotic, and one hyperparakeratotic.

Changes in basal and spinous cell layers

In four biopsies a signet-cell-like degeneration was observed, mainly occurring in the spinous cell layer, Fig. 4. A slight lique-

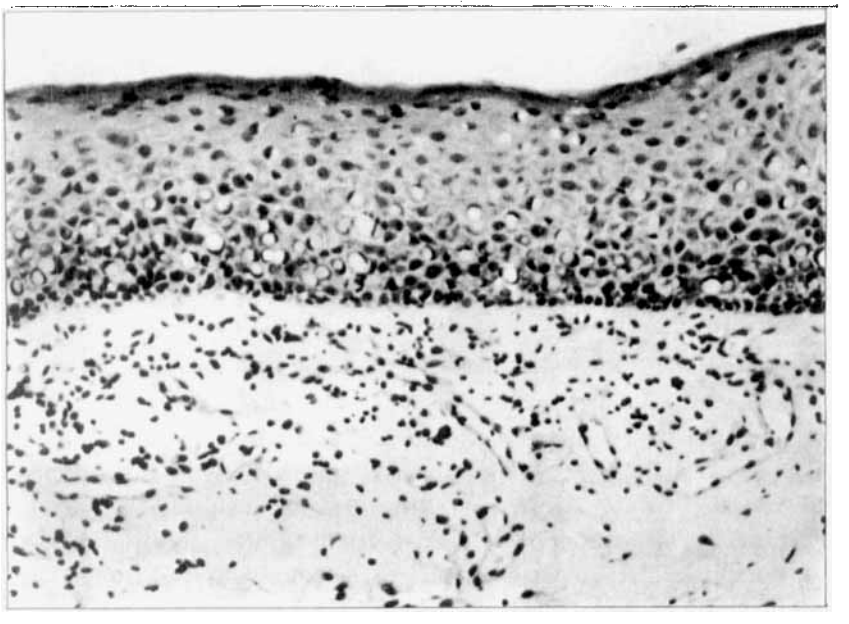

Fig. 4. Atrophic epithelium with signet cell-like degeneration in buccal mucosa of 40-year-old male Indian with oral submucous fibrosis. × 155.

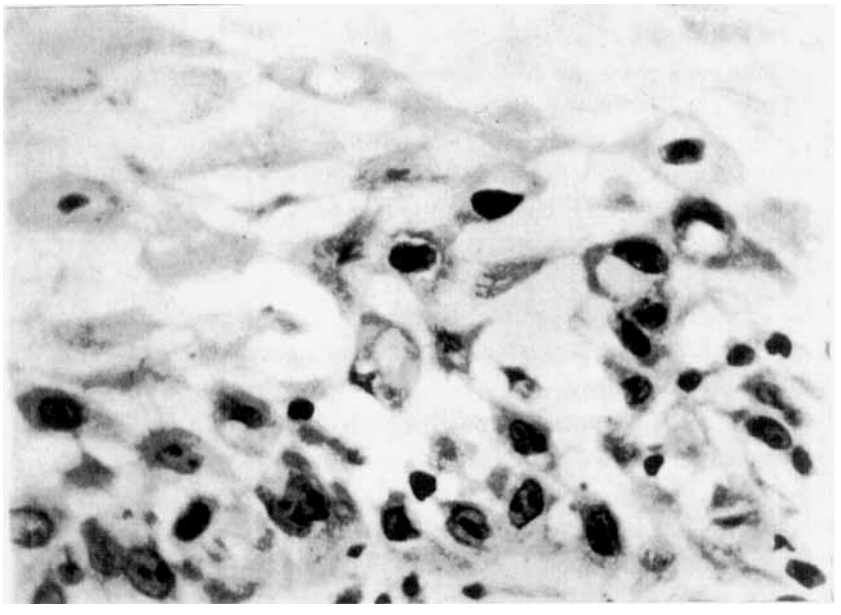

Fig. 5. Marked intercellular edema in lower lip epithelium from 50-year-old male Indian with oral submucous fibrosis. × 600.

faction in the basal cell layer was noticed in six biopsies. The lower part of the spinal cell layer and the basal cell layer were the seats of an intercellular edema in 3 cases, Fig. 5. In one biopsy from the buccal mucosa a subepithelial vesicle was seen. This lesion has been described in detail elsewhere (*Pindborg & Singh*, 1964).

Precancerous and malignant changes

In one biopsy of a lesion clinically diagnosed as papilloma, a well-differentiated squamous cell carcinoma was found. This lesion occurred in the soft palate, and the histologic examination showed the tumor confined to the lamina propria. In the remaining 33 biopsies a rough estimation of the mitotic activity was made. In three cases the rate of cell division was judged to be increased. Clinically, these three lesions had presented a mixture of blanched and red (atrophic) mucosa.

DISCUSSION

In contrast to the majority of previous investigations in which thickening of the epithelium in submucous fibrosis was found, cases studied in this investigation unequivocally show that the epithelium suffers a marked atrophy. The reason for epithelial atrophy may lie in the fact that the underlying connective tissue is markedly changed*). As *Sirsat & Khanolkar* (1957) have pointed out, the changes consist in a fibro-elastotic transformation of the lamina propria. A hyalinized tissue surrounds the blood vessels, and this may cause a reduced nutrition of the epithelium.

Atrophy of the oral mucosa associated with achlorhydria has been reported as a precancerous condition by *Sharp* (1956). The atrophic changes in the epithelium in submucous fibrosis should, therefore, lend support to the suspicion that they also are precancerous changes. In three of the biopsies in this investigation, an increased mitotic activity was noted, and the clinical picture was that of a lesion of speckled appearance, almost identical with the picture sometimes seen in leukoplakias. From studies by *Pindborg, Renstrup, Poulsen & Silverman* (1963) it is known that the speckled type of leukoplakia is often associated with premalignant changes. Therefore, we feel that patients suffering from submucous fibrosis who show red-white oral lesions should be followed closely.

Normally, the human buccal mucosa is unkeratinized. In the present study, 14 out of 29 biopsies from the buccal mucosa had an unkeratinized epithelium. The remaining biopsies exhibited different types of cornification. The role of the submucous fibrosis in this metaplasia cannot be considered as established. In all the patients with this change, the mucosa was habitually exposed to tobacco, which could also lead to cornification.

The significance of the occasional signet-cells in the spinous cell layer and that of the liquefaction in the basal cell layer are not clear. *Sharan* (1959) reported a similar liquefaction-degeneration, but does not comment further upon it. It would be interesting to compare in a larger number of cases the liquefac-

*) The connective tissue changes in the present material will be reported in subsequent papers.

tion zone in submucous fibrosis with the same phenomenon in lichen planus. Clinically, the atrophic type of lichen planus has certain similarities with the speckled type of submucous fibrosis. It should be added that the atrophic type of lichen planus is the one most likely to undergo malignant transformation (*Andreasen & Pindborg,* 1963).

SUMMARY

Thirty-four biopsies, predominantly from the buccal mucosa in 23 patients with oral submucous fibrosis, were analysed with regard to epithelial changes. In contrast to findings of previous investigators a marked atrophy of the epithelium with disappearance of rete pegs was observed, in 91 % of the specimens examined. In a few biopsies signet-cells and liquefaction degeneration were noticed. Increased mitotic activity was seen in three biopsies and squamous cell carcinoma in one. The significance of an atrophic oral epithelium as a possible precancerous condition is discussed.

RÉSUMÉ

ALTÉRATIONS ÉPITHÉLIALES DANS LA FIBROSE SOUS-MUQUEUSE DE LA CAVITÉ BUCCALE

34 biopsies, provenant principalement de la muqueuse des joues, chez 23 patients présentant une fibrose sous-muqueuse de la cavité buccale ont été analysées en ce qui concerne les altérations épithéliales. Contrairement aux résultats antérieurs d'autres observateurs, une atrophie marquée de l'épithélium avec disparition des digitations épithéliales a été observée, dans 91 % des specimens examinés. Dans quelques biopsies, on a constaté des cellules en forme de sceau et une dégénération par liquéfaction. Une augmentation de l'activité mitotique a été observée dans trois biopsies et un épithélioma malpighien spino-cellulaire dans une biopsie. La signification d'une atrophie de l'épithélium buccal en tant qu'altération précancéreuse possible, fait l'objet d'une discussion.

ZUSAMMENFASSUNG

EPITHELIALE VERÄNDERUNGEN BEI ORALER SUBMUKÖSER FIBROSE

Bei 23 Patienten mit oraler submuköser Fibrose wurde 34 Gewebsproben vorzugsweise der bukkalen Mukosa entnommen und hinsichtlich epithelialer Veränderungen analysiert. Im Gegensatz zu Funden früherer Forscher wurde eine deutliche Atrophie des Epithels mit Schwund von Epithelzapfen beobachtet, was bei 91 % der untersuchten Proben der Fall war. In einigen der Proben wurden Siegelzellen und Verflüssigungsdegeneration beobachtet.

Eine erhöhte mitotische Aktivität wurde bei 3 Proben und ein Plattenepithelzellenkarzinom in einer Probe festgestellt. Die Bedeutung atrophischen oralen Epithels als ein möglicherweise präkanceröser Zustand wird erörtert.

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