

Snuff-induced lesions in Finnish recruits

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Abstract - Snuff-induced lesions from 21 snuff users were studied clinically, histologically and by electron microscopy. Clinically most lesions appeared coarsely wrinkled, grayish white and slightly elevated. All lesions were found in the upper vestibular area. Histologically, epithelial thickening, acanthosis, vacuolation of surface cells and a slight subepithelial inflammatory reaction were seen. The electron microscopic findings revealed an intact basement lamina, increased tonofilament concentration moving up towards the surface of the epithelium, widening of intercellular spaces in the spinous cell layer and partial keratinization of surface cells. The salivary flow of resting saliva showed a slightly significant increase compared to controls. That of stimulated saliva was not significantly increased among snuff users.

Key words: electron microscopy; epidemiology, oral; oral mucosa, diseases; snuff-induced lesion; tobacco habits.

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The use of snuff is a worldwide phenomenon. What has been mainly an adult habit seems to have become a popular habit among adolescents and even children (1, 2). The use of snuff, snuff dipping, consists of placing a pinch of smokeless tobacco in the labial or buccal sulcus. The time of dipping varies greatly but some persons keep the quids in place most waking hours. Lesions associated with the use of snuff have been well documented, especially in the United States, Denmark and Sweden (2-7). The clinical and histologic picture of these lesions has been shown to be very similar in different

studies (3-6). The possible carcinogenicity of snuff has received special attention and has been the subject of controversy.

According to some Scandinavian studies and some reports from the United States there is no clear correlation between snuff dipping and oral cancer (7-11) while other studies suggest a positive relation (1, 3, 12-17). Axéll (3), for example, found an annual incidence of one case of oral cancer per 200 000 male snuff dippers. On the other hand, Smith (7) could find no oral cancer or epithelial dysplasia in 157 biopsies of clinically severe cases of snuff induced lesions.

Studies on the use of snuff have not been made earlier in Finland. The aim of the present investigation was to study the clinical, histologic and ultrastructural appearance of snuff-induced lesions and to assess the frequency of snuff dipping among a selected group of Finnish recruits and to study the salivary flow and the buffer capacity of saliva among these snuff dippers.

Material and methods

The material for the present study consisted of 441 recruits aged 17-29 at the military unit Nylands Brigad in Tammsaari, Finland. The recruits completed a questionnaire with eight questions concerning snuff habits, smoking and drinking habits and frequency of dental care. 48 snuff users, aged 17-21 with a mean of 18.9, were identified on the basis of the questionnaire. Each snuff user was subjected to a thorough examination of the mucosa where the snuff-induced lesions were clinically registered and photographed in color.

Biopsy - Biopsies were obtained from 21 snuff users with oral lesions under local anesthesia. Of the remaining 27 snuff users 12 showed no alterations of the mucosa. Of these, eight had given up the habit when they joining the military unit (3 wk earlier) and four had started 2-3 wk earlier. The remaining 15 were either indisposed or would not submit to a biopsy. The biopsy specimens were cut in two. One part was fixed in a 10% formalin solution, dehydrated, embedded in paraffin, cut serially in 2- μ m-thick sections and stained with hematoxylin-eosin. These specimens were then studied under the light microscope. The other part was fixed for 60 min in a 2% glutaraldehyde solution and transferred to a 0.1 M phosphate buffer solution. After refixation in 1% osmium-tetroxide the specimens were dehydrated and embedded in Epon, sectioned in 1- μ m-thick sections for light microscopy and in 40-60-nm-thick sections for electron microscopy. These specimens were then studied under a Jeol JEM-100 CX electron microscope.

Saliva - Before biopsy resting and stimulated salivary excretion were measured. Measurements were undertaken between 8 and 9 p.m. and none of the subjects were allowed to use snuff for 1 h prior to collection of saliva. The resting saliva was

collected by letting the saliva flow unaided into a measuring glass. The stimulated saliva was collected in the same manner using a piece of paraffin as salivation-stimulator. The collecting time was 5 min. The stimulated saliva collected was then studied concerning buffer capacity (Dentobuff, Orion Diagnostica, Espoo, Finland). The saliva of 10 non-snuff using controls was collected and studied using the same method.

Results

Approximately 11% of the recruits examined used snuff. The mean duration of the snuff habit was 4.2 yr ranging from 2 wk to 12 yr. The onset of the habit ranged from 8 yr of age to 20 with a mean of 14.4 yr. The frequency of dipping ranged from 1 to 20 per day with a mean exposure time of approximately 45 min. All snuff users kept the quid in the maxillary labial sulcus. 83% of the snuff dippers used the same brand of wet snuff ("Strengberg's grov snus", Finland; pH approximately 8.5) whereas the rest used various Swedish brands. The lesion corresponded to the localization of the quid and included the alveolar and labial mucosa to varying degrees. Eleven lesions appeared as



Fig. 1. Snuff-induced lesion in maxillary left vestibulum of a 19-yr-old man caused by continuous use of snuff for 5 yr. Note wrinkled, "dried mud" appearance and slight elevation of lesion.

a milk-like whitish coloration of the mucosa whereas 25 lesions showed varying degrees of coarse wrinkling resembling dried mud in appearance (Fig. 1). The color was whitish to gray with a frequent brown discoloration. Most lesions appeared slightly raised and irregular in outline. The only symptom reported was a slight itching from the first quid of the day.

LIGHT MICROSCOPIC FEATURES

Epithelial hyperplasia and acanthosis was found in all cases. Large vacuolated cells with rests of cell nuclei were noted in the surface layers. This layer varied considerably in thickness. Hyperorthokeratinization was noted in 12 cases and hyperparakeratinization in nine cases. In one case a Chevron-type of keratinization could be demonstrated. A mild subepithelial inflammatory cell infiltrate consisting mainly of lymphocytes was noted in all cases (Fig. 2). In one case mild epithelial dysplasia was noted con-

sisting of atypical and increased mitoses and loss of basal cell polarity.

ELECTRON MICROSCOPIC FEATURES

In the basal cell region a single and intact basement lamina and an increase in the amount of tonofilaments in basal cells was noted. In 10 cases out of 21, capillaries were seen lying only 1–3 μ m from the basal cells (Fig. 3). An abundance of glycogen rosettes was seen in the spinous cell layer. In the spinous cell layer and moving towards the surface an increase in the amount of tonofilaments was noted in all specimens. Lamellated "Odland bodies" were found in the spinous cell layer of 12 specimens. Keratohyaline granules and keratohyaline masses of irregular arrangement were observed in the spinous cell layer. Here widening of the intercellular spaces and intercellular edema was noted. The surface cells showed degenerative changes and few cell organelles. All specimens showed keratinized and transitional cells (Fig. 4).



Fig. 2. Histologic section of lesion in Fig. 1. Note vacuolated epithelial surface layer, acanthosis and slight subepithelial inflammation. H&E, $\times 120$.

SALIVA

The resting salivary flow was slightly higher among the snuff users than among the controls, 0.51 ml/min vs. 0.38 ml/min. This difference is statistically slightly significant ($t = 2.07$, 29 df, $P < 0.05$). The stimulated salivary flow was somewhat higher among the snuff users than among the controls. The corresponding means for stimulated saliva were 1.73 ml/min vs. 1.23 ml/min. This difference is, however, not statistically significant ($t = 2.01$, 29 df, $P > 0.05$). No differences in buffer capacity were noted.

Discussion

It should be stressed that the figures given in this paper present a selected material as more than 50% of the recruits studied came from the western part of Finland, the Ostro-

botnia, where snuff dipping seems to be much more frequent than in other parts of Finland. Therefore, the percentage of snuff dippers, 11%, in our study should be considered high compared to the average figure for Finnish young men.

The histologic changes demonstrated in this study correspond well to those found in earlier investigations (3-6). However, the chevron-type of parakeratinization demonstrated by PINDBORG (5) could be found in only one of our specimens. Nor could we demonstrate any subepithelial deposits like those found by other investigators (3, 18, 19). The finding of a case of mild epithelial dysplasia would suggest a positive relation

between snuff dipping and malignant changes. It must be kept in mind, however, that this may be a reactive change directed towards the subepithelial inflammatory cell infiltrate. The ultrastructural changes were limited to the epithelium. Our findings are similar of FRITHIOF (4) but less dramatic, which may be explained by the relatively short exposure time of snuff to our subjects. The basement lamina was intact in all our specimens, giving no suggestion of invasive changes. The submucosal filamentous material found by FRITHIOF (4) could not be demonstrated in our specimens. This finding may be due to a specific brand of snuff or a reaction to prolonged exposure of snuff. The



Fig. 3. Electron micrograph of the lesion in Fig. 1. Epithelial basal cell layer shows increased amount of tonofilaments and widened intercellular spaces. A single and intact basal lamina is seen (arrows). Also note large capillary (c) lying immediately below the basal cell. N, nucleus. Electron micrograph, $\times 13000$.

finding of a slightly significant increase in resting salivary flow among snuff users is probably only a reaction to this local irritant. Experimental studies using rats and hamsters (8, 9, 20) have shown that exposure of snuff to the oral mucous membranes for most of the animal's life span cause changes that are limited to the epithelium. No malignancies have developed in these animals. However, these tests were done in hamster cheek pouches or artificially made test canals in rats which anatomically and functionally differ from human oral mucosa. Furthermore the life span of these test animals may not be long enough for snuff to cause malignancies. Some of our subjects had given up

snuffing only recently after dipping for many years and showed a clinically healthy mucosa. This supports the findings by FRITHIOF (4) and PINDBORG & RENSTRUP (5) that snuff-induced lesions are reversible, especially in the early stages. A prolonged exposure time will, however, increase the possibility of malignant development and patients should therefore be informed about the risks involved in snuff dipping and encouraged to give up the habit.

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Fig. 4. Surface of same lesion. Note narrow intercellular spaces and typical keratin pattern (k). Electron micrograph, $\times 26\,000$.

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