Clinical classification of Swedish snuff dippers' lesions supported by histology

Gunilla Andersson[1], Tony Axéll[1] and Åke Larsson[2]

Departments of [1]Oral Surgery and Oral Medicine, [2]Oral Pathology, Lund University, Malmö, Sweden

Andersson G, Axéll T, Larsson Å: Clinical classification of Swedish snuff dippers' lesions supported by histology. J Oral Pathol Med 1991; 20: 253–7.

From a total material of 184 Swedish users of loose packed moist snuff and 68 users of portion-bag packed moist snuff, cases were selected from subgroups based on a four-point clinical grading scale. The selected material for the study comprised 70 cases (ten from each clinical grade group, no Degree 4 lesion was found among portion-bag users). Features recognized in biopsies from these cases together with findings in previous studies correlated well with the use of a four-point scale for the grading of clinical changes, especially in the context of discriminating lesions for which special efforts should be undertaken to make the patient stop or change the snuff dipping habit and for selecting patients in whom regular clinical follow-up including a biopsy should be carried out. In this article is also discussed the labeling of the clinical oral mucosal changes seen at the site where a quid of snuff is regularly placed. The conceptual use of "snuff dippers' lesions" is recommended instead of e.g. snuff-induced leukoplakia.

Key words: leukoplakia; mouth disease; oral mucosa; pathology; snuff; tobacco, smokeless.

Gunilla Andersson, Department of Oral Surgery and Oral Medicine, Faculty of Odontology, Lund University, S-214 21 Malmö, Sweden.

Accepted for publication December 21, 1990.

The habitual use of oral snuff, snuff dipping, is a habit where a pinch of powdered or particulate tobacco is placed in contact with the oral mucosa. In Sweden, by far the most frequent site of placing a quid of snuff is the vestibular area inside the upper lip and almost exclusively non-fermented moist snuff is used (1).

Almost invariably, a clinically visible change can be found on the site of the oral mucosa where the snuff is regularly placed (2). This change has been called snuff dippers' lesion (2–3, 4), snuff dippers' keratosis (5), snuff-induced oral leukoplakia (6), and snuff-induced lesion (7–9). In the present article the label snuff dippers' lesion will be used.

Subdivision of a diagnosis into subgroups may be useful for many reasons. It may be used to study various aspects of a lesion and its different appearances and it may also form the basis for recommendations on clinical routines. A four-point scale for subgrouping snuff dipper's lesions, suggested by AXÉLL (2), was used in the present study. This scale is based on clinical criteria including wrinkling, thickening and color changes of the oral mucosa.

The four-point scale has previously been used in several studies on snuff related lesions (1, 4, 7, 10, 11). A modified classification has been used by GREER & POULSON (12) and GREER *et al.* (13) who reduced the four-point scale to a three-point scale, since in their studies of teenagers, adults, and geriatric patients they were able to classify all lesions into one of Degrees 1–3. HOLMSTRUP & PINDBORG (14) have speculated on whether the three-point scale is applicable on a world-wide basis, but they state that this must await future studies. The aim of the present study was to analyse whether the four-point scale is relevant or justified based on its correlation to the histologic appearance in tissue biopsies.

Material and methods

The material for the analysis of the clinical grading comprises 252 men who, at the sampling and recruitment procedures, were all using Swedish moist snuff on a daily regular basis; 184 were using loose snuff and 68 portion-bag snuff. Sampling and examination procedures including the taking of biopsies are detailed in articles by ANDERSSON & AXÉLL (1) and ANDERSSON *et al.* (10). The distribution of lesions on the four-point scale, as well as consumption data, are detailed in Table 3 in (1).

Snuff dippers' lesions were subgrouped according to the mentioned four-point scale (2). *Degree 1:* a superficial lesion with a color similar to the surrounding mucosa, and with a slight wrinkling. No obvious mucosal thickening. *Degree 2:* a superficial, whitish or yellowish lesion with wrinkling. No obvious thickening. *Degree 3:* a whitish-yellowish-to-brown, wrinkled lesion with intervening furrows of normal mucosal color. Obvious thickening. *Degree 4:* a marked, white-yellowish-to-brown and heavily wrinkled lesion with intervening, deep and reddened furrows and/or a heavy thickening.

Selected for histologic analysis in the present study were specimens from 10 consecutive subjects from each "clinical lesion group" comprising the following fractions of the total collected material. From loose snuff users were selected all 10 Degree 1 lesions, 10 of 33 Degree 2 lesions, 10 of 130 Degree 3 lesions and 10 of 11 Degree 4 lesions. From portion-bag snuff users were selected 10 of 13 Degree 1 lesions, 10 of 31 Degree 2

Table 1. Age and consumption factors for 10 consecutive subjects of loose and portion-bag snuff users with lesions of Degree 1 through Degree 4.

Product	Clinical grading	Age Mean±SD	Consumption h/Day Mean±SD	g/day Mean±SD	Yr Mean±SD
Loose	1	40.2±8.9	7.1±4.5	10.6±6.7	10.5±5.7
Loose	2	36.0±8.9	5.9±3.1	17.1±9.8	10.4±6.5
Loose	3	43.2±18.0	8.9±3.8	19.8±9.5	16.6±3.4
Loose	4	39.6±14.1	11.8±4.0	26.5±13.1	15.8±7.7
Portion-bag	1	37.9±15.6	8.1±4.0	9.8±3.5	3.5±3.3
Portion-bag	2	36.7±5.3	9.2±3.1	9.9±4.2	3.0±2.4
Portion-bag	3	38.0±7.4	10.7±3.3	12.6±5.3	4.2±2.8

No Degree 4 lesion was recorded, in portion-bag users

lesions and 10 of 24 Degree 3 lesions. No Degree 4 lesion was encountered among portion-bag snuff users. The number of specimens selected for analysis thus totalled 70. Age and consumption data for the subjects from whom the biopsies were secured are shown in Table 1.

Histologic criteria were the same as those used in previous reports based on the total material (10, 11, 15). Among these, two major epithelial surface patterns, Types 1 and 2, were recorded. The most commonly encountered pattern was Type 1, characterized by a variably thickened surface layer, composed of vacuolated cells and often showing "chevron-type patterns". This feature was always rhodamine B negative. Type 2 changes were characterized by a variable degree of keratinization, staining positive with rhodamine B. The surface could also be recorded as a thin homogeneous structureless zone, staining eosinophilic and rhodamine B negative. This necrotic surface zone could be recorded alone or in combination with the Type 1 change.

Results

The histologic findings related to the clinical grading of the lesions are shown in Table 2 and in Figs. 1–8.

Changes of the surface layer – These changes were subtle in Degree 1 lesions and became increasingly pronounced in Degrees 2–4. A necrotic rhodamine B negative surface zone was a common finding either alone or in combination with Type 1 changes. Type 2 changes were most frequent in lesions of clinical Degrees 1 and 2.

Other histologic observations – Atrophy, hyperplasia, mitoses and basal cell hyperplasia were increasingly more often recorded in lesions with a higher clinical degree. However, three cases of hyperplasia in combination with increased mitotic rate were identified in portion-bag users with Degree 1 lesions, also comprising the three lesions with Type 1 surface changes indicated in Table 2. These three portion-bag users had the highest daily exposure to snuff within this group. In those specimens where increased basal cellularity was recorded, an increased mitotic rate was also seen. A combination of atrophy and hyperplasia was recorded in two cases of loose snuff users showing clinical Degree 4 lesions, comprising also the two cases which showed a necrotic surface zone, but no typical Type 1 or Type 2 changes. In the Degree 4 lesions, three specimens showed loss of cohesion. One of these cases also showed a non-specific ulcer.

Various degrees of non-specific chronic inflammation was observed in all cases. Hyalinization in the connective tissue close to the epithelium was found in a few lesions, predominantly of Degree 4.

The observations in both habit groups can be summarized as follows. In Degree 1 lesions of *portion-bag users* only subtle histologic alterations were seen (Fig. 1), with an occasional Type 1 or Type 2 surface change. Almost all of the portion-bag users exhibiting clinical Degree 2 lesions showed Type 1 (Fig. 2, most common) or Type 2 changes. In addition, 50% of these cases demonstrated an increased mitotic rate. All except one of the portion-bag users presenting with a clinical Degree 3 lesion showed histologic Type 1 changes, often with a necrotic surface zone. The majority of these cases also showed an increased mitotic rate and a few an increased cellular density (Fig. 3). Almost all *loose snuff users* exhibiting clinical Degree 1 lesions showed evidence of Type 1 epithelial changes, often combined with a necrotic surface zone (Fig. 4). The pattern of tissue changes among the loose snuff users exhibiting a clinical Degree 2 or 3 lesion (Figs. 4, 5) was very much in accordance with that observed of the corresponding lesions of portion-bag users. Clinical Degree 4

Table 2. Histologic features in specimens from 10 consecutive subjects of loose and portion-bag snuff users with lesions of Degrees 1, 2, 3 and 4.

Product	Clinical degree	Surface changes: Normal	Only necrotic zone	Type 1	Type 2	Atrophy	Hyperplasia	Increased mitotic rate	Increased cellular density	Loss of cohesion
Loose	1	1	–	8 (6)*	1	–	–	–	–	–
Loose	2	0	2	5 (3)	3	3	1	1	1	–
Loose	3	0	2	6 (3)	2	2	6	4	1	–
Loose	4	0	2	7 (5)	1	5	5	7	5	3
Portion-bag	1	1	5	3 (1)	1	–	3	3	–	–
Portion-bag	2	1	3	4 (3)	3	1	1	5	1	–
Portion-bag	3	0	1	9 (7)	0	3	3	8	2	–

No Degree 4 lesion was recorded in portion-bag users.
* ( ) = number of biopsies showing necrotic surface zone adjacent to type 1 change

lesions, recorded only among loose snuff users, invariably showed more extensive histologic changes, including epithelial atrophy, a high mitotic rate, occasional loss of cohesion and increased cellular density (Figs. 6–8).

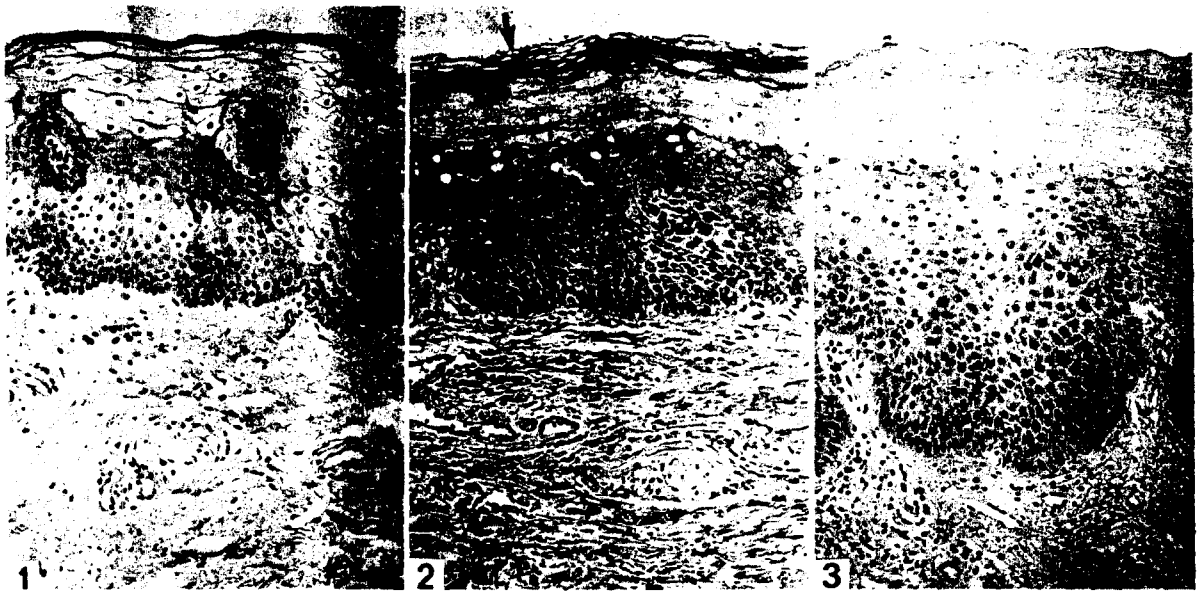

Fig. 1. 48-yr-old man with clinical Degree 1 lesion following use of portion-bag snuff (7 h daily, 8 g a day, 2 yr with regular habit). Normal looking surface epithelium (cf 10) with vacuolated cells typical of this area with only few inflammatory cells. × 140. *Fig. 2.* 28-yr-old man with clinical Degree 2 lesion following use of portion-bag snuff (10 h daily, 12 g a day, 1 yr with regular habit). Typical Type 1 histologic change with thickened surface layer of swollen cells, in this case also accompanied by necrotic surface zone (arrow). This case also showed increased mitotic rate (cf arrow head). × 140. *Fig. 3.* 41-yr-old man with clinical Degree 3 lesion following use of portion-bag snuff (10 h daily, 12 g a day, 10 yr with regular habit). Widely thickened and swollen surface layer (Type 1, cf Fig. 2) and slightly increased basal cell layer is seen. Increased rate of mitoses was also recorded (arrow-heads). × 140.

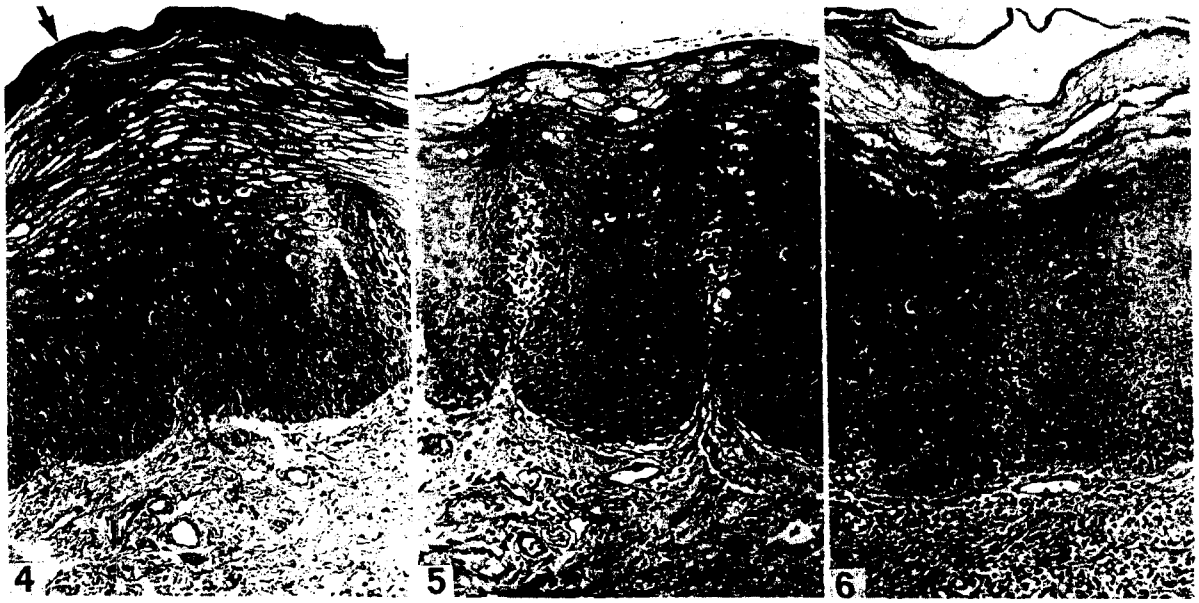

Fig. 4. 48-yr-old man with clinical Degree 1 lesion following use of loose-snuff (13 h daily, 7 g a day, 2 yr with regular habit). Slight change is observed, with thin necrotic surface zone (arrow), small degree of cellular swelling and also some inflammation. × 140. *Fig. 5.* 49-yr-old man with clinical Degree 2 lesion following use of loose snuff (8 h daily, 7 g a day, 10 yr with regular habit). Thin necrotic surface zone (cf Fig. 4) is accompanied by thickened layer of swollen cells (Type 1 change) and also some inflammation. × 140. *Fig. 6.* 30-yr-old man with clinical Degree 3 lesion following use of loose snuff (10 h daily, 33,3 g a day, 15 yr with regular snuff habit). Type 1 epithelial change, with thick surface layer of swollen cells, and also some inflammation. This case showed increased mitotic rate. × 140.

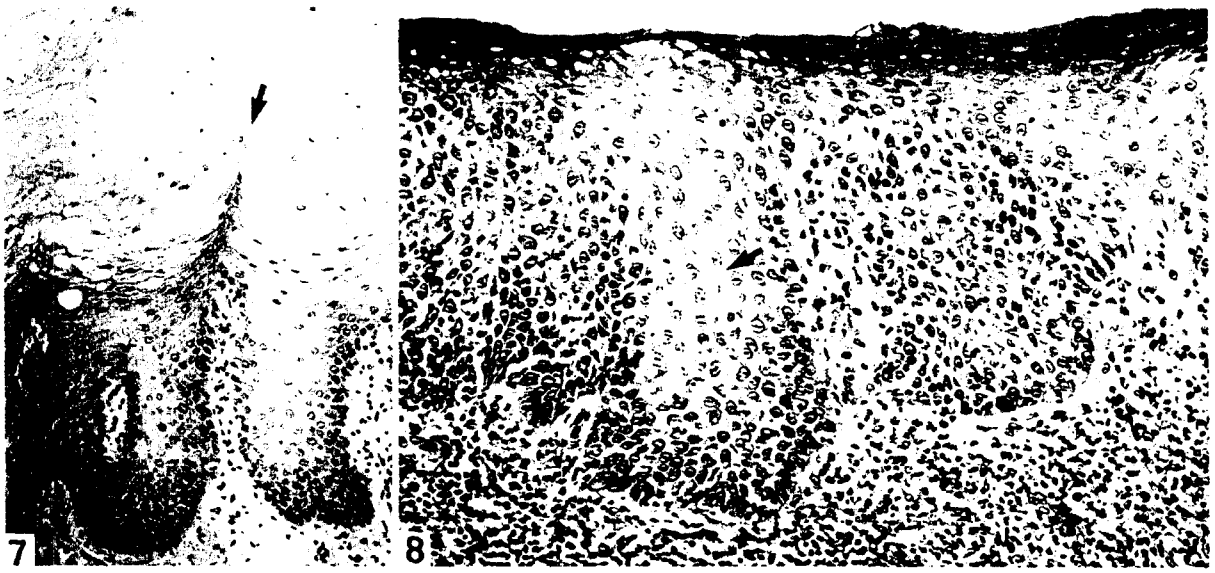

Fig. 7. 35-yr-old man with clinical Degree 4 lesion following use of loose snuff (14 h daily, 40 g a day, 16 yr with regular habit). Heavily swollen surface layer with the typical "chevron pattern" (arrow) and slight inflammation. This case also showed increased mitotic rate and localized areas of epithelial atrophy. × 130. *Fig. 8.* 70-yr-old man with clinical Degree 4 lesion following use of loose snuff (14 h daily, 13 g a day, 8 yr with regular habit). Slightly atrophic epithelium with thin necrotic surface zone and with evidence of loss of cellular cohesion (arrow) combined with heavy inflammation. This case also showed increased mitotic rate, increased cell density and eosinophilic infiltration (This was reported by LARSSON *et al.* (15) as one of the rebiopsied cases with changed habit, resulting in reduced changes at follow-up). × 180.

Discussion

In the present study, a relatively consistent pattern of tissue changes was recorded, indicating that a relationship frequently exists between the presently used clinical grading of the lesions and the histologic changes. In clinical Degree 1 lesions, there was a slight inflammation, but only subtle, if any, epithelial changes. In Degree 2 lesions, the epithelium showed a slightly increased thickness of the surface layer with or without an accompanying surface zone of necrosis. A considerably thickened surface layer of Type 1 (10) characterized Degree 3 lesions. In Degree 4 lesions, a marked thickening of the surface layer may be combined with areas of atrophy and of heavy inflammation. The mitotic rate increased with increasing clinical grading. This might be a physiologic expression of an increased demand for epithelial repair. Increased basal epithelial cell density and hyalinization of the connective tissue were most common in clinical Degree 4 lesions. Loss of cohesion was only recorded in Degree 4 lesions. These findings indicate that more extensive tissue changes could be expected to be present in clinical Degree 4 lesions compared with findings in Degrees 1–3. These more pronounced changes may, thus, appear in a small fraction of snuff dipper's lesions. The character of these changes has been reported and discussed in detail in a follow-up study on clinical and histologic changes associated with snuff use (15).

It should be emphazised that there is no clear cut difference between each of the clinical degrees, either clinically or histologically and, thus, an overlap between the degrees is logical and sometimes occurs. However, subdivision of snuff dipper's lesion is highly justified. Without subdivision, evaluations and analyses presented in several studies on snuff dipper's lesion would not have been possible. Further, the use of a four-point scale for grading clinical changes obviously gives the opportunity of selecting those snuff dipping patients for whom special efforts should be made to make them stop or change their habit, and also to select those patients for whom a regular clinical follow-up program, including a biopsy, should be recommended.

The question whether the grading of snuff dipper's lesion should comprise a three- or four-point scale has been raised (13, 14). From the present findings it may be concluded that the four different clinical degrees employed to register snuff dipper's lesions generally correspond to a fairly consistent set of tissue changes.

In previous articles it has been pointed out that there is a clinical, as well as histologic, difference between the changes encountered among loose and portion-bag snuff users. In this study, histologic differences were observed especially in clinical Degree 1 lesions. With increasing degree, the changes recorded among portion-bag users tend to resemble the histologic pattern of loose snuff users. This is in accordance with previous observations in the analysis of the total material from which the present material was retrieved (10). However, the most important difference in tissue specimens from users of the two package forms of snuff is that, some of the more pronounced histologic parameters e.g. loss of cohesion, were not recorded among portion-bag users. Also no clinical Degree 4 lesion was encountered in this group.

In clinical work and research, diagnostic labels could be helpful tools provided that they are carefully described with clear, easily understandable criteria and also that they are generally accepted. The use of varying diagnostic labels for the same lesion or condition, as for snuff induced oral mucosal changes, is therefore unfortunate. According to a report from an international seminar on tobacco-related oral mucosal lesions, whitish lesions associated with, and thought to be due to, the use of tobacco should be classified as precancerous lesions of tobacco-associated leukopla-

kia (16). However, as pointed out by AXÉLL (2, 17) snuff dipper's lesion should not be considered as a form of leukoplakia, but rather as a separate entity like e.g. smoker's palate, because it is not always whitish. Moreover, according to epidemiologic data from Sweden (18) precancerous potential of Swedish moist snuff has not been established.

It is also most likely that whatever substance is regularly placed at a specific site in the oral mucosa some change may appear. Depending on the contents of the "quid" this change may show varying clinical and/or histologic alterations. Such a "quid lesion" should preferably be recorded as a separate entity and not included among leukoplakias, *inter alia* for purposes of follow-up on the development of that specific "quid lesion".

Based on the findings in this study, we suggest that oral mucosal changes associated with the use of snuff should be labelled snuff dipper's lesion and be graded on a four-point scale.

Acknowledgments – This study was supported by grants from the Faculty of Odontology, Lund University, Malmö, Sweden and from the Swedish Tobacco Research Council (project No. 8716).

References

1. ANDERSSON G, AXÉLL T. Clinical appearance of lesions associated with the use of loose and portion-bag packed Swedish moist snuff: a comparative study. *J Oral Pathol Med* 1989; **18**: 2–7.
2. AXÉLL T, MÖRNSTAD H, SUNDSTRÖM B. The relation of the clinical picture to the histopathology of snuff dipper's lesion in a Swedish population. *J Oral Pathol* 1976; **5**: 229–36.
3. SMITH JF, MINCER HA, HOPKINS KP, BELL J. Snuff dipper's lesion. A cytologic and pathologic study in a large population. *Arch Otolaryngol* 1970; **92**: 450–6.
4. MÖRNSTAD H, AXÉLL T, SUNDSTRÖM B. Clinical picture of snuff dipper's lesion in Swedes. *Community Dent Oral Epidemiol* 1989; **17**: 97–101.
5. ARCHARD HO, TARPLEY TM. Clinicopathologic and histochemical characterization of submucosal deposits in snuff dipper's keratosis. *J Oral Pathol* 1972; **1**: 3–11.
6. ROED-PETERSEN B, PINDBORG JJ. A study of Danish snuff-induced oral leukoplakias. *J Oral Pathol* 1973; **2**: 301–13.
7. HIRSCH J-M, HEYDEN G, THILANDER H. A clinical histomorphological and histochemical study on snuff-induced lesions of varying severity. *J Oral Pathol* 1982; **11**: 387–98.
8. FRITHIOF L, ANNEROTH G, LASSON U, SEDERHOLM C. The snuff induced lesion: a clinical and morphological study of a Swedish material. *Acta Odontol Scand* 1983; **41**: 53–64.
9. JUNGELL P, MALMSTRÖM M. Snuff-induced lesions in Finnish recruits. *Scand J Dent Res* 1985; **93**: 442–7.
10. ANDERSSON G, AXÉLL T, LARSSON Å. Histologic changes associated with the use of loose and portion-bag packed Swedish moist snuff: a comparative study. *J Oral Pathol Med* 1989; **18**: 491–7.
11. ANDERSSON G, AXÉLL T, LARSSON Å. Impact of consumption factors on soft tissue changes in Swedish moist snuff users – histological study. *J Oral Pathol Med* 1990; **19**: 453–8.
12. GREER JR RO, POULSON TC. Oral tissue alterations associated with the use of smokeless tobacco by teen-agers. *Oral Surg Oral Med Oral Pathol* 1983; **56**: 275–84.
13. GREER JR RO, POULSON TC, BOONE ME, LINDEMUTH JE, CROSBY L. Smokeless tobacco associated oral changes in juvenile, adult and geriatric patients: clinical and histomorphologic features. *Gerodontics* 1986; **2**: 87–98.
14. HOLMSTRUP P, PINDBORG JJ. Oral mucosal lesions in smokeless tobacco users. *CA-A Cancer J Clin* 1988; **38**: 230–5.
15. LARSSON Å, AXÉLL T, ANDERSSON G. Reversibility of snuff dipper's lesion in Swedish moist snuff users: a clinical and histologic follow-up study. *J Oral Pathol Med* 1991; **20**: 000–000.
16. AXÉLL T, HOLMSTRUP P, KRAMER IRH, PINDBORG JJ, SHEAR M. International seminar on oral leukoplakia and associated lesions related to tobacco habits. *Community Dent Oral Epidemiol* 1984; **12**: 145–54.
17. AXÉLL T. Occurrence of leukoplakia and some other oral white lesions among 20333 adult Swedish people. *Community Dent Oral Epidemiol* 1987; **15**: 46–51.
18. AXÉLL T, MÖRNSTAD H, SUNDSTRÖM B. Snusning och munhålecancer – en retrospektiv studie. *Laekartidningen* 1978; **2**: 2224–6.