

SMOKELESS TOBACCO: ANOTHER FORM OF HAZARDOUS TOBACCO

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Summary

This review deals with the smokeless tobacco products, their use, composition, systemic and oral diseases associated with it. It is evident that smokeless tobacco is carcinogenic to human and causes various systemic and oral diseases. One of the major cancers caused by smokeless tobacco use is oral cancer and other oral diseases like leucoplakia, dental caries, smokeless keratosis, and other negative influences of smokeless tobacco on oral cavity including staining of teeth, bad breath, mouth sores, attrition and abrasion. This review also tries to describe the possible tobacco cessation intervention in dental office.

Key words: Smokeless tobacco; Systemic diseases; Oral diseases; Tobacco cessation.

Bezdýmný tabák: jiná forma nebezpečného tabáku

Souhrn

Tato práce se zabývá bezdýmnými tabákovými produkty, jejich užíváním, složením a systémovými onemocněními a chorobami ústní dutiny spojenými s jejich účinky. Je zřejmé, že bezdýmný tabák je pro člověka karcinogenní a způsobuje různá systémová onemocnění a choroby ústní dutiny. Jednou z nejčastějších nemocí způsobených užíváním bezdýmného tabáku je rakovina ústní dutiny – další jsou např. leukoplakie, zubní kaz, bezdýmná keratóza a jiné negativní vlivy bezdýmného tabáku na ústní dutinu, včetně zbarvení zubů, zápachu z úst, boláků, opotřebování a abraze. Práce rovněž popisuje snahu zubních lékařů o to, aby pacienti přestali užívat tabákové produkty.

Klíčová slova: Bezdýmný tabák; Systémová onemocnění; Onemocnění ústní dutiny; Skončení užívání tabáku.

Introduction

Tobacco, in general, is used as smoking and smokeless form (ST) (46). The negative health consequences of cigarette smoking are understood very well. Because smoking is declining in the modern world, the tobacco industry has to look for other products that can keep the old customers and attract new ones. Different forms of ST are currently massively promoted and are gaining importance (35). The recent trend has been boosted by marketing of a few types of ST as a harmless alternative to smoking cigarettes (47). In recent years, some health scientists have even suggested ST to be actively promoted among cigarette smokers as a safer (i.e. a harm-reduction product) alternative for those having difficulty to quit smoking (21). Some people even think ST is safe or less harmful than cigarettes. Most people, including smokers, and some health care professionals know almost nothing about ST

products, or even worse, are completely misinformed about the basic characteristics of ST products. Thus, it is important to understand these products, how they are used, their contents and ill effects. There is also a growing interest in the possible adverse health effect of ST because of the increasing popularity of ST use among youth adults.

This review article gives a brief picture about the different types of ST products, their composition and method of use, as well as about their systemic and oral effects. Finally, the possibility of tobacco cessation intervention in dental practice is discussed.

Smokeless tobacco products

ST is a very broad term that refers to more than 30 different types of products around the world (26). ST products are those in which there is no combustion or pyrolysis at the time of use (40). Types,

composition and pattern of use of ST products are highly variable in different parts of the world and within regions (45, 9). ST is normally consumed orally or nasally, and includes products that are placed in mouth, cheek or lip and sucked (dipped) or chewed (26). ST products exist in two major forms: snuff and chewing tobacco. Snuff may be moist or dry. Moist snuff is usually taken orally (25). Normally, a pinch of snuff is placed in the gingival fold under the upper lip, close to the midline frenulum, where it is kept in place for a varying period of time and frequently replaced. The total daily exposure can vary from less than an hour to twenty hours. Snuff is considered a safe alternative to smoking and is socially widely accepted in countries like Sweden. Its popularity was further promoted by introduction of the portion-bag pack, which makes the habit more discreet and easier to handle than the earlier form of loose weight tobacco (47). Dry snuff is usually inhaled through the nose and less commonly used. Chewing tobacco is coarser than snuff and exists in three forms: loose-leaf (sold in a soft package or pouch), plug (sold in a small block) and twist (dried tobacco leaves that are twisted into strands). Chewing tobacco is usually placed in the oral buccal vestibule, and it is called as “chaw” or “quid”. This quid may be retained in the mouth for hours, and the user expectorates saliva that mixes with the tobacco extract (25). Another type of ST product also includes paste or powder that is used on the gums or teeth (26). ST products are placed in contact with oral or nasal cavities against the mucosal site that permits the absorption of nicotine into the human body (45). Cigarette smoking is pandemic, affecting large proportions of the population worldwide. In contrast, the use of ST is endemic, mainly restricted to certain geographical areas such as North America, the Scandinavian countries, India, Bangladesh, Southeast Asia and part of Africa (4). South Asia is a major producer and net exporter of tobacco. Over one-third of tobacco consumed regionally is ST (14). Oral ST (moist snuff) is popular in Sweden and Norway, but it is banned from sale within the majority of the European Union countries (39). The use of moist snuff is widespread in Sweden. In 2004, approximately 800,000 Swedes were daily users, which corresponds to 22% of the male population and 3% of the female population (2). There are approximately 100 million users of ST products in India and Pakistan (40). In developing countries ST

is mostly chewed with other ingredients. Chewing is practiced in different ways: the main ingredients are usually areca nut (betel), leaf, lime and tobacco (9). This mixture is referred to as betel quid (45). The main types of ST in western countries are chewing tobacco and oral snuff (9). Worldwide, several names are used to denote different ST products; plug, gutkha, khiwan, khani, iq'milk, zarda, naswar, nass, chimo, toobak, shamma, gudhaku, gul, mishri, maras and moist snus (44).

ST is a complex chemical mixture, including not only components of the tobacco leaf, but also chemicals added during the manufacturing process. ST contains addictive chemical nicotine and more than 20 cancer-causing chemical substances (31), but the actual number of carcinogens found is fewer than in cigarette smoke (44). The most important carcinogens identified in ST are tobacco-specific N-nitrosamine (TSNA), N'-nitrosonornicotine (NNN), and 4(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). NNN and NNK are formed from nicotine during curing, ageing and especially during fermentation of tobacco (17). Moreover, chemicals including radium-226 and lead-210 are also found in ST products (25). Tobacco-specific nitrosamines are the most prevalent strong carcinogens in ST products. Carcinogens and other chemicals present in ST products can vary widely in different parts of the world. It has been reported that the levels of tobacco-specific nitrosamines in ST products used in India are considerably higher than those found in most ST products marketed in Europe and North America (40). On the base of epidemiological study (Cogliano, 2004), the International Agency for Research on Cancer (IARC) concluded that there is ‘sufficient evidence’ that the oral use of ST is carcinogenic to humans (8).

Smokeless tobacco and systemic disease

Generally, the youth start experimenting with ST products at the age of 9 to 16, less possibly after the age of 20 (41). One of the important systemic effects of ST is nicotine dependence or addiction compared to cigarette smoking. Because it contains higher levels of addictive nicotine (one can of snuff delivers as much nicotine as 60 cigarettes) and prolonged mean usage time, it can be harder to quit compared to cigarettes (3, 23). Withdrawal symptoms

such as drowsiness, nervousness, headache, irritability, and cravings have been reported (25). Oral ST causes a duration-dependent increase in oxidative stress (34). ST is a risk factor for osteoporosis in populations where its use is prevalent (27) and also associated with cataract (29), cardiovascular diseases (9), and immediate increase in blood pressure and heart rate (5). A recent study to find the influence of tobacco chewing on cardiovascular risk found that the risk is similar in chewing tobacco and cigarette use (13).

The increased risks of mortality or morbidity among ST users include stomach, rectal, prostate (1) and pancreatic cancers (1, 6). Tobacco chewing (mostly tobacco with areca nut/betel quid) is a highly significant risk factor for laryngeal and esophageal cancer (9, 14). A recent study from Pakistan reported that many women with bladder carcinoma had a long history of smokeless tobacco use (28). In a few countries, exposure to ST with extremely high nitrosamine concentrations has been found to induce cancers in the head-neck region (22). The metabolites of nitrosamines, primarily NNN and NNK, are found locally in saliva of the oral cavity of ST users as well as in their body fluids. These agents are known to cause toxic effects, particularly cancer and other cellular and DNA changes, at the local placement site or by indirect systemic effects (44).

In females, ill effects of smoking over the reproductive system are well documented (24). The same types of ill effects over the reproductive system are also seen in female ST users. The consumption of ST during pregnancy decreases the gestational age at birth and birth weight (15), and increases stillbirth risk (16). Pregnant women in India who used ST have a threefold increased risk of stillbirth and a two- to threefold increased risk of having a low birth weight infant (14). Preeclampsia is also associated with ST use (10). Neurobehavioral signs occur in neonates born to women who use ST (18). In males, a decrease in sperm quality and, to a lesser extent, with oligoasthenozoospermia or azoospermia was found in a group of tobacco chewing men who are undergoing infertility evaluation (33).

In the Indian subcontinent, inhalation of nasal snuff is a common habit (37). Morphological and functional changes in the nasal mucosa happen due to chronic abuse (35), and a form of chronic rhinitis develops as a consequence of which the nose is blocked and becomes stuffy (37).

Smokeless tobacco and oral disease

Oral cancer

ST is very strongly related to cancer of the cheek and gums, locations typically in direct contact with tobacco (9, 44). This association is evident from the studies in the US, Scandinavia, and also from Asia and Africa where ST is used extensively. The risk of oral cancer increases with the length of exposure, and is greatest at the anatomic site where ST product is held in contact with oral mucosa for the longest time (44).

Carcinogenic tobacco-specific nitrosamines are likely to be the procarcinogen acting at the target site (45). ST users are 50 times more likely to get oral cancer than non-users (19). Even ST products that claim to be low in nitrosamines are likely to raise the risk among users up to 30% risk of oral cancer in smokers (44). It is reported that the chronic stimulation of the lymphoid tissues in oral mucosal membrane may be related to the increase in oral cancer (3). The risk of oral cancer from ST tobacco varies in different parts of the world; one possible explanation for this is the qualitative difference in the production of ST and different contents of carcinogenic tobacco-specific N-nitrosamines (47). The two most common forms of cancers found in association with ST use are verrucous carcinoma and squamous cell carcinoma (25, 44).

Dental caries

Especially people who use chew tobacco appear to have more dental caries than non-users (46). A review of studies conducted from 1988–1990 on oral consequences of snuff and chewing tobacco use among professional baseball players in the US found that ST use shows a significantly higher prevalence of root caries than comparable sites in non-smokers (32). The data from the multipurpose health survey (Third National Health and Nutrition Examination Survey) conducted in the USA from 1988 to 1994 were used to examine the relationship between chewing tobacco and other forms of tobacco use and decayed or filled coronal or root surface caries. Chewing tobacco users had a slightly higher mean number of decayed and filled coronal surfaces than individuals using other forms of tobacco. In addition, the mean number of decayed and filled root surfaces in those who used chewing tobacco was four times higher than in those who did not use tobacco. It is important to note that the

decayed or filled surfaces tended to match that side of the mouth on which the ST was used although this did not reach statistical significance. The results showed that the mean number of decayed and filled root surfaces rose with the increasing number of chewing tobacco packages used per week and duration of use in years (43). A biologically reasonable explanation for an association between chewing tobacco use and dental caries is that the high levels of fermentable sugar in ST products can stimulate growth of cariogenic bacteria (12, 43).

Leucoplakia and snuff dippers lesion

Oral leucoplakia, a precancerous lesion to oral cancer, is strongly linked to ST use (44). Oral leucoplakia occurs in up to 60% of ST users within 6 months to 3 years after starting of ST use, mostly occurring at the site of ST use; it is mainly the result of local irritation (40). A typically wrinkled appearance at the site of placement of the moist snuff and chewing tobacco was described by Axell and his colleagues. The severity of the leucoplakia lesion associated with ST rises with the increasing amount and duration of use, suggesting a dose-response relationship (44). Betel quid chewing is an important risk factor for precancerous lesion oral submucous fibrosis and oropharyngeal cancer in South Asia (14).

Another well-recognized and predictable lesion that appears at the site where ST is held in oral cavity is snuff dipper's lesion. This lesion appears white keratotic in nature and is translucent rather than opaque whiteness (36), and is present in 15% of chewing tobacco users and 60% of snuff tobacco users (41). It is reversible when the affected person discontinues the habit (36). This lesion is also known by some other names – tobacco pouch keratosis or smokeless keratosis, and is mostly seen in snuff dippers (44).

Other oral effects

In addition to the above mentioned conditions, ST is found to be associated with the periodontal disease (11). Acute Necrotizing Ulcerative Gingivitis (ANUG), gingivitis, and periodontitis are found in ST users. Gingival recession and attachment loss are generally seen in the area adjacent to where the ST is held (25). Cessation of ST use does not reverse the gingival recession – it is estimated to be present in 7 to 27% of ST users (41).

Other negative effects include stained teeth, bad breath and mouth sores (19). The use of ST is also associated with tooth abrasion of the incisal and occlusal surface of the teeth (25). Especially tobacco chewing is positively associated with both moderate and severe tooth wear (20). Abrasive materials found in tobacco products like silica or silicon may contribute to dental attrition in chronic users of ST (7).

Tobacco cessation intervention in dental practice

The number of tobacco using patients visiting dentists for a regular dental treatment is quite high. A dental office with well motivated dental staff can be a good place for headstart starting of the tobacco cessation intervention. In 1996, the World Dental Federation (FDI) recognized the role of dentists as professional interventionists; the body also urged to instigate tobacco use prevention and cessation program into daily dental routine and daily dental care (30). Recognizing of patients according to the psychological status of cessation habits can be grouped as precontemplation, contemplation, preparation, action, and maintenance (38). The action plan of intervention has to be individually planned according to the above mentioned patient groups. Dentists and dental hygienists can motivate patients who are adversely thinking about quitting the tobacco use. For motivated patients they can draw a road map to retrieve from the habit with a time frame. The continuous encouragement of such patients can be psychologically rewarding for them during the recall of general dental treatment. And dentists have an opportunity to assess the stages of quitting the patients' habits.

The five major steps recommended for tobacco cessation activity in the dental office are popularly known as "5 As" (ask, advise, assess, assist, arrange) (30, 42). These steps, if followed effectively by the professional and patient, result in an effective outcome of the treatment, in other words in cessation of the tobacco habit (Table 1).

Conclusion

Smoking is considered to be a risk factor for multiple diseases. The myth that ST is less harmful than smoking is not well justified. The fact that

tobacco in any form is not safe is universal truth. The ST form causes multiple oral reversible and irreversible pathological changes mostly where it comes in close contact with oral mucosa. The limited data are available on the carcinogenicity of smokeless tobacco products in organs other than the mouth.

Table 1

Summary of the five major steps recommended for tobacco cessation activity in dental office

ASK Identify tobacco users	Develop one to one relationship Tobacco use assessment questionnaire Recording of the relevant facts Identifying cessation intervention
ADVICE Urging the tobacco users to quit	Explain the health hazards of tobacco use Personalized strong oral communication Benefits of cessation of tobacco usage Record psychological readiness to cessation of the habit
ASSESS Assessment of willingness of quit attempt (with in 30 days)	Assist the patient in attempt to quit Motivate the unwilling patient Provide additional information about adverse effects of tobacco Record the patient's decision
ASSIST Help the patient to quit	Designing the road map to quit with time bound concrete plan Specific problem related counseling Providing medical assistance (nicotine withdrawal therapy) Stipulating recall
ARRANGE Designing follow-up programme	Recording and rewarding of the progress Provide continuous support to recommit on quitting Assessment of medical intervention Referring the patients to more intensive treatment



EFFECTIVE TREATMENT OUTCOME

The literature focused on ST use and its ill effects is still rather limited, especially when compared to literature dealing with smoking of cigarettes. Little research has been done in relation between ST use and mortality from chronic diseases.

As ST is becoming popular among children and youth around the world, it is important for the scientific community to pay more attention towards

research in this particular area. In the daily routine practice, dentists come across many tobacco users of various categories. So it becomes mandatory for the dentists to provide counseling on tobacco cessation to prevent oral diseases associated with tobacco. Dentists who are interested in tobacco cessation services should be provided with adequate training in tobacco cessation counseling so that it becomes a normal part of the oral health motivation among patients.

Literature

1. ACCORTT, NA., et al. Cancer incidence among a cohort of smokeless tobacco users (United States). *Cancer Causes Control.*, 2005, vol. 16, p. 1107–1115.
2. ANDERSSON, G. – WAHLIN, A. – BRATTHALL, G. The effect of Swedish and American smokeless tobacco extract on periodontal ligament fibroblasts in vitro. *Swed. Dent. J.*, 2006, vol. 30, p. 89–97.
3. ARAL, M., et al. Comparison of effects of smoking and smokeless tobacco "Maras powder" use on humoral immune system parameters. *Mediators Inflamm.*, 2006, vol. 3, p. 85019.
4. ASPLUND, K., et al. Smokeless tobacco as a possible risk factor for stroke in men: a nested case-control study. *Stroke*, 2003, vol. 34, p. 1754–1759.
5. ASPLUND, K. Smokeless tobacco and cardiovascular disease. *Prog. Cardiovasc. Dis.*, 2003, vol. 45, p. 383–394.
6. BOFFETTA, P., et al. Smokeless tobacco use and risk of cancer of the pancreas and other organs. *Int. J. Cancer*, 2005, vol. 114, p. 992–995.
7. BOWLES, WH., et al. Abrasive particles in tobacco products: a possible factor in dental attrition. *J. Am. Dent. Assoc.*, 1995, vol. 126, p. 327–331.
8. COGLIANO, V., et al. Smokeless tobacco and tobacco-related nitrosamines. *Lancet Oncol.*, 2004, vol. 5, p. 708.
9. CRITCHLEY, JA. – UNAL, B. Health effects associated with smokeless tobacco: a systematic review. *Thorax*, 2003, vol. 58, p. 435–443.
10. ENGLAND, LJ., et al. Adverse pregnancy outcomes in snuff users. *Am. J. Obstet. Gynecol.*, 2003, vol. 189, p. 939–943.
11. FISHER, MA. – TAYLOR, GW. – TILASHALSKI, KR. Smokeless tobacco and severe active periodontal disease, NHANES III. *J. Dent. Res.*, 2005, vol. 84, p. 705–710.
12. GOING, RE. – HSU, SC. – POLLACK, RL. Sugar and fluoride content of various forms of tobacco. *J. Am. Dent. Assoc.*, 1980, vol. 100, p. 27–33.
13. GUPTA, BK., et al. Cardiovascular risk factors in tobacco-chewers: a controlled study. *J. Assoc. Physicians India*, 2007, p. 27–31.
14. GUPTA, PC. – RAY, CS. Smokeless tobacco and health in India and South Asia. *Respirology*, 2003, vol. 8, p. 419–431.
15. GUPTA, PC. – SREEVIDYA, S. Smokeless tobacco use, birth weight, and gestational age: population based, prospective cohort study of 1217 women in Mumbai, India. *BMJ*, 2004, vol. 328, p. 1538.

16. GUPTA, PC. – SUBRAMONEY, S. Smokeless tobacco use and risk of stillbirth: a cohort study in Mumbai, India. *Epidemiology*, 2006, vol. 17, p. 47–51.
17. HOFFMANN, D. – DIJORDEVIC, MV. Chemical composition and carcinogenicity of smokeless tobacco. *Adv. Dent. Res.*, 1997, vol. 11, p. 322–329.
18. HURT, RD., et al. Iqmik – a form of smokeless tobacco used by pregnant Alaska natives: nicotine exposure in their neonates. *J. Matern. Fetal Neonatal Med.*, 2005, vol. 15, p. 281–289.
19. KOZLOWSKI, LT. – O'CONNOR, RJ. Apply federal research rules on deception to misleading health information: an example on smokeless tobacco and cigarettes. *Public. Health Rep.*, 2003, vol. 118, p. 187–192.
20. MILOSEVIC, A. – LO, MS. Tooth wear in three ethnic groups in Sabah (northern Borneo). *Int. Dent. J.*, 1996, vol. 46, p. 572–578.
21. NELSON, DE., et al. Trends in smokeless tobacco use among adults and adolescents in the United States. *Am. J. Public. Health*, 2006, vol. 96, p. 897–905.
22. NILSSON, R. De minimus non curat lex--virtual thresholds for cancer initiation by tobacco specific nitrosamines--prospects for harm reduction by smokeless tobacco. *Int. J. Occup. Med. Environ. Health*, 2006, vol. 19, p. 202.
23. PHILLIPS, CV. – WANG, C. – GUENZEL, B. You might as well smoke; the misleading and harmful public message about smokeless tobacco. *BMC Public. Health*, 2005, vol. 5, p. 31.
24. POLANSKA, K. – HANKE, W. Influence of smoking during pregnancy on children's health – overview of epidemiologic studies. *Przegl. Epidemiol.*, 2005, vol. 59, p. 117–123.
25. PRISCILLA, M., WALSH – JOEL, B., EPSTEIN. The Oral Effects of Smokeless Tobacco. *J. Can. Dent. Assoc.*, 2000, vol. 66, p. 22–25.
26. PROKHOROV, AV., et al. Youth tobacco use: a global perspective for child health care clinicians. *Pediatrics*, 2006, vol. 118, p. 890–903.
27. QUANDT, SA., et al. Smokeless tobacco use accelerates age-related loss of bone mineral density among older women in a multi-ethnic rural community. *J. Cross Cult. Gerontol.*, 2005, vol. 20, p. 109–125.
28. RAFIQUE, M. Clinico-pathological features of bladder carcinoma in women in Pakistan and smokeless tobacco as a possible risk factor. *World J. Surg. Oncol.*, 2005, vol. 3, p. 53.
29. RAJU, P., et al. Influence of tobacco use on cataract development. *Br. J. Ophthalmol.*, 2006, vol. 90, p. 1374–1377.
30. REIBEL, J. Tobacco and oral diseases. Update on the evidence, with recommendations. *Med. Princ. Pract.*, 2003, vol. 12, p. 22–32.
31. RICHER, P. – SPIERTO, FW. Surveillance of smokeless tobacco nicotine, pH, moisture, and unprotonated nicotine content. *Nicotine Tob. Res.*, 2003, vol. 5, p. 885–889.
32. ROBERTSON, PB. – WALSH, M. – GREENE, JC. Oral effects of smokeless tobacco use by professional baseball players. *Adv. Dent. Res.*, 1997, vol. 11, p. 307–312.
33. SAID, TM. – RANGA, G. – AGARWAL, A. Relationship between semen quality and tobacco chewing in men undergoing infertility evaluation. *Fertil. Steril.*, 2005, vol. 84, p. 649–653.
34. SAMAL, IR. – MANEESH., M. – CHAKRABARTI, A. Evidence for systemic oxidative stress in tobacco chewers. *Scand. J. Clin. Lab. Invest.*, 2006, vol. 66, p. 517–522.
35. SAPUNDZHIEV, N. – WERNER., JA. Nasal snuff: historical review and health related aspects. *J. Laryngol. Otol.*, 2003, vol. 117, p. 686–691.
36. SHAM, AS., et al. The effects of tobacco use on oral health. *Hong Kong Med. J.*, 2003, vol. 9, p. 271–277.
37. SREEDHRAN, S., et al. Effect of snuff on nasal mucosa. *Am. J. Otolaryngol.*, 2005, vol. 26, p. 151–156.
38. STAFNE, EF. – BAKDASH, B. Tobacco cessation intervention: how to communicate with tobacco using patients. *J. Contemp. Dent. Pract.*, 2000, vol. 1, p. 37–47.
39. STENSTROM, B., et al. Swedish moist snuff accelerates gastric cancer development in Helicobacter pylori-infected wild-type and gastrin transgenic mice. *Carcinogenesis*, 2007. [Epub. ahead of print].
40. STEPANOV, I., et al. Tobacco-specific nitrosamines in smokeless tobacco products marketed in India. *Int. J. Cancer*, 2005, vol. 116, p. 16–19.
41. TAYBOS, G. Oral changes associated with tobacco use. *Am. J. Med. Sci.*, 2003, vol. 326, p. 179–182.
42. TOMAR, SL. Dentistry's role in tobacco control. *J. Am. Dent. Assoc.*, 2001, vol. 132, p. 30–35.
43. TOMAR, SL. – WINN, DM. Chewing tobacco use and dental caries among U.S. men. *J. Am. Dent. Assoc.*, 1999, vol. 130, p. 1601–1610.
44. WARNAKULASURIYA, KA. – RALHAN, R. Clinical, pathological, cellular and molecular lesions caused by oral smokeless tobacco – a review. *J. Oral Pathol. Med.*, 2007, vol. 36, p. 36–37.
45. WARNAKULASURYA, S. Smokeless tobacco and oral cancer. *Oral Dis.*, 2004, vol. 10, p. 1–4.
46. WINN, DM. Tobacco use and oral disease. *J. Dent. Educ.*, 2001, vol. 65, p. 306–312.
47. ZATTERSTROM, UK., et al. Oral cancer after using Swedish snus (smokeless tobacco) for 70 years – a case report. *Oral Dis.*, 2004, vol. 10, p. 50–53.

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