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REVIEW ARTICLE

Smokeless tobacco: a gateway to smoking or a way away from smoking

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Abstract

Recently, tobacco companies have been marketing moist smokeless tobacco products that are 'spitless'. These products have lower concentrations of tobacco-specific nitrosamines and of other harmful chemicals than other tobacco products, but can deliver relatively high doses of nicotine. They are packaged in small sachets, similar to tea bags that are placed between cheek and gum. Global promotion of smokeless tobacco products is hotly debated among tobacco control and public health experts. Proponents point to the Swedish experience where snus (Swedish moist snuff) is widely used as an alternative to cigarette smoking among men. Meanwhile, Sweden has low rates of smoking and a lower rate of respiratory diseases and lung cancers by comparison to other developed countries. The opponents argue that snus has its own risks, that no form of tobacco should ever be promoted; and that 'snus is culture-bound and not transferable to other settings'. Critics also suspect that the tobacco industry will use snus marketing as a 'gateway' to promote cigarettes among young people. Research on the effects of marketing snus to smokers is too limited to support using snus as a harm-reduction tool, and the epidemiological data are not conclusive.

Keywords: *Snus; smokeless tobacco*

History of smokeless tobacco

Plant geneticists have established that the area in which the tobacco plant was first cultivated is located in the Peruvian/Ecuadorian Andes. The first tobacco cultivation is estimated to have occurred 5000–3000 BC (Gately 2001). The genus *Nicotiana* comprises 64 species. Only two of these, namely *Nicotiana tabacum* (a tall, annual, broad-leafed plant) and *Nicotiana rustica* (shorter and fleshier leaves) are utilized for human consumption. The latter variety is planted and consumed mainly in Russia, Poland, in other East European countries, and in parts of Asia and Africa. *Nicotiana tabacum* is preferred in America and in European countries because of the plasticity of its leaves and agronomic variety of its species.

Historians believe Native Americans began using tobacco for medicinal and ceremonial purposes before 1 BC. Tobacco was sniffed, chewed, eaten and drunk (Gately 2001). First evidence that tobacco was being smoked is conveyed by a pictorial record on Guatemalan pottery which is dated 600–1000 AD.

Tobacco was introduced to Europe after the discovery of America. Tobacco began its European life in palace gardens where court physicians were interested in its medicinal potential. Jean Nicot, a French ambassador to Portugal used an ointment made from tobacco leaves 'to cure' the tumour of a man in Lisbon. Nicot's experiments became widely known and his name was immortalized by labelling the genus, '*Nicotiana*'. Meantime, in 1565, Nicolas Monardes, a doctor of Seville, published a pamphlet entitled 'Joyful News' listing the herb's healing properties and claimed that tobacco can cure 36 maladies (Gately 2001). By 1570 European physicians used tobacco as a universal cure for every human illness, including cancer. Tobacco was also produced for pipe smoking, chewing and sniffing. In the 1800s cigars became popular. Egyptian soldiers were credited with the invention of modern cigarettes in 1832. The invention of

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matches 20 years later was a great convenience to smokers. The 20th century history of cigarette manufacture and consumption was, of course, closely tied to technological advances and recognition of smoking as a way to relieve stress and to stimulate at the same time.

Types of smokeless tobacco products and their use

Today, several types of smokeless tobacco (ST) products are available that can be used orally or nasally. Chewing tobacco comes as twist, plug and scrap leaf. Twist tobacco is made of leaves of air-cured or fire-cured Burley tobacco that is flavoured and braided. Plug tobaccos are a blend of cured Burley, cigar type and the flavourful oriental tobaccos. Such blends are sweetened, moistened, and flavoured with sugars, syrups, honey, liquorice, then are pressed into plugs. Scrap leaf is a blend of air-cured and fermented cigar leaf tobacco, to which different amounts of sweeteners are added and then loosely packed. Snuff comes in dry and moist forms; dry snuff is finely powdered tobacco that can be used orally or nasally (it contains ≤ 10% moisture). Moist snuff is flavoured, finely ground or shredded, air-cured and fire-cured tobacco, (containing 20–50% moisture); it is sold loose or in tea-bag type packets (sachets). Chewing tobacco and snuff are placed in the mouth, cheek or on the lips to be chewed or sucked (dipped).

Several countries have developed specific types of ST. In India, Central and East Asia, as well as in China, betel quid chewing is prevalent. It often involves mixtures of betel and tobacco leaves, *Areca* nut and lime which are pulverized and aged (IARC 2004). In the Sudan and in Algeria people practice the oral and nasal use of toombak made of *Nicotiana rustica*. Toombak contains a large percentage of stems, and it is fermented, aged for 1 year, and treated with sodium bicarbonate (Idris et al. 1994). Alaskan natives use Iq-mik, a mixture of tobacco leaves with ash derived from punk fungus that grows on the bark of birch trees (Renner et al. 2005). Moist snuff and chewing tobacco stimulate saliva flow and may require spitting, thus they are called 'spit tobacco'. Newly introduced ST products are 'spitless'. In Sweden, moist snuff (snus) used to be the prevalent form of ST. The processing of Swedish snus involves heat treatment or pasteurization rather than fermentation. The heating process purports to kill bacteria, producing a more sterile product; concomitantly, it leads to lower levels of tobacco-specific nitrosamines (TSNAs). The manufacturer of snus has introduced voluntary standards, called GothiaTek® that set limits for certain oral tobacco constituents and allows only those additives and flavourings that are already permitted in foods (Hatsukami et al. 2007). The pH levels of snus products range from 7.8 to 8.5. This is important because it renders nicotine as a free base that is rapidly absorbed through the mucosal membrane.

Chewing tobacco was the leading form of tobacco use at the turn of the 20th century in the USA. Then sales of ST declined as the popularity of cigarettes increased and reached its peak in the 1960s. However, with the introduction of moist snuff in the 1970s, the sale of ST began to rise again, and its consumption increased significantly during the past 20 years. In 2005, 3.2% of Americans, more commonly non-Hispanic young white men were current ST users (Tomar 2003). In India about 22% of men and 12% of women use ST, while 8% of the population use both ST and smoke tobacco products at the same time. About 40% of the males and 10% of females in the Sudan use Toombak. About 23% of men in Sweden are reported to use snus (Critchley & Unal 2003).

Major toxicants in smokeless products

An expert group at the International Agency for Research on Cancer (IARC) has concluded that ST is carcinogenic to humans and contains about 30 cancer-causing agents (IARC 2008). One class of harmful carcinogens in ST is that of the TSNAs which are formed during growing, curing, fermenting, and aging of tobacco. Other toxicants in ST are *N*-nitrosamino acids, volatile nitrosamines, aldehydes such as formaldehyde, acetaldehyde and crotonaldehyde, metals such as arsenic, nickel, chromium, cadmium, lead, polonium-210, as well as polycyclic aromatic hydrocarbons, ethyl carbamate, hydrazine, 1,1-dimethylhydrazine and others. Swedish snus has been claimed to contain lower levels of some harmful agents than many brands available in North America, and products used in India and in the Sudan. Concentrations of total TSNA in Swedish snus were reported to be ≤ 2 μg/g tobaccos; in the USA total TSNA ranged from 0.2 to 9 μg g^{-1} tobaccos. By contrast the levels of TSNA in Indian products range from 1.2 to 128 μg g^{-1} product (Hatsukami et al. 2007), and in Sudanese products levels of NNK were reported in the range of 188 to 7870 μg g^{-1} dry product (Foulds et al. 2003).

ST delivers nicotine comparable to doses typically absorbed from cigarette smoke and about twice as high as those obtained from nicotine-replacement therapy. The main difference from smoked tobacco is the somewhat slower nicotine absorption and a lack of the higher concentration arterial bolus that results from nicotine inhalation (Foulds et al. 2003).

Health effects of smokeless tobacco

The available evidence suggests that adverse health consequences vary by specific type of ST, the use of which

is strongly associated with geography. Even ST products that claim to be low in TSNA and other toxicants are likely to present a health risk for users. ST can cause cancer in humans (Cullen et al. 1986), and the evidence is strongest for cancer of the oral cavity, particularly at the site of tobacco placement, and for pancreatic cancer. ST use can also lead to the development of non-cancerous oral conditions, particularly, oral precancerous leukoplakia. Lesions in the local epithelium are reversible on quitting but gingival retractions are not (Warnakulasuriya & Ralhan 2007, Anderson et al. 1994). Swedish studies claim that portion-bag users exhibit less pronounced clinical changes of the oral mucosa than do the users of loose snus (Anderson et al. 1994). In India, a 10-year follow-up study has shown that oral cancers arise from pre-existing leukoplakia. Snuff was more frequently associated with development of oral mucosal lesions than was the use of chewing tobacco (Daniels et al. 1992). Studies in India, Pakistan and the Sudan describe large increases in the risk of oral cancers related to use of different smokeless products. Studies from Sweden are controversial. A Swedish cohort study followed 279 897 male construction workers for 20 years and claims that snus use is associated with an increased risk of pancreatic cancer relative risk (RR) = 2 (95% confidence interval (CI) 1.2–3.3) but that it is unrelated to incidence of oral RR = 0.8 (CI 0.4–1.7) and lung cancers RR = 0.8 (CI 0.5–1.3) (Luo et al. 2007). However, another cohort study comprised 9976 men who participated in a population-based followed up survey, from 1973–74 to 2002, found a statistically significant increase in the incidence of oral and pharyngeal (combined) cancer among daily users of snus RR = 3.1 (95% CI 1.5–6.6) (Roosaar et al. 2008). The relative risks of oral cancer attributed to ST use vs non-tobacco users in males reported by Boffetta et al. are: in the USA, RR = 2.6 (95% CI 1.3–3.5); in Nordic countries (Norway and Sweden) RR = 1.0 (0.7–1.3), and in males in Canada, RR = 2.6 (1% population is exposed); in the Sudan, RR = 7.3 (34%); and in India, RR =5.1 (27%) (Boffetta et al. 2008). Meta-analysis of the relationship between European and American ST-related oral cancer based on 38 studies suggests an odds ratio of 1.87 (95% CI 1.40–2.48) (Weitkunat et al. 2007). Smokeless tobacco use is also associated with other health consequences. Swedish data suggest a causal link between snus use and risk of type 2 diabetes, and increasing evidence incriminates insulin resistance and abnormal glucose metabolism as risk factors for development of pancreatic cancer (Foulds et al. 2003). The association between ST use and adverse cardiovascular effects has been controversial (Critchey & Unal 2003). Studies probing the relationship between tobacco use and cardiovascular mortality in 135 036 in Swedish male construction workers recruited in 1971–1974 and followed up for 12 years, found that snus users had slightly higher risk of cardiovascular disease than non-users RR = 1.4 (95% CI 1.2–1.6) (Bolinder et al. 1994). Meta-analyses from cohort, case–control and cross-sectional studies indicate an increase of heart disease in ST users compared with non-smokers RR = 1.12 (95% CI 0.99–1.27, $n = 8$), stroke RR = 1.42 (1.29–1.57, $n = 5$) and CHD RR = 1.25 (1.14–1.37, $n = 7$) (Lee 2007). Use of snus during pregnancy affects the weight of infants. Snus users gave birth to babies weighing on average 40 g less than infants of non-tobacco users; the corresponding weight reduction for smokers' babies was 206 g (Foulds et al. 2003).

Is snus a 'gateway' to smoking or a pathway away from smoking?

Cigarette smoking has been a major health concern worldwide. The goal of preventive medicine is to have people refrain from smoking, or to quit the habit. However, for a smoker who cannot quit or does not want to quit, one school of thought believes that a less harmful alternative product should be available, another school believes in the 'quit or die' dogma. One alternative of harm reduction is by means of nicotine-replacement products. However, because of their low dose and delivery rate such products are not highly effective, and most smokers find them not satisfying as a cigarette substitute. Another alternative that is gaining some support in the public health community, but is also intensely disputed, is to go along with the use of moist snuff that has low toxicants and TSNA content, as a complete substitute for cigarettes. In the USA, in general, moist snuff use conveys lower risk for morbidity and mortality, than does cigarette smoking. Median mortality risks relative to smoking were estimated to be 2–3% for lung cancer, 10% for heart disease, and 15–30% for oral cancer (Levy et al. 2004). The sale of moist snuff is illegal in Australia and is banned in the European Union countries. Sweden is exempt from the ban and moist snuff use is permitted in the USA and Canada. Since 1980 snus consumption has increased drastically and smoking has declined among Swedish men. Using the WHO MONICA dataset from Northern Sweden, consisting of population-based surveys in 1986, 1990, 1994 and 1999, investigators compared the prevalence amongst various subgroups, namely smokers, former snus users now smoking, current snus users who also smoke, snus users who are ex-smokers and those using snus exclusively. The study found that among men 'all forms tobacco use' were stable from 1986 to 1999 in all four survey years at a level of about 40%, but the prevalence of smoking declined from 23% in 1986 to 14% in 1999, whilst the use of snus increased from 22 to 30%. This study demonstrates that although cigarette smoking declined drastically among Swedish men, overall tobacco use did not change

(Radu et al. 2002). Despite this high prevalence of snus use, tobacco-related mortality in Sweden is among the lowest in the developed world. There is also a lower rate of oral cancer that continues to decline. Some studies suggest that the decline in tobacco-induced diseases is attributed to switching from smoking to the use of snus (Foulds et al. 2003). An epidemiological modelling also indicates that there are only small differences in life expectancy between smokers who quit smoking at age 35 or 40 years and those who switch to snus at the age of 35 or 40 (Garner & Hall 2008). Proponents of ST use suggest that if the goal of tobacco control is to reduce tobacco-related disease, rather than tobacco use per se, then – based on the Swedish experiment – the promotion of snus use by smokers is a promising public health measure.

Opponents of snus promotion have raised several concerns. One problem is that research reports concerning the health effects of snus use are somewhat conflicting as was discussed above. A second problem is that increased use of snus may facilitate a pathway into nicotine dependence, leading to smoking as a 'gateway effect', hooking young people on nicotine. On the other hand, snus can act as a form of nicotine replacement and thus provide an 'exit' strategy. The review published in the 1994 US Surgeon General's report describes the results as mixed with some showing that ST use is a precursor to smoking and other studies showing that smoking preceded smokeless tobacco use.

It has been suggested that for ST to be judged a causal gateway to cigarette smoking for an individual, it is important to know which product was used first. Recent Swedish data indicated that among those starting a tobacco habit with snus, 20% later go on to smoking (Ramstrom 2003). These observations suggest that the gateway more likely favours cessation from smoking rather than an entrance to cigarette use. The USA data imply that 77.2% can be classified as non-gateway users in that 35% had only used ST and 42.2% had smoked cigarettes before choosing the smokeless product (Kozlowski et al. 2003). Those who used cigarettes before moist snuff were 2.1 times more likely to have quit smoking than cigarette only users.

In summary, changing from smoking to smokeless products can be beneficial or harmful to health depending on how the levels of toxicants in the products are controlled, how the products are used and who is using them. To assure that the public health is protected it is necessary to tightly regulate tobacco products. Such regulation would permit standards to be established for allowable levels of toxins delivered from tobacco products and enable controlling the degree of potential addiction to a product. In addition, consumers must be accurately informed about each product. The past experience with the failure of 'light' cigarettes to decrease anticipated health risks, due in part to compensation through smoking behaviour (such as smoking a greater number of cigarettes/day, inhaling more intensely, smoking cigarettes down to a smaller butt length) and other factors, should alert us to the fact that, ideally, pilot clinical studies precede the marketing of new products. Recent studies indicate that smokers who have smoked light cigarettes are indeed not exposed to higher levels of toxins by comparison to smokers who smoke regular cigarettes. However, at low exposures the metabolic conversions of toxins, measured as urinary metabolites, are greater (Melikian et al. 2007a, b). A similar phenomenon may occur in dual use when some cigarettes are substituted by less harmful ST products (slightly lower toxin exposure); formation of some of the toxic metabolites may increase rather than decline.

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