Abstract: Tobacco use contributes to many oral and general health disorders. While cigarette smoking is the most hazardous and prevalent form of tobacco use in the industrialized countries, consideration also needs to be given to non-cigarette use such as bidi smoking in India, reverse smoking by several rural populations and use of snuff and chewing tobacco.

Clinical Relevance: Health professionals should encourage and aid cessation of tobacco use as a part of prevention of oral and other cancers.

Dent Update 2005; 32: 394-401

The evidence is clear that the use of tobacco is the major risk factor for oral cancer and potentially malignant lesions – oral leukoplakia and erythroplakia. Counselling by doctors and dentists can profoundly increase smokers’ motivation to stop smoking but is not applied in a systematic or frequent manner to people presenting with potentially malignant lesions of the oral cavity.

Tobacco use is the leading preventable cause of premature death world-wide.1 Possibly 4.9 million people died of tobacco-related illness in the year 2000.2 Tobacco is a major independent risk factor for the development of oral and pharyngeal cancer and is causally related to at least 16 types of human cancer (Table 1 and Dent Update 32: 204–212).

Tobacco is consumed in a variety of different ways, though smoking of manufactured cigarettes is the most prevalent form of use. Tobacco use is complicated by strong nicotine dependence.

Epidemiology of tobacco use

In most countries at least one-quarter of the population smoke (Table 2). In the US about 25% smoke, while in the UK the rates are currently around 27%. The highest reported rates are from China.

Cancer Sites and Organs

Lung
Colon and rectum
Oral cavity
Nasal cavities and nasal sinuses
Pharynx
Larynx
Oesophagus
Stomach
Pancreas
Liver
Urinary bladder
Kidney
Uterine cervix
Myeloid leukaemia

Table 1. Tobacco smoking and cancers.
where around 63% of males are smokers. A global summary of estimates on tobacco use is available from: http://www.who.int/tobacco/global_data/country_profiles/en/

In most countries a higher proportion of males smoke, notable exceptions are Denmark, New Zealand and the United Kingdom where female rates closely parallel those of males. Furthermore, hundreds of millions of people world-wide are addicted to smokeless tobacco.

**Tobacco and oral cancer**

The main cause of oral cancer has long been known to be cigarette smoking. Several case-control studies from Europe and USA show an increased risk varying from 3 to 35-fold, particularly in the presence of other synergistic factors. Over 90% of patients diagnosed with oral cancer use tobacco, either smoking or chewing it. Chewing tobacco, tobacco used with betel quid, tobacco and lime mixtures (nass) and moist snuff used in some parts of Europe and the USA are reported to be carcinogenic to humans.

The risk of oral cancer appears to fall over a 5–10 year period following giving up smoking or quitting other uses of tobacco.

Public knowledge on tobacco as a cause of oral cancer is varied. Population surveys among adults on oral cancer have demonstrated an alarming lack of knowledge on tobacco as a risk factor and, despite some recent campaigns, knowledge deficits remain.

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**Nicotine dependence**

Nicotine affects mood and performance and is a drug of addiction. Both smoking or chewing tobacco give rise to physical and psychological dependency.

Nicotine facilitates the release of several brain neurotransmitters, including acetylcholine, dopamine, noradrenaline, serotonin, beta-endorphin and glutamate, and the rewarding properties are believed to be mediated by dopamine release in the nucleus accumbens, as is the case with other psychostimulant drugs of abuse. Nicotine can thus produce a sense of well-being, reduce anxiety, help to maintain cognitive vigilance, and have both arousing or relaxing effects. Cigarettes on average contain 10 mg of nicotine of which the smoker typically absorbs 10%. Nicotine withdrawal symptoms, which are believed to be the reason why tobacco users relapse in the short-term, have been studied more thoroughly in smokers than in smokeless tobacco users. They include irritability, impatience, restlessness, difficulty concentrating, difficulty sleeping, increased appetite particularly for sweet high carbohydrate foods, weight gain, anxiety and depressed mood. The craving or urges to smoke cigarettes, increased appetite and weight gain can continue for many months after quitting. Although data are much more limited on the acute withdrawal effects from smokeless tobacco, the symptoms appear to be very similar, though they may be less intense and fewer in number.

**Nicotine dependence treatment**

Although 70% of smokers want to quit and 35% attempt to quit each year, less than 5% succeed. The low rate of successful quitting and the high rate of relapse are related to the effect of nicotine addiction (Figure 1). Formal assistance is available, which includes:

- Behaviour modification;
- Use of medication;
- Nicotine replacement therapy (NRT);
- Zyban (bupropion).

**Diagnosis, screening and brief interventions**

In the UK, around 40% of smokers make an attempt at quitting after having been advised to do so by their doctor. Unfortunately, about 95% of these quit attempts will fail because the smoker leaves the consultation motivated to stop but then embarks on a poorly planned quit attempt on his/her own without support or medication (Figure 1). The challenge is to harness this now motivated population and ensure that they receive sufficient help with their quit attempt so as to maximize their chances of quitting.
There is now a very convincing evidence base indicating that both short- and long-term abstinence rates are significantly increased by both counselling and the adjunctive use of pharmacotherapy.\(^1\)

**Brief clinical intervention**

Even the simplest forms of counselling can be beneficial, so healthcare staff should be prepared to undertake at least brief counselling on a routine basis with all their tobacco-using patients. In primary care settings it is often not feasible to offer the optimal counselling intensity for maximizing success rates. However, the extremely wide ‘reach’ into the population of lower intensity interventions more than compensates for their lower efficacy and, if practised by all healthcare staff as recommended in the US and UK guidelines,\(^1\) would have an enormous impact on prevalence of tobacco use, morbidity and mortality rates.

### Intensive clinical interventions

Intensive interventions produce higher success rates than do brief interventions. Ideally, when faced with a motivated tobacco user wishing to make a serious quit attempt, clinicians should try to offer a minimum of four counselling sessions each lasting about 15 minutes, or six sessions each lasting 10 minutes, with the first post-quit session being not more than a week after ‘Quit Day.’ If this weekly pattern is continued, it implies a treatment course lasting around 4–6 weeks in total. This time scale takes ex-tobacco users a little beyond the period when withdrawal symptoms are most troublesome and therefore the period where they are likely to need the most support. Specialist smokers’ clinics in the UK are used by only about 2% of smokers. These clinics are usually staffed by psychologists and nurses who have had specialist training in the treatment of tobacco dependence. Intensive interventions differ from minimal interventions primarily in the programme intensity. Treatment may be provided on an individual one-to-one basis or in group treatment format. Particular types of counselling, including psychoeducational, behavioural skills training and cognitive...
behavioural therapy are utilized in this setting, along with strong encouragement to use appropriate pharmacotherapy. An indication of short- to medium-term success rates across the country achieved through smoking counsellors is illustrated in Table 3.

**Pharmacotherapy (Table 4)**

Nicotine replacement therapy (NRT) The rationale for nicotine replacement therapy (NRT) is to reduce the severity of nicotine withdrawal symptoms by providing weaning doses of nicotine in a ‘clean’ form to smokers for about 8–12 weeks after stopping smoking. The objective of therapy is to increase short- and long-term quit rates and reduce the risk of a relapse. In many countries some, or all, of the products are available either over the counter (OTC) for pharmacy sales or on general sale (eg in supermarkets) in addition to being prescribable by a doctor. This reflects the fact that these products have such a good safety profile.13

NRT roughly doubles the quit rates compared with a placebo, irrespective of the amount of additional counselling support with which it is used, or the clinical setting.14 It is for this reason that clinicians should encourage patients contemplating quitting to use NRT.

There are a few medical contra-indications for the use of NRT (unstable angina, recent myocardial infarct, serious arrhythmia, accelerated hypertension). Though NRT is contra-indicated in pregnancy and breast feeding women, recent recommendations encourage these populations to use the product if a risk benefit assessment warrants it. Similarly, it can be used in adolescents on the recommendation of a doctor, though no trials have yet demonstrated efficacy over a placebo in this population.

All six NRT products developed to date deliver pure nicotine (derived from tobacco) to the user’s bloodstream without the dangerous toxins that are present in tobacco or tobacco smoke, which are very largely responsible for the damaging health effects. The products differ in terms of the speed of nicotine delivery, the frequency and ease of use, type of local sensory side-effects, amount of ‘behavioural’ substitution they provide, and the extent to which they

<table>
<thead>
<tr>
<th>Type of NRT</th>
<th>Route</th>
<th>Dose</th>
<th>Delivery system</th>
<th>Adverse effects</th>
<th>Notes to prescriber</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transdermal patches</td>
<td>Skin</td>
<td>15mg, 10mg, 5mg</td>
<td>Worn during waking hours</td>
<td>Local skin irritation</td>
<td>Start with highest strength and move to lower after 4-6 weeks Select dose on the basis of frequency of smoking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21mg, 14mg, 7mg</td>
<td>Worn over 24 hours</td>
<td>Sleep disturbance</td>
<td></td>
</tr>
<tr>
<td>Nicotine gum</td>
<td>Oral</td>
<td>2 or 4mg</td>
<td>Gum is chewed gently to release nicotine</td>
<td>Jaw ache, Gastric irritation. Not suitable for denture wearers</td>
<td>4mg for smoking &gt;20 or smoking within 30 minutes of waking. Foods and beverages should be avoided during chewing</td>
</tr>
<tr>
<td>Nicotine lozenges</td>
<td>Oral</td>
<td>1, 2 or 4mg</td>
<td>Suck until the taste is strong then park until dissolution</td>
<td></td>
<td>4mg for more dependent smokers</td>
</tr>
<tr>
<td>Sub-lingual tablets</td>
<td>Oral</td>
<td>2mg</td>
<td></td>
<td>Should not chew or suck</td>
<td></td>
</tr>
<tr>
<td>Inhaler/ Inhalator</td>
<td>Mouth</td>
<td>6 cartridges per day (max 12)</td>
<td>Nicotine cartridge Puff steadily for about 20 minutes per hour or two hours</td>
<td>Addresses the behavioural habit of smoking (puffing) and handling</td>
<td></td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>Nose</td>
<td>2x 0.5mg in each nostril</td>
<td>1-2 doses per hour for 2 months gradually stop</td>
<td>Irritation of nasal mucosa</td>
<td>Effective for heavy smokers with urge to smoke</td>
</tr>
</tbody>
</table>

Table 4. A summary of NRT therapies for the practitioner.
enable the user to titrate their dose as and when needed.

Based on the rate of delivery, NRTs can be divided into two main types:
- Constant dose (transdermal patches) and
- More flexible, self-administered dosing (gum, lozenge, sublingual tablet, inhalator, nasal spray).

There is no good evidence that any one product is more effective than another and clinicians are advised to take the patient’s preference into account. A few studies have examined the effect of using more than one NRT concurrently, usually the patch for easy steady state nicotine replacement, combined with a faster-acting product for dealing with break-through cravings. Table 4 is a general guide to update the practitioner on the use of different NRT products but more detailed information could be found elsewhere.⁶

Safety of NRT

Nicotine administered as a medication is always safer than that obtained by tobacco use. While in theory all forms of NRT have some potential to sustain nicotine dependence, only a very small proportion of NRT users become long-term users.⁷ The active ingredient in NRT is nicotine but, in its pure form, has no known risk in tobacco-related cancers and is not implicated in chronic obstructive lung disease.⁸ There is no known increased cardiovascular risk with NRT, except with acute disease mentioned earlier. The possibility of endogenous formation of carcinogenic nitrosamines from nicotine metabolites has been suggested,⁹ but there is no evidence. While NRT may be considered a neurotoxin, the currently available NRT products – without the several hundred other chemicals in tobacco – are much safer than the most widely used source of nicotine, ie cigarettes.

Bupropion SR (Zyban)

The efficacy of bupropion (or amfebutamone) as a smoking cessation aid was a serendipitous discovery made while it was being used as an anti-depressant in the US under the trade name Wellbutrin SR. Bupropion is the only non-nicotine medication, approved by US Food and Drug Administration (FDA), used in the UK and the European Union for smoking cessation treatment. It became available for use in 2000. Like NRT, bupropion roughly doubles long-term abstinence rates compared to the placebo treatment. It is marketed as Zyban for smoking cessation (BNF). Its mechanism of action for smoking cessation is not known for certain but it blocks neural re-uptake of dopamine and/or norepinephrine, both of which have a central role in nicotine addiction. Interestingly, it is also a non-competitive nicotine receptor antagonist which might explain smokers’ reports that it makes smoking less enjoyable or satisfying.

Bupropion significantly enhances short- and long-term cessation rates, and reduces craving and other tobacco withdrawal symptoms. This medication is prescription-only and dosing starts 1–2 weeks before a subject quits smoking in order for therapeutic blood levels to be reached. Therapy begins with 150 mg once daily for 6 days, usually increased to twice daily from day 7 onwards for about 7–9 weeks, but the license in some countries allows maintenance therapy to continue for 6 months post-cessation. Bupropion interacts with a number of commonly used drugs, including some antidepressants (MAOI), type 1c antiarrhythmics and antipsychotics. There are many more contra-indications and precautions or drug interactions than with NRT, including pregnancy or breast feeding, previous history or predisposition to seizure disorders, current or prior bipolar eating disorder, and use of a monoamine oxidase inhibitor (MAOI) in the previous 14 days. The most common adverse effects reported are insomnia (35–40%), dry mouth (10%) and headache. Zyban is associated with a dose-related risk of seizure with an estimated incidence of approximately 0.1%, similar to other antidepressants. Alcohol moderation is recommended to reduce a risk of seizure. No trials of bupropion have been done in smokers aged under 18, and the drug is not licensed or recommended for smoking cessation in this group.

Bupropion may also help in smokeless tobacco cessation.

Other interventions: alternative approaches to reduce tobacco use

Hypnosis and acupuncture have been suggested as useful but there is not sufficient evidence to recommend their use. Although tailored computer-based counselling programs have proven effective for people who are unwilling to visit smoking cessation clinics, there is little empirical evidence on the efficacy of internet-based cessation programmes, despite the huge number of websites which have sprung up in recent years.

Conclusions

Tobacco is the major risk factor for oral cancer (and many other cancers). Oral cancer is, to a great degree, preventable. The disease has a long developmental period during which secondary prevention could reduce risk; early interventions could alter the natural history of the disease limiting malignant transformation. Dentists, through their individual efforts, could improve the oral health of the public by engaging in tobacco education. Primary care dentists could contribute to preventing cancer, saving lives and diminishing suffering from cancer through education, advocacy and clinical care.

Other cancer prevention approaches related to alcohol moderation, quitting betel quid use and improving diet are also discussed in articles in this series.

References


**Book Review**


Since the first edition was published 20 years ago, Oral Pathology by Soames and Southam has become an essential reference book for undergraduate and postgraduate dental students, as well as general and hospital dental practitioners. A wide range of oral diseases is covered and subsequent editions have incorporated advances in knowledge while emphasizing the core of basic information and retaining the readable, concise style. The aetiology, risk factors, clinical features and pathology of oral diseases are discussed and, where appropriate, progress of disease and prognosis, with correlations between histopathology and prognosis. The depth of coverage is appropriate for postgraduate studies but the clear layout of the fourth edition makes it easy for undergraduate students to understand the essential basic information. Much greater use is made of colour-coded information boxes containing tables, classifications, summaries and key points on the topics covered in each chapter. These stand out well from the rest of the text and provide useful quick references and aids to revision. Each chapter begins with a list of the conditions that are discussed, for ease of reference, and concludes with suggestions for further reading.

The fourth edition includes many advances in areas such as developmental control genes, DNA content in leukoplakia and genetic abnormalities in oral cancer. Changes in classification, such as the classification of periodontal disease and the new European criteria for diagnosis of Sjogren's syndrome, have been included. The text is very generously illustrated with full-colour clinical and histological photographs.

This new edition of an old favourite will appeal to a wide readership including specialists, general practitioners, undergraduate and postgraduate students. It is a valuable addition to any dental library.

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