



Title	The effects of tobacco use on oral health
Author(s)	Sham, ASK; Cheung, LK; Jin, LJ; Corbet, EF
Citation	Hong Kong Medical Journal, 2003, v. 9 n. 4, p. 271-277
Issued Date	2003
URL	http://hdl.handle.net/10722/44551
Rights	Creative Commons: Attribution 3.0 Hong Kong License

ASK Sham 岑思勁
LK Cheung 張念光
LJ Jin 金力堅
EF Corbet 高弼文

The effects of tobacco use on oral health

吸煙對口腔健康的影響

Objective. To review the effects of tobacco use on oral health, with particular emphasis on the effects of periodontal diseases, dental implant failures, and risk of development of oral cancers and precancers.

Data sources. Medline literature search (1977-2002).

Study selection. Key words for the literature search were ‘tobacco smoking’, ‘periodontal disease’, ‘dental implant’, and ‘oral cancers and precancers’.

Data extraction. Evidence-based literature review.

Data synthesis. The prevalence and severity of periodontal diseases in their various forms are higher among smokers than among non-smokers. The success of dental implant treatments is significantly influenced by addiction to tobacco smoking. The failure rate of implant osseointegration is considerably higher among smokers, and maintenance of oral hygiene around the implants and the risk of peri-implantitis are adversely affected by smoking. The risks of developing oral cancers and precancers are greater in smokers. Betel nut chewing and smokeless tobacco produce similar risk to cancer incidence as tobacco smoking. Cessation of tobacco use has a beneficial effect on halting the progression of periodontal diseases and on the outcome of periodontal therapy.

Conclusions. Medical and dental teams should be aware of oral problems associated with tobacco use. Counselling on smoking cessation and smoking prevention programmes should be an integral component of medical and dental teaching and practice.

Key words:

Dental implants;
Mouth neoplasms;
Periodontal diseases;
Smoking;
Tobacco

關鍵詞：

牙科植入體；
口腔腫瘤；
牙周病；
吸煙；
煙草

Hong Kong Med J 2003;9:271-7

Faculty of Dentistry, The University of
Hong Kong, Prince Philip Dental Hospital,
34 Hospital Road, Hong Kong

ASK Sham, MSc, FIBMS
LK Cheung, PhD, FHKAM (Dental Surgery)
LJ Jin, PhD, Odont Dr
EF Corbet, FDSRCS, FHKAM (Dental
Surgery)

This paper is a summary of the symposium on “Smoking and Oral Health” presented at the 6th Asia Pacific Conference on Tobacco or Health, “Youth Fight Back”, 26-29 October 2001, Hong Kong.

Correspondence to: Prof LK Cheung
(e-mail: lkcheung@hkucc.hku.hk)

目的：綜述吸煙對口腔健康的影響，特別著重牙周病、牙科植入體的失敗，以及引致口腔癌症和癌前期疾病的危機。

資料來源：Medline 1977 至 2002 年的文獻。

研究範圍：以 “tobacco smoking”、“periodontal disease”、“dental implant”、“oral cancers and precancers” 為關鍵詞檢索文獻。

資料選用：實證文獻回顧。

資料綜合分析：與非吸煙者相比，吸煙者患上各類型牙周病的情況更為常見，而病情亦更為嚴重。吸煙與否對牙科植入體治療的成敗影響很大，骨結合性植入體手術失敗率相當高，而吸煙也不利於保持植入體周圍的口腔衛生，更增加了患上植入體周圍炎的機會。此外，口腔癌症和癌前期疾病在吸煙者中的病發率也相對較高。嚼檳榔和用無煙的煙草，跟吸煙一樣會引致癌症。戒煙能有效防止牙周病進一步惡化，並有助改善牙周病的治療效果。

結論：醫生和牙醫要留意與吸煙有關的牙患，而戒煙輔導和控煙計劃應要納入醫科和牙科的教學課程裏，行醫時也應提供這類服務。

Introduction

Tobacco smoking is linked with many serious illnesses, such as cancer, cardiovascular diseases, low birthweight, as well as with many health problems.¹ It is also linked to a detrimental impact on oral health, such as increasing risk of periodontal (gum) diseases. In addition, dental implant failure is more common among smokers than among non-smokers, and peri-implantitis among smokers is also more prevalent.² Tobacco can be consumed through the mouth in a variety of forms, varied from smoking to smokeless tobacco chewing on itself or combined with betel nut. These may induce a variety of oral manifestations of diseases (Box 1). These lesions most likely result from the many irritants, toxins, and

Box 1. Oral lesions and conditions associated with tobacco use

Oral precancerous lesions
• Leukoplakia
• Erythroplakia
• Smokeless tobacco keratosis
Oral cancers
<i>Squamous cell carcinomas of the</i>
• Tongue
• Floor of the mouth
• Lip
• Gingiva
<i>Verrucous carcinomas of the</i>
• Buccal mucosa
• Gingiva
• Alveolar ridge
Periodontal diseases
• Increased plaque and calculus depositions
• Ischaemia
• Gingival inflammation
• Periodontal pockets
• Gingival recession
• Alveolar bone loss
Root caries
Peri-implantitis
Halitosis
Taste derangement
Stained teeth and restorations

carcinogens found in the smoke emitted from burning tobacco, but they may also arise from drying of the mucosa by the high intra-oral temperature, pH change, alteration in immune response, or altered resistance to fungal or viral infections. Other effects include halitosis, staining of teeth and composite restorations,³ decreased ability to taste and smell, and nicotinic stomatitis and keratosis.⁴ Most of these problems are reversible after cessation of tobacco use.⁵

The aim of this article is to present an evidence-based comprehensive literature review for medical and dental practitioners on the effect of tobacco smoking on oral health, particularly on the risk of periodontal diseases, dental implants, and oral cancers.

Tobacco smoking and periodontal diseases

Periodontal diseases, including gingivitis and periodontitis, are common human bacterial infections that affect the gingiva and bone supporting the teeth. Gingivitis is a form of inflammation limited to the marginal gingival tissues, and is usually caused by the accumulation of dentogingival plaque due to inadequate oral hygiene. Gingivitis is reversible with professional treatment and good oral care at home. Untreated gingivitis may advance to periodontitis under certain conditions when plaque accumulates below the gingival line. Periodontitis refers to the destructive inflammation that results in irreversible loss of periodontal attachment and tooth-supporting alveolar bone. Approximately 17% of the adult population in Hong Kong has

severe chronic periodontitis.⁶ Gingival recession may result from periodontal destruction and exposure of part of the root surfaces of teeth to the oral environment. The exposed root surfaces are at risk of developing root surface caries. Furthermore, root surface caries among individuals with gingival recession is more prevalent among tobacco smokers than among non-smokers.⁷

Effects of smoking on the prevalence and severity of periodontal diseases

Epidemiological studies have demonstrated that tobacco use is a significant risk factor for the development of periodontal diseases.^{8,9} Disease severity increases with the frequency of smoking.^{9,10} Smokers accumulate markedly more dental calculus than do non-smokers, and the quantity of calculus is correlated with the frequency of smoking.^{11,12} Smoking is also associated with an increased risk of periodontal attachment loss and formation of periodontal pockets, as well as alveolar bone loss (Fig 1). The adverse effects of smoking on the periodontium correlates well with both the quantity of daily consumption and the duration.^{13,14} Approximately half of the cases of periodontitis in the United States have been attributed to smoking.¹⁵ Smokers were recorded to have a 2.5 to 3.5 times greater risk of severe periodontal attachment loss.⁸ In analyses that adjusted for different oral hygiene habits, patient age, sex, and socio-economic level, smokers had deeper periodontal pockets, increased alveolar bone loss, increased tooth mobility, and more tooth loss than did non-smokers.¹⁶ In addition, emotional stress and poor oral hygiene seem to play an important interactive role with tobacco smoking.¹⁷

Acute necrotising gingivitis is also strongly correlated with tobacco use.¹⁸ Although the precise cause of this disease remains unknown, it tends to occur most frequently in teenagers and young adults. Some patients with acute necrotising gingivitis have defective neutrophil function, thereby allowing bacterial, or possibly viral (cytomegalovirus) invasion of gingival tissues.¹⁹ The gingival bleeding in smokers is 'less severe' than in non-smokers, which could be related to the vasoconstrictive effect of the nicotine.²⁰ The main vasoconstrictive property of nicotine exerts its effect at the end-arterial vasculature of the gingivae,²⁰ and

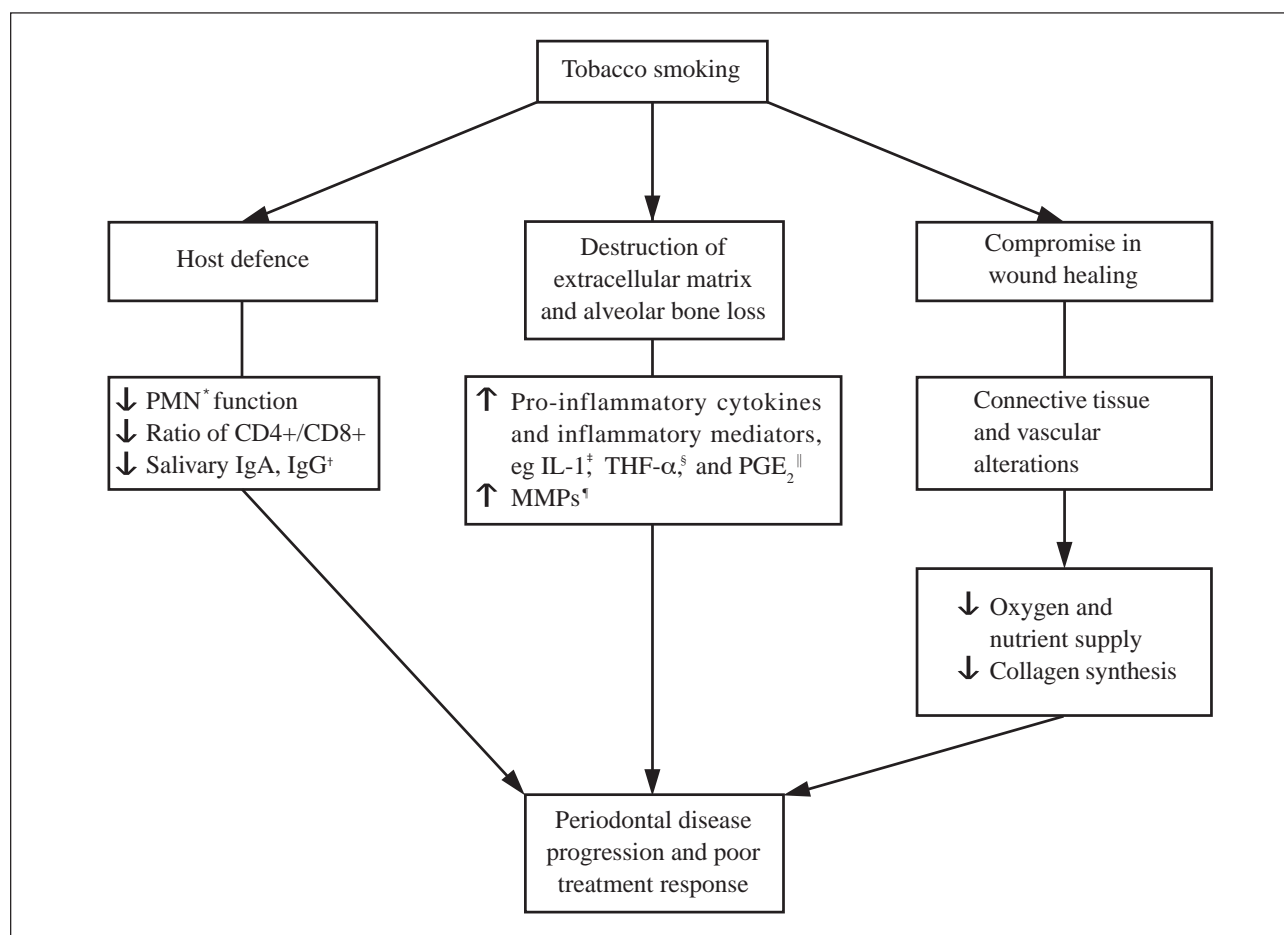


Fig 1. A heavy smoking subject with generalised chronic periodontitis

other tobacco components can also induce tissue necrosis and ulceration seen in the disease. Smokeless tobacco users have an incidence of gingivitis and gingival bleeding that is similar to the incidence among non-users. Nevertheless, use of this form of tobacco is known to produce a painless loss of gingival tissues and alveolar bone destruction in the area of chronic tobacco contact, as a result of collagen breakdown due to increased release of collagenase.²¹ Nicotine inhibits the growth of gingival fibroblasts and their production of fibronectin and collagen.²¹ Furthermore, oral leukocytes, especially neutrophils, may exhibit diminished ability to migrate and phagocytose, and they contribute to the inactivation of tissue proteinase inhibitors.²² Tobacco smoking may exert a masking effect on gingival symptoms of inflammation, which might give smoking patients a false sense of assurance of gingival health.²³ Smoking upregulates the expression of pro-inflammatory cytokines, such as interleukin-1, which contributes to increased tissue damage and alveolar bone resorption.²² Interleukin-1 genotype-positive smokers are more susceptible to severe adult periodontitis.²⁴ The effect of tobacco smoking on periodontal tissues is summarised in Fig 2.

Effects of smoking on periodontal therapy outcomes

Smokers respond less favourably than non-smokers to non-surgical^{25,26} and surgical periodontal therapy.²⁷ Smokers exhibited less improvement when compared with non-smokers, in terms of pocket depth reduction, resolution of gingival inflammation, and clinical attachment level.^{25,26,28} Heavy smokers (ie smoking >10 cigarettes per day) exhibited a lower degree of probing-depth reduction and less gain in clinical attachment level than did ex-smokers and non-smokers during active periodontal treatment.^{29,30} In addition, current smokers have poor healing ability, which may be associated with persistent subgingival infection with *Bacteroides forsythus* and *Porphyromonas gingivalis* following subgingival scaling and root planning when compared with ex-smokers and non-smokers.³¹ Cigarette smoking adversely affects outcomes of guided-tissue regeneration treatment (which aims to encourage regeneration of lost periodontal attachment) in terms of reduction in recession, gain of clinical attachment and probing-bone, and root coverage.^{32,33} However, up to 90% of refractory periodontitis patients are smokers.³⁴ Because smokers have different treatment response patterns



- * PMN polymorphonuclear leukocytes
 † IgA, IgG immunoglobulin A, immunoglobulin G
 ‡ IL-1 interleukin-1
 § TNF- α tumour necrosis factor- α
 || PGE₂ prostaglandin E₂
 ¶ MMPs matrix metalloproteinases

Fig 2. Effects of tobacco smoking on periodontal tissues

and healing dynamics, a short-term study conducted by Jin et al³⁵ suggested that smoking patients need a more intensive treatment regimen to achieve a better treatment outcome.

Periodontal effects of smoking cessation

Smoking cessation is beneficial to periodontal treatment outcomes and periodontal health. An encouraging finding is that periodontal disease progression also slows down in individuals who quit smoking. Smoking cessation may even restore the normal periodontal and microbial healing responses: the healing response of ex-smokers can even become similar to that of non-smokers.^{30,31}

Smokers who have been treated for periodontal diseases should be recalled more frequently for professional examination, reinforcement of oral hygiene instruction, intensive scaling, and prophylaxis after completion of treatment. Smoking is known to influence the composition of the subgingival microflora in adult patients with periodontitis, and the habit may predispose to the development of a specific population of periodontal pathogens.³⁶ Therefore, a combination of antibiotic therapy and participation in a smoking cessation programme may be the most effective treatment of smoking-induced periodontal diseases.^{37,38}

Dental implant failure

Tobacco smoking contributes to increased tooth mobility³⁹ and tooth loss occurs 1.53 times more frequently in smokers than in non-smokers.^{40,41} Tooth loss reduces the oral chewing function and quality of life and leads to the subsequent demand for tooth replacement, such as dentures or implant-supported prostheses.

Furthermore, smoking addiction is directly related to dental implant failure,^{42,43} and there is a general consensus on the negative effect of smoking on implant survival.⁴⁴ Significantly greater proportions of implant failures occur in smokers than in non-smokers (11.28% versus 4.76%).⁴³ Furthermore, Wallace⁴⁵ showed a failure rate of 16.6% in smokers, compared with 6.9% in non-smokers after a review of 56 patients having 187 endosseous dental implants over a 4-year period; shorter implants (<10 mm in length) were more susceptible to failure in smokers.⁴⁵ In this study, the failure rate before loading the implants was 9% in smokers versus 1% in non-smokers, which was statistically significant, even though the bone quality in both groups was comparable.

Peri-implantitis is the formation of deep mucosal pockets around dental implants, inflammation of the peri-implant tissues, and increased resorption of implant-surrounding bone. Chronic peri-implantitis results in implant failure when left untreated.² Tobacco use may directly compromise the osseointegration of root-form dental implants.⁴⁵ The difference in peri-implant bone loss is significant in the

mandible between smokers and non-smokers but insignificant in the maxilla.^{46,47} The combination of smoking and plaque-induced inflammation significantly influences bone loss around the implants,⁴⁶ whereas occlusal loading has only a minor role.

Smoking cessation protocols show considerable promise in improving the success rate of osseointegration in smokers who overcome the addiction, with significant differences between failure rates between non-smokers and smokers and between smokers who adopted the smoking cessation protocol and those who continue smoking.⁴⁸

Oral precancerous lesions

Leukoplakia and erythroplakia

A clinical definition of leukoplakia was formulated by the World Health Organization in 1978. Oral leukoplakia is currently defined as a predominantly white lesion of the oral mucosa that cannot be characterised as any other definable lesion; some of these lesions will develop into cancer (Fig 3).⁴⁹ The recent classification and staging system also incorporates provisional and definitive diagnoses on the basis of histopathological features of persistent lesions lasting longer than 2 to 4 weeks, such as the size of the leukoplakia and the presence of epithelial dysplasia. A diagnosis of oral leukoplakia results from the recognition of several levels of certainty (C), an approach that is analogous to the use of the C-factor in the tumour-node-metastasis classification system.⁴⁹ Smokers with oral premalignant lesions such as leukoplakia and erythroplakia (red patches or plaques that cannot be characterised clinically or pathologically as any other conditions) have an annual cancer transformation rate of about 5% (Fig 4).⁵⁰ A case-control study, conducted by Shiu et al⁵¹ in Taiwan, showed that the adjusted ratio for betel nut chewing and smoking on the occurrence of leukoplakia were 17.43 and 3.22, respectively. These findings suggested that stopping smoking may reduce the number of leukoplakia cases by 36%, while elimination of betel nut influence may prevent 62% cases of leukoplakia and 26% of cases of malignant transformation to oral carcinoma.

Smokeless tobacco keratosis

Snuff pouch or smokeless tobacco keratosis is a white keratotic lesion. It has a translucent appearance rather than an opaque whiteness. The microscopic appearance of tissue from a lesion does not reveal excessive keratinisation, which is characteristic of leukoplakia. This lesion is located only in areas of direct contact with snuff or chewed tobacco and is reversible when the affected patients stop the habit.

Many oral cancers, on the other hand, do not go through a premalignant stage, and not all premalignant lesions will become malignant; some may even regress with time.⁵² The degree of histological epithelial dysplasia and the clinical characteristics are the most reliable markers in predicting malignant potential.



Fig 3. Homogenous leukoplakia on the left alveolar gingiva of the mandible

Oral cancer

Oral cancer is dominated by squamous cell carcinoma (present in 90%-95% of all oral cancers), and the role of tobacco in the development of oral squamous cell carcinoma is well recognised (Fig 5). The long-term prognosis is quite poor, and treatment can lead to further functional and cosmetic problems. Tobacco use, including reverse smoking (smoking with the lit end inside the mouth), chewing of betel quid (a mixture of areca nut, slaked lime, and tobacco wrapped in betel leaf), and use of smokeless tobacco (smokeless tobacco products are not licensed for sale in Hong Kong⁵²), increases the risk of cancers of the upper aerodigestive tract. Oral cancer is also associated with alcohol consumption.^{53,54} Alcohol is capable of making the mucosa more susceptible to malignant transformation by the tobacco carcinogens, such as polycyclic aromatic hydrocarbons, formaldehyde, and nitrosamines. Tobacco smoking and betel nut chewing with or without smokeless tobacco use may induce mutations in *p53* and *Rb* tumour suppressor genes.^{55,56} Glutathione S-transferase M1 (*GSTM1*) and T1 (*GSTT1*) enzymes are both involved in the metabolism of environmental carcinogens, including tobacco-derived carcinogens. The prevalence of null genotypes of *GSTM1* and *GSTT1* is high among cases of oral cancer,⁵⁷ with both null genotypes occurring together in 60.2% of cases in one study.⁵⁸

Carcinogenesis of squamous cell carcinoma in the lung and oral cavity due to carcinogens present in tobacco and tobacco smoke may be correlated. Genetic polymorphisms of glutathione synthesis and glutathione-dependent enzymes have been studied with respect to the susceptibility to lung cancer.⁵⁹ Genetic combinations, such as mutations in the gene encoding cytochrome P450 (*CYP*) 1A1 and the *GSTM1*-null genotype, may predispose the lung and oral cavity of smokers to an even higher risk of carcinogenesis or DNA damage.⁶⁰ Major classes of carcinogens present in tobacco and tobacco smoke can be converted into DNA-reactive metabolites by *CYP*-related enzymes, but a study conducted in Japan showed that the *GSTM1*-null genotype



Fig 4. Tongue lesion with (A) epithelial dysplasia at the whitish area and (B) carcinoma at the ulcerative area



Fig 5. Invasive squamous cell carcinoma on the posterior mandible in a 66-year-old smoker

had only a weak correlation with oral cancers and genetic polymorphism of *GSTT1*, *CYP1A1*, and *CYP2E1* genes were not associated with such cancers.⁶¹ Retinoids or beta-carotene, isothiocyanates and tea polyphenols have also been identified as possible chemo-preventive agents for cancers of the lung and oral cavity, but study results remain controversial.⁶⁰ More molecular epidemiological evidence is required to confirm the gene-to-gene and gene-to-environment interactions in the development of oral cancers influenced by the different forms of tobacco smoking, especially among different ethnicities and races.

Smoking cessation strategies

Smoking is a chronic condition that requires long-term management. Dental treatment outcomes may be unpredictable for patients who continue to smoke. The financial burden may be increased when a more intensive treatment plan is required to achieve oral health. The most substantial decreases in management costs may be achieved for patients who stop smoking at an early stage.

Smoking cessation efforts are divided into two broad categories: pharmacological and behavioural. Pharma-

ological approaches currently include two general strategies: nicotine replacement and bupropion therapy. In April 2002, the National Institute for Clinical Excellence in the United Kingdom released guidelines to health care professionals on the use of nicotine replacement therapy (NRT) and non-NRT, such as bupropion (Zyban; Glaxo Wellcome, London, UK) for smoking cessation.⁶² Nicotine replacement therapy reduces physical withdrawal symptoms. Nicotine gum, transdermal patch, nasal spray, inhalers, sublingual tablets, and lozenges are examples of NRT products available.⁶³ Chewing nicotine gums and applying skin patches allow nicotine to be absorbed through the mucosa of the oral cavity and skin, respectively, thereby reducing the craving for nicotine and allowing patients to focus on changing their behaviour. Bupropion is the first prescribed non-nicotine pharmacological agent shown to be effective for smoking cessation, and it has been approved by the United States Food and Drug Administration for that use.⁶⁴ Bupropion is an antidepressant that acts on dopaminergic pathways in the central nervous system.⁶⁵

The combination of bupropion with NRT via a transdermal system has the highest success rates of cessation treatments.⁶⁵ Success of smoking cessation using pharmacotherapy-based treatment can be more effective when accompanied by individual or group-based behavioural therapy programmes conducted by specialised counsellors.⁶⁶ The most important factor for successful smoking cessation still lies on patients' willingness to quit smoking. Local smoking cessation services are provided by, among others, the Department of Health and Hospital Authority in Hong Kong (Box 2).

Conclusion

Periodontal diseases, dental implant failure, oral cancers, and precancerous development are linked closely with the tobacco use. Advising patients to quit tobacco use is a dental professional responsibility, and the dentists may take an active role in nicotine replacement counselling. Smoking cessation should be incorporated as an integral teaching

component of the undergraduate dental curriculum, particularly with respect to the prevention and diagnosis of tobacco-induced oral lesions and complications. Close collaboration of both dentists and physicians with smoking cessation programmes is advocated in the treatment of tobacco-smoking patients.

References

1. Wald NJ, Hackshaw AK. Cigarette smoking: an epidemiological overview. *Br Med Bull* 1996;52:3-11.
2. Haas R, Haimbock W, Mailath G, Watzek G. The relationship of smoking on peri-implant tissue: a retrospective study. *J Prosthet Dent* 1996;76:592-6.
3. Asmussen E, Hansen EK. Surface discoloration of restorative resins in relation to surface softening and oral hygiene. *Scand J Dent Res* 1986;94:174-7.
4. Mehta FS, Jalnawalla PN, Daftary DK, Gupta PC, Pindborg JJ. Reverse smoking in Andhra Pradesh, India: variability of clinical and histologic appearances of palatal changes. *Int J Oral Surg* 1977;6:75-83.
5. Hedin CA, Pindborg JJ, Axell T. Disappearance of smoker's melanosis after reducing smoking. *J Oral Pathol Med* 1993;22:228-30.
6. Holmgren CJ, Corbet EF, Lim LP. Periodontal conditions among the middle-aged and the elderly in Hong Kong. *Community Dent Oral Epidemiol* 1994;22:396-402.
7. Ravald N, Birkhed D, Hamp SE. Root caries susceptibility in periodontally treated patients. Results after 12 years. *J Clin Periodontol* 1993;20:124-9.
8. Bergstrom J. Cigarette smoking as risk factor in chronic periodontal disease. *Community Dent Oral Epidemiol* 1989;17:245-7.
9. Amarasekera N, Ekanayaka AN, Herath L, Miyazaki H. Tobacco use and oral hygiene as risk indicators for periodontitis. *Community Dent Oral Epidemiol* 2002;30:115-23.
10. Haber J, Kent RL. Cigarette smoking in a periodontal practice. *J Periodontol* 1992;63:100-6.
11. Bergstrom J. Tobacco smoking and supragingival dental calculus. *J Clin Periodontol* 1999;26:541-7.
12. Muller HP, Stadermann S, Heinecke A. Longitudinal association between plaque and gingival bleeding in smokers and non-smokers. *J Clin Periodontol*. 2002;29:287-94.
13. Martinez-Canut P, Lorca A, Magan R. Smoking and periodontal disease severity. *J Clin Periodontol* 1995;22:743-9.
14. Machuca G, Rosales I, Lacalle JR, Machuca C, Bullon P. Effect of cigarette smoking on periodontal status of healthy young adults. *J Periodontol* 2000;71:73-8.
15. Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: findings from NHANES III. National Health and Nutrition Examination Survey. *J Periodontol* 2000;71:743-51.
16. Grossi SG, Zambon JJ, Ho AW, et al. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol* 1994;65:260-7.
17. Horning GM, Cohen ME. Necrotizing ulcerative gingivitis, periodontitis, and stomatitis: clinical staging and predisposing factors. *J Periodontol* 1995;66:990-8.
18. Johnson BD, Engel D. Acute necrotizing ulcerative gingivitis. A review of diagnosis, etiology and treatment. *J Periodontol* 1986;57:141-50.
19. Slots J, Contreras A. Herpesviruses: a unifying causative factor in periodontitis? *Oral Microbiol Immunol* 2000;15:277-80.
20. Clarke NG, Shephard BC, Hirsch RS. The effects of intra-arterial epinephrine and nicotine on gingival circulation. *Oral Surg Oral Med Oral Pathol* 1981;52:577-82.
21. Tipton DA, Dabbous MK. Effects of nicotine on proliferation and extracellular matrix production of human gingival fibroblasts in vitro. *J Periodontol* 1995;66:1056-64.
22. Travis J, Pike R, Imamura T, Potempa J. The role of proteolytic enzymes in the development of pulmonary emphysema and periodontal disease. *Am J Respir Crit Care Med* 1994;150:143S-146S.
23. Bergstrom J, Preber H. Tobacco use as a risk factor. *J Periodontol* 1994;65(5 Suppl):545S-550S.

Box 2. Contact details of smoking cessation groups

Tobacco Control Office
 Cessation hotline: (852) 2961 8883
 Enquiries: (852) 2961 8823
 Fax: (852) 2575 8944
 Website: <http://www.tobaccocontrol.gov.hk/>

Hospital Authority Smoking Counselling and Cessation Centres
 Cessation hotline: (852) 2300 7272
 Fax: (852) 2890 7726
 E-mail: haquitsmoking@ha.org.hk

Smoking Cessation Health Centre
 Telephone: (852) 2855 0787

Cessation hotline
 Quitline (provided by the University of Hong Kong in collaboration with the Hong Kong Council in Smoking & Health [COSH])
 Telephone: (852) 2855 9557

24. Meisel P, Siegemund A, Dombrowa S, Sawaf H, Fanghaenel J, Kocher T. Smoking and polymorphisms of the interleukin-1 gene cluster (IL-1alpha, IL-1beta, and IL-1RN) in patients with periodontal disease. *J Periodontol* 2002;73:27-32.
25. Preber H, Linder L, Bergstrom J. Periodontal healing and periopathogenic microflora in smokers and non-smokers. *J Clin Periodontol* 1995;22:946-52.
26. Grossi SG, Skrepcinski FB, DeCaro T, Zambon JJ, Cummins D, Genco RJ. Response to periodontal therapy in diabetics and smokers. *J Periodontol* 1996;67(10 Suppl):1094S-1102S.
27. Bostrom L, Linder LE, Bergstrom J. Influence of smoking on the outcome of periodontal surgery. A 5-year follow-up. *J Clin Periodontol* 1998;25:194-201.
28. Ah MK, Johnson GK, Kaldahl WB, Patil KD, Kalkwarf KL. The effect of smoking on the response to periodontal therapy. *J Clin Periodontol* 1994;21:91-7.
29. Norderyd O, Hugoson A. Risk of severe periodontal disease in a Swedish adult population. A cross-sectional study. *J Clin Periodontol* 1998;25:1022-8.
30. Kaldahl WB, Johnson GK, Patil KD, Kalkwarf KL. Levels of cigarette consumption and response to periodontal therapy. *J Periodontol* 1996;67:675-81.
31. Grossi SG, Zambon J, Machtei EE, et al. Effects of smoking and smoking cessation on healing after mechanical periodontal therapy. *J Am Dent Assoc* 1997;128:599-607.
32. Trombelli L, Scabbia A. Healing response of gingival recession defects following guided tissue regeneration procedures in smokers and non-smokers. *J Clin Periodontol* 1997;24:529-33.
33. Trombelli L, Kim CK, Zimmerman GJ, Wikesjo UM. Retrospective analysis of factors related to clinical outcome of guided tissue regeneration procedures in intrabony defects. *J Clin Periodontol* 1997;24:366-71.
34. Johnson GK, Slach NA. Impact of tobacco use on periodontal status. *J Dent Educ* 2001;65:313-21.
35. Jin L, Wong KY, Leung WK, Corbet EF. Comparison of treatment response patterns following scaling and root planing in smokers and non-smokers with untreated adult periodontitis. *J Clin Dent* 2000;11:35-41.
36. Eggert FM, McLeod MH, Flowerdew G. Effects of smoking and treatment status on periodontal bacteria: evidence that smoking influences control of periodontal bacteria at the mucosal surface of the gingival crevice. *J Periodontol* 2001;72:1210-20.
37. Winkel EG, Van Winkelhoff AJ, Timmerman MF, Van der Velden U, Van der Weijden GA. Amoxicillin plus metronidazole in the treatment of adult periodontitis patients. A double-blind placebo-controlled study. *J Clin Periodontol* 2001;28:296-305.
38. van Winkelhoff AJ, Bosch-Tijhof CJ, Winkel EG, van der Reijden WA. Smoking affects the subgingival microflora in periodontitis. *J Periodontol* 2001;72:666-71.
39. Worthington H, Clarkson J, Davies R. Extraction of teeth over 5 years in regularly attending adults. *Community Dent Oral Epidemiol* 1999;27:187-94.
40. Yoshida Y, Hatanaka Y, Imaki M, Ogawa Y, Miyatani S, Tanada S. Epidemiological study on improving the QOL and oral conditions of the aged-Part 2: Relationship between tooth loss and lifestyle factors for adults men. *J Physiol Anthropol Appl Human Sci* 2001;20:369-73.
41. Ragnarsson E, Eliasson ST, Olafsson SH. Tobacco smoking, a factor in tooth loss in Reykjavik, Iceland. *Scand J Dent Res* 1992;100:322-6.
42. Widmark G, Andersson B, Carlsson GE, Lindvall AM, Ivanoff CJ. Rehabilitation of patients with severely resorbed maxillae by means of implants with or without bone grafts: a 3- to 5-year follow-up clinical report. *Int J Oral Maxillofac Implants* 2001;16:73-9.
43. Bain CA, Moy PK. The association between the failure of dental implants and cigarette smoking. *Int J Oral Maxillofac Implants* 1993;8:609-15.
44. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. *Eur J Oral Sci* 1998;106:721-64.
45. Wallace RH. The relationship between cigarette smoking and dental implant failure. *Eur J Prosthodont Restor Dent* 2000;8:103-6.
46. Lindquist LW, Carlsson GE, Jemt T. Association between marginal bone loss around osseointegrated mandibular implants and smoking habits: a 10-year follow-up study. *J Dent Res* 1997;76:1667-74.
47. Carlsson GE, Lindquist LW, Jemt T. Long-term marginal periimplant bone loss in edentulous patients. *Int J Prosthodont* 2000;13:295-302.
48. Bain CA. Smoking and implant failure-benefits of a smoking cessation protocol. *Int J Oral Maxillofac Implants* 1996;11:756-9.
49. van der Waal I, Axell T. Oral leukoplakia: a proposal for uniform reporting. *Oral Oncol* 2002;38:521-6.
50. Lee JJ, Hong WK, Hittelman WN, et al. Predicting cancer development in oral leukoplakia: ten years of translational research. *Clin Cancer Res* 2000;6:1702-10.
51. Shiu MN, Chen TH, Chang SH, Hahn LJ. Risk factors for leukoplakia and malignant transformation to oral carcinoma: a leukoplakia cohort in Taiwan. *Br J Cancer* 2000;82:1871-4.
52. The Smokeless Tobacco Products (Prohibition) Regulations (Chapter 132BW), Hong Kong Government.
53. Gupta PC, Bhonsle RB, Murty PR, Mehta FS, Pindborg JJ. Epidemiologic characteristics of treated oral cancer patients detected in a house-to-house survey in Kerala, India. *Indian J Cancer* 1986;23:206-11.
54. Zavras AI, Douglass CW, Joshipura K, et al. Smoking and alcohol in the etiology of oral cancer: gender-specific risk profiles in the south of Greece. *Oral Oncol* 2001;37:28-35.
55. Jones A. A general review of the p53 gene and oral squamous cell carcinoma. *Ann R Australas Coll Dent Surg* 1998;14:66-9.
56. Tanaka N, Odajima T, Mimura M, et al. Expression of Rb, pRb2/p130, p53, and p16 proteins in malignant melanoma of oral mucosa. *Oral Oncol* 2001;37:308-14.
57. Hung HC, Chuang J, Chien YC, et al. Genetic polymorphisms of CYP2E1, GSTM1, and GSTT1; environmental factors and risk of oral cancer. *Cancer Epidemiol Biomarkers Prev* 1997;6:901-5.
58. Nair UJ, Nair J, Mathew B, Bartsch H. Glutathione S-transferase M1 and T1 null genotypes as risk factors for oral leukoplakia in ethnic Indian betel quid/tobacco chewers. *Carcinogenesis* 1999;20:743-8.
59. Vineis P, Malats N, Lang M, et al. Metabolic polymorphisms and susceptibility to cancer. International Agency for Research on Cancer, IARC Scientific Publications No. 148, Lyon: IARC; 1999.
60. Nair U, Bartsch H. Metabolic polymorphisms as susceptibility markers for lung and oral cavity cancer. *IARC Sci Publ* 2001;154:271-90.
61. Katoh T, Kaneko S, Kohshi K, et al. Genetic polymorphisms of tobacco- and alcohol-related metabolizing enzymes and oral cavity cancer. *Int J Cancer* 1999;83:606-9.
62. Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation. National Institute for Clinical Excellence Technology Appraisal Guidance No. 39. 2002 Apr. National Institute for Clinical Excellence website: www.nice.org.uk. Accessed December 2002.
63. Rennard SI, Daughton DM. Smoking cessation. *Chest* 2000;117(5 Suppl 2):360S-364S.
64. Hughes JR, Goldstein MG, Hurt RD, Shiffman S. Recent advances in the pharmacotherapy of smoking. *JAMA* 1999;281:72-6.
65. Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *N Engl J Med* 1999;340:685-91.
66. West R, McNeill A, Raw M. Smoking cessation guidelines for health professionals: an update. Health Education Authority. *Thorax* 2000;55:987-99.