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REVIEW ARTICLE

The impact of cigarette/tobacco smoking on oral candidosis: an overview

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Smoking is associated with a variety of changes in the oral cavity. Cigarette smoke has effects on saliva, oral commensal bacteria and fungi, mainly *Candida*, which causes oral candidosis, the most common opportunistic fungal infection in man. How cigarette smoke affects oral *Candida* is still controversial. This brief overview is an attempt to address the clinical findings on the relationship between smoking and oral candidosis and possible mechanisms of pathogenicity.
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Introduction

Many factors can predispose to oral *Candida* infection (Almeida and Scully, 2002). Whether tobacco smoking is included as one of these factors has been considered for many years. During the past two decades a number of studies have found that smoking, either alone or in combination with other factors, appears to be an important predisposing factor for oral candidosis, although the exact pathogenic influence of smoking is yet to be resolved (Arendorf *et al*, 1983; Arendorf and Walker, 1984).

Epidemiological studies on oropharyngeal candidosis (OPC) in Human Immunodeficiency Virus (HIV)-positive persons have identified cigarette smoking as a major risk factor for symptomatic infection in those with higher CD4 cell counts than those usually predisposing to infection (200–500 cells μl^{-1}), with possible immunological consequences (Galai *et al*, 1997; Palacio *et al*, 1997; Schuman *et al*, 1998; Greenspan *et al*, 2000). Evidence for this possibility comes from the observation that HIV-positive and OPC-positive smokers with CD4 counts ≥200 cells μl^{-1} exhibited decreased interferon-gamma (IFN-γ) concentrations and a trend toward increased interleukin-4 (IL-4) concentrations in whole saliva compared with HIV-positive and OPC-negative non-smokers with ≥200 cells μl^{-1}. OPC-positive smokers and non-smokers with <200 cells μl^{-1} had increased IL-4 concentration compared with OPC-negative persons with ≥200 cells μl^{-1} ($P < 0.004$ and 0.0005 respectively). Individuals with CD4 cell counts ≥200 cells μl^{-1} were more likely to have OPC if they smoked, whereas smoking was not a factor in subjects with CD4 cell counts <200 cells μl^{-1} (Slavinsky *et al*, 2002). Although the association of OPC with smoking is unclear, hypotheses have included increased fungal burden caused by *Candida* (Alkumru and Beydemir, 1992), reduced numbers of Langerhans cells (Daniels *et al*, 1992), and/or increased prevalence of human papillomavirus (Burger *et al*, 1993) in smokers.

In this brief overview we discuss the clinical findings on the relationship between tobacco smoking and candidal carriage and the possible mechanisms of pathogenicity.

The relationship between tobacco smoking and candidal carriage

The literature reveals that the rate of oral candidal carriage in tobacco smokers was higher than in non-smokers (Abu-Elteen and Abu-Elteen, 1998; Willis *et al*, 1999). Tobacco smoking is one of the local factors, which influences oral *Candida* (Fongsmut *et al*, 1998). Arendorf and Walker (1980) studied 54 healthy dentate subjects and found a significantly higher carriage rate of *Candida* among smokers compared with non-smokers ($P < 0.01$). The same group of workers later studied the relationship of tobacco smoking in 40 patients with candidal leukoplakia and another 40 age- and sex-matched normal subjects and found that tobacco smoking was significantly more frequent in the test group than in the control group (Arendorf *et al*, 1983). Further Daftary *et al* (1972) reported that 98% (48 of 49) of Indian villagers with candidal leukoplakia were smokers, and Holmstrup and Bessermann (1983) documented that 10 patients with chronic hyperplastic candidosis had their lesions resolved after cessation of

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tobacco use without antimycotic treatment. Furthermore, clinical expertise suggests that some candidal infection invariably disappear following smoking cessation alone (Johnson and Bain, 2000). A study by Masipa *et al* (1992), to detect the oral carriage of *Candida* in 148 healthy adults found that there was no significant difference in prevalence between smokers and non-smokers. However smoking males showed a significantly higher prevalence of candidal carriage than the non-smoking males ($P < 0.05$). In a recent study, using 180 healthy subjects, a significant relationship ($P = 0.021$) was found between smoking and oral candidal carriage, the more heavily the individual smoked the more likely to carry *Candida* in the oral cavity (Shin *et al*, 2003).

The importance of tobacco smoking and denture wearing in the etiology of median rhomboid glossitis (MRG) in 39 patients was evaluated by Arendorf and Walker (1984). More of the MRG patients (85%) smoked tobacco compared with the 39 healthy age- and sex-matched control subjects (41%). The number of MRG patients, who were both tobacco smokers and denture wearers, were significantly high suggesting that these local factors may play a role in the development of MRG, by favoring the local proliferation of *Candida albicans* on the dorsum of the tongue (Arendorf and Walker, 1984). A study by Guggenheimer *et al* (2000) using insulin-dependent diabetes mellitus (IDDM) patients found that the variables significantly associated with the presence of *Candida* pseudohyphae in the diabetic population, were poor glycemic control, current cigarette smoking and use of dentures. Presence of *Candida* pseudohyphae, could therefore have contributed to the pathogenesis of MRG. In another study by Tapper-Jones *et al* (1981) who examined 50 diabetic patients and 50 healthy volunteers matched for age, sex, dental status and smoking habits, found that smoking increased the candidal carrier rate in both diabetics and the healthy. Four of every five (80%) diabetics who smoked carried the yeast. Smoking did not significantly influence the overall candidal densities in either group. However, recently it has been found that diabetic patients with oral candidosis who were smokers had significantly higher candidal load than diabetic patients with oral candidosis who were ex-smokers or who did not smoke (Willis *et al*, 1999).

Crockett *et al* (1992) using an imprint culture technique in a group of full denture-wearing patients with erythematous candidosis found that denture wearers who smoked tobacco had a significantly greater incidence of erythematous candidosis than controls. Sixty-eight denture wearers from two independent cohorts were evaluated for denture-related stomatitis. Among risk factors evaluated, wearing dentures at night and smoking were associated with the most extensive inflammation (Barbeau *et al*, 2003). Furthermore, smoking was associated with increased prevalence of denture stomatitis in IDDM patients, in addition to other factors such as longer duration of IDDM, and elevated glycosylated hemoglobin (Guggenheimer *et al*, 2000).

There is a substantial body of epidemiological data, accumulated over a very short period, emphasizing oral candidosis in HIV-infected individuals Samaranayake, 1990. It is considered the commonest oral manifestation in this patient group. A study by Conley *et al* (1996) using 232 HIV-infected males, found that cigarette smoking was significantly associated with oral candidosis ($P < 0.01$) and cigarette smokers developed oral candidosis more rapidly than non-smokers ($P = 0.031$). In a similar study using 2499 HIV-1 seropositive men who had baseline $CD4^+$ cell counts $> 200\ \mu l^{-1}$, smoking was associated with a 40% increase in pseudomembranous candidosis ($P \leq 0.01$) (Galai *et al*, 1997). Therefore cigarette smoking seems to have an effect on the incidence of pseudomembranous candidosis in immunocompromised individuals. In a recent study, among HIV+ subjects a significant association between *Candida* carriage and smoking was observed, even though such an association was not seen in relation to *Candida* density (Campisi *et al*, 2002). *Candida* species isolated from oral rinses of 130 HIV-infected patients were compared with those of 130 healthy non-matched volunteers. Smoking was significantly associated with oral carriage of non-*C. albicans* species such as *C. glabrata*, *C. dubliniensis* and *C. tropicalis* ($P < 0.05$). Hence these findings suggest that smoking may contribute to oral carriage of such species (Schoofs *et al*, 1998). HIV-positive individuals were also more likely to be OPC positive if they smoked cigarettes ($P < 0.001$) (Slavinsky *et al*, 2002). Significant variables were CD4 cell count and smoking, and further analysis showed a significant interaction ($P < 0.001$) between these two variables. HIV-positive smokers with ≥ 200 cells μl^{-1} were 50 times more likely to be OPC positive than non-smokers (Slavinsky *et al*, 2002). Although there seems to be a trend existed for smokers to have predominantly erythematous OPC on the tongue ($P = 0.059$), the likelihood of having erythematous OPC on the tongue if the individual had ≥ 200 cells μl^{-1} was much greater ($P < 0.005$) (Slavinsky *et al*, 2002). Salivary secretory leukocyte protase inhibitor (SLPI) suppresses the growth of *Candida*. Chattopadhyay *et al* (2004), on the effect of SLPI on oral candidosis in a group of HIV-infected persons found that smoking was associated with a fourfold increase in having a positive history of OPG ($P = 0.04$). While cigarrette smoke supresses salivary SLPI levels, exposure to *Candida* may lead to an upregulation of salivary SLPI that may overcome the suppressive effects of smoking (Chattopadhyay *et al*, 2004).

A group of 27 patients under radiation therapy for head and neck malignancies also showed that smoking enhanced oral colonization by *Candida* during radiation therapy ($P = 0.045$) (Epstein *et al*, 1993). However, in a study by Ramirez-Amador *et al* (1997) using 46 patients undergoing radiation therapy for head and neck carcinoma showed smoking was not a significant risk factor for increased candidal colonization ($P = 0.085$). A more in depth coverage on the relationship between radiotherapy and oral candidosis has recently been reviewed (Soysa *et al*, 2004) and is beyond the scope of this discussion.

In contrast to foregoing information others have failed to show a positive correlation between smoking

and oral candidosis. Kadir *et al* (2002) using 55 diabetic and 45 non-diabetic patients, failed to demonstrate a correlation between oral candidal carriage and smoking. Furthermore, Gergely and Uri (1966) and Colman *et al* (1976) have also reported that neither tobacco nor cigarette smoking causes quantitative disturbances in oral yeasts. Similarly, Bastiaan and Reade (1982) who studied the prevalence of *C. albicans* in 127 patients with oral mucous membrane keratosis and their tobacco smoking habits arrived at a similar conclusion. Oliver and Shillitoe (1984) in a study of 100 healthy individuals found that the prevalence of oral *Candida* was the same (35%) in both smokers and non-smokers. In a recent study a significant correlation was not found between smoking habits and diabetic status, presence of dentures with oral yeast or the amount, species or genotype of the yeast isolated ($P > 0.05$; Manfredi *et al*, 2002). Whilst it is generally believed that smoking predisposes to oral carriage of *Candida* these data clearly reveal that this relationship is far from resolved.

Mechanism of pathogenicity

The exact mechanism by which candidal carriage may be affected by cigarette or cigar smoke is not yet established. However Arendorf and Walker (1980) have suggested that smoking may lead to localized epithelial alterations, which facilitate candidal colonization. In a study by the same research group using 53 candidal leukoplakia patients suggested smoking as a prime etiological factor in oral candidal leukoplakia. In the same study group of 40 tobacco-smoking patients 36 were continuous denture wearers. This suggests that palatal lesions found in denture wearers involving the unprotected mucosa provides circumstantial evidence for a direct mucosal insult by tobacco smoke in the pathogenesis. Tobacco smoking associated with denture friction on the oral mucosa also alters the mucosal surface, which may facilitate candidal colonization (Arendorf *et al*, 1983).

An alternative hypothesis is that cigarette smoke may contain nutritional factors for *C. albicans*. This has important implications as aromatic hydrocarbons contained in cigarette smoke may be converted by inducible enzyme systems present in *Candida* species to carcinogen end products (Hsia *et al*, 1981). This together with other observations that *C. albicans* could catalyze the formation of *N*-nitrosobenzylmethylamine (Krogh *et al*, 1987), may partly explain why smokers may be more prone to candidal leukoplakia and has a higher potential for malignant changes than other leukoplakias.

Immunoglobulins, polymorphonuclear leukocytes and normal bacterial flora are important in inhibiting the colonization of *Candida* in the oral cavity (Samaranayake, 1990). Smoking depress the activity of oral leukocytes and reduce gingival exudate with the consequences that the carriage of leukocytes and immunoglobulins is likely to diminish which may also enhance candidal colonization in the mouth (Macgregor, 1989). Smoking and increased salivary glucose have been implicated as independent risk factors for increased oral candidal carriage. Smoking may have an indirect effect on candidal carriage and candidosis by elevating glycosylated hemoglobin levels (Lundman *et al*, 1990). Salivary glucose may form chemically reversible glycosylation products with proteins in tissues during hyperglycemic episodes (Brownlee *et al*, 1988). It is possible that accumulation of such glycosylation products on buccal epithelial cells may increase the number of available receptors for *Candida*. Furthermore, tobacco smoke increases adrenaline levels in blood (Ritz *et al*, 1998), and blood glucose levels in diabetic smokers were significantly higher than non-smokers due to the effect of smoke on adrenaline.

A review of the literature indicates that the most consistent data on smoking and oral candidosis comes from the immunosuppressed populations especially the HIV-infected subjects. Data in other populations (diabetes, denture wearers, etc.) who are largely immunocompetent are much less consistent with regard to the impact of smoking. Cell-mediated immunity (CMI) by Th1-type $CD4^+$ T cells is considered the most important host defense mechanism against *C. albicans* at mucosal surfaces as demonstrated by the high incidence of mucosal candidosis in those with reduced $CD4^+$ T cells (Reichart *et al*, 2000). Evaluation of systemic CMI in a cohort of HIV^+ individuals with and without mucosal candidosis revealed that *Candida*-specific CMI is not different between HIV-positive persons with OPC or vulvovaginal candidosis and HIV-negative persons. Thus, the correlation of reduced $CD4^+$ cell numbers to OPC may be explained by the requirement for a threshold number of systemic $CD4^+$ cells to protect the oral mucosa together with the status of local immunity (Fidel, 2002). In as much as OPC occurs frequently under CMI immunocompromised conditions, it can also occur when $CD4^+$ T cell levels are normal, which indicates that other mechanisms are involved in host defense, presumably at the local level (Steele *et al*, 2000). It has been postulated that oral epithelial cells inhibit the growth of blastoconidia and/or hyphal phases of *Candida* through a cell surface carbohydrate moiety with a requirement for cell contact and with no demonstrable role for soluble factors (Steele *et al*, 2001). Therefore it is likely that this oral epithelial cell anti-candidal activity is reduced in HIV+ persons with OPC and is thus considered an innate host defense against oral candidosis. In a recent study by Arredondo *et al* (2001) it was found that nicotine in tobacco can cause structural and functional changes in oral keratinocytes. Hence, with the known effects of smoking on epithelial cells, a reduction of this activity when other more primary host defenses (CD4 cells) are reduced or begin to fail could increase susceptibility to OPC.

Interferon-γ and IL-12 are associated with resistance to mucosal and/or systemic *Candida* infection, where as IL-4 and IL-10 have been associated with susceptibility to infection (Romani *et al*, 1996). IFN-γ concentrations in saliva of OPC-positive smokers with $\geq$200 cells μl^{-1} were significantly lower than those in saliva of OPC-negative persons with $\geq$200 cells μl^{-1} ($P < 0.001$).

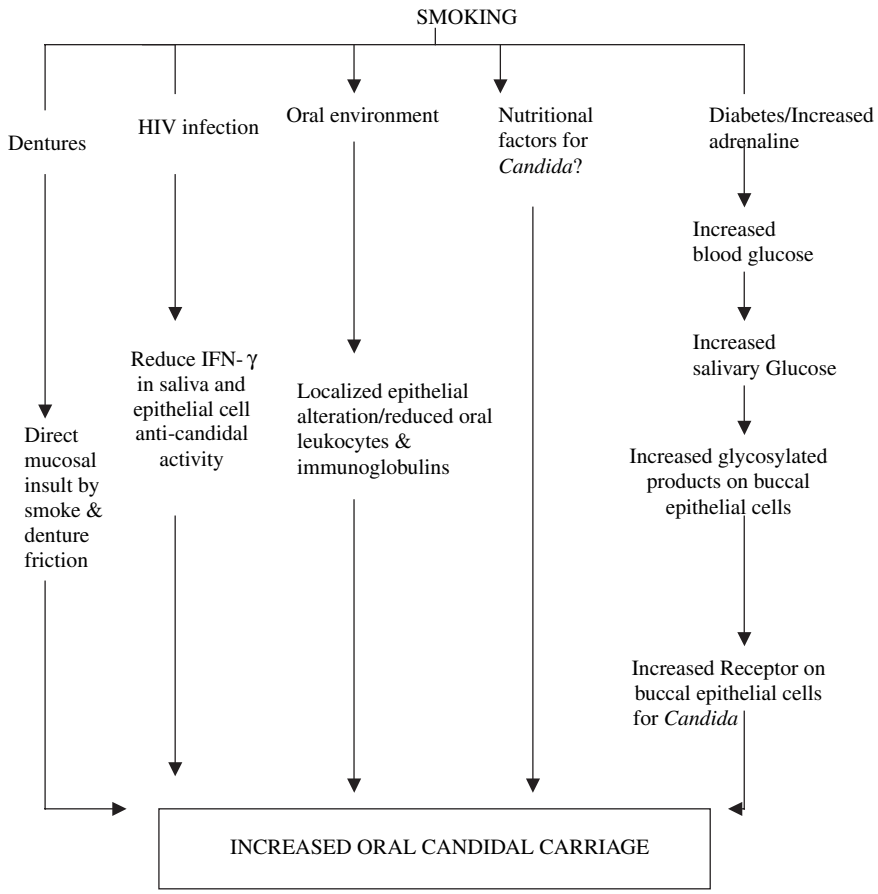

Figure 1 Impairment of local immunity including cytokine changes and epithelial cell-mediated anti-candidal activity along with other possible mechanism by which smoking may increase oral candidal carriage

Hence, these findings suggest that smoking in HIV-positive persons has an inhibitory effect on local immunity (i.e. antigen presentation, innate resistance and cytokine production) that systemic CD4 cells, at levels that are normally considered protective, cannot overcome (Slavinsky *et al*, 2002). Alternatively, smoking together with HIV infection may adversely affect the blood CD4 cells resulting in reduced immunity. The foregoing data clearly reveals that the impact of smoking can only be realized when the status of the immune system is reduced while other factors such as diabetes and dentures are contributory. A schematic diagram depicting the potential factors of smoking on oral candidosis is shown in Figure 1.

Conclusion

A number of studies have found that smoking either alone or in combination with other factors appear to be an important predisposing factor for oral candidosis, although this relationship or its pathogenic influence on oral *Candida* is far from resolved. However, the impact of smoking on local and oral immune mechanisms, and the mechanisms by which *Candida* proliferate intra-orally as a result of cigarette smoking, necessitates probing to clarify these unresolved concepts. As most consistent data on smoking and oral candidosis comes from the immunosuppressed populations, the answer to these important questions regarding the mechanism of smoking on local immune function, however require longitudinal oral immune analyses of smokers throughout HIV disease progression.

References

Abu-Elteen KH, Abu-Elteen RM (1998). The prevalence of *Candida albicans* populations in the mouths of complete denture wearers. *New Microbiol* **21:** 41–48.

Alkumru HN, Beydemir K (1992). The prevalence of *Candida albicans* in complete denture and removable partial denture wearers: a comparative study. *J Marmara Univ Dent Fac* **1:** 218–222.

Almeida OP, Scully C (2002). Fungal infections of the mouth. *Braz J Oral Sci* **1:** 19–26.

Arendorf TM, Walker DM (1980). The prevalence and intraoral distribution of *Candida albicans* in man. *Arch Oral Biol* **25:** 1–10.

Arendorf TM, Walker DM (1984). Tobacco smoking and denture wearing as local aetiological factors in median rhomboid glossitis. *Int J Oral Surg* **13:** 411–415.

Arendorf TM, Walker DM, Kingdom RJ *et al* (1983). Tobacco smoking and denture wearing in oral candidal leukoplakia. *Br Dent J* **155:** 340–343.

Arredondo J, Nguyen VT, Chernyavsky AI *et al* (2001). A receptor-mediated mechanism of nicotine toxicity in oral keratinocytes. *Lab Invest* **81:** 1653–1668.

Barbeau J, Seguin J, Goulet JP *et al* (2003). Reassessing the presence of *Candida albicans* in denture-related stomatitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **95:** 51–59.

Bastiaan RJ, Reade RC (1982). The prevalence of *Candida albicans* in the mouths of tobacco smokers with and without oral mucous membrane keratoses. *Oral Surg Oral Med Oral Pathol* **53:** 148–151.

Brownlee M, Cerami A, Vlassara H (1988). Advanced glycosylation end products in tissue and the biochemical basis of diabetic complications. *N Engl J Med* **318:** 1315–1321.

Burger MP, Hollema H, Gouw AS *et al* (1993). Cigarette smoking and human papillomavirus in patients with reported cervical cytological abnormality. *BMJ* **306:** 749–752.

Campisi G, Pizzo G, Milici ME *et al* (2002). Candidal carriage in the oral cavity of human immunodeficiency virus-infected subjects. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **93:** 281–286.

Chattopadhyay A, Gray LR, Patton LL *et al* (2004). Salivary secretory leukocyte protease inhibitor and oral candidiasis in human immunodeficiency virus type 1-infected persons. *Infect Immun* **72:** 1956–1963.

Colman G, Beighton D, Chalk A *et al* (1976). Cigarette smoking and the microbial flora of the mouth. *Aust Dent J* **21:** 111–118.

Conley LJ, Bush TJ, Buchbinder SP *et al* (1996). The association between cigarette smoking and selected HIV-related medical conditions. *AIDS* **10:** 1121–1126.

Crockett DN, O'Grady JF, Reade PC (1992). *Candida* species and *Candida albicans* morphotypes in erythematous candidiasis. *Oral Surg Oral Med Oral Pathol* **73:** 559–563.

Daftary DK, Mehta FS, Gupta PC *et al* (1972). The presence of *Candida* in 723 oral leucoplakias among Indian villagers. *Scand J Dent Res* **80:** 75–79.

Daniels TE, Chou L, Greenspan JS *et al* (1992). Reduction of Langerhans cells in smokeless tobacco-associated oral mucosal lesions. *J Oral Pathol Med* **21:** 100–104.

Epstein JB, Freilich MM, Le ND (1993). Risk factors for oropharyngeal candidiasis in patients who receive radiation therapy for malignant conditions of the head and neck. *Oral Surg Oral Med Oral Pathol* **76:** 169–174.

Fidel PL Jr (2002). Immunity to *Candida*. *Oral Dis* **8:** 69–75.

Fongsmut T, Deerochanawong C, Prachyabrued W (1998). Intraoral *Candida* in Thai diabetes patients. *J Med Assoc Thai* **81:** 449–453.

Galai N, Park LP, Wesch J *et al* (1997). Effect of smoking on the clinical progression of HIV-1 infection. *J Acquir Immune Defic Syndr Hum Retrovirol* **14:** 451–458.

Gergely L, Uri J (1966). Day-by-day variation in the mycotic flora of the mouth. *Arch Oral Biol* **11:** 15–19.

Greenspan D, Komaroff E, Redford M *et al* (2000). Oral mucosal lesions and HIV viral load in the Women's Interagency HIV Study (WIHS). *J Acquir Immune Defic Syndr* **25:** 44–50.

Guggenheimer J, Moore PA, Rossie K *et al* (2000). Insulin-dependent diabetes mellitus and oral soft tissue pathologies: II. Prevalence and characteristics of *Candida* and candidal lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **89:** 570–576.

Holmstrup P, Bessermann M (1983). Clinical, therapeutic and pathogenic aspects of chronic oral multifocal candidosis. *Oral Surg Oral Med Oral Pathol* **56:** 388–395.

Hsia CC, Sun TT, Wang YY *et al* (1981). Enhancement of formation of esophageal carcinogen benzylmethylnitrosoamine from its precursors by *Candida albicans*. *Proc Natl Acad Sci U S A* **78:** 1878–1881.

Johnson NW, Bain CA (2000). Tobacco and oral disease. EU-Working Group on Tobacco and Oral Health. *Br Dent J* **189:** 200–206.

Kadir T, Pisiriciler S, Akyuz S *et al* (2002). Mycological and cytological examination of oral candidal carriage in diabetic patients and non-diabetic control subjects: thorough analysis of local aetiologic and systemic factors. *J Oral Rehabil* **29:** 452–457.

Krogh P, Hald B, Holmstrup P (1987). Possible mycological etiology of oral mucosal cancer: catalytic potential of infecting *Candida albicans* and other yeasts in production of N-nitrosobenzylmethylamine. *Carcinogenesis* **8:** 1543–1548.

Lundman BM, Asplund K, Norberg A (1990). Smoking and metabolic control in patients with insulin-dependent diabetes mellitus. *J Intern Med* **227:** 101–106.

Macgregor ID (1989). Effects of smoking on oral ecology. A review of the literature. *Clin Prev Dent* **11:** 3–7.

Manfredi M, McCullough MJ, Al-Karaawi ZM *et al* (2002). The isolation, identification and molecular analysis of *Candida* spp. isolated from the oral cavities of patients with diabetes mellitus. *Oral Microbiol Immunol* **17:** 181–185.

Masipa JN, Hauman CH, Raubenheimer EJ (1992). Oral carriage of *Candida* species in patients visiting the Medunsa Dental Clinic. *J Dent Assoc S Afr* **47:** 407–409.

Oliver DE, Shillitoe EJ (1984). Effects of smoking on the prevalence and intraoral distribution of *Candida albicans*. *J Oral Pathol* **13:** 265–270.

Palacio H, Hilton JF, Canchola AJ *et al* (1997). Effect of cigarette smoking on HIV-related oral lesions. *J Acquir Immune Defic Syndr Hum Retrovirol* **14:** 338–342.

Ramirez-Amador V, Silverman S Jr Mayer P *et al* (1997). Candidal colonization and oral candidiasis in patients undergoing oral and pharyngeal radiation therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **84:** 149–153.

Reichart, PA, Samaranayake LP, Philipsen HP (2000). Pathology and clinical correlates in oral candidiasis and its variants: a review. *Oral Dis* **6:** 85–91.

Ritz E, Benck U, Franek E *et al* (1998). Effects of smoking on renal hemodynamics in healthy volunteers and in patients with glomerular disease. *J Am Soc Nephrol* **9:** 1798–1804.

Romani L, Puccetti P, Bistoni F (1996). Biological role of Th cell subsets in candidiasis. *Chem Immunol* **63:** 115–137.

Samaranayake LP (1990). Host factors and oral candidosis. In: Samaranayake LP, MacFarlane TW, eds. *Oral candidosis* London, UK: Butterworth and Company Ltd, pp. 66–103.

Schoofs AG, Odds FC, Colebunders R *et al* (1998). Cross-sectional study of oral *Candida* carriage in a human immunodeficiency virus (HIV)-seropositive population: predisposing factors, epidemiology and antifungal susceptibility. *Mycoses* **41:** 203–211.

Schuman P, Ohmit SE, Sobel JD *et al* (1998). Oral lesions among women living with or at risk for HIV infection. *Am J Med* **104:** 559–564.

Shin ES, Chung SC, Kim YK *et al* (2003). The relationship between oral *Candida* carriage and the secretor status of blood group antigens in saliva. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* **96:** 48–53.

Slavinsky J, Myers T, Swoboda RK *et al* (2002). Th1/Th2 cytokine profiles in saliva of HIV-positive smokers with oropharyngeal candidiasis. *Oral Microbiol Immunol* **17:** 38–43.

Soysa NS, Samaranayake LP, Ellepola ANB (2004). Cytotoxic drugs, radiotherapy and oral candidiasis. *Oral Oncol* **40:** 971–978.

Steele C, Leigh J, Swoboda R *et al* (2000). Growth inhibition of *Candida* by human oral epithelial cells. *J Infect Dis* **182:** 1479–1485.

Steele C, Leigh J, Swoboda R *et al* (2001). Potential role for a carbohydrate moiety in anti-*Candida* activity of human oral epithelial cells. *Infect Immun* **69:** 7091–7099.

Tapper-Jones LM, Aldred MJ, Walker DM *et al* (1981). Candidal infections and populations of *Candida albicans* in mouths of diabetics. *J Clin Pathol* **34:** 706–711.

Willis AM, Coulter WA, Fulton CR *et al* (1999). Oral candidal carriage and infection in insulin-treated diabetic patients. *Diabet Med* **16:** 675–679.