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Tobacco Smoking and Vertical Periodontal Bone Loss

By

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Stockholm 2005

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إلى القنديلان اللذان لن ولن يطفئ بينهما ولن يخبأ ضبا وُ صما هي دنيا وجودي ومدى حياتي
واللذان سيطلقان يضيوان نفسي ما حبت بنور الله
إلى من وبياني على حب العلم والمعرفة إلى من أكرمني الله من أجلمو.....
إلى والدتي العزيزة إلى والدي العزيز.....
حفظهما الله

إلى وفريقي في رحلة الحياة ومن وفرت لي السبل إلى من حملت معي المجاهد
وطرقت معي الأمواج العاتية إلى من حاولت أن تخفي الدموع وتضيئ الشموع هي
بحولي إلى زوجتي قاربي وشراعي

إلى أبنائي ونور عيني..... تبوا ... جميل ... بكر...
حفظهم الله
إلى صوك أصدى ثماره ذا الجسد المتواضع
فاقبلوه بكل الحب الذي عمدته منكم مدى الدوام

محبكم

مصطفى جميل بلجون

ABSTRACT

Cigarette smoking is associated with increased prevalence and severity of destructive periodontal disease in terms of periodontal pocketing, periodontal bone loss, and tooth loss. The smoking destructive effect on periodontal bone may be of even "horizontal" and vertical "angular" pattern. The vertical bone loss or the "vertical defect" is a sign of progressive periodontal breakdown that involves the periodontal bone. Water pipe smoking has a sharp rise by the popularity in the recent years by men and women in Middle East countries.

The general objective of this thesis was to investigate the relationship between tobacco smoking and vertical periodontal bone loss cross-sectionally and longitudinally.

This thesis is based on two study populations, Swedish musicians and a Saudi Arabian population. All participants had a full set of intra-oral radiographs including 16 periapical and 4 bitewing projections that were assessed with regard to presence or absence of vertical defects.

In Study I, the number of defects per person increased with age. Vertical defects were more common in the posterior as compared to the anterior region of the dentition and the distribution of defects within the maxilla as well as the mandible typically revealed a right - left hand side symmetry. Cigarette smoking was significantly associated with the prevalence and severity of vertical bone defects (Studies II and III). The relative risk associated with cigarette smoking was 2 to 3-fold increased. The impact of water pipe smoking was of the same magnitude as that of cigarette smoking and the relative risk associated with water pipe smoking was 6-fold increased compared to non-smoking. In addition, the risk of vertical defects increased with increased exposure in cigarette smokers as well as water pipe smokers (Study III). In Study IV, the proportion of vertical defects increased over a 10-year period and the increase over time was significantly associated with smoking. Moreover, the 10-year vertical bone loss was significantly greater in heavy exposure smokers than in light exposure smokers suggesting an exposure-response effect of smoking. Compared to non-smokers the 10-year relative risk was 2.4-fold increased in light exposure smokers and 5.8-fold increased in heavy exposure smokers.

In conclusion, the present observations indicate that there is a significant relationship between tobacco smoking and vertical periodontal bone loss. Tobacco smoking should be considered a risk factor for periodontal vertical bone loss.

Key words: Age, angular bone defect, bone loss, cigarette smoking, periodontal disease, radiography, Saudi Arabia, tobacco, vertical bone defect, water pipe smoking.

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PREFACE

The thesis consists of an introductory text with original research articles appended. These are listed below and will be referred to in the text by their Roman numerals I-IV:

- I. **Baljoon M**, Natto S, Bergström J. The occurrence of vertical bone defects in dentally aware individuals. *Acta Odontol Scand* 2003; 61: 47-51.
- II. **Baljoon M**, Natto S, Bergström J. The association of smoking with vertical periodontal bone loss. *J Periodontol* 2004; 75: 851-858.
- III. **Baljoon M**, Natto S, Abanmy A, Bergström J. Smoking and vertical bone defects in a Saudi Arabian population. *Oral Health Prev Dent* 2005. Accepted.
- IV. **Baljoon M**, Natto S, Bergström J. Long-term effect of smoking on vertical periodontal bone loss. *J Clin Periodontol* 2005; 32: 370-378.

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Other related publications by the same authors:

- Natto S, **Baljoon M**, Abanmy A, Bergström J. Tobacco smoking and gingival health in a Saudi Arabian population. *Oral Health Prev Dent* 2004; 2: 351-357.
- Natto S, **Baljoon M**, Dahlén G, Bergström J. Tobacco smoking and periodontal microflora in a Saudi Arabian population. *J Clin Periodontol* 2005; 32: 628-634.
- Natto S, **Baljoon M**, Bergström J. Tobacco smoking and periodontal health in a Saudi Arabian population. *J Periodontol* 2005; Accepted.
- Natto S, **Baljoon M**, Bergström J. Tobacco smoking and periodontal bone height in a Saudi Arabian population. *J Clin Periodontol* 2005; Accepted.

GLOSSARY

Incidence	Number who get disease over a period of time in relation to the number of people at risk during that period
Odds ratio	A comparison of the presence of a risk factor for disease in a sample of diseased subjects and non-diseased
Precision	Estimation of random error in the measurements.
Prevalence	The proportion of a population that has disease at a specific point in time.
Reliability	The capacity to give the same result-positive or negative, whether correct or incorrect- on repeated application in a person with a given level of disease.
Risk factor	Characteristic, or exposure, that increases the probability developing a disease or may lead to a measurable change in health status. Identified in prospective longitudinal studies.
Severity	The frequency of diseased sites in relation to the frequency of sites measured in the individual
Vertical defect	A one-sided bone resorption of the interdental marginal bone of at least 2 mm that had a typical angulation towards either the mesial or distal aspect of the root. In addition the lamina dura of the affected tooth showed widening

LIST OF ABBREVIATIONS

ANOVA	Analysis of variance
BL	Baseline
CI	Confidence interval
CS	Cigarette smokers
FS	Former smokers
FU	Follow-up
GI	Gingival index
KVP	Kilo volt per person
LSD	Fisher Least Square Difference Test
NS	Non-smokers
OR	Odds ratio
PI	Plaque index
<i>s</i>	Precision
SD	Standard deviation
VD	Vertical defects
WPS	Water pipe smokers
κ	Cohen's kappa statistic

GENERAL INTRODUCTION

Periodontal disease

Periodontal disease is one of the most widespread diseases of mankind. No nation and no area of the world is free from it and has a high prevalence affecting almost the entire adult population (Burt 1993). Periodontal disease varies from localized mild gingivitis to general severe periodontal destruction that may end by tooth loss. It is no longer warranted to consider all individuals to be at the same level of risk of developing periodontal disease. Certain groups of the population are at a higher risk than others. Epidemiologists are focusing on what characteristics are peculiar to such groups and how they might be identified in time for preventive action to be taken.

Destructive periodontal disease is unlike many other chronic inflammatory diseases in that the presence of the infectious agents *per se* do not inevitably lead to the development of periodontal tissue loss. Although there is strong evidence implicating microorganisms in the etiology of periodontal disease (Haffajee & Socransky 1994, Albandar et al. 2001), there is a lack of correspondence between the somewhat high prevalence of periodontal pathogens and loss of periodontal tissue in the affected individual and tooth site (Albandar 2002). Some potential risk factors, however, have been identified such as age and smoking (Preber et al. 1980, Burt et al. 1982, Bergström & Flodérus-Myrhed 1983, Feldman et al. 1983, Ismail et al. 1983, Genco & Loe 1993, Burt 1994, Bergström 2003, 2004).

The height and density of the alveolar bone are normally maintained by equilibrium, regulated by local and systemic influences between bone formation and bone resorption. When resorption exceeds formation, bone height and/or bone density are reduced.

In periodontal disease, periodontal bone loss occurs as a consequence of inflammation to the supporting periodontal structures. The most common pattern of interdental bone resorption in periodontal disease is the horizontal bone loss. The bone is reduced in height, but the bone margin remains roughly perpendicular to the tooth surface (Carranza 2002). Occasionally, specific resorption patterns occur such as osseous craters and infrabony defects. The radiographic representation of infrabony destruction is commonly referred to as vertical or angular defects (Grant 1988, Goaz & White 1994, Carranza 2002). Vertical defects occur in an oblique direction, leaving a hollowed-out trough in the bone alongside the root. Vertical defects are considered a sign of progressive or advanced disease and

have been associated with further periodontal bone loss and tooth loss (Papapanou & Wennström 1991).

Just like all other hard connective tissue, the alveolar bone is subject to change with age. It has been noted that, with increasing age, the periodontal surfaces of alveolar bone become jagged and that collagen fibers insert less regularly into the bone (Ive et al. 1980). Although moderate loss of periodontal bone is common in the elderly, severe periodontal breakdown is not a natural consequence of aging and age alone in healthy adults does not lead to a critical loss of periodontal support (Burt 1994). The increased severity of periodontal disease with age, however, is not because of greater susceptibility among elderly but represent the disease accumulation over time (Burt 1992). Clinical indices used to register periodontal disease that measure the cumulative effects of past disease have overestimated the periodontal disease prevalence in elderly.

Tobacco smoking and general health

The adverse effect of smoking on health is well documented (Doll et al. 1994, D'Agostino et al. 1995, Bartholomew & Knuiman 1998, Iribarren et al. 1999, Peto et al. 2000, Hannan et al. 2000, Sitas et al. 2004, Boyle 2005, McGhee et al. 2005, Ebihara et al. 2005). The over all tobacco smoking worldwide prevalence ranges from 20-30% in Scandinavian countries to 70% in the developing countries (Nordlund et al. 1999, Tessier et al. 1999, Rahman et al. 2005) and is considered the single most important environmental factor contributing to illness, disability and death. Tobacco smoke is a complex mixture of chemicals, many of which may contribute to human disease. Nicotine is one of the chemicals with pharmacological and toxicological negative effects on human health (Hukkanen et al. 2005). The nicotine is on average 8-9 mg in one cigarette tobacco. Smokers absorb 1 mg of nicotine per cigarette that may lead to activation of the sympathetic nervous system, acceleration of heart rate, and increased blood pressure (Benowitz 1997). The mouth acts as a primary target for tobacco smoke, hence positive associations have been shown between smoking and hyperkeratinization, leukodema, leukoplakia, and cancer of oral mucosa (Bastiaan & Reade 1976, Axell & Henriksson 1981, Fisher et al. 2005).

Cigarette smoking plays a major role in the pathogenesis of coronary heart diseases, peripheral vasoconstriction, vascular diseases and renal failure (Woodward et al. 1999, James et al. 2000, Fennessy et al. 2003, Amarenco 2005, Iseki 2005, Zieske et al. 2005).

Furthermore, smoking increases the rate of bone loss in other parts of the skeleton such as the radius, femoral neck, hip, and lumbar spine (Vogel et al. 1997, Krall & Dawson-Hughes 1999, Hannan et al. 2000, Tanaka et al. 2001, Naves et al. 2004). In addition, smoking is observed to induce peripheral vasoconstriction (Fennessy et al. 2003) and oral, pharyngeal and laryngeal cancers (Franceschi et al. 1999).

Water filtered tobacco smoking or water pipe smoking (known as hubble-bubble, nargila, argila, hookah, or sheesha, Fig. 1) is attributable to old traditions. A sharp rise in the popularity of the water pipe smoking has been noted in recent years among men and women in the South Asia, the Middle East and North Africa. The water pipe smoking prevalence ranged from 20% to 40% of sampled populations (Shihadeh et al. 2004). Water pipe smoking is commonly viewed as healthy compared to cigarette smoking among young smokers.

The harmful health effects of water pipe smoking are marked in increased blood carboxyhemoglobin levels, reduced ventilatory capacity, and increased risk of developing obstructive airway disease (Zahran et al.1985, Al-Fayez et al.1988, Kiter et al.2000). Lip cancer and coronary heart diseases have been associated with water pipe smoking (El-Hakim & Uthman 1999, Radwan et al. 2003). Unlike popular belief, water pipe smoke has the same harmful components as found in cigarette smoke (Shihadeh 2003). The tobacco used for water pipe smoking contains 2-4% nicotine (Kiter et al. 2000). A special device is needed for water pipe smoking and the tobacco is burnt using a piece of charcoal. The produced smoke passes a long tube and through a water trap at the base of the device that is meant to act as a filter and reduce nicotine inhalation.

Tobacco smoking and periodontal health

Smoking has been proven to be an important risk factor in the prevalence and progression of periodontal disease (Preber et al. 1980, Bergström & Flodérus-Myrhed 1983, Feldman et al. 1983, Ismail et al. 1983, Bolin et al. 1993, Bergström 2003, 2004). The negative impact of smoking appears as anti-inflammatory and anti-haemorrhagic effect, increased pocket depth and/or pocket frequency, increased attachment loss and higher rates of tooth loss. The precise mechanisms of action of tobacco smoke on the periodontal tissue are not well understood but it seems highly likely that the periodontal bone is one of the most susceptible tissues and that smoking has a specific effect on the bony component of the periodontal tissue support. The evidence of the role of smoking in periodontal bone

destruction is provided by retrospective and prospective studies that showed a significant effect on the periodontal bone seen by horizontal (Bergström & Flodérus-Myrhed 1983, Bergström & Eliasson 1987b, Feldman et al. 1987, Bolin et al. 1993, Grossi et al. 1995, Machtei et al. 1997, Norderyd & Hugoson 1998, Krall et al. 1999, Norderyd et al. 1999, Bergström et al. 2000a,b, Payne et al. 2000, Jansson & Lavstedt 2002) and vertical patterns of bone loss (Persson et al. 1998a).

The noxious effect of smoking has been shown to be dose dependent implicating that the morbidity rate of the periodontal structures increase with increasing exposure to smoking, i.e., the greater the daily consumption and/or the longer the duration of the smoking habit, the greater the severity of the disease. The lower level of periodontal disease in former smokers compared to current smokers is the strongest available evidence that smoking may cause the disease (Bergström 2004).

In this thesis an effort has been made to evaluate and explain the current understanding and some basic concepts regarding the factors that may place an individual at increased risk for vertical bone loss. A key question arises as to whether or not tobacco smoking can be considered a risk factor for vertical bone loss.



Fig. 1. Water pipe (Sheesha, Argila).

AIMS

General aim

The general objective of this thesis was to investigate the relationship between tobacco smoking and vertical periodontal bone loss cross-sectionally and longitudinally.

Specific aims

- To investigate the prevalence and severity of vertical bone defects in a Swedish population consisting of dentally aware individuals (Study I).
- To investigate the association between cigarette smoking and the prevalence and severity of vertical bone defects in a Swedish population (Study II).
- To investigate the association between various tobacco smoking habits particularly water pipe smoking and the prevalence and severity of vertical bone defects in a Saudi Arabian population (Study III).
- To investigate the long-term influence of cigarette smoking on vertical bone loss in a prospective study over 10 years (Study IV).

MATERIAL AND METHODS

Study populations

This thesis work is based on Swedish and Saudi Arabian study populations.

Swedish study population (Studies I, II, and IV)

The Swedish populations were derived from full-time musicians in the following Stockholm orchestras: The Royal Orchestra ($n = 107$), The Swedish Radio Symphony Orchestra ($n = 103$), and The Stockholm Philharmonic Orchestra ($n = 98$).

In 1982, the investigation was carried out at the School of Dentistry, Stockholm, between January 1982 and February 1983. All 308 musicians were invited, and a total of 250 (212 men and 38 women) appeared for examination. Of the 58 individuals who did not appear for examination, 28 could be reached by telephone but did not want to take part because their own dentists had recently examined them. By further contact with the dentists in question, available clinical and radiographic data were reviewed. These data were not included in the study but there seemed to be little evidence of any crucial differences between these individuals and those taking part. The other 30 individuals could not be reached or did not allow further inspection of their dental records.

In 1992, the professional musicians from the above cited orchestras were invited for investigation, and 258 (192 men and 66 women) in the age range 20-70 years took part. The majority had not taken part in the 1982 investigation, but 101 individuals (40%) were participating both in 1982 and 1992 (Fig. 2, Table 1). The mean (SD) age was 43.2 (11.2) years in 1982 and 42.3 (12.1) years in 1992. Participants of this population were considered “dentally aware” in 1982 owing to the findings that the vast majority (94%) visited a dentist on a regular basis and 87% brushed their teeth twice daily (Bergström & Eliasson 1985).

Table 1. Characteristics of the study populations.

	Study I	Study II	Study III	Study IV
Participants (<i>n</i>)				
1982	251	249	355	101
1992	247	229		101
Male (%)				
1982	86	86	71	89
1992	76	76		
Female (%)				
1982	14	14	29	11
1992	24	24		
Age (year)				
1982	43.2	43.2	36.9	51.0
1992	42.3	42.3		61.1
Remaining teeth (Mean)				
1982	26.4	26.4	26.4	26.7
1992	27.1	27.1		25.8
Plaque index (Mean)				
1982	0.9	0.9	1.2	1.1
1992	0.8	0.8		0.8
Gingival index (Mean)				
1982	1.24	1.24	0.9	1.31
1992	1.13	1.13		1.28

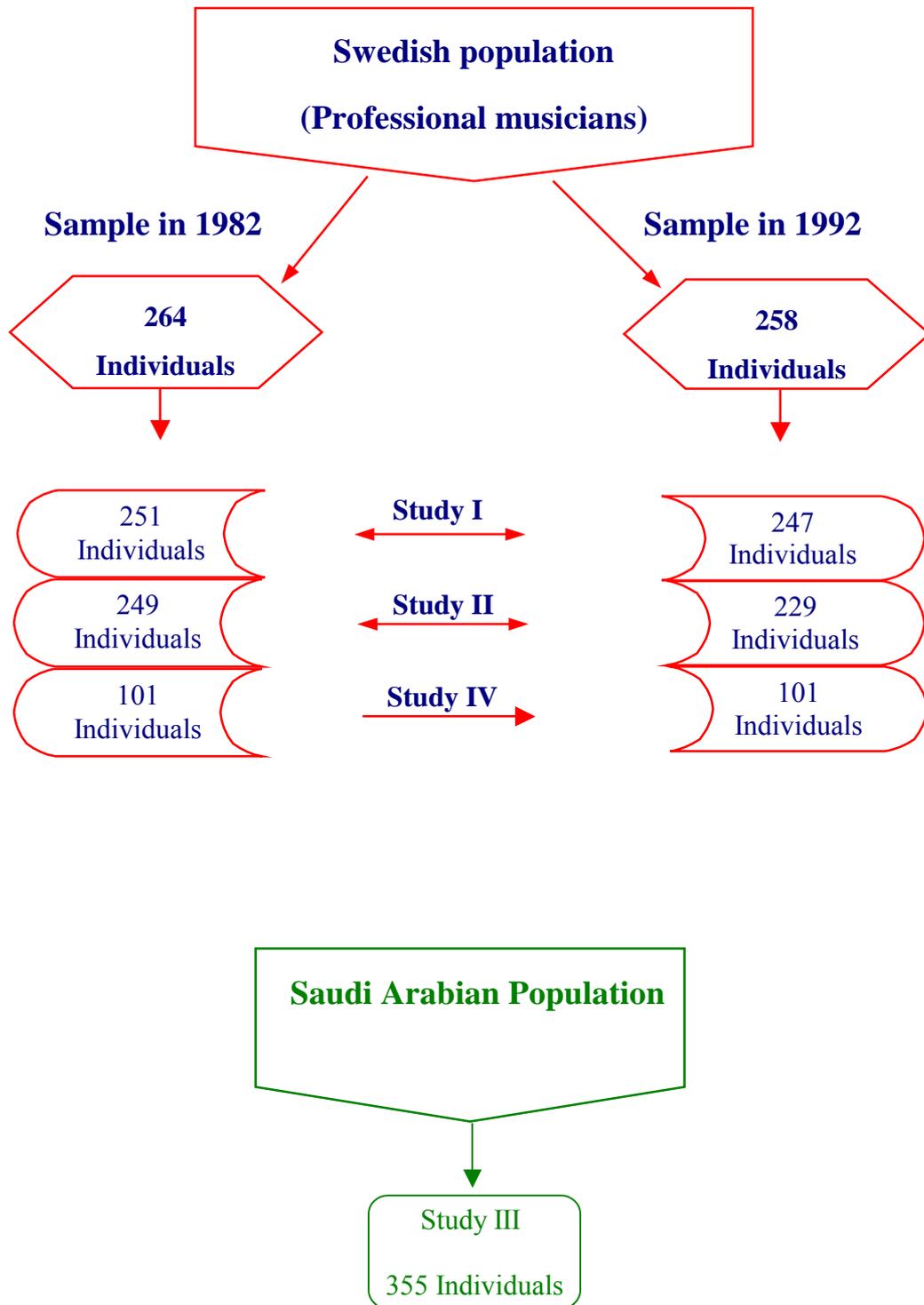


Fig 2. The stratification of the study populations in Studies I-IV.

Saudi Arabian study population (Study III)

Saudi residents in Jeddah city, Saudi Arabia were invited to participate in the study by means of announcements in newspapers. To be included potential participants were required to exhibit a minimum of 20 teeth and not being pregnant. Out of 355 individuals who fulfilled the inclusion criteria, responded to a standardized questionnaire, and had full-mouth radiographic examination, 262 (74%) also volunteered for clinical examination (Table 1). The radiographic and clinical examinations were carried out at King Faisal Specialty Hospital and Research Center, Jeddah, Saudi Arabia.

The mean (95% CI) age was 36.9 (36.8; 37.9) years. There was an overall significant association between smoking habit and age ($F = 5.9$, $p < 0.001$). The age of mixed smokers was significantly lower than that of water pipe smokers, cigarette smokers, and non-smokers ($p < 0.05$).

Studies I, II, and IV were approved by the local ethics committee of Karolinska Institutet, Stockholm in accordance with the Helsinki Declaration of 1975 and as revised in 1983. The study III was approved by the local ethics committee of King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia, in accordance with the Helsinki Declaration of 1975 and as revised in 1983.

Questionnaire

For both study populations the total examination included collection of interview data, recording of clinical variables, and a full-mouth radiographic survey. Each participant was interviewed at the time of the clinical examination. The questionnaire included questions about dental care habits, oral hygiene habits, education levels, and smoking habits.

For the Swedish population, information regarding dental care visits and oral hygiene were obtained in accordance with a predetermined questionnaire (Bergström & Eliasson 1985). For the Saudi population, oral hygiene habits were shown by three questions concerning the frequency of tooth brushing, and dental care habits were revealed by the participant's stated reason for visiting the dentist (Natto et al. 2004). In addition, formal education status was classified on a five-point scale according to the school system in Saudi Arabia.

Tobacco smoking

Based on self-reports in Study II, subjects were classified as current smokers who were smokers at time of investigation (33% and 21% in 1982 and 1992, respectively), former

smokers who had quit smoking already before the commencement of the investigation and not taken up smoking again (26% and 25%, respectively), and non-smokers who denied smoking (41% and 54%, respectively). Based on self-reports in Study III, subjects were classified as water pipe smokers (33%), cigarette smokers (20%), smokers of both water pipe and cigarettes (labeled mixed smokers 19%), and non-smokers (28%). Former smokers were excluded ($n = 4$). Study IV included 24 individuals who were smokers in 1982 (baseline) and had continued smoking over the 10-year period (smokers), 24 individuals who had quit smoking already before the commencement of the baseline investigation and not taken up smoking again (former smokers), and 43 individuals who denied smoking both at baseline and follow-up (non-smokers, Table 2).

Tobacco smoking exposure

In Studies II - IV, the smoking exposure was expressed in terms of consumption, i.e., the number of cigarettes or water pipe runs consumed per day, duration, i.e., the number of years of smoking, and lifetime exposure, i.e., the accumulated exposure over time as formed by the product of daily consumption and years of duration (“cigarette-years” or “run-years”). In the Swedish population (Study II), the mean (SD) cigarette consumption of current and former smokers was 13.2 (7.3) cig/day and 18.0 (10.0) cig/day, respectively, in 1982 and 13.3 (7.5) cig/day and 15.1 (8.6) cig/day, respectively, in 1992. The mean (SD) smoking duration of current and former smokers was 20.8 (11.3) years and 16.0 (9.9) years, respectively, in 1982 and 20.4 (12.8) years and 13.0 (9.2) years, respectively, in 1992. The mean (SD) time since quitting smoking among former smokers was 12.6 (9.6) years in 1982 and 12.5 (9.0) years in 1992.

In the Saudi Arabian population (Study III), the mean (95% CI) consumption for cigarette smokers and water pipe smokers was 15.9 (14.7; 17.2) cig/day and 2.8 (2.1; 3.1) run/day, respectively, where a run is the completion of the water pipe smoking until the tobacco is burnt. The mean (95% CI) duration for cigarette smokers and water pipe smokers was 12.8 (11.2; 14.3) years and 11.5 (10.1; 13.0) years, respectively. The mean (95% CI) life-time exposure for cigarette smokers and water pipe smokers was 230.4 (193.4; 267.5) cigarette-years and 56.8 (48.0; 65.6) run-years, respectively. The mean (95% CI) consumption for mixed smokers was 12.1 (10.4; 14.6) cig/day and 1.5 (1.1; 1.9) run/day. The mean (95% CI) duration for mixed smokers was 11.8 (10.1; 13.4) years. The mean (95% CI) life-time

exposure for mixed smokers was 174.0 (141.0; 206.9) cigarette-years and 23.8 (17.9; 29.5) run-years (**Table 2**).

Table. 2 Smoking characteristics of the study populations

	Study II	Study III	Study IV
Cigarette smokers (<i>n</i>)			
1982	81	72	24
1992	48		
Water pipe smokers (<i>n</i>)	✘	117	✘
Mixed smokers (<i>n</i>)	✘	67	✘
Former smokers (<i>n</i>)			
1982	65	✘	24
1992	57		
Non-smokers (<i>n</i>)			
1982	103	99	43
1992	124		
Consumption			
cigarette smokers (cig/day)			
1982	13.2	15.9	13.9
1992	13.3		13.6
water pipe smokers (run/day)	✘	2.8	✘
mixed smokers			
(cig/day)	✘	12.1	✘
(run/day)		1.5	
Duration			
cigarette smokers (years)			
1982	20.8	12.8	19.9
1992	20.4		27.9
water pipe smokers (years)	✘	11.5	✘
mixed smokers (years)	✘	11.8	✘
Life-time exposure			
cigarette smokers (cig-yr)			
1982	321.5	230	297.9
1992	288.9		424.9
water pipe smokers (run-yr)	✘	56.8	✘
mixed smokers			
(cig-yr)	✘	174.0	✘
(run-yr)		23.8	
former smokers (cig-yr)			
1982	299.4		227.5
1992	232.2	✘	✘

Clinical conditions

The inflammatory condition of the gingiva was evaluated according to the gingival index method of Løe & Silness (1963) and supragingival dental plaque was scored following the plaque index system of Silness & Løe (1964). The depth of the sulci or pockets was probed to the nearest 1mm level at 4 sites (buccal, mesial, distal, lingual) around all teeth using a Hilming probe. Probing depths of 4 mm or more were recorded in mm whereas sites with a probing depth below 4 mm were set to 2 mm. For each individual a mean probing depth value was computed based on all available sites.

The overall mean (SD) Silness & Løe plaque index was 0.86 (0.38) in 1982, 0.76 (0.36) in 1992 in the Swedish population, and 1.2 (0.17) in the Saudi Arabian population. The overall mean (SD) Løe & Silness gingival index was 1.2 (0.03) in 1982, 1.1 (0.04) in 1992 in the Swedish population, and 0.9 (0.07) in the Saudi Arabian population. The mean (95% CI) number of remaining teeth in the Swedish population was 26.4 (24.8; 26.9) and 27.1 (26.8; 27.5) in 1982 and 1992, respectively (Bergström & Eliasson 1985). The mean (95% CI) number of remaining teeth in the Saudi Arabian population was 26.4 (26.1; 26.7), (Table 1, Natto et al. 2004).

Radiographic assessment

The radiographic examinations of the Swedish population in Studies I, II, and IV were performed at the Department of Oral Radiology, Institute of Odontology, Karolinska Institutet, Stockholm by specially trained assistants (Bergström & Eliasson 1986). The radiographic examination of the Saudi Arabian population in Study III was performed at the Department of Dentistry, King Faisal Specialist Hospital and Research Center, Jeddah. A full set of intraoral radiographs including 16 periapical and 4 bitewing projections was available for each individual. The modified parallel long distance technique was used. The film was placed in a film holder as parallel as possible to the long axis of the teeth. The X-ray machines used operating at 65-70 kVp, were equipped with a rectangular tube giving at least 0.20 m target-to-skin distance. Kodak Ekta Speed film (speed group E) was used. The radiographic assessment was done with the aid of a Mattsson viewer that gives 2 times magnification and a light table with good illumination. A vertical bone defect was defined as a one-sided bone resorption of the interdental marginal bone ≥ 2 mm that had a typical angulation towards either the mesial or distal aspect of the root. In addition the

lamina dura of the affected tooth showed widening (Goaz & White 1994, Carranza 2002), (Fig. 3). All teeth except third molars were assessed as to the presence or absence of a vertical defect. However, if a first or second molar was missing the third molar of the same quadrant was included. Two observers (M.B and S.N) independently assessed all radiographs at the Department of Oral Radiology, Institute of Odontology, Karolinska Institutet, Stockholm. In the event of disagreement between the examiners the final decision was taken after a consensus of all authors. The prevalence of vertical bone loss was estimated from the proportion of individuals exhibiting one or more vertical defects. In Study IV, the 10-year cumulative incidence was estimated from the proportion of individuals who became affected over time. The term severity of vertical bone loss was used to describe the frequency of sites with a vertical defect in relation to the frequency of sites measured in the individual. The severity was expressed as number or % per person. Radiographic assessments were performed blinded with reference to the smoking status of the individual. Furthermore, for the purpose of Study IV, the radiographic data from baseline and 10-year follow-up were assessed independently.

In Studies I, II, and IV the interdental bone height was measured from the same set of intraoral radiographs. The bone height was measured mesially and distally to all teeth and expressed as % of the root length. For single-rooted teeth the length of the root was defined as the mean of the mesial and distal distances from the cemento-enamel junction to the dental apex. In multi-rooted teeth the root length was defined as the distance from the cemento-enamel junction to the apex and determined on the distal aspect of the distal root and on the mesial aspect of the mesial root. The height of the alveolar bone was determined as the distance from the apex to a point where the lamina dura become continuous with the compact bone of the interdental septum. If the periodontal space was widened, the height was determined at the level where the width of the periodontal space did not exceed 1 mm. When no dental or bony landmark could be identified, owing, for example, to restoration or overhanging, the tooth was excluded (Bergström & Eliasson 1986).

Error of radiographic measurements

In Studies I and II, the reproducibility of the method was estimated following the principle of repeated measurements resulting in an estimate of the precision of the method. The precision (s) was expressed as the standard deviation of a single measurement as found from the relation

$$s = \sqrt{\Sigma d^2 / 2n}$$

where d denotes the difference between replicates and n the number of the differences. The reproducibility was evaluated in a sub-sample of 73 individuals of the 1982 sample and 69 individuals of the 1992 sample. The precision was $s = 0.3$ and $s = 0.6$ for the 1982 and 1992 sample, respectively. The error pertaining to the mean was $s_{\text{mean}} = 0.02$ and 0.04 in 1982 and 1992, respectively. It is concluded that the influence the intra-observer variation on group means of the vertical defects per person is negligible.

In Studies III and IV, the interexaminer reliability with respect to vertical bone defects measurements was estimated from 100 and 30 randomly selected individuals (representing 5200 and 1584 sites, respectively) using Cohen's kappa statistic (κ) according to the formula

$$\kappa = \frac{A_o - A_c}{1 - A_c},$$

where A_o is the proportion of agreements that was actually observed and A_c the proportion of agreements that could be expected by chance (Cohen 1960). The interexaminer reliability found was $\kappa = 0.89$ and 0.93 , respectively, indicating "perfect" agreement (Landis & Koch 1977). It is concluded that the error related to interexaminer variability of assessments did not substantially influence the outcome.

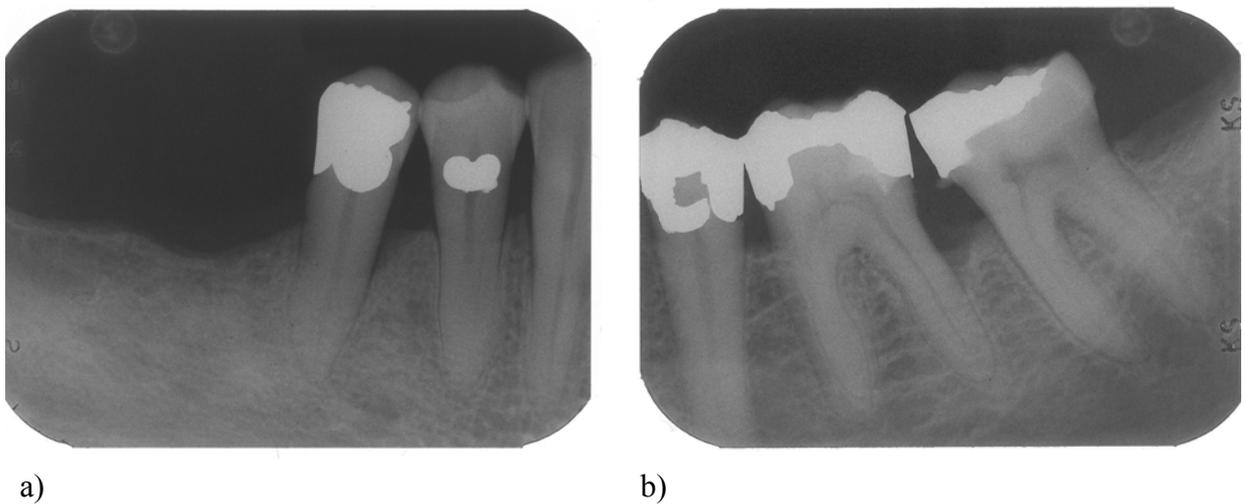


Fig. 3. The vertical defects a) at mesial side of tooth 45; b) at distal side of tooth 36.

Statistical analysis

The number or proportion of proximal sites with vertical defects per person was presented as means and standard deviation (SD) or 95% confidence intervals (CIs). This variable was non-normally distributed and, therefore, primarily tested with non-parametric methods (Chi-square and Kruskal-Wallis ANOVA). Furthermore, the 10-year differences in the number of teeth and proportion of vertical defects were non-normally distributed and, therefore, tested with Friedman ANOVA (Study IV). Additional statistical analysis was performed by means of 1-, and 2-factor ANOVA, or 2-factor repeated measures ANOVA (Study IV), including *post hoc* multiple comparisons testing according to Scheffe. Intra-individual differences between means of various regions of the dentition were tested with the Wilcoxon test of matched pairs (Study I).

Multiple linear regression analysis was run with the proportion of vertical defects in Studies II and III and with the 10-year difference in the proportion of vertical defects as the dependent variable in Study IV. Smoking was transformed into dummy variables including current smoking (current smokers vs non-smokers and former smokers) and former smoking (former smokers vs non-smokers and current smokers) in Studies II and IV. In Study III, a dummy variable including water pipe smokers, cigarette smokers, and mixed smokers versus non-smokers was applied.

Logistic regression was used to estimate the relative risk expressed as odds ratio and 95% confidence interval (OR and 95% CI). The proportion of vertical defects was used as the dependent variable, dichotomized ($> 0 = 1$, else = 0) in Studies II and III. In Study IV, the 10-year difference in the proportion of vertical defects was used as the dependent variable, dichotomized ($> 1 = 1$, else = 0). The individual was the statistical unit in the analyses and statistical significance was accepted at $p < 0.05$. The data were analyzed using the STATISTICA (6.0) program.

RESULTS

I) Cross-sectional observations

Distribution of vertical defects within the dentition

The distribution of vertical defects within the dentition had a typically symmetrical appearance. The mean proportions of vertical defects per person according to tooth type and site (maxilla and mandible) in the Swedish 1982 and 1992 population are shown in Figs 4 and 5, respectively. The mean (SD) proportion of vertical defects per person was 1.8% (4.2%) and 2.4% (5.9%) in the maxilla and mandible, respectively, in 1982 and 1.6% (4.5%) and 1.7% (4.5%), respectively, in 1992. The difference was not statistically significant neither in 1982 nor 1992 (Wilcoxon, $Z = 1.6$ and 0.8 , respectively, $p > 0.05$). The mean (SD) proportion of vertical defects per person in the right and left hand sides of the dentition was 2.1% (4.9%) and 2.1% (5.3%), respectively, in 1982 and 1.8% (4.8%) and 1.5% (4.1%), respectively, in 1992. The difference was not statistically significant neither in 1982 nor 1992 (Wilcoxon, $Z = 0.7$ and $Z = 1.1$, respectively, $p > 0.05$).

The mean (SD) proportion of vertical defects per person in the anterior and posterior regions of the dentition was 0.16 (0.61) and 0.72 (1.31), respectively, in the Swedish population in 1982, and 0.12 (0.47) and 0.64 (1.51), respectively, in 1992. Expressed as % the means (SD) of the anterior and posterior regions were 0.8% (3.4%) and 3.4% (7.3%), respectively, in 1982 and 0.6% (2.3%) and 2.7% (7.0%), respectively, in 1992. Irrespective of mode of expression the difference between the anterior and posterior regions was statistically significant in both 1982 and 1992 populations (Wilcoxon, $Z = 6.6 - 6.9$ and $5.8 - 6.0$, respectively, $p < 0.001$).

The same appearance was observed in the Saudi Arabian population suggesting that the proportion of vertical defects was significantly greater in the posterior compared to the anterior regions (Wilcoxon, $Z = 4.1$, $p < 0.001$). However, the difference in the proportion of vertical defects per person was not statistically significant neither between the right and left hand sides of the dentition nor between maxilla and mandible (Wilcoxon, $Z = 1.0$ and $Z = 1.3$, $p > 0.05$).

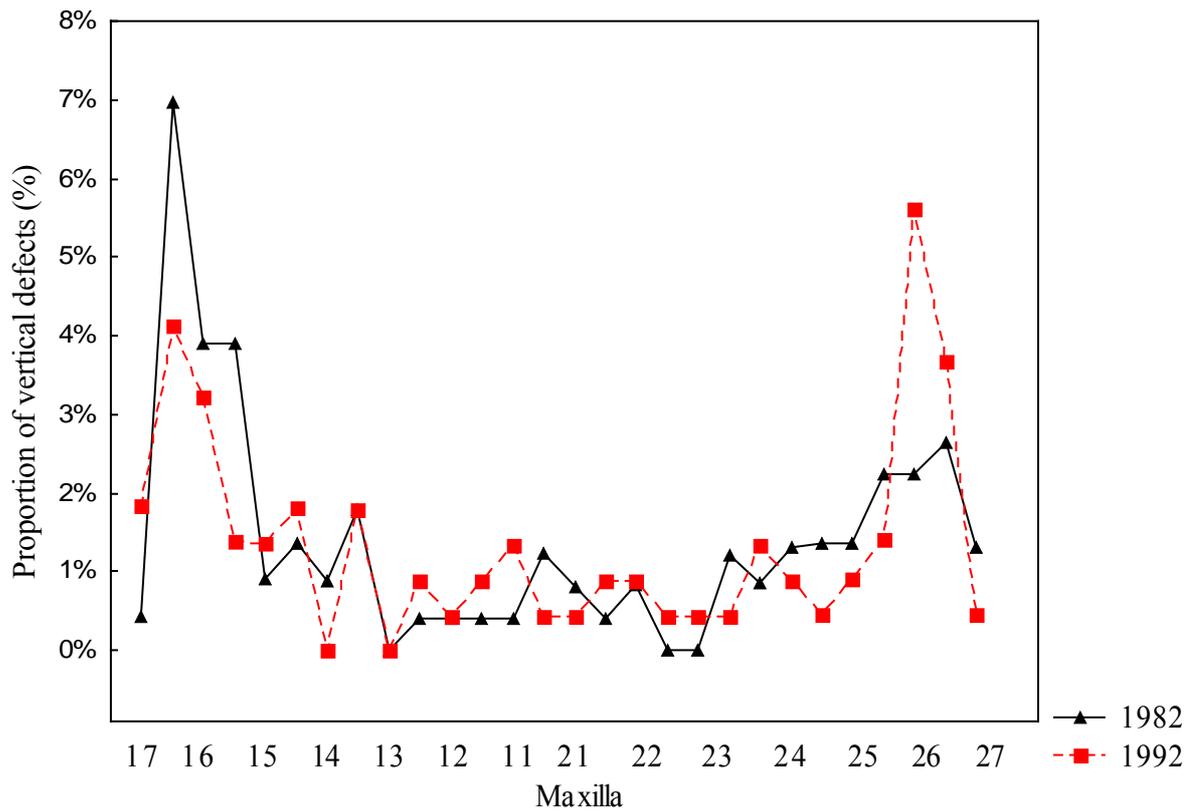


Fig. 4. Proportion of vertical defects per person in the Swedish population in 1982 and 1992 according to tooth and sites in the maxilla

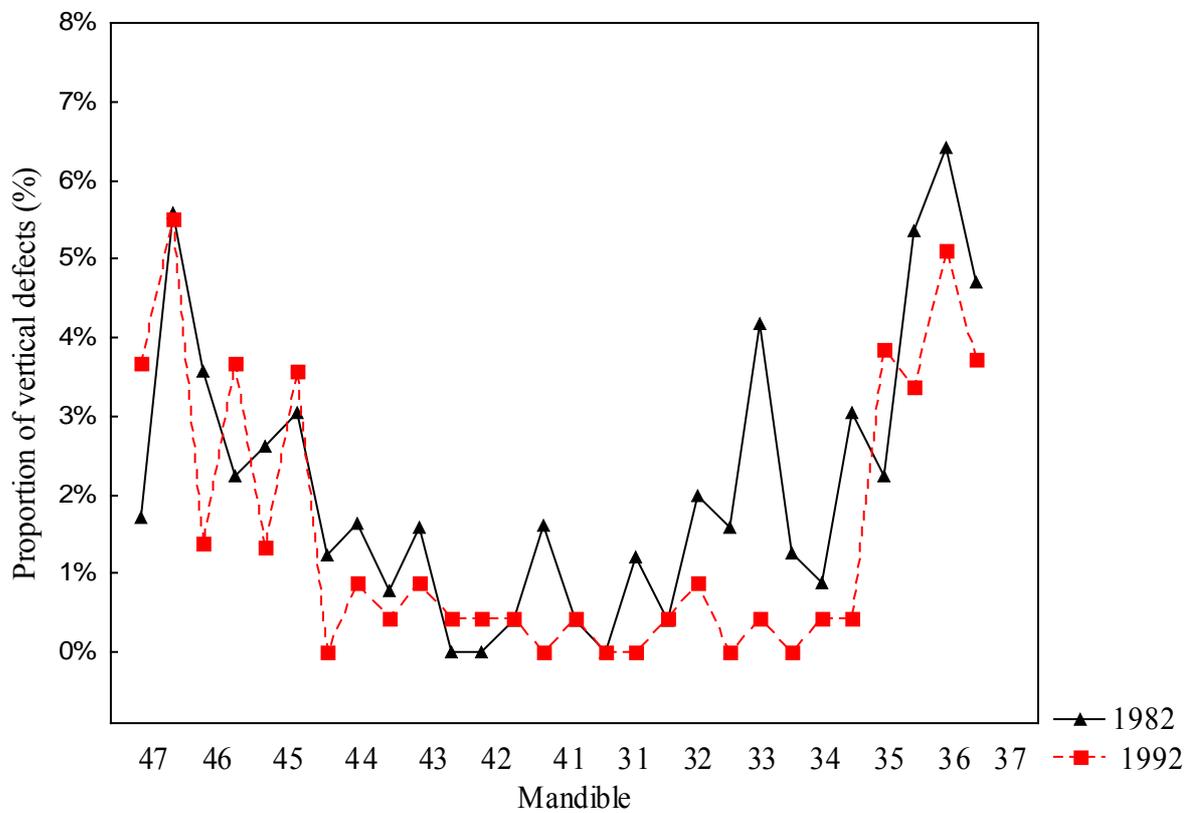


Fig. 5. Proportion of vertical defects per person in the Swedish population in 1982 and 1992 according to tooth and sites in the mandible

Prevalence

a) Age

The overall prevalence of individuals exhibiting one or more vertical defects was 38% in 1982, 27% in 1992 in the Swedish population (Study I), and 39% in the Saudi Arabian population (Study III).

In the Swedish population, the prevalence increased with increasing age from 11% in age group 21-30 years to 64% in age group 51-70 years in 1982 and from 7% to 47%, respectively, in 1992 (Fig. 6). In the Saudi Arabian population, the prevalence increased from 16% in age group 17-30 years to 57% in age group 41-60 years. The increase with age was statistically significant in all three populations ($\chi^2 = 21.7$, $\chi^2 = 18.9$, and $\chi^2 = 41.8$, $p < 0.001$).

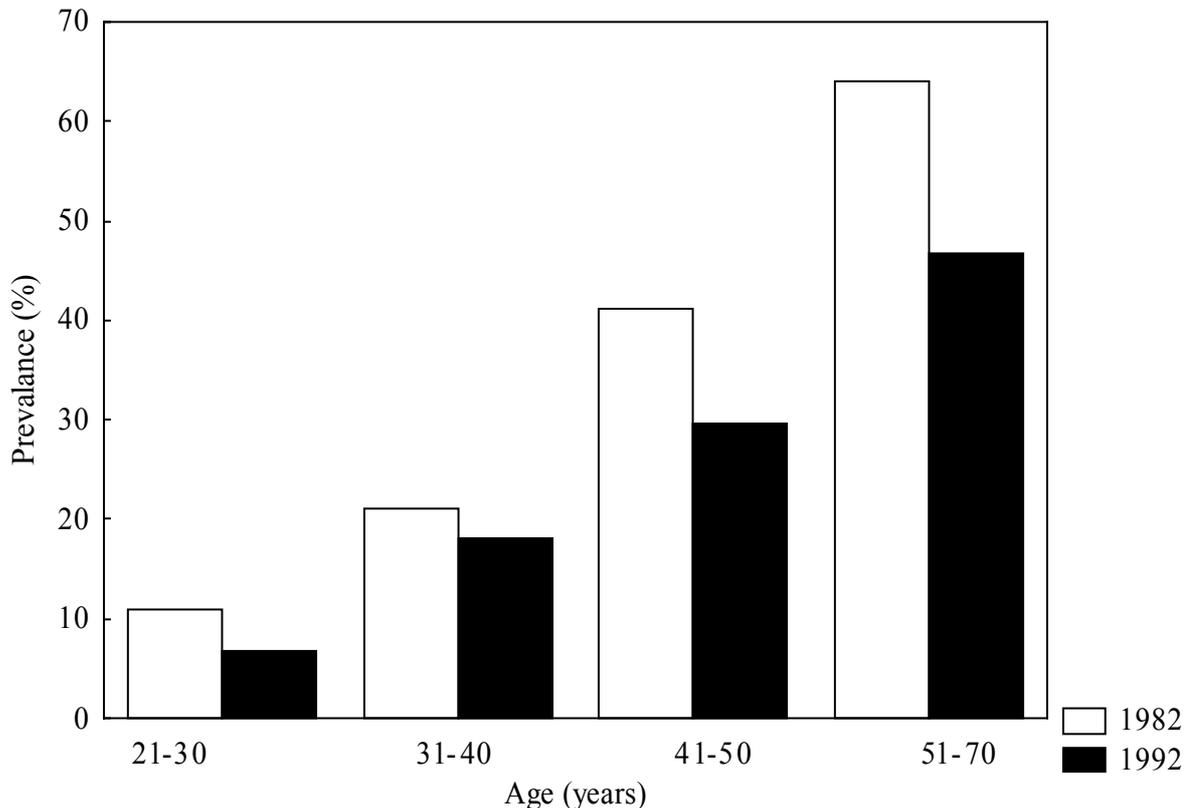


Fig. 6. Age specific prevalence in 1982 and 1992 samples of the Swedish population.

b) Smoking

The smoking specific prevalence of vertical defects in the Swedish population in 1982 was 47% in current smokers, 49% in former smokers, and 24% in non-smokers. In 1992 the prevalence was 42%, 28%, and 19% for current smokers, former smokers, and non-

smokers, respectively (Fig. 7). The smoking specific prevalence in the Saudi Arabian population was 54% in cigarette smokers, 47% in water pipe smokers, and 23% in non-smokers. The prevalence was significantly related to smoking habit in all three study populations ($\chi^2 = 14.4$, $\chi^2 = 9.9$, and $\chi^2 = 21.5$, respectively, $p < 0.001$).

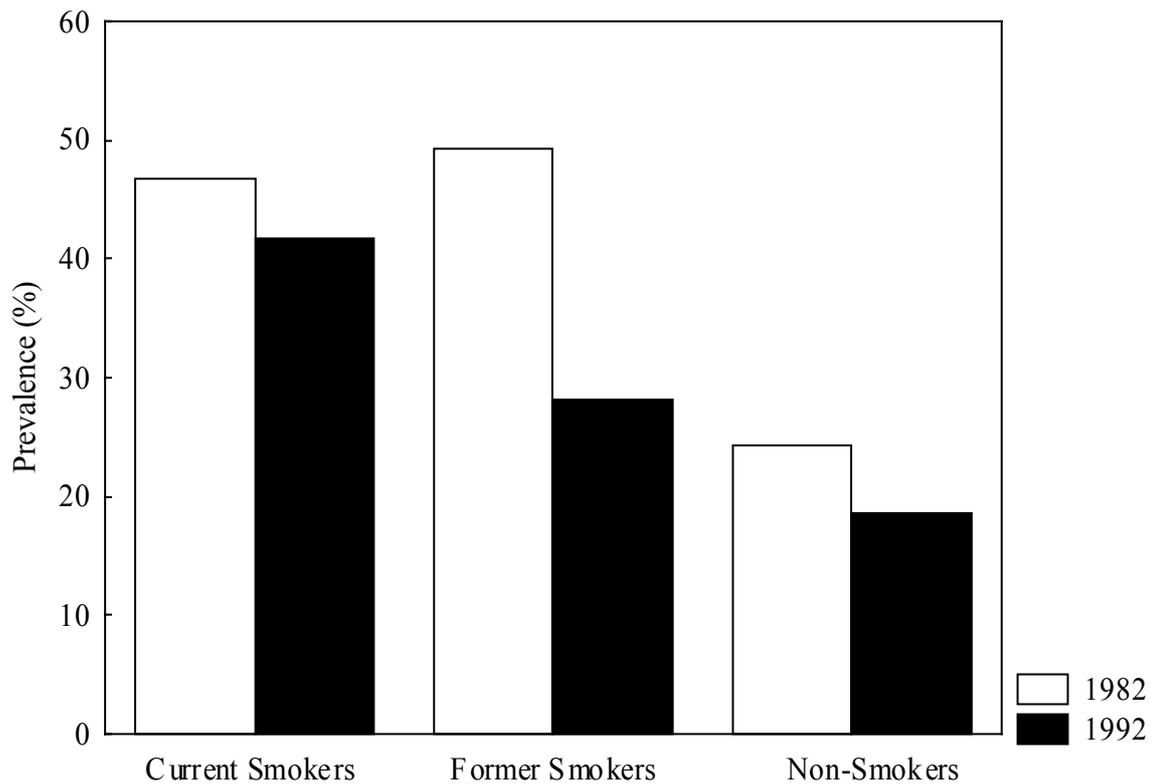


Fig 7. Prevalence of individuals with vertical defects according to smoking habit in the Swedish population of 1982 and 1992.

In study II, the smoking specific prevalence in age stratum 41-70 years was 62%, 56%, and 38% in 1982 and 59%, 40%, and 35% in 1992 for current smokers, former smokers and non-smokers, respectively. The difference between current smokers and non-smokers was statistically significant ($\chi^2 = 4.6$ and $\chi^2 = 3.7$, respectively, $p < 0.05$). In Study III, there was a trend towards a greater prevalence in water pipe smokers, cigarette smokers, and mixed smokers than in non-smokers in all age groups (Fig. 8). The trend was statistically significant in the 17-30 year age group ($\chi^2 = 11.4$, $p < 0.001$).

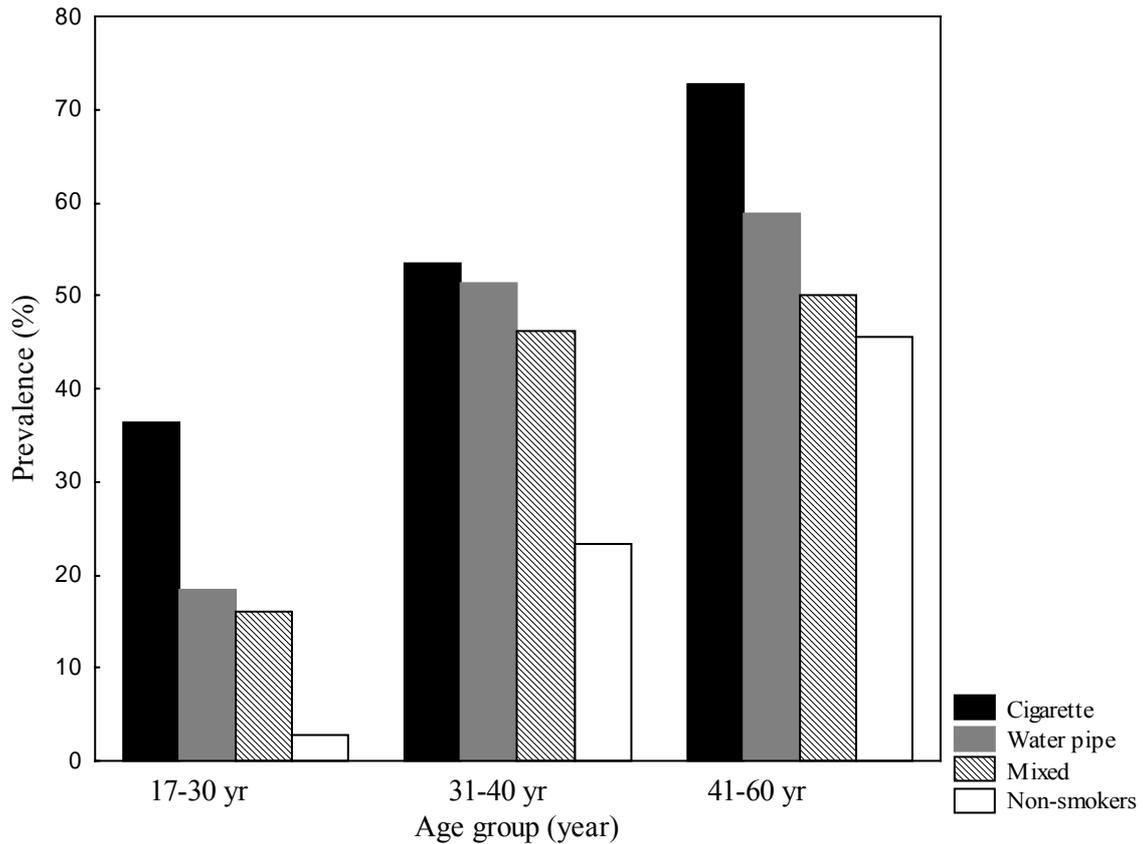


Fig. 8. Prevalence of individuals with vertical defects according to age and smoking habit in the Saudi Arabian population.

Severity

a) Age

In Study I, the overall severity expressed as the mean (SD) number of vertical defects per person in the Swedish population in 1982 and 1992 was 0.88 (1.63) and 0.76 (1.78), respectively, or expressed as the proportion of available sites 4.2% (10.4%) and 3.3% (9.2%), respectively. The difference between the 1982 and 1992 study populations was statistically significant (Mann-Whitney $Z = 2.5$, $p < 0.05$). The mean (SD) number of defects increased with age from 0.11 (0.32) in age group 21-30 years to 1.89 (2.3) in age group 51-70 years in 1982 and from 0.09 (0.37) to 1.61 (2.65), respectively, in 1992. The increase across age groups was statistically significant in both study populations (Kruskal - Wallis $H = 51.3$ and 33.1 , respectively, $p < 0.001$).

In the Saudi Arabian population of Study III, the overall mean (95% CI) severity expressed as the proportion of vertical defects per person was 2.2% (1.7; 2.6); increasing from 0.8% (0.4; 1.2) in age group 17-30 years to 3.9% (2.9; 4.8) in age group 41-60 years.

The increase across age groups was statistically significant (Kruskal-Wallis $H = 44.4$, $p < 0.001$).

b) Smoking

In Study II, the severity of vertical bone loss expressed as the mean (SD) proportion of vertical defects per person was 5.4% (8.9%) for current smokers, 4.3% (6.6%) for former smokers, and 2.2% (6.5%) for non-smokers in 1982 (Fig. 9). In 1992 the corresponding means (SD) were 6.8% (13.0%), 2.3% (5.3%), and 2.2% (6.7%), respectively (Fig. 9). The association between smoking and the proportion of vertical defects controlling for age was statistically significant in both 1982 and 1992 (Kruskal-Wallis $H = 16.9$, $p < 0.001$ and $H = 10.5$, respectively, $p < 0.01$).

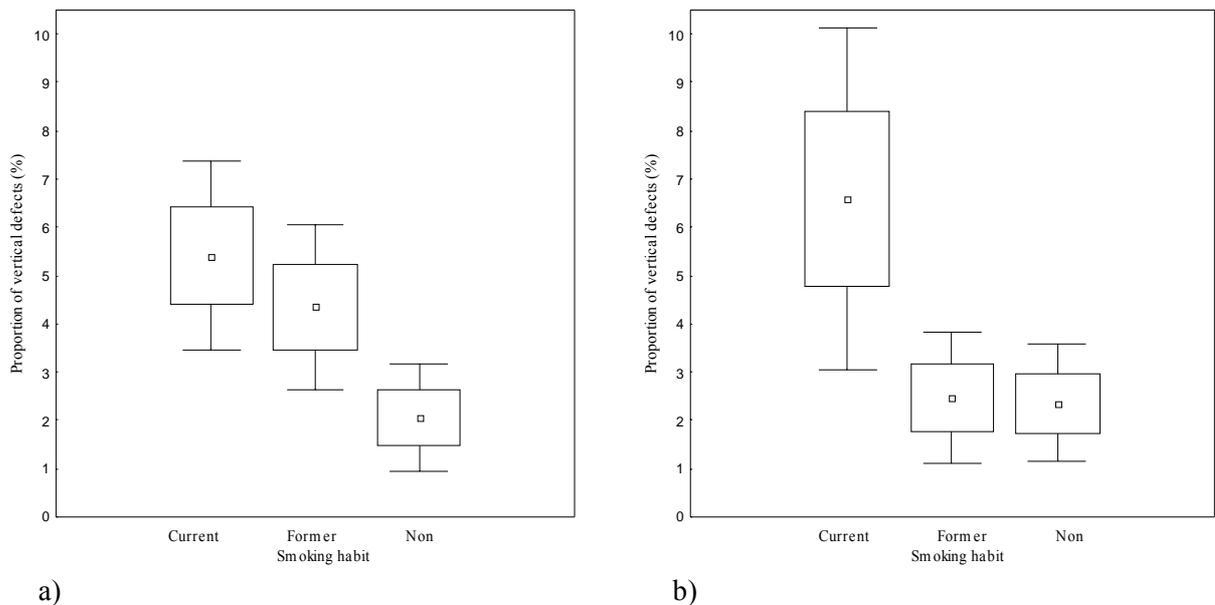


Fig. 9. Proportion of vertical defects per person. Mean and 95% CI according to smoking habit in the Swedish population, a) in 1982, b) in 1992.

In Study III, the mean (95% CI) severity was 2.8% (1.7; 3.8) for cigarette smokers, 2.6% (1.9; 3.3) for water pipe smokers, 1.9% (1.1; 2.8) for mixed smokers, and 1.3% (0.6; 2.0) for non-smokers (Fig. 10). The association between smoking and the proportion of vertical defects was statistically significant (Kruskal-Wallis $H = 19.4$, $p < 0.001$). The significance was attenuated when controlling for age (ANOVA $F(3,2) = 2.4$, $p = 0.065$). *Post hoc* comparisons testing, however, indicated statistically significant differences between water

pipe smokers and non-smokers, and between cigarette smokers and non-smokers ($p = 0.003- 0.014$).

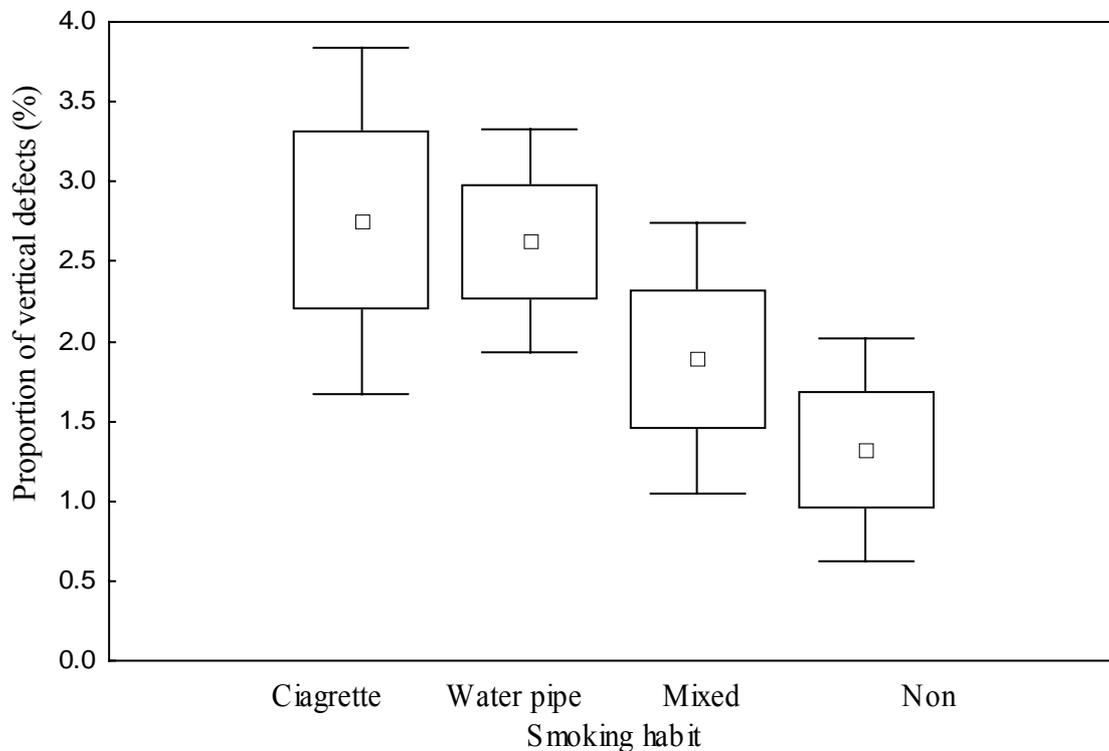


Fig. 10. Proportion of vertical defects per person. Mean and 95% CI according to smoking habit in the Saudi Arabian population.

Smoking exposure

In Study II, in the 1982 Swedish population, the association between life-time smoking exposure and the proportion of vertical defects was statistically significant (Kruskal-Wallis $H = 17.9$, $p < 0.001$). Controlling for age, the association became weaker and significance was lost. *Post hoc* comparisons, however, suggested that there was a significant difference between heavy and light exposure smokers but not between light exposure smokers and non-smokers (Table 3).

Also in the 1992 Swedish population, a statistically significant association between life-time smoking exposure and the proportion of vertical defects was observed (Kruskal-Wallis $H = 12.4$, $p < 0.01$). Controlling for age, the association lost significance. However, *post hoc* comparisons suggested that there was a significant difference between heavy and light exposure smokers (Table 3).

Table 3. Two-Factor ANOVA with the proportion of vertical defects as the dependent variable and life-time smoking exposure as independent variable together with age as co-factor. *Post hoc* tests between smoking exposure group in the Swedish population in 1982 and 1992. Means and 95% confidence intervals (CI)

Exposure	1982		1992	
	Mean	95% CI	Mean	95% CI
Non	1.1	0.4; 1.7	1.5	1.0; 1.9
Light	1.5	1.0; 2.0	1.6	0.8; 2.3
Heavy	3.0	1.4; 4.6	4.3	2.8; 5.8

* $p < 0.05$ *** $p < 0.001$

In the Saudi Arabian population of Study III, the association between life-time smoking exposure and severity of vertical defects was statistically significant within water pipe smokers as well as cigarette smokers (Kruskal-Wallis $H = 92.6$ and $H = 50.8$, respectively, $p < 0.001$). The associations remained significant when controlling for age (ANOVA $F = 21.8$ and $F = 11.4$, respectively, $p < 0.001$). *Post hoc* comparisons testing indicated that the differences between light and heavy exposure smokers were statistically significant among water pipe as well as cigarette smokers (Scheffe test $p < 0.001$, Table 4).

Table 4. Two-factor ANOVA with the proportion of vertical bone defects as the dependent variable and life-time smoking exposure as independent variable together with age as co-factor. *Post hoc* tests between exposure groups in water pipe and cigarette smokers in the Saudi Arabian population. Means and 95% confidence intervals (CI)

Exposure	Water pipe smokers		Cigarette smokers	
	Mean	95% CI	Mean	95% CI
Non	2.6	1.2; 4.1	2.6	1.2; 4.1
Light	0.6	0.2; 0.9	1.3	0.4; 2.2
Heavy	11.3	9.1; 13.5	9.9	5.9; 13.9

*** $p < 0.001$

Multiple regression and risk assessment

The proportion of vertical defects as the dependent variable could be predicted from the variables age, current smoking, former smoking, number of teeth, bone height, number of pockets, gingival index, and dental plaque entered in one block. In the Swedish population in 1982, 40% of the total variation in the dependent variable was explained by these

factors ($R^2 \text{ adj} = 0.40$ $F(7, 228) = 23.0$, $p < 0.001$). Number of teeth, bone height, and number of pockets were the strongest and only statistically significant predictors. When the primary significant factors were excluded from the analysis, age and current smoking became significant ($p < 0.001$ and $p = 0.05$) and the prediction dropped ($R^2 \text{ adj} = 0.16$). Very similar effects were obtained in 1992; once again, number of teeth, bone height and number of pockets were the strongest and only statistically significant predictors ($R^2 \text{ adj} = 0.40$). Current smoking was borderline significant ($p = 0.060$). When the primary significant factors were excluded from the analysis, age and current smoking became significant ($p < 0.001$ and $p < 0.001$) and the prediction dropped ($R^2 \text{ adj} = 0.18$).

In the Saudi Arabian population, 23% of the total variation in the dependent variable was explained by these factors ($R^2 \text{ adj} = 0.23$, $p < 0.001$). Age ($p = 0.006$), smoking ($p = 0.024$), and number of teeth ($p = 0.000$), were the only statistically significant predictors.

Logistic regression analysis was run to estimate the relative risk for the occurrence of vertical defects. In the Swedish population, the relative risk associated with current smoking compared to non-smoking after adjustment for age was 2.0 (95% CI 1.4 – 4.9, $p < 0.05$) in 1982 and 3.4 (95% CI 1.5 – 8.0, $p < 0.01$) in 1992. The age adjusted relative risk associated with former smoking was almost significant in 1982 (OR= 2.0, 95% CI 1.0 – 4.2, $p = 0.053$) but not significant in 1992 (OR= 1.1, 95% CI 0.5 – 2.5, $p > 0.05$).

In the Saudi Arabian population, the relative risk associated with smoking was 3.3-fold increased compared to non-smoking after adjustment for age (OR= 3.3, 95% CI 1.9- 5.8, $p < 0.001$). The risk run by water pipe and cigarette smokers was 3.1-fold and 5.7 elevated, respectively, compared to non-smokers after adjustment for age (OR= 3.1, 95% CI 2.6- 6.5, $p < 0.001$ and OR= 5.7, 95% CI 2.5- 7.1, $p < 0.001$).

II) Longitudinal observations

10-year tooth loss

The possible long-term influence of smoking on vertical defects was prospectively studied over 10 years in a longitudinal cohort of the Swedish population. The mean (95% CI) number of teeth at baseline and 10-year follow-up was 27.0 (26.2; 27.3) and 26.4 (25.9; 26.8), respectively. The difference was statistically significant ($t = 4.9$, $p < 0.001$). The mean (95% CI) frequency of retained teeth at baseline was 27.3 (26.1; 28.0), 26.8 (25.2; 27.9), and 26.9 (24.7; 27.8) for smokers, former smokers, and non-smokers, respectively. The corresponding mean (95% CI) frequencies at follow-up were 26.9 (25.5; 27.3), 25.8 (23.3; 27.3) and 26.3 (23.7; 27.9), respectively. There were no statistically significant differences between smoking groups ($p > 0.05$). The decrease in the number of teeth over the 10 years was statistically significant in all three smoking groups (Friedman ANOVA $\chi^2 = 4.2$, $\chi^2 = 3.7$, and $\chi^2 = 3.1$, respectively, $p < 0.05$). The 10-year decrease was not significantly associated with smoking (repeated measures ANOVA $F = 0.9$, $p > 0.05$).

The mean (95% CI) number of teeth at baseline and 10-year follow-up among 29 individuals who lost teeth to follow-up was 26.0 (23.3; 27.7) and 24.1 (21.7; 26.5), respectively, as against 27.4 (26.3; 27.9) among 62 individuals who did not lose teeth. As further described in Table 5, the 29 loser individuals lost a total of 55 teeth or on average 1.9 teeth per individual. 5 smokers lost 9 teeth affected by 6 vertical defects, 11 former smokers lost 23 teeth affected by 2 vertical defects, and 13 non-smokers lost 23 teeth affected by 7 vertical defects. The mean (95% CI) number of vertical defects at baseline was 1.0 (0.06; 2.6) in individuals who lost teeth over 10 years (2.0, 0.9, and 0.8 in smokers, former smokers, and non-smokers, respectively) compared to 0.3 (0.6; 1.2) in individuals who did not lose any teeth (0.7 in smokers, 0.2 in former smokers, and 0.1 in non-smokers). The difference between loser and non-loser individuals was statistically significant (Kruskal-Wallis $H = 8.1$, $p < 0.01$).

The increase in the number of vertical defects over the 10-year period was greater in non-loser than loser individuals. The increase was 1.5, 2.0, and 1.6-fold, respectively, in smokers, former smokers, and non-smokers who lost teeth to follow-up compared to 3.7, 8.8, and 9.7-fold, respectively, in smokers, former smokers, and non-smokers who did not lose teeth to follow-up (Table 5). Individuals who lost teeth were significantly older ($p <$

0.001) and had an inferior bone height level at baseline ($p < 0.001$). There was an interaction effect of smoking and bone height on lost teeth ($p < 0.05$).

When evaluating the 10-year changes in vertical bone loss only teeth that were present both at baseline and follow-up were considered.

Table 5. Number of teeth and vertical bone defects (VD) at baseline and follow-up and number of teeth lost to follow-up. Means in loser and non-loser Swedish individuals according to smoking habit. n = number of individuals in the Swedish population, N = number of teeth or vertical defects.

Smoking habit	Teeth lost	Teeth at baseline	Teeth at follow-up	Teeth at 10-year loss	VD at baseline	VD at follow-up	VD per tooth at baseline	VD per tooth at follow-up	Relative increase	VD 10-year change
	<i>N</i>	<i>Mean</i>	<i>Mean</i>	<i>Mean</i>	<i>N</i>	<i>N</i>	<i>Mean</i>	<i>Mean</i>		<i>Mean</i>
Smoker										
Loser ($n = 5$)	9	27.4	25.6	1.8	10	14	0.073	0.109	1.5	0.036
Non-loser ($n = 19$)	0	27.2	27.2	0	13	48	0.025	0.093	3.7	0.068
Former smoker										
Loser ($n = 11$)	23	26.0	23.9	2.1	10	18	0.035	0.069	2.0	0.034
Non-loser ($n = 13$)	0	27.5	27.5	0	2	19	0.006	0.053	8.8	0.047
Non-smoker										
Loser ($n = 13$)	23	25.5	23.7	1.8	10	15	0.030	0.049	1.6	0.019
Non-loser ($n = 30$)	0	27.5	27.5	0	3	32	0.004	0.039	9.7	0.035
Total										
Loser ($n = 29$)	55	26.0	24.1	1.9	30	47	0.040	0.067	1.7	0.027
Non-loser ($n = 62$)	0	27.4	27.4	0	18	99	0.011	0.058	5.3	0.047

10-year incidence

Excluding teeth lost to follow-up the prevalence at baseline was 21% (33% in smokers, 25% in former smokers, and 12% in non-smokers). The prevalence at follow-up was 55% (67% in smokers, 55% in former smokers, and 49% in non-smokers). Although the prevalence estimates were throughout greater in smokers, the differences between smoking groups were not statistically significant ($p > 0.05$).

Excluding teeth lost to follow-up, the 10-year cumulative incidence of individuals who became affected by one or more vertical defects was 50% in smokers, 39% in former smokers, and 42% in non-smokers (Table 6). The incidence was not significantly different between smoking groups ($\chi^2 = 1.3$, $p > 0.05$). In addition, the 10-year cumulative incidence was 58% in age group 20-40 years as compared to 29% in age group 41-60 years. The difference between age groups was statistically significant ($\chi^2 = 9.2$, $p < 0.01$).

Table 6. Frequency of individuals with “affected” or without “unaffected” vertical defects at baseline and follow-up, and 10-year cumulative incidence. Estimates according to smoking after exclusion of teeth lost to follow-up in the Swedish population.

Smoking habit	Baseline		Follow-up		10-year incidence
	Non-affected <i>n</i>	Affected <i>n</i>	Non-affected* <i>n</i>	Affected* <i>n</i>	%
Smoker	16	8	8	8	50
Former	18	6	11	7	39
Non	38	5	22	16	42
Total	72	19	41	31	43

* Out of non-affected at baseline

10-year severity change

Excluding teeth lost to follow-up the mean (95% CI) proportion of vertical defects per person at baseline was 1.3% (0.2; 2.4) in smokers, 0.9% (0.0; 1.8) in former smokers, and 0.3% (0.0; 0.6) in non-smokers. The association between smoking and the proportion of vertical defects at baseline was almost statistically significant (Kruskal-Wallis $H = 2.7$, $p = 0.071$). The *post hoc* difference between smokers and non-smokers using 1-factor ANOVA and Scheffe test was statically significant ($p < 0.05$).

The 10-year change in the proportion of vertical defects implied statistically significant increases in all smoking groups (Friedman ANOVA $\chi^2 = 13.0$, $\chi^2 = 12.0$, and $\chi^2 = 22.0$ in smokers, former smokers, non-smokers, respectively, $p < 0.001$). The increase was statistically significantly associated with smoking (repeated measures ANOVA $F = 3.7$, p

< 0.05, Table 7). The *post hoc* difference between smokers and non-smokers was statistically significant (Scheffe test $p < 0.01$). Controlling for baseline condition of vertical defects the significance was attenuated ($F = 3.0$, $p = 0.052$). The *post hoc* difference between smokers and non-smokers, however, remained significant (Scheffe test $p < 0.01$). The same held true controlling for age or plaque level at baseline ($F = 3.0$, $p = 0.053$ and $F = 2.9$, $p = 0.060$, respectively, Scheffe test $p < 0.01$).

Table 7. Proportion (%) of vertical bone defects at baseline and 10-year follow-up. Mean and 95% CI according to smoking in the Swedish population.

Smoking habit	Baseline	Follow-up	F	p
	Mean (95% CI)	Mean (95% CI)		
Smoker	1.3 (0.2; 2.4) *	4.5 (1.8; 7.1) *	3.5	< 0.001
Former	0.9 (0.0; 1.8)	2.9 (1.3; 4.5)	3.2	< 0.01
Non	0.3 (0.0; 0.6)	1.7 (1.0; 2.5)	4.1	< 0.001
Total	0.7 (0.3; 1.1)	2.8 (1.9; 3.6)	3.6	< 0.01

* Significantly different from non-smokers ($p < 0.05$)

The effect of baseline life-time smoking exposure on the 10-year change in the proportion of vertical defects was statistically significant (repeated measures ANOVA $F = 5.6$, $p < 0.001$) with a significant *post hoc* difference between heavy and light exposure smokers (Scheffe test $p < 0.01$) but not between light exposure smokers and non-smokers. The same held true controlling for baseline condition of vertical defects or plaque ($F = 3.5$ and $F = 7.3$, respectively, $p < 0.05$, Scheffe test $p < 0.01$). Controlling for age, the overall significance was lost ($F = 2.4$, $p > 0.05$), but the *post hoc* difference between heavy and light exposure smokers remained significant (Scheffe test $p < 0.01$). The life-time exposure effect became stronger as the analysis was restricted to smokers (repeated measures ANOVA $F = 8.1$, $p < 0.001$, Fig. 11) and disappeared as run in former smokers alone (repeated measures ANOVA $F = 1.7$, $p > 0.05$).

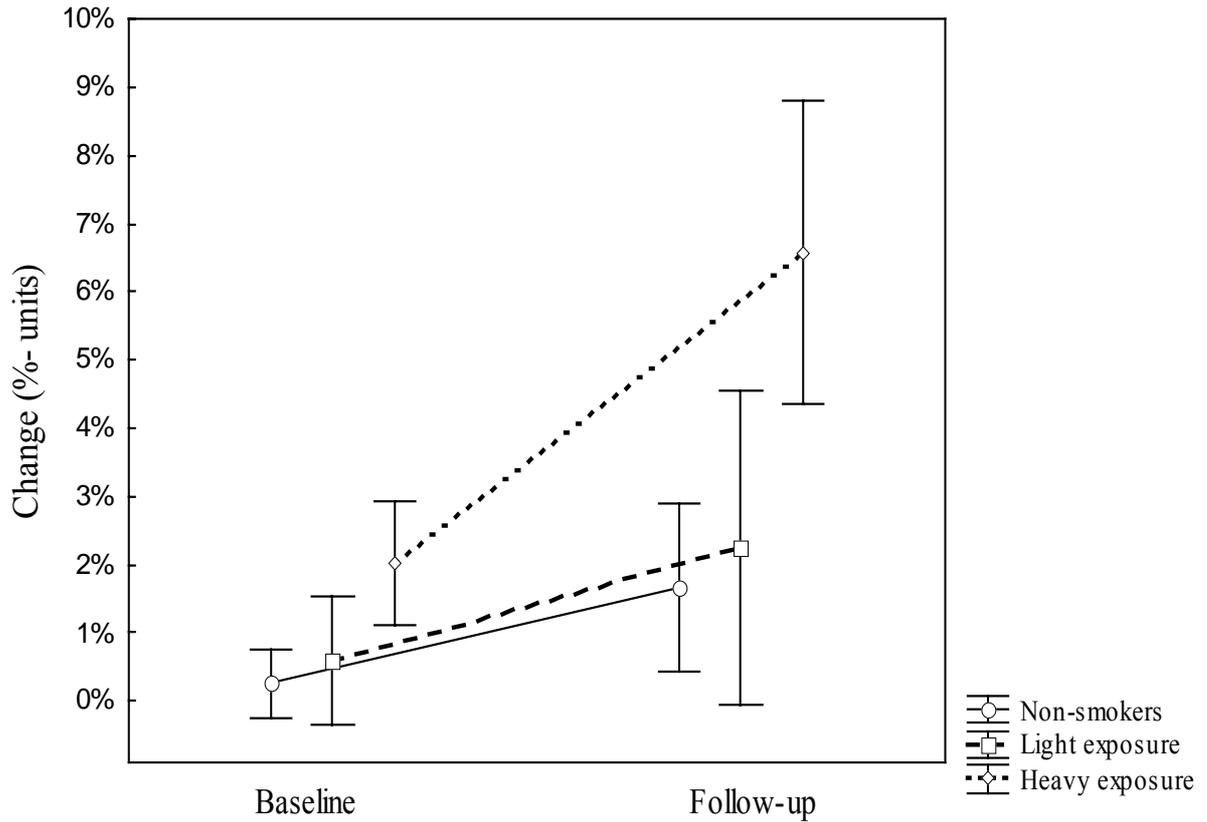


Fig. 11. Ten-year change in proportion (%) of vertical bone defects. Mean and 95% CI in light and heavy life-time exposure smokers and with non-smokers as control in the Swedish population.

Multiple linear regression and risk assessment

Using multiple linear regression, the 10-year change in the proportion of vertical defects as the dependent variable could be predicted from the variables age, life-time exposure at baseline, number of teeth at baseline, bone height at baseline, number of pockets at baseline, gingival index at baseline, and plaque index at baseline as predictors entered in one block. The variables explained 19% of the variance in the dependent variable (R^2 adj = 0.19, $F(7, 84) = 3.5$, $p < 0.01$, Table 8). The strongest predictors were life-time exposure at baseline and number of teeth at baseline. Also in a forward stepwise approach, life-time exposure at baseline and number of teeth at baseline turned out the only significant factors (R^2 adj = 0.20, $F(4, 88) = 6.0$, $p < 0.001$).

Table 8. Multiple regression analysis with 10-year change in the proportion of vertical defects as dependent variable in the Swedish population. Standard model (R^2 adj = 0.19)

Variable	Parameter	Standard error	t	P
Age baseline	0.00034	0.00049	0.80	0.423
Plaque index baseline	0.00007	0.00018	0.60	0.547
Gingival index baseline	-0.00005	0.00013	-0.03	0.969
Bone height baseline	-0.00091	0.00068	-1.37	0.172
Number of pockets baseline	0.00028	0.00023	1.44	0.153
Number of teeth baseline	0.00407	0.00184	2.21	0.029
Life time exposure baseline	0.00005	0.00002	2.67	0.009

The relative risk for 10-year increase in the proportion of more than one vertical defect associated with life-time smoking exposure was estimated from logistic regression analysis. In smokers and former smokers combined, the relative risk was 2.3-fold increased in light exposure smokers and 5.3-fold increased in heavy exposure smokers compared to non-smokers (OR = 2.3, 95% CI 1.1 – 4.9 and OR = 5.3, 95% CI 1.2 – 24.3, $p < 0.05$). Adjustment for age, bone height at baseline, vertical defects at baseline, plaque level at baseline, or number of teeth at baseline did not substantially influence the relative risk estimates. In smokers alone, the age adjusted relative risk of light and heavy smokers was 2.4-fold (OR = 2.4, 95% CI 1.0 – 5.6) and 5.8-fold (OR = 5.8, 95% CI 1.1 – 13.2), respectively, increased compared to non-smokers. The relative risk was not significantly elevated neither in light nor heavy exposure former smokers when compared to non-smokers.

GENERAL DISCUSSION

The overall aim of this thesis was to investigate the relationship between tobacco smoking and vertical bone loss. In order to elucidate this problem two different populations were studied and two kinds of investigational approach, the cross-sectional and longitudinal, were employed.

The overall occurrence of vertical defects in the present populations was a rare event. Out of a total of approximately 14 000-19 000 tooth sites examined, less than 2% exhibited the characteristics of a vertical defect according to the definition used corresponding to a prevalence of 30-40%. It is considerably less than the prevalence observed in patient populations (Papapanou et al. 1988, Papapanou & Wennström 1991) but comparable to the reported prevalence of 32% in a large scale Swedish population study in 1989 (Wouters et al.1989).

A feature common to both populations of the present thesis was the observation that the prevalence increased with increasing age. The increase across age groups was approximately 6-fold in the 1982 Swedish population (11% - 64%), approximately 7-fold (7% - 47%) in 1992 Swedish population, and approximately 4-fold (16% - 57%) in the Saudi Arabian population. This is in general agreement with previous studies suggesting a gradual increase in the vertical defects with increasing age (Nielsen et al. 1980, Wouters et al. 1989, Papapanou et al. 1988). In addition, our findings have demonstrated an association between tobacco smoking and prevalence of vertical bone defects. Cigarette smokers and water pipe smokers exhibited a higher frequency of vertical bone defects than non-smokers.

The distribution of individuals with regard to the frequency of vertical defects was typically skewed to the left, i.e., most individuals were not at all or only slightly affected. Moreover, approximately 60% to 80% of the affected individuals in both populations had a maximum of 2 defects and, as a consequence, a minority only was severely affected. The presently found distribution characteristics resemble those reported by others (Persson et al. 1998a, Wouters et al. 1989).

The severity in terms of mean number of defects per person was on average 1.0 vertical defect per person, or expressed as the proportion of affected sites per person approximately 2-4% in all studied populations. Only one earlier study has elucidated the

severity aspect (Wouters et al. 1989). The severity reported seems to be of the same magnitude as that observed in the present thesis. Moreover, the severity was more pronounced in cigarette smokers and water pipe smokers compared to non-smokers. However, it is notable that former smokers or mixed smokers were less affected than "pure" cigarette smokers or "pure" water pipe smokers. The explanation for this reduced severity in mixed smokers is that the mean age was lower in the mixed smokers group compared to the other smoking groups. The present findings of a significant association between water pipe smoking and periodontal bone loss as diagnosed by an increased number of vertical defects are in general agreement with the results of previous studies with emphasis on cigarette smoking and periodontal bone loss (Bergström & Eliasson 1987a, Persson et al. 1998b, Norderyd et al. 1999, Bergström et al. 2000a,b, Jansson & Lavstedt 2002, Bergström 2004). The impact of other forms of tobacco smoking such as cigar and pipe on the periodontal bone has been studied (Feldman et al. 1983, Krall et al. 1999). According to the study by Krall et al (1999) cigar and pipe smokers were at similar risk of experiencing bone loss as cigarette smokers. The present observations add to the information of these investigations suggesting that water pipe smoking is another form of tobacco consumption that is detrimental to the periodontal bone.

The present thesis suggests that the distribution of vertical defects within the dentition followed a symmetrical right and left hand side pattern. Such a symmetry has also been noted by others (Persson et al. 1998a, Wouters et al. 1989). Moreover, in agreement with an earlier study (Nielsen et al. 1980), the frequency of vertical defects was the same in the mandible and the maxilla, whereas it was significantly greater in the posterior as compared to the anterior region of the dentition. There was a tendency toward a greater frequency of vertical defects at mesial sites as compared to distal sites which is consistent with one earlier study (Wouters et al. 1989) but not with another (Nielsen et al. 1980).

Longitudinal observations

The longitudinal observations of Study IV suggested that vertical bone loss was influenced by smoking, since the 10-year severity increase was significantly greater in smokers compared to non-smokers. The prevalence of vertical bone loss estimated at baseline was 34% before exclusion of teeth lost to follow-up. This was close to the prevalence found in the total 1982 population suggesting that the longitudinal cohort although including only 40% was largely representative of the total population at baseline. The results confirm the

cross-sectional findings of Studies II and III indicating an effect of smoking on vertical bone loss, and, furthermore, agree with long-term studies on smoking and periodontal bone loss in general (Feldman et al. 1987, Bolin et al. 1993, Norderyd et al. 1999, Bergström et al. 2000b, Payne et al. 2000, Jansson & Lavstedt 2002, Bergström 2004).

In spite of a low tooth mortality rate, there was a significant loss of teeth over the 10 years in all three smoking groups. Furthermore, tooth loss influenced the estimation of vertical defects since individuals who lost teeth developed fewer new defects than individuals who did not lose any teeth. Loss of teeth reduces the probability of attracting new vertical defects and at the same time increases the probability of losing existing defects, thus resulting in an underestimation. Although loss of teeth was not significantly different in the smoking groups, the effect of tooth loss on vertical bone loss seemed to be greater in smokers since they were more affected at baseline. For the same reason, the 10-year relative increase in the number of vertical defects in individuals who did not lose teeth was comparably less pronounced in smokers (Table 5). This might have resulted in a comparably greater underestimation in smokers. The effect of tooth loss on estimates of vertical bone loss has to be considered in longitudinal studies.

The present and earlier cross-sectional studies suggest that prevalence as well as severity of vertical bone loss increase with increasing age (Nielsen et al. 1980, Wouters et al. 1989, Persson et al. 1998b). According to the present longitudinal observations the effect of age seemed to be the result of an accumulation of vertical defects over time. This was evidenced by the observations that the 10-year cumulative incidence was relatively greater in young (20-40 yr) compared to old (41-60 yr) individuals. Furthermore, the 10-year severity increase, i.e. the vertical bone loss rate was not dependent of age. This seems to agree with some previous long-term observations suggesting that the bone loss rate is not influenced by age (Bergström 2004).

Tobacco smoking exposure

The association between tobacco smoking and vertical bone loss is exposure dependent suggesting a dose-response relationship. This effect was most evident comparing individuals with heavy and light smoking exposure, whereas the contrast between individuals with light exposure and non-exposed individuals was not evident.

In Study IV, the 10-year increase in vertical periodontal bone loss depended on smoking exposure confirming our earlier cross-sectional observations suggesting that the vertical bone loss was more pronounced in comparably more exposed individuals. The effect of heavy exposure increased the 10-year risk for vertical bone loss by 5 to 6 times compared to non-smokers. Furthermore, the observation that former smokers who had given up smoking in the past exhibited a 10-year progression rate on a par with non-smokers suggests that an exposure abolishment has a beneficial effect. The findings of a dose-response relation agree with earlier cross-sectional (Bergström & Eliasson 1987a, Feldman et al. 1993, Wouters et al. 1993, Grossi et al. 1995, Norderyd & Hugoson 1998) and longitudinal (Feldman et al. 1987, Bolin et al. 1993, Krall et al. 1997, Machtei et al. 1997, Norderyd et al. 1999, Bergström et al. 2000a, Payne et al. 2000, Jansson & Lavstedt 2002) investigations. The observation of an exposure response effect is important since it is commonly accepted that this strengthens the plausibility of a causal relationship between the risk factor and the dependent variable (Hill 1983, Rothman 1986). Although the risk estimates were uncertain as is seen from the comparably large confidence intervals, the magnitude of the estimated risk is reasonable when compared to other studies on smoking associated periodontal bone loss (Norderyd & Hugoson 1998, Norderyd et al. 1999).

In the Swedish population, the results referring to former smokers were less consistent than those referring to current smokers. The former smokers were more similar to current smokers than to non-smokers in the 1982 population but more similar to non-smokers than to current smokers in the 1992 population. This was probably due to the fact that former smokers of the 1982 population were on average older than former smokers of the 1992 population. Moreover, former smokers of the 1982 population had been smoking for a longer duration before quitting than those of the 1992 population.

Multiple regressions and risk assessment

The influence on the severity of vertical bone defects by other factors including age, gender, number of remaining teeth, bone height, probing depth, gingival bleeding and dental plaque was studied by means of multiple regression. The influence of smoking, however, was independent of plaque level, gingival condition, and gender as was evident from the multivariate analyses performed. Age was associated with the prevalence and severity of vertical defects, which was evident in the oldest age group (41-60 years). This finding, in accordance with earlier findings, may not be unexpected due to the cumulative

effect of periodontal bone destruction over time (Nielsen et al. 1980, Papapanou et al. 1988, Wouters et al. 1989, Hugoson & Laurell 2000). Beside age, the proportion of vertical defects was positively correlated with the number of teeth, bone height, and number of pockets. This in agreement with the results of Persson et al (1998b) suggesting a strong correlation between overall periodontal bone loss and frequency of severe vertical defects. It may not be unexpected that the severity of vertical defects is closely correlated with intrinsic factors such as these, since vertical defects are considered the result of bone loss and pocket formation. Excluding these intrinsic factors, the extrinsic factors such as smoking were significantly correlated with the severity of vertical defects. Although intrinsic factors may considerably contribute to the explanation of the statistical model, they may not offer explanatory power about the occurrence of vertical defects from a causal point of view. Smoking as an extrinsic factor, however, might infer a causal effect on the development and occurrence of vertical defects. Interestingly, plaque was not significantly related to the severity of vertical defects neither in the Swedish nor the Saudi Arabian population. This is in agreement with previous observations suggesting that the effect of smoking on the periodontal bone height is independent of plaque infection (Bergström & Eliasson 1991, Bergström et al. 2000a, b). In Study IV, the influence of age, number of pockets, gingival index, and plaque index on the 10-year vertical bone loss was marginal if any as found from the multiple regression analysis. Of the local or “periodontal” factors included in the analyses baseline tooth frequency contributed most to the explanation of vertical bone loss. However, only about 20% of the variation in the dependent variable was explained by the factors studied, and, therefore, uncontrolled confounding might remain from other factors such as trauma from occlusion (Glickman & Smulow 1965) and deficient root cementum (Blomlöf et al. 1987).

The estimated risk for the occurrence of vertical defects was about 2 to 6-fold elevated in tobacco smokers compared to non-smokers suggesting that the impact of smoking on the periodontal bone was within the range of that reported earlier regarding the effect of cigarette smoking on periodontal bone loss (Norderyd & Hugoson 1998, Norderyd et al. 1999, Bergström 2003).

Methodological considerations

The individuals of the Swedish population were professional musicians and they are regarded as dentally aware since they have been shown to exhibit a high standard of oral

hygiene and regular dental care habits (Bergström & Eliasson 1985, Eliasson & Bergström 1997). An advantage of utilizing a Swedish population of dentally aware people for the study of vertical defects is the circumstance that the number of retained teeth in such individuals can be expected to be high. In fact, all individuals had on average more than 26 remaining teeth. This is an important feature of the present study since a high number of retained teeth is a prerequisite for an accurate estimation of the frequency of vertical defects. In previous studies of vertical bone loss the populations studied mostly consisted of patients seeking dental care (Nielsen et al. 1980, Papapanou et al. 1988, Persson et al. 1998a.). It can be assumed that the level of tooth retention is lower in dental care seekers than in a dentally aware population. Only one previous study concerned a random selection of individuals (Wouters et al. 1989). The level of tooth retention, however, was comparably low also in that study, particularly in older age groups. When the number of teeth is low the estimates of the prevalence and particularly the severity of vertical defects become inaccurate and unreliable. In the present study no differences were observed between the smoking groups regarding the number of retained teeth whereas in other studies smokers had a lower number of retained teeth (Holm 1994, Krall et al. 1997, Kerdvongbundit & Wikesjö 2002). The present thesis is the first study to allow estimates of vertical bone defects based on a high level of tooth retention throughout all age groups. In addition, it is the first thesis to investigate the vertical bone loss over time.

The main limitations of this thesis are the gender bias towards a male predominance throughout (Studies I-IV) and the limited sample size of the longitudinal cohort (Study IV). These circumstances together with the fact that the dental awareness was above average may put some restraints on the generalization of the findings. In addition, participation in Study III was limited to individuals who responded to newspaper announcements designed to attract individuals with various smoking habits. This resulted in a higher smoking prevalence than in the Saudi population at large that is estimated to 35% (Siddiqui et al. 2001). A further limitation is the assignment of individuals to different smoking groups on the basis of self-reporting alone which might have resulted in some underreporting. An alternative approach to self-reports that may more accurately estimate the exposure to tobacco is to assess tobacco metabolites such as cotinine, carbon monoxide, or thiocyanate (Dolcini et al. 2003). On the other hand, the self-reported smoking checked by interview questionnaire is considered a valid method that is widely used for recording smoking history (Petitti et al. 1981). Similar estimates of smoking

prevalence have been obtained when self-reports have been compared to salivary cotinine measures (Dolcini et al. 2003).

Although not representative of the Swedish or Saudi population at large, the present populations are considered representative of the middle class, which is a major proportion of the Swedish and the Saudi populations. In addition, the smoking prevalence in the Swedish study populations was 30% and 20%, respectively, which largely corresponds to the Swedish average at the time of examination.

In determining risk, it is of value to examine the relationship between the degree of exposure to the risk factors under study. The ability to demonstrate a dose-response relation strengthens the evidence of risk factor status and the biological plausibility of an interference (Rothman 1986). However, the absence of a dose-response relationship does not necessarily rule out a causal relationship, since a threshold may exist above which disease develops.

The mean consumption of cigarette smokers in the Swedish population was similar in 1982 and 1992 about 13 cig/day, whereas it was 15 cig/day for cigarette and 3 run/day for water pipe smokers in the Saudi population. The mean duration of smoking was almost the same about 20 years in the Swedish population in 1982 and 1992 whereas it was considerably less in the Saudi population, 12 years. The mean life-time exposure of cigarette smokers was about 300 cigarette-years in the Swedish population, whereas somewhat less in the Saudi population, about 230 cigarette-years. However, the mean age was lower by 7 years in the Saudi Arabian population. If it is assumed that one run of water pipe smoking corresponds to the smoking of 4-5 cigarettes, the life-time smoking exposure of water pipe smokers was close to that of cigarette smokers in the Saudi Arabian population.

The mean life-time exposure in the Swedish population in 1982 was about 150 cigarette-years in light and about 500 cigarette-years in heavy smokers, and 90 cigarette-years and 450 cigarette-years in light and heavy smokers, respectively, in 1992. The life-time exposure in the Saudi Arabian population was about 100 cigarette-years and about 300 cigarette-years in light and heavy cigarette smokers, respectively, and about 30 run-years and about 90 run-years in light and heavy water pipe smokers, respectively. One possible reason for the slightly different outcomes in the populations may have been the stratification of exposure variables. The stratification was not based on a *priori* definitions

of “light” and “heavy”, but on the intention to create substrata of approximately the same size.

In all studies, the radiographic examination procedures were similar and performed by experienced personnel. A full set of intraoral radiographs including 16 periapical and 4 bitewing projections was available for each individual. Standardized radiographic and development techniques were ensuring radiographs of a high quality to be assessed. A Mattsson viewer that gives 2 times magnification and a light table with good illumination were used for the radiographic assessment. Exclusion of radiographs due to non-readability was less than 2% in both studied populations. As the number of retained teeth was high, no consideration was made to the unreadable sites in the analysis.

In the present series of studies, a vertical defect was defined as a resorption of the interdental marginal bone of at least 2 mm that had a typical angulation towards either the mesial or distal aspect of the root. No quantitative criteria of defect size or defect depth were applied in the assessment of vertical bone defects. In analogy with previous studies (Nielsen et al. 1980, Papapanou et al. 1988, Wouters et al. 1989) the minimum vertical dimension of the defect was 2 mm. This limitation may have resulted in an underestimation of changes in severity over time. Nevertheless, the definition of defect has important bearings on the prevalence and severity. As shown by Persson et al (1998a) a shift from 1 mm to 3 mm in the vertical dimension will result in a prevalence reduction from 70% to 30%, i.e., by more than 50%. Similarly, the number of defects of a given size is of importance. It can be seen from the present observations that shifting the number of defects required to be labeled “affected” from 1 to 5 will cause a reduction in prevalence in the Swedish population from 38% to 5%, i.e., by almost 90%.

The intra- and the interexaminer reliability were estimated following the principle of repeated measurements resulting in an estimate of the precision of the method. The reproducibility of the method has been shown to be satisfactory for the purpose of the studies and it is concluded that the error related to intra- and interexaminer variability of assessments did not substantially influence the outcome.

Biological mechanisms

The present observations are consistent with ample documentation that smoking increases the rate of bone loss in other parts of the skeleton such as the radius, femoral neck, hip,

and lumbar spine (Vogel et al. 1997, Krall & Dawson-Hughes 1999, Hannan et al. 2000, Tanaka et al. 2001, Naves et al. 2004).

The biological mechanisms responsible for the effect of smoking on the periodontal tissues are still elusive. Several possibilities have been described, and both locally and systemically induced effects have been suggested (Kinane & Chestnutt 2000). Cytotoxic substances such as nicotine and its major metabolic cotinine can be detected in the saliva, gingival cervical fluid, serum, and urine demonstrating their systemic availability (McGuire et al. 1989). It is possible that the effect of nicotine is related to vascular changes, resulting in insufficient vascular supply and indirectly leading to bone tissue breakdown. There is experimental evidence to suggest that nicotine as well as cigarette smoke have detrimental effects on bone cells and osteoprogenitor cells (Liu et al. 2001, 2003, Walker et al. 2001, Akmal et al. 2004, Oda et al. 2004). It is further readily realized that several other agents in cigarette smoke may exert a toxic action on bone cell metabolism causing increasing bone resorption, decreasing bone formation or both. Such an action would lead to an imbalance between build-up and breakdown functions (Oncken et al. 2002).

Based on the present observations it may be argued that exposure to cigarette smoke exerts an effect on the periodontal bone such that the probability of being affected by bone loss, including vertical defects, is elevated in chronic smokers. Since smoking was antecedent to the effect observed in the longitudinal study (Study IV), whereas the abolishment of smoking inhibited the effect, the argument favours the contention that smoking is a cause of periodontal bone loss. Smoking may not be, however, the only cause of such an event, nor necessarily a sufficient one. Most likely, additional factors, usually referred to as component causes (Rothman 1986), are needed to form a sufficient cause that eventually can provoke the effect. This is synonymous to stating that for periodontal bone loss to occur in a smoker, the smoker has to be susceptible. Unfortunately, little is presently known about what makes a susceptible smoker (Kocher et al. 2002). Other sets of component causes may exist that can cause periodontal bone loss. Such sets, however, have not yet been shown to possess the same strength as sets where smoking is a component cause. Findings from previous studies, however, suggest that the presence of angular bone defects is associated with increased risk for further bone loss or even tooth loss (Papapanou et al. 1989, Papapanou & Wennström 1991). Although the likelihood of exhibiting vertical bone defects increases with age it is not fully known whether the

occurrence of single defects signify the onset of disease. On the other hand, it is highly likely that the occurrence of multiple vertical defects is indicative of a disease process.

CONCLUSIONS

On the basis of the results obtained, it is concluded that:

- The present radiographic studies in the populations investigated indicate that the prevalence of vertical defects was in the range 30-40%. Multiple vertical defects, however, were observed in only a minor proportion (Studies I-III).
- There was an association between cigarette smoking and vertical periodontal bone loss. Cigarette smokers consistently exhibited increased levels of prevalence as well as severity of vertical bone defects as compared to non-smokers. The estimated relative risk for vertical bone loss was two to three-fold elevated in smokers (Study II).
- Water pipe smoking was associated with increased levels of prevalence and severity of vertical periodontal bone defects. The association of vertical bone loss with water pipe smoking was comparable to the association with cigarette smoking. The relative risk was 3-fold increased in water pipe smokers (Study III).
- Cigarette smoking had a significant long-term influence on vertical periodontal bone loss (Study IV).

GENERAL CONCLUSION

There is a significant relationship between tobacco smoking and vertical periodontal bone loss. Tobacco smoking should be considered a risk factor for vertical periodontal bone loss.

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