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Prosthodontics, Periodontology, Biology, Research and Systemic Conditions

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ORAL HEALTH CARE – PROSTHODONTICS, PERIODONTOLOGY, BIOLOGY, RESEARCH AND SYSTEMIC CONDITIONS

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Notice

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Meet the editor

Dr. Mandeep Singh Virdi, Bds, MDs, received his graduate and post-graduate dental education at AB Shetty Memorial Institute of Dental Sciences in Mangalore, Karnataka State, India. He received his first degree from the Mangalore University, and his postgraduate degree from Rajiv Gandhi University of Health Sciences, Karnataka. Dr. Virdi is presently the Head of, and Professor of, Pediatric and Preventive Dentistry at PDM Memorial Dental College and Research Institute in Sarai Aurangabad, Bahadurgarh, Haryana, India. He is an active member of the Indian Society of Pediatric and Preventive Dentistry, Indian Dental Association (IDA), and an affiliate member of the American Dental Association, and Vice President of West Delhi IDA.

Contents

Preface

Oral Health Care, commonly referred to as Dentistry, is the branch of medicine that is involved in the study, diagnosis, prevention, and treatment of diseases, disorders, and conditions of the oral cavity, maxillofacial area, and the adjacent and associated structures, and their impact on the human body. Oral Health Care is considered necessary for overall health.

The present work is a companion book of Oral Health Care - Pediatric, Research, Epidemiology and Clinical Practices and is aimed at completing the whole range of Oral Health Care. These books are using the internet, information technology's most potent tool, for its storage, retrieval, and dissemination amongst its target audience of general practitioners, academicians, and research scholars of Oral Health Care Sciences and Practices.

InTech-Open Access Publisher took the initiative in organizing the publication of this book and its companion book, and to make it available on the internet with free access to all those who may be interested in the subject.

The book has contributions from specialists in various subjects of Oral Health Sciences, and is divided into four chapters, namely geriatric dentistry and prosthodontics, periodontology and oral biology, research in oral health, and systemic conditions.

We expect the present work to be accepted as a reference material and initiator of research in the areas covered, as it traces developments on the specific issues and reflects the trend of current research.

The editor wishes to thank all specialist contributors and Publishing Process Manager Ms Irena Voric of InTech for their contributions without which this book would not have been possible. It will not be out of place to acknowledge with gratitude the contribution of my family, who were kind enough to bear with me during the process of developing this book.

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Part 1

Geriatric Dentistry and Prosthodontics

1

Relationship Between Chewing and Swallowing Functions and Health-Related Quality of Life

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1. Introduction

Population aging has advanced rapidly in developed countries. In particular, Japan has already become a "Super Aging Society" (MHLW, 2010), and this trend exists in other Asian countries such as South Korea as well (Fig. 1). The increase in life expectancy has led to a decreased ratio between people of working-age and older individuals. At present, the aging problem is most common in developed and mid-developed countries.

During the last 6 decades, the types of diseases found in Japan have changed greatly with socio-economic development (Matsuda, 2008). For example, the present major causes of death in Japan are non-communicable diseases (NCD) such as malignant neoplasm, cardiovascular disease, and cerebrovascular disease (WHO, 2011). With an aging population, the need for geriatric dentistry has increased greatly in Japan. Oral health is important in the elderly; it helps maintain the ability to chew, swallow, and speak clearly, which are important for quality of life (QOL) (Pereira et al., 2006; Sonies et al., 1984).

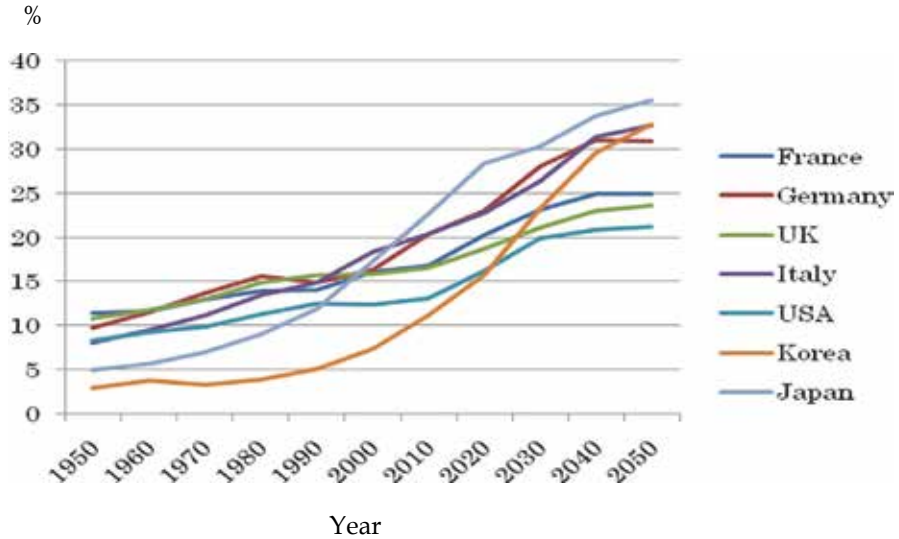

Fig. 1. Percentage of elderly people in the population of 7 countries, including Japan

1.1 QOL improvement and successful aging

Psychosocial approaches to successful aging focus on high social functioning and life satisfaction (Britton et al., 2008; Peel et al., 2005). In particular, sustaining good health is essential for maintaining QOL. Health-related QOL (HRQOL) refers to the perception of overall satisfaction with life and involves the measurement of functional status in the physical, mental, and social realms (Coons et al., 2000). Successful aging is a key concept for improving the quality of life. Application of this broader perspective helps to explain why dental treatment of elderly individuals is more likely to succeed if it addresses oral problems that disturb self-image and social interactions, rather than an approach based solely on function.

Previous studies have reported that QOL is closely related to health and financial status (Robert et al., 2009; Yamazaki et al., 2005), and maintaining satisfactory health, in particular, is essential to successful aging. Thus, HRQOL is a key issue for the elderly.

1.2 Evaluation of HRQOL

Previous studies reported different methods for evaluating HRQOL. Representative evaluation methods are SF-36 (Brazier et al., 1992), SF-8 (Ware et al., 2001), Sickness Impact Profile (Berger, 1981), WHOQOL-BREF (WHO, 2011), and EuroQOL (EuroQOL Group, 1990). In particular, SF-36 and SF-8 have been translated into many languages, including Japanese. More specific evaluations, for example, are EROTC QLQ for cancer (Asronzon et al., 1993), KDQOL (Hays, 1994) for kidney disease, and GOHAI for oral health (Atchinson et al., 1990) . These methods are also very useful for assessing comprehensive health status among the elderly.

1.3 Geriatric oral health in Japan

In Health Japan 21, a national health campaign to improve the population's health status, the followings were identified as focus areas: nutrition, physical activity, mental health, tobacco control, alcohol control, oral health, diabetes control, prevention of heart diseases, and prevention of cancer (MHLW, 2011). Oral health goals in Health Japan 21 were as follows: (1) prevention of dental caries among infants, (2) prevention of dental caries at school age, (3) prevention of periodontal disease, and (4) prevention of tooth loss. The "prevention of tooth loss" is particularly important for the oral health of aging people.

Table 1 shows baseline and intermediate oral health results after 5 years of the Health Japan 21 initiative. The goals relevant to the elderly are to increase the percentage of: 80-year-olds retaining 20 or more teeth; 60-year-olds retaining 24 or more teeth; the increased numbers of people receiving tooth scaling and cleaning; and the increased number of individuals receiving a periodontal checkup. According to the intermediate report (Ministry of Health, Labour, and Welfare, 2007), the dentition of the elderly has greatly improved. Figure 2 shows the national data regarding the percentage of individuals retaining more than 20 teeth. In Japan, the "8020 movement," which means to keep 20 teeth at 80 years, has already been a very popular oral health initiative (Shinsho 2001).

1.4 Oral health and overall health

The oral cavity is important for its eating and speaking functions; eating is necessary for survival, and speaking is essential for satisfactory verbal communication. Many epidemiological studies have shown that good oral health contributes to greatly improving

the physical health of community-dwelling elderly individuals in Japan (Miura et al., 1997; Miura et al., 1998; Miura et al., 2005; Moriya et al., 2011). The scientific evidence contained in these studies provides a useful guidance to other mid-developed countries.

Goals	Age of target population	Percent of population		
		Baseline	Mid-term	Final target
Increase of the proportion of persons with 20 or more teeth	80	11.5%	25.0%	>20%
Increase of the proportion of persons with 24 or more teeth	60	44.1%	60.2%	>50%
Increase of the proportion of persons with dental scaling each year	60	15.9%	43.2%	>30%
Increase of the proportion of persons with periodontal checkup each year	60	16.4%	35.7%	>30%

Table 1. Mid-term evaluation of the oral health initiative goals in 2006 from Health Japan 21 for the prevention of tooth loss

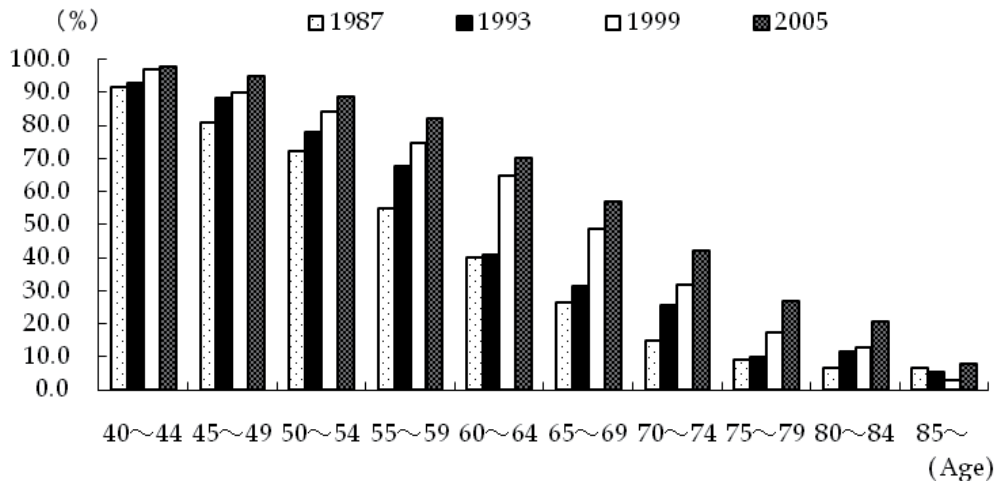

Fig. 2. Persons retaining 20 or more teeth from 1987 to 2005 in Japan (MHLW, 2006)

Chewing and swallowing disorders are prevalent in frail elderly people. In particular, masticatory problems in the disabled elderly are frequently related to tooth loss and ill-fitting dentures. Mastication is necessary for the reduction of food mass, and therefore, inadequate chewing may cause dysphagia symptoms, particularly in the elderly. Several cross-sectional studies revealed that preservation of a person's ability to chew contributed

greatly, not only to physical health, but to QOL as well (Miura et al., 2000; Mori et al., 2010). Furthermore, subsequent studies provided a new perspective for assessing the HRQOL of subjects who suffer from systemic disease with oral symptoms or dysfunction; whereas dysphagia may be the functional focus, patients with dysphagia often have inadequate diets that also produce systemic problems (Foley et al., 2009).

Eating is a pleasure for most people in daily life; therefore, the relationship between improvement in dysphagia and QOL, especially for the elderly, is an important issue. Because consumption of food and drinks form integral to social events and symbolize acceptance, friendship, and community, it is not surprising that swallowing problems evoke a host of distressing psychosocial responses, such as anxiety, shame, embarrassment, fear, and lowered self-esteem (McHorney et al., 2000).

1.5 Purpose of the present study

A decline in chewing and swallowing functions among the elderly is closely related to an increase in overall health risks, such as malnutrition and aspiration pneumonia. Insufficient chewing and swallowing functions could result in a lower HRQOL. In this chapter, we report on our field survey on the relationship between chewing, swallowing, and HRQOL in the elderly.

2. Subjects and methods

2.1 Subjects

The cross-sectional survey was conducted from September 2010 to January 2011 in the northern area of Miyazaki Prefecture, located in Southern Japan. Our initial target sample was 675 community-dwelling individuals who were older than 65 years. Before the survey, we explained in detail the intent of the present survey and obtained informed consent from 541 persons (response rate = 80.1%). The present study was approved by the Institutional Review Board of National Institute of Public Health of Japan.

2.2 Measurements

The respondents were asked to complete a structured questionnaire regarding the following items: (i) demographic variables, (ii) dysphagia risk, (iii) HRQOL, and (iv) overall satisfaction with diet. The decline in the ability to chew and swallow was assessed using the dysphagia risk assessment for the community-dwelling elderly (DRACE), which was developed by Miura et al. (2006). Table 2 shows the assessment items of DRACE. Dysphagia risk was determined according to the criteria of our previous study (Miura et al., 2007); thus, subjects who had >2 positive scores on DRACE were classified as at risk for dysphagia.

HRQOL among community-dwelling elderly people was evaluated using the Japanese version of the SF-8 Health Survey (Fukuhara et al., 2004). The SF-8 represents a major advance in the application of SF technology for purposes of achieving both brevity and comprehensiveness in population health surveys. The SF-8 is widely used to assess QOL, including health status, and comprises the following 8 health subsets: physical functioning (PF), role physical (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). Levels of subjective satisfaction with diet were measured by the question: "Are you satisfied with your present diet?" Subjects categorized themselves by using the 5 Likert scale.

The following questions are related to your ability to swallow food and beverages.
Please select the option that best describes your experience in the last year.
(1) Have you had at least one episode of fever?
2 Frequently 1 Occasionally 0 Never
(2) Have you felt that you take a longer time to eat than before?
2 Much longer 1 Slightly longer 0 Not at all
(3) Have you had difficulties with swallowing beverages?
2 Frequently 1 Occasionally 0 Never
(4) Have you had difficulties with chewing hard food?
2 Frequently 1 Occasionally 0 Never
(5) Have you experienced food spilling out of your mouth?
2 Frequently 1 Occasionally 0 Never
(6) Have you ever choked while eating?
2 Frequently 1 Occasionally 0 Never
(7) Have you ever choked while drinking beverages?
2 Frequently 1 Occasionally 0 Never
(8) Have you ever swallowed food and had it go up your nose?
2 Frequently 1 Occasionally 0 Never
(9) Have you ever had a change in your voice after a meal?
2 Frequently 1 Occasionally 0 Never
(10) Have you ever produced sputum during a meal?
2 Frequently 1 Occasionally 0 Never
(11) Have you ever felt like you had a lump in your throat while swallowing?
2 Frequently 1 Occasionally 0 Never
(12) Have you ever had food or liquid from your stomach come back up into your throat?
2 Frequently 1 Occasionally 0 Never

Table 2. Dysphagia risk assessment for community-dwelling elderly (DRACE)

2.3 Analyses

Bivariate analyses were performed using Pearson correlation coefficients, and partial correlation coefficients were determined to control typical demographic variables such as age and gender. Then, a stepwise multiple regression was performed with the DRACE score treated as the dependent variable for each independent variable (F = 2.5) in order to detect the factors with the largest influence on the risk of dysphagia among the elderly. All statistical procedures were performed using SPSS ver.18.0 (Chicago, IL, USA).

3. Results

3.1 Univariate analysis

Table 3 shows the characteristics of the elderly subjects, DRACE scores, and SF-8 mean value and standard deviation. Each of the SF-8 sub-scores was similar to the standardized

value of Japanese elderly population. The distribution of DRACE scores among the respondents is shown in Figure. 3. In the present survey, 45.0% of individuals had dysphagia risk.

Satisfaction with diet	Frequency (%)
Very satisfied	59.9
Satisfied	33.4
Fair	5.1
Unsatisfied	0.9
Very unsatisfied	0.3

(a)

Variable	Mean	SD	Median
Age	76.06	6.75	75.00
DRACE score	3.02	2.09	2.00
SF-8 sub scores			
PF	48.48	6.32	48.52
RP	48.06	7.36	48.47
BP	46.43	7.97	46.19
GH	49.41	6.71	50.71
VT	49.87	6.48	54.48
SF	48.30	7.80	54.74
RE	49.64	7.48	49.07
MH	50.22	6.63	50.28

(b)

Table 3. Univariate analyses on characteristics of the elderly subjects (N = 541)

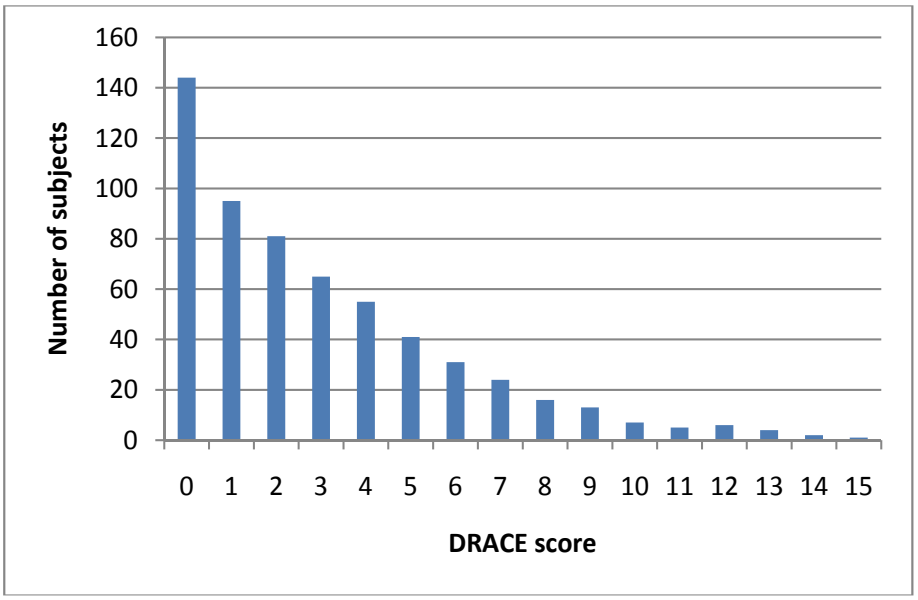

Fig. 3. Distribution of DRACE scores among the survey respondents

3.2 Bivariate analysis

Table 4 shows the matrix of Pearson correlation coefficients among DRACE, SF-8 sub-scores, and subjective satisfaction with diet. DRACE scores significantly related to all sub-scores of SF-8 and subjective satisfaction on diet ($p < 0.001$). In particular, sub-scores of SF-8 regarding mental health status closely associated with DRACE scores. Table 4 also shows the partial correlation coefficients controlled for age and gender between DRACE and the other variables. In the analyses of partial correlation coefficients, DRACE also significantly related to all sub-scores of SF-8 and subjective satisfaction with diet ($p < 0.001$). In particular, MH of SF-8 revealed higher correlation coefficients to DRACE score.

Pearson correlation coefficients			Partial correlation coefficients controlled for age and gender		
DRACE score versus:	Pearson correlation	P value	DRACE score versus:	Partial correlation	P value
Age	0.262	<0.001			
Satisfaction with diet	0.295	<0.001	Satisfaction with diet	0.238	<0.001
SF-8 sub-score			SF-8 sub-score		
PF	-0.304	<0.001	PF	-0.219	<0.001
RP	-0.374	<0.001	RP	-0.270	<0.001
BP	-0.260	<0.001	BP	-0.237	<0.001
GH	-0.310	<0.001	GH	-0.244	<0.001
VT	-0.356	<0.001	VT	-0.284	<0.001
SF	-0.373	<0.001	SF	-0.272	<0.001
RE	-0.388	<0.001	RE	-0.274	<0.001
MH	-0.374	<0.001	MH	-0.350	<0.001

Table 4. Matrix of correlation coefficients among DRACE score, SF-8 sub-scores, and subjective satisfaction with diet

3.3 Multivariate analysis

Table 5 shows the results of a stepwise multiple regression analysis to find the most influential factor on the DRACE score. Finally, we determined that the 4 most influential factors were as follows: mental health (MH), age, role physical (RP), and subjective satisfaction with diet. The final regression coefficient was 0.445 ($p < 0.01$), and the adjusted coefficient of determination was 0.192 ($p < 0.01$).

Variable	Beta	T value	P value
SF-8 MH	-0.225	-4.711	<0.001
Age	0.184	4.184	<0.001
SF-8 RP	-0.123	-2.432	0.015
Satisfaction with diet	0.102	2.247	0.025

Multiple correlation coefficient (R) = 0.445.
Adjusted coefficient of determination (R^2) = 0.192.

Table 5. Factors related to dysphagia risk in stepwise regression analyses

4. Discussion

The present findings indicate that a decline in chewing and swallowing functions are closely related to HRQOL. Multivariate analysis revealed that chewing and swallowing functions had a significantly higher correlation to mental health status than to physical status.

4.1 Evaluation of the risks of dysphagia

Dysphagia frequently occurs among frail elderly individuals (Siebens et al., 1986; Eliot et al., 1988) and enhances the risk of aspiration pneumonia, which are clinically-occult. Therefore, conducting appropriate screening to identify the potential for aspiration is important. DRACE is a useful assessment tool for detecting the risk of mastication and swallowing disorders among community-dwelling elderly people (Miura et al., 2007). Because there are only 12 items to assess, DRACE is a very simple survey compared to the other available options.

4.2 Evaluation of HRQOL

In order to assess HRQOL issues of the elderly, their heath needs must be identified; maintaining HRQOL is directly associated with an extended healthy life expectancy. There are many methods for assessing HRQOL; however, SF-8 is an international scale of comprehensive HRQOL that has been widely used in Japan because the standard values for a cross section of Japanese residents have previously been reported (Fukuhara, 2004). The SF-8 is almost equivalent to SF-36; SF-8 is an 8-item version of the SF-36 that yields a comparable 8-dimension health profile and comparable estimates of summary scores for the physical and mental components of health. This study found that the SF-8 sub-scores were similar to the previously established values for the Japanese elderly.

4.3 Dysphagia and HRQOL

The ability to chew and swallow satisfactorily is necessary for maintaining a well-balanced diet for the elderly. Dysphagia affects physical health, including the nutrition status of senile individuals (Morris, 2006). Severe dysphagia can lead to reduced food selection, which can cause malnutrition. In addition, the ability to chew affects food selection and intake. The dietary data from the National Diet and Nutrition Survey showed that energy intake was lower in edentate people (Sheiham et al., 2001). Thus, a decline in chewing and swallowing function is significantly related to physical health.

In the present study, it was very interesting that there was a stronger correlation between DRACE and factors related to mental health than to factors related to physical health. A previous study has also shown a significant relationship between oral function and poor mental health (Friedlander and Norman, 2002). It was very interesting that the enhancement of chewing and swallowing function contributes not only physical health, but mental health as well.

The negative spiral caused by the decline of chewing and swallowing functions is illustrated in Fig. 4. A well-balanced diet would greatly improve a person's comprehensive QOL, including both physical and mental aspects.

4.4 Dysphagia and satisfaction with diet

Satisfaction with diet has been involved various aspects such as quality of diet, oral function and dietary environment. The present findings revealed the subjective evaluation on diet

closely related the risk of dysphasia among elderly community residents. Healthy chewing and swallowing function is connected to maintain healthy diet. A previous study regarding oral health-related QOL reported that Japanese elderly persons especially have developed a culture enjoying seasonal foods and a variety of foods (Naito, 2011), thus satisfaction with diet has been useful indicator to grasp the risk of dysphagia.

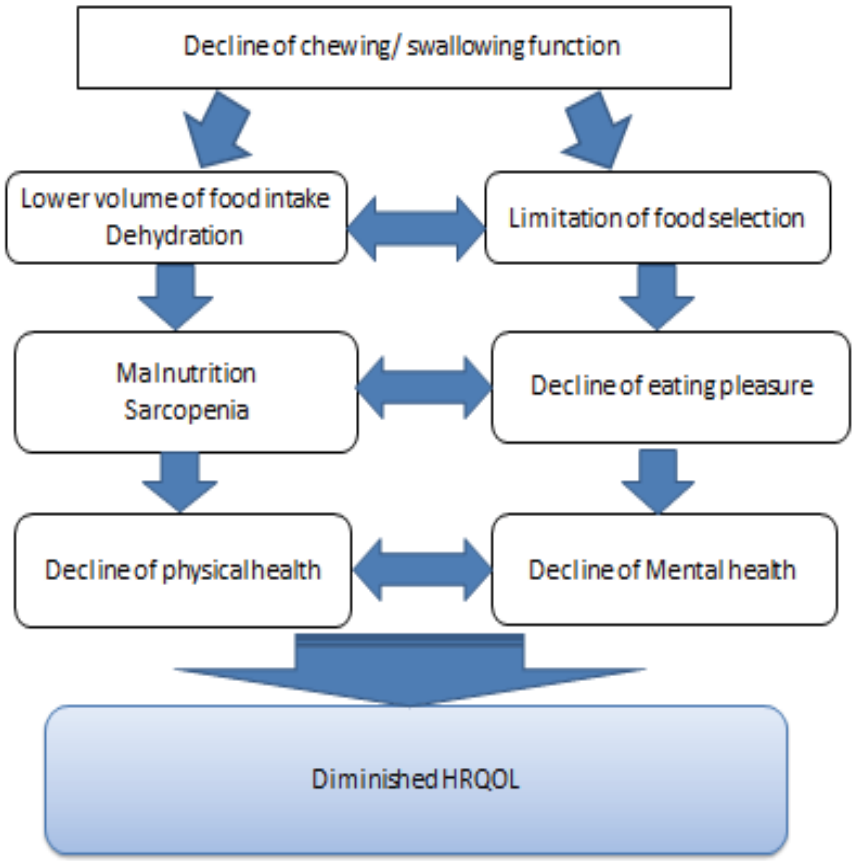

Fig. 4. Negative spiral caused by dysphagia in elderly people

4.5 Limitation of the present study

A limitation of the present study was the need to exclude elderly people with severe physical or mental disabilities in order to obtain reliable answers. Nevertheless, the present findings suggest that improvement of chewing and swallowing functions are very important for the maintenance of a healthy aging society.

5. Conclusion

Mastication and swallowing are essential functions for the maintenance of a healthy dietary life. A decline in these functions could induce not only the deterioration of physical health, but also mental health. To avoid the negative spiral caused by poor chewing and

swallowing, an oral function improvement program will be necessary as the population ages. The retention of the ability to chew and swallow is a key to a prolonged and healthy life. The creation of health programs that enhance the swallowing function, such as exercises to activate orofacial muscles, could improve QOL in elderly individuals.

In conclusion, the present findings suggest that the ability to chew and swallow is significantly related to HRQOL and subjective satisfaction with diet. These results will contribute to the creation of a conceptual model of QOL for the elderly and the impact of any decline in chewing and swallowing functions.

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2

Residual Ridge Resorption – Revisited

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1. Introduction

Residual ridge resorption (RRR) is a term that is used to describe the changes which affect the alveolar ridge following tooth extractions, and which continue even after healing of the extraction socket. The most significant feature of this healing process is that the residual bony architecture of the maxilla and mandible undergoes a life-long catabolic remodelling. The rate of reduction in size of the residual ridge is maximum in the first three months and then gradually tapers off. However, bone resorption activity continues throughout life at a slower rate, resulting in loss of varying amount of jaw structure, ultimately leaving the patient a 'dental cripple'.

Rehabilitation of a totally edentulous patient using a conventional complete removable denture is a routine clinical procedure, yet at times it can be a difficult and challenging process. All these patients have been through a period of edentulousness that varies from weeks to months or even years and the promise of having 'teeth' again often makes their expectations unrealistically high. The challenges facing the clinician are therefore manifold and this is the reason why there remains a wide variation in the predictability of clinical success.

Even experienced clinicians know fully well that it is not possible to completely satisfy all the needs of edentulous patients, even with a well-fabricated prosthesis. There is a wide range of variation seen within the community as regards the needs, expectations, and responses to treatment. Before initiating treatment it is therefore, essential that the dental surgeon provide all patients with sufficient information regarding treatment options and the expected outcome of each. This allows them to make adequately informed decisions regarding their needs. The treatment options are to be presented in such a manner that each modality of treatment has a perspective that is relevant to the patient's needs and expectations. It is also imperative that all treatment advice should be in consonance with the clinical findings and physical parameters of the existing oral condition.

2. Residual ridge remodelling

Immediately following tooth extraction, a cascade of inflammatory mediators is initiated, which results in the formation of a blood clot which is the first step in the eventual closure of the extraction wound. The clot then undergoes organisation and is gradually replaced by granulation tissue towards the periphery and base of the alveolar socket. After a span of

seven to ten days, new bone formation is evident, with osteoid matrix present as non-calcified bone spicules. Mineralization progresses from the alveolar socket base in a coronal direction and two-thirds of the socket is filled in approximately 5 to 6 weeks. (Schropp et al, 2003)

The bony remodelling that subsequently takes place occurs in two phases: an initial and fairly rapid phase that can be observed in the first 3 months and the subsequent slow, minimal yet continuous resorption that continues life-long. During the initial period there is new bone formation with loss of almost all of the alveolar crest height and simultaneous reduction of approximately two-thirds of the ridge width. These changes continue over the initial ten to twelve week period. Between six and twelve months, part of the new laid-down bone undergoes further remodelling resulting in the further reduction of the alveolar ridge width until it is reduced to approximately half. The rate of resorption then slows down to minimal levels, yet since it is continues throughout the individual's life there is a significant reduction in bony volume seen in geriatric patients.

This unique phenomenon is known as residual ridge resorption (RRR). The rate of RRR varies, from one individual to another; at different phases of life and even at different sites in the same person. The clinical significance of such remodelling is that the functionality of removable prostheses, which rely greatly on the quantity and architecture of the residual ridge, may be adversely affected.

Residual ridge resorption is often clinically evident yet the actual physiological changes that follow tooth extraction are not well-understood. Atwood first postulated the four main factors namely anatomic, prosthetic, metabolic, and functional factors that are responsible for the loss of alveolar bone. (Atwood, 1957, 1962) Since then, numerous investigators have made an attempt to analyse the changes in the form of the residual alveolar ridge using lateral cephalograms, panoramic radiographs, or diagnostic casts as standardized measurements. (Carlsson & Persson, 1967) The main aim of these investigators was to isolate the factor or factors that could explain a pathologic origin in severe cases of RRR. Despite best efforts, till date, no study has been able to conclusively provide evidence to any one factor or causative agent. What is clinically proven is that the use of ill-fitting removable prostheses, which generate localised mechanical stress onto the alveolar bone affect the rate of bone loss of residual ridges. Among the other systemic causes, only postmenopausal osteoporosis has been shown to have a cause-effect relationship with RRR. (Kribbs, 1990, Nishimura et al, 1992) Since residual ridge resorption exhibits such a wide variation in its clinical presentation it can be reasonably assumed that a myriad of factors all play a part in determining the ultimate rate and extent of bone loss in a particular individual.

3. Factors affecting resorption of the residual ridge

3.1 Anatomic factors

It is postulated that RRR varies with the quantity and quality of the bone of the residual ridges. Thus it is likely that the more bone volume there is, more the quantum of resorption will be seen. Another anatomic factor that is crucial to an increased rate of resorption is the bone density of the ridge. However, it is important to remember that the

density at any given moment does not indicate accurately the current metabolic status of the ridge and that osteoclastic activity will resorb the bone irrespective of the degree of calcification.

3.2 Localised mechanical stress from removable prostheses

Kelly first described the "combination syndrome" wherein patients with remaining mandibular natural teeth against a maxillary complete denture were shown to have an exaggerated loss of anterior segment of maxillary residual ridge. (Kelly, 1972) Carlsson and others conducted a prospective clinical study on a group of partially edentulous patients. Cases of Kennedy Class I edentulous situation were studied under three groups; the first without any mandibular denture, second were those wearing partial denture with bilateral free-end saddles, and the third group were those having a partial denture with anterior lingual bar. The results of the study revealed an increased rate of RRR of the edentulous ridge in the groups wearing dentures for prolonged periods. (Carlsson, 1967) It was assumed that excessive mechanical stresses were responsible for the increased degree of resorption, as greater loss of residual ridge volume was observed in patients who wore their dentures for long hours as compared to the edentulous ridges of the patients who wore their dentures less frequently.

3.3 Stress and strain effect

It is well known that osteoid tissue that receives constant mechanical stimuli maintains a balance between osteoclastic and osteoblastic activity. When bone is in a state of immobilization or a weightless environment, the reduced mechanical stress cannot sustain the normal remodelling process which results in a decrease of calcified bone mass which is known as disuse atrophy. On the other hand, it has been demonstrated physiologically that applied mechanical force can stimulate bone apposition. The oral and facial musculature during functional jaw movements such as mastication, swallowing, produce forces on the occlusal surface of artificial teeth, which is transmitted via the denture base to the underlying residual ridge. Removable partial or complete dentures which are primarily 'tissue-borne' transmit the stress through the mucosa directly to the residual ridge, making it the primary stress bearing area.

3.4 Role of inflammatory mediators

Various inflammatory mediators, mainly prostaglandins, have been regarded by many workers as playing a role in increasing the rate of residual ridge resorption. A study by Yeh and Rodan (1984) showed that when osteoblastic cells were subjected to repetitive mechanical stresses in-vitro there was a significant increase in prostaglandin E2 synthesis. In a separate study that used edentulous rats, the daily administration of indomethacin, an inhibitor of cyclooxygenase (an enzyme required for the prostaglandin synthesis), reduced the rate of RRR to 50% within the experimental period. When systemic delivery of prostaglandin E2 was initiated the inhibitory effect of indomethacin was reduced thus leading the investigators to believe that this could be one factor that could mediate the residual ridge bone resorption activity.(Nishimura et al, 1988) The cause-effect direct relationship between prostaglandin-mediated bone resorption, resulting in severe form of RRR, and the stress related resorption of the residual ridge

has not been successfully demonstrated. (Devlin & Ferguson, 1991) The synthesis of certain biologically active substances by the edentulous mucosa may play a role in enhancing osteoclastic activity of residual ridge alveolar bone, but these are yet to be identified.

3.5 Osteoporosis and post-menopausal osteoporotic changes

The extent of RRR is proportional to the time lapsed after the teeth have been extracted as well as the age of the patient. (Humphries et al, 1989) Osteoclastic activity occurs primarily on the surface of the residual ridge and hence there is a three-dimensional change in the shape of the ridge. The maxillary residual ridge has been reported to be significantly smaller in postmenopausal osteoporotic women while their edentulous mandible remained the same as the age related controls. (Kribbs, 1990) When bone resorption occurs at the labial and lingual surfaces of the residual ridge in preference to the occlusal surface the result is a knife-edged ridge. Studies have exhibited that postmenopausal women with lower bone densitometric scores showed a tendency to have a knife-edge lower alveolar ridge. (Nishimura et al, 1992) This may occur in combination with a small maxillary ridge which may be a disadvantage to successful rehabilitation using a conventional removable prosthesis. Histological studies of residual ridges indicate that extraction sockets heal with active synthesis of trabecular bone. Trabecular bone formation is seen around the borders of post-extraction socket and the large amount of bone resorption due to osteoclastic activity occurs towards the crestal region. This often results in a distinctive porosity on the crest of the residual ridge alveolar bone. (Araújo & Lindhe, 2005)

4. Differential resorption rate in maxilla and mandible

It is a clinically acknowledged fact that the anterior mandible resorbs 4 times faster than the anterior maxilla. The probable reasoning for this fact are difference in the square area of the maxilla and the mandible; the property of the mucoperiosteum that has a 'shock absorber' effect and the variation in the quality of bone of the two jaws.

Woelfel et al have cited the projected maxillary denture area to be 4.2 sq in and 2.3 sq in for the mandible; which is in the ratio of 1.8:1. If a patient bites with a pressure of 50 lbs, this is calculated to be 12 lbs/sq in under the maxillary denture and 21 lbs/sq under the mandibular denture. The significant difference in the two forces may be a causative factor to cause a difference in the rates of resorption. (Woelfel et al, 1974, 1976) The mucoperiosteum due to its 'spongy' nature has a 'dampening effect' on the forces that are transmitted to the alveolar ridge. Since the overlying mucoperiosteum varies in its viscoelastic properties from patient to patient and from maxilla to mandible, its energy absorption qualities may influence the rate of RRR.

Cancellous bone is ideally designed to absorb and dissipate the forces it is subjected to. The maxillary residual ridge is often broader, flatter, and more cancellous than the mandibular ridge. Trabeculae in maxilla are oriented parallel to the direction of compression deformation, allowing for maximal resistance to deformation. The stronger these trabeculae are, the greater is the resistance. These anatomical variations may result in the observed differences in the RRR of the upper and lower jaw.

5. Importance of reducing ridge resorption

Every clinician is aware that the proportions of the residual ridge are critical to denture success, and so it is vital to preserve the dimensions of the post-extraction ridge. There will be a significant decrease in patient morbidity if all attempts are made to maintain its ideal vertical and horizontal proportions instead of reconstructing it at a later date. (Darby et al, 2009) Therefore, any technique that ensures the preservation, augmentation or reconstruction of the alveolar ridge height, thickness and quality, immediately after dental extraction, either with bone regeneration procedures or with the placement of endosseous implants, must be carried out for the maintenance of its vertical and horizontal dimensions. This would very often diminish the need for complex procedures such as augmentation with bone grafts and increase the success of the final prosthesis. (Aimetti et al, 2009; Lekovic et al, 1998)

Several methods have been suggested to facilitate bone formation in freshly extracted sockets, thus minimizing the loss of bone height and buccolingual width. These include guided bone regeneration, with or without grafting material, grafting with bone substitutes, osteogenic materials, such as autogenous bone marrow and plasma rich in growth factors (PRGF); and other biomaterials. (Fiorellini et al, 2005; Mardas et al, 2011; Serino et al, 2003, 2008) The grafting materials used as bone fillers after tooth extraction provide mechanical support and prevent the collapse of both the buccal and lingual bone walls, thus delaying residual ridge resorption and remaining in the place until new bone formation. The ideal bone substitute should be both osteoinductive and osteoconductive in nature, stimulating and serving as a scaffold for bone growth.

6. Surgical options for highly resorbed ridges

Whenever there is significant loss of alveolar bone volume and associated mucosa, the functional and esthetic potential of the prosthesis is severely compromised and patients are often resigned to the fact that they can never be able to function with a removable prosthesis. In recent years the advent of suitable augmentation methods and materials as well as the ability to regenerate maxillary and mandibular bone and soft tissue with subsequent placement of implants has brought new hope to these former 'dental cripples'. (De Coster et al, 2011, Iasella et al, 2003) When there is severe ridge resorption, alveolar distraction osteogenesis can facilitate a substantial amount of both hard and soft-tissue regeneration. Alveolar distraction may be followed by implant placement and prosthetic rehabilitation. Augmentation of the intended implant site makes it possible to achieve an aesthetically acceptable and functional prosthetic restoration. (McCarthy et al, 2003)

In the maxilla, advanced bone resorption may result in pneumatization of the maxillary sinus and subsequent decrease in the height and width of the alveolar bone of the maxilla. In such cases, different grafting techniques such as sinus lift osteotomies followed by onlay grafting can achieve aesthetic and functional restorations. (Branemark et al, 1984; Summers, 1994; Tatum, 1986) Another treatment alternative is alveolar distraction osteogenesis. The concept of distraction osteogenesis was first demonstrated by Ilizarov as a means of lengthening long bones. The procedure is based on the theory of bone distraction along a vector that is transverse to the long axis of the bone, which results in

bone formation. (Ilizarov, 1989) It was later applied to the human mandible, and more recent clinical reports have shown that alveolar distraction osteogenesis is effective for treating severe forms of alveolar ridge atrophy. (Chin & Toth, 1986) A primary advantage of distraction osteogenesis is that there is no need for additional surgery at the donor site. Another benefit is the coordinated lengthening of the bone and associated soft tissues. The alveolar bone in the anterior maxilla is one of the sites in the dental arch where distraction osteogenesis is used with encouraging results. (Aragon & Bohay, 2005; Gaggl et al, 2000; Uckan et al, 2002) The vertical height of the residual ridge may be increased using this technique with subsequent implant placement and rehabilitation using overdentures.

7. Prosthodontic principles to reduce RRR

Certain general principles must be kept in mind during fabrication of complete dentures which will help to reduce the stress transmission and help preserve the alveolar ridge. This may be achieved by having broad area of coverage under the denture base (to reduce the force per unit area). A decrease in the number of denture teeth; decrease in the buccolingual width of teeth; improved occlusal tooth design form (to decrease the amount of force required to penetrate a bolus of food) are some of the other techniques that may also be used. During tooth setup the aim should be to reduce the number of inclined planes (to minimize dislodgement of dentures and shear forces) and achieve a centralization of occlusal contacts (to increase stability of dentures and to maximize compressive load). Accurate recording of maxillomandibular relationship will ensure optimum vertical rest dimension which will decrease the frequency and duration of tooth contacts, thereby giving adequate rest to the underlying ridges. (Kapur & Soman, 1964; Van Waas, 1990)

8. Prosthodontic rehabilitation of resorbed ridges

8.1 Conventional complete dentures

For many decades complete tissue-supported removable prostheses have been regarded as the treatment of choice for edentulous patients. The primary reason for this was the absence of a viable alternative. The treatment outcome of rehabilitation with complete dentures cannot be predicted, and it is a common clinical experience that there is a wide variation in the patient response to this treatment modality. Despite the fact that complete dentures are known to have poor masticatory capability, patients seem to accept this as part of the ageing process. Clinically the commonest reason in patients reporting for treatment is the 'loosening' of the dentures – which is often due to the continual resorption of the alveolar ridge. The expectations of clinicians seem to be different from than that of the patients when it comes to evaluation of removable complete dentures. Though the clinician may not be satisfied for a variety of reasons it is the patients who seem to be generally happy with conventional dentures. Despite all the controversy, for the appropriate age and oral condition, general health, and socioeconomic status, a carefully fabricated complete removable denture may be a safe, predictable, and cost-effective treatment to restore an edentulous patient, especially in developing countries.

8.2 Implant supported overdentures

The field of prosthodontic rehabilitation has been irreversibly transformed with the advent of osseointegrated titanium implants. The predictable clinical success of osseointegrated implants has ensured that the concept of an implant-supported prosthesis as a reliable protocol in the management of complete edentulism is now accepted world-wide. The evolution of implants as a means of ensuring support, retention and stability of an implant retained overdenture have revolutionised the treatment concepts and should be made the treatment of choice, wherever possible. In most cases there is improved stability, greater functional efficiency, and improved levels of patient satisfaction with the implant-retained and tissue-supported mandibular overdenture, as compared to the conventional removable dentures.

In the developed countries a mandibular 2-implant retained overdenture treatment modality is, by and large, considered the 'gold standard' for the treatment of the edentulous mandible. This is based on the efficacy of this treatment modality as regards function, nutrition, and overall quality of life, balanced with patient preferences and expectations, treatment planning, prosthodontic management, and predicted costs. In lesser developed nations, however, the cost factor for such treatment over conventional dentures appears to be the only area of concern regarding its acceptability among all practitioners. Though, it is generally agreed that, when all other treatment options have failed, the only recourse is to use implant-supported overdentures for the management of the edentulous patient with an advanced degree of ridge resorption. The cost versus performance benefit for these two modalities of prosthodontic treatment should be employed by practitioners to facilitate their patients to make informed choices. There is the distinct possibility that with the increasing competition and marketing strategies adopted by the implant manufacturers, the cost of such implants will be sufficiently lowered for them to become affordable across the economic spectrum of patients. This will make implant supported prostheses a realistic option to rehabilitate all patients with poor ridges effectively and economically.

9. Conclusion

The ultimate aim of a successful prosthesis is stability in function and excellent esthetics. The expectations of edentulous patients are highly variable and therefore the outcome of patient treatment varies significantly from one individual to another. The overall degree of patient satisfaction is influenced by social and cultural influences, financial resources, and adaptive capability. A host of other socioeconomic, regional, cultural, age, and gender influences, educational background, knowledge and experience of the clinician play a vital role in the patient acceptance of a particular treatment modality. In the light of present day understanding of the sequelae of residual ridge resorption it is imperative for all clinicians to allow their patients to be partners in making informed treatment choices. The patients should be educated regarding the type and extent of treatment that is ideal for them, the prognosis of the treatment outcomes with various types of removable or fixed prostheses and the alternatives that are available. The end result will be the successful rehabilitation of an increased number of edentulous individuals and many more satisfied clinicians.

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Improvement of Patient's Satisfaction and Oral Health-Related Quality of Life by the Implant and Prosthodontic Treatment

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1. Introduction

Improvement of oral health and quality of life is the main goal of contemporary dentistry, since it has been considered as an important part of patient's well-being. Eliminating oral pain and the problems connected to chewing and speech, as well as the improvement of aesthetic contributes the improvement of oral health.

When assessing the outcomes of dental treatment, it is important to consider the clinicians' as well as the patients' point of view. Therefore, the four basic parameters have been identified, which describe these objective and subjective outcomes:

- biologic and physiologic parameters (health of oral structures, nutrition, chewing, and esthetics),
- longevity and survival rate (of teeth, restorations, implants),
- psychosocial parameters (treatment satisfaction, self-esteem, body image, quality of life, benefit, utility)
- and economic parameters (cost-effectiveness, direct and indirect cost) (Anderson, 1998; Guckes et al., 1996).

The first two categories have been investigated extensively so far by the clinicians, while in the last few decades the psychosocial outcomes have also gained lots of interest (Buck & Newton, 2001).

According to Assunção et al. (2007), patient satisfaction depends on factors such as chewing, stability, comfort (fit), esthetics, taste and speech. In addition to these clinical aspects, an understanding of the impact of denture on a patient's well-being is required to help patient and dentist to make the decision which treatment option would be the most appropriate in prosthodontic rehabilitation. To evaluate the effect of prosthetic therapy on patient satisfaction psychosocial outcomes factors (general satisfaction, social impact, self-esteem) also have to be used (Assunção et al., 2007). In other words, outcomes of treatment have to be assessed by subjective perceptions of the patient, as well as by objective tests. In some articles only subjective or objective assessments have been used, while in the other both

outcomes have been evaluated (Attard et al., 2006; Burns et al., 1994; Heydecke et al., 2004; Kleis et al., 2010; Zani et al., 2009).

Since the interest to evaluate psychosocial factors has been increased in the last two decades, many publications used only subjective outcomes. Their wide usage is based on low cost and simplicity since already one single questionnaire can measure changes in patients' perceptions regarding satisfaction and oral health related quality of life (OHRQoL) outcomes before and after treatment. Other type of questionnaire has been used in retrospective studies to remember the patients of their experience with previous dentures and rate the change after receiving new denture (Kimoto & Garrett, 2005). Since the retrospective studies rely on patient memory, the data can also be unreliable and inaccurate (Allen et al., 2001b).

Oral health-related quality of life (OHRQoL) is an important patient-centered endpoint to be considered when assessing the impact of oral diseases and evaluating professional interventions (Heydecke et al., 2003b). In other words, it can be defined as a person's assessment of how functional, psychological and social factors and pain/discomfort affect his or her well-being—in the context of oral health (Inglehart & Bagramian, 2002). This opens new opportunities in clinical work, research and education. According to Locker different aspects of OHRQoL have different levels of importance to an individual, depending on their age and general health status (Locker & Miller, 1994).

OHRQoL is a multidimensional construct that has been assessed by various questionnaires that collect data not only about oral health status, but also about other oral health dimensions that affect quality of life. They should reflect the influence of the oral status on personal and social well-being (Elinson, 1974). Some questionnaires measure different dimensions, while others are focused on a particular dimension of oral health (Inglehart & Bagramian, 2002). The most of the questionnaires are trying to describe the negative effect of oral conditions like loss of teeth and denture therapy on OHRQoL. One problem of nonspecific, broad questions is the high number of false-positive responses; therefore, they should always be complemented by more specific items. The questions are mostly related to general satisfaction, as well as to more specific items like chewing, speech, comfort and esthetics. According to Awad these items are the most relevant ones (Awad et al., 1998). Concerning the prosthodontic, patient's physical and psychosocial negative experiences with previous dentures are of high importance, since they may influence on decision and satisfaction with new implant and prosthodontic rehabilitation (Kapur et al., 1999).

The high-general satisfaction score in many studies may be a result of general questions that give more positive response than narrowly focused questions (Strassburger et al. 2006). The development of validated, multi-item questionnaires for the measurement of OHRQoL has made significant progress, since they have good measuring characteristics to assess the type of therapy and its success. This led to the development of longer, more complex instruments. Some questionnaires, like the Oral Health Impact Profile (OHIP) (Slade & Spencer, 1994) have been translated into different languages and have been accepted worldwide.

Most of the questionnaires haven't been standardized what makes the results less valid, less meaningful and less comparable (Strassburger et al., 2006), while the standardization and validation of the questionnaires makes them reliable and allows comparison of results

(Strassburger et al., 2004). It would be best to compare the data between the studies, but since the most of them used self-made questionnaires and different graduation scales, this would be inappropriate (Melas et al., 2001).

To avoid the bias in the study clinician shouldn't be involved in the study, since the patients would assign better scores not to offend their dentist (Allen et al., 2001b). Problem, which is often encountered in studies, is also the lack of a control group not allowing the comparison of results with a non-treated general population and assessment of real treatment effects (Boerrigter et al., 1995a). Another problem is a short follow-up period, which is very important in the group of patients with slow adaptation capabilities (Roumanas et al., 2003).

Finally, we could conclude that the selection of the appropriate psychometric instrument for evaluating OHRQoL has a powerful influence on the final result, as instruments specifically designed for problems related to the oral cavity. In many publications self-made questionnaires have been used, but recently more studies asked to complete an Oral Health Impact Profile (OHIP), that is apparently more sensitive than generic ones that assess the health-related quality of life (Allen et al. 1999; Allen & McMillan, 2003; Heydecke et al., 2003b).

The OHIP is a self-administered instrument specifically designed to measure the impact of oral health on psychosocial well-being and quality of life (Slade & Spencer, 1994). This questionnaire includes 49 items that cover seven domains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap. The five categories of choice per item are: never, rarely, occasionally, often, and very often; and are coded from 0 to 4, with the higher scores indicating more serious problems.

OHIP and its modifications (several shortened versions) show reasonable degree of cross-cultural consistency, discriminance and hence good construct validity properties. As it is oral specific, it will be of greater use in measuring outcomes of oral disorders than generic measures such as SF-36. It was concluded that sensitivity to change of the OHIP was good. This property was not improved by using statement weights (Allen et al., 2001b).

The important part of the standardization is the usage of the same scale, such as the Lickert scale (from 1 to 5) or VAS (visual analog scale). The VAS consists of a line 10 cm in length representing a spectrum of feeling between two extremes identified by end-phrascs. For example, in response to the question, "do you feel discomfort with your mandibular prosthesis," the left side end-phrasc would represent the response "always," whereas the right side would represent "never." In another words the line represents the graduation from zero point or percentage to the 100% value and the most favorable response for the question. A vertical mark on the line represents their feelings at that time, or the degree of comfort in the example (Cibirka et al., 1997). This finding will be relevant when considering the use of health-related quality of life measures to target resources and measure the outcome of clinical intervention (Allen et al., 1999).

The other widely used standardizes generic health status questionnaire is SF36, a generic health status measure developed in the United States (Ware & Sherbourne, 1992). The SF36 consists of 35 statements divided into eight subscales (physical functioning, social functioning, role limitation-physical, role limitation-emotional, mental health, vitality, pain and general health perception). There is also a self-assessed global transition statement asking respondents to compare their general health status with one year previously.

In general population, the number of teeth has the strongest impact on the OHRQoL (Allen & McMillan, 1999). In elderly, tooth loss has an adverse effect on different aspects of quality of life, particularly in institutionalized individuals where the loss of teeth may constitute a severe handicap (Sheiham et al., 2001). As pointed out by Blomberg (1985), the teeth do not only serve as a part of the masticatory system, but as the part of the oral region have also an important part in speech and psycho-sexual functioning. Therefore, the loss of teeth is equivalent to the loss of an organ with several implications to the individual (Albrektsson et al., 1987).

Although the prevalence of edentulism is falling (Steele et al., 2000), the percentage of older people is still increasing in population (Thompson & Kreisel, 1998). Since the missing occlusal units are related to OHRQoL impairment (Baba et al., 2008) it is necessary to provide a treatment to reconstruct their number and provide satisfactory oral function. To replace the missing tooth different treatment possibilities have been proposed. Until recently two main options for restoring the function and esthetics of non-restored or inadequately restored spaces were tooth-supported fixed partial dentures (FD) and conventional removable dentures (CD). Loss of more teeth and their inappropriate position requested denture as only option. Due to lack of denture retention and stability in many denture-wearing patients diet is poor and speech is unclear (Kapur, 1987). Therefore, the success of classical denture treatment very often depends on a patient's adaptive capacity to overcome these limitations (Carlsson, 1998).

In recent years the implementation of implant therapy has gained more importance and significance as a therapy option, as it provides significant improvement in stability, retention and OHRQoL of edentulous patients (Assunção et al., 2009; Strassburger, 2006). Many studies evaluated the outcomes of two-implant supported mandibular overdentures (IOD) opposed by conventional maxillary prostheses (Awad et al., 2000; Cibirka et al., 1997; de Bruyn et al., 1997; De Grandmont et al., 1994; Kent & Johns, 1991; Kiyak et al., 1990; Pera et al., 1998; Tang et al., 1997).

The impact of different non-implant and implant dental treatments on patient's OHRQoL has been assessed. Detailed questions with regard to specific aspects of the dentures give insight into aspects that have been improved by the treatment. Such factors include satisfaction with comfort, chewing, stability and esthetic. To date, clinical studies have mainly been focused on OHRQoL outcomes of partial and complete dentures (CD) (Celebic & Zlataric 2003; Forgie et al., 2005). In the last two decades some studies also evaluated implant therapy by changes of the patient's OHRQoL (Allen et al., 2001b; Allen & McMillan 2003; Strassburger et al., 2006; Zani et al., 2009), and their number increases constantly (Strassburger et al., 2004). According to some studies, quality of life has been significantly improved after the treatment with implant-supported overdentures (IOD) in comparison to the previous experience of wearing CD (Awad et al., 2003b). With respect to chewing (Geertman et al., 1996a), bite force (Fontijn-Tekamp et al., 1998), comfort, function, speech, esthetic, self-image and dental health (Cibirka et al., 1997), IODs provided greater improvement of oral health. Concerning the rehabilitation in elderly, improvement of functional aspects and oral health has been confirmed (Allen et al., 2001b; Heydecke et al., 2003b), as well as after the rehabilitation with implant-supported fixed dentures (IFD) (Berretin-Felix et al., 2008). Despite some articles and general opinion that patients who have IOD are less satisfied and have lower OHRQoL than the patients with IFDs (Heydecke et al.,

2003a), some authors found out that both patient groups have been equally satisfied (Zani et al., 2009).
All these studies confirmed that patient based outcome measures are necessary in clinical decision making, and that specific instruments are needed to clinicians and researchers to assess the these outcomes. A shift from clinical longevity toward health status assessments has been made in order to improve patients benefit. For clinician this information means enhancement to design therapeutic interventions. The argument for the use of these measures must be made on practical not theoretical grounds. Therefore, it is important to prove to clinicians that measuring health status is useful in improving patient care and that these measures are important tools in the service of their patients (Hayes, 1998).

2. Aim of the study

The aim of this chapter was to undertake systematical search (electronic and manual) of the current dental literature to identify and classify articles (according to their level of evidence) on satisfaction and oral-health related quality of life (OHRQoL) outcomes after implant-prosthodontic rehabilitation. The collected literature was systematically reviewed and outcome variables analyzed trying to summarize the characteristics of the studies published so far. The aim was also to induct the future direction according to missing or deficient data.
It was hypothesized that the number of studies based on high-level evidence, using patient-based outcomes is small in some areas, and that some treatment possibilities haven't been investigated.

3. Materials and methods

3.1 Search strategy and inclusion/exclusion criteria

We conducted a systematic dental literature search until July 2011 in the Medline (PubMed) electronic databases. For this purpose a detailed search strategy for Medline was developed (Fig. 1.). Groupings of words were created which were internally combined with the Boolean term 'OR'. The first group consisted of the terms connected to the treatment: implant supported, dental implant, dental implantation, denture, overdenture, dental prosthesis, dental prostheses, prosthodontic, fixed prosthodontic, fixed prosthesis, fixed prostheses, and fixed partial denture. The second group consisted of the terms related to the outcomes of interest: satisfaction, patient satisfaction, patient outcome, quality of life, dental health surveys, health status measures, oral health, oral health–related quality of life, oral health impact profile and visual analog scale. These two groups of terms were then combined using the Boolean term 'AND'.
The titles and abstracts were screened by two of the authors (NP and KRS) to identify articles with the focus on the satisfaction and OHRQoL outcomes after implant-prosthodontic rehabilitation.
Full review of publications was done according to inclusion/exclusion criteria (Fig. 2.) and level of evidence (Fig. 3.).
The articles that did not evaluate the psychosocial outcomes were excluded, no matter if they included clinical outcomes. Further exclusion criteria were insufficient description of the sample characteristics or the therapeutic intervention, and missing or unclear hypotheses. Only the articles published in English were included since their international recognition.

Search #1	Search #2	Search #3: (#1) AND (#2)
implant supported (5922)	satisfaction (116664)	
dental implant (23213)	patient satisfaction (69431)	Limits Activated: English, Humans, All Adult: 19+ years, Review, Meta-Analysis, Randomized Controlled Trial, Controlled Clinical Trial, Clinical Trial
dental implantation (16242)	patient outcome (613578)	
denture (42373)	quality of life (164691)	
overdenture (2982)	dental health surveys (18037)	
dental prosthesis (81884)	health status measures (31232)	
dental prostheses (83109)	oral health (31232)	
prosthodontics (91866)	oral health–related quality of life (1123)	
fixed prosthodontics (11626)	oral health impact profile (624)	
fixed prosthesis (11626)	visual analog scale (64045)	
fixed prostheses (16266)		
fixed partial denture (8526)		
OR (106450 hits)	OR (905141 hits)	AND (1410 hits)

Fig. 1. Strategy for the electronic search (July 2011)

Inclusion criteria	Exclusion criteria
• Implant/prosthodontic focus • Use of a patient-based outcome (measurement of OHRQoL or satisfaction) • English language	• No clear research question or hypothesis • Missing or insufficient reporting of data • Patients under 18 years

Fig. 2. Inclusion and exclusion criteria

Ia	Evidence obtained from a meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomization
IIb	Evidence obtained from at least one other type of well-designed quasiexperimental study
III	Evidence obtained from well-designed non experimental studies, such as comparative, correlational, or case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

Fig. 3. Classification of the levels of evidence of the articles by the US AHCPR

3.2 Assessment of publication quality

The levels of evidence of the articles were classified following the guidelines of the US Agency for Health Care Policy and Research (AHCPR) and are presented in Fig. 3. (Agency for Health Care Policy and Research, 1992).

The number of studies with high evidence level has increased in the last two decades improving the quality of the conducted trials. Therefore, a satisfactory number of articles of the high levels of evidence, (level I and II) have fulfilled our criteria and are included in this chapter.

The whole range of publications of lower levels of evidence has been identified, but they were omitted since they were retrospective and non-experimental and may compromise the findings (Assunção et al., 2009).

3.3 Data collection and statistical analysis

All identified publications were obtained from the University Library and electronically. From each article the following data were collected: year of publication, level of evidence, follow-up period, patients number and their average age, intervention characteristics, jaw treated, main outcomes (general satisfaction, oral and general health-related quality of life), number and type of implants. For data analysis the SPSS statistical software was used.

4. Results

Through the MEDLINE search a total of 1410 articles were identified and abstracts were reviewed according to inclusion criteria. According to the aim of the study 10 publications fulfilled criteria for edentulous maxilla treatment, 72 for edentulous mandible treatment and 9 for partial edentulous treatment; all together 87 articles were detected for implant treatment outcomes.

The number of studies with a high level of evidence dealing with patient's satisfaction and OHRQoL has increased steadily over the last 2 decades (Fig. 4.). However, one of the major short-comings of these studies has been usage of non-standardized questionnaires, which results can not be compared between the studies. Only 11 studies have been identified that used a standardized questionnaire, such as OHIP (Allen & McMillan, 2003; Allen et al., 2001b; Attard et al., 2006; Awad et al., 2000, 2003b; Berretin-Felix et al., 2008; Heydecke et al., 2003b, 2005a; Kleis et al., 2010; Zani et al., 2009;) and SF-36 (Allen & McMillan, 2003; Heydecke et al., 2003b).

Period of publication	Percentage of studies
1960-1990	4,45 %
1991-1995	14,29 %
1996-2000	25,27 %
2001-2005	30,77 %
2006-2011	25,27 %

Fig. 4. Shematic diagram of articles considering evaluation criteria

The average number of included patients in all studies that met inclusion criteria was 66.59, with the mean age of 58.85 of all patients. More than the half of the studies used short

follow-up period of only few months, with the longest period of 10 years (Naert et al., 2004). Therefore, the everage follow-up period was 27.96 month. In most of the cases Branemark implants were inserted (14 articles), followed by Straumann implants (5 articles).

4.1 Treatment option for the edentulous maxilla

For implant-supported dentures in the edentulous maxilla two main options have been proposed; the fixed screw-retained implant denture (IFD) and the removable implant overdenture (IOD). Both fixed and removable prostheses can be attached to the edentulous maxilla, but different results concerning the efficacy of the treatment have been proposed. Both designs have been tested in clinical studies, but since the denture design shouldn't be selected randomly or only on the clinical findings, patient's preferences have been investigated as well.

Only 10 investigations with evidence level I and II have been published about patients' assessment of the implant rehabilitation outcomes in the edentulous maxilla (Table 1). VAS and categorical scales have been used to assess the outcomes after the treatment.

Concerning the IOD treatment, 7 found a higher level of satisfaction than for CD (Aarts et al., 2008; de Bruyn et al., 1997; Heydecke et al., 2003a, 2004; Naert et al., 1998; Watson et al., 1997; Zitzmann & Marinello, 2000;). The advantage of the this treatment is significantly better mastication and speech demonstrated (de Bruyn et al., 1997; Heydecke et al., 2003a, 2004; Naert et al., 1998, Watson et al., 1997), as well as comfort, stability, and esthetics (de Bruyn et al., 1997; Naert et al., 1998; Watson et al., 1997; Zitzmann & Marinello, 2000). On the other hand, de Albuquerque et al. (2000) demonstrated different outcomes. According to his within-subject crossover trial outcome ratings of the IOD were not significantly higher than for new maxillary CD. Therefore, de Albuquerque suggests that maxillary IOD should not be considered as a general treatment of choice in patients with good bony support. The result of the study also showed absence of the difference between dentures with and without the palate coverage.

This result is supported by the general fact that the lower percent of the patients complain on their maxillary than on mandibular CD. In other words, the satisfaction with maxillary dentures was higher than for mandibular dentures, which again reflects common clinical findings. The reason is better anatomical condition that provides better stability and retention of maxillary CD, therefore better function and higher satisfaction.

Concerning the IFD treatment, all 4 publications agree that patient satisfaction is higher after the treatment (de Bruyn et al., 1997; Fischer & Stenberg, 2006; Heydecke et al., 2003b; Peñarrocha et al., 2007). High patient satisfaction was confirmed by the fact that 90 % of the patients would undergo the same treatment again (de Bruyn et al., 1997). There is a strong belief among clinicians and patients that IFD provide greater patient acceptance and satisfaction than IOD. But the clinical studies currently available indicate the advantage of IOD over the IFD treatment, and concluded higher degree of general satisfaction, better esthetic, better speech quality and easier cleaning with IOD than with IFD (Heydecke et al., 2003b, 2004). In the within-subject crossover trial by Heydecke et al. (2003b) the majority of the patients chose the IOD at the end of the trial.

A prospective clinical trial (fixed vs. removable) by Zitzmann & Marinello (2000) demonstrated that the both denture designs were associated with significant improvements in comfort (fit), stability and retention, function, esthetics and appearance, taste, speech, and

self-esteem. No difference was found between the patients assessment of these two treatment option. However, the results indicated that patients after receiving IOD experienced greater differences between pretreatment and post treatment scores for the parameters esthetics, taste, and speech.

It would be very interesting to analyze the cost-benefit of each treatment option, but the number of these studies is very low. One study demonstrated that the treatment cost per unit was significantly higher in IFD than in IOD group of patients (Zitzmann & Marinello, 2000). The overall positive results from the VAS questionnaire indicate that cost-utility and cost-benefit justify the expense in this 6-months period. The author suggested that the number of years that dentures last should be included, as well as the observation period should be prolonged to fully assess the cost of the treatment.

Clinical studies including the speech improvement showed advantage of IOD treatment. Heydecke et al. (2004) demonstrated in their within-subject crossover clinical trial that the speech is often perturbed after the treatment. Placement of maxillary long-bar IOD, no matter of palate coverage, produced a significantly higher percentage of sounds correctly than with IFD. Similar findings were published in other studies, where the IOD patients assessed speech with high ratings after the treatment (Heydecke et al., 2003b; Naert et al., 1998; Zitzmann & Marinello, 2000).

Placement of more implants seems to have a great role in maxilla, since the most studies included implant-retained hinging overdentures on four implants with the promising results (de Albuquerque et al., 2000; Naert et al., 1998). Some authors also presented cases with 5 to 6 inserted implants with high rating results (Fischer & Stenberg, 2006). The results indicate that the maxillary IOD supported by multiple implants may provide patients with better oral function than IFD treatment. (Heydecke et al., 2003b).

Many different types of attachments have been used for implants. For maxilla low number of studies was available. A bar showed satisfactory results and high patients ratings. Therefore, a use of a long-bar (de Albuquerque et al., 2000; Heydecke et al., 2003b) or just inter-implant bar attachment (Watson et al., 1997) was proposed as a reliable retention solution.

Furthermore, the 64.7% of the participants preferred the physiologic occlusion, while the 35.3% preferred the lingualized occlusion (Aarts et al., 2008). However, when the general satisfaction, general ability to chew and general function were analyzed together no significant differences between the occlusion concepts were observed.

Type of implant has been a focus of the study by Peñarrocha et al. (2007), where a patient satisfaction was compared between a group with zygomatic implant-supported IFD and the other group with conventional implants. General satisfaction was similar, but the patients in the zygomatic group demonstrated higher scores for esthetics.

The predictability of the loading protocols has been well documented, but only one study demonstrated patient satisfaction depending on the time of implant loading. A study by Fischer & Stenberg (2006) presented that the early loading protocol is a viable alternative to the standard protocol in the rehabilitation of the edentulous maxilla patients concerning the patient's point of view.

The general opinion is that the implants in the edentulous maxilla are a recommended treatment option, no matter if the IOD or IFD has been used as a prosthodontic suprastructure, especially for the patients that have a problem to adapt to CD (de Albuquerque et al., 2000; Heydecke et al., 2003b; Naert et al., 1998).

Outcome	Removable implant overdenture	Fixed implant denture
General satisfaction	- Very high ratings (Heydecke et al., 2003b; Naert et al., 1998; Watson et al., 1997) - High ratings (Aarts et al., 2008; Watson et al., 1997), - High improvement, ratings the same as for CD, no difference with and without palate (de Albuquerque et al., 2000)	- High satisfaction (de Bruyn et al., 1997; Fischer & Stenberg, 2006; Peñarrocha et al., 2007), - Very high ratings 3-years post treatment (de Bruyn et al., 1997), - Significantly less satisfaction as with IOD (Heydecke et al., 2003b)
Esthetics	- Great difference between pretreatment and post treatment scores (Zitzmann & Marinello, 2000), - Very high ratings (Naert et al., 1998)	- Very high ratings 3-years post treatment (de Bruyn et al., 1997), - Significantly lower ratings comparing to IOD (Heydecke et al., 2003b)
Chewing	- Very high ratings (Naert et al., 1998), - Significantly better than CD (Heydecke et al., 2003b, 2004; Watson et al., 1997)	- 90% have optimal chewing (de Bruyn et al., 1997), - High satisfaction (Heydecke et al., 2003b)
Cleaning	- Easier to clean compared to IFD (Heydecke et al., 2003b)	- Significantly harder to clean than IOD (Heydecke et al., 2003b)
Stability, Comfort	- Very high ratings (Naert et al., 1998; Watson et al., 1997; Zitzmann & Marinello, 2000)	- Optimal for 90% of patients (de Bruyn et al., 1997)
Speech	- Better pronunciation than IFD (without difference with and without palate) (Heydecke et al., 2004), - Very high ratings (Naert et al., 1998; Watson et al., 1997), - Better speak quality compared to IFD (Heydecke, 2003b), - Great difference between pretreatment and post treatment scores (Zitzmann & Marinello, 2000)	Significantly worse than IOD (Heydecke et al., 2003b)
Taste	Great difference between pretreatment and post treatment scores (Zitzmann & Marinello, 2000)	
Cost		Treatment costs per unit were significantly higher than in IOD (Zitzmann & Marinello, 2000)

Table 1. Edentulous Maxilla – treatment outcomes

4.2 Treatment option for the edentulous mandible

Until recently, the only option to treat edentulousness was by giving the patient removable CD. The main problem in the beginning was a poor fitting, but contemporary technical procedures resulted with their more precise fabrication and comfortable wearing.

Outcome	Removable implant overdenture	Fixed implant denture
General satisfaction	- Significant improvement (Aarts et al., 2008; Allen & Locker 2002; Allen et al., 2001; Boerrigter et al., 1995a, 1995b; Bouma et al., 1997; Cibirka et al., 1997; Cune et al., 2005, 2010; Davis & Packer, 1999; De Grandmont et al., 1994; Ellis et al., 2009; Fenlon et al., 2001; Geertman et al., 1996b; Heydecke et al., 2003, 2008; Kapur et al., 1998; MacEntee et al., 2005; Mericske-Stern et al., 2009; Naert et al., 1997, 1999; Pan et al., 2008; Pera et al., 1998; Raghoebar et al., 2003; Rashid et al., 2011; Stellingsma et al., 2003; Tang et al., 1997; Timmerman et al., 2004; Walton et al., 1997, 2002; Wismeijer et al., 1997) - 96% of the patients satisfied (Pan et al., 2007)	- Significant improvement (De Grandmont et al., 1994) - Very high ratings 3-years post treatment (Allen & Locker, 2002; de Bruyn et al., 1997; Gregory et al., 1990) - Significant improvement, confidence in themselves, part of their body (Blomberg, 1985; Walton et al., 2009;)
Esthetics	- Significant improvement (Cibirka et al., 1997; De Grandmont et al., 1994; Watson et al., 1997; Fenlon et al., 2002; Walton et al., 2002)	- Significant improvement (Blomberg, 1985; de Bruyn et al., 1997; De Grandmont et al., 1994; Walton et al., 2009;)
Chewing	- Significant improvement in chewing hard and soft foods (Allen & Locker, 2002) - Significantly better than CD (Awad et al., 2000; Geertman et al., 1996) - Improved chewing (Boerrigter et al., 1995a, 1995b; Cibirka et al., 1997; De Grandmont et al., 1994; Fenlon et al., 2002; Kapur et al., 1998; Meijer et al., 2001; Pera et al., 1998; Raghoebar et al., 2003; Rashid et al., 2011; Roumanas et al., 2003; Tang et al., 1997; Walton et al., 2002; Watson et al., 1997; Wismeijer et al., 1997)	- Optimal chewing function (Blomberg, 1985; De Grandmont et al., 1994; Gregory et al., 1990) - Problems decreased (de Bruyn et al., 1997; Walton et al., 2009) - Significantly better than CD (Allen Locker, 2002)
Cleaning	- Decisive factor in comparison to IFD (De Grandmont et al., 1994)	- Difficult cleaning in comparison to IOD (De Grandmont et al., 1994)

Outcome	Removable implant overdenture	Fixed implant denture
Stability, Comfort	- Good retention (with bar and ball attachment) (Naert et al., 1997; 1999) - Two implants and ball attachments less satisfied than bar splinted implants (Timmerman et al., 2004) - Improved comfort (Burns et al., 1995; Kapur et al., 1998; Meijer et al., 2001; Pan et al., 2007; Tang et al., 1997; Walton et al., 2002; Watson et al., 1997; Wismeijer et al., 1997) - Bar improved comfort (Mericske-Stern et al., 2009) - Better in long-bar overdenture supported by more implants (Tang et al., 1997) - High comfort with ball (Rashid et al., 2011)	- Optimal (Blomberg, 1985; de Bruyn et al., 1997; Gregory et al., 1990; Walton et al., 2009)
Speech	- Significant improvement (Cibirka et al., 1997; De Grandmont et al., 1994; Rashid et al., 2011; Watson et al., 1997; Wismeijer et al., 1997;)	- Significant improvement (Blomberg, 1985; de Bruyn et al., 1997; De Grandmont et al., 1994; Walton et al., 2009;)
Cost	- More cost-effective than CD (Attard et al., 2006) - No difference in cost between immediate and conventional loading protocol (Attard et al., 2006)	
OHRQoL	- Significant improvement (lower post-treatment OHIP scores) (Awad et al., 2000) - High (Allen & Locker, 2002; Allen et al., 2001, 2006; Attard et al., 2006) - Better in long-bar overdenture supported by 4 implants than in two-implant hybrid bar overdenture (Tang et al., 1997) - Significant improvement one-year after the treatment (Bouma et al., 1997; Kleis et al., 2010) - Improved (Cibirka et al., 1997) - Improved by 33% (Heydecke et al., 2005b).	- Significant improvement (OHIP49-31-point within group) (Allen & Locker, 2002) - Equally satisfied as IOD (Zani et al., 2009) (OHIP)

Table 2. Edentulous Mandible - treatment outcomes

Despite the great improvement in denture quality, poor retention of the mandible denture is still a great problem for many patients, especially in the patient with a great loss of alveolar bone volume, intolerance of the denture or chewing problems, that led to feelings of insecurity and inferiority and considerable psycho-social problems (Albrektsson et al., 1987). For this population a CD is unsatisfactory treatment.

Forty-four investigations have been published with evidence level I and II concerning the rehabilitation of the edentulous mandible with implant-supported complete dentures (Table 2.). All the publications found a higher level of satisfaction for IOD, while no article confirmed the same level of satisfaction as for CD treatment (Fig 4). Concerning the IFD treatment, all 7 publications agree that patient satisfaction is higher after the treatment (Allen & Locker, 2002; Blomberg, 1985; Blomberg & Lindquist, 1983; de Bruyn et al., 1997; De Grandmont et al., 1994; Gregory et al., 1990; Zani et al., 2009). Zani et al. (2009) assessed IFD treatment equally satisfactory as IOD treatment, while De Grandmont et al. (1994) determined cleaning as a decisive factor in comparison to IOD.

In the most of the articles new denture in the upper jaw has been produced (Awad et al., 2000; Cune et al., 2005; de Bruyn et al., 1997; De Grandmont et al., 1994; Heydecke et al., 2003; Roumanas et al., 2003; Tang et al., 1997), giving a more objective results of the mandibular IOD. Still, the better fitting of the new upper CD doesn't mean that the presence of any problems should be attributed to the lower IOD. Furthermore, most of the studies included control group with a lower CD (Allen et al., 2006; Awad et al., 2000; Cibirka et al., 1997; Geertman et al., 1996b; Heydecke et al., 2003; Kent & Johns, 1991; Kiyak, et al., 1990; Pan et al., 2008; Pera et al., 1998; Raghoebar et al., 2003; Roumanas et al., 2003) to compare the results and present the advantage of the IOD. Absence of the control group, like the study by Walton et al. (2009), may compromise the results, making them less objective and reliable.

Studies that compared implant-supported dentures with CD demonstrated higher patients' general satisfaction and OHRQoL after implant insertion (Aarts et al., 2008; Allen & Locker, 2002; Allen et al., 2001, 2006; Awad et al., 2000; Blomberg, 1985; Boerrigter et al., 1995a, 1995b; Bouma et al., 1997; Burns et al., 1995; Cibirka et al., 1997; Davis & Packer, 1999; De Grandmont et al., 1994; Ellis et al., 2009; Emami et al., 2009; Fenlon et al., 2002; Geertman et al., 1996a, 1996b; Gregory et al., 1990; Heydecke et al., 2003, 2005b, 2008; Kapur et al., 1998; Kleis et al., 2010; Meijer et al., 1999; Naert et al., 1997, 1999; Pan et al., 2008; Pera et al., 1998; Roumanas et al., 2003; Tang et al., 1997; Walton et al., 2002; Wismeijer et al., 1997). Based on two meta-analysis (Emami et al., 2009; Thomason, 2010) IOD treatment has been confirmed as more satisfying for edentulous patients than new CD, resulting with the improved OHRQoL. Still the magnitude of IOD effect stayed uncertain. Therefore, Emami et al. (2009) proposed inclusion of cost-effectiveness analyses to better assess the impact of conventional and implant treatments.

According to Heydecke et al. (2008), in IOD patients post treatment satisfaction meets the pretreatment expectation (especially in middle-aged patients), but it is not the case in CD group (Heydecke et al., 2003). This confirms that the patients have been informed about the advantages of the IODs. Kapur et al. (1998) demonstrated overall satisfaction as well as improved chewing and comfort. Therefore, he considered IOD for patients experiencing chronic irritation and/or chewing discomfort.

Since the implant therapy includes surgical pretreatment and higher cost, some patients refuse implants despite having problems with their old dentures (Ow et al., 1997). We also

have to consider that in the most of the cases the problem is not in dentures as a treatment option but the way the treatment has been done. Therefore we shouldn't eliminate the denture as a treatment option, instead to repeat the denture should be the first treatment option (Strassburger et al., 2006).

To verify the advantages of implants, an assessment of OHRQoL outcomes after IOD treatment has been done. Awad et al. (2000) and Allen et al. (2006) attempted to investigate the impact of implant treatment on OHRQoL (measured with OHIP questionnaire) and reported significant improvement among subjects who received IOD. In addition, Heydecke et al. (2005b) reported improvement of OHRQoL by approximately 33%, what justifies the difference in cost according to the author. Furthermore, a series of publications confirms the improvement of OHRQoL (Assunção et al., 2007; Awad et al., 2000, 2003b; Berretin-Felix et al., 2008; Boerrigter et al., 1995a, 1995b; Burns et al., 1994; Cibirka et al., 1997; Fenlon et al., 2002; Geertman et al., 1996; Heydecke et al., 2003; Kapur et al., 1998; MacEntee et al., 2005; Meijer et al., 1999, 2003; Melas et al., 2001; Pera et al., 1998; Raghoebar et al., 2003; Thomason et al., 2003; Walton et al., 2002; Wismeijer et al., 1997), while fewer studies concluded that there is no differences in OHRQoL between IOD and CD (Allen et al., 2001; Assunção et al., 2007; Bouma et al., 1997; Kapur et al., 1999; Kimoto & Garrett, 2005; Wismeyer et al., 1995).

The implant-prosthodontic treatment results also in improvement of retention and stabilization of dentures (Salonen, 1994), furthermore their function and OHRQoL (Allen et al., 2001; Att & Stappert, 2003; Awad et al., 2003; Heydecke et al., 2003). Some authors confirmed that the use of implant supported dentures provides more comfort in comparison to conventional ones (Heydecke et al., 2005). According to Boerrigter et al. (1995a, 1995b) the absence of the satisfactory stability and retention is the greatest problem of CD, and the reason why so many edentulous people are dissatisfied with their lower CDs. Resulting functioning problems, as well as other factors (denture quality, the small denture bearing area, previous denture experiences, the patient's personality and psychologic well-being) are also important problems why more and more patients are seeking for IOD treatment as a solution for their problems. After construction of a lower IOD general functional complaints significantly diminish, confirming the advantage of the IOD over the CD (Boerrigter et al., 1995a). A positive response to treatment was confirmed by the 96% of the patients that felt satisfied with new IOD and reported their fit comfortably (Pan et al., 2007). Concerning the sex differences, they remained in the CD group after the 12 months observation period, but in the IOD group the both, males and females, rated their satisfaction as equal (Pan et al., 2008).

De Grandmont et al. (1994) observed significant improvement after implant treatment and demonstrated higher scores (VAS scale) to both types of implant supported prostheses (IOD and IFD) than to their original CD for general satisfaction, as well as for the chewing, esthetic, cleaning and speech. Patients paid more attention to what they ate with the CD and much less using the implant-supported dentures because of the stability provided. Concerning the fit and retention again the implant-supported dentures were evaluated as better. Improving the stability and retention patients don't have to support their CD with the tongue and cheeks and use them for better pronunciation. Therefore, the speech was rated as better as well.

The most of the publications deal with mastication problems that greatly determine the general satisfaction with IOD. These implant-supported dentures offer the possibility of overcoming some of the limitations of CD in terms of chewing efficiency (Allen & Locker,

2002; Boerrigter et al., 1995a; Fenlon et al., 2002; Geertman et al., 1996; Rashid et al., 2011; Watson et al., 1997;). Subjects who received IOD reported significant improvement in chewing hard and soft foods, but still 30–50% of them avoided eating hard food. This suggests that successful prosthetic rehabilitation improved chewing ability does not necessarily result in a satisfactory food selection and diet (Allen & Locker, 2002). Roumanas et al. (2003) proposed dietary counseling as a part of implant and complete denture therapy. After the adaptation period to new IOD, patients only consumed less difficult-to-chew foods than with their original CD, what was more frequent in lower jaw (Roumanas et al., 2003).

The superiority of the implant treatment in patients with atrophic ridge has been a focus of certain number of studies. At the l-year evaluation study by Boerrigter et al. (1995b) IODs were compared to CDs, as well as to CDs made after a vestibuloplasty and deepening of the floor of the mouth. Results indicated vastibuloplasty as a more satisfactory solution for denture-related problems than CD, but still IOD group showed better scores and superior results. In his multicentre randomised clinical trial (RCT) Boerrigter et al. (1995a) once again confirmed dental implants to provide a more satisfactory solution to denture-related problems for patients with a severely resorbed mandible. These findings were confirmed in the study by Pera et al. (1998), who reported high satisfaction and masticatory efficiency after implant-anchorage of the denture in atrophic ridge. Furthermore, the study by Bouma et al. (1997) demonstrated that the denture satisfaction was more favorable in the IOD group when compared to the preprosthetic surgery group to enlarge the denture-bearing area. One year after treatment, all three dental treatment modalities had a comparably positive effect on dental health-related quality of life (Wismeyer et al., 1995). Therefore, the implant-retained overdentures are a favourable treatment modality for edentulous patients with lower denture problems (Raghoebar et al., 2003).

Several studies concerning the type of implant are available. Geertman et al. (1996a) observed the differences between the transmandibular and the endosseous implant with respect to satisfaction, complaints, and subjective chewing ability, and found no statistical significance. Similar findings were presented by Meijer et al. (2001). Analyzing the advantage of these implants over the augmentation of the mandible followed by four endosseous implants, the 1-year evaluation study in extremely resorbed mandible found no difference between these three treatment modalities. However, in terms of discomfort and pain during the augmentation using an autologous bone graft from the iliac crest followed by inserting four endosseous implants appeared the least favorite option (Stellingsma et al., 2003).

Implant immediate and early loading protocols are becoming more and more popular because of the shorter treatment period, no matter of fixed or removable denture suprastructure. The advantages are less appointments, faster treatment and reduction of costs. Attard et al. (2006) compared different loading protocols with measured outcomes, such as degree of satisfaction and impact on quality of life. Significant improvement in perceived oral health status has been observed for both loading protocols (immediate and conventional loading), what confirms IOD as a more cost-effective treatment than CD (Attard et al., 2006). No difference in time cost was observed and the immediate protocol was not confirmed as a cheaper alternative.

In the most of the investigations 2 implants in the interforaminal region have been inserted supporting IOD (Assunção et al., 2007; Cune et al., 2010; Ellis et al., 2009; Meijer et al., 2001; Mericske-Stern et al., 2009; Naert et al., 2004; Rashid et al., 2011; Timmerman et al., 2004;).

Most of the articles confirmed this treatment option as a reliable and satisfactory that improves OHRQoL of patients, proposing this option as a standard procedure. Measured by OHIP questionnaire higher values were detected in implant patients (Awad et al., 2000; Heydecke et al., 2003b, 2008; Kleis et al., 2010). In some studies more implants were inserted, like four or five (De Grandmont et al., 1994; Stellingsma et al., 2003), but insertion of more implants doesn't seem to further increase patients' satisfaction (Geertman, 1996b). Meijer et al. (2001) demonstrated that putting 4 implants no difference in comparison to 2- implant systems will occur.

When the type of retention was analyzed, it was observed that in the most of the publications a bar or a ball were used as an attachment connection to overdenture. The most used treatment option was two-implant IOD retained by ball attachments and single- or triple-bar. Some studies suggest that a mandible overdenture retained by 2 implants with a single bar may be the best treatment strategy for edentulous people with atrophic ridges (Naert et al., 2004; Timmerman et al., 2004), while some authors presented the results of high satisfaction with the new dentures no matter of the attachment connection (a bar or a ball) (Cune et al., 2010; MacEntee et al., 2005; Naert et al., 1997, 1999).

The widely accepted treatment option is insertion of 4 implants and overdenture retained by a cast bar with extracoronal attachments, what resulted with good denture fit (Pan et al., 2007). According to Wismeijer et al. (1995) no significant difference was found between the three treatments strategies (two implants with ball attachments, two implants with an interconnecting bar, and four interconnected implants); therefore, the simple implant treatment such as an overdenture retained by two ball attachments author suggested as sufficient treatment. Recently, high and comparable satisfaction has been presented inserting a single midline implant; therefore this option was suggested as an alternative to the customary two-implant overdenture for maladaptive denture patients (Walton et al., 2009).

Magnets as an attachment system have been presented in limited number of publications. Although they provide viable treatment options and high general satisfaction (Davis & Packer, 1999; Naert et al., 1997, 1999;), still the low retention force (Naert et al., 1997, 1999) and unsatisfactory comfort (Naert et al., 2004) makes it the last desirable option. This attachment option was included in the study by Cune et al. (2005). The results showed that patients strongly preferred bar-clip (10/18 subjects) and ball-socket attachments (7/18 subjects) over magnet attachments (1/18 subjects) (Cune et al., 2005). Similar results were presented by Burns et al. (1995) and Ellis et al. (2009), i.e. a strong preference for the ball over the magnets. The magnetic attachment has a low resistance to lateral forces, and the subsequent immediate loss of retention might be the reason for such a low satisfaction with this type of retention.

Locator® attachment system has been recently used in dentistry, but there is a lack of clinical studies on this attachment system for two-implant-retained overdentures in the edentulous mandible. Only one study compared it with two other traditional designs and no significant difference in the patients' OHRQoL was found between them (Kleis et al., 2010).

Tang et al. (1997) compared a within-subject crossover clinical trial for two forms of removable prostheses which are frequently prescribed for the edentulous mandible: a long-bar overdenture supported by 4 implants and a two-implant hybrid bar overdenture. Subjects rated significantly better general satisfaction, quality of life, stability, retention,

comfort, esthetics and chewing using long-bar overdenture. This was expected since the two implant hybrid denture transfers a part of the occlusal forces on the bearing area, while the longer bar accepts almost all forces. To establish an adequate occlusal table the distal cantilever extensions (10 to 20 mm) could be created (De Grandmont et al., 1994), or U-shaped triple-bar construction with 2 cantilever extensions (Meijer et al., 2001). These options were confirmed as reliable ones and rated with high satisfaction by the patients.
A limited number of studies confirmed improvement after IFD treatment (Allen & Locker, 2002; Blomberg, 1985; Cibirka et al., 1997; de Bruyn et al., 1997; De Grandmont et al., 1994; Gregory et al., 1990; Walton et al., 2009). The majority of them state that there has been a significant improvement in their lives, that they have regained confidence in themselves, and that, in contrast to a conventional denture, they accept the IFD as part of their body. High percentage of patients (90%) rated comfort and stability as «optimal» (Blomberg, 1985; Walton et al., 2009). There was considerable evidence of improved well-being of patients, who felt more secure following treatment and, as a result, their personal and social relationships improved (Gregory et al., 1990).
The most clinicians believe that IFD constitute generally the treatment of choice for edentulous patients, providing better comfort (fit), stability and retention; therefore providing better function and esthetics. On edentulous mandible patients this assumption does not appear to hold. De Grandmont et al. (1994) demonstrated in a within-subject cross-over trial that the scores given for both types of prostheses did not differ with regard to general satisfaction, esthetics, and ability to speak and to chew. This confirms IOD as a equally satisfactory option (Zani et al., 2009), concerning the cleaning even the superior to IFD (De Grandmont et al., 1994). Similar results were published by Feine et al., (1994) in their within-subject cross-over clinical trial, where they observed that IOD patients rated ease of cleaning as the most important factor, while the IFD group rated stability and ability to chew as significantly better than with IOD. Perhaps the reason is construction that allows easier cleaning but also deposition of food, since a 2-3-mm relief between the residual ridge and the IFD was left free. Feine et al. (1998) concluded also that about half of all patients preferred IOD to IFD.
When comparing chewing outcome the most clinicians would prefer IFD. According to De Grandmont et al. (1994) no significant differences between the IOD and IFD were detected except for the difficulty of chewing carrot, apple, and sausage, which were rated with higher values in IFD patients. The results confirm the clinical impression that IFD are more efficient than IOD for eating harder types of foods. Despite this result level of general satisfaction with the IFD wasn't assessed as higher. In other words patients in this within-subject cross-over clinical trial were equally satisfied with both types of implant-supported dentures, despite the general clinical belief.
Based on the findings of these studies, the general conclusion is that mandibular overdentures are more satisfactory than conventional dentures, and 90% of patients indicated that they were ready to repeat the treatment if necessary (de Bruyn et al., 1997).

4.3 Treatment options for the partially edentulous patients

Dental implants are expanding their use among partially edentulous patients. However, whether implants can improve the OHRQoL of these patients has not been sufficiently examined (Table 3.). Kuboki et al. (1999) presented higher OHRQoL levels for dental implant patients than those with removable partial denture or no restoration. The results of

this study confirmed the ability of IFD restoration to promote oral condition related quality of life of unilateral mandibular distal extension edentulism.

Outcome	Fixed implant partial denture
General satisfaction	- 90% satisfied (Kapur, 1991), - Highly satisfied (de Bruyn et al., 1997; Farzad et al., 2004; Schropp et al., 2004; Yi et al., 2001)
Esthetics	- Improved and satisfactory, the same as in the control group with natural teeth (Yi et al., 2001) - High (de Bruyn et al., 1997) - 7% better than RPD (Kuboki et al., 1999)
Chewing	- 28% better than RPD (Kuboki et al., 1999) - Improved and satisfactory, the same as in the control group with natural teeth (Yi et al., 2001) - High (de Bruyn et al., 1997; Kapur, 1991)
Cleaning	- More difficult than RPD (Feine et al., 2002) - Satisfactory (de Bruyn et al., 1997; Kapur, 1991)
Stability, Comfort	- 14% better than RPD (Kuboki et al., 1999) - Improved and satisfactory, the same as in the control group with natural teeth (Yi et al., 2001) - Problem eliminated (de Bruyn et al., 1997) High (Kapur, 1991)
Speech	- 10% better than RPD (Kuboki et al., 1999) - Improved and satisfactory, the same as in the control group with natural teeth (Yi et al., 2001) - Satisfactory (de Bruyn et al., 1997; Kapur, 1991)
OHRQoL	- Significant improvement in shortened dental arch (OHIP) (Kuboki et al., 1999)

Table 3. Partially Edentulous Jaw - treatment outcomes

Wearing dentures is often a not pleasing experience for the patients because of unsatisfactory fit and stability. As a result of unsatisfactory retention comfort problems occur. Therefore, Kapur (1991) observed that the improvement in social life has been better after IFD treatment. The results of de Bruyn et al. (1997) also demonstrated high patient's satisfaction since comfort problems diminished after IFD treatment. Concerning the cleaning, studies demonstrated more difficult cleaning with IFD than with although the cleaning was easier in removable partial denture group (Feine et al., 2002; Kapur, 1991).
High VAS values regarding satisfaction were also presented for the implant-supported crown (Schropp et al., 2004). Improved and satisfactory oral function after rehabilitation has been confirmed also in periodontally compromised patients (Yi et al., 2001). Comparing the results between the IFD group and dentate group, no significant difference was observed for mastication, phonetics, chewing comfort and aesthetics. Some studies published in this field

examined difference in satisfaction depending of the loading protocol. In general, the patients were highly satisfied with the outcome of the both loading protocols (early and delayed) (Schropp et al., 2004; Schropp & Isidor, 2008). Still, the appearance with the IFD was assessed as significantly greater in the immediate group than in the delayed group (Schropp et al., 2004).
The results of the analyzed publications allow us to conclude that patients were generally very satisfied with IFD treatment outcome in the posterior mandible (Farzad et al., 2004; Kapur, 1991). Therefore, IFD treatment is proposed as a reliable treatment option in partially edentulous patients.

5. Conclusion

This review attempted to identify published articles describing the effect of implant and prosthodontic treatment on patient satisfaction and OHRQoL outcomes. The data and conclusions of the high level evidence publications were collected and summarized with the aim to establish the general treatment benefits in comparison to other therapy solutions and to confirm it as a reliable and superior treatment option. Patient-centered approaches to the assessment of treatment efficacy are highly relevant to today's prosthodontist, whose goals are the improvement of function and quality of life for their patients. The implementation of implant therapy has further induced the number of studies to assess the patient's opinion about this treatment option. It was hypothesized that the number of studies based on high-level evidence, using patient-based outcomes in some areas is small and that some treatment possibilities haven't been investigated.
The high number of publications from this area confirms progression in the last decades. Despite a huge number of OHRQoL studies, only few of them assessed specific prosthodontic treatments in edentulous areas and particular effects on the improvement of the OHRQoL in elderly population. Most studies on the OHRQoL investigated similar types of dentures (egg mandible 2 implants and bar or ball) and include middle-age groups. Methodically more specified studies are required to assess the outcomes of some specific fields of OHRQoL.
While improvement of OHRQoL has been reported for both treatment options (IOD and IFD), it is also important to demonstrate their superiority over the conventional treatments for every edentulous possibility in completely or partially edentulous arch. Therefore, all studies should include control group and patients should be observed for a longer period of time.
The effect of the technical correctness and quality of prosthetic restorations has also been scarcely investigated. This should be included as well to properly assess the advantages and cost-benefit of a specific treatment. Furthermore, to establish a direct comparison between the studies it would be necessary to standardize the sampling methodologies, meaning questionnaires and follow-up periods.
Within the limitation of the literature review, it can be concluded that most of the studies confirmed higher patient satisfaction and OHRQoL improvement using 2 implant bar and ball attachment mandibular IOD in comparison with CD. Four implants connected by a bar were showed as a reliable option for edentulous maxilla. In contrast to common belief, based on the results collected, placing IFD has not been confirmed as a superior treatment to IOD. This result was not expected, since the IFD treatment was stated as most likely to be physiologically and psychologically incorporated into the oral cavity.

Since most of the information available is limited to outcomes of IOD therapy in mandibular edentulous jaw, more randomized controlled trials studies are needed to obtain IFD effectiveness data, regardless of the jaw and number of the teeth that are missing. The data presented should help future researchers to develop and improve study designs with broader outcome measures that will support dentist to make appropriate therapeutic decisions for every individual patient.

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4

Association Between Tooth Loss and Cancer Mortality in Elderly Individuals

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1. Introduction

Over the past decade, much evidence has emerged showing an association between oral health and systemic health condition, though few have studied the relationship between impaired dental status and cancer mortality. Although tooth loss is a good clinical indicator of poor oral health because it is less prone to measurement error, results of epidemiological research using tooth loss as a measurement of oral health are limited, likely because periodontal disease has been a particular focus of attention in recent years. The aim of this study was to review the outcomes in other reports that suggest associations between dental status, especially tooth loss, and cancer mortality and morbidity. Furthermore, several potential mechanisms related to those associations are discussed.

2. Assessment of dental status: Which is better, tooth loss or periodontal disease?

Most studies published to date have used tooth loss and/or periodontal disease to assess dental status. However, a persistent problem with this point is that diagnosis of periodontal disease is subjective and not straightforward, and it is questionable whether periodontal indices such as probing can reliably reveal underlying disease status. First, the process of calibration between examiners performing periodontal assessments, with both probing and non-probing indices, is time consuming. When several dentists are used as examiners, they must be calibrated both before and during the survey using some of the same subjects or volunteer patients. The kappa value determined by replicate examinations by probing of periodontal tissue is generally not high, at most around 0.7 to 0.8. Second, different cut-offs for periodontal disease have been used (Hujoel et al., 2000; Wu et al., 2000). In contrast, measurment of the number of missing teeth is straightforward and seems to be a reliable indicator of dental health status. Therefore, in the present study, we focus on research that investigated the associations between tooth loss and cancer risk.

Tooth loss typically results from trauma, caries, or periodontal disease, with that in older individuals more likely to be caused by periodontal disease, while tooth loss in younger ages is usually caused by dental caries (Papapanou et al., 1996). Thus, we consider that tooth loss as described in this review is an indicator of periodontal disease and the

number of missing teeth can be viewed as an index of lifetime accumulation of poor oral health.

3. Methods for assessment of tooth loss

In general, 2 methods are used for assessment of tooth loss. One is an oral examination by a dentist or tooth counting by medical personnel, while the other is self-reporting by use of a questionnaire that includes the question, "How many teeth do you have remaining?". Three reports (Michaud et al., 2008; Hiraki et al., 2008; Stolzenberg-Sollomon et al., 2003) have been presented based on answers to that question, while 3 different reports (Cabrera et al., 2005; Tu et al., 2007; Abnet et al., 2005) were of results obtained by direct data collection using panoramic photographs or oral examinations. Previous report suggested that self-reported number of teeth is highly correlated with actual number of teeth found in clinical assessments of a general population (Douglass et al., 1991).

4. Relationship between tooth loss and cancer mortality

4.1 Tooth loss and all-site cancer mortality

To date, 4 known studies have reported the associations between tooth loss and risk of cancer death (Abnet et al., 2005; Cabrera et al., 2005; Tu et al., 2007; Michaud et al., 2008). When reviewing those articles, it is important to note carefully whether the outcomes investigated were morbidity or mortality, as the former 3 studies were based on mortality, while the most recent was based on the incidence of cancer, or morbidity. Here, we would like to present a step by step review of 3 of those reports (Table 1).

Authors	Year	Nation	Length	Sample size	Expose	Outcome	HR (95% CI)
Cabrera et al.	2005	Sweden	24 years	1,462 women	>10 missing teeth	Mortality	1.16 (0.90-1.49)
Michaud et al.	2008	USA	18 years	48,375 men	0-16 vs. 25-32 teeth	Morbidity	1.26 (1.15-1.38) 1.09 * (0.99-1.20)
Ansai, et al.	2010	Japan	12 years	697 80-yr-old	Edentulous vs. 20 or more teeth	Mortality	1.77 (0.76-4.17)

Table 1. Summary of longitudinal studies evaluating relationship between tooth loss and all-site cancer mortality/morbidity
*Fully adjusted model

The association between tooth loss and cancer mortality is controversial. A prospective cohort study of 1462 Swedish women study showed there were no associations between number of missing teeth and cancer mortality over a period of 24 years [hazard ratio (HR) 1.16, 95% confidence interval (CI) 0.90-1.49 per 10 missing teeth] after adjustments for age, waist-hip ratio, body mass index, smoking, age at first birth, parity, and husband's

occupational category, while there was a significant association between tooth loss and cardiovascular disease mortality (HR, 1.34, 95%CI, 1.05-1.71) after adjustments for the same confounding factors (Cabrera et al., 2005). A study of US male health professionals showed that fewer teeth at baseline was associated with a significant increase in incidence rate of total cancer for those with 0-16 teeth vs. those with 25-32 teeth (HR, 1.26, 95%CI, 1.15-1.38), with adjustments for age, ethnic origin, physical activity, history of diabetes, alcohol consumption, body mass index, geographical location, height, calcium intake, total calorific intake, red meat intake, fruit and vegetable intake, and vitamin D score (Michaud et al., 2008). However, in a fully adjusted model that included smoking history (never, past quit ≤10 years, past quit >10 years, current 1-14 cigarettes per day, 15-24 cigarettes per day, 25+ cigarettes per day) and pack-years, the association was insignificant for tooth loss (HR, 1.09, 95%CI, 0.99-1.20).

On the other hand, evidence from Asian populations is scarce and only 3 reports are known to date. One is a case-control study conducted in Japan (Hiraki et al., 2008), and the other 2 are prospective cohort studies showing an association between tooth loss and cancer mortality (Abnet et al., 2005; Ansai et al., 2010). The case-control study was based on a Hospital-based Epidemiologic Research Program in Japan, and investigated associations between tooth loss and incidence rates of 14 common cancers. Although the risk for total cancer was not described, their findings showed that a greater number of missing teeth was associated with increased risks of head and neck, esophageal, and lung cancers, and decreased risk of prostate cancer (Hiraki et al., 2008). Also, for head and neck and esophageal cancers, stratified analyses by sex and age showed clear associations between tooth loss and cancer risk in women and younger subjects, but less clear associations in men and older subjects. In another Japanese survey, which was our prospective cohort study of 697 Japanese individuals (80 years old at baseline), there were no associations between number of teeth (treated as a categorical variable) and cancer mortality during a 12-year follow-up period (HR, 1.77; 95% CI, 0.76-4.17 for edentulous vs. those with 20 or more teeth), while a significant association was observed between the number of teeth and all causes of mortality (HR, 1.66; 95% CI, 1.17-2.35 for edentulous vs. those with 20 or more teeth), with adjustments for gender, smoking status, serum total cholesterol, fasting serum glucose, body mass index, and systolic blood pressure (Ansai, 2010). A population study conducted in China did not mention an association between tooth loss and total cancer mortality, though it showed that tooth loss significantly increased the risk of death from upper gastrointestinal cancer (HR, 1.35, 95%CI, 1.14-1.59), while there were no significant associations between tooth loss and death from other cancers (Abnet et al., 2005).

4.2 Tooth loss and specific-site cancer mortality

As noted above, epidemiologic studies have associated tooth loss with a higher risk of cancer. Next, recent evidence is presented concerning the associations between tooth loss and morbidity/mortality due to cancer in specific sites (Table 2).

4.2.1 Tooth loss and oral cancer morbidity

There are no known reports regarding associations between tooth loss and mortality due to oral cancer. Although case-control studies have been reported, the relationship between

Authors	Year	Nation	Length	Sample size	Expose	Outcomes	HR (95% CI)
Abnet et al.	2005	China	15 years	29,584	Median number of teeth	Gastric cancer mortality	1.35 (1.14-1.59)
Hujoel et al.	2003	USA	10 years	11,328	Edentulous	Lung cancer mortality	1.37 (0.72-2.60)
Michaud et al.	2008	USA	18 years	48,375 men	0-16 vs. 25-32 teeth	Lung cancer morbidity	1.70 (1.37-2.11)
Tu et al.	2007	UK	57 years	9,569 men, 2,654 women	Number of missing teeth	Lung cancer mortality	1.01 (0.97-1.06)
Stolzenberg-Solomon et al.	2003	Finland	12 years	29,104 men	Edentulous vs. 0-10 missing teeth	Pancreatic cancer morbidity	1.63 (1.09-2.46)
Michaud et al.	2008	USA	18 years	48,375 men	0-16 vs. 25-32 teeth	Pancreatic cancer morbidity	0.91 (0.56-1.47)
Michaud et al.	2007	USA	18 years	48,375 men	Past 4-year tooth loss	Pancreatic cancer morbidity	1.61 (1.13-2.31)
Michaud et al.	2008	USA	18 year	48,375 men	0-16 vs. 25-32 teeth	Prostate cancer morbidity	0.70 (0.50-0.97)
Michaud et al.	2008	USA	18-yr	48,375 men	0-16 vs. 25-32 teeth	Skin melanoma morbidity	0.62 (0.41-0.93)

Table 2. Summary of longitudinal studies evaluating relationships between tooth loss and specific-site cancer mortality/morbidity

tooth loss and mortality due to oral cancer remains unknown. Nevertheless, strong associations between tooth loss and oral cancer even after adjusting for smoking and alcohol

consumption have been noted (Zheng et al., 1990; Bundgaard et al., 1995; Marshall et al., 1992; Garrote et al., 2001; Rosenquist et al., 2005), and those reports were recently reviewed (Meyer et al., 2008). After removing smoking and alcohol consumption as factors, those results showed that tooth loss increases the risk of oral cancer by 2- to 3-fold. In addition, those findings revealed significant interactions between tooth loss and smoking and alcohol use. A more extensive study recently explored the relationship between oral health status and squamous cell carcinoma of the head and neck and esophagus (Guha et al., 2007). Their findings indicated that as oral health condition worsened, the risks of cancers of the head, neck, and esophagus increased. However, scant information regarding those associations in Asian populations is available. One report noted a significant association between tooth loss and esophageal squamous cell carcinoma in a Chinese cohort (Abnet et al., 2001), while Hiraki et al. reported a significant positive association between tooth loss and risk of head and neck and esophageal cancers in a Japanese population after adjustment for potential confounders in a case-control study (Hiraki et al., 2008).

4.2.2 Tooth loss and gastric cancer mortality

Two early studies indicated that tooth loss may be associated with gastric cancer incidence (Wolff & Lauter, 1976; Demirer et al., 1990). In the 21st century, 2 studies from China provided information on the link between tooth loss and gastric cancer (Abnet et al., 2001, 2005). The population for both studies was recruited from the Linxion province, where provision of dental care is poor and there is a high prevalence of gastric cancer. In the former study, tooth loss, especially in subjects below the age of 50 years, was significantly associated with gastric non-cardia adenocarcinoma (HR, 3.3, 95%CI, 0.85-12.4), following adjustments for age, gender, smoking, and alcohol use. In another follow-up study of the same population, there was a significant relationship found between tooth loss and mortality due to gastric cancer, as tooth loss was associated with a 35% increased risk. Also, the risk for gastric cancer associated with tooth loss was higher in male never-smokers than in male smokers (HR, 1.59, 95% CI, 1.03-2.45; HR, 1.39, 95% CI, 1.06-1.83, respectively). In contrast, there was not a significant association in females. Age was also shown to be a significant effect modifier of gastric cancer mortality and tooth loss association. In that study, 547, 1121, and 957 cases of gastric cancer were found in subjects aged <50, 50-59, and ≥60 years, respectively, with HRs of 1.25 (95% CI, 1.06-1.48), 1.18 (95% CI, 1.05-1.33), and 0.99 (95% CI, 0.87-1.13), respectively, for those 3 age strata.

4.2.3 Tooth loss and lung cancer mortality

Three studies of the association between tooth loss and lung cancer mortality/morbidity have been presented (Hujoel et al., 2003, Tu et al., 2007; Michaud et al., 2008). The earliest presents data from the NHANES I epidemiological follow-up study (Hujoel et al., 2003). The subjects in that study underwent periodontal assessments based on the Russell Index, and included those with and without periodontal disease, gingivitis, and an edentulous condition. Those with an edentulous condition, which was defined as total tooth loss, had an elevated risk for mortality due to fatal neoplasms in the lung and bronchus. After adjustments for demographic factors and risk factors for lung cancer, edentulous condition had an HR of 1.37 (95% CI, 0.72-2.60). In the survey of health professionals in the US, fewer

teeth at baseline (0-16) was associated with an increase in morbidity from lung cancer (HR, 1.70, 95% CI, 1.37-2.11) as compared to subjects with 25-32 teeth (Michaud et al., 2008). However, in never-smokers, no association was noted for lung cancer. On the other hand, there was no significant association between tooth loss as a continuous variable and lung cancer mortality in a Scottish study, both with adjustment for baseline smoking status (HR, 1.01, 95% CI, 0.97-1.06) and without (HR, 1.02, 95% CI, 0.98-1.07) (Tu et al., 2007). Even when tooth loss was treated as a categorical variable, similar results have been obtained, as HRs were 1.29 (95% CI, 0.81-2.06) for 5-8 missing teeth and 1.36 (95% CI, 0.71-2.61) for ≥9 missing teeth, following adjustments (Tu et al., 2007).

4.2.4 Tooth loss and pancreatic cancer incidence

There is increasing evidence that tooth loss is a risk factor for pancreatic cancer. A Finnish study showed that tooth loss, especially edentulous condition, was associated with an increasing cancer incidence risk in a prospective cohort study conducted for 12 years (Stolzenberg-Solomon et al., 2003). The multivariate HR was 1.63 (95% CI, 1.09-2.46; P for trend, 0.02) for edentulism as compared with missing teeth (0-10 teeth) and 1.23 (95% CI, 0.82-1.85) for 11-31 missing teeth as compared with 0-10 missing teeth, with adjustments for age, number of years of smoking, education, urban living, and height. More convincing information has come from the US health professionals survey (Michaud et al., 2007). Their data showed that tooth loss was not significantly associated with an increased incidence of pancreatic cancer. However, another study of the same sample showed that tooth loss during the past 4 years was significantly associated with pancreatic cancer incidence (Michaud et al., 2007). In that study, the multivariate HR was 1.61 (95% CI, 1.13-2.31) with adjustment for multiple confounders including age, smoking history, profession, race, geographic location, history of diabetes, body mass index, height, history of cholecystectomy, nonsteroidal anti-inflammatory drug use, multivitamin use, dietary intake of fruits and vegetables, vitamin D, calcium, sucrose, total calories, and baseline number of teeth. Furthermore, periodontal disease with recent tooth loss in the past 4 years was associated with an increase in pancreatic cancer, as compared with no periodontal disease and no recent tooth loss (HR, 2.71, 95% CI, 1.70-4.32).

4.2.5 Tooth loss and prostate cancer incidence

A case-control study conducted in Japan showed that a decreased number of remaining teeth was associated with the incidence of prostate cancer with a lower odds ratio (OR) of 0.49 (95%CI, 0.19-1.26) (Hiraki et al., 2008), while a similar finding was reported in follow-up investigation of the US male health professionals study (Michaud et al., 2008). The multivariate HR value reported in that study was 0.7 (95%CI, 0.50-0.97) for subjects with 0-16 teeth vs. those with 25-32 teeth. Interestingly, both results showed significant inverse associations, though interpretation of this association requires caution, as unmeasured confounders could explain the association, which is the case with any epidemiological study.

4.2.6 Tooth loss and incidence of melanoma of the skin

A significant inverse association between tooth loss and the incidence of melanoma of the skin was found in the US male health professionals follow-up study (Michaud et al., 2008).

However, this is the only evidence presently available, since no other survey concerning such an association has been performed. The multivariate HR was 0.60 (95%CI, 0.40-0.89) with adjustments for age, ethnic origin, physical activity, history of diabetes, alcohol consumption, body mass index, geographical location, height, calcium intake, total calorific intake, red-meat intake, fruit and vegetable intake, and vitamin D score. Furthermore, even in a fully adjusted model including smoking history and pack-years, the association for tooth loss remained significant (HR, 0.62, 95%CI, 0.41-0.93).

4.2.7 Tooth loss and other cancers

A recent Japanese case-control study investigated the associations between tooth loss and other cancers (Hiraki et al., 2008), and reported no significant associations for cancers of the colon, liver, breast, uterus, ovary, bladder, thyroid, and lymphoma. Another report conducted in the United States found showed no significant associations between tooth loss and oropharyngeal, colorectal, kidney, bladder, hematopoietic, and brain cancers (Michaud et al., 2008). In contrast, that report found a significant association between history of periodontal disease and kidney cancer, and between history of periodontal disease and hematopoietic cancers.

5. Possible mechanism for relationship between tooth loss and cancer mortality/morbidity

As noted above, associations between tooth loss and cancer mortality/morbidity have been reported, though the potential causal mechanism remains unknown. As for the primary mechanisms behind the associations, 2 have been hypothesized; a chronic inflammation pathway and a nutritional pathway. On the other hand, other possible factors may be more indirect, such as sarcopenia, brain activity, quality of life (QOL), and socioeconomic status. Here we present several findings to support these pathways and factors.

5.1 Chronic inflammation pathway

Tooth loss in older age is a consequence of chronic bacterial infections, such as periodontitis (Papapanou, 1996). Thus, tooth loss may be an indicator of past bacterial load and perhaps the presence of endogenous bacteria in general. Host response to periodontal disease might lead to systemic exposure to proinflammatory cytokines. For example, host response to *Helicobacter pylori*-induced inflammation has been reported to play a role in gastric cancer (Correa P et al., 2003). In this regard, periodontal disease may increase the risk of cancer by chronic release of inflammatory mediators. Another important point is that periodontal disease may influence carcinogenesis through increased generation of carcinogens, such as nitrosamines. Oral flora is known to preferentially produce carcinogenic by-products and is more effective for reducing nitrates to nitrites, which then spontaneously react with amines and become converted to carcinogenic nitrosamines (Shapiro KB et al., 1991). Another metabolic product of significance that has carcinogenic potential is acetaldehyde (Homann et al., 2001). These can spontaneously combine with other dietary components to form nitrosamines. Periodontal disease and attendant increased loss of teeth might result in greater endogenous nitrosamine production, and an associated greater risk of cancer.

5.2 Nutritional pathway

Tooth loss reduces chewing ability and may lead to consumption of a less healthy diet, which may be associated with cancer. Studies performed in the United Kingdom (Sheiham et al., 2001) and Japan (Kanmori et al., 2003) found that poor chewing ability influences total calorie intake. Also, tooth loss may influence the types and intake of nutrients. Yoshihara et al. (2005) reported a comparison of nutrient intake between individuals with 20 or more teeth and those with less than 20 teeth. They found that the former group had increased intake of vegetables and fish as well as vitamins, including vitamin D, vitamin B1, vitamin B6, niacin, and pantothenic acid. The Japanese National database study also reported that subjects with reduced chewing ability had lower intake of minerals, such as calcium, magnesium, and zinc, as well as dietary fiber, while they had much more starch intake. In the UK, subjects with lower chewing ability had lower intake of dietary fiber, proteins, calcium, iron, niacin, vitamin C, and vitamin E (Sheiham et al., 2001). Furthermore, in the report of male health professionals performed in the US, subjects who lost 5 or more teeth during an 8-year period had significantly lower intake of dietary fiber, fruit, polyunsaturated fat, and vitamin E as compared to subjects who had lost no teeth (Hung et al., 2003). In another report conducted in the US, edentulous subjects had lower intake of dietary fiber, carotenes, and vitamin C than fully dentate subjects (Nowjack-Raymer et al., 2003). In general, vitamins such as vitamin C, vitamin E, and carotene are known to be anti-cancer nutrients. The consumption of vegetables, specifically bright red, green, and yellow vegetables, and solid fruit may lead to prevention of diseases including cardiovascular or gastrointestinal diseases (Joshipura et al., 1999; Cheng et al., 1996). The WHO recommends intake of vegetables in amounts greater than 400 g/day. In a Japanese survey, subjects with lower chewing ability had a higher prevalence of gastrointestinal disease (Ikebe et al., 1999), with a similar outcome reported elsewhere (Cheng et al., 1996). Furthermore, the effects of denture wearing have also been studied. Subjects with dentures had a lower intake of vegetables and dietary fiber as well as vitamin C and beta-carotene (Nowjack-Raymer et al., 2003), while a recent report also found that subjects wearing any kind of removable dentures had lower intakes of vegetables and fruit with associated increased nutritional risk as compared to subjects with fixed dentures (Tsai et al., 2011).

5.3 Sarcopenia

Sarcopenia is defined as muscle power decline or decreased muscular volume with aging, leading to decreased levels of basal metabolism and energy consumption by the whole body, which results in lower energy intake and a decrease in synthesis of proteins in the body. To the best of our knowledge, no study concerning the association between chewing ability (tooth loss) and sarcopenia has been presented, though it is considered that elderly individuals with sarcopenia may also develop the condition in the oral cavity region, which has been supported by several reports. For example, subjects with stable occlusion, eg., Eichner index (EI; Eichner, 1955) Class A were shown unlikely to stumble (Yoshida, 2005). EI, long used as an indicator of occlusal condition, are based on existing natural tooth contacts between the maxilla and mandible in the bilateral premolar and molar regions. Class A represents contact in all 4 support zones. Some reports have been presented regarding associations between stable occlusion and physical fitness ability (Yamaga et al., 2002), chewing ability and physical fitness (Takata et al., 2004), and walking speed and oral

function (Okada et al., 2011). In a recent longitudinal study of Japanese elderly subjects, partial or complete loss of occlusion was associated with a decline in leg extensor power or decrease in one-leg standing time with eyes open (Okuyama et al., 2011). Sarcopenia may have a negative influence on both chewing ability and oral function. A Japanese survey of elderly individuals (60 to 87 years old) reported that significant factors related to occlusal power were handgrip strength in males, walking speed for 5 m in both genders, and body muscle volume in females (Kono, 2009). These findings suggest the possibility that oral sarcopenia induces a negative spiral of systemic health conditions including decreased levels of appetite and activities of daily living, as well as deterioration of psychosomatic health conditions, such as occurrence of depression, though the causal relationship remains unclear.

5.4 Brain activity

Functional magnetic resonance imaging (fMRI) is a new tool for testing specific hypotheses regarding the anatomical regions involved in processing sensory and motor information in the human brain. Onozuka et al. (2002) assessed the effects of aging on brain regional activity associated with chewing in subjects with intact dentition. Chewing resulted in a bilateral increase in blood oxygenation level-dependent (BOLD) signals in the sensorimotor cortex, cerebellum, thalamus, supplementary motor area, and insula, and a unilateral increase in the right prefrontal area. Interestingly, the increase in the right prefrontal area was remarkable in aged subjects and up to 4 times higher than that seen in young subjects (Onozuka et al., 2003). Grady et al. (2001) showed that increased right prefrontal cortex activity is associated with better memory performance. In elderly individuals, it is possible that chewing stimulates neuronal activity within a network between the right prefrontal cortex and hippocampus, which might be useful for maintaining cognitive function. Tooth loss/decreased chewing ability may lead to decreased cognitive ability or occurrence of dementia, which may or may not be a direct cause of cancer morbidity, though those would make the pathological conditions worse.

5.5 Quality of life

As described above, tooth loss results in decreased chewing ability and may influence the latitude of food selection. Consequently, comfort at the table as a major part of QOL may be decreased (Grath et al., 2000). Eating behavior may be related to the will to live and is expected to have a positive psychological effect (Teraoka et al., 1992). Since 1986, there have been several indexes presented for QOL assessment, such as Geriatric Oral Health Index (GOHAI) (Atchison & Dolan, 1990) and Oral Health Impact Profile (OHIP) (Slade, 1997). In a comparison among 3 groups based on number of functional teeth, the GOHAI score in subjects with 24 to 32 teeth was higher than that in those with 0 to 19 and 20 to 23 teeth (Ikebe et al., 2007). In particular, factors related to chewing, eating, and speech influence QOL scores. In a Japanese intervention study of institutionalized elderly subjects, GOHAI scores were improved when denture treatment was performed (Naito et al. 2010). Another recent study reported a significant association between decreased chewing ability and decreased OHIP score (Inukai et al., 2010).

5.6 Socioeconomic status

The number of teeth is an indicator of lifetime oral health, and therefore highly associated with socioeconomic status and access to dental care. Tooth loss can partly be explained as a

consequence that reflects unhealthful behavior, which may be associated with socioeconomic status. A recent prospective cohort study of 1462 Swedish women investigated the relationship between tooth loss and cancer mortality/morbidity (Cabrera et al., 2005). Tooth loss independent of socioeconomic status variables was associated with increased all-cause mortality and cardiovascular disease mortality (HR, 1.36, 95%CI, 1.18-1.58, and HR, 1.46, 95%CI, 1.15-1.85 per 10 missing teeth, respectively), while no associations were found between tooth loss and cancer mortality (HR, 1.16, 95%CI, 0.90-1.49). Thus, the authors proposed that socioeconomic status was a stronger predictor of cancer as compared to tooth loss, while tooth loss may be more related to cardiovascular events, though the precise mechanism remains unknown. On the other hand, due to several limitations including the timing of tooth loss and residual confounding factors, a comment regarding their article noted that additional longitudinal studies with randomized controlled trials will be required before conclusions can be drawn (Joshipura & Richie, 2005).

6. Conclusion

Herein, we reviewed the associations between cancer and tooth loss as a more objective assessment of dental status as compared to periodontal disease. Significant associations have been shown between tooth loss and site-specific cancer, including gastric, lung, and pancreatic cancers. However, evidence regarding tooth loss and cancer mortality/morbidity reported to date is somewhat equivocal, and does not suggest that the general population should be warned of an increased risk of developing cancer. Some of the associations require further investigations and evidence of possible mechanisms is needed. However, all members of the dental profession are encouraged to promote good oral health and this advice should be extended to targeted populations. Routine dental care as well as public dental health interventions may lead to promotion of overall health and longevity.

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5

Geriatric Oral Health – Appreciating and Addressing It with a Team Approach

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1. Introduction

It is universally accepted that the body undergoes physiological change and development throughout life. The period of growth peaks at approximately 21 years of age before it begins to decline slowly until the person dies. The geriatric age lies somewhere towards the end of this continuum and is generally acknowledged to be around 65 years and older.

Ageing is part of the cycle of life. In the past, many communities did not have the privilege of experiencing this part of the cycle due to the ravages of war, infectious diseases, poor sanitation and malnutrition. This has, however, changed and it is projected that by 2040, about 14% of the global population, or almost 1.3 billion people, will be aged 65 years or older. 1 Such a demographic change poses pressing concerns for the healthcare fraternity as an increasingly geriatric population brings with it a host of health issues including chronic diseases such as diabetes, hypertension and stroke. Declining oral health also tends to be common among the elderly and this is an issue which warrants close attention. One of the enlightenments of the 21st century has been the recognition of oral health as an essential and integral part of systemic health. For example, the close association between periodontal disease and diabetes is well documented. 2,3,4. Increasingly, evidence of a close association between periodontal disease and cardiovascular disease 5,6 is also emerging.

While the link between oral and systemic health is complex, it is easier to understand how poor oral health substantially influences one's overall quality of life as the ability to enjoy food and speak properly as well as social confidence can be grossly affected 7,8 by oral diseases. A British national nutrition survey showed that the intake of most nutrients, such as non-starch polysaccharides, protein, calcium, non-haem iron, niacin, and vitamin C, was lower in edentate than dentate subjects. The survey also revealed that subjects with 21 or more teeth consumed more of most nutrients, especially the non-starch polysaccharides. 7

Indeed, oral health is an integral and important part of one's overall health but it is often neglected due to prevailing misconceptions which include a general apathy towards oral health since many conditions affecting the oral cavity are non-life threatening. Therefore, while people are willing to attend annual health checks for their blood pressure, blood sugar, height and weight; the same interest for dental check-ups is generally lacking.

2. Common oral diseases affecting the elderly

2.1 Dental caries and periodontal disease

Dental caries (tooth decay) and periodontal disease (gum disease) are the two most common dental conditions which affect the general adult population and their prevalence tends to increase with increasing age. 7,8

Dental plaque is a key contributing factor in the aetiology of dental caries and periodontal disease. This composite of saliva, partially digested food and bacteria sticks to the tooth surfaces. Acidic by-products of bacteria metabolism causes erosion of the tooth structure giving rise to dental caries. The elderly with lower masticatory ability tend to consume carbohydrate-rich foods and this exacerbates a vicious cycle for dental caries as such foods are excellent bacterial substrates in the oral cavity. In general, oral health has generally improved over the years and the prevalence of edentulism has decreased. 9 With more teeth in the mouth over a longer period of time, it is unsurprising that the incidence of dental caries is higher among the elderly. Gingival recession (Figure 1), common with increasing age, also puts teeth at increased risk for root caries.

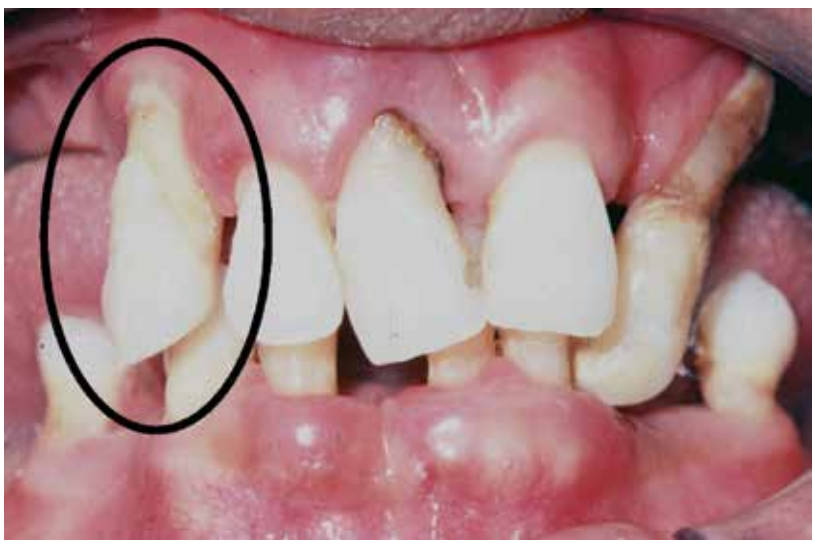

Fig. 1. Gingival recession (circled) increases the risk of root caries

In the initial stage, dental caries usually presents with little or no signs and symptoms. Often noticed as an initial white patch on the tooth surface, it can easily go undetected especially by the lay person. Left unmanaged, the caries progress further giving rise to a cavitation in the tooth. At this stage, sensitivity and pain manifest to suggest the onset of dental caries (Figure 2).

The teeth are supported in their positions in the mouth by the periodontium which comprises the alveolar bone, periodontal ligament, gingiva (gums) and cementum. The bacterial by-products of dental plaque cause gingival inflammation and sets the stage for periodontal disease to set in. Prolonged accumulation of dental plaque around and in the gingival tissues initiates a host-mediated destruction of soft tissue caused by hyperactive leukocytes, cytokines, eicosanoids and bacterial by-products. This leads to an irreversible resorption of the surrounding bone supporting the teeth resulting in drifting, mobility and

eventually loss of teeth. 25 Common signs and symptoms of periodontal disease include redness and swelling of the gingival tissue, bleeding even on gentle brushing, longer looking teeth, mobility of teeth, malodour and pain.

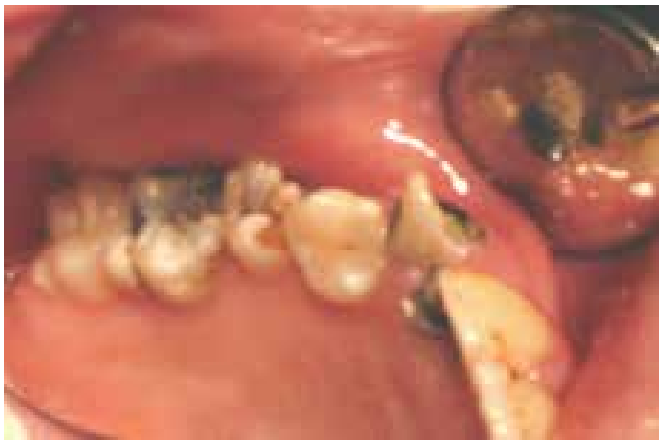

Fig. 2. Carious teeth

Certain medical conditions such as diabetes mellitus, hyposalivation as well as medications like anti-hypertensives can also predispose individuals to dental caries and periodontal disease.

2.2 Retained roots

Retained roots and carious teeth broken beyond repair, are commonly found among the institutionalised elderly. Various studies on oral health status and treatment needs in nursing homes show that 20% to 36% of the residents require at least one dental extraction. 10,11 The risks of infection arising from these retained and carious teeth is a cause of concern among the elderly especially those who are immunocompromised.

2.3 Prevention of dental caries and periodontal disease

The prevention of dental caries and periodontal disease can be easily instituted at home with regular toothbrushing using fluoridated toothpastes and dental flossing. Dietary control to limit the intake of sugars, which are excellent substrates for the bacteria in the mouth, is also crucial for the prevention of dental caries. In high-risk individuals, the use of fluoride varnishes or mouthrinses, saliva substitutes or sugar substitutes may be necessary to complement the home care as additional caries prevention measures. Regular dental visits are highly recommended, even for the elderly, as this will facilitate the early detection and management of dental conditions which may otherwise be left to deteoriate and cause great pain and suffering.

2.4 Mucosal lesions

The main causes of mucosal lesions in the oral cavity are trauma from dentures and food, *Candidal* infections, mucosal changes due to nutritional deficiencies and neoplastic changes.
One of the biggest culprits of mucosal lesions is poorly fitting dentures. Denture wearers have a higher likelihood of succumbing to denture stomatitis, *Candidal* infection and ulcers.

With increasing age, the oral mucosa tends to lose its elasticity, have diminished blood supply and exhibit atrophy of epithelial cells. These changes can be exacerbated by conditions, such as xerostomia and iron or vitamin deficiency, commonly associated with the elderly. This makes the oral mucosa more friable and susceptible to inflammation and ulcers. 12,13

Denture wearers are generally advised to remove their dentures before sleeping, brush off all food debris from the denture surfaces and soak the dentures in a denture cleanser or diluted Milton's solution. Soaking the dentures in antiseptic solutions reduces the bacterial and fungal load in the porous acrylic resin denture base. Furthermore, the oral mucosa needs to be exposed to the protective antibodies and enzymes in saliva to minimise denture stomatitis.

2.5 Xerostomia

Xerostomia, otherwise known as dry mouth, is relatively common among the elderly and results from reduced salivary flow. This reduction in saliva is often a result of diseases such as Sjorgrens' Syndrome, sarcoidosis, primary biliary cirrhosis and cystic fibrosis. It may also be the result of polypharmacy and radiotherapy. Many drugs including anticoagulants, antihypertensives, antihistamines, antipsychotics, antidepressants and anticholinergics can also result in reduced salivary flow as a side effect. 26

Saliva serves many important functions. It helps in speaking, chewing and swallowing. It offers protection against dental caries with its capacity to buffer the drop in pH associated with the onset of dental caries. Xerostomic individuals are, therefore, at increased risk of developing dental caries. Saliva helps to hydrate the oral mucosa and a reduced salivary flow can cause a burning sensation or soreness of the mucosa. Saliva also plays a pivotal role in complete denture retention and xerostomia poses a challenge for fully edentulous elderly patients.

2.6 Bisphosphonates

The use of bisphosphonates in the treatment of osteoporosis, Paget's disease of the bone, multiple myeloma and breast cancer is common. One possible side effect of this is osteonecrosis of the jaw bone following dental surgery or infection, which can be challenging to manage. To prevent such complications, it is advisable for all potential foci of dental infection to be removed before starting bisphosphonate therapy. 26 27

3. Management of oral diseases

Tooth loss is mainly caused by dental caries 14,15 and periodontal disease. However, trauma and other iatrogenic causes may also contribute towards tooth loss. Due to current advancements in dental restorative procedures, more people are retaining their teeth for longer than before. Among those who still have teeth, many of the remaining teeth are heavily restored with fixed prostheses and even implant retained ones. Re-restoration of complex restorations in an ageing dentition is therefore a growing and emerging challenge of this century.

Dental prostheses (Figure 3) to replace missing teeth have been used for centuries. Missing teeth should only be replaced if necessary to fulfil the needs of aesthetics, function or comfort. Prostheses must be recognised as aids that require maintenance and care for its continued function.

Fig. 3. Crowns used to replace extensively carious teeth

Complete dentures have been used for over a hundred years. The ubiquitous acrylic resin dentures (Figure 4), which came into use in the early 1950s, are now commonly used all over the world. They are generally affordable, well-tolerated by patients and simple to fabricate.

Fig. 4. Acrylic upper complete denture

Studies have shown that worn and broken dentures cause more oral lesions than having no teeth or dentures! In fact, prolonged chronic irritation can often lead to pre-cancerous lesions. This underscores the need for regular dental check-ups even with a dental prosthesis in the mouth. Complete dentures rely on suction for retention and they need to be professionally cleaned and maintained, with the borders checked and adjusted for over-extension and occlusion modified to accommodate uneven wear of the tooth surfaces. It is also recommended to have new ones made every 3 to 5 years.

One of the main problems with dentures is the retention of the mandibular denture as the bony ridges which support the prostheses in the lower jaw tend to be highly resorbed with increasing age. Osseointegrated dental implants, first introduced in the late 1950s in an experimental way, are now readily available at most dental practices and their costs are no longer overly prohibitive. The implant retained lower complete denture (Figure 5) is fast becoming the prosthesis of choice and almost synonymous with the expected standard of

Fig. 5. Implant-retained mandibular complete denture

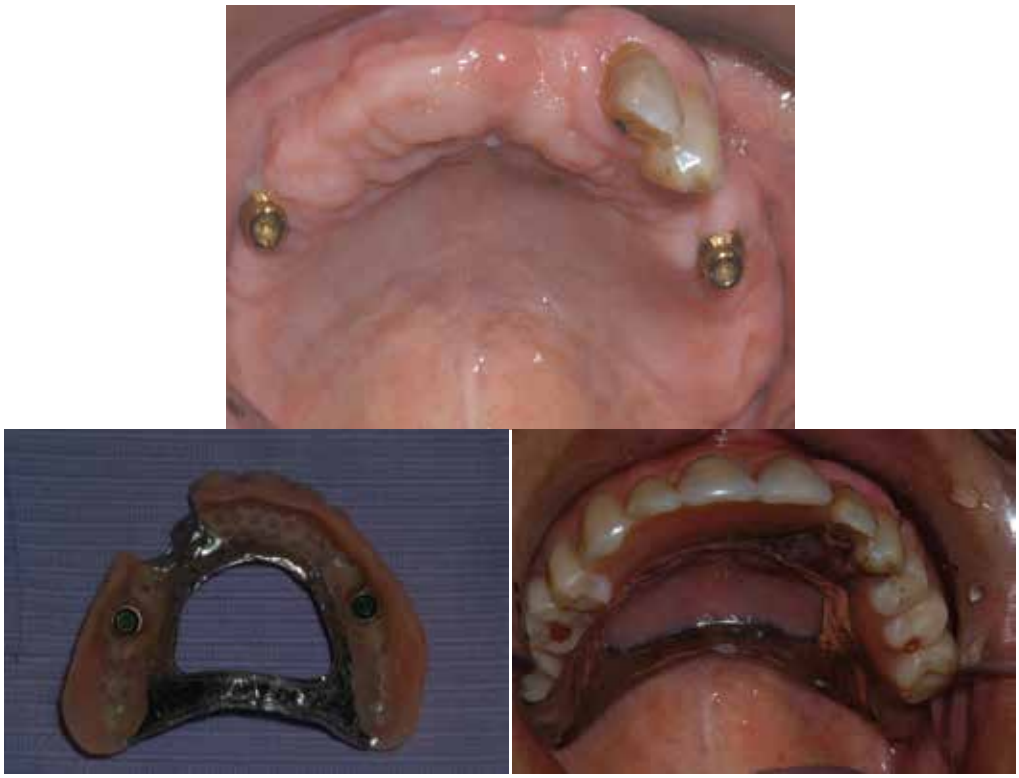

Fig. 6. Implant retained maxillary partial denture

care for edentulous persons in many developed countries. However, not everyone, is suitable for dental implants and the contra-indications for such a treatment option include smokers, patients with diabetes and those on oral bisphosphonates.
Fixed partial dentures or bridges are commonly prescribed for those with one or two teeth missing. These are more challenging to maintain than the removable ones and cleaning around them needs to be more meticulous. Such prostheses often fail when the supporting neighbouring teeth become mobile, carious or fracture with time.

4. Embracing a team approach to oral health

General medical practitioners provide comprehensive and holistic health care for individuals in the community, including the elderly. As more people visit their general medical practitioners each year than any other health care professional, they are well poised to promote health, anticipate health needs and offer opportunistic prevention by proactively targeting high-risk elderly individuals who may not be fully aware of their conditions and the need for follow-up care and management. In fact, this close contact with the medical practitioners is even more so for the elderly as many of them have chronic conditions which require regular follow-ups with their doctors.
Oral health is part and parcel of an individual's general health and wellbeing. An alliance can be forged with the general medical practitioner to empower them to identify early signs of oral diseases and alert their elderly patients to seek further follow-up with their dental practitioners. 19 For example, when a doctor performs a routine tonsil examination, a quick glance at the rest of the mouth for signs of oral disease can help the patient a long way. Early referral to a dental surgeon or an oral health therapist (e.g. dental hygienist; dental therapist) can enhance the patient's overall quality of life.
In line with this, oral health has been included as one of 6 functional domains of functional independence for the elderly in Singapore.23 To facilitate an assessment of oral health, the Oral Health Assessment Tool (OHAT) has been incorporated within a set of Functional Screening Guidelines for Older Adults in the Community in Singapore. 24 The OHAT was modified from the Kayser-Jones Brief Oral Health Status Examination (BOHSE) and validated for use in nursing homes in Australia. 18 With this tool, non-dental healthcare professionals such as doctors and nurses can recognise and identify less than optimum states of oral health so that patients can be referred for necessary follow-up with the dental surgeon.
Apart from the doctor, other members of the healthcare team including allied health professionals such as nurses can be rallied to identify common oral conditions and alert the elderly or their caregivers to seek dental treatment and management. For example, occupational therapists can also be involved to reach out to the cognitively impaired residents helping them to carry out activities of daily life including tooth and denture brushing. 16 In Singapore, a pilot project was conducted for nursing staff from the intensive care and geriatric wards in a hospital. With this project, the nursing staff were trained in the fundamentals of oral hygiene education 22 to empower them to address the oral hygiene of the patients as part of the overall in-patient care. The staff responded favourably to the training and were positive about what they could do for their patients with the newly acquired knowledge and skills. Volunteer dentists in Singapore have been working closely with nursing home administrators and clinical staff to run regular dental clinics in their

premises. Many of these homes are staffed by non-dental professionals who display a commendable interest in oral health and proactively look into the oral health needs of the residents. 20,21

It must be emphasised that the primary role of the non-dental healthcare partners is to recognise and identify less than optimal states of oral health and refer the patient to a dental surgeon or oral health therapist for further management. They should not be expected to dispense oral hygiene instructions but if they do, that will be a real bonus for the patient!

This team approach to oral healthcare is not a new idea and has been proposed by many researchers and public health dentists and also practised in some countries.16,17 The dental fraternity needs to step out of its comfort zone and embolden itself to engage their medical colleagues from the general medical practices, hospitals and even nursing homes to establish a collaborative relationship which will benefit the health and wellbeing of the elderly population in the long-term.

5. Conclusion

Oral health is a fundamental and pivotal aspect of health for the elderly as it can significantly influence their overall quality of life. It is therefore crucial to embrace the new paradigm to include oral health care as part of one's overall health and holistic wellbeing. Traditionally, oral health has been viewed as the sole responsibility of the dental fraternity. However, with increasing awareness of a team approach to healthcare, the dental fraternity needs to work collaboratively with their counterparts from the medical fraternity to forge alliances with them and empower them to identify and detect early signs of oral conditions among the elderly for early dental referrals and management. This will allow the elderly easy access to oral health advice from multiple touchpoints.

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6

Research and Clinical Applications of Facial Analysis in Dentistry

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1. Introduction

Anthropometry is the study of human body measurement for use in anthropological classification and comparison in living subjects (Farkas et.al., 2005). It has been applied in medical areas such as plastic surgery, craniofacial development, forensic science and bioengineering as well as in diverse industries such as clothing, glasses and shoes manufacturing (Farkas et.al., 2005; Germec-Cakan et.al., 2010; Fourie et.al., 2011). This traditional method of finding required body dimensions by manual measurements has many sociological, logistical and technical drawbacks such as prolonged time, skilled researcher for consistency and accuracy of measurements, undesirable physical contact between the subject and the researcher, required presence of people from different demographic categories or travel of researcher with equipment. If these dimensions are extracted from the stored digital human models, above drawbacks can be eliminated (Nechala et.al., 1999; Lucas et.al., 2009; Fourie et.al., 2011).

Current literature presents a range of techniques and methods to measure human body parts for both research and clinical purposes. Photogrammetry, which is a method that encloses the image acquisition to obtain such measurements, is one of these techniques (Nechala et.al., 1999; Germec-Cakan et.al., 2010; Fourie et.al., 2011). It has been adopted by medicine in the middle of the 19th century, though, without exhibiting any useful applications. Nowadays, due to its recent technical advances this noninvasive procedure is related to particular relevant advantages as follows: the absence of soft tissue compression, usefulness with low cost and easy transportation. In addition, the image registration is an important source of documentation enabling to compare results among studies and their reproducibility (Nechala et.al., 1999; Gomes et.al., 2006; Lucas et.al, 2009; Germec-Cakan et.al., 2010; Maal et.al., 2010; Fourie et.al., 2011). For all these reasons, photogrammetry has reacquired enormous popularity in research and clinical practice.

Facial anatomy is a primary characteristic by which individuals present themselves to the external world. This influences the subjective perception of a given person by another person, for instance in terms such as 'attractive' or 'notable' (Frush and Fisher, 1958;

Ackerman et.al., 1998; Gomes et.al., 2006; Gomes, et.al. 2008; Gomes et.al., 2009; Lucas et.al., 2009). In Dentistry, particularly during rehabilitation treatments of the dentofacial dimensions, limited accepted protocols are available to provide the esthetic quality desired by the patient. Usually, a natural appearance is pursued (Frush and Fisher, 1958). The facial analysis performed during the first dental clinical exam has been used successfully to offer essential evidences for treatment planning mainly when associated to photogrammetry (Gomes et.al., 2006; Gomes et.al., 2008; Lucas et.al, 2009; Germec-Cakan et.al., 2010; Fourie et.al., 2011). The issue of increased productivity in a dental practice is of great interest to dentists, not only because of its economic implication but also because the demand by the public for more dental services is ever increasing. The armamentarium of facial cosmetic, orthognatic and maxillofacial surgery allows correction of greater portion of facial abnormalities. However, surgical correction reaches far beyond the scope of this chapter. The following discussion is limited strictly to methods of recognition and diagnosis of faults in the balance of the face.

2. Esthetic diagnoses

Many professionals in both medical and dental literature have expressed interest in facial balance, harmony, and unity. The diagnosis and the careful acquisition of complementary exams are the basis of the suitable treatment planning (Frush and Fisher, 1958; Germec-Cakan et.al., 2010). However, successful esthetic outcomes of dentofacial restorations comprise of existing skills that are associated to much more than the ability of diagnosing and correcting functional and pathological irregularities. Esthetic restorations are not only associated with pathology and function but also with patient's attitudes related to his/her appearance, personality, career fields and social life. It is, therefore, influenced by culture and self-image (Frush and Fisher, 1958).

Any scientific analysis of a physically beautiful face of a patient ultimately must be approached on a mathematical basis. Proportion is the certain ratio between parts, and proportional means a proper correlation of parts among themselves. Efforts in the past were made to find principles of esthetic and functional equilibrium for use as guides in clinical practice. It is reputed, that knowledge about "Gold Proportion" Pythagor has got from products of the Egyptian and Babylon scientists (Mack, 1991; Preston, 1993). The Golden Section is also known as the Golden Ratio, the Golden Mean, the Golden Cut or the Divine proportion. It has been considered for a long period to present proportions that is most appealing, soothing, or attractive to the human psyche, but its implications extend to encompassing space or time and the very foundations of physics and abstract science. The proportions of pyramids in Giza, home appliances and ornaments from Tutanhamon tomb testify, that under their creation the Egyptian masters were guided by a principle of "Gold Proportion". The facade of ancient Greek temple Parthenon was also built by the same principle. During archeological digs of this temple the compasses which sculptors and architects of an ancient world used has been found. The "Gold Proportion" is mentioned in the work which has reached us "Beginning" the author is the scientist of antique epoch Euclid (Ricketts, 1981; Mack, 1991; Preston, 1993).

According to Vadachkoriia et. al. (2007), Luka Pacholi published the book of the "Divine Proportion" illustrated by Leonardo de Vinci, in 1509, Italy. This work has been recognized as a "Hymn of a Gold Proportion". In 1885, the German researcher professor Zeising published his work "Aesthetic researches". When Zeising has received numerical values of

piece length, he saw that they coincided with figures of some numerical sequence, which was offered by the great Italian mathematician of Middle Ages Fibonacci (or Leonardo Pisano). In his composition the "Abacus Book" Leonardo Fibonacci showed aforesaid sequence of numbers, by means of which he has explained the formula of duplication of rabbits. In sequence of Fibonacci, in some division of its term on previous, it is received irrational number 1,61803398875.., known as Fibonacci. It is used in the reduced, approximated kind as F = 1,618 or phi = 0,618 (Ricketts, 1981; Mack, 1991; Preston, 1993). In the past, dental professionals used these concepts as a guide in the facial analysis of patients, and approximate conformity with these principles was considered one of the objectives of treatment (Ricketts, 1981; Nanda and Ghosh, 1995).Classic studies produced aesthetic canons in which the dimensions of nose, lips, and chin were stated to follow to mathematical ratios (Ricketts, 1981; Mack, 1991). In his works Rickets has specified, that mentioned data is necessary to be considered in aesthetic stomatology during teeth reconstruction. For example, Rickets (1982) stated that the distance between the base of the nose to the rima oris is in Golden Proportion to the distance between the rima oris to the chin. Also, the interalar width is suposed to be in golden proportion with the lip comissure distance. Marquardt (2002), an oral and maxillofacial surgeon from California, analyzed human face from ancient times to modern day and discovered that beauty is not only related to phi but can be defined for both genders and for all races and cultures, with a method and apparatus for analyzing facial configurations and components named the "Beauty Mask". This method patented from 1997 to 1999 (number 5867588) analyzes the form and proportion of faces and components of those faces (e.g., eyes, nose, mouth, etc.) and establishes a reference system to analyze human faces for surgical, cosmetic, and identification purposes.

Nowadays, some studies have suggested that, in general, there are no concrete evidences to consider the Golden Proportion as the ideal aesthetic standard to rehabilitate neither human face or in the anterior dental segment (Nikgoo et.al., 2011; Condon et.al., 2011; Al-Johany et.al., 2011). Recent observations of 81 Brazilian undergraduate students (37 females and 44 males), with mean age of 21 years old, showed that facial architecture was not significantly dimensioned according to Divine Proportion. Table 1 and 2 present, respectively, the horizontal and vertical measurements of the face (mean and standard deviation) obtained through photogrammetry for the total sample and when divided to gender. For the total sample and when it was divided to gender, table 3, 4 and 5 present the mean ratios and standard deviation found to each facial relationship compared, as well as the percentage of golden ratio found in each comparison with the highest percentages highlighted.

The lack of Divine Proportion among dental and facial structures are also stated in recent literature (Bukhary et.al., 2007; Murthy and Ramani, 2008; Mizumoto et.al., 2009; Nikgoo et.al., 2011; Condon et.al., 2011; Al-Johany et.al., 2011) attesting this proportion as an unsuitable method to relate dentofacial dimensions with natural or even 'attractive' appearance during rehabilitation treatments.

According to the values presented on table 3, the lip commissure distance was in Golden Proportion to the interalar distance only in 1,3% of the total sample (LCD-IAD), and the mean ratio found was 1,395 instead of 1,618 as stated by Rickets (1981). Another relationship tested was the upper lip length (distance from the base of the nose to the lips) and the lower third of the face (UL-LT). As shown on table 4, no significant percentage for Golden Proportion (0,0%) was found and the mean ratio corresponded to 0,334 instead of 0,618 (see table 3).

	Total		Female		Male	
Horizontal	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
RE	3.185	0.212	3.128	0.212	3.258	0.191
LE	3.205	0.213	3.135	0.172	3.296	0.229
MCE	3.438	0.312	3.391	0.295	3.498	0.328
MPD	6.846	0.434	6.690	0.405	7.049	0.388
RE+MCE	6.622	0.400	6.520	0.404	6.756	0.358
LE+MCE	6.643	0.410	6.527	0.382	6.795	0.401
LCE	9.828	0.545	9.655	0.518	10.052	0.501
IAD	4.081	0.350	3.911	0.314	4.302	0.260
LCD	5.670	0.439	5.469	0.321	5.931	0.438
BZG	14.178	0.808	13.787	0.716	14.686	0.621

Table 1. Mean, in centimeters, and standard deviation (SD) of the horizontal facial measurements for the total sample and when divided to gender: RE (right eye width), LE (left eye width), MCE (distance between the medialis canthus of the eyes), MPD (mid-pupillary distance), RE-MCE and LE-MCE (distance between the lateral canthi of one eye – right or left – to the medial canthi of the other eye), LCE (distance between the lateral canthus of the eyes), IAD (interalar distance), LCD (lip commissure distance), BZG (bizigomatic width)

	Total		Female		Male	
Vertical	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
UT	6.318	0.792	6.025	0.696	6.699	0.755
MT	6.685	0.494	6.632	0.513	6.754	0.468
LT	7.393	0.643	7.083	0.511	7.797	0.574
UT-LT	20.396	1.310	19.740	1.065	21.250	1.096
UL	2.471	0.268	2.404	0.230	2.556	0.293
LL-C	4.818	0.463	4.567	0.345	5.144	0.390
LE-C	12.191	0.998	11.694	0.633	12.838	1.022
RE-C	12.284	0.865	11.765	0.583	12.960	0.689
LE-LC	7.477	0.567	7.205	0.455	7.831	0.503
RE-LC	7.518	0.567	7.245	0.449	7.872	0.508

Table 2. Mean, in centimeters, and standard deviation (SD) of the vertical facial measurements for the total sample and when divided to gender: UT (upper third), MT (middle third), LT (lower third), UL (upper lip length), LL-C (distance between the lower lip to the chin), LE-C and RE-C (distance between the eyes – left or right – to the chin), LE-LC and RE-LC (distance between the eyes – lefts or right – to the lip commissure)

	Total			Female			Male		
Horizontal	**MR**	**SD**	**GR**	**MR**	**SD**	**GR**	**MR**	**SD**	**GR**
MCE:IAD	0.846	0.083	0.0%	0.870	0.079	0.0%	0.815	0.080	0.0%
LCD:IAD	1.395	0.112	1.3%	1.406	0.126	2.3%	1.380	0.091	0.0%
IAD:MPD	0.597	0.044	27.6%	0.585	0.045	27.9%	0.611	0.040	27.3%
BZG:IAD	3.488	0.221	0.0%	3.541	0.256	0.0%	3.419	0.141	0.0%
LCE:IAD	2.420	0.183	0.0%	2.480	0.192	0.0%	2.342	0.136	0.0%
LCD: LCE	0.578	0.043	19.7%	0.567	0.037	18.6%	0.591	0.046	21.2%
LCD:MCE	1.660	0.173	11.8%	1.622	0.143	14.0%	1.709	0.198	9.1%
LCD:MPD	0.830	0.062	0.0%	0.819	0.057	0.0%	0.843	0.068	0.0%
LCD:BZG	0.400	0.028	0.0%	0.398	0.030	0.0%	0.404	0.026	0.0%
MCE-LCE	2.071	0.127	0.0%	2.082	0.118	0.0%	2.056	0.138	0.0%

Table 3. Mean ratio (MR), standard deviation (SD) and the percentage of the Golden Ratio (GR) found after comparing all horizontal facial measurements for the total sample and when divided to gender. See footnotes table 1

	Total			Female			Male		
Verticais	**MR**	**SD**	**GR**	**MR**	**SD**	**GR**	**MR**	**SD**	**GR**
(UT+ MT):LT	1.769	0.170	1.3%	1.769	0.170	1.3%	1.769	0.170	1.3%
LT:UT-LT	0.923	0.007	0.0%	0.923	0.007	0.0%	0.923	0.007	0.0%
LT:LE-C	0.608	0.047	42.1%	0.608	0.047	42.1%	0.608	0.047	42.1%
LT:RE-C	0.602	0.030	43.4%	0.602	0.030	43.4%	0.602	0.030	43.4%
LE-LC:LE-C	0.614	0.031	63.2%	0.614	0.031	63.2%	0.614	0.031	63.2%
RE-LC:RE-C	0.612	0.022	60.5%	0.612	0.022	60.5%	0.612	0.022	60.5%
UL:LE-LC	0.331	0.028	0.0%	0.331	0.028	0.0%	0.331	0.028	0.0%
UL:RE-LC	0.329	0.027	0.0%	0.329	0.027	0.0%	0.329	0.027	0.0%
LL-C:LE-LC	0.646	0.058	21.1%	0.646	0.058	21.1%	0.646	0.058	21.1%
LL-C:RE-LC	0.642	0.059	23.7%	0.642	0.059	23.7%	0.642	0.059	23.7%
LL-C:LT	0.652	0.027	28.9%	0.652	0.027	28.9%	0.652	0.027	28.9%
UL:LT	0.334	0.024	0.0%	0.334	0.024	0.0%	0.334	0.024	0.0%

Table 4. Mean ratio (MR), standard deviation (SD) and the percentage of the Golden Ratio (GR) found after comparing all vertical facial measurements for the total sample and when divided to gender. See footnotes table 2

The dentist and health professionals that work with esthetics overemphasize attractive dentofacial architecture not only from form and functions with stereotyped orientated dimensions but also from organic expressions of the patient's personality, lifestyle, and

other features that differentiate one individual from another. Accordingly, the evaluation of facial beauty is subjective, since the balance and harmony of its components are not indicative that the face is attractive. In fact, asymmetric and disproportionate dentofacial dimensions contribute significantly with esthetic problems, but fortunately they can be recognized and diagnosed objectively (Ras et.al., 1995; Aksu et.al., 2010; Germec-Cakan et.al., 2010).

	Total			Female			Male		
Horizontal and Vertical	**MR**	**SD**	**GR**	**MR**	**SD**	**GR**	**MR**	**SD**	**GR**
UL:LCD	0.437	0.051	0.0%	0.441	0.049	0.0%	0.433	0.055	0.0%
LCD:LL-C	1.185	0.118	0.0%	1.205	0.121	0.0%	1.158	0.110	0.0%

Table 5. Mean ratio (MR), standard deviation (SD) and the percentage of the Golden Ratio (GR) found after comparing vertical and horizontal facial measurements for the total sample and when divided to gender. See footnotes table 1 and 2

3. Facial analysis protocol

Photographs of a patient's face provide an enormous amount of information for to guide diagnosis and treatment planning, as well as to document preoperative and postoperative conditions. It can be said that, for the ideal diagnosis of dentofacial imbalances, the evaluation begins with the face of the patient being visualized in frontal and lateral view followed by the dental clinical exam. Facial analysis was underestimated for a long time due to the lack of clinical parameters such as those used in radiographic images. However, radiography produces inaccurate soft tissues registration, and consequently, avoids their esthetic evaluation (Nechala et.al., 1999; Edler et.al., 2003; Good et.al., 2006; Fourie et.al., 2001). Additionally, traditional anthropometry produces inaccurate values due to the soft tissue compression. Though, to perform photogrammetry accurately a standardized protocol must be followed during the image registrations, to guarantee a mathematical relationship between the real and the image dimensions. The following section of this chapter discusses reliable approach to obtaining frontal and profile photographs of the face. Careful use of the equipment and techniques described in this part will enable clinicians and researchers to make useful full-face and profile records of patients when needed.

3.1 Materials and equipment

A single-lens reflex (SLR) camera system with a 90 mm or longer focal length is needed. Shorter focal lengths tend to distort the subject's face in the center of the image. This distortion is known in general photography as "barrel distortion." Barrel distortion is a lens effect resulting in images that are "spherized" at their center (Vargas, 2003). The camera should be held in a tripod, in front of the object to avoid having blurry edges because of unsteady hands or other instable support. The background makes the image stand out properly and for this reason is important to improve the visualization of the object. A

nonreflective background of black, light-gray or light-blue is commonly used (Vargas, 2003). The subject must be positioned about 120 centimeters in front of the background to avoid shadows from the subject on the background. A piece of black or blue velvet is ideal due to the absorption of the light by the fabric (Vargas et.al., 2003; Lucas et.al, 2009). A white background does not provide sufficient distinction with the subject. Shiny or hard surfaces will detour the absorption of light rays, and for this reason neutral gray backgrounds are preferred. The light also plays an important part in the photographic process. The light rays that are emitted from sunlight and artificial light (tungsten light bulbs or fluorescent light) are different. Also, the angle of the light rays reflecting or being absorbed by the object will produce different effects (Laws, 2001). The Illumination of the subject can be obtained with two studio flashes attached to the camera or activated by a remote-control unit. The flashes must be positioned 45 degree angle each side in relation to the sagittal plane of the face (facial median line). Flash units used in intraoral photography can be used, but these may not illuminate the subject properly, resulting in the appearance of undesirable shadows in the background (Vargas, 2003). When a studio flash is not accessible and an intraoral flash must be used, some restrictions on quality should be expected. The intraoral flash does not have the power to evenly illuminate the subject, necessitating the use of large apertures and resulting in a shallow depth of field, teeth frontal aspects for example. If a nonblack background is used, remove the flash from the lens and hold it above the camera to eliminate "red eye" as well as undesirable shadows over the background. The natural light source is recommended instead of a single flash close to the camera, such as is obtained with an intraoral unit.

3.2 Facial positioning

The patient's posture is essential to assure standardized digital image. The head must be positioned at the center of the image. Also, the head during the image registration must be positioned according to the three reference section planes: transverse, coronal and sagittal (Gomes et.al. 2006, Gomes et.al., 2008; Gomes et.al., 2009; Lucas et.al., 2009). Including the patient's ears in the image may be important. The ears (porion, the superior aspect of the external auditory meatus) and the eyes (orbitale, the inferior point of the orbital rim) define the Frankfort horizontal plane. The horizontal plane of Frankfort is the reference for transverse plane and it may be parallel to the floor plane. The mid-pupillary line must also be parallel to the floor plane, with the patient looking forward (horizon line). Regarding the sagittal plane, facial median line must be perpendicular to the floor. Figure 1 A and B illustrates facial positioning for anterior and lateral analysis, respectively.

The lower third of the face can have far reaching effects on facial aesthetics, not just on the peri-oral areas but on the whole face (Mohindra and Bulman, 2002; Gomes et.al, 2008). Mandibular posture greatly depends on head posture. Thus, it is compulsory to state if the subject is in rest vertical dimension (RVD) [1] or in occlusal vertical dimension (OVD) with the teeth in contact. The seated or supine position may also influence since it is the habitual mandibular position is determined by the stiffness that results from the postural muscle tone acting on the mandible (Woda et.al., 2001).

[1] Craniofacial muscles are in tonic balance, with labial and mental muscles relaxed.

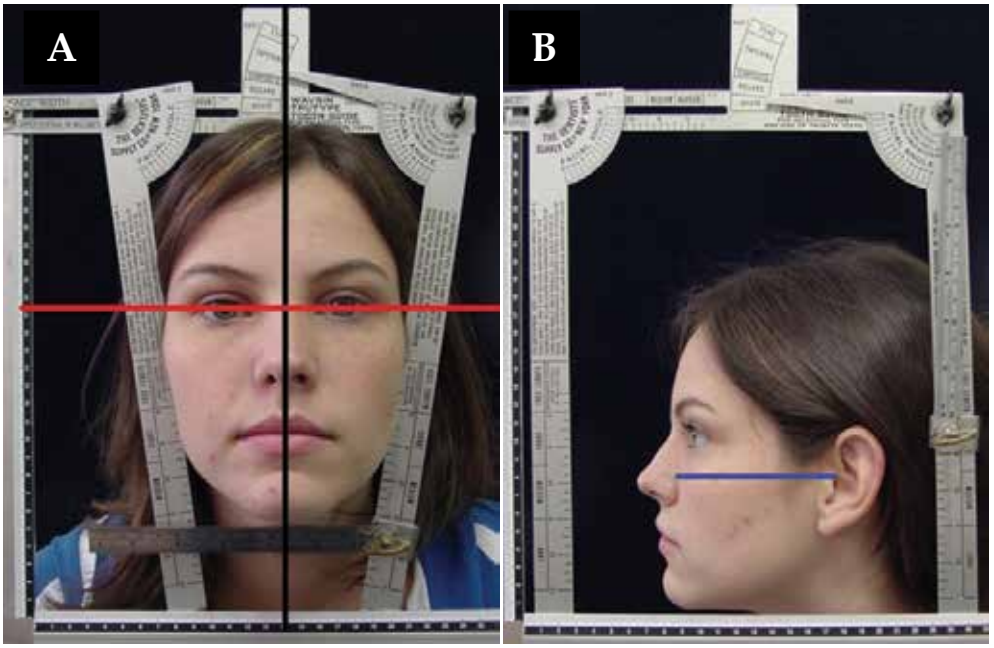

Fig. 1. Reference lines for facial positioning: A- Frontal view: mid-pupillary line (red) and facial median line (black); and B- Frankfort plane (blue)

3.3 Anatomical parameters

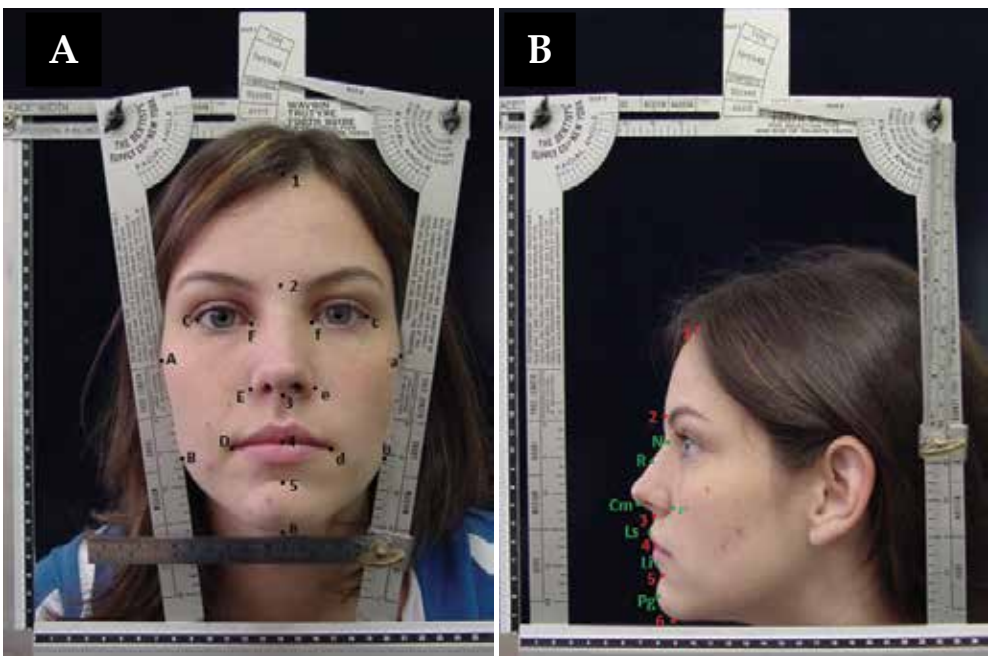

Fig. 2. Biometric Points for facial analysis: A- Frontal view; C- Lateral view

3.3.1 Frontal view

Considering the facial median line (Figure 1A), the face must be examined in a frontal view to evaluate bilateral symmetry and horizontal proportions among facial structure's sizes: nasal width, width of the eyes and the masseter muscles conditions. The vertical proportions of the face must be evaluated in the same facial position, however, with the pupil lines as the reference (Figure 1A). The vertical proportion enables to classify the facial pattern as well as the division of the face in three thirds. Figure 2A illustrates biometric points for dividing the face in three thirds: (1) upper third, between points 1 and 2; (2) middle third, between points 2 and 3; and (3) lower third, between points 3 and 6. Also, the lower third can be divided in upper lip length (between points 3 and 4), lower lip length (between points 4 and 5) and the chin corresponding to the mental region (between points 5 and 6). Thus, the frontal view is important to calculate facial asymmetry and disproportions considering the laterolateral and longitudinal axis.

3.3.2 Lateral view

In the lateral view, not only the vertical thirds but also the maxillomandibular relationship can be assessed allowing both the anatomic evaluation of the lips and the classification of the facial profile. As seen on figure 2B, biometric points are used to measure vertical dimensions. In this view, angular measurements can also be assessed: nasofacial angle, nasolabial angle and mentolabial angles. So, the lateral view enables the estimation of the vertical disproportions on the longitudinal axis and the horizontal discrepancies on the anteroposterior axis.

4. Relationship between dentofacial structures

It is questionable if the Golden Proportion can really reproduce the natural appearance during the restoration of dentofacial proportions. Baker and Woods (2001) concluded that there is no correlation between esthetic rating and divine proportion in various facial and cephalometric ratios, either before or after orthodontic/orthognatic surgical treatment. However, it is a consensus that facial architecture is correlated (Powell and Humphreys, 1984; Gomes et. al. 2006; Gomes at. al, 2008; Gomes et. al., 2009). The mathematical relationship between dentofacial structures can improve mainly the rehabilitation of the dental dimensions of the maxillary anterior segment for patients with tooth agenesis from craniofacial anomalies or those who lost their teeth from oral pathology or craniofacial traumas (Gomes et.al., 2009; Lucas et.al., 2009; Germec-Cakan et.al., 2010).

When anthropometric methods were introduced into clinical practice, features differentiating various races/ethnic groups were revealed. Farkas et. al. (2005) published anthropometric values found after evaluating in a preliminary study, 1470 healthy subjects (18 to 30 years), 750 males and 720 females. The largest group (780 subjects, 53.1%) came from Europe, all of them Caucasians. Three groups were from the Middle-East (180 subjects, 12.2%), five groups from Asia (300 subjects, 20.4%) and four groups from peoples of African origin (210 subjects, 14.3%). From all facial measurements, the orbital regions exhibited the greatest variations in identical and contrasting measurements in comparison to North American White (NAW) subjects. Nose heights and widths contrasted sharply: in relation to NAW the nose was very or extremely significantly wide in both sexes of Asian and Black ethnic groups. Among Caucasians, nose height significantly differed from NAW in three

ethnic groups, with one shorter and two greater. In the Middle Eastern groups nose width was identical to those of NAW but the height was significantly greater.
Normative data of facial measurements are indispensable to precise determination of the degree of deviations from the normal. Surgeons require access to craniofacial databases based on accurate anthropometric measurements in order to study and to treat successfully congenital or post-traumatic facial disfigurements in members of different groups. Comparison among the ethnic groups' databases offered the most suitable way to select a method for successful treatment. The following section of this chapter discusses reliable mathematical relationships obtained from photogrammetry to guide oral rehabilitation treatments. Concepts and techniques described in this part will enable clinicians and researchers to understand dentofacial architecture.

4.1 Frontal view

Three different conditions can be registered in frontal aspect: smiling, in RVD or in OVD. In addition to displaying anterior tooth dimensions, the image of the patient's smile is suggested when the lip-tooth relationship is the aim of the observer.
According to Johnson and Moore (1997) the lips are fleshy folds consisting of skin superficially and mucous membrane internally, with muscle, loose connective tissue, nerves and blood vessels contained between them. The sphincter of the lips is the orbicularis oris. It consists of circular fibres surrounding the orifice of the mouth. Some of its fibres are contained entirely within the lips while others are contributed from the dilator muscles and especially from buccinator. The central fibres of buccinator decussate at the corner of the mouth so that those from above pass to the lower lip and vice versa. Many of the fibres that are contained entirely within orbicularis oris pass obliquely through the thickness of the lips from the dermis of the skin on the outer labial surface to the mucous membrane on the inner aspect. Lee (1988) stated that the muscle fibres decussate in the midline and vertical as well as oblique muscle fibre extensions insert into the dermis in the region of the midline philtral groove and the philtral ridges. A dynamic role is postulated of the role of orbicularis oris muscle in giving rise to the unique configuration of the philtrum. Contraction of orbicularis oris compresses the lips against the teeth as well as closing the oral orifice. Due to its instability, the measurement of this facial part is a complex procedure. Ackerman and Ackerman (2002) used photogrammetry to measure the patient's dynamic lip-tooth relationship. Through this method the clinician can incorporate smile analysis into routine treatment planning. Esthetic smile design is a multifactorial decision-making process that allows the clinician to treat patients with an individualized, interdisciplinary approach.
The upper and lower lips frame the display zone of the smile. Within this framework, the components of the smile are the teeth and the gingival scaffold (Fig. 3). The soft-tissue determinants of the display zone are lip thickness, intercommissure width, interlabial gap, smile index (width/height), and gingival architecture. Although the commissures of the lips form lateral borders of the smile, the eye can perceive inner and outer commissures, as delineated by the innermost and outermost confluences, respectively, of the vermillion of the lips at the corners of the mouth (Fig.3). The curve formed by the incisal edges of the maxillary anterior teeth was named by Ackerman and Ackerman (1998) of "smile arc" (Figure 4). The smile arc is described as consonant when there is a parallelism between the smile arc and the curvature of the lower lip, and as less esthetic if the smile arc is flat.

Fig. 3. Anatomy of the lips: (IC) inner commissure, (OC) outer commissure

Fig. 4. Anatomy of the lips: in green, the inter-commissure line; in blue, the smile arc; and in black, the curvature of the lower lip

Conventionally, the length of the maxillary anterior teeth is established by the length of the upper lip. However, there is a lack of consensus regarding the suitable anatomical parameter for the estimation of the width of these teeth. Berry (1905), House and Loop (1939) found the width of the maxillary central incisor as 1/16 of the facial width, measured between the zigomatic bone. Cesario and Latta (1984) and Latta et.al. (1991) published that the mid-pupillary distance was supposed to be the width of the maxillary central incisor multiplied by the factor of 6.6.

A recent research developed at the Department of Prosthodontics and Dental Materials at the Faculty of Dentistry of the Federal University of Uberlandia (Brazil) evaluated 70 facial photographs of undergraduated students. The following facial measurements were compared to the width of the maxillary central incisors: mid-pupillary distance and bizigomatic width of the face. Table 6 presents the ANOVA and Tucky test's results after to apply the techniques mentioned above. Only the bizigomatic width technique (BZG) showed values similar to the real width of the maxillary anterior teeth.

Comparisons for tooth width	Mean	Results
Maxillary central incisor	8.745	A1
BZG/16	8.808	A1
MPD/6.6	10.278	A2

Table 6. Tucky test's results for the techniques to select the width of the central incisors. Footnotes see table 1

The length of the maxillary central incisor is usually said to be the facial length also divided by a factor of 16 (Berry, 1905; House and Loop, 1939). In the same study, facial length was measured both from glabella to mental region and from hair line to mental region, corresponding to the sum of the three facial thirds. Regarding the length of this tooth, the facial length measured in both ways, cannot be used safely to estimate the real length of the maxillary central incisor (Table 7).

Comparisons for tooth length	Mean	Results
Maxillary central incisor	9.574	A1
(MT+LT)/16	8.747	A2
(UT+MT+LT)/16	12.688	A3

Table 7. Tucky test's results for the techniques to select the lenght of the central incisors. Footnotes see table 2

Usually, when it is necessary to observe facial pattern, maxillomandibular relations and facial muscle conditions, the vertical dimension of rest position is recommended. In this situation, photogrammetry can also allow identifying associations between the width of facial structures, such as the nasal width (Gomes et.al., 2009) or the distance between the medialis angles of the eyes (Lucas et.al 2009), and the width of the six maxillary anterior teeth.

The measurement of the vertical dimension of the face can also be evaluated through photogrammetry, compulsory for those patients with posterior tooth loss or reduced teeth size by oral parafunction. Significant correlations were found between the distance from the outer canthus of the eyes to the labial commissure and the lower third of the face while the patient is in vertical dimension of rest position (Gomes et al., 2008).

Another research developed at the Department of Prosthodontics and Dental Materials at the Faculty of Dentistry of the Federal University of Uberlandia (Brazil) evaluated 82 facial photographs of undergraduated students to evaluate the lower third of the face (figure 5). The length of the upper lip was measured from the base of the nose to the rima oris (UL).

The distance between the rima oris and the mental region was also measured (LL-C), corresponding to the length of the lower lip and the chin (figure 5). The distances were compared to the lower third (LT) of the face registered while the subject was in rest vertical dimension. Table 8 presents mean values, standard deviations (SD) and student t test's results for differences according to gender for these measurements. As shown on table 9, all measurements are correlated. Values for the relationship between the lower lip length to the lower third (LLC-LT) are the most significant (r=0.903; p=.000). Figures 6-8 illustrate mathemathical equation from linear regression for these mathematical relationships.

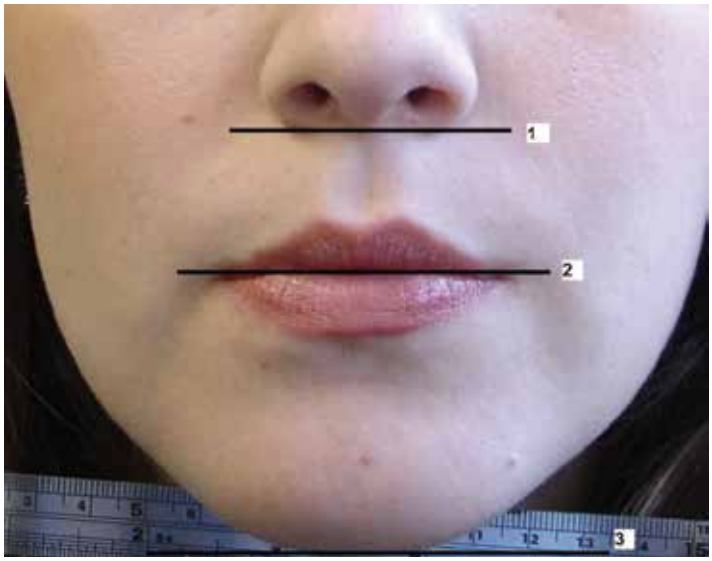

Fig. 5. Frontal view of the lower one-third of the face and landmarks used to guide measurements in digital image

Variables	Total (SD)	Male (SD)	Female (SD)	p
UL	24,71 (2,68)	25,57 (2,93)	24,04 (2,30)	0,008
LL-C	48,18 (4,63)	51,44 (3,90)	45,67 (3,45)	0,000
LT	73,93 (6,43)	77,97 (5,74)	70,83 (5,11)	0,000

Table 8. Mean values and standard deviation (SD) for the total sample and when it was divided according to gender. Footnotes see table 2. Results of Student's *t* Test for differences according to gender (p<.05)

Variables	r	P-value
LL-C x UL	0.439	0.000*
UL x LT	0.745	0.000*
LL-C x LT	0.903	0.000*

Table 9. Pearson's correlation coefficient (r) and their probabilities (P) in a bilateral test

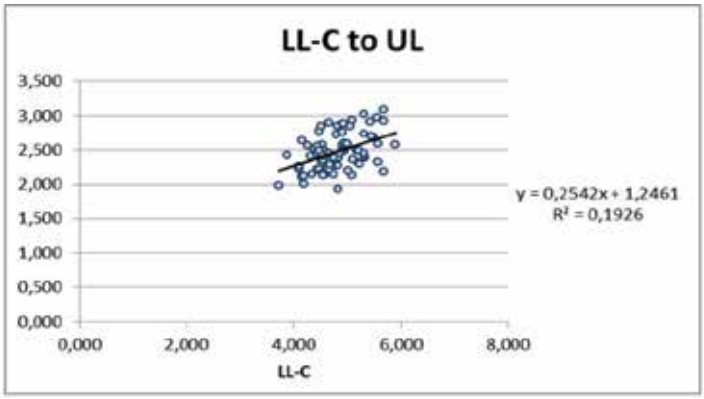

Fig. 6. Scatter plot to show correlation between the values of UL (y) and LL-C (x), and mathematical equation from linear regression

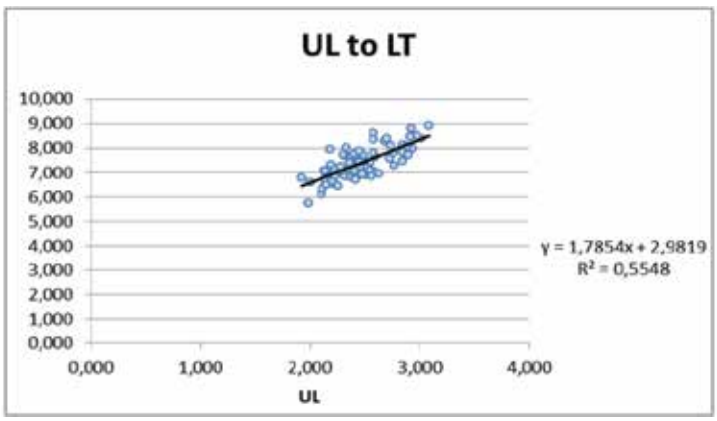

Fig. 7. Scatter plot to show correlation between the values of LT (y) and UL (x), and mathematical equation from linear regression

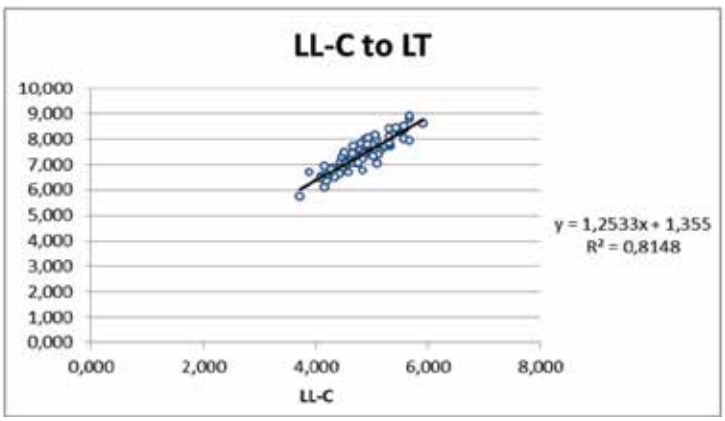

Fig. 8. Scatter plot to show correlation between the values of LT (y) and LL-C (x), and mathematical equation from linear regression

4.2 Lateral view

The success of an oral rehabilitation treatment is frequently related to the improvement in the patient's facial appearance, which includes the soft tissue profile. Unfortunately, during the orthodontic treatment, for instance, traditional cephalometric measurements do not provide all the answers to the aesthetic considerations of the face and dentition, particularly in relation to the soft tissues (Powell and Humphreys, 1984; Gomes et. al. 2006; Gomes at. al, 2008; Gomes et. al., 2009; Aksu et.al, 2010).

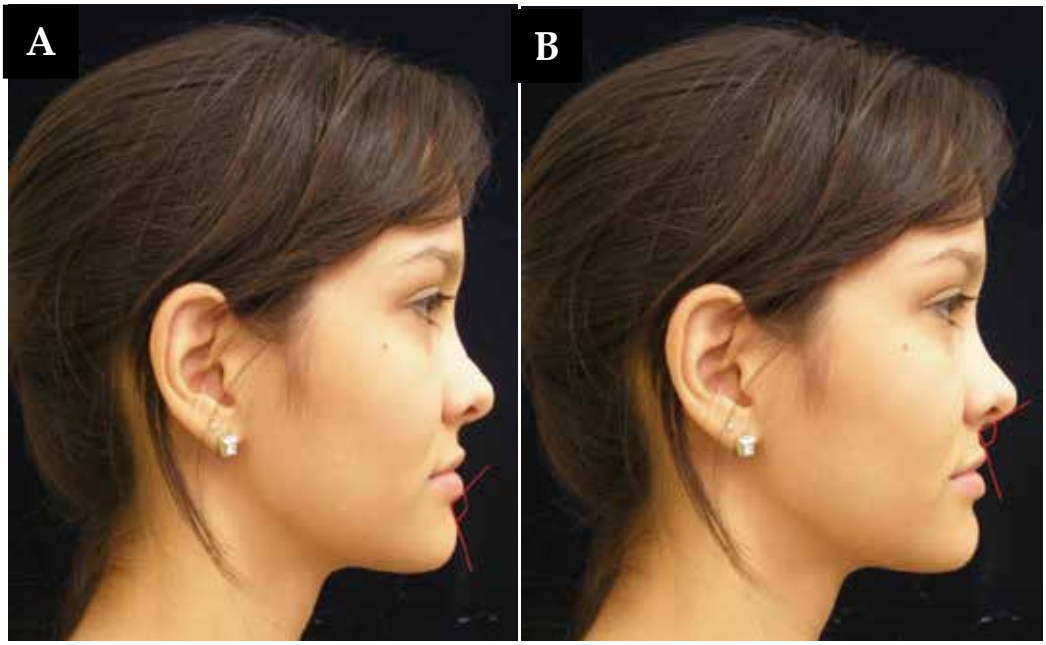

Fig. 9. Mentolabial and Nasolabial angles

Lateral photographs of the subject's face allow the aesthetic analysis to be rapidly carried out, providing the determinants for the horizontal positions of the soft tissue chin, upper lip, lower lip, upper incisors, and lower incisors in relation to the profile (see biometric points on figure 2B). Also, angular measurements can be observed improving the esthetic treatment planning. Table 10 presents mean values for nasolabial and mentolabial angles measured on 18 Brazilian undergraduated students (aged between 18- 25 years old). Figure 7A and B illustrates how those angles were measured.

	Nasolabial angles	Mentolabial angle
Mean (SD)	107.3 (8.2)	128.3 (15.4)

Table 10. Mean values and standard deviation (SD) of the nasolabial and mentolabial angles for total sample

5. Future research

Anthropometry techniques have gained large interest in the last decades to study and to identify human body parts. Two types of approaches are distinguished: direct

measurements with simple instruments and indirect measurements through digital images. While direct approach generates inaccurate results, due to differences in soft tissues compression among observers, indirect measurements requires a standardize image registration of body parts. In this chapter, the use of photogrammetry in dentistry were introduced and discussed. It consists of a steady measurement technique to perform facial analysis offering anatomical parameters for surgical, orthodontic, prosthetic treatments and for researches. Several dentofacial associations to guide oral rehabilitation treatments were shown to implement the diagnosis and restoration of dentofacial irregularities, of craniofacial development, and of facial reconstruction in forensic medicine. Future studies are recommended to define normative data for different ethnic groups as well as other reliable mathematical associations among dentofacial structures to guarantee esthetic quality and natural appearance after oral rehabilitation treatments.

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Part 2

Periodontology and Oral Biology

7

Clinical and Histological Evaluation of Barberry Gel on Periodontal Inflammation

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1. Introduction

Gingivitis and periodontitis are the most common inflammatory oral diseases (Newman et.al./2006). Gingivitis is the most common periodontal disease in children and adolescents (Mc Donald et.al./2011). Periodontitis is an inflammation of the tissues and ligaments that support teeth (that could lead to loosening and subsequent tooth loss) due to infections with microorganisms participate in dental plaque (Newman et.al./2006).
Gingivitis involves primarily inflammation of gingival tissues (Newman et.al./2006). Clinically, it appears as an inflammation of the gingival tissues next to the tooth. Microscopically, it is characterized by the presence of an inflammatory exudates and edema, destruction of collagenous gingival fibers, and ulceration and proliferation of the epithelium facing the tooth and attaching the gingival to it (Mc Donald et.al./2011).
Various studies have shown increased, world-wide gingivitis prevalence rates, especially in developing countries. For example, only 11.3% of 15-19 year-old Iranians had healthy periodontal tissues, 12% had bleeding during probing, 46% presented with gingival calculus, 30.4% had shallow dental pockets and 0.3% had deep pockets in their jaw sextants (Kazemnejad et. al./ 2008, Khordimood & Makarem /2002).
Despite of the changing concepts on the etiology that considered plaque as an etiologic factor for periodontal diseases, an oral self care (for plaque control) is still an essential step in the prevention and treatment of gingivitis (Marsh &Bradshaw1993.Makarem et.al.2006).
Bacterial plaque is composed of soft bacterial deposits that adhere firmly to the teeth and form a complex, metabolically interconnected, highly organized bacterial system consisting of dense masses of microorganisms embedded in an inter microbial matrix. *In sufficient concentration, this microbial matrix can disturb the host-parasite relationship and cause dental caries and periodontal diseases (Mc Donald et.al./2011).*
Since most individuals, especially children and adolescents seem to have difficulty in achieving perfect plaque control by mechanical means, investigations have been directed towards the dentifrices (Pooreslami & Makarem /2002).

2. Plaque control

Chemical plaque control and prevention has been focused on various periodontal preventive strategies since 1980 and include the use of antibiotics (e.g., metronidazole),

enzymes (e.g., dextranase), antiseptics (e.g., chlorhexidine), quaternary ammonium compounds (e.g., cetylpyridinium), phenols, oils, and herbal compounds (Mc Donald et.al./2004).

Recently, novel therapies have included the use of herbal-based pharmaceutical products that have been used world wide, including the increased use of herbal toothpaste over the last decade in the United States, since the perception of many consumers is that herbal-based products are often safer and more effective than chemical-based products (Sean Lee, et.al./2004). Makarem, Khordimood & Pooreslami have shown that herbal agents have effective antiplaque characteristics which make them appropriate as possible antiplaque and tooth cleansing agents (Pooreslami & Makarem /2002 Khordimood & Makarem /2002).

Pradeep AR, et al. concluded that Gumtone gel may be a useful herbal formulation for chemical plaque control agent and improvement in plaque and gingival status (Pradeep /2010).

Adamkova H et al performed a clinical trial to investigate the effectiveness of a herbal-based dentifrice in the control of gingivitis. Forty volunteers were participated in a 84-days study. All subjects were balanced for measured parameters – plaque index (PI), community periodontal index of treatment needs (CPITN) and papillary bleeding index (PBI). The dentifrice was effective in reducing symptoms of gingivitis as evaluated by the CPITN and PBI indices (Adamkova).

Berberine is an alkaloid agent which has previously shown high antimicrobial effects (Makarem & Khalili/2006). This alkaloid is the most active alkaloid (isoquinolines group) extracted from the root and stem of the plant barberry which grows in Europe, Africa, America and central Asia and also in Iran (Makarem & Khalili /2006).

Its scientifically name is "Berberis Vulgaris", the herb known as "Barberry" is a thorny shrub with yellow flowers, small red fruits. It grows along with other shrubs at the edge of fields or forests. This herb is a little pretentious regarding the type of soil it grows on; the types of barberry with caducous leaves are heliophile, and those with persistent leaves can be cultivated in the shade.

In the traditional Chinese medicine, barberry has been mentioned for the past 3000 years. Barbarry is known to contain the potent active agent Berberine, which has numerous usages in controlling different illnesses (stimulates digestion and reduces the gastrointestinal pains). It is also known as a substance that toughens the immune system. Apart from berberine, there are numerous active substances present in the different parts of plant. The bark contains a large number of alkaloids (berberine, berbarine, oxyacantha) and tanines. Barberry fruits contain glucose, fructose, malic acid, pectin, vitamin C. The active substances from the herb bring about the following effects: haemostatic, diuretic, vasodilator, hypertensive, antibacterial, and anti-inflammatory.

Only the dry crust from the roots and stem is being used in medicinal purposes. Barberry can be found on the market under the forms of tea, tincture, pills and ointment. Usually the percentage of berberine from those products is between 8 and 12%. The tincture should be consumed three times a day in doses of 1.2 ml.

Barberry decoct as gargling is effective against sore throats while using of cataplasms with powdered barberry crust is recommended for conjunctivitis.

Anti-inflammatory

The effects of the alkaloid constituents are primarily responsible for the historical use of Berberidaceae species extracts in inflammatory conditions. Berberine and oxycanthine

alkaloids from *Berberis vulgaris* were administered in acute inflammation (paw edema). In comparison, Oxycanthine was less effective than berberine in the studies (Ivanovska & Philipov /1996).
An in vivo study using Turkish Berberis species demonstrated that all alkaloids (from this species of *Berberis*) inhibited inflammation with dose dependent activity. Berberine, palmatine and berbamine were the most effective in topical and oral administration.

3. History

Barberry has a long history of use in traditional eastern and western herbalism. In ancient Egypt, barberry fruit was used with fennel seeds to ward off pestilent fevers (Chevallier / 2001). Indian ayurvedic physicians used barberry in the treatment of dysentery and traditional Iranian medicine uses the fruit as a sedative (Kunwar et.al./2006, Fatehi-Hassanabad.al/2005). In northern Europe barberry was used to treat gall bladder and liver problems, while in Russia and Bulgaria it was used in the treatment of abnormal uterine bleeds and rheumatism (Ivanovska &, Philipov/ 1996, Imanshahidi & Hosseinzadeh/ 2008). In North America, the Eclectics used barberry to treat malaria and as a general tonic (Mills & Bone / 2000). The American Indians found it useful in improving appetite and used the dried fruit as a gargle (Imanshahidi & Hosseinzadeh /2008, Bone / 2003).

4. Major active constituents

The key active constituents of barberry root and stem bark are isoquinoline alkaloids. Two classes of alkaloids have been identified – protoberberines (berberine, berbamine, jateorrhizine and palmatine) and bisbenzlisoquinolines (oxycanthine). Berberine is the main active constituent and the most studied alkaloid. It is found throughout the plant; however, it is more concentrated in the roots, bark and stems (Imanshahidi & Hosseinzadeh/2008, Bone /2003).

5. Actions

5.1 Traditional

antimalarial, antirheumatic, antiseptic (Imanshahidi & Hosseinzadeh /2008, astringent Tierra/*1988*), bitter tonic (Imanshahidi & Hosseinzadeh /2008), depurative (Tierra/*1988*), diuretic (Ivanovska & Philipov /1996), dysmenorrhea (Imanshahidi M & Hosseinzadeh /2008), purgative (Mills & Bone/2000, sedative (Fatehi-Hassanabad et.al./2005).

5.2 Contemporary

amoebicidal , antibacterial (Chevallier / 2001), antibiotic (Van Wyk &, Wink /2004), antiemetic (Thomsen / 2005, Bone / 2007), anti-inflammatory (Thomsen / 2005), antimicrobial, antiparasitic (Bone / 2007), antiprotozoic , antipyretic (Thomsen/2005), bitter tonic (Kunwar et.al./2006,Van Wyk &,Wink /2004, Bone /2007), cholagogue (Thomsen /2005, Bone /2007, choleretic (Van Wyk &, Wink /2004), hepatic (Bone / 2007), laxative (Bone /2003, Bone /2007), spleen tonic (Thomsen/2005).
The Makarem and co workers study (Makarem & Khalili /2006) indicates that the barberry dental gel effectively controls microbial plaque and gingivitis in the school aged children; therefore, the use of barberry dental gel is strongly recommended. They also concluded that a dental gel preparation containing berberine reduced dental plaques by 56% and their study resulted in a 33% improvement in the GI (Makarem & Khalili /2006).

The study of Moeintaghavi , Makarem et al, was performed to evaluate the clinical and histological efficacy of a topical gel containing a barberry extracts in patients with periodontitis needing periodontal surgery. They concluded that Tissues treated with barberry gel extract had reduced numbers of inflammatory cells at the time of surgery. However, the GI and PI scores were not different between treated groups.

6. The study protocol

6.1 Sample size

Based on the study by Makarem *et al*., 11 patients were the minimum needed to carry out the proposed study; however, 14 patients were recruited to account for confounders.

6.2 Study design

This randomized clinical trial study was performed on 14 patients (11 female, 3 male) with a mean age 45±4 years that were referred to the Department of Periodontology at the Mashhad School of Dentistry, Iran. All patients presented with moderate to severe periodontitis according to criteria established by the American Academy of Periodontology (AAP) and also needed periodontal surgery.

The study protocol was approved by the Medical Ethics Committee of Mashhad University of Medical Sciences. Subsequent to receiving information regarding the study process, informed consent was obtained. Patients with the following conditions were excluded from the study: Patients with conditions that could aggravate periodontal infections (such as hematologic disorders, diabetes, immunodeficiencies), antibiotic use during the preceding three months, patients on contraceptives, patients using antibacterial mouthwashes or patients with a history of smoking.

6.3 Gel preparation

Berberis vulgaris branches were collected in the autumn and dried outdoors for three weeks. The degree of dehydration was verified periodically by measuring the weight of the collected branches. The branches were ground to a particle size of 1000 ± 250 µ. A total of 200 g of the ground was extracted following the reflux protocol over a 24 h period with 700 ml of 96% ethanol using Soxhlet instrument. The alcohol extract was concentrated to give 40 gm using vacuum evaporating at 40°C water bath. The extract was standardized using UV spectroscopy at 340 nm on the basis of the berberin concentration of the primary plant alkaloid that comprises 0.005% of the total dried branch weight.

The 5% aqueous gel specimens were prepared by geometrically triturating 5 g of the extract with 95 g of gel base under clean conditions using mortar and pestle. The gel base was an aqueous solution of 5% polyvinyl alcohol. The placebo gel was prepared in a same manner without addition of the concentrated berberin extract. Fifteen grams of either the berberin gel preparation or the placebo were packed in aluminum tubes on the same day of delivering to the patients under clean conditions.

6.4 Berberin gel testing

Plaque (PI) and gingival (GI) indices of enrolled patients were recorded at the time of the study (base line) and again one-week later. In addition, scaling and root planning were carried out for all patients using an ultrasonic scaler (Dentsply,Cavitron; BOBCAT, 11136,

L.I city, N.Y, USA) following standard protocols. An impression was taken of the jaw and a soft splint made with a medial gap. Patients were asked to fill half of the splint with b erberine gel and half with placebo each night for a period of two weeks at which time the PI and GI were again measured prior to surgery. To control for patient use errors, each patient received two coded tubes containing berberine gel or placebo. Patients were asked to return the tubes after the two weeks and the content of the respective tubes identified when the patients returned to the clinic at the end of the two-week period.
Three weeks after scaling and root planning, periodontal surgery was performed and specimens harvested from both sides of the jaw and analyzed histologically. Samples were fixed in 10% formalin for 24 h, paraffin embedded and cut into 4-5 μm thick sections that were hematoxylin and eosin (H&E) stained and then examined at 400 and 1000X using an optical microscope (Leitzlabarlux microscope, Vermont Optechs, Charlotte, VT).

6.5 Histological evaluation

Acute and chronic inflammation was defined by characterizing the nature of infiltrating polymorphonuclear (PMN) cells and lymphocytes. The severity of inflammation was categorized according to the number of inflammatory cells present in respective microscopic fields. Degrees of inflammation were defined as follows: 0-2 inflammatory cells, no inflammation; 2-5 inflammatory cells, mild inflammation; 5-10 inflammatory cells, moderate inflammation and 10 or more inflammatory cells, severe inflammation. The number of blood vessels identified in 5 microscopic fields (0.2 mm^2) was calculated and compared to the number of blood vessels present in samples harvested from the control specimens. In addition, changes in epithelial thickness were compared to epithelial thickness of normal tissues and results defined as either hyperplastic or atrophic. The examiner, surgeon and statistician were all blinded to the medication applied to respective samples. Two patients were excluded due to non-compliance.

6.6 Statistics

Gingival and plaque indices for the two groups were analyzed using the Friedman test. The Chi-square and Wilcoxon tests were used to compare inflammation rates and vessel densities between groups.

7. Results

Fourteen patients were enrolled in this study to assess the effect of berberin gel on periodontal inflammation. Two patients were excluded due to non-compliance. Of the 12 remaining patients (2 men, 10 women) differences in respective GI values were observed between baseline and follow up visits in each group (Table 1 and 2), however, no GI differences between the respective groups at each time point were observed even though the PI decreased significantly between the first and third visits. The most commonly identified inflammatory cell type in respective samples were lymphocytes and plasma cells. However, no significant differences in the type of inflammatory cells present between treatment groups, the degree of angiogenesis ($P=0.102$) nor in the degree of edema ($P=0.214$) was observed between samples from respective treatment groups. In addition, the amount of collagen fibers identified remained unchanged between groups. The only significant difference observed was a reduction in the number of inflammatory cells

present in samples examined from portions of the jaw treated with berberin gel (P=0.011) (Figs 1-4).

Visit	Test Mean ± SD	Control Mean ± SD	P-Value*
First	1.57± 0.43	1.68± 0.4	0.214
Second	1.37± 0.26	1.28± 0.4	0.386
Third	1.07± 0.42	1.09 ± 0.29	0.779
P-value**	0.037	0.002	

*Wilcoxon signed Rank Test
**Friedman Test

Table 1. Gingival Index reading of the test and control groups at each visit

Visit	Test Mean ± SD	Control Mean ± SD	P-Value*
First	1.82± 0.43	1.72± 0.77	0.114
Second	1.46± 059	1.42± 0.61	0.715
Third	1.04± 0.8	1.1 ± 0.75	0.068
P-value **	0.013	0.019	

*Wilcoxon signed Rank Test
**Friedman Test

Table 2. Plaque Index readings of the test and control groups at each visit

Intensity	Test		Control		P-value
	Number (n)	Percent (%)	Number (n)	Percent (%)	
Mild	5	41.7	0	0	
Moderate	5	41.7	7	58.3	
Severe	2	16.7	5	41.7	
Total	12	100	12	100	P=0.011

Table 3. Inflammatory cell infiltrate intensity

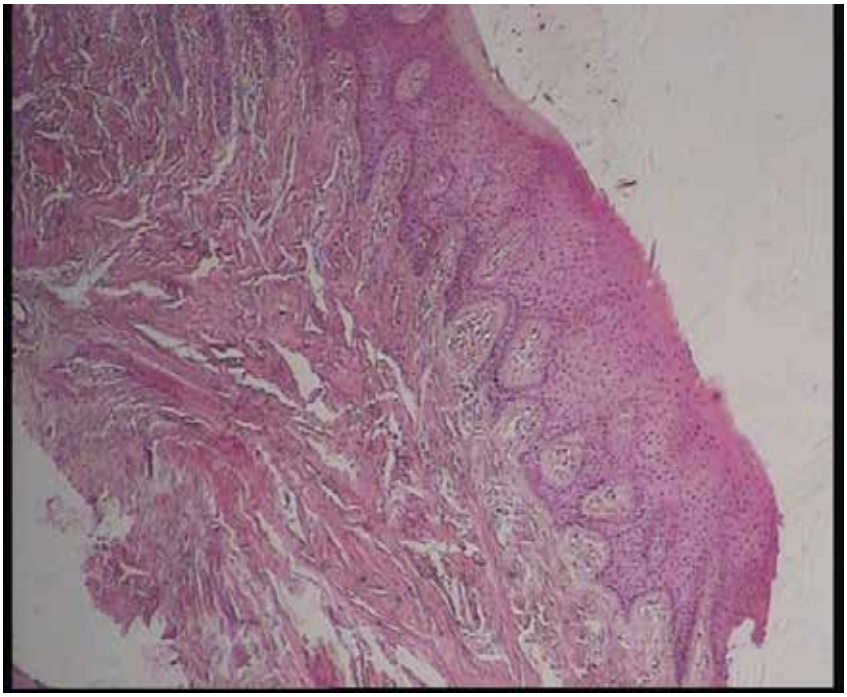

Fig. 1. Histologic aspect of a test specimen (H & E staining, magnification 40^{X})

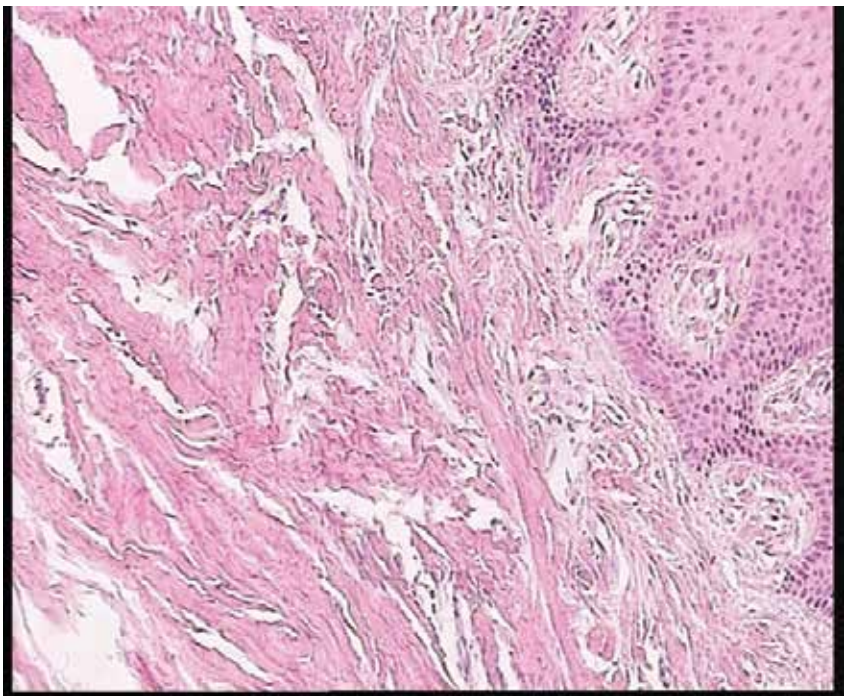

Fig. 2. Histological aspect of a test specimen (H & E staining, magnification 100^{X})

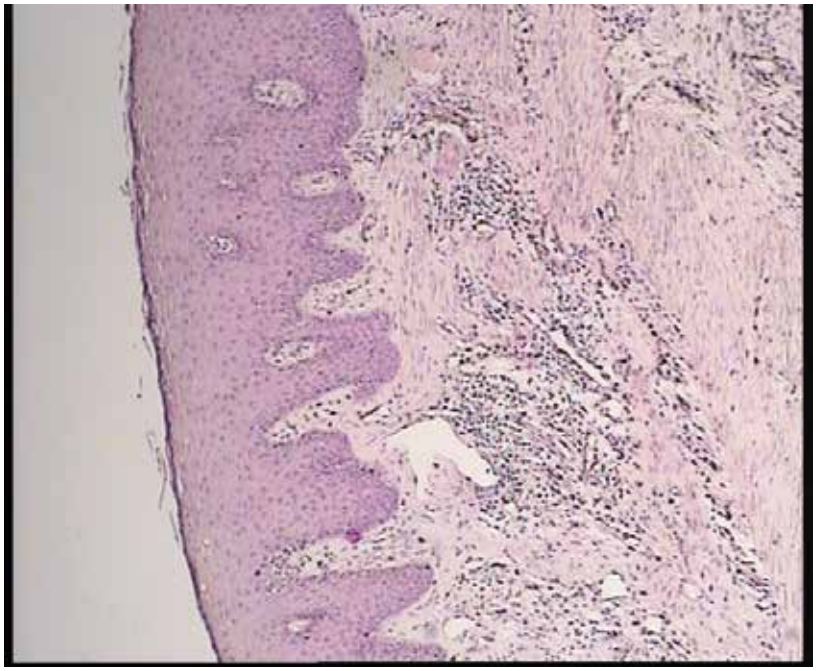

Fig. 3. Histologic aspect of a control specimen with chronic inflammation (H & E staining, magnification 40X)

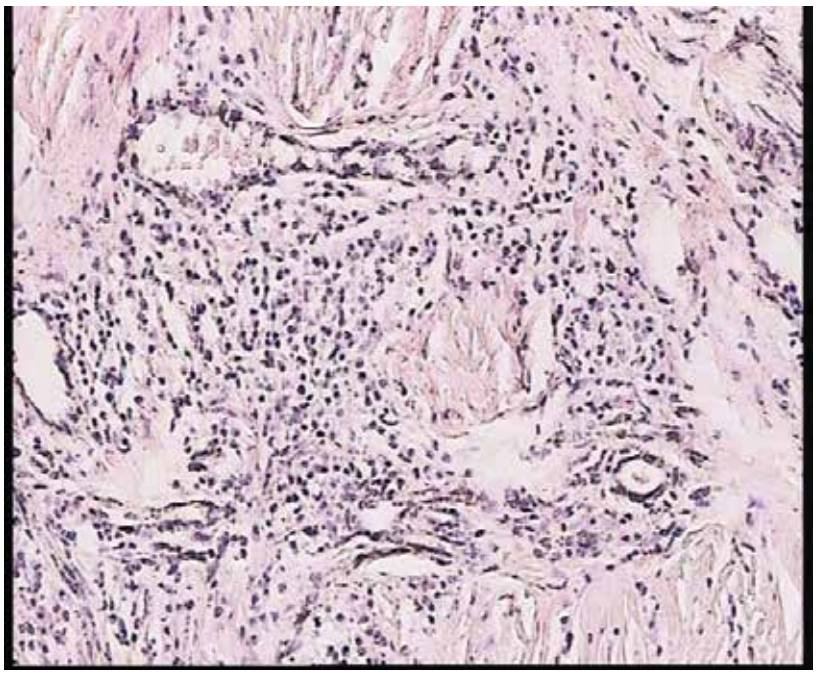

Fig. 4. Histological aspect of a control specimen with chronic inflammatory cells infiltration (H & E staining, magnification 100X)

8. Discussion

Gingivitis and periodontitis are two common inflammatory diseases of periodontal tissues. Inflammation is limited to gingival tissues in gingivitis but periodontitis is also associated with the destruction of tooth supporting structures. In both cases, inflammation is the result of microorganisms present in dental plaque (Newman et. al. /2006). Therefore, either mechanical or chemical plaque control methods have been used to reduce plaque-related inflammation of the oral mucosa.

Since it has been suggested that there is an association between periodontal disease and systemic diseases like coronary heart diseases, diabetes, stroke or preterm low birth weights, control of periodontal infections could be important not only in controlling oral mucosa infections but also in the maintenance of overall health.

Today, chemical plaque control using mechanical methods has increased the efficacy of periodontal treatments along with antibiotic treatments and essential oils used for plaque control (Mc Donald et.al./2004). Since herbal derivatives are less harmful than synthetic medications (Lee et.al./2004) significant efforts have been made to identify novel, herbal extracts for use as anti-plaque agents.

Barberry is a plant that grows in different parts of the world including parts of Europe, Africa and in Asia it is found only in Iran (Makarem & Khalili /2006). Berberin is the most effective alkaloid derived from Barberry plants and has been added to tooth pastes and mouth washes due to its antimicrobial activities. Since it was demonstrated by Makarem et al. that berberin gel reduced both the PI and GI in gingivitis patients (Makarem & Khalili /2006), the present study was carried out to evaluate the clinical and histological effects of berberin gel in periodontitis patients. Our findings showed that PI and GI decreased significantly between baseline and the second and third visits in both groups, likely due to mechanical debriment, in contrast to the data presented by Makarem et al. (Makarem & Khalili /2006) that suggested the reduction in both PI and GI was due to the berberin present in the toothpaste and not a consequence of mechanical debriment. To eliminate the mechanical debridment component from this study, our patients used the gel during their sleep and not during teeth cleaning.

Data from studies that required patients to carry out some of the study procedures at home demonstrated that patients could be influenced by factors that may mask the efficacy of a test agent compared to the control. One factor is the Hawthorn effect (Fletcher et.al/1997) that suggests the clinical trial participants may experience some improvement not associated with the therapeutic properties of the test agent, but rather due to behavioral modifications as a consequence of participating in the trial. For example, patients participating in oral hygiene studies improved their oral care practices regardless of the group in which they were enrolled. Since this study had a split mouth design and each patient acted as a test and a control, risk of Hawthorne effect bias was reduced. However, it is possible that the 3-week period of the study was insufficient to show significant effects of the berberin gel over the placebo due to a potential lack of compliance with using the gel.

Although, it has been demonstrated that berberine and related derivatives (such as oxycanthine) poses antibacterial properties (Amin AH et. al./1969) and can inhibit bacterial attachment to human cells (Sun/ 1988) we did not observe significant effects of berberin over placebo with the exception of the intensity of the inflammatory cell infiltrate which was reduced in berberin-treated tissues. This might have been due to the anti inflammatory

effects of berberin and berbamine (Wong et. al. / 1992), other alkaloids shown to improve immune cell function (Kumazawa et. al. /1984).

9. Conclusion

The use of a barberry-derived gel (compared to the placebo) did not alter GI or PI scores, inflammatory cell profiles or the severity of edema but reduced the degree of inflammatory cell infiltrates in the oral mucosa.

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11. Conflict of interest and sources of funding statement

The authors declare that there were no conflicts of interest in this study.
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8

Periodontal Disease and Carotid Atherosclerosis: Mechanisms of the Association

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1. Introduction

Despite advances in its diagnosis and management, cardiovascular disease remains the leading cause of death in western countries. Many risk factors are involved in the development of cardiovascular disease; recently, periodontal disease was recognized as a new risk factor in many epidemiological studies. The association between dental and cardiovascular disease is intriguing for the potential clinical implications, and it is independent of other risk factors. This association has been demonstrated for several localization of atherosclerotic plaques, involving coronary, cerebral and/or peripheral arteries. The finding that patients with periodontitis show also more evident carotid atherosclerotic plaques is clinically important because this disease localization is the most important cause of cerebral ischemia, in turn the main cause of disabilities in western world (A.H.A, 2002).

On this basis, the following chapters highlight the links between periodontal disease and carotid atherosclerosis, focusing on the mechanisms of this association: inflammation, dental pathogens and toxins, endothelial dysfunction, with the addition of hemorheology as a new evidence.

In details, the first chapters exploit the main features of these processes (chronic periodontitis, atherosclerosis, wall shear stress in hemorheology); then, we report and analyze a series of cross sectional, prospective and intervention studies in this field. In the last section will elucidate the interplays between periodontal disease, hemodynamic forces and atherosclerosis.

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2. Chronic periodontitis

Chronic periodontitis affects a large proportion of the adult population; it can be regarded as a progression of infection and inflammation of gingivae into the deep tissues of the periodontium (Mitchell DA et al, 2003).

All periodontitis develops out of gingivitis but not all gingivitis progresses to periodontitis. In fact, even if it is true that gingivitis is a successful response to the bacterial onslaught, in certain occasion it may progress to periodontal disease in which the soft tissues and bone are destroyed (Cawson RA et al, 2009).

Dental plaque is the principal etiological factor in nearly all forms of periodontal disease although the role of bacteria is unclear; current hypotheses suggest that periodontal disease may be due to bacterial accumulation irrespective of its composition, or the result of an infection with a single specific pathogen, or the result of infection with a relatively small number of interacting bacterial species (Palmer R. M. et al, 2008). There are a number of currently identified risk factors for the progression of the disease such as poor plaque control, smoking, age, systemic diseases, stress, genetics and various other medical conditions. Therefore, periodontitis is initiated and sustained by microbial plaque but host factors determine the pathogenesis and rate of progression of disease. In most cases progression is slow to moderate but periods of rapid tissue destruction may occur.

Periodontal disease is characterized by breakdown of periodontal fibre bundles at the cervical margin, resorption of alveolar bone, and apical proliferation of junctional epithelium beyond the amelocemental junction.

Periodontal abscess, a complication of periodontitis, is a localized collection of pus within a periodontal pocket. Clinically there may be swelling, pus from pocket or sinus, pain tenderness to percussion and signs of periodontitis.

The diagnosis of periodontal disease is based on a thorough clinical examination of periodontal tissues, instrumental examinations and laboratory tests. All this is addressed to appreciate the degree of oral hygiene (presence of plaque and tartar), predisposing local factors (incongruous restorations, abnormal shape and position of teeth), clinical signs of gingival inflammation (redness, swelling, bleeding), destruction of periodontal tissues (gingival recession, clinical attachment loss, alveolar bone loss).

The gingival recession and loss of clinical attachment is measured using the periodontal probe, looking at the gingival margin and periodontal pockets, producing standard quantitative periodontal parameters of disease. Gingival plaque is generally evaluated with Plaque Index by Silness and Löe, which comprises visual clinical evaluation of each tooth on the mesial, distal, buccal and lingual aspect (Silness J et al, 1964). Inflammation of gingiva is evaluated by Gingival Index: 24 gingival margins are scored 0 to 3 upon inspective signs of inflamed mucosa, and bleeding (Loe H, 1967). Probing depth is a clinical measure of inflammation involving the other periodontal structures of periodontal ligament, dental cementum and alveolar bone; detected in millimeters at 6 sites in each tooth (mesial, center and distal of the buccal and lingual aspects), it gives Pocket Deep index (Ramfjord SP, 1959). Gingival margin is a reference point for reading of values during probing. A global index is DMFT, the number of Decayed, Missing and Filled Teeth. The loss of alveolar bone is measured by X-ray.

Although periodontal disease is a localized chronic inflammation, it may have important effects on distant organs (Lindhe J et al, 2003). In particular, periodontitis can interfere with

the systemic circulation. Therefore, in the last decade numerous studies have been conducted on the atherosclerotic process in particular. This effect of periodontitis was explained by the possible translocation of periodontal pathogens from the oral cavity to the circulatory system. Furthermore, a large local periodontal production of mediators could invade the circulatory apparatus and inflammation could then cause damage to sites distant from the point of origin. Recently, some other interesting mechanisms of this association have been proposed; these new findings are delineated below, together with an overview of the pathophysiology of the arterial system.

3. Atherosclerosis

Atherosclerosis is commonly considered a chronic inflammatory disease that affects large and medium-sized arteries (Ross R, 1999). Atherosclerotic lesions are at the basis of common cardiovascular disease as myocardial infarction, stroke, claudicatio intermittens. Common risk factors for atherosclerosis development include arterial hypertension, diabetes mellitus, dyslipidemia, obesity (A.H.A, 2002). Although all arteries are exposed to the risk of atherosclerotic lesions, plaques grow in areas of disturbed blood flow and altered hemodynamic forces, in particular at arterial bifurcations (Chatzizisis YS et al., 2007).

Atherosclerotic lesions develop during many years and in a stepwise manner. Anatomically, earliest lesion is represented by the so-called "fatty streak": this is a yellow lesion of few millimeters, that develops from the first years of life as demonstrated at autopsy. Histologically, this lesion consists in *foam cells* (macrophages that absorb oxidized – Low Density Lipoproteins and other fats, then migrate under tunica intima of the vessels) with some T-lymphocytes, platelets and smooth muscle cells.

Later, the progression of atherosclerosis leads to the atheroma formation. In fact, it continues the deposition of lipids, platelets and macrophages; these cells release growth factors that leads to SMC proliferation. SMC create a cap that contains a *core* of intra- and extracellular lipids (Cotran R et al, 1999).

The final stage is represented by the complication of atherosclerotic plaque: the rupture of the atheroma. In fact, for inflammation and/or production of metalloprotease, the rupture of the fibrous cap may occur; consequently, the exposition of thrombogenic lipid material to the circulating platelets induces thrombus formation in the lumen. Intraluminal thrombus can occlude arteries (e.g. coronary occlusion), but more often it detaches, moving downstream and eventually occluding smaller branches (thromboembolism, e.g. stroke as a complication of carotid atherosclerosis) (Davies MJ, 1998).

Recently, a subclinical early level of atherosclerosis has been recognized in a microscopic alteration called intima-media thickening. It is the increase of the thickness of intimal and medial layers of arterial wall, usually measured by external ultrasound. Intima-media thickening appears as a hypo- or iso-echogenic space delimitated by two hyper-echogenic lines. These lines are generated by the lumen-intima interface and the media-adventitia interface. The measurement of intima-media thickening using ultrasound has been evaluated and validated by in vitro measurements of specimens of common carotid arteries and in vivo measurement in normal subjects (Coll B et al, 2008). A large number of studies have demonstrated that intima-media thickening is a risk factor and a marker for coronary heart disease that accurately represents subclinical vascular disease but not plaque formation or atherosclerosis per se (Johnsen SH et al, 2009).

However, probably there is a earlier step of atherosclerotic process, the *response to endothelial injury* or *endothelial dysfunction* (Ross R, 1998).

4. Endothelial dysfunction

In order to give a definition of endothelial dysfunction, a brief overview about anatomy and physiology of the arteries is needed (Chien RS et al, 1987).
First of all, the arterial tree can be divided into different compartments, from central to peripheral arteries: elastic arteries, muscular arteries, and arterioles. Large elastic arteries have a dominant role in cushioning against pressure oscillations that result from ventricular ejection and they tend to transform pulsatile flow into a steady flow to better supply oxygen and nutrients to the tissues. Muscular arteries and even more arterioles regulate the amount and distribution of the blood in peripheral tissues.
These physiological mechanisms are warranted by healthy structure and function of the arteries. In fact, it is well known that arteries not only provide a conduit for the blood, but synthesize and release several vasoactive substances in order to meet the peripheral metabolic demand. Among these substances, nitric oxide has a pivotal role in protecting against the initiation and progression of atherosclerosis via its vasodilator activity and its inhibitory activity against vascular smooth muscle cells growth, transcription of cell adhesion molecules, platelet aggregation, and leukocyte adhesion to endothelial cells.
Therefore, in pathophysiology, endothelial dysfunction can be defined a pathological state of the endothelium (the inner lining of blood vessels) characterized by an imbalance between vasodilating and vasoconstricting substances produced by the endothelium. Recently, some physical forces generated by blood movements have been recognized as important players in endothelial dysfunction.

5. Hemodynamic forces

Many physical forces are generated during blood circulation (Bevan JA et al, 1991). Wall shear stress is the frictional force of the flowing blood on the endothelial surface of the arterial wall. It is the product of the blood viscosity and shear rate (wall shear stress = blood viscosity x blood velocity /arterial internal diameter). In fact, shear rate is an expression of the velocity of the blood as a function of radial position in the vessel. According to this formula, apart from blood viscosity changes during circulation, arterial regions with increased internal diameter or reduced blood velocities have a low shear stress.
The features of fluid flow through a tube is also dependent on flow velocity and on the presence of geometric irregularities like arterial bending and/or bifurcation, stenosis etc. Fluid flow is laminar or turbulent. Laminar flow or streamline flow, occurs when a fluid flows in parallel layers, with no disruption between the layers. In turbulent flow the velocity at any given point varies continuously over time, even though the overall flow is steady. In fluid dynamics, a measure of flow turbulence is determined by Reynolds number; for low Reynolds values, flow is laminar, whereas for high Reynolds values (typically above 2,000), flow is turbulent. In relatively straight arterial segments, wall shear stress is pulsatile and unidirectional with a magnitude that varies within a range of 5 to 70 dyne/cm^2 for mean shear stress. In contrast, mainly in regions of disturbed laminar flow, oscillating or reverse wall shear stress occurs. Wall shear stress could be low also in straight arteries of old or

diseased individuals, in particular if affected by arterial hypertension, excessive body weight or diabetes mellitus.
Wall shear stress deeply influences endothelial cell pathophysiology. Luminal endothelial cell surface is equipped with numerous mechanoreceptors capable of detecting and responding to shear stress stimuli. After activation of mechanoreceptors, a complex network of several intracellular pathways is triggered, a process known as mechanotransduction. In arterial regions of healthy people without flow problems, where wall shear stress varies among individuals within a physiological range, the endothelial cells express various atheroprotective genes and suppress the production of several pro-atherogenic substances, leading to arterial stability and a proper endothelial function in that region. In contrast, in regions where low and/or disturbed wall shear stress occurs, the atheroprotective genes are suppressed and the pro-atherogenic genes are upregulated, thereby promoting endothelial dysfunction and atherosclerotic process (Chatzizisis YS et al., 2007).

6. Endothelial function measurement

Many efforts have focused on the development and improvement of non-invasive diagnosis of atherosclerosis based on ultrasound technology in order to evaluate arterial structure and function. Celermayer developed an ultrasound technique known as flow mediated dilation to study arterial function. This test allows evaluation of endothelial response to an ischemic stimulus. Briefly, brachial artery is visualized and baseline diameter measured. Then, ischemia is created by inflating a cuff around the forearm. Ischemia causes arteriolar dilation; this, in turn, induces reactive hyperemia for the reduced forearm resistance after cuff release. Reactive hyperemia increases blood flow through the brachial artery creating a wall shear stress elevation which increases arterial diameter. The percentage increase in diameter, calculated by measuring the diameter before and after the test, is an estimate of endothelial function in response to ischemia (Celermajer DS et al, 1992).
Vasodilation generated by the increase in shear stress following ischemia is mediated by nitric oxide, a local vasodilator. Impaired vasodilator reaction is among the earliest changes to occur during the development of atherosclerosis (Agewall S, 2003). A different method to assess vascular function is nitroglycerin mediated vasodilation of brachial artery (an index of endothelium-independent dilatation) or acetylcholine mediated vasodilation (an endothelium-dependent vasodilator) (Kasprzak JD et al, 2006).
The alteration of flow mediated dilation is important for its potential clinical implications; indeed, as demonstrated in the Cardiovascular Health Study, brachial flow mediated dilation is a predictor of future clinical cardiovascular events in older adults, even after adjustment for other conventional cardiovascular disease risk factors (Yeboah J, 2007). Moreover, another study has demonstrated its strong association with coronary artery disease, evaluated by angiography (Neunteufl T et al, 1997).
An epidemiological association has been verified between endothelial dysfunction and periodontal disease, as exploited in the following chapter.

7. Periodontitis and endothelial dysfunction: Epidemiological association

Periodontal disease is linked with endothelial dysfunction assessed with both flow mediated dilation and acetylcholine mediated dilation.

A case-control study published in 2003 demonstrated for the first time an endothelial vasomotor dysfunction in a conduit artery in patients with severe periodontal disease. Authors assessed both flow mediated dilation and nitroglycerin-mediated dilation of the brachial artery in 26 subjects with advanced periodontal disease compared with 29 control subjects. Subjects were free of traditional risk factors and underwent a vascular examination. Patients with advanced periodontal disease had lower flow-mediated dilation compared with control patients matched for age and sex. Nitroglycerin-mediated dilation was equivalent in the two groups (Amar S et al, 2003).

Focusing on the additive role that periodontitis may play with traditional risk factors in the impairment of endothelial function, Higashi et al assessed forearm blood flow responses to acetylcholine and sodium nitroprusside in various subtypes of patients with periodontal disease. Aim of this study was to define the effects of periodontitis on endothelial function in humans avoiding the possible confounding factor of endothelial function alterations caused by other factors as hypertension, heart failure, atherosclerosis, hypercholesterolemia, diabetes mellitus, smoking, aging, and menstrual cycle. A normal control group (20 men; 26±3 years of age) was compared with a group of 32 patients with periodontitis without other cardiovascular risk factors (32 men; 25±3 years of age), and hypertensive patients without periodontitis (28 men and 10 women; 56±12 years of age) were compared with hypertensives with periodontitis (18 men and 6 women; 54±13 years of age). Both in healthy and in hypertensive subjects, forearm blood flow responses to acetylcholine were significantly smaller in the periodontitis groups than in the control groups. Sodium nitroprusside–stimulated vasodilation was similar in the 2 groups. Periodontitis impaired endothelium-dependent vasodilation in healthy young men. In patients with hypertension who have impaired endothelial function, clinical complications of periodontitis greatly increased the magnitude of endothelial dysfunction (Higashi Y et al, 2008).

Looking at more advanced atherosclerotic conditions, also carotid intima-media thickening and/or carotid plaques, the commonest cause of cerebral ischemia, resulted associated to periodontal disease.

8. Periodontitis and carotid atherosclerosis: Epidemiological association

Many studies report the association between periodontal disease and clinical or subclinical carotid atherosclerosis. It has been demonstrated, in cross-sectional and longitudinal studies, that periodontal disease is closely related with subclinical carotid atherosclerosis. The ARIC study, a large cross sectional study performed between 1996 and 1998, demonstrated for the first time the relationship between periodontitis and intima-media thickening. The participants received a clinical periodontal examination, and a carotid scan using high-resolution B-mode ultrasound. The results of the study showed that individuals with severe periodontal disease had 1.3 times the odd of thicker carotid arterial walls (>=1 mm) compared with individuals with less severe disease, after adjustment for traditional risk factors for atherosclerosis. The edge of 1 mm for intima-media thickening was chosen because a larger value is associated with an increased risk of cardiovascular events. (Beck JD et al, 2001).

Later, a similar study, carried out in 711 subjects with no history of stroke or myocardial infarction, demonstrated also a significant association between teeth loss, considered as a sign of past periodontitis, and carotid artery plaque prevalence. Among patients with 0 to 9

missing teeth, 46% had carotid artery plaque, whereas among those with 10 or more missing teeth, carotid artery plaque prevalence was 60% (Desvarieux M et al, 2003).
Shortly after, INVEST cross-sectional study demonstrated that carotid IMT correlated with periodontal microbiota. The analysis was adjusted for age, gender and traditional risk factors. Overall, periodontal bacterial burden was related to carotid intima-media thickening (Desvarieux M et al, 2005).
The relationship between periodontal disease and carotid atherosclerosis was further highlighted in longitudinal studies.
In fact, Soder et al. assessed the role of periodontitis in the development of atherosclerosis, evaluating the relationship between periodontal disease and development of subclinical signs of carotid atherosclerosis. Eighty two subjects with periodontitis 16 years before were compared to 31 patients without periodontitis. In the follow up, patients with periodontal disease developed significantly more intima media thickening than patients without documented periodontitis. This result confirm in a longitudinal manner that periodontal disease is associated with the development of early atherosclerotic carotid lesions (Söder PO et al, 2005).
Moreover, chronic oral inflammatory diseases seem responsible of atherosclerotic plaque progression. Another longitudinal study with a follow-up of 7.5 months showed that dental and periodontal disease was significantly associated with progression of carotid atherosclerosis. The authors used known periodontal indexes: DMFT as a measure of global teeth status was predictor of prevalence and progression of the disease, irrespective of traditional cardiovascular risk factors and baseline degree of stenosis. Edentulous patients also had a significantly increased risk for disease progression as compared with dentate patients. Particularly, during the follow-up period, 11.7% of patients showed progression of carotid atherosclerosis: they had significantly higher DMFT indices compared with patients with stable carotid disease. A further analysis of the subcategories of DMFT revealed that the number of missing teeth was strongly associated with disease progression, whereas filled teeth showed only a borderline significance, and the number of decayed teeth was not significantly associated with progressive disease (Schillinger T et al, 2006).
But the presence of periodontitis is linked to carotid atherosclerosis and at its earlier step, endothelial dysfunction, also in intervention studies.

9. Periodontitis, carotid atherosclerosis and endothelial dysfunction: Intervention studies

A strong evidence for the link between endothelial dysfunction and periodontitis comes from intervention studies, evaluating patients with periodontal disease before and after dental treatment.
Apart from previous reports, (Mercanoglu F et al, 2004; Seinost G et al, 2005), in 2007 a large study showed that periodontal treatments lead to an improvement of endothelial function. One hundred twenty patients with severe periodontitis were randomized to receive current periodontal care or intensive treatment. Endothelial function was assessed with flow-mediated dilatation before the treatment and up to 6 months after treatment. Twenty-four hours after treatment, flow-mediated dilatation was significantly lower in the intensive-treatment group than in the control-treatment group. Then, flow-mediated dilatation was

greater in the intensive-treatment group than in the control-treatment group 60 and 180 days after therapy. The degree of improvement was associated with improvement in measures of periodontal disease. Therefore, intensive periodontal treatment resulted in acute, short-term systemic inflammation and endothelial dysfunction. Thereafter, the improvement of oral health was associated with improvement in endothelial function.
Furthermore, recently, an intervention study has been performed in a small sample of patients suffering from periodontal disease. This study confirmed that periodontal therapy decreases total oral bacterial load, inflammation biomarkers, adhesion and activation proteins, and in addition it showed a regression of carotid IMT (Piconi S et al, 2009).

10. Mechanisms of association

Studies reporting the association between periodontitis, atherosclerosis and endothelial dysfunction have been discussed above. The present chapter elucidates the mechanisms linking these factors.
First of all, it has been demonstrated that oral pathogens as Porphyromonas gingivalis can infect endothelial cells (Deshpande RG et al, 1998). Furthermore, exposure of cultured endothelial cells to this pathogen is associated with endothelial activation and expression of cell adhesion molecules (Khlgatian M et al, 2002).
However, probably the key event driving patients affected by periodontal disease to atherosclerosis development is systemic inflammation characterizing periodontal disease. In fact, severe periodontal disease was associated with increased serum C-reactive protein levels, Interleukin-6 and many others inflammation factors (De Nardin E, 2001); furthermore, intervention studies reported a reduction of these indexes after therapy (Elter JR et al, 2006). There are at least three ways by which inflammation in periodontal disease might cause a carotid atherosclerotic development (Figure).
First, chronic inflammation leads to endothelial dysfunction, as demonstrated by the findings that patients with chronic inflammatory disease like systemic lupus erythematosus have impairment of flow mediated vasodilation in brachial artery (Lima DS et al, 2002). The reason of this finding can be found in experiments conducted in cell cultures. In fact, in vitro experiments have demonstrated that elevated levels of C-reactive protein, characteristics of inflammatory state, lead to reduction of nitric oxide through a reduction of nitric oxide synthase mRNA; this might impair brachial flow mediated dilation (Verma S et al, 2002).
Moreover, a systemic inflammatory state leads to an impairment of wall shear stress also in carotid artery territory. Recently it has been demonstrated for the first time, a relationship between periodontal disease and low wall shear stress. Different periodontal indices were evaluated during dental examination: Plaque Index, Gingival Index, Pocket Deep. Common carotid wall shear stress was associated with extension and severity of periodontitis. This association was independent of classical cardiovascular risk factors and age (Carallo C et al, 2010). This is important because it has been demonstrated a strong association between low wall shear stress and intima-media thickening increase (Gnasso A et al, 1997). The way through which periodontitis influences hemodynamic forces might be systemic inflammation, by an enlargement of arterial diameter as in rheumatoid arthritis (Irace C et al, 2004). Furthermore, low shear stress might in turn also locally enhance vascular inflammation (Ridger V et al, 2008). As above reported, in regions where low shear stress

occurs, the atheroprotective genes are suppressed and the pro-atherogenic genes are upregulated, promoting the atherosclerotic process.
Finally, systemic chronic inflammation could cause atherosclerosis per se. Ridger et al demonstrated that the presence of chronic respiratory, urinary tract, dental, and other infections amplified the risk of atherosclerosis development in the carotid arteries. Moreover, among subjects with chronic infections, atherosclerosis risk was higher in those with a prominent inflammatory response (Ridger V et al, 2008).

11. Conclusions

In conclusion, periodontal diseases, mainly by a consequent systemic inflammation, have a deep influence on several old and new vascular parameters that are strictly interrelated each other, as endothelial function and hemodynamic forces. This mechanisms might contribute to explain the link between major cardiovascular disease and oral affections.

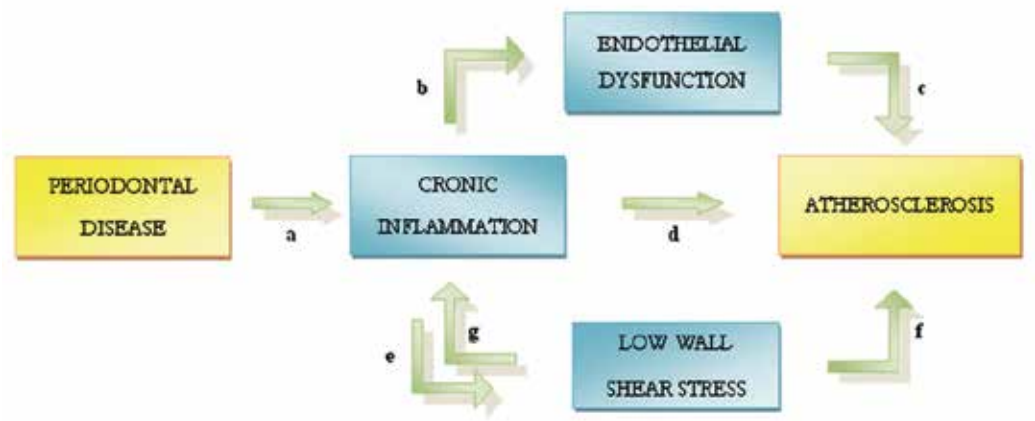

Fig. 1.

Figure describes the relationship between periodontal disease and atherosclerosis, showing that this link might be mediated by various factors. First of all, periodontitis is characterized by systemic inflammation (arrow 'a'); chronic inflammation itself leads to development of atherosclerotic disease (arrow 'd'). Chronic inflammation could act also via endothelial dysfunction (arrow 'b'), that represents the first step of atherosclerotic disease (arrow 'c'). Moreover, periodontal disease is linked with an impairment of hemodynamic force of wall shear stress, probably via the inflammation (arrow 'e'). In turn, low wall shear stress could cause a worsening of atherosclerosis directly (see arrow 'f') or via a worsening of chronic inflammation (arrow 'g').

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9

Relationship Between Oral Malodor and Oral Microbiota

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1. Introduction

Oral malodor, also called halitosis or bad breath, is one of the major complaints made by patients visiting the dentist, ranking behind only dental caries and periodontal disease. It can originate from either systemic or oral conditions, but is usually related to an oral cause. Clinical causes of oral malodor include periodontitis, poor oral hygiene, tongue debris, deep caries, inadequately fitted restorations, endodontic lesions, and low salivary flow [1-5]. Under such conditions, it is thought that either bacterial cell numbers increase or oral bacterial communities shift towards a composition producing high levels of malodor. The major compounds that contribute to oral malodor are volatile sulfur compounds (VSCs), such as hydrogen sulfide (H_2S), methyl mercaptan (CH_3SH), and dimethyl sulfide (CH_3SCH_3) [6, 7]. In addition, methylamine, dimethylamine, propionic acid, butyric acid, indole, scatole, and cadaverine are reported to cause oral malodor. About 90% of the VSCs in mouth air are H_2S and CH_3SH [7], which are produced through bacterial metabolism of sulfur-containing amino acids, such as cysteine and methionine. Gram-negative anaerobes are important producers of VSCs. Persson *et al.* [8] reported that periodontal pathogens isolated from subgingival plaque, such as *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythensis* and *Treponema denticola*, generated significant amounts of H_2S and CH_3SH. An examination of the microbiota composition of the tongue biofilm of individuals with no periodontitis, or only a slight degree of periodontitis, suggested that the major species of H_2S-producing bacteria were *Veillonella*, *Actinomyces*, and *Prevotella* [9]. On the other hand, Gram-positive oral bacteria, primarily streptococci, may also promote VSC production by Gram-negative bacteria [10]. Recently, Takeshita *et al.* [11] determined the bacterial composition of saliva, based on terminal-restriction fragment length polymorphism (T-RFLP) profiles using hierarchical cluster analysis, and associated the global composition of indigenous bacterial populations with the severity of oral malodor. The human oral cavity contains more than 500 bacterial species that interact both with each other and host tissues, suggesting that various bacteria may be related to malodor production.

Oral-derived malodor is classified into physiological and pathogenic odor. The microbial composition of the oral cavity varies according to clinical condition; therefore, the most appropriate management strategy may also differ. However, the common goal of regimen for the treatment of oral malodor is the acquisition of a healthy oral condition, including

normal microbiota. In this chapter, we review and summarize previous studies of the relationship between oral malodor and oral bacteria, and discuss oral microbiota-focused therapeutic strategies in addition to mechanical oral hygiene.

2. VSC-producing bacteria and oral malodor

Periodontopathic bacteria

Periodontal disease is the primary cause of pathogenic oral malodor [7, 12]. The majority of the bacterial species isolated from subgingival microbiota produces H_2S and CH_3SH [8]. In particular, bacterial strains forming large amounts of H_2S from L-cysteine were found in the genera *Peptostreptococcus*, *Eubacterium*, *Salenomonas*, *Centipeda*, *Bacteroides*, and *Fusobacterium*, and CH_3SH from L-methionine was formed by some members of the genera *Fusobacterium*, *Bacteroides*, *Porphyromonas*, and *Eubacterium* [8]. Periodontopathic bacteria have been isolated from the tongue coating and saliva, in addition to the periodontal pocket, in subjects with periodontal disease [13, 14]. In particular, the tongue coating is considered a major source of malodor in both periodontally diseased and healthy individuals, because VSC-producing bacteria have easy access to nutrients, such as desquamated epithelium and food debris, in the tongue coating [12, 15, 16]. It is generally observed that patients with chronic periodontitis have far more tongue coating and higher VSC levels than healthy individuals [15, 16]. Tanaka *et al.* [13] quantified five periodontopathic bacteria, including *P. gingivalis*, *T. forsythensis*, *P intermedia*, *Prevotella nigrescens*, and *T. denticola*, in the tongue debris of patients complaining of halitosis, using real-time polymerase chain reaction (PCR). They found a strong positive correlation between the proportions of periodontopathic bacteria and VSC levels. Furthermore, their data suggest that the proportions of *P. intermedia* and *P. nigrescens* on tongue dorsa are correlated with H_2S concentration. In addition, the proportions of *P. gingivalis* and *P. nigrescens* also showed a strong correlation with CH_3SH concentration. Among the different surfaces in the oral cavity, the bacterial composition of saliva is most similar to that of the tongue coating [17], and bacteria that inhabit other oral surfaces can also be recovered from saliva [18-20]. Therefore, many investigators have used saliva samples to evaluate the relationship between oral malodor and oral microorganisms as reflecting the overall condition of the oral cavity [11, 14, 21]. Awano *et al.* [14] detected the presence of *T. forsythensis*, *P. gingivalis*, *Aggregatibacter actinomycetemcomitans*, and *P. intermedia* by PCR in the saliva of patients complaining of halitosis. They suggested that the presence of *T. forsythensis*, *P. gingivalis*, and *P. intermedia* influenced VSC production, and the presence of *T. forsythensis* in subjects with periodontitis was strongly correlated with VSC concentration in mouth air. One study investigating the relationship between oral malodor and the menstrual cycle reported that VSC, bleeding on probing (BOP), and *P. intermedia* numbers in saliva significantly increased during ovulation in females with periodontitis [21]. In a previous study, we examined the presence of *Helicobacter pylori*, which can cause peptic ulcers and gastric cancer [22, 23] and may cause periodontitis and halitosis [24, 25], in the saliva of patients complaining of halitosis [26]. The presence of *H. pylori* correlated with CH_3SH concentration and periodontal parameters including tooth mobility, periodontal pocket depth, and occult blood in the saliva. Collectively, several periodontopathic bacteria involved in malodor production have been identified and studied.

Normal inhabitants of the tongue

Physiological halitosis in periodontally and systemically healthy people is caused mainly by VSC-producing commensal bacteria that inhabit the tongue coating [27]. According to a study of the topographic distribution of bacterial types on the tongue surface in periodontally healthy subjects, the dorsal posterior to the circumvallate papillae consistently carried the highest load of all bacterial groups [28]. Furthermore, anaerobic, Gram-negative, and VSC-producing (*P. gingivalis*, *F. nucleatum*, and *P. intermedia*) bacterial counts on the dorsal posterior surfaces increased with malodor intensity, whereas aerobic bacterial and *Streptococcus salivarius* counts decreased. An examination of the composition of the microbiota in tongue biofilm suggested that the major species of H_2S-producing bacteria were *Veillonella*, *Actinomyces*, and *Prevotella* in both the odor and no/low odor groups, and the numbers of these bacteria in tongue biofilm were significantly higher in the odor group than in the no/low odor group [9]. The study subjects did not have severe periodontitis (the number of teeth with probing depth ≥ 4 mm was 1.6 and the largest probing depth was 4.0 mm) and therefore these species may contribute to H_2S-production in physiological halitosis.

3. Gram-positive bacteria and oral malodor

VSCs are produced by enzymes that transform *S*-amino acids into their corresponding sulfides. The proteolytic activity of Gram-negative bacteria is closely associated with this process [29, 30]. Many of the available proteins in the oral cavity are glycoproteins [31], which require removal of their carbohydrate side-chains before the protein core can be degraded [32]. Some researchers have suggested that various glycosidases, such as the β-galactosidase produced by Gram-positive oral bacteria, cleave carbohydrate side-chains of salivary glycoproteins and contribute to VSC-production by Gram-negative oral bacteria [33, 34]. In an *in vitro* study using a model *P. gingivalis*-mediated malodor system, addition of *Streptococcus salivarius* promoted mucin degradation and concomitant malodor production [33]. A clinical study using volunteers reported that the presence of β-galactosidase activity in saliva showed a positive relationship with the organoleptic test score (OLS) of the whole mouth or tongue dorsum [34]. Another study of patients complaining of halitosis reported that the β-galactosidase-positive group showed significantly higher OLS and VSC concentrations as measured by gas chromatography, and tongue-coating scores [35]. Recently, Masuo *et al.* [36] quantified β-galactosidase activity in the saliva of subjects complaining of halitosis, and reported a positive correlation between enzymatic activity in whole saliva and OLS and VSC concentrations in the periodontally healthy group, but not in the periodontitis group. In addition, the plaque index and tongue coating score were positively correlated with β-galactosidase activity in the periodontally healthy group. A bacterial quantitative analysis showed that the numbers of total bacteria, *F. nucleatum*, and *S. salivarius* were positively associated with β-galactosidase activity in the periodontally healthy group. These previous studies suggest that β-galactosidase produced by Gram-positive bacteria plays an important role in physiological oral malodor, although the predominant species are Gram-negative bacteria.

4. Malodor-associated microbiota

As described above, several bacteria involved in malodor production have been identified and studied. The accumulation of investigations regarding VSC-production by specific bacterial species may lead to the discovery of the mechanisms underlying oral malodor. On the other hand, analysis of human oral flora has been limited by conventional culture-dependent methods; thus, a significant proportion of oral bacteria remain uncultured and uncharacterized. Malodor producers are members of the oral microbial ecosystem, which is regulated by numerous interactions among the inhabitants. Recently, a molecular approach based on 16S rRNA was been applied to investigate the diversity of both cultivable and uncultivable species in the human oral cavity [37-39]. Several investigators have attempted to identify the oral bacterial species associated with halitosis by PCR amplification of tongue-debris samples, and cloning and sequencing of 16S rRNA genes [40-42]. Although the size of the study populations was limited (11, 13, and 32, respectively) and their oral condition was not described, the data showed some similarities. The diversity of bacterial species in subjects with halitosis was greater than in those with no halitosis. *Solobacterium moorei* was a key bacterial species identified only in subjects with halitosis.

Despite the lack of fully resolved phylogenetic analyses at the species level, T-RFLP analysis is an effective 16S rRNA-based molecular approach for the rapid assessment and comparison of large numbers of complex bacterial communities [43]. Takeshita *et al.* [11] divided the bacterial composition of the saliva of 240 subjects complaining of halitosis into groups based on T-RFLP using hierarchical cluster analysis. Four types of bacterial community compositions were detected (clusters I, II, III, and IV). Oral malodor parameters, including VSC concentration in mouth air and the OLS, were lower in cluster I. Cluster III exhibited an intermediate pattern both in terms of oral malodor parameters and T-RFLP profile. Bacterial genera corresponding to T-RFs with greater peak area proportions in cluster I were *Streptococcus*, *Granulicatella*, *Rothia*, and *Treponema*. Bacterial candidates representing cluster II, which showed the highest VSC and OLS, were *Veillonella* and *Prevotella*. Bacterial candidates representing cluster IV, which showed the second-highest VSC and OLS, were *Neisseria*, *Haemophilus*, *Aggregatibacter*, *Lautropia*, *Parvimonas*, *Fusobacterium*, and *Porphyromonas*. Two types of bacterial communities (clusters II and IV) were implicated as malodor-associated microbiota. Further studies examining the factors that influence differences in microbial composition are needed.

5. Therapeutic approach to manage oral halitosis from an etiologic standpoint

Basic therapeutic approach

Since malodor originating from the mouth is due to the metabolic degradation of available proteinaceous substrates to malodorous gases by certain oral microorganisms, it can be improved by the reduction of bacterial load and/or nutrient availability, and conversion of VSC to non-volatiles. Prevention and treatment of oral malodor is a primarily a matter of oral hygiene, meaning brushing teeth, flossing, cleaning dentures, and cleaning of the tongue dorsum. Tongue cleaning is considered the most important strategy for the

prevention of oral malodor [44]. In addition, treatment of pathogenic oral malodor requires treatment of oral diseases, such as periodontitis, gingivitis, deep caries, inadequate restorations, endodontic lesions, and dry mouth [45, 46]. Chemical approaches using mouthrinses with antimicrobial properties can reduce oral malodor by reducing the number of microorganisms. The active ingredients in these products are chlorhexidine, essential oils, triclosan, and cetylpyridinium chloride [47]. Other chemical agents can reduce halitosis by chemically neutralizing VSCs. The active ingredients in these products are most commonly zinc and chlorine dioxide [48]. Metal ions with a high affinity for sulfur inhibit the formation of VSCs, which is likely also related to the antibacterial properties of the metal [49, 50]. Chlorine dioxide and the chlorite anion consume amino acids such as cysteine and methionine, which are VSC precusors [51]. In addition, the chlorite anion is powerfully bactericidal [52]. A combination of chemical agents markedly reduced VSC concentrations [53, 54].

Biological therapeutic approach

Biological therapeutic agents, such as lactoferrin and probiotic bacteria, have been employed to control oral malodor [55, 56]. These treatments may involve fewer side effects and are environmentally safe. The expected effects–other than antimicrobial activity–of these agents are diverse and the goal of the treatment is the acquisition of a healthy oral condition, including normal microbiota. Lactoferrin, a member of the transferrin family and a component of milk, saliva, tears, and secondary neutrophil granules, demonstrates immuno-modulatory effects and regulates both cell proliferation and iron uptake, in addition to antimicrobial activity [57, 58]. A study using tablets containing bovine lactoferrin and lactoperoxidase in healthy volunteers reported that CH_3SH levels were significantly lower in the test group 10 min after ingestion as compared with the placebo group [56]. No difference in the numbers of salivary bacteria was detected by culturing or quantitative PCR; however, T-RFLP analysis detected one fragment with a significantly lower copy number at 2 h in the test group as compared with the placebo group. Probiotic bacteria, defined as live microorganisms that confer a health benefit on the host when administered in adequate amounts (FAO/WHO 2001), are thought to play a role in the maintenance of oral health [59]. Recently, some studies concerning the effect of probiotic bacteria on maintaining oral health have been reported [60-62]. An open-label pilot trial using tablets containing *Lactobacillus salivarius* WB21 and xylitol reported that VSC levels (H_2S and CH_3SH) and OLS were significantly lower at two weeks in subjects with physiologic halitosis, and OLS and bleeding on probing were significantly lower at four weeks in subjects with oral pathologic halitosis [55]. Quantitative analysis by real-time PCR found that *L. salivarius* and *P. intermedia* numbers were significantly increased in subjects with oral pathologic halitosis at two weeks, but levels of other VSC-producing periodontal bacteria and total bacteria in the saliva were unchanged. Another clinical trial reported that taking a tablet containing *L. salivarius* WB21 reduced the number of *T. forsythensis* in the subgingival plaque of healthy volunteers at four weeks [63]. Thus the effects of biological agents on oral malodor have been confirmed, but no quantitative change in oral bacteria was apparent. Therefore, these effects may be dependent on oral conditions. We also investigated changes in bacterial composition after administration of *L. salivarius* WB21 in subjects with periodontitis. Total bacteria in saliva was significantly reduced in

the test group at two weeks; however, T-RFLP analysis found no difference in bacterial composition between the test and placebo groups (unpublished data). A long-term and large-scale study may be required to clarify the effects of biological agents on oral microbial composition.

6. Conclusions

The present review describes the oral microorganisms and microbiota involved in the production of oral malodor. The oral cavity contains complex, multispecies microbial communities. Residents of these communities display extensive interactions while forming biofilm, carrying out physiological functions, and inducing microbial pathogenesis [64]. The bacterial composition of the oral cavity changes depending on the oral environment; therefore, the bacterial communities associated with oral malodor also differ according to the conditions in the oral cavity. Accumulating information on VSC-producing bacteria, other organisms contributing to the process of oral malodor, and the key species detected in bacterial communities with oral malodor, and comparisons between the bacterial composition of healthy individuals versus those with physiological and pathologic malodor will serve as a basis for exogenously modulating the interactions between biofilm constituents, thus resulting in novel approaches for controlling biofilm activities. In the future, oral malodor therapy approaches should be modified from "remove and kill all" to "acquire healthy oral microbiota."

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10

Oral Health and Nutrition

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1. Introduction

Nutrition and diet affects the development and integrity of the oral cavity as well as progression of diseases of the oral cavity, and are major multifactorial environmental factors in the aetiology and pathogenesis of oro-facial diseases and disorders (US Department of Health and Human Services 2000). Oral health means more than good teeth; it is integral to general health and essential to well-being (Petersen 2003). The interrelationship between oral health and general health has been proven. Severe periodontal disease, for example, is associated with diabetes (Grossi & Genco 1998). The strong correlation between several oral diseases and noncommunicable chronic diseases is primarily the result of common risk factors (Sheiham &Watt 2000). Oral health and nutrition have a synergistic relationship. Oral infectious diseases, as well as acute, chronic and terminal systemic diseases with oral manifestations, impact on the functional ability to eat while also having an impact on diet and nutrition status. Despite great achievements in the improvement of oral health of populations globally, problems still remain in many communities. The significant role of socio-behavioural and environmental factors in oral disease has been demonstrated by a large number of epidemiological surveys (Petersen 2003).

Dental caries is a global disease with few populations exempt from its effects. In developed countries, widespread reduction of dental caries in childhood has led to the development and recognition of high caries risk communities who have failed to benefit from prevention and are often excluded from regular use of healthcare systems (Gratrix & Holloway 1994). The communities are often of low socio-economic status, where minority ethnic groups are over-represented and general health and living conditions are poor (Acheson 1998).

In developing countries, as development increases, so does dental caries, and children are at the forefront of disease disadvantage (Chen 1995). Internationally, there is a growing realization of the need to accurately identify high caries risk groups, to commence prevention from a young age and to examine the effect of early intervention in childhood on general and dental health with both population and high-risk approaches (Pine 1997). Critical aspects to consider include the social and cultural aspects around child development, including family stress, and access and use of health services; nutrition, including access to fluoride and use of sugar; composition and activity of the oral microflora; and a recognition of behavioural and biological impacts on health. Published research has looked at associations between key risk factors and the development of dental caries cross-sectionally and some longitudinally (Hausen 1998). However, in developing countries, little is known of the interactions vertically in the paradigm between molecular

impacts and psychosocial impacts, particularly within and between ethnically diverse or disadvantaged, impoverished populations.

2. Dental caries

Diet and nutrition have a direct influence on the progression of tooth decay. The overall nutrient adequacy of an individual's diet may be the best indicator of caries risk. Diets that promote variety and moderation are going to contribute to both oral and general health (Mobley, 2003). Dental caries is a diet-dependent infectious disease primarily attributed to the presence of oral bacteria. Its prevalence and progression is influenced by other factors including saliva, fluoride and the integrity of enamel (Konig, 2000). Preventive dental regimens are designed to maintain the equilibrium in the dynamic demineralization–remineralization of the tooth surface (Featherstone 2000). Nutrition systemically influences teeth during the pre-eruptive stage, including prenatal, perinatal and postnatal periods. Protein energy malnutrition and deficiencies of vitamins A and D have been associated with enamel hypoplasia and an increase in the susceptibility to caries (Alvarez, 1995).

The evidence shows that sugars are undoubtedly the most important dietary factor in the development of dental caries and the disease is most strongly associated with sugar consumption, in the absence of regular exposure to fluoride (Burt & Satishchandra, 2001). The ability of oral bacteria, most notably *Streptococcus mutans,* to ferment sucrose and other sugars into acid, producing a sustained pH lower than 5.5, is the basis of the demineralization process that is capable of destroying tooth enamel and eventually leading to tooth loss. The biochemistry of disaccharide breakdown and the formation of sticky levans and dextrans in the formation of plaque on the tooth surface, providing a protected reservoir for bacterial acid production right on the tooth surface, is also well-established.

The frequency and the total amount of sugar-rich foods consumed have both been strongly correlated to dental caries and also to each other, suggesting that strategies to control one variable will contribute to controlling the other (Sheiham 2001). Other researchers (Ismail *et al*. 1984; Jamel *et al*. 1997) have shown the danger of consuming sugar in forms that are very sticky (have strong adhesive properties) as these are cleared from the mouth by saliva very slowly. Factors determining the cariogenic, cariostatic and anti-cariogenic properties of the diet are food consistency (liquid, solid, sticky, long-lasting), frequency of consumption of sugar and other fermentable carbohydrates, nutrient composition, potential to stimulate saliva, sequence of food intake and combinations of food (Papas *et al*. 1995; DePaola *et al*. 1999; König 2000).

The role of diet in dental caries incidence and prevalence is reflected in dietary patterns that are a combined consequence of food choices, the food eaten and the frequency of dietary intake in a specific time period (Mobley, 2003). Strategies need to be developed to assess food choices that combine caries-promoting and cariostatic foods. Calcium and fluoride-rich foods enhance the potential for remineralisation.

3. Nutrition and early childhood caries

A child's diet has a profound ability to influence cognition, behaviour, emotional development, physical growth and development. Nutrients from food provide energy for growth, serve as structural components and partake in the metabolic functions of the body.

Guidelines for dietary habits and food choices are designed to provide adequate energy and nutrient intake to support growth.

Dental caries is widely recognized as a preventable infectious disease that is strongly modified by diet. The main players in the aetiology of the disease are cariogenic bacteria, fermentable carbohydrates and a susceptible tooth and host. However, in young children, bacterial flora and host defence systems are in the process of being developed, tooth surfaces are newly erupted and may show hypoplastic defects, and carers must negotiate the dietary transition through breast/bottle feeding, first solids and childhood tastes and it has been reported that there may be unique risk factors for caries in infants and young children (Seow 1998).

Early childhood caries (ECC) in infants and preschool children is a preventable dental disease. It affects a disproportionate number of children from low socio-economic groups and ethnic minorities. Milnes (1996) reported that while the prevalence rate of ECC varied from 1% to 12% in developed countries, in developing countries and within disadvantaged populations of developed countries (immigrants, ethnic minorities), the prevalence rate is as high as 70%. The presentation of a child suffering from rampant caries is, as described by Fass (1962), a shocking experience. He published the first comprehensive description of caries in infants, which he termed 'nursing bottle mouth'. The clinical appearance of ECC includes the form of caries affecting all the primary upper anterior teeth, upper and lower primary first molars and the lower canines (the lower anterior teeth remain unharmed) to rampant caries affecting all the teeth in the mouth or small 'pockets' of decay affecting a single tooth in children between 1 and 5 years old.

The causes of early childhood caries are complex, but understanding the aetiology of the disease has a direct influence on public policy. In the United Kingdom, the British Society of Paediatric Dentistry recommends a reduction in sugar intake by the whole child population in the country, whereas its American counterparts' view is that sugar restrictions can be relaxed in a society where fluoride is used frequently, particularly for children who have low or no caries (British Society of Pediatric Dentistry 1992; American Academy of Pediatric Dentistry 1989). The aetiology of ECC is multifactorial – the presence of oral bacteria and fermentable carbohydrates are necessary, but proper oral hygiene and regular fluoride exposure reduce the risk of caries. The design of interventional programmes set up to prevent the disease is influenced by how the aetiology is interpreted. It has been established that a group of cariogenic micro-organisms, oral streptococci, is associated with ECC. Oral levels of these bacteria, which are generally acquired from the mother, were found to be elevated in children with ECC (Tinanoff & O'Sullivan 1997). Other contributing factors that predispose children to ECC include prolonged and night-time bottle feeding of milk and/or sweetened juice in infants and toddlers, nocturnal breastfeeding after 12 months of age, linear hypoplasia of primary teeth associated with malnutrition and the prolonged use of a pacifier covered with honey, sugar or other sweetened foods (Tinanoff & O'Sullivan 1997; van Palenstein Helderman et al 2006).

3.1 Protein energy malnutrition/failure to thrive

ECC has also been implicated as contributing to other health problems: children with ECC were shown to weigh less than 80% of their ideal weight and to be in the lowest 10th percentile for weight (Acs *et al*. 1999). Protein energy malnutrition is defined as weight or height less than the 5th or 10th percentile for age and failure to thrive implies a deficit in expected growth and in one or more areas of psychosocial development (Wright, 2000). The mean age of 'low weight' patients with ECC was significantly greater than for patients at or

above their ideal weights, indicating that progression of ECC may affect growth adversely. In addition, the quality of life of the child suffers – pain or infections associated with ECC may make it difficult for the child to eat. Alternatively, poor nutritional practices may be responsible for both the reduced weight and caries. Low *et al*. (1999) reported on the effect of severe caries on the quality of life in young children. They found that there was a significant change in pain complaint, eating preferences, quantity of food eaten and sleep habits before and after treatment of dental caries. Finally and most importantly, the cost of restoring decayed teeth in ECC is extremely high (Weinstein 1998).

3.2 Implications of early childhood caries

Early childhood caries is characterized by a high prevalence, high impact and high resource requirements. Its seriousness and societal costs continue to be a significant public health issue, especially among racial or ethnic minorities (Tinanoff & O'Sullivan 1997). There is considerable evidence that children who experience ECC continue to be at high risk for new lesions as they grow older, both in the primary and permanent dentitions (Johnsen *et al*. 1987; Kaste *et al*. 1992; O'Sullivan & Tinanoff 1996). It has not been established whether it is the high levels of infection by cariogenic organisms or the establishment of poor nutritional practices that are the determinants of caries progression (Litt *et al*. 1995).

Treatment of ECC is expensive, often requiring extensive restorative treatment and extraction of teeth at an early age. In the US, the estimated costs of restoring teeth alone is thought to exceed U$1000 per child (Jones *et al*. 1995). In addition to these expenses, general anaesthesia or deep sedation may be required because such young children lack the ability to cope with surgical procedures. Thus, the consequences of ECC are a significant problem not only in monetary terms to parents and the government, but also in potential risks to health and comfort of the child.

3.3 Prevention of early childhood caries

There are three general approaches that have been used to prevent ECC. The first is a community-based strategy that relies on the education of mothers or caregivers in the hope of influencing their dietary habits as well as those of their infants (Ripa 1988). This approach also uses water fluoridation and community preventive programmes in high-risk communities. The second approach is based on the provision of examination and preventative care in dental clinics. The third involves the development of appropriate dietary and self-care habits at home. All three approaches use the mothers or caregivers to follow healthy dietary and feeding habits in order to prevent the development of ECC, as patterns in the introduction of foods and when eating behaviours are established, may be influential in its prevention and treatment (Garcia-Godoy *et al*. 1995; Tinanoff & Palmer 2003). The goal of the educational initiative is to increase the knowledge of the mother and to improve the dietary and nutritional habits of the infants and mothers. It is assumed that an increase in the knowledge f mothers or caregivers will influence their self-care habits and dietary practices and in turn improve the dietary and oral hygiene habits of the infants leading to the prevention of ECC.

4. The role of fluoride in nutrition

There is no specific nutritional requirement for fluoride and it is usually recommended as a means of caries prevention. The role of fluoride in protecting teeth against dental caries is

well-established (Warren & Levy, 2003). It remains the cornerstone of caries prevention and there are a variety of sources that contribute to the dietary intake of fluoride. However, the association between the frequency of sugar intake and dental caries is negated only partly by the presence of fluoride (Stecksen-Blicks & Holm 1995). In fact, the beneficial effects of fluoride vary according to the amount of sugars consumed (Kunzel & Fischer 1997). For example, there is a dramatic increase in the prevalence and severity of dental caries when sugar intake increases from around 15 kg to 35 kg per person per year (Takahashi 1961; Sheiham 1987). On the basis of this evidence, Sheiham (1991) recommended that in the presence of fluoride, a 'safe' intake of sugars would be up to 15kg per person per year and in the absence of fluoride, up to 10 kg.

5. Water fluoridation – Where are we now?

With the availability of fluorides targeted at individuals and the decline in dental caries, the need for water fluoridation has been questioned (Kumar, 2008). Water fluoridation is the process of adjusting the amount of fluoride that is present naturally in a community's water to the optimal level for protection against tooth decay. It is a cheap and efficient public-health measure for the delivery of fluoride in many countries. It is the most cost-effective way of preventing tooth decay. Optimum fluoride levels in the water strengthen the teeth and reduce tooth decay by up to 60% (Pizzo *et al*. 2007). It is 18 times cheaper than toothpaste and 61 times cheaper that filling one tooth (van Wyk *et al*. 2001). The advantages of water fluoridation include its ability to deliver low levels of fluoride in saliva frequently and the potential to reduce oral health disparities by creating a healthy environment. Communities need to discuss issues about fluoridation with regard to available caries-prevention strategies, disease burdens, feasibility, cost and use of other forms of fluorides. Currently, water fluoridation remains the best tool to combat caries and to reduce disparities among socially disadvantaged groups within communities.

6. Dental erosion

Dental erosion is the chemical dissolution of dental hard tissues by extrinsic and/or intrinsic acids without bacterial involvement. It is commonly associated with dietary practices involving the frequent intake of acidic food and beverages (Scheutzel 1996; Zero 1996; Parry *et al*. 2001) that weaken the integrity of the tooth and increase caries risk. Extrinsic dietary acids include citric, phosphoric, ascorbic, malic, tartaric and carbonic acids that are found in fruits, fruit juices, soft drinks and vinegar. Dental erosion may progress into the dentine and pulp, with consequent tooth sensitivity, altered occlusion and poor aesthetics. The scientific interest in dental erosion has dramatically increased during the last decade and it is now recognized as an important cause of loss of tooth tissue in children. Furthermore, the reduced thickness of enamel and greater acid solubility in the primary dentition contribute to a higher susceptibility to erosion (Shaw *et al*. 1998; Harley 1999). Age-related increases in dental erosion have been shown to be greater in those with the highest intake of soft-drinks.
The prevalence of erosion is associated with social and dietary factors (Millward *et al*. 1994; Hinds & Gregory 1995; Malik *et al*. 2001; Luo *et al*. 2005).There is a positive correlation between higher parental educational levels and erosion in children. Previous studies reported inconsistent findings on the relationship between erosion and social factors: Luo *et al*. (2005) and Millward *et al*. (1994) found that children from low socio-economic groups had

less erosion, while others found an inverse relationship that as social deprivation worsened, the presence of dental erosion increased (Hinds & Gregory 1995; Harding *et al*. 2003). A focus on the importance of improved dietary habits for good oral health as well as good general health should be included in counselling.

7. Periodontal diseases

Periodontal diseases are oral infectious diseases involving inflammation and loss of bone and supporting tissues of the teeth. Gingivitis and periodontitis are chronic infectious diseases. Although its pathogenesis involves bacteria, there are local and systemic host and environmental factors that influence the severity and progression of the disease (Nishida *et al*. 2000).

Dental plaque is a complex environment called a biofilm. Nutrition has both direct and indirect effects on the development and composition of plaque biofilm (Boyd & Maddon, 2003): (i) through a direct supply of nutrients (such as sugar) as substrates for energy, nitrogen or carbon for the bacteria; (ii) by having an effect on the production of metabolic by-products from one organism that provides nutrients for other organisms (Bowden & Li, 1997); (iii) through the production of specific polymers by other bacteria and finally (iv) by altering the environment of the biofilm and thereby influencing bacteria to colonise the biofilm.

The interaction between nutritional status and the immune response to the bacterial challenge is an underlying factor in the progression of periodontal disease. Nutrient deficiencies (vitamin C and calcium) may compromise the systemic immune response to inflammation and infection and alter nutrient needs (Nishida *et al*. 2000; Krall 2001). In addition, it can also compromise the associated inflammatory response and wound healing (DePaola *et al*. 2002). Nutritional status has a direct influence on the synthesis and release of cytokines and their action (Psoter *et al*. 2005). Consequently, malnutrition is associated with increased needs for calories and protein to promote repletion, wound healing and an improved immune response. Malnutrition also has an adverse effect on the volume, composition, antibacterial and physiochemical properties of saliva. Undernutrition exacerbates the severity of oral infections and may eventually lead to other life-threatening diseases such as noma (Enwonwu 1995).

Good nutritional status and dietary practices combined with the removal of the stimuli of the inflammatory periodontal response are important in reducing the severity of periodontal diseases and to promote optimal periodontal health.

8. HIV/AIDS

The oral manifestations of HIV infection include fungal, viral and bacterial infections. Neoplasms, periodontal disease, salivary gland disease and lesions of uncertain origin are also seen. Oral lesions such as candidiasis, herpetic ulcers and Kaposi's sarcoma are among the first symptoms of HIV infection. Deterioration of oral health is highly correlated to deterioration of general health, making it essential for the patient to be well nourished to respond to the challenge of HIV and other infectious diseases.

Malnutrition at a global level is the most widespread condition associated with immunosuppression in humans (Enwonwu & Warren, 1994). Malnutrition in Africa is of a staggering magnitude, and worsening in some countries, especially in Sub-Saharan Africa

(Berg, 1992). Malnutrition and wasting are prominent manifestations of the late stages of HIV infection (Hecker & Kottler, 1990) and a growing number of single nutrient deficiencies have been reported in AIDS patients (Enwonwu & Warren, 1994). There is marked overlap between the immunological abnormalities caused by malnutrition and by HIV infection (Chandra, 1991). Inadequate nutrition may influence the progression from asymptomatic HIV infection to the full blown condition of AIDS as well as intensify the susceptibility to opportunistic infections and contribute to the severity of HIV-related diseases (Raiten, 1990). Protein-energy malnutrition (PEM) is a major nutritional problem and is a common complication of HIV infection (Enwonwu, 1992; Kottler, 1990). The oral mucosa and the gastrointestinal tract have relatively high cell turnovers. In PEM, the fundamental problem is poor cell production resulting in mucosal atrophy. In the oral cavity, malnutrition-induced mucosal disruptions in combination with poor oral hygiene, are expressed as candidiasis, angular chelitis, stomatitis and severe periodontal lesions (Samarayanake, 1986). Hypofunction of salivary glands in PEM results in xerostomia and failure to protect oral tissues against the numerous potentially pathogenic oral microbial organisms (FDI, 1992).

Patients with HIV infection are at risk for oral disease with accompanying nutritional and systemic consequences. For example, oro-pharyngeal candidiasis may cause a burning, painful mouth and dysphagia. Herpes simplex and cytomegalovirus infections lead to chronic, painful ulcerations. These conditions cause discomfort, difficulty with swallowing, eating restrictions and may reduce an already compromised appetite and intake. Due to the magnitude and impact of HIV-associated oral disease on dietary intake and nutritional status, dental intervention together with nutrition management is an essential component of care. Nutritional strategies need to be developed to reduce the occurrence of opportunistic infections in immuno-compromised patients.

9. Infants and children

Adequate nutrition and nutrients are needed pre-, peri- and postnatally for normal craniofacial growth and development of the oral cavity (Alvarez 1995; DePaola *et al*. 1999; DePaola *et al*. 2002). A single episode of mild to moderate malnutrition in the first year of life and/or folate deficiency was found to be associated with an increased incidence of caries in deciduous and permanent teeth later in life (Alvarez 1995).

Diet counselling is an integral part of anticipatory guidance during the infant oral health visit. Similar to dietary instructions for children of all ages, the primary emphasis is on sugar intake frequency. Maxillary anterior incisor caries as manifested in ECC is mainly due to feeding practices and is the major nutrition-related oral disease found in young children. As mentioned above, the combination of infant/ child feeding practices and repeated sequential consumption of fermentable carbohydrates, such as sweetened beverages or highly processed starchy/ sugary foods, increases caries risk.

There are, however, other infant-specific dietary issues that must also be addressed during the infant oral health visit. Bottle-fed infants should not be put to sleep with the bottle. Weaning from the bottle should be encouraged by 12–14 months of age. Infants older than 6 months and with exposure to less than 0.3 p.p.m. fluoride in their drinking water need dietary fluoride supplements of 0.25 mg fluoride per day. Only 4–6 oz of fruit juice should be consumed by infants per day. Infants should not be given powdered beverages or fizzy drinks, as these pose an increased risk for dental caries. Iron-fortified infant cereals, along

with breast milk or infant formula, should be consumed by infants who are over 6 months of age. Cow's milk should be avoided in the first year of life and restricted to less than 24 oz per day in the second year (Naidoo & Myburgh, 2007). Parents should be cautioned regarding the potential of various foods to constitute a choking hazard for infants (Nainar & Mohummed 2004; Sayegh *et al*. 2005). For school-age children, meal and snack behaviours should involve food choices that promote oral health. Other conditions that may affect oral health include developmental anomalies that alter eating ability and require specialized feeding strategies and cranio-facial surgery, which often requires increased energy, protein and nutrient needs for wound healing.

Nutrition education and counselling for the purposes of reducing caries in children are aimed at teaching parents the importance of reducing high frequency exposures to obvious and hidden sugars. Guidelines include: avoiding frequent consumption of juice or other sugar-containing drinks in bottle or cup; discouraging the behaviour of a child sleeping with a bottle; promoting non-cariogenic foods for snacks; fostering eating patterns consistent with Food Guide Pyramid and those food that have been fortified; limiting cariogenic foods to mealtimes; rapidly clearing cariogenic foods from the child's oral cavity, either by tooth brushing or by consumption of protective foods and restricting sugar-containing snacks that are slowly eaten (e.g. sweets, lollipops, suckers). Along with nutritional factors, a comprehensive approach to preventing dental caries in pre-school children must include improved general dietary habits, good oral hygiene, appropriate use of fluorides, and access to preventive and restorative dental care (Tinanoff & Palmer 2003). Policies and health promotion strategies need to be targeted to mothers from less advantaged backgrounds. Appropriate advice on infant feeding, dietary practices and oral hygiene measures should be the major focus.

10. Concluding remarks

Nutrition plays an important role in the maintenance of the optimal functioning of the immune response. Individuals who are undernourished have impaired immune responses including abnormalities in adaptive immunity, phagocytosis and antibody function. Many countries that are undergoing nutritional transitions may not have adequate exposure to fluoride. There is a call for the promotion of adequate fluoride exposure via appropriate vehicles like affordable toothpastes, water, salt and milk (WHO/FAO, 2003).

Because a healthy, functioning oral cavity is a necessary part of mastication and digestion, a comprehensive oral health module should be incorporated into the training of all health sciences students. The outcomes should include detection of nutrition and diet-related risk factors for oral health and referral to an oral healthcare worker for any abnormal findings. The need for oral health professionals to facilitate patient referrals has been identified (Greenspan *et al*. 1995; Touger-Decker & Gilbride 1997). Health sciences students should be given opportunities to work in oral health settings together with dental students to provide competency in oral examination, identification of oral risk, nutrition and diet advice and interventions.

The joint World Health Organization/Food and Agricultural Organization (WHO/FAO) expert recommendation (WHO/FAO 2003) calls for international organizations to recognize nutrition as an essential part of training of oral health professionals, as well as an important part of educational programmes for dietetics and other health professionals. Oral health and nutrition experts should assume leadership in promoting this dual curriculum content area

of allied health professionals. Oral health professionals need to form networks with other members of the healthcare team (physicians, nurses, speech and language therapists, etc.) to advance health promotion and preventive initiatives that promote oral health and nutrition as they relate to general health.

Partnerships need to be forged between national dental organizations, local and national governmental structures and the private sector to alleviate the barriers (physical, cultural, racial, ethnic, social, educational, environmental and healthcare delivery) that prevent people from achieving oral health and to enhance and support appropriate research that explores new ways of improving nutrition and oral health for all.

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11

Use of Polyols in Oral Biology Research

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1. Introduction

The use of polyol (sugar alcohol) sweeteners in oral biologic research has predominantly stemmed from their anticipated non-cariogenicity in human nutrition and their inclusion in certain oral hygiene products (such as dentifrices) as humectants. The wide-spread use of polyols in food manufacturing, and in pharmacologic and cosmetic products, presumes that the oral effects of polyols must be well researched. The metabolism and safety of most of the common dietary polyols is indeed well known. Occasional reports on polyols applied in biomaterials research have also been published. Most alditol-based information published in the field of dentistry has generated from caries-associated research. Most studies have unfortunately dealt with xylitol and D-glucitol (sorbitol) only, leaving researchers unaware of the potential of other alditols. From the dental and nutritional point of view, however, naturally only alditols with sufficient sweetness have raised interest, since they have been originally used as sweeteners, i.e. to replace sugar in confectioneries and other food items. Several medical applications, however, rely on the osmotic effects of alditols, such as D-glucitol and D-mannitol.

What makes polyols chemically such interesting research objects in biomedicine? The chemical and physiologic rationales behind the interest in polyols generate from their ubiquitous presence in nature, their promising applications in various fields of medicine and technology, and their well-known molecular structure and metabolism. The latter aspects have been reviewed in numerous articles and can be summarized as follows:

i. The common dietary polyols, such as erythritol, xylitol, D-glucitol, D-mannitol, and related alditols (the term used in the subsequent text to include the above and similar molecules) are normal constituents of virtually all living tissues in the plant and animal kingdoms, although significant differences exist between species, and, regarding plants, also between seasons. Since simple straight-chain polyols can be regarded as reduced forms of corresponding aldoses and ketoses, it is possible that the corresponding alditol molecules preceded aldoses and ketoses in the chemical evolution in the early oxygen-poor environment of the Earth. Synthetic dietary disaccharide polyols include maltitol and lactitol. Hydrogenated glucose or maltose syrups may contain higher polyols consisting of more than two monosaccharide units. Industrial-scale polyol syrups often derive their sweetness from D-glucitol and maltitol, with traces of reducing sugars also contributing to sweetness.
ii. The above alditol molecules are characterized by the absence of a reducing carbonyl group, by the chemical reducing power they can exert in biologic environments (owing to the "extra" hydrogen atoms present in the alditol molecules), by their complexation

ability (alditols can complex, for example, calcium atoms, designated as Ca(II) below), by their free-radical-scavenging ability, by their ability to strengthen hydrophobic interactions of proteins (increasing protein stability), by their hydrophilicity, and other properties.

Regardless of the above, general polyol properties, all polyols naturally also exert their own specific effects on metabolic processes and, therefore, on health and disease. Therefore, from a physiologic point of view, alditols cannot be regarded as identical substances; their metabolism and detailed physicochemical properties differ. Each member of the homologous series also affects the nutrition and metabolism of cariogenic and periodontopathic organisms differently. In the present article, this homologous series consists of tetritols, pentitols, and hexitols, containing 4, 5, or 6 hydroxyl groups, respectively. The diverse effects of these substances on mammalian and microbial metabolism result from the detailed molecular configuration and ability to interact with water molecules. The simple ladder structure formulas of several alditols are shown in Fig. 1. The structures shown include some alditols whose oral biologic effects have not been studied but which, based on their detailed chemical configuration, warrant future investigation as potential chemical effectors of dental plaque.

Several text books and research papers have elucidated the chemistry and physiology of alditols in detail (Carr & Krantz, 1945; Lohmar, 1962; Touster & Shaw, 1962; Mills, 1974; Angyal et al., 1974; Gekko & Satake, 1981; Georgieff et al., 1985; Mäkinen, 2000, 2010, 2011). There is an ever-growing body of research describing the medical, pharmaceutical, nutritional, technical, cosmetic, and other applications of alditols. The volume of such investigations is simply too overwhelming for any review article to cover them all. Therefore, this review will predominantly focus on the following oral biologic processes or conditions where alditols have been shown to exert specific oral biologic effects: 1) complexation of Ca(II) and stabilization of the salivary Ca(II) phosphate system; 2) nitrogen and protein metabolism of whole-mouth saliva and dental plaque, and their carbohydrase activities; 3) oral counts of mutans streptococci (MS), and growth of dental plaque. A substantial number of "forgotten", significant oral biologic studies were conducted during the 1970s and 1980s. The importance of some of the results obtained then presumes their re-evaluation. Consequently, this review will first recall some important earlier observations made in this field of oral biology, and will subsequently discuss reports on new applications of alditols in oral biologic research where specific alditol effects, listed under (*ii*) above, are assumed to play a role. Specifically, these earlier observations will focus on MS, on the microbial and chemical composition of dental plaque and whole-mouth saliva, and on certain aspects of periodontal disease and gingival inflammation. The alditols will be examined together, which should render their comparison convenient. A few studies outside oral biology will finally be mentioned owing to their possible relevance to future dental research.

2. The significance of the "extra" hydrogen atoms

Important polyol properties include— the chemically reduced state of the alditol molecules, as compared to the corresponding ketoses and aldoses. This chemical feature plays a role in all oral biologic effects of alditols. The multifaceted nature of the biomedical effects of alditols thus receives a chemical explanation when one examines the chemical profile of the alditol molecules. Alditols are substances that can produce abundant NADH and NADPH.

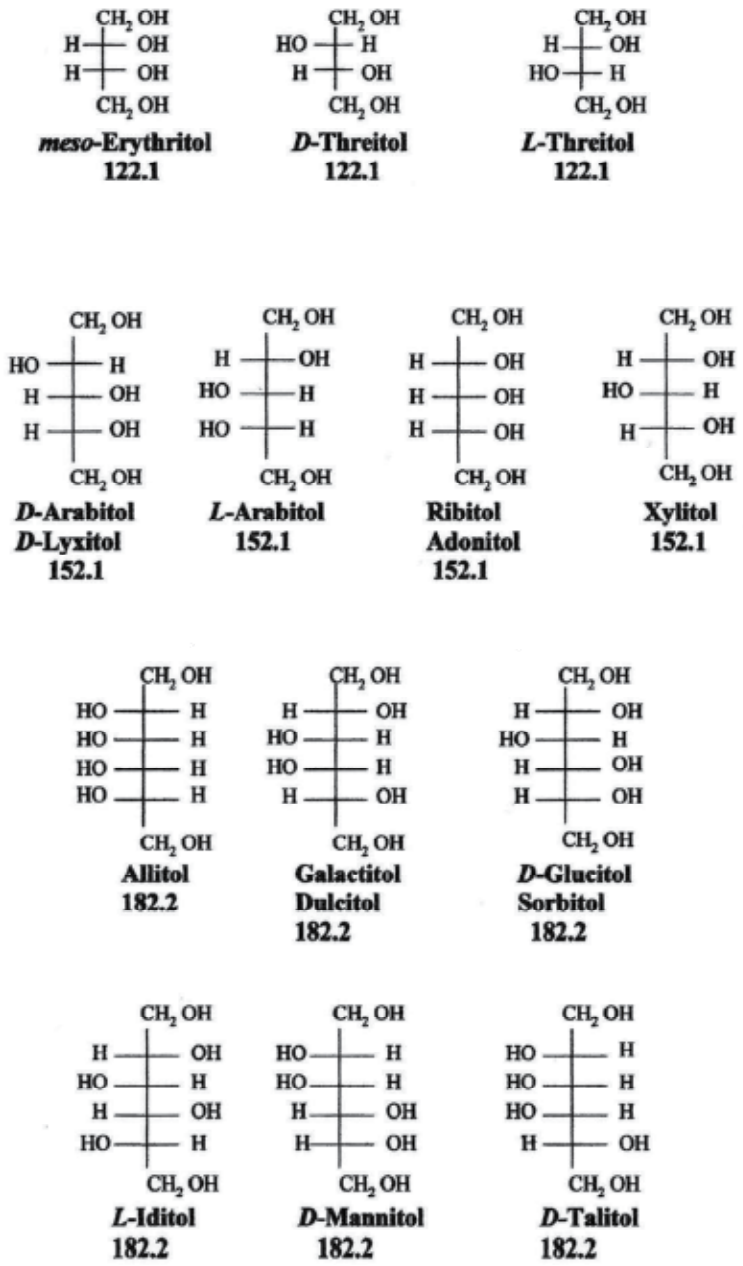

Fig. 1. Simple "ladder" structure formulas of several alditol molecules. The molar mass of each alditol is shown with one-decimal accuracy (in g/mol). It is important to recall that the differences between the molar masses play a significant role in the metabolic fate of these molecules in dental plaque and in the human body after ingestion. Although no oral biologic research has been carried out on some of the rare alditols shown, they are included here since their molecular configuration and conformation may bring about interesting oral biologic effects

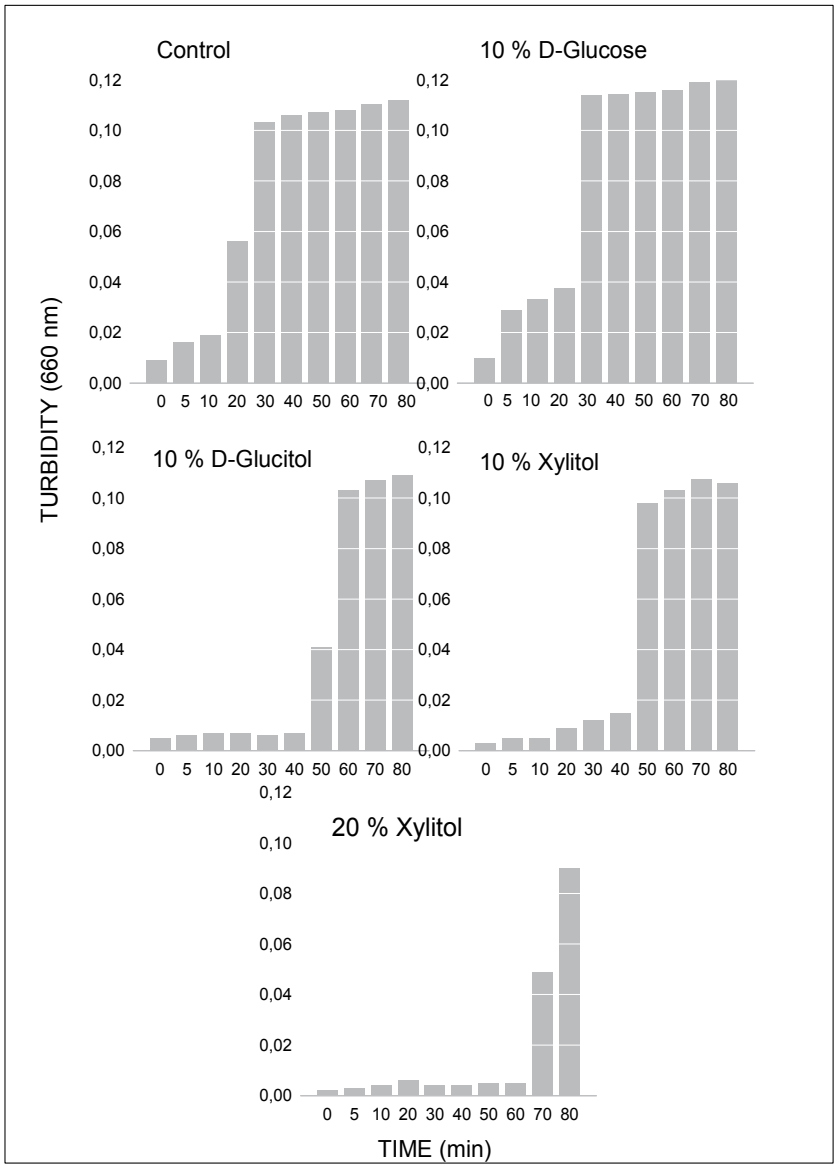

Fig. 2. An example of the stabilizing effect of alditols on the calcium phosphate system in an aqueous solution at pH 7.4. Inhibition by D-glucose, D-glucitol, and xylitol of Ca(II) phosphate precipitation at 37°C. The reactions were carried out using $CaCl_2$ as the source of Ca(II) and NaH_2PO_4 as the source of phosphate (starting Ca(II) and phosphate concentrations were 2.40 mM and 1.44 mM, respectively). The formation of Ca(II) precipitates was monitored over a period of 80 min by measuring the turbidity of the mixtures at 660 nm. The procedures have in principle been described in Mäkinen & Söderling, 1984

These reduced forms of coenzymes can in turn affect the cellular redox potential, which in turn can regulate the levels of other coenzymes and hormones. The alditol molecules can thus be regarded as reservoirs of "extra" hydrogen atoms which can be enzymatically

deposited onto other molecules, eventually generating reduced forms of coenzymes (such as NADH and NADPH). Alditols are of the type $(CH_2O)_n2H$, whereas aldoses and ketoses are of the type $(CH_2O)_n$.
Dental plaque contains microbial enzymes that can convert aldoses and ketoses to their corresponding alditols. Using aldoses as precursors, the formation and naming of some alditols can be shown as follows:

Precursor	Alditol
D- or L-erythrose + 2H	erythritol (*meso*-erythritol)
D-arabinose + 2H	D-arabitol (D-arabinitol)
D- or L-ribose + 2H	ribitol (adonitol)
D- or L-xylose + 2H	xylitol
D-glucose + 2H	D-glucitol (sorbitol)
L-glucose + 2H	L-glucitol
D- or L-galactose + 2H	galactitol (dulcitol)
D-mannose + 2H	D-mannitol

In the same way maltose + 2H results in the formation of maltitol and lactose + 2H in the formation of lactitol, respectively. The term *meso* (used above with erythritol) stands for optical inactivity owing to internal compensation in the molecule. Some sources use the *i*-prefix. These erythritol prefixes have been omitted in the present text.

3. Biochemical consequences in dental plaque after ingestion of alditols

3.1 Stabilization of the Ca(II) phosphate system by alditols; effect on protein stability

Complex formation between carbohydrates and metal cations is a well-studied bioinorganic research area. Complexation of Ca(II) with alditols, such as erythritol and xylitol, may play a role in the remineralization of caries lesions—an interesting possibility that has been discussed elsewhere (Mäkinen, 2010, 2011). In the present review, another oral biologic effect of alditols will be recalled: stabilization of the Ca(II) phosphate system of the oral cavity. This effect is predominantly directed at the solubility of salivary (or plaque fluid) Ca(II) and phosphate, rendering their prolonged, dissolved, supersaturated state possible, compared with the effects of, say, sucrose, D-glucose, or D-xylose, or similar non-polyol carbohydrates. The latter substances tend to initiate instantaneous precipitation of Ca(II) and phosphate from saliva, thus eliminating a part of those substances from remineralization. Consequently, the alditols' role in whole-mouth saliva and plaque fluid is one of stabilization: Ca(II) and phosphate are stabilized in the presence of alditols and will remain in solution even at supersaturated concentrations. Although the stability constants of the Ca(II)-alditol complexes in simple and well-characterized chemical mixtures are known, no such information is available on the possible differences between alditols in complex biological systems, such as saliva and plaque fluid. In principle, this alditol-associated stabilization of the Ca(II) and phosphate system resembles the one caused by innate salivary polypeptides, such as statherin. One particular biological role of those peptides is to govern the precipitation/crystallization kinetics of Ca(II) and phosphate in the oral cavity.
The above stabilizing effect will be illustrated here first in a simple aqueous solution consisting of Ca(II) and phosphate (Fig. 2). Depending on conditions, calcium phosphate salts will eventually start to precipitate in the mixture. The formation of precipitates can be graphically followed by measuring the turbidity of the mixtures at 660 nm. Fig. 2 shows the

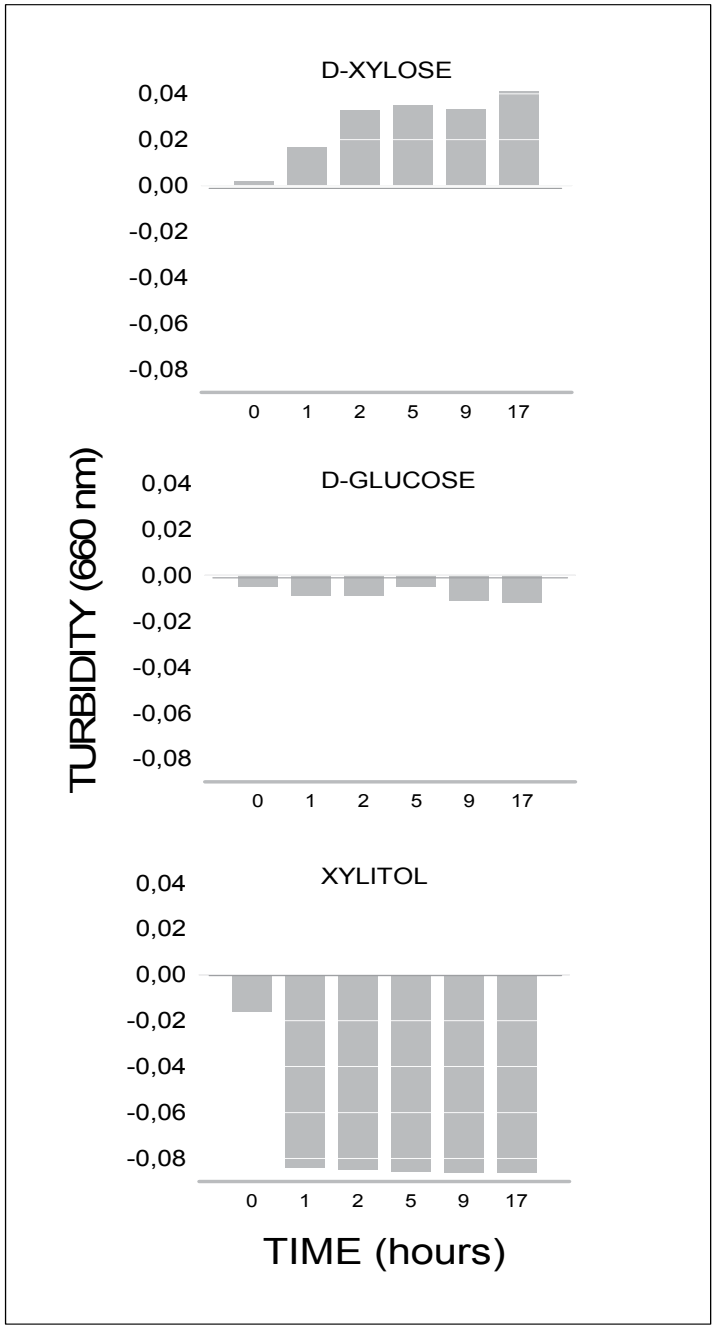

Fig. 3. Stabilizing of the Ca(II) phosphate system by 10% xylitol in human whole-mouth saliva (following centrifugation and Millipore-treatment of saliva) at 37°C in long-term incubations (17 h). The stabilizing effect of xylitol (shown by negative turbidity development) was compared with that of two aldoses (10% D-xylose and 10% D-glucose). Adapted from Mäkinen et al., 1989

pronounced stabilizing effect, observed during a period of 80 min, of 10% and 20% xylitol, and of 10% D-glucitol, on the Ca(II)-phosphate system, compared with 10% D-glucose. The stabilizing effect of the alditols and D-glucose differ significantly. Fig.3 illustrates a similar stabilizing effect observed over a period of 17 h, measured in Millipore-treated human whole-mouth saliva. Again, in the presence of 10% xylitol, a clear stabilizing effect was observed as compared to D-xylose and D-glucose. Fig. 4 in turn depicts a similar experiment with a commercial dextran preparation, D-xylose, and xylitol, this time monitored over a period of 120 min. Clearly, the polyol nature of the alditols played an important role in the system's stabilization. The stabilizing effect prevailed under the conditions described over at least a period of 17 h (Fig. 3). The exact biological role of this stabilizing effect on oral health is not known. However, these effects are real and based on well-researched basic physicochemical properties of alditols. Although several alditol effects on oral bacteria can be predominantly explained in terms of bacterial biochemistry, the above complexation and stabilizing aspects cannot be ignored.

Another specific property of alditols (or polyhydroxy alcohols in general), is their ability to protect protein molecules against denaturation (such as unfolding) caused by heat and other physical and chemical factors. The physical chemistry of these effects has been actively researched (Gekko & Satake, 1981; reviewed in Mäkinen, 1985). A recent paper (Liu et al., 2010) elucidated the molecular mechanism of structural stability of a protein (chymotrypsin inhibitor 2) in polyol solutions (glycerol, xylitol, D-glucitol: also trehalose and sucrose were included). The protein protection by polyols was positively correlated with the molecular volume and the fractional polar surface area. There was preferential hydration on the protein surface, and polyol molecules clustered around the protein at a distance of about 4 Å (Liu et al., 2010). Such preferential exclusion of polyols leads to indirect interactions, preventing the protein molecule from unfolding. The water structure also becomes more ordered with the increase of the molecular weight of the polyol. The bearing of these effects on oral health is not known. However, the point here is to elucidate the versatile effects alditols can exert on biological systems in general. Therefore, even when an investigating team focuses on one particular feature (such as the growth of MS) in an alditol-based clinical program, all of the above-described physicochemical, bioinorganic, and physiologic effects of alditols act simultaneously with full force.

3.2 Nitrogen and protein metabolism; carbohydrase activities

Remarkable differences between sucrose- and xylitol-consuming subjects were found in the activity levels of combined invertase-sucrase enzymes obtained from whole-mouth saliva and dental plaque (Fig. 5). The consumption of xylitol significantly reduced the activity levels of these enzymes. These studies did not reveal which enzyme group, invertases or sucrases, was involved, but an important point here is that both enzymes can be regarded as sucrose-splitting, and thus as sucrose-exploiting. Reduced sucrose-hydrolyzing capacity in whole-mouth saliva (which normally contains large quantities of plaque bacteria) and in dental plaque itself is most likely associated with reduced acidity in dental plaque. Xylitol loading tests have shown that also the activity levels of salivary amylase are affected: consumption of sucrose increased these activities, whereas xylitol consumption reduced them significantly (Fig. 5). Such results can be regarded as normal and expected: habitual consumption of larger quantities of a carbohydrate substrate normally elicits the formation of enzymes that hydrolyze those substrates or which are otherwise involved in the latter's metabolism.

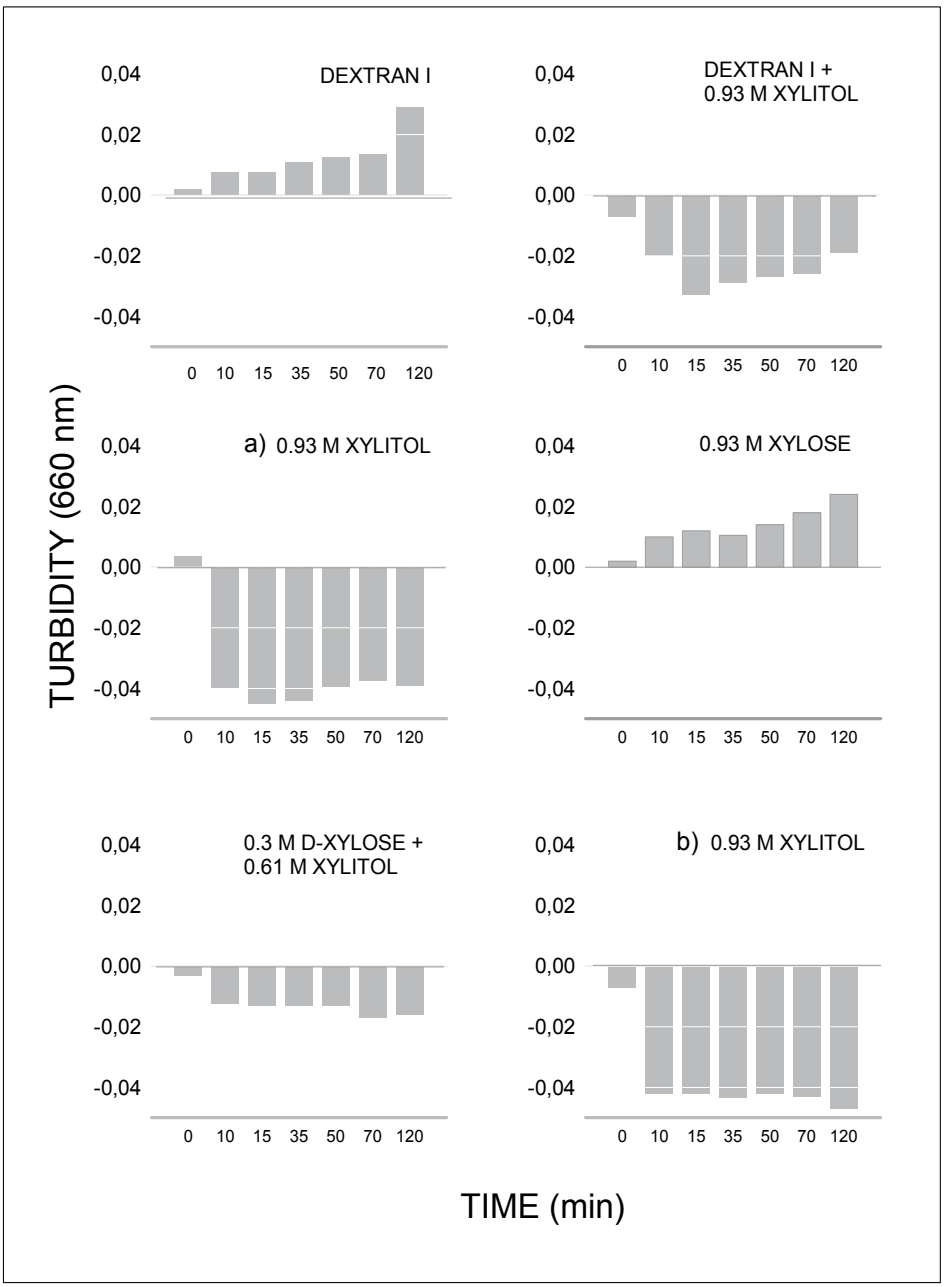

Fig. 4. Stabilizing of the Ca(II) phosphate system by xylitol in human whole-mouth saliva (following centrifugation and Millipore-treatment of saliva) at 37°C in short-term incubations. The stabilizing effect was monitored by measuring the turbidity of the mixtures at 660 nm and was compared to the effect occasioned by "dextran I" (1×10^6 – 2×10^6 daltons) and 0.93 M D-xylose. 0.93 M xylitol prevented turbidity formation over at least 120 min (negative values). a) and b) represent two separate tests with 0.93 M xylitol. Adapted from Mäkinen et al., 1989

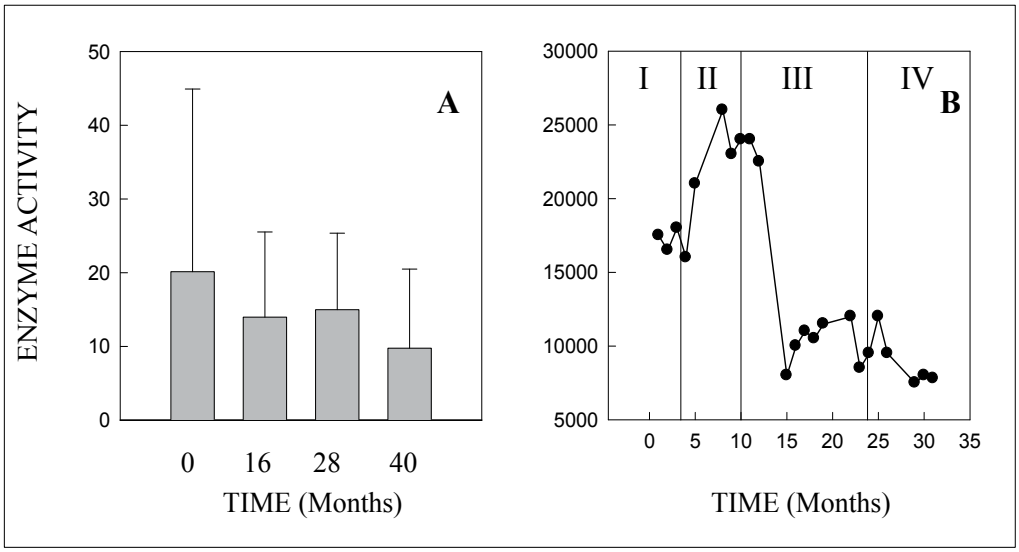

Fig. 5. Examples of the effect of habitual xylitol consumption on carbohydrate-splitting enzymes present in human whole-mouth saliva. Panel A: Activity levels of the combined invertase-sucrase system in initially 8-year-old subjects during 40-month use of xylitol chewing gum (maximum daily intake of xylitol: 9 g per subject). The difference between baseline and 40 months was significant ($p<0.05$) and indicative (p value approach significance) between baseline and 16- and 28-month measurements, respectively. The enzyme activity was determined by means of the neocuproine assay which measures the amount of reducing sugars formed (in nmol/min/mg). The data were adapted from Mäkinen et al. (1966) which also described the general methodology used. Panel B: Activity levels of whole-mouth saliva amylase in a 30-day xylitol loading test consisting of period I (normal diet), period II (formula diet + 70–100 g of sucrose daily), period III (formula diet + 70–100g of xylitol daily), and period IV (normal diet). The study was carried out on nine adult subjects who had habitually used xylitol during a period of 4.3 to 5.3 years. The enzyme activity is shown in amylase units per ml. Note the strong dependency of enzyme activities on the presence of xylitol in daily diet. Low activity levels persisted during period IV (no measurements after day 31 were made). The general methodology was described by Mäkinen et al. (1982). The data are from the present author's files

The partial metabolic inertness of xylitol in human dental plaque leads to various biochemical phenomena that clearly differ from those associated with the consumption of sucrose or hexitols. Provided that the consumption levels of xylitol are large enough, such as those consumed by the Turku Sugar Study subjects (i.e. 10-100 g/day) (Mäkinen & Scheinin, 1975), the plaque microorganisms may become deprived of their preferred substrates (such as C_6-based carbohydrates) and start to synthesize extracellular proteolytic enzymes for the hydrolysis of proteins and peptides present in the medium. For example, when cells of *S. mutans* (strain Ingbritt) were maintained in a medium containing xylitol instead of D-glucose, the cells showed no measurable uptake of ^{14}[C(U)]-xylitol, but exhibited strong increase in the extracellular proteinase activity (Fig. 6) (Knuuttila & Mäkinen, 1981). Xylitol thus behaved as an inert carbohydrate with respect to increases in the extracellular proteolytic activities. This observation is most likely associated with a general increase in

protein and nitrogen metabolism upon starvation of a fermentable carbohydrate (D-glucose). Similar increases in proteinase activities, although not as pronounced, occurred in whole-mouth saliva and dental plaque when high quantities of xylitol were consumed. Owing to the obvious non-specificity of the proteinases discovered, they may attack salivary proteins and peptides *in vivo*. Increased proteinase activity against denatured haemoglobin was found in whole-mouth saliva of subjects habitually receiving high amounts of xylitol. Because saliva contains glycoproteins, it may be considered understandable that the activity levels of plaque glycosidases also increased during xylitol consumption (Mäkinen & Scheinin, 1975). These metabolic events may be related to decreased use of gluconeogenetic enzymes in dental plaque. The nitrogen and protein metabolism are simultaneously increased. Thus, when sucrose is replaced with xylitol, there is an increased search for metabolizable proteinaceous substrates of the medium (i.e. saliva and plaque extracellular phase), with a concomitant increase in the general nitrogen metabolism. Consumption of larger quantities of xylitol thus also leads to an increase in the size of the free amino acid pool of saliva and to a decrease in the production of lactic acid in plaque. The increase of the pool of free amino acids also renders higher deamination rates possible. This can in turn boost the production of ammonia in dental plaque, a phenomenon that has been observed to take place in long-term and short-term xylitol feeding studies (Mäkinen & Scheinin, 1975; Pakkala et al., 1981). The presence of D-glucose in the growth medium of *S. mutans* reduces the pool of free amino acids while the presence of xylitol increases the size of the pool.

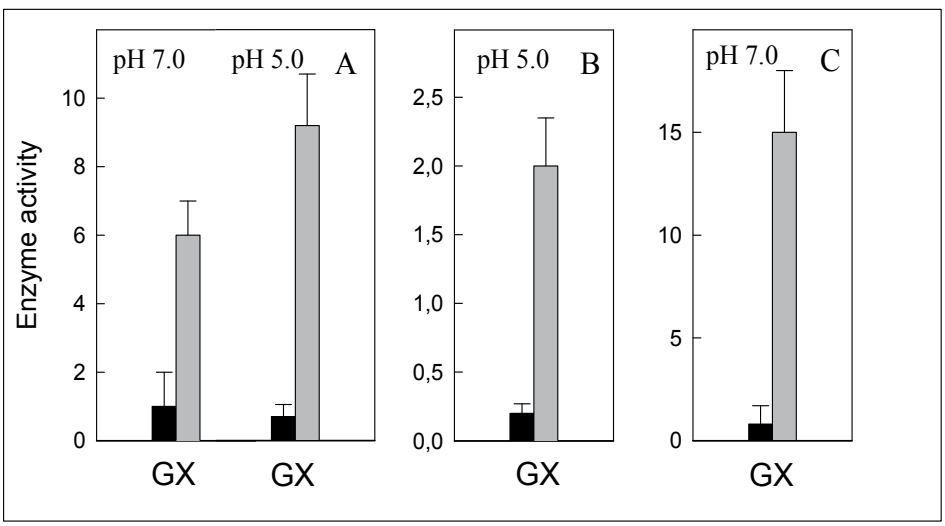

Fig. 6. Extracellular hydrolase (proteinase) activity of the cells of the oral bacterium *Streptococcus mutans* (strain Ingbritt) grown on D-glucose (G) or xylitol (X). The illustration demonstrates the appearance of new or enhanced proteinase activity when the bacterial cells were stored in the presence of 0.25% xylitol or 0.25% D-glucose (for 18 months) at 5°C. The induced proteinase activity supported the growth of the cells and was associated with generally increased protein and nitrogen metabolism of the xylitol-grown cells. Panel A: Hydrolysis of casein at pH 7.0 and 5.0. Panel B: Hydrolysis of a chromophore-collagenase substrate (4-phenylazobenzyloxycarbonyl-L-prolyl-L-leucylglycyl-L-prolyl-D-arginine dihydrate) at pH 5.0. Panel C: Hydrolysis of native collagen at pH 7.0. General methodology is described in Knuuttila & Mäkinen, 1981. The data are from the present author's personal files

The above findings suggest that quantification of dental plaque by means of its protein and nitrogen content cannot be correct. Plaque grown in the presence of xylitol may contain increased protein and nitrogen levels although its volume, mass, adhesiveness, and other caries-associated properties may have decreased. Thus, studies exploiting nitrogen assay of plaque, and claiming that xylitol therefore increases plaque growth (Scheie et al., 1998), do not necessarily reflect the true clinical situation.

3.3 Effect of alditols on oral bacterial counts and dental plaque

Oral biologic literature is replete with studies on the effects of alditols on the growth and metabolism of MS, lactobacilli, and occasionally other oral bacteria and yeasts. A large number of long-term and short-term studies have attempted to evaluate the effects of alditols on the mass and adhesiveness of dental plaque. Typical examples of such studies will be discussed below.

The World Health Organization-associated field trials in Hungary included various oral biologic studies which unfortunately have received little attention. One of those studies investigated 3-year habitual use of fluorides or xylitol on the visible plaque index (VPI) in 688 institutionalized children initially aged 7 to 10 years (Szöke et al., 1985). Although the determination of the VPI may be regarded as a relatively rough clinical procedure, the consistent pattern of the results increases confidence in the results (Fig.7). Regardless of the age group investigated, the VPI values remarkably and consistently declined during the last intervention year in children who had received xylitol. These results are in agreement with those obtained in other long-term xylitol intervention studies, such as the Turku Sugar Studies, which demonstrated a 50% reduction in plaque growth in xylitol-consuming subjects (Mäkinen & Scheinin, 1975). The total number of experiments showing xylitol to reduce the growth and adhesiveness of dental plaque currently amounts to over fifty, with fewer than ten showing a nugatory plaque-reducing effect.

Most studies have shown that D-glucitol and D-mannitol, owing to their hexitol nature, support the growth of MS and dental plaque. Erythritol in turn has been shown to reduce the growth of MS almost to the same extent as xylitol (Mäkinen et al., 2005), although published information is still scant (reviewed in Mäkinen, 2010). Recently, Yao et al. (2009) reported in a Chinese study that the growth and acid production of *S. mutans* were higher in low (2% and less) concentrations of erythritol than in similar concentrations of xylitol, while they were lower at higher (<8%) erythritol levels than at corresponding xylitol levels. This finding may support an earlier (Mäkinen et al., 2005) contention that the mechanism of the inhibitory effect of erythritol and xylitol on the growth of MS differ, and that perhaps combinations of these alditols may turn out to be effective in caries limitation. Another Chinese study reported that maltitol chewing gum may lead to similar reduction of dental plaque as xylitol chewing gum (Li, 2010).

Several recent studies have confirmed the generally accepted idea that xylitol exerts a special growth-retarding effect on MS (Ribelles et al., 2010; Paula et al., 2010; Fraga et al., 2010; Duane, 2010; Söderling et al., 2011; Campus et al., 2011). The study by Duane (2010) demonstrated that children receiving 4.24 g xylitol daily (in five chewing episodes) in the form of chewing gum showed reduced bacterial counts even when the gum contained hexose-based polyols. This study also emphasizes a point that has received serious attention owing to occasional implementation of clinical trials whose very design has nullified the anticipated xylitol effects already in advance (Mäkinen, 2010, 2011). Some points of concern

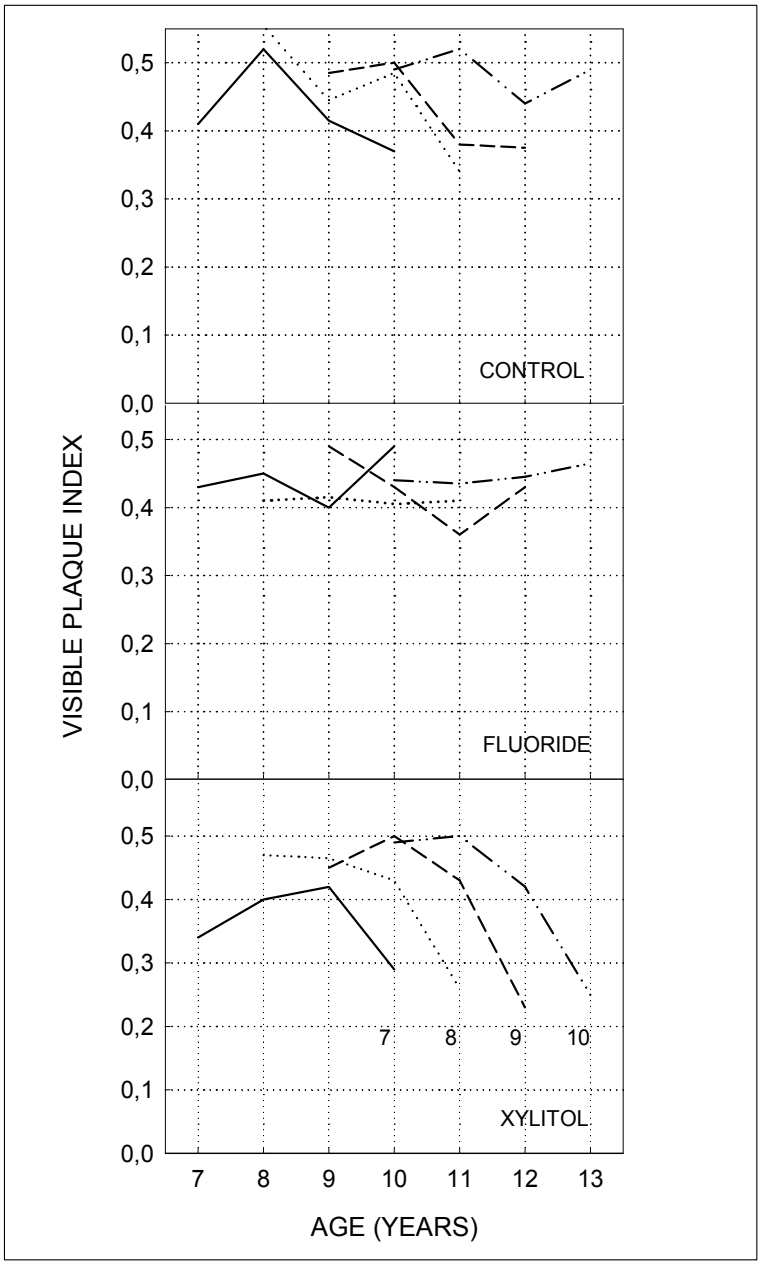

Fig. 7. Effect of three-year xylitol and systemic fluoride treatments on oral hygiene in institutionalized children aged 7 to 10 years at baseline. Oral hygiene was assessed by means of the visible plaque index (VPI). The baseline ages are shown in the lower panel. Fluoride was administered in milk or drinking water and xylitol (maximum daily intake 20 g per subject) was consumed in the form of confectioneries. Note the change in the xylitol group VPI values during the last year of the study, and the consistent pattern of VPI decrease in all age groups. Adapted from Szöke et al., 1985

are that in the recruitment of subjects, it has not always been considered whether the subjects harbour sufficiently high oral MS counts and whether sufficiently frequent daily exposure to xylitol has been observed. Several studies have impoverished the xylitol program by using too-small daily xylitol doses that have been administered only three times per day in subjects with relatively pronounced caries resistance. In most successfully completed studies the daily xylitol dose has been at least 5–10 g per subject.

The study by Söderling et al. (2011) in turn re-emphasizes the close biochemical relationship between plaque MS and xylitol. Xylitol reduced the counts of these bacteria in dental plaque while the effect of salivary MS levels was nil and the microbial composition of the dental plaque (and whole-mouth saliva) in general was not affected. Since the enamel hydroxyapatite surface constitutes the natural growth site of MS in humans, the presence of those organisms in whole-mouth saliva normally results from shedding of the bacteria from plaque. Therefore, determination of oral counts of MS should normally be carried out on dental plaque, although several reports do exist on successful effects also in whole-mouth saliva provided that the growth of dental plaque has been abundant and the plaque MS levels high. The report by Campus et al. (2011) suggested that a combination of xylitol and magnolia bark extract reduces the salivary MS levels, plaque acidogenicity, and bleeding on probing.

The above findings and earlier clinical observations on the caries-limiting role of xylitol receive interesting support from the Raman spectroscopy studies of Palchaudhuri et al. (2011), who suggested that uptake of xylitol by Gram-positive and Gram-negative pathogens occurs even in the presence of other high-calorie sugars. Stable integration of xylitol within the bacterial cell wall may discontinue bacterial multiplication. Much earlier animal experiments by Havenaar et al. (1984) showed that xylitol can limit dental caries even when mixed with a highly cariogenic diet.

4. Alditols in periodontal research

Laboratory experiments and clinical studies have not reported periodontally detrimental effects upon the use of xylitol and D-glucitol in the diet. There is no information on the effect of other alditols on periodontal and gingival health. Differentiation between xylitol and D-glucitol has been difficult, although xylitol, owing to its pentitol nature, has been more effective than D-glucitol in reducing the growth and adhesiveness of dental plaque. More specifically, researchers have come to the following conclusions concerning the relationship between xylitol and periodontal disease: 1) No known periodontopathic organism seems to use xylitol as an important energy source; 2) Xylitol inhibits the growth of several periodontopathogens; 3) Xylitol consumption reduced the adhesiveness of dental plaque (Rekola, 1981); 4) *In vivo* experiments using a hamster cheek pouch microcirculation system suggested that gingival exudate obtained from xylitol-consuming subjects was less inflammatory than that obtained from subjects who received regular sucrose diet or fructose diet (Luostarinen et al., 1975); 5) A bone culture experiment indicated that xylitol plaque was less inflammatory than plaque obtained from sucrose-using substrates (Tenovuo et al., 1981); 6) A study in which 5-day old dental plaque was tested suggested that xylitol plaque was less irritating to macrophages and bone tissue than sucrose plaque (Mielityinen et al., 1983); 7) A study involving experimental gingivitis showed that xylitol mouth rinses were periodontally less harmful than sucrose rinses (and equal to non-sugar Na-cyclamate rinses) (Paunio et al., 1984); 8) A later hamster cheek pouch microcirculation study suggested that

sucrose plaque (obtained after sucrose rinses) caused inflammation to a much greater extent than plaque obtained from subjects who used xylitol or Na-cyclamate rinses (Luostarinen et al., 1984); 9) Two consecutive experiments on young subjects indicated that the use of chewable tablets and candies containing xylitol was associated with reduced plaque mass and lowered gingival bleeding (Harjola et al., 1978; Pakkala et al., 1981). More recently, xylitol was shown to inhibit cytokine expression by a lipopolysaccharide from *Porphyromonas gingivalis*, which is one of the suspected periodontopathic organisms (Han et al., 2005).

One of the laboratory studies that has dramatically illustrated the differences that may occur between dietary sugars is number 4) above (Luostarinen et al., 1975). Fig. 8 shows results from hamster cheek pouch microcirculation measurements involved in the study in question. Gingival crevicular exudate that was obtained from subjects who habitually consumed a xylitol-containing diet was significantly less inflammatory to microcirculation than plaque received from sucrose- or fructose-consuming subjects. The difference shown between the three dietary carbohydrates can be considered remarkable and may in part explain why long-term xylitol administration has in general turned out to be periodontally harmless.

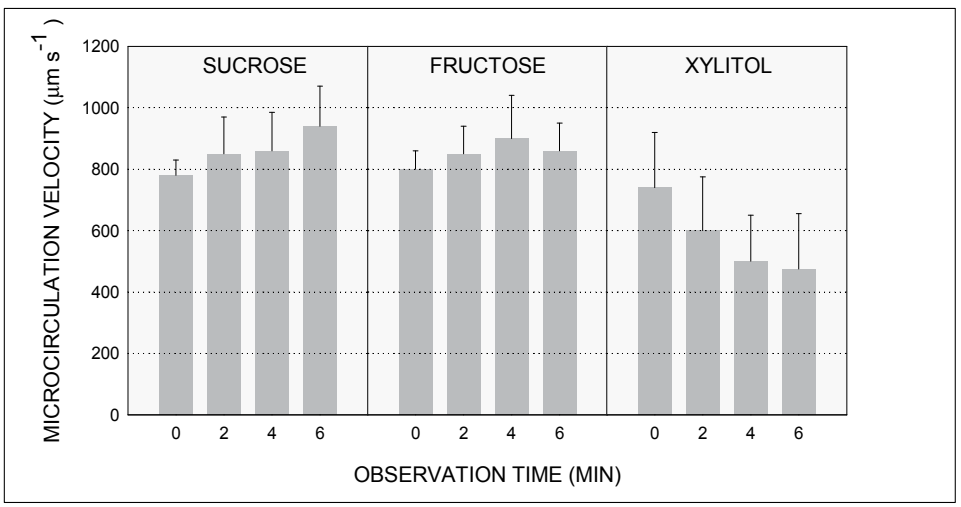

Fig. 8. Effect of gingival exudate on the microcirculation of hamster cheek pouch. Gingival exudate samples were obtained by means of a filter paper method from subjects who had habitually used sucrose, fructose, or xylitol diets over a period of 12 to 13 months. The exudate samples (normally 10 μl) were investigated by means of an intravital microvasculature study using hamster cheek pouches (adapted from Luostarinen et al., 1975). The velocity of circulation was determined at 110x magnification using the "flying spot technique". Measurements of corpuscular velocity were performed every 30-60 sec during the first 6 min. The values shown are means±SD. The number of subjects was 8 in the sucrose and fructose groups, and 14 in the xylitol group

A similar intravital technique was used to assess the response to microcirculation of plaque extracellular fluid (Fig. 9) (Luostarinen at al., 1984). The samples of dental plaque were obtained from subjects who had refrained from oral hygiene for a period of 12 days. During

this period, the subjects rinsed their mouth six times a day either with 0.4 M xylitol, 0.4 M sucrose, or 0.01 M sodium cyclamate solutions. Plaque fluid obtained from the sodium cyclamate and xylitol groups produced a slight increase in the blood velocity in the microcirculation, whereas plaque fluid obtained from the sucrose group displayed a strong decrease in velocities. Consequently, plaque fluid and gingival exudate caused opposite effects on microcirculation, exemplifying the complex nature of the pathophysiological responses involved. However, the occurrence of leucocytes and their attachment to capillary walls diminished after the application of plaque fluid from the xylitol and sodium cyclamate groups. The levels of histamine at the site of irritation in the cheek pouch were highest after treatment with plaque from the sucrose group. However, these results generally suggested that long-term neglect of oral hygiene with simultaneous use of sucrose mouthrinses increases the capacity of dental plaque to cause inflammation and that rinsing the mouth with a xylitol solution is much less inflammatory. These tests essentially compared sucrose with xylitol and leave the question of the effects of other alditols unanswered. However, an important point here is to recall earlier results that have received less attention but provide impressive evidence on the oral biologic differences that can exist between dietary sweeteners.

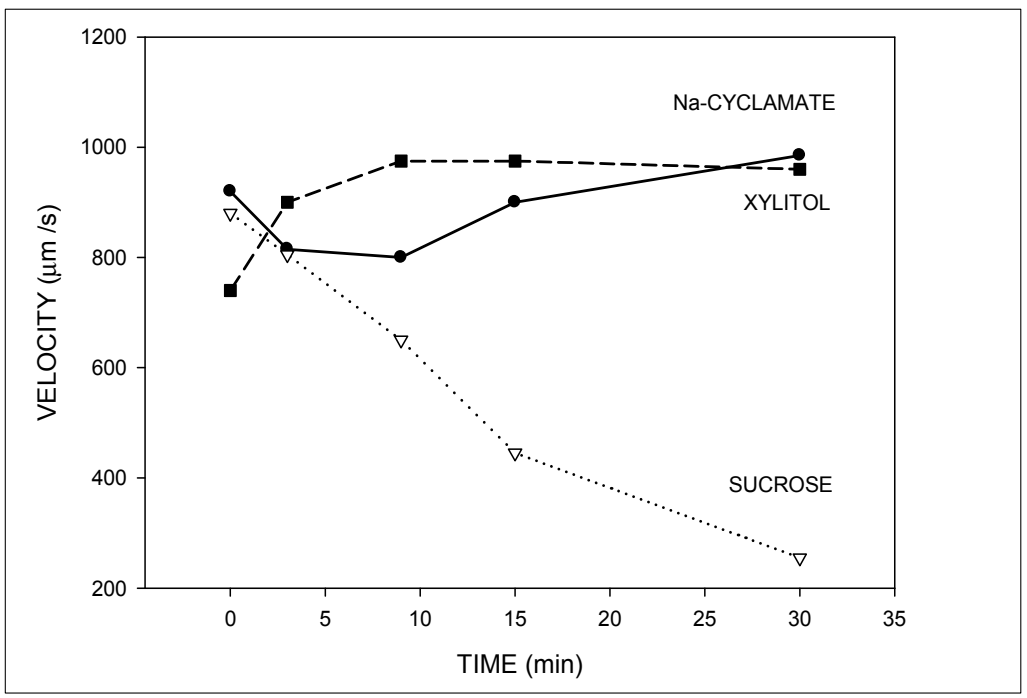

Fig. 9. Effect of the extracellular fluid of dental plaque on hamster cheek pouch microcirculation. Plaque fluid was obtained from young adult subjects who refrained from oral hygiene over a period 12 days and who rinsed their mouth during this period with aqueous solutions containing either sucrose (0.4 M), xylitol (0.4 M), or Na-cyclamate (0.01 M) (n = 11 in each group). The curves show the effect on microcirculation by pooled plaque fluid. The effect on microcirculation by 10 µl samples was measured as in Fig. 8. Measurement with individual plaque samples followed the general pattern shown. Adapted from Luostarinen et al. (1984)

5. Comments on the use of alditols in nutrition

Although several sugar alcohols may generate interest owing to their chemical effects on dental plaque and dental caries, a number of practical reasons limit their application. Firstly, the sweetness of some alditols and higher polyols may be insufficient from the point view of consumer acceptance. The sweetest sugar alcohols seem to be xylitol and erythritol, whose sweetness, as assessed by most test panels, is comparable to that of sucrose. The sweetness of D-glucitol and D-mannitol is about 0.5 compared to the value (1.0) given for sucrose. Another feature of dietary sugar alcohols is their normally slow rate of absorption. This may cause osmotic diarrhoea in unadapted subjects, particularly if the consumption levels are high. This property is common to all slowly absorbed substances, such as D-fructose. In the case of sugar alcohols, the cathartic effect naturally depends on the molecular weight of the substance, D-glucitol (a hexitol), for example, being more effective than xylitol and erythritol (a pentitol and a tetritol, respectively). Erythritol, owing to its small molecular weight, normally causes no harmful gastrointestinal effects. De Cock and Bechert (2002) ranked some common dietary polyols based on the maximum bolus dose not causing laxation. D-glucitol had the lowest value, i.e. 0.17 (in g/kg body weight), while xylitol, maltitol, and isomalt gave a value of 0.3, which can be compared to that of 0.66, assessed for erythritol. Habitual use of dietary sugar alcohols often leads to increased tolerability.

6. Recent advances made in biomaterials and other biomedical research

Some alditols, such as erythritol, xylitol, and D-glucitol (along with ethylene glycol and glycerol) have been tested as dentine primers (Ohhashi et al., 1997). Contraction gap formation was completely prevented in an aqueous solution of 62.5% ethylene glycol (wt/wt), although 37.5% erythritol was also effective. The other alditols were less effective. Since the required polyol levels were very high, the mechanism of action of the polyols tested must be related to their pronounced hydrophilicity and replacement of water molecules. Earlier studies had shown that esterification of methacrylate with glycerol and erythritol also prevented the formation of a contraction gap by a commercial light-activated resin composite (Manabe et al., 1991). Both esters thus contain hydrophobic and hydrophilic groups. The above tests with mere polyols suggest that hydrophobic interactions may not be necessary in the process.

In a study investigating the biocompatibility of dental restorative materials, ascorbic acid increased in a dose-dependent manner the toxic effect of most of those restorative materials tested (Soheili Majd et al., 2003). However, D-mannitol was found to neutralize the toxicity of ascorbic acid. Another application of xylitol resulted from its polycondensation reactions with sebacic acid (1,8-octanedicarboxylic acid). The substances synthesized can be used as biodegradable elastomers. These elastomers exhibited increased biocompatibility compared with, for example, poly(L-lactic-co-glycolic acid) (Bruggeman et al., 2010).

Using a particular wound biofilm model, Dowd et al. (2009) showed that biofilm formation was completely inhibited by 20% xylitol and 10% erythritol. More specifically, xylitol displayed an increasing inhibitory effect on *Pseudomonas aeruginosa* at all concentrations tested, while erythritol had an inhibitory effect on *P. aeruginosa* and *Staphylococcus aureus* at over 5% concentrations. Also these findings support the contention that the biochemical

mechanism of action of erythritol and xylitol on common pathogenic microorganisms can differ remarkably. Biofilm production was also effectively controlled using a combination of xylitol and chlorhexidine (Paula et al., 2010). Xylitol also interfered with the biofilm formation by *Streptococcus pneumoniae* and lowered the autolysin-encoding gene lytA expression levels (Kurola et al., 2011). However, the presence of D-glucose and D-fructose abolished the xylitol effect. This is an important observation that should be considered when planning clinical trials on xylitol in otitis media patients.

Although xylitol cannot be said to prevent dental erosion, it may be possible to alleviate this problem by first eliminating the erosion-inducing conditions and adding a suitable xylitol program to the treatment strategy. Using bovine enamel as a model, 20% xylitol treatment appeared to partially reduce enamel erosion (Souza et al., 2010; Rochel et al., 2011). Indirectly related to these findings is the potential of xylitol as a component in saliva stimulants designed for Sjögren-syndrome patients (de Silva Margues, et al., 2011). Since xylitol may act effectively in preventing irritative dermatitis, suppressing the sodium lauryl sulphate-induced transepidermal water loss (Korponyai et al., 2011), it is possible that xylitol (along with glycerol) could indeed be tested as a potential constituent in saliva substitutes designed for Sjögren-syndrome patients.

Results with possibly remarkable practical value were reported by Uittamo et al. (2010) who showed that 0.11 M xylitol can inhibit the formation of carcinogenic acetaldehyde (produced from ethanol) by *Candida* species. Xylitol reduced acetaldehyde production from ethanol below the mutagenic level of 40-100 μM.

The team of Knuuttila et al. have shown during the past 20 years that dietary alditol administration can elicit beneficial effects on the bone and connective tissue metabolism of rats (earlier studies reviewed in Mäkinen, 2000). Recently, these contentions received support in a study by Sato et al. (2011): bone density increased in the femurs of rats receiving 10% and 20% xylitol in their diet. These results should be contemplated against the ability of xylitol to complex with Ca(II), as discussed in several connections (Angyal et al., 1974; Mäkinen, 2000, 2010).

Finally the potential of erythritol as a safe and efficacious sugar substitute in oral biologic applications must be emphasized. Regarded as a "sweet antioxidant" (de Cock & Bechert, 2002; den Hartog et al., 2010), this alditol has been shown to yield promising results in preliminary caries and laboratory tests (dentally related literature reviewed in Mäkinen, 2010). Potential future alditol applications may include the study of combinations of erythritol and xylitol. Such studies are indeed warranted because it is possible that the mechanism of action of these alditols on MS differ (Mäkinen et al., 2005), making their combined effects additive and possibly clinically more effective than when using either one of these alditols separately.

7. Conclusions

Most of the polyols discussed in this review are simple dietary alditols or disaccharide sugar alcohols. These molecules are characterized by several common "polyol properties" such as the absence of reducing chemical groups in the molecular structure, pronounced hydrophilicity, ability to strengthen hydrophobic interactions of protein molecules, tendency to form complexes with divalent cations, and other properties. Each alditol or disaccharide polyol also constitutes a unique molecular species of its own; these polyols are

by no means exactly identical regarding their physiologic and pharmacologic effects and their detailed chemical behaviour in biological environments. Therefore, oral biologic research can benefit from the diversity of these specific polyol effects. Although regular medical and physicochemical researchers have been familiar with the existence of specific polyol effects, some oral biologic and dental researchers have experienced difficulties in adopting this inevitability. Numerous ordinary physicochemical papers have routinely reported important differences between alditols. Such differences often result from differences in water activities in alditol solutions which in turn lead to different networks of hydrogen bonds that differ from alditol to alditol. Physicochemical research has shown that the mobility of water molecules around each individual oxygen atom of the alditol molecule differs remarkably, resulting in differences in the chemical behaviour of the alditol. Such differences are eventually likely to manifest themselves also in biological systems.

Regarding oral pathological processes such as dental caries and periodontal disease, decisive factors that can lead to different polyol effects in disease prevention include the length of intervention, the daily amount of alditol used, and the frequency of use per day (Mäkinen, 2011). Therefore, new attempts to design alditol-based caries trials (Bader et al., 2010) are welcome but will not provide final answers if the consumption level of the alditol, the frequency of alditol use, or the overall duration of intervention, are defective. Regarding xylitol, for example, customary instructions call for preferably 5x/daily use, the required daily dose being at least 5 to 7 g xylitol (in some trials 10 g has been administered daily) during a period extending beyond three years. Deliberate impoverishment of a clinical program and failure to pay attention to the above requirements may not provide valid evidence-based research findings. Serious errors have been made in polyol-based caries trials by investigating inherently caries-resistant patient cohorts. A trial aimed at studying a preventive instrument must be implemented on patients who represent normal predisposition to the disease involved. Other errors made in clinical trials include saliva stimulation (for example, by gum chewing) that extends beyond 10 min. In some studies 20-30-min chewing episodes have been used. Prolonged chewing will lead to so-called salivary effects only, masking possible pharmacologic, alditol-based effects. The present author has mostly used 5-min stimulation.

Future oral biologic alditol research should elucidate the biochemical mechanism of action of erythritol in caries prevention. Future clinical trials on sugar alcohols should also investigate possible caries-limiting potential of their mixtures. Preliminary experiments suggest that mixtures of xylitol and erythritol may be more effective in affecting the growth of MS than those of D-glucitol and xylitol (Mäkinen et al., 2005). It has been suggested that the caries-limiting potential of common dietary alditols will increase as the number of hydroxyl groups decreases (Mäkinen, 2010). This assertion would concern hexitols, pentitols, and tetritols, which would be represented by D-glucitol or D-mannitol, xylitol, and erythritol, respectively. This suggestion is right now largely based on theoretical considerations and on cultivation of MS in the presence of xylitol and erythritol (Mäkinen et al., 2005). Clearly, future studies should elucidate the caries-reducing potential of the above alditols so that the alditols will be compared in the same, truly long-term trial. Likewise, it is possible that combinations of xylitol with maltitol and combinations of xylitol, erythritol, and maltitol, would turn out to be clinically promising. Such clinical trials should be accompanied by concerted oral biologic analyses of the chemistry and microbiology of dental plaque and whole-mouth saliva.

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12

Virulence Mechanisms of Leukotoxin from *Aggregatibacter actinomycetemcomitans*

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1. Introduction

Aggregatibacter actinomycetemcomitans is a gram-negative bacterium that is present in the oral cavity of a large proportion of the human population (Zambon et al., 1983; Henderson et al., 2010) The bacterium is acquired through transmission from infected individuals and thought to initially colonize oral mucosa as a facultative intracellular pathogen (Fine et al., 2006). When the bacteria translocate to a site in the subgingival crevices, a persistent colonization may lead to periodontal destruction and development of periodontitis in susceptible individuals (Fig. 1) (Philstrom et al., 2005; Darveau 2010). The prevalence of this bacterium shows a great variation depending on geographic origin, age and life stile of the examined population (Kinane et al., 2008; Habek 2010). *A. actinomycetemcomitans* is a part of the normal flora in many healthy individuals but it is also a major agent in some aggressive forms of periodontitis (Fine et al., 2006). Periodontitis is a chronic infection characterized by the destruction of tooth-supporting structures (Darveau 2010). The number and composition of bacteria in the subgingival dental plaque, as well as life stile and genetic predisposition are factors that determine the outcome of the disease activity (Philstrom et al., 2005; Darveau 2010). The genetic diversity among different isolates of *A. actinomycetemcomitans* is great and its ability to express and release virulence factors varies (Henderson et al., 2010). The different adhesins and fimbriae expressed by this bacterium have been shown to be important factors that promote colonization at the various ecological niches of the human oral cavity (Fine et al., 2006).

A. actinomyctemcomitans expresses two exotoxins, a cytolethal distending toxin (Cdt) and a leukotoxin. Cdt´s are expressed by a number of gram-negative bacteria and causes death of the host cells by blocking their proliferation (Belibasakis et al., 2004). The leukotoxin selectively affects human cells of hematopoetic origin by binding to the lymphocyte function associated receptor 1 (LFA-1) and cause disruption of the membrane integrity (Lally et al., 1999). Leukotoxin belongs to the Repeat in Toxin family (RTX) and shares genomic organization and molecular structures with RTX proteins produced by a number of other gram-negative bacteria (Linhortavá et al., 2010). The expression of leukotoxin and Cdt varies among different *A. actinomycetemcomitans* isolates and high leukotoxin expression has been shown to correlate with disease while the role of Cdt still is more unclear (Henderson et al.,

2010). The genetic features and the molecular structure of leukotoxin have recently been described in detail (Kachlany 2010; Johansson 2011). This chapter focuses on the functional aspects of the leukotoxin as a virulence factor associated with pathogenic cellular mechanisms.

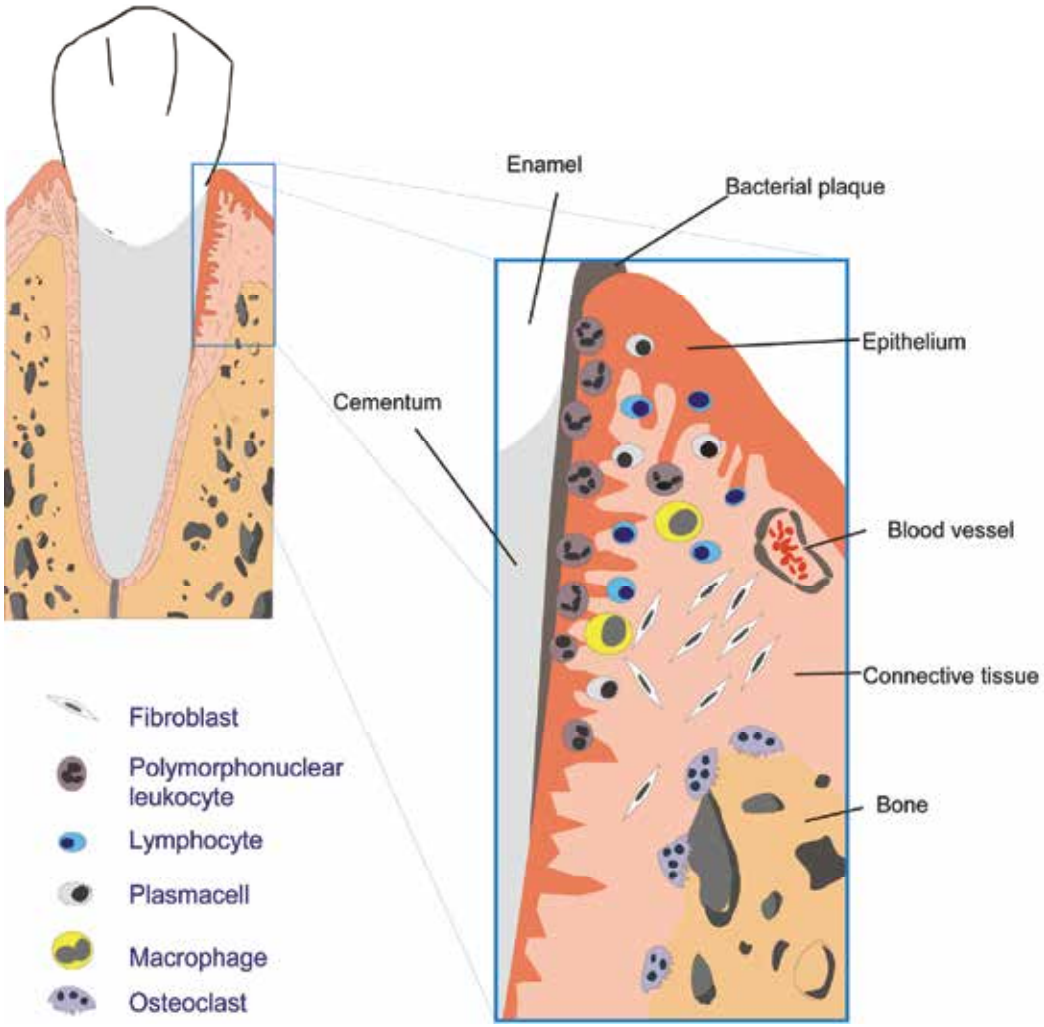

Fig. 1. Schematic illustration of cells and tissues involved in the pathogenesis of periodontal diseases. Microbes adhere to the epithelium and tooth surface and form a biofilm (microbial plaque). Persistent presence of this biofilm activates an inflammatory response in the surrounding tissues, which recruits a substantial number of immune cells from the peripheral circulation to the inflamed site. An imbalance in the host response might lead to degradation of the tooth supporting tissues, bone and connective tissue, and finally to tooth loss. A large number of microbial components, such as toxins and proteases that are released from the biofilm can affect the cellular response of the host.

2. *Aggregatibacter actinomycetemcomitans* and its association to disease

As mentioned, periodontitis is a chronic inflammatory condition in the periodontal tissues, which leads to periodontal attachment loss and destruction of the alveolar bone that houses the teeth. Based on clinical characteristics, several forms of periodontitis are recognized. Most prevalent is the slowly progressing chronic periodontitis while the so called aggressive form shows a more rapid tissue loss and often occurs in young subjects (Pihlstrom et al., 2005).

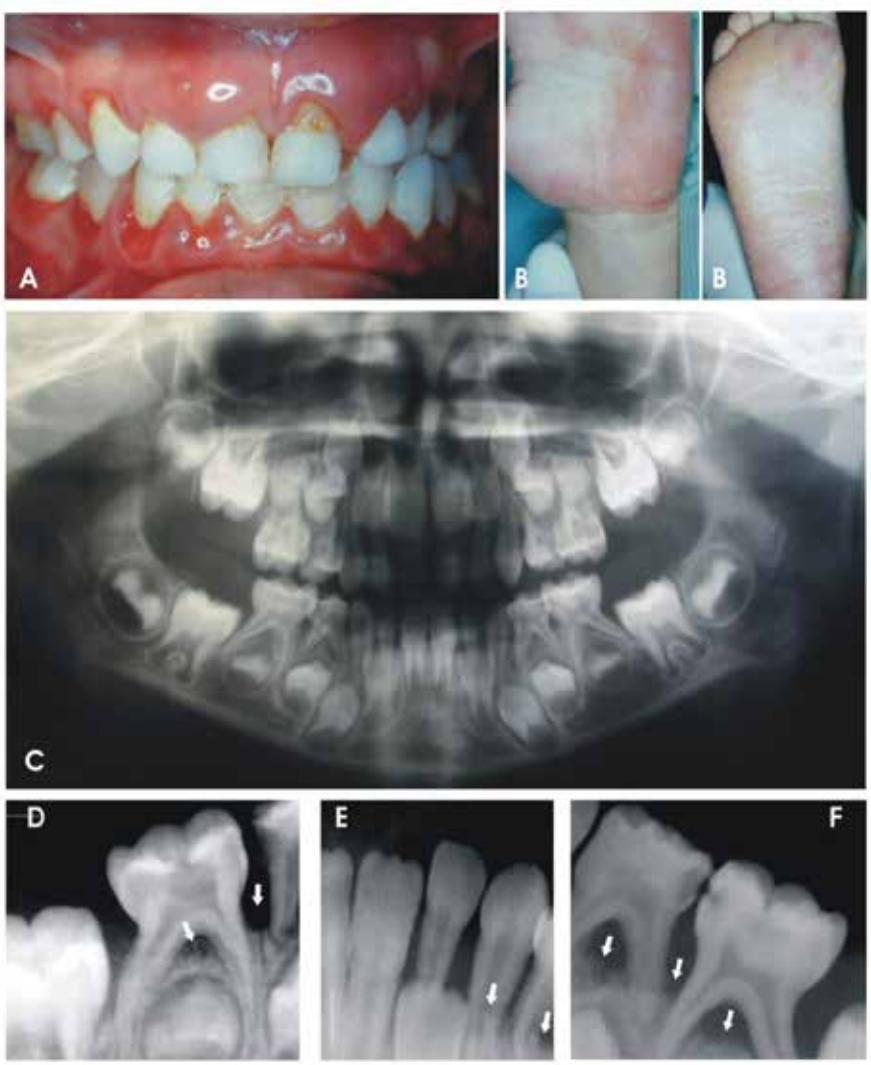

Fig. 2. Papillon-Lefèvre syndrome in a 6-year old child. A. Clinical manifestation of the extended periodontal inflammation affecting the primary dentition. B. Hyperkeratotic palmo-plantar skin lesions C-F. Radiographs showing the severe bone loss (arrows) around the teeth. Cultures of samples from the periodontal pockets revealed the rich presence (up to 70% of the total sample flora) of *A. actinomycetemcomitans.* (unpublished data of author SK).

Periodontitis can also be developed in conjuction with systemic diseases or medication and its severity depends on the underlying condition, the most severe forms being found in patients with disorders in the cellular defense, mostly in neutrophils, e.g. Papillo-Lefèvre syndrome, Kostmann syndrome, various neutropenias, and Chediak-Higashi syndrome (Fig. 2) (Reichart & Dornow 1978; Deasy et al. 1980; Deas et al. 2003; Tempel et al. 1972; Saglam et al. 1995; Defraia & Marinelli 2001; De Vree et al. 2000).

The etiology of periodontitis is microbial. The infection is caused in most cases by consortia of bacteria with a predominance of gram-negative anaerobic rods that colonize the periodontal pocket (Pihlstrom et al., 2005; Darveau 2010). Approximately 700 different bacterial species can be detected in samples from the subgingival plaque biofilm (Socransky & Haffajee 2005). The majority of these species can be isolated from samples of both healthy and periodontally diseased subjects. In plaque samples from diseased sites, the number and proportion of pathogenic organisms are elevated (Berezew & Darveau 2011; Nishihara & Koseki 2004).

In some forms of aggressive periodontitis *A. actinomycetemcomitans* is often found in high numbers in subgingival plaque samples from the affected tooth sites (Fine et al., 2007). Especially in patients with certain neutrophil disorders, *A. actinomycetemcomitans* is the main pathogen colonizing the periodontal area (Stabholz et al. 1995; Kleinfelder et al. 1996; Velazco et al. 1999; Pütsep et al., 2002). These epidemiological data indicate that establishment of *A. actinomycetemcomitans* in the periodontium as the main pathogen and development of inflammation depends on the lack of functional neutrophils in this area.

Besides the pathogens in the oral biofilm, genetic and environmental host factors contribute to periodontitis development (Nishihara & Koseki 2004). Furthermore, an association between periodontal infections and other inflammatory systemic diseases, such as cardiovascular diseases and diabetes, is well established, but the underlying specific mechanism is still unknown (Pihlstrom et al., 2005).

The prevalence of *A. actinomycetemcomitans* in subgingival plaque samples can be estimated by traditional culture methods, as well as by molecular (PCR-based) techniques (Fine et al., 2007). In an examined population, the proportion of *A. actinomycetemcomitans* positive individuals varies with periodontal status, age, ethnicity and geographic origin (Fine et al., 2007). Genetic differences of both patients and potential pathogens are of importance for a better insight into the etiology of periodontal diseases (Rylev & Kilian 2008). Longitudinal studies have shown that periodontally healthy children that harbour *A. actinomyctemcomitans* have an increased risk to develop Localized aggressive periodontitis (LAP) (Van der Velden et al., 2006; Fine et al., 2007). A specific clone (JP2) is strongly associated with LAP in subjects of African origin, and differs from other clones of this species by several genetic peculiarities, including a 530-bp deletion in the promotor region of the leukotoxin gene operon, which results in an enhanced expression of leukotoxin (Brogan et al. 1994; Haubek et al., 2007 & 2008). Healthy adolescents harbouring this clone were shown to have an 18-fold increased risk to develop periodontal attachment loss within a 2-year follow up period compared to the *A. actinomycetemcomitans* negative controls (Haubek et al., 2008). In contrast to the promoter deletion in the JP2, in a Japanese strain was shown that an insertion mutation increases the expression of the leukotoxin operon (He et al., 1999). However, no reports are yet available that associates the presence of this specific highly toxic clone with the onset and progression of aggressive periodontitis in this population.

3. Genetic characteristics of *Aggregatibacter actinomycetemcomitans*

A. actinomycetemcomitans is a member of the bacterial family *Pasteurellaceae* (Kilian et al., 2006). Recently, it was reclassified in the new genus *Aggregatibacter* together with its close relatives *Aggregatibacter* (*Haemophilus*) *aphrophilus* and *Aggregatibacter* (*Haemophilus*) *segnis* (Nørskov-Lauritsen & Kilian 2006). Molecular genetics has demonstrated a degree of biodiversity in the oral microflora and *A. actinomycetemcomitans* is genetically heterogeneous and comprises distinct clonal lineages that may have different virulence potentials (Kittichotirat et al., 2011). Seven serotypes have been identified among *A. actinomycetemcomitans* isolates; each serotype represents a distinct clonal lineage (Kaplan et al., 2002; Kilian et al., 2006; Takada et. al., 2010). The complete genome sequence of *A. actinomycetemcomitans* serotype b strain HK1651 from the JP2 clone has been available since 2002 (http://www.genome.ou.edu/act.html). Genome sequencing of 14 different strains from *A. actinomycetemcomitans* species have identified a pangenome consisting of 3301 genes, including 2034 core genes and 1267 flexible genes (Kittichotirat et al., 2011). The natural competence of this bacterium for horizontal gene transfer might explain the substantial genetic diversity shown within this species (Wang et al., 2002). The within-species variable virulence may be attributed to a strain-to-strain variation in genome content and regulation of virulence gene expression (Kittichotirat et al., 2011). Future work with genomic characterization of *A. actinomycetemcomitans* might contribute to identify specific virulent clones other than the already well characterized highly leukotoxic JP2 clonal types (Haubek 2010; Kittichotirat et al., 2011). In addition, population genetic analyses of this bacterium have been giving information about global dissemination of this species and its strict horizontal transfer pattern together with the presence of several genetic peculiarities give also information about population trades (Kilian et al., 2006; Habek et al., 2007).

4. Expression and secretion of *A. actinomycetemcomitans* leukotoxin

The leukotoxin operon consists of four coding genes designated *ltx*C, *ltxA, ltx*B and *ltx*D and an upstream promoter gene (Lally et al., 1989; Kraig et al., 1990). *ltxA* is encoding for the structure of the toxin, *ltx*C for components required for posttranslational acylation of the toxin and *ltxB* and *D* for transport of the toxin to the bacterial outer membrane. The leukotoxin operon is organized as illustrated in fig. 3, this pattern being similar to the gene organization found for other proteins of the RTX-family (Welch et al., 2001; Linhartová et al., 2010).

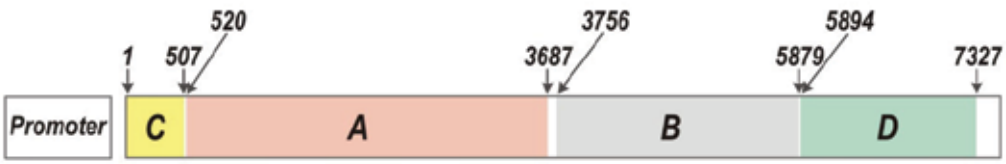

Fig. 3. Schematic illustration of the operon organization of *A. actinomycetemcomitans* leukotoxin.

There is a great variation in leukotoxin expression *in vitro* (Fig. 4), although all *A. actinomycetemcomitans* strains harbor a complete leukotoxin operon (Henderson et al., 2010).

Zambon and co-workers (1983) showed that *A. actionomycetemcomitans* isolated from periodontally diseased subjects exhibited significantly enhanced leukotoxicity compared with isolates from periodontally healthy subjects. Interestingly, certain clones of the bacterium with enhanced leukotoxin expression have been shown to have a modified promoter in the leukotoxin operon (Brogan et al., 1994; He et al., 1999). The cellular and molecular mechanisms in which a modified leukotoxin promoter enhances the expression of leukotoxin are not known. The most well known phenomenon is the highly leukotoxic JP2 clonal strains of *A. actinomycetemcomitans* characterized by a 530-bp deletion in the promoter of the leukotoxin operon (Haubek 2010). Hypertonic NaCl extracts of bacteria from this clone analyzed by SDS-PAGE and Comassie staining reveald a protein pattern that was dominated by a 116 kDa band shown to be the leukotoxin (Johansson et al., 2000a) (Fig. 6). Presence of the JP2 clone is highly associated to aggressive forms of periodontitis and shown to correlate with disease onset of adolescents in Morocco (Haubek et al., 2008). This highly leukotoxic clone (JP2) has recently been reported to also colonize subjects with, by genotyping confirmed, North-European origin (Claesson et al., 2011). Clonal diversity analysis of JP2-like isolates have shown that all strains of this clone have a common ancestor from Northern Africa (Haubek et al., 2007). The high accumulation of this clone in subjects of African origin has indicated a possible host tropism, but could also be a result of the strict vertical transmission pattern of this bacterium (Kilian et al., 2006; Haubek 2010).

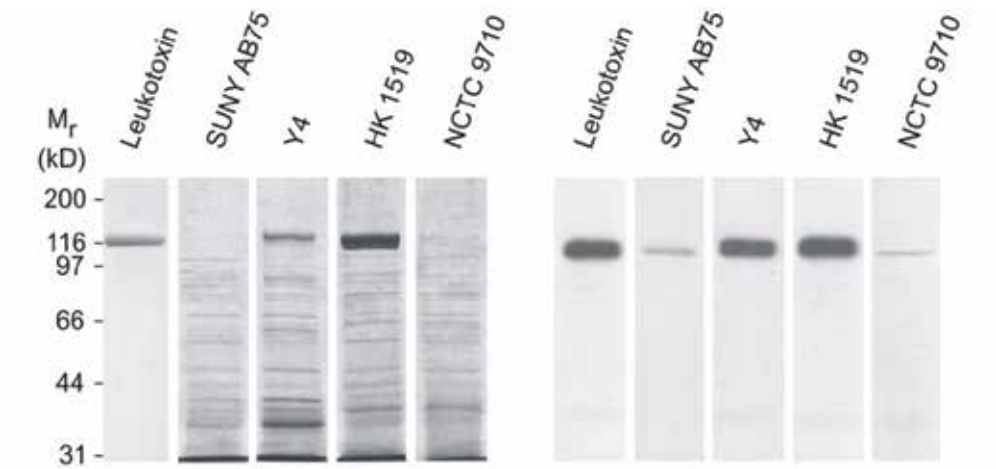

Fig. 4. The left figure shows NaCl extracts from different strains of *A. actinomycetemcomitans* separated on 8% SDS-PAGE and stained with Comassie blue. The left lane contain the purified leukotoxin and the other 4 lanes contain extract from 3 strains representing 3 different serotypes (SUNY AB75 serotype a, Y4 serotype b and NCTC 9710 serotype c) and having intact leukotoxin promoter and 1 strain serotype b from the highly leukotoxic JP2 clonal type (strain HK1519). The right figure shows the same SDS-PAGE separated extracts blotted on a PVDF membrane and visualized by western blot technique with a leukotoxin specific rabbit antiserum.

The expression of leukotoxin is also regulated by environmental factors, such as growth conditions and substrates (Kachlany et al., 2010). The expression of leukotoxin by various strains of *A. actinomycetemcomitans* at the infected site of the host is still unknown.

The expressed leukotoxin is transported to the bacterial outer membrane by a type I secretion system (Kuhnert & Christensen 2008). Three proteins, LtxB, LtxD and TdeA, are reported to be required for export of the toxin to the bacterial outer membrane and are organized in accordance to the figure below (Fig. 5) (Crosby & Kachlany 2007).

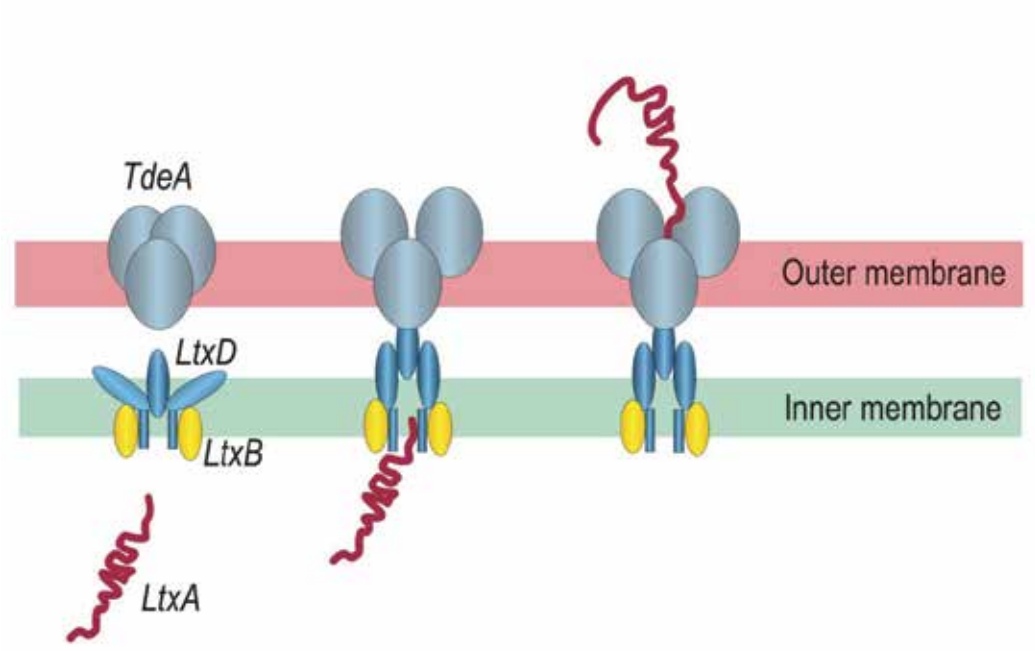

Fig. 5. Schematic illustration of the type I secretion system required for export of the expressed *A. actinomycetemcomitamns* leukotoxin to the bacterial outer membrane (OM). IM = Inner membrane and TdeA = a TolC like proten.

In addition, presence of serum proteins also mediates a similar release of the toxin from the bacterial outer membrane, which indicates involvement of competitive mechanisms (Johansson et al., 2003). Different culture conditions have been shown to determine the distribution of the expressed toxin between the bacterial outer membrane and the culture supernatant (Kachlany et al., 2000; 2010). Whether leukotoxin remains associated to the bacteria in the periodontal pocket is not known. However, the serum mediated release of the toxin (Johansson et al., 2003), as well as the intense systemic immune response to the toxin (Brage et al., 2011), possibly indicate a release of the toxin from bacteria in the biofilm *in vivo*. Among the different proteins of the RTX family, *A. actinomycetemcomitans* leukotoxin differ from the other toxins by its high isoelectric point, as well as the membrane association of the expressed protein (Welch 2001; Linhortavá et al., 2010). This property of leukotoxin further supports the importance of electrostatic forces for its association to the bacterial outer membrane.

The secreted leukotoxin has been shown to be easily inactivated by environmental proteases and superoxide radicals (Johansson et al., 2000b, 2001; Balashova et al., 2007). This degradation of the toxin molecule can be inhibited by the presence of superoxide dismutase

(SOD) produced by *A. actinomycetemcomitans* and the naturally occurring protease inhibitors of human serum (Johansson et al., 2001; de Haar et al., 2006; Balashova et al., 2007). In 1981, McArthur and co-workers showed that the activity of leukotoxin in interaction with polymorphonuclear leukocytes (PMNs) was enhanced by the presence of human serum (McArthur et al., 1981). This phenomenon could later be explained by the protective effect of the serum protease inhibitors on leukotoxin degradation caused by lysosomal enzymes released by the affected PMNs (Johansson et al., 2001).

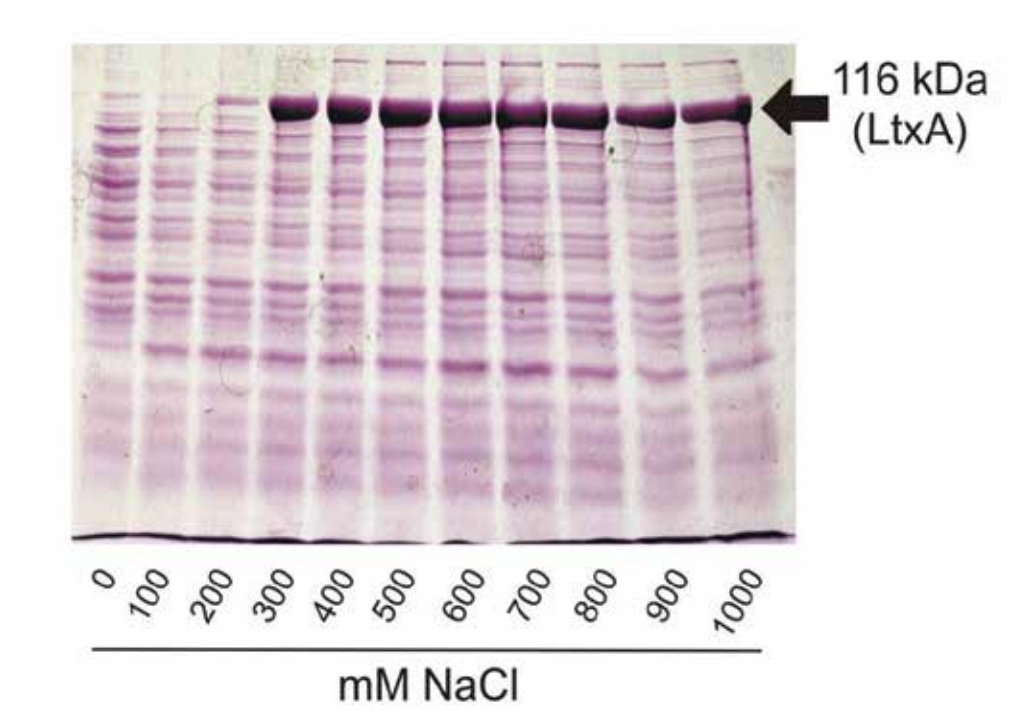

Fig. 6. Surface extract of bacteria from a highly leukotoxic (JP2) strain of *A. actinomycetemcomitans* (HK1619) separated by SDS-PAGE and stained with Comassie blue. The 116 kDa leukotoxin is released from the bacterial surface at NaCl concentration ≥300 mM, becoming the dominant band in the protein profile of the extracts (Johansson et al., 2000a).

5. Molecular aspects of *A. actinomycetemcomitans* leukotoxin

5.1 Structure

Leukotoxin (LtxA) expressed by *A. actinomycetemcomitans* is a large pore-forming protein that belongs to the RTX family of proteins. Leukotoxin consists of 1055 amino acids encoded by the leukotoxin gene in the leukotoxin operon (Lally et al., 1989; Kraig et al., 1990). The molecule can be divided into four regions based upon analysis of the amino acid sequence, the N-terminal region, the central region, the repeat region and the C-terminal region (Fig. 7) (Lally et al., 1996).

The N-terminal region at residues 1-408 exhibits alternating hydrophobic and hydrophilic clusters. The pore-forming regions of RTX proteins have been suggested to be mediated by

the hydrophobic clusters located between residues 175-400 (Welch et al., 2001). The central region at residues 409-729 contains large hydrophilic domains and the two acylation sites of leukotoxin located at $lysine_{562}$ and $lysine_{687}$ (Balashova et al., 2009). The fatty acids at these positions have been shown necessary for the activity of the toxin and suggested to contribute to the anchorage at the target cell membrane. The repeat region consists of tandem repeats of a cassette with nine amino acids located between residues 730-900 and 14 such repeats have been identified in this region of leukotoxin (Stanley et al., 1994). The target cell receptor LFA-1 binds to the repeat region and this interaction has been shown to determine the host cell specificity of leukotoxin (Stanley et al., 1994; Lally et al., 1994). In addition, the glycine rich repeats in this region have a strong capacity to bind Ca^{2+} and presence of these cations mediates increased binding of the toxin to leukotoxin-sensitive LFA-1 expressing cells (Lally et al., 1997). Finally, residues 901-1055 at the C-terminal end have been shown to be needed for export of the toxin to the bacterial outer membrane by interactions with secretory proteins (Stanley et al., 1991; Sato et al., 1993). This region of leukotoxin contains 20 additional basic amino acid residues, which differs the leukotoxin from the other RTX-proteins and confers its high isoelectric point (9.7) (Kraig et al., 1990). The four regions of leukotoxin described above are shared among the various toxins in the diverse family of pore forming RTX proteins but their amino acid sequence homology is limited to about 40-50%, with the highest homology between their repeat regions and the lowest between their C-terminal regions (Kraig et al., 1990). A partial denaturation of the leukotoxin molecule has been reported to enhance its leukotoxicity, which indicates that conformational changes affect the activity of the toxin (Lear et al., 2000). Some minor differences have been identified on the leukotoxin genes between different *A. actinomycetemcomitans* isolates but whether these differences interfere with leukotoxicity is not known (Lally et al., 1989; Kraig et al., 1990; Chen et al., 2009, Kittichotirat et al., 2011). The crystalline structure of leukotoxin has not yet been solved, which limits the available information about the molecular structures of the protein.

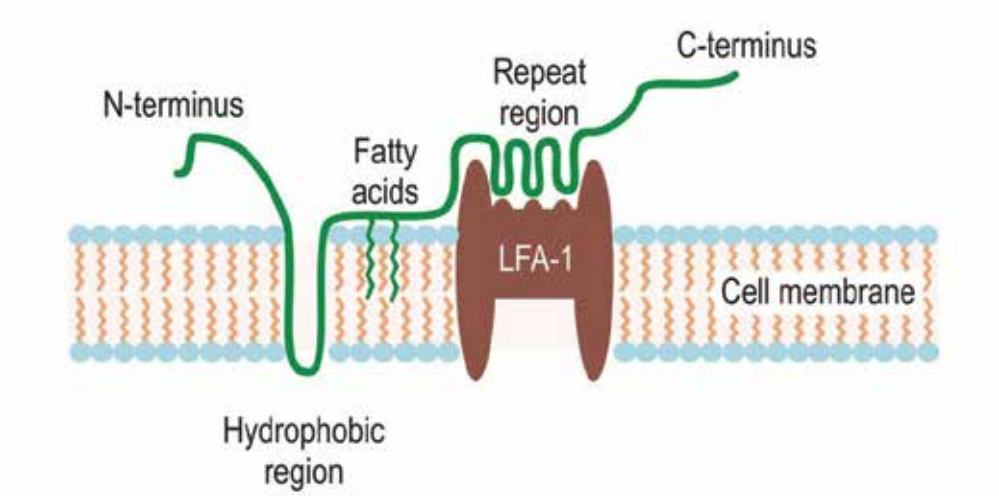

Fig. 7. Schematic illustration of the molecules involved in the interaction between *A. actinomycetemcomitans* leukotoxin and the target cell membrane.

5.2 Interaction with the target cell membrane

Leukotoxin exhibits a unique specificity to cells of haematopoetic origin from humans and some other primates (Lally et al., 1994). This restricted host cell specificity indicates that the species-specific effect of leukotoxin is mediated through a unique receptor on the target cells and that a precise region in the toxin recognizes and interacts with the receptor (Dileepan et al., 2007; Kieba et al., 2007). The principal feature of this species recognition region of leukotoxin is a series of 14 tandemly repeated amino acid sequences in the repeat region of the toxin (Stanley et al., 1994).

The leukotoxin has been shown to bind to surfaces of toxin-sensitive LFA-1-expressing cells, as well as toxin-resistant cells without LFA-1 expression (Lally et al., 1997). It has been suggested that the role of LFA-1 in leukotoxin-mediated cell lysis is to help the protein to have a correct orientation on the target cell membrane (Fig. 7) (Lally et al., 1999). Further, the two fatty acids strengthen the anchorage of the toxin when inserted in the target cell membrane and the hydrophobic domain forms small pores in the membrane. It has been stated that low concentration of the toxins might induce apoptosis through loss of membrane integrity caused by the small pores and that higher concentration of the toxin allows oligomerization of leukotoxin-LFA-1 complexes on the target cell membrane mediating a rapid and complete membrane collapse (Lally et al., 1999). In addition, leukotoxin has been shown to require lipid rafts for target cytotoxicity, which also indicates the importance of a high mobility on the target cell membrane (Fong et al., 2006).

The domain of leukotoxin that recognizes the target cell receptor has been determined to residues 688-941 examined by epitope mapping with monoclonal antibodies (Stanley et al., 1994). The LFA-1 molecule identified as the leukotoxin target cell receptor is a heterodimer consisting of the α_L (CD11a) and β_2 (CD18) subunits. The residues 1-128 on human CD11a has been shown to determine the human specificity of leukotoxin-induced cell lysis (Kieba et al., 2007). In addition, the extracellular region of human CD18 (residues 500-600) has been shown critical for conferring susceptibility to leukotoxin-induced cell lysis (Dileepan et al., 2007). The most important ligand of LFA-1 is the intercellular adhesion molecule 1 (ICAM-1), but this interaction does not coincide with the residues identified for leukotoxin binding (Dileepan et al., 2007; Kieba et al., 2007, Dustin et al., 2004). This finding indicates that the intracellular signaling mediated by the LFA-1 ligand binding is not activated by the leukotoxin binding. Three different affinity states (low, intermediate, high) of LFA-1 that interfere with ligand binding have been described (Shimaoka et al., 2003). If these different affinity states of the leukotoxin receptor interfere with the interactions between leukotoxin and its target cells is not known.

6. Cellular and molecular host response against *A. actinomycetemcomitans* leukotoxin

The ability of *A. actinomycetemcomitans* extracts to cause death of leukocytes was first shown more than 30 years ago (Baehni et al., 1979; Tsai et al., 1979). A protein named leukotoxin was indentified as the responsible molecule for this effect that was restricted to affect human PMNs and monocytes (Baehni et al., 1979; Tsai et al., 1979; Taichman et al., 1980). It has later been shown that leukotoxin also can affect human lymphocytes and erythrocytes from human and animal origin, however, at higher toxin concentrations than those lysing

PMNs and monocytes (Mangan et al., 1991; Balashova et al., 2006). Even though leukotoxin affects all subsets of human immune cells it is highly immunogenic and induces a specific acquired systemic immune response in the infected host (Ebersole 2003; Brage et al., 2011).

6.1 Acquired humoral immune response against leukotoxin

The specific role of humoral immunity in periodontal disease progression has not been fully elucidated, although the production of antibody response is suggested to be beneficial to the host in fighting periodontal infections (Ebersole 2003). On the other hand, the acquired immune response against periodontal pathogens has been shown to mediate disease associated mechanisms, such as bone resorption (Taubman et al., 2005; Teng 2003). It has clearly been shown that leukotoxin specific antibodies are present in the peripheral circulation of both periodontally healthy and diseased subjects (Kachlany et al., 2000; Califano et al., 1997). Plasma samples from the subjects with specific immunoreactivity against leukotoxin have been shown to neutralize leukotoxin activity and have also enhanced antibody titers against whole cells of *A. actinomycetemcomitans* in comparison with samples from subjects without immunoreactivity to leukotoxin (Califano et al., 1997). It has also been shown that systemic leukotoxin neutralization is correlated to the presence of this bacterium in the subgingival plaque (Källestål et al., 1991; Sjödin et al., 1995; Carlsson et al., 2006). The prevalence of systemic leukotoxin antibodies has been shown to be present in >50% in samples from adults and without significant differences in relation to periodontitis (Brage et al., 2011; Johansson et al., 2011). Interestingly, systemic leukotoxin neutralization correlates to decreased risk of the incidence of stroke in woman (Johansson et al., 2005). The mechanism behind this phenomenon has not yet been determined but a possible role of leukotoxin is suggested in the association seen between peridontitis and cardiovascular diseases (Pihlstrom et al., 2005).

A general opinion is that the humoral immune response against antigens of the oral subgingival microbiota is both local and systemic (Ebersole 2003). Whether the leukotoxin activity can be neutralized in the gingival pocket by specific antibodies is not known and there has been no report about the presence of leukotoxin neutralizing antibodies in the gingival crevicular fluid. The strong correlation between prevalence of higly leukotoxic *A. actinomycetemcomitans* and the development of attachment loss (Haubek et al., 2008) indicates a minor role of neutralizing antibodies in the infected periodontal pocket. However, it can be assumed that systemic leukotoxin neutralizing antibodies are an important protection against the systemic side effects, such as increased risk for diabetes and cardiovascular diseases that are associated with periodontitis. It has previously been shown that systemic antibodies against leukotoxin completely neutralize its activity even at high dilutions of the positive sera (Brage et al., 2011). In addition, the systemic leukotoxin-neutralizing capacity negatively associates to stroke while the systemic immunoreactivity to *A. actinomycetemcomitans* also shows a negative association to rheumatoid arthritis (Johansson et al., 2005; Okada et al., 2011). The mechanism behind these negative associations has not been elucidated. It could be speculated that the ability of leukotoxin to specifically affect the immune cells, in particular the antigen presenting monocytes/macrophages, causes a delayed acquired immune response in a primary *A. actinomycetemcomitans* infection.

6.2 Polymorphonuclear leukocytes

PMNs are the first defense cells to be recruited in the acute phase of an inflammation, as in a periodontal infection (Kantarci & van Dyke 2005). These defense cells are often found at high numbers in the infected periodontal pocket, attracted from the peripheral circulation through chemotaxis towards a gradient of molecules released from the dental plaque, as well as activated host cells. Although PMNs are crucial for phagocytizing and killing bacteria, they also release substances that mediate tissue destruction in aggressive forms of periodontitis (Kantarci et al., 2003). PMNs in the periodontium have been described as a "double-edged sword", capable of producing periodontal disease as well as protecting against the disease (Lamster et al., 1992). Leukotoxin as well as leukotoxic bacteria have been shown to efficiently cause death of human PMNs and consequently the leukotoxin is assumed to protect *A. actinomycetemcomitans* against phagocytic killing (Henderson et al., 2010). The protection occurs in relation to the leukotoxin production of the bacterial population (Johansson et al., 2000c). In a mixture of low-leukotoxic bacteria, human serum and PMNs (25 bacteria/PMN), which is agitated at 37°C under anaerobic condition, the bacteria are efficiently phagocytized and killed (Johansson et al., 2000c). In contrast, in the presence of highly leukotoxic (JP2-clone) bacteria and under the same conditions, the PMNs failed to phagocytize and kill the bacteria. Transmission electron microscopy pictures of the exposed PMNs showed a peripheral translocation of the granules in cells exposed to the highly leukotoxic bacteria (Fig. 8). Further analysis of PMNs exposed to leukotoxin showed an extracellular release of proteolytic enzymes from both primary and secondary granules (Johansson 2000b). More over, the interaction between leukotoxin and PMNs mediates activation and release of matrix metalloproteinase 8 (Claesson et al., 2002). Taken together these findings indicate that leukotoxin before causing death of the PMNs induces activation and release of proteolytic enzymes from these cells, which can contribute to periodontal tissue destruction.

Whether leukotoxin can exist as a biologically active protein in the infected periodontal pocket has not yet been examined. The presence of serum proteins and the relatively high pH (≈8) in the pocket indicates that leukotoxin is released from the bacterial surface in this ecological niche (Kraig et al., 1990; Johansson et al., 2003). The released toxin is an easy target for inactivation by several of the components present in the periodontal pocket, such as superoxide radicals and proteinases released from the host defense cells or the colonizers of the subgingival biofilm (Johansson et al., 2000a, 2003; Balashova et al., 2007). In addition, systemic leukotoxin specific antibodies neutralize leukotoxic activity, but if these antibodies are functional in the environment of the infected periodontal pocket is not known (Brage et al., 2011). There are also molecules that can protect leukotoxin from inactivation, such as the serum proteinase inhibitors and SOD expressed by *A. actinomycetemcomitans* (Johansson et al., 2001; Balashova et al., 2007). Probably, the great variation over time in the balance between these factors and the leukotoxin produced at a site of infection affects the progression of periodontal destruction.

As mentioned above, impaired PMN function is closely associated with periodontitis and functional PMNs seem to be of certain importance for combating *A. actinomycetemcomitans* establishment in the subgingival biofilm (de Haar et al., 2006; Kantarci et al., 2003; Carlsson et al., 2006; Pütsep et al., 2002). For instance, PMNs of subjects with Kostmann´s syndrome are immature and expresses truncated LL37, a cathelicidin with antibacterial effect against

A. actinomycetemcomitans (Pütsep et al., 2002). Furthermore, subjects with Papillon-Lefèvre syndrome have truncated PMN serine proteases, this causing an enhanced leukotoxin sensitivity due to impaired capacity to degrade extracellular leukotoxin by the released lysosomal PMN enzymes (de Haar et al., 2006).

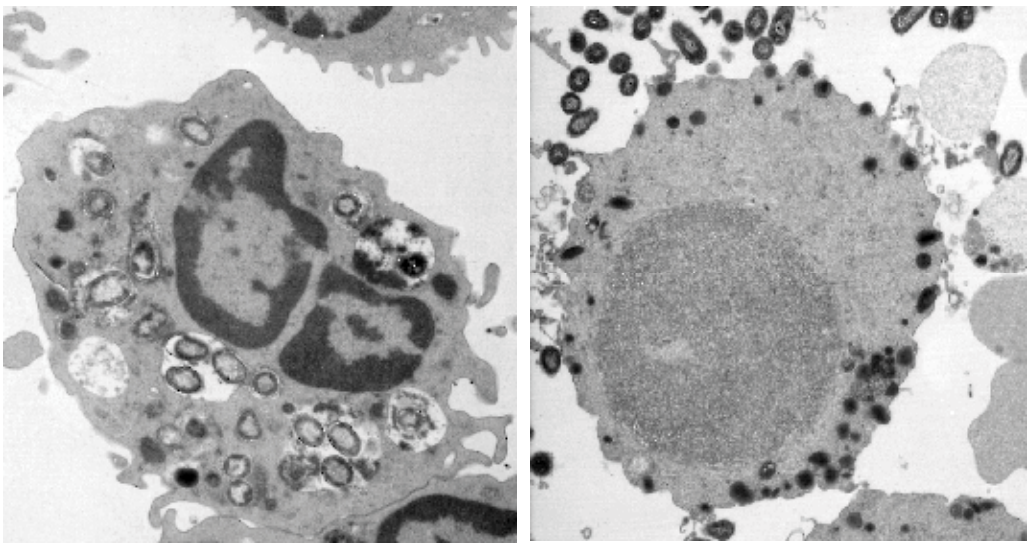

Fig. 8. PMNs exposed to alive *A. actinomycetemcomitans* (25 bacteria/PMN) for 10 min in the presence of 10% human non-immune sera. The mixture was gently agitated at 37°C in an anaerobic atmosphere. The minimally leukotoxic bacteria are phogocytized and killed by the PMN, while the highly leukotoxic bacteria (JP2) resist PMN phagocytosis and causes extracellular release of lysosomal components (Johansson et al., 2000c).

6.3 Lymphocytes

The lymphocytes were initially described as leukotoxin resistant cells (Baehni et al., 1979; Tsai et al., 1979). The first observation of leukotoxin susceptible cells of lymphocytic origin was by Simpson and co-workers (Simpson et al., 1988) who showed that several lymphoid cell lines were killed in the presence of leukotoxin. In addition, leukotoxin was shown to suppress function of peripheral blood lymphocytes (Shenker et al., 1994). A few years later, Mangan and co-workers (1991) showed that T-cells isolated from human peripheral blood were affected by leukotoxin. This leukotoxin-induced T-cell death was a slow process compared to the lysis of human cells of myeloid origin, the death being caused through apoptosis (Mangan et al., 1991). Human natural killer (NK) cells are affected by leukotoxin in a similar way as the T-cells, while the effects of leukotoxin to human B-cells or plasma-cells have not been studied (Shenker et al., 1994). Human lymphocytes show a great heterogeneity in regard to leukotoxin sensitivity and a subgroup of these cells are shown to be lysed at approximately the same concentrations as human PMNs (Kelk et al., 2003). The

lymphocytes with different leukotoxin sensitivity was not further characterized in this study but analysis of CD11a expression on the cell membrane showed a heterogenic distribution pattern for this cell population. The reason for the variation in leukotoxin sensitivity between PMNs and lymphocytes is not known. The suggested oligomerization of leukotoxin-LFA-1 complex and the need of lipid rafts on the target cell membrane may indicate that the composition of membrane molecules on the target cells determines the source of leukotoxin-induced death mechanisms (Lally et al., 1999). In cells from the human myeloid carcinoma cell line HL-60, low concentrations of leukotoxin cause apoptosis while higher concentrations lead to necrosis (Korostoff et al., 1998).

Cells of lymphoid origin are rare in the infected periodontal pocket but they reside at high numbers in the surrounding tissues as well as in the lymph glands (Kinane et al., 2002). It has been known for >30 years that the development of periodontitis involves a switch from a T cell lesion to one involving large numbers of B-cells and plasma cells. A shift in the balance between Th1 and Th2 subsets of T-cells is found in periodontal inflammation, with the Th2 cells to associate with chronic periodontitis (Ohlrich et al., 2009). More recently, T regulatory (Treg) and Th17 cells have been detected in periodontal tissues indicating that these cells also are of importance in the host response and pathogenesis of periodontal disease (Garlet 2010). The strong humoral immune response induced by leukotoxin indicates direct contact between this molecule and cells of lymphoid origin (Brage et al., 2011; Califano et al., 1997). The ability of leukotoxin to induce apoptosis in lymphocytes might impair the acquired immune response of periodontal infections. The ability of leukotoxin to affect the lymphocytes also indicates a possible role of this molecule in Th1/Th2/Th17 differentiation, a process that seems to be of importance in the pathogenesis of inflammatory diseases.

6.4 Monocytes/macrophages

It was early shown that human monocytes were as sensitive to leukotoxin, as human PMNs (Tsai et al., 1979). Killing of monocytes by the toxin proceeds through three distinct phases 1) cessation of the membrane undulating folding and an accumulation of granulae in the perinuclear area, 2) abnormal membrane movement and strings of cytoplasm projecting from the cell, and 3) explosive release of cytoplasmic material from the cells (Taichman et al., 1980). However, it should be taken into consideration that these studies were made with a crude leukotoxin extract that contained a lot of other bacterial components. Rabie and co-workers (Rabie et al., 1988) showed that purified leukotoxin caused a rapid death of human monocytes in mixtures of the toxin with peripheral blood mononuclear leukocytes (MNL).

More recently, analyses of different subsets of leukocytes separated from peripheral blood of a single donor showed that monocytes had an enhanced sensitivity to leukotoxin compared to PMNs and lymphocytes (Kelk et al., 2003). The leukotoxin-induced monocyte lysis was shown to involve activation of caspase-1, which indicates involvement of pro-inflammatory intracellular signalling (Fig. 9). Caspase-1 is a cytosolic cysteine proteinase that specifically induces activation and secretion of the pro-inflammatory cytokines interleukin-1β (IL-1β) and interleukin-18 (IL-18) (Dinarello, 2009a, 2010). The two cytokines are expressed as biologically inactive precursors and have to be cleaved by caspase-1 for activation and secretion. Caspase-1 is activated by incorporation in a cytosolic multimer

complex named the inflammasome (Latz 2010). The intracellular signalling pathways involved in leukotoxin-induced inflammasome activation in human monocytes/macrophages have not yet been determined. A partial characterization of this process indicates involvements of activation of the purogenic receptor $P2X_7$ (Kelk et al., 2011). Caspase-1 activation is also caused by several other gram-negative pathogens, such as *Salmonella* and *Shigella* species, and has been shown to be an important innate immune effector mechanism against intracellular bacteria (Miao et al., 2010).

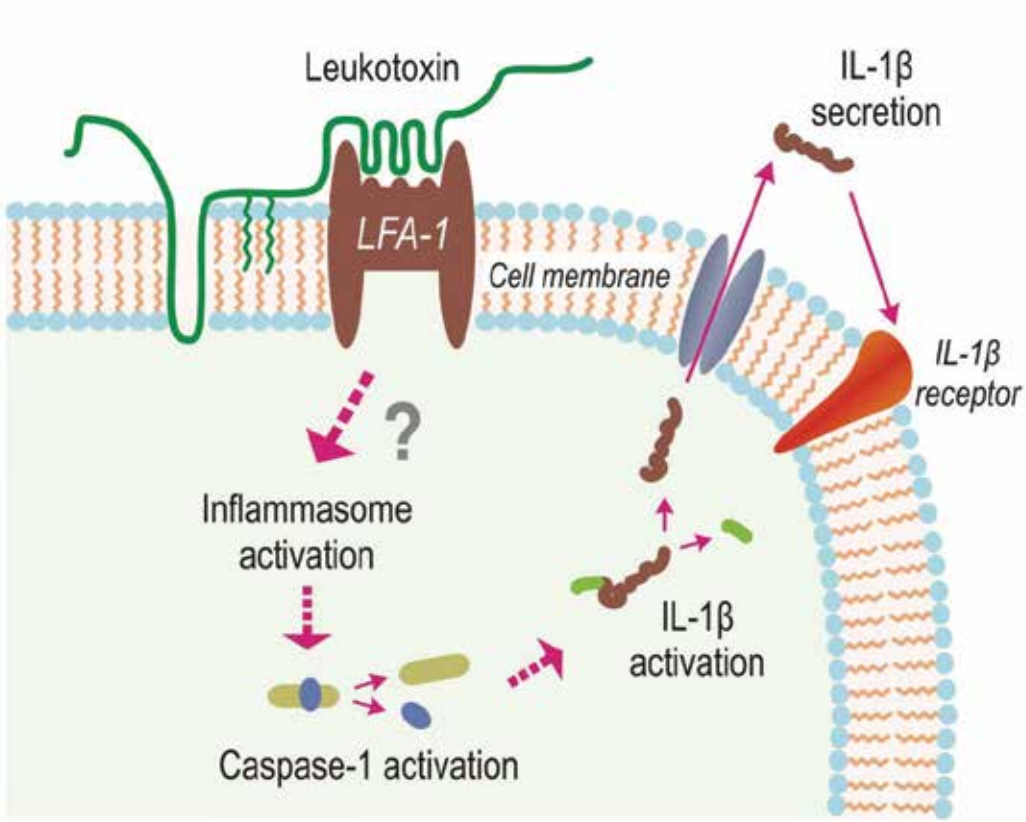

Fig. 9. Schematic illustration of the leukotoxin interaction with macrophages. Leukotoxin adheres to the cell membrane through binding to the LFA-1 dimer and it further anchors by inserting the fatty acid into the membrane lipid bilayer. The hydrophobic domain of the toxin is thought to cause small pores in the cell membrane. Through still undefined intracellular signalling pathways, this interaction with the target cell causes activation of caspase-1 and IL-1β that is secreted in a bioactive form from the affected cell.

IL-1β is a key component involved in acute and chronic inflammation, which makes the discovery of the leukotoxin induced IL-1β activation relevant and important (Kelk et al., 2005; Dinarello, 2011). IL-1 is an important regulator of bone resorption, which associates this cytokine to the alveolar bone loss seen in periodontitis (Schett, 2011; Dinarello, 2011;

Preshaw & Taylor, 2011). Analysis of gingival exudates have shown increased IL-1 concentration associated to periodontitis (Reinhardt et al., 2010; Preshaw & Taylor, 2011). Periodontal pockets examined from the same subject have indicated an association between high levels of *A. actinomycetemcomitans* and increased IL-1β concentration (Kelk et al., 2008).

The finding that leukotoxin induces activation of caspase-1 in human inflammatory defence cells indicates a new role of this virulence factor as a mediator of pro-inflammatory host response. Human macrophages (adherent blood monocytes) exposed to leukotoxin activates a rapid and abundant secretion of bioactive IL-1β (Kelk et al., 2005). Culture supernatants of leukotoxin-exposed macrophages activate bone resorption in cultured mouse calvaria, while presence of monoclonal antibodies against IL-1β abolishes this activation. This data indicate that bone resorption caused by culture supernatants of leukotoxin-exposed macrophages is mainly caused by released IL-1β. Moreover, exposure of human macrophages to components of gram-negative oral pathogens causes an increased accumulation of cytosolic pro-IL-1β that was not activated and released (Kelk et al., 2008). Leukotoxin or leukotoxic *A. actinomycetemcomitans* activates cleavage and secretion of this accumulated macrophage IL-1β, while *A. actinomycetemomitans* mutants without leukotoxin expression fail to cause this phenomenon. IL-1β secretion was activated already at a ratio of 1 bacterium/macrophage when using a highly leukotoxic *A. actinomycetemcomitans* strain or at a 10 times higher ratio when strains with low leukotoxicity were used (Kelk et al., 2008). Taken together, these data show that leukotoxin is the major *A. actinomycetemcomitans* component that induces activation and release of IL-1β from human macrophages and that this effect is further enhanced by priming the macrophages with other bacterial components.

Macrophages are rare cells in the healthy periodontium but are often found in high numbers in tissues from periodontal lesions (Kinane & Lappin, 2002). These cells are recruited to the infected site from the peripheral blood monocytes that are attracted by ICAM-1 expressing endothelial cells. The monocytes are passing through the vessel wall and are migrating in the connective tissue towards a gradient of chemoattractants that are released from the biofilm and the activated host cells (Geissmann et al., 2010). During diapedesis the monocytes differentiate into macrophages with a concomitant up-regulation of their inflammatory machinery, which continues during the migration. This process involves an accumulation of pro-inflammatory precursor molecules, such as IL-1β and IL-18, in the migrating macrophages (Dinarello, 2009b). A secondary stimulus is needed to induce activation and release of the accumulated precursors of IL-1β and IL-18 in the primed macrophages (Dinarello, 2010). In the case of an infection containing *A. actinomycetemcomitans,* the gradient of bioactive components in the connective tissue will contain leukotoxin, and the migrating macrophages will sooner or later meet leukotoxin concentrations that activate secretion of cytokines in the surrounding tissues. If this process is activated in the tooth supporting tissues in vicinity to the infection it might cause imbalance in the host inflammatory response and it might promote pathogenic cellular mechanisms. Some preliminary results indicate an association between enhanced IL-1β levels in gingival crevicular fluid and high number of *A. actinomycetemcomitans* in the periodontal pocket (Kelk et al., 2008). Interestingly, recent results suggest that IL-1β is transported into the *A. actinomycetemcomitans* cells and binds to the trimeric form of

intracellular ATP synthase subunit β (Paino et al., 2011). This specific mechanism might universally enhance biofilm resistance to host defence by binding IL-1β during inflammation.

The strong systemic immune response of the host to leukotoxin in *A. actinomycetemcomitans* infected subjects indicates direct contact between the antigent-presenting macrophages and leukotoxin (Califano et al., 1997; Brage et al., 2011). The enhanced leukotoxin-sensitivity of human macrophages indicates that these antigen presenting cells might be affected during a primary infection with leukotoxic *A. actinomycetemcomitans,* which might cause a delayed acquired immune response.

The pro-inflammatory response associated to degenerative diseases is at focus of research in many different medical disciplines (Dinarello, 2010). A variety of safe and effective anti-inflammatory agents are available today and commonly used in treatments of many autoimmune or auto-inflammatory disorders, neurodegenerative disease, or cancer. Increased knowledge of the cellular and molecular mechanisms involved in the pathogenesis of periodontitis might open up possibilities for new specific therapeutic agents and strategies in the future. The cellular and molecular targets for specific blockage of the inflammatory response to infection, as well as the possible therapeutic agents now and in the future, have recently been extensively reviewed (Dinarello, 2011).

6.5 Erythrocytes

The ability of some strains of *A. actinomycetemcomitans* to cause β-hemolysis on blood agar plates has been known for many years (Kimuzuka et al., 1996). Later, it was found that red blood cell lysis caused by *A. actinomycetemcomitans* involved an interaction with leukotoxin (Balashova et al., 2006). Different strains of the bacterium with various expressions of leukotoxin show a specific pattern when cultured on blood agar plates containing fresh horse blood. Red blood cells lack the receptor LFA-1, a key molecule for leukotoxin-induced leukocyte lysis (Lally et al., 1994). The cellular and molecular mechanisms for the hemolytic effect of leukotoxin are unknown. The lysis of erythrocytes by the leukotoxin has recently been reviewed (Kachlany 2010). It remains to be answered whether the hemolytic capacity of leukotoxin is an important virulence factor in periodontitis.

7. Conclusions

The ability of leukotoxin to cause death of all subsets of cells with hematopoetic origin might contribute to help the bacterium to survive the host immune response and also to release compounds essential for bacterial growth (Fig. 10). The more recent discoveries that leukotoxin mediates activation and release of proteolytic enzymes from PMNs and pro-inflammatory cytokines from monocytes/macrophages indicate a more direct role of leukotoxin in the disease pathogenesis. Unfortunately there is no animal model available for studying the virulence mechanisms of leukotoxin because of its specificity against defense cells of human or old world monkey origin. However, the strong correlation between presence of highly leukotoxic (JP2-clone) *A. actinomycetemcomitans* and development of attachment loss in adolescents indicates an important role of leukotoxin in the pathogenesis of aggressive periodontitis (Haubek, 2010).

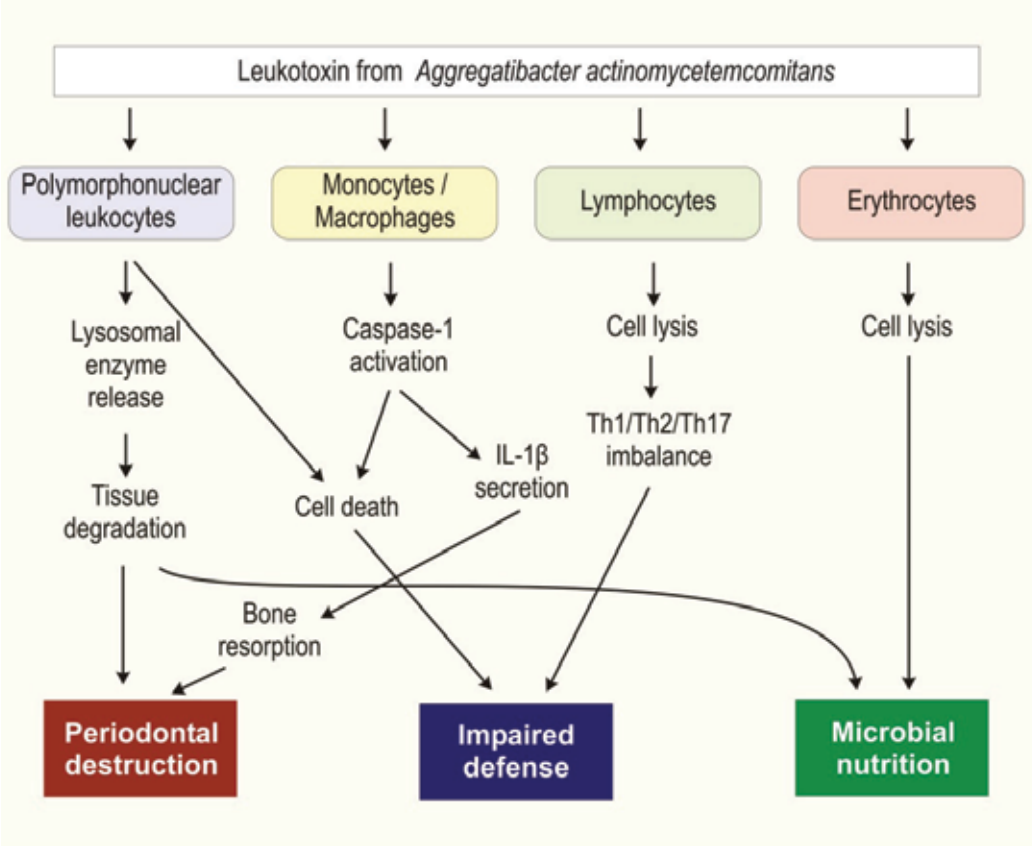

Fig. 10. Effects of importance for development of periodontal inflammation and local tissue destruction derived from the interactions of *A. actinomycetemcomitans* leukotoxin with human blood cells.

8. Acknowledgment

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Transformation of Nitrite and Nitric Oxide Produced by Oral Bacteria to Reactive Nitrogen Oxide Species in the Oral Cavity

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1. Introduction

Nitrate and nitrite are present in the human oral cavity. The main origin of these components is nitrate that is contained in leafy vegetables such as lettuce and spinach (Tamme et al., 2006). Ingested nitrate is absorbed into human body by the intestine, and part of the absorbed nitrate is secreted into the oral cavity as a component of saliva. In the oral cavity, nitrate is reduced to nitrite by nitrate-reducing bacteria (Doel et al., 2004, 2005; Zetterquist et al., 1999), and nitrite is reduced to nitric oxide (NO) by nitrite-reducing bacteria (Palmerini et al., 2003). If NO is produced from nitrite by nitrite-reducing bacteria, NO can autoxidize to dinitrogen trioxide (N_2O_3) and can react with superoxide anion radical (O_2^-) to produce a strong oxidant peroxynitrite ($ONOO^-$/ONOOH, pKa = 6.8) (ONOOH/NO_2, $E^{o\prime}$ = 2.10 V at pH 7) (Halliwell & Gutteridge, 1999). In the oral cavity, two peroxidases are present; one is salivary peroxidase that is derived from saliva and the other is myeloperoxidase that is derived from leukocytes migrated into the oral cavity. Nitrite can be oxidized by these peroxidases producing nitrogen dioxide (NO_2) (van der Vliet et al., 1997). The $E^{o\prime}$ of NO_2/NO_2^- at pH 7 is 0.99 V (Halliwell & Gutteridge, 1999). If the pH in the oral cavity decreased around 5, nitrite ion is protonated to produce nitrous acid (pKa = 3.3) that can be transformed to NO, N_2O_3, NO_2, and NO^+ (NO^+/NO, $E^{o\prime}$ = 1.21 V at pH 7) by self-decomposition (Oldrreive & Rice-Evabs, 2001). In this way, the formation of nitrite and NO by oral bacteria results in the production of reactive nitrogen oxide species (RNOS) by various reactions. This chapter deals with the mechanisms of production of RNOS in the human oral cavity under neutral and acidic conditions. Taking the mechanism into consideration, we discuss that the decrease in pH in the oral cavity results in the injury of oral tissue cells.

2. Measurements of RNOS

Production of RNOS in the oral cavity can be measured by (1) trapping of NO with Fe-*N*-(dithiocarboxy)sarcosine [$Fe(DTCS)_3$] complex, (2) transformation of 4,5-diaminofluorescein (DAF-2) and 3-amino-4-monomethylamino-2′,7′-difluorofluorescein

(DAF-FM) to their triazole forms, (3) oxidative degradation of aminophenyl fluorescein (APF) to fluorescein, (4) nitration of 4-hydroxyphenyl acetic acid (HPA), and (5) oxidation of uric acid.

Two preparations obtained from mixed whole saliva are use to study the formation RNOS in the oral cavity. One is saliva filtrate prepared by filtration of mixed whole saliva through two layers of nylon filter net, and the other is bacterial fraction prepared by centrifugation of the saliva filtrate.

2.1 NO-trapping

$Fe(DTCS)_3$ is prepared by addition of 0.03 mL of 100 mM $FeCl_3$ to 1 mL of 10 mM DTCS in 50 mM sodium phosphate (pH 7—7.6) (Fujii et al., 1996). The $Fe(DTCS)_3$ solution (0.2 mL) is added to 0.2 mL of saliva filtrate or bacterial fraction (Takahama et al., 2008a). $Fe(DTCS)_3$ is transformed to NO-$Fe(DTCS)_2$ after tapping NO. The formation of NO-$Fe(DTCS)_2$ was measured using an electron spin resonance (ESR) spectrometer with a quartz flat cell (0.05 mL). ESR spectra were recorded at room temperature under the following conditions: microwave power, 10 mW; scanning speed, 5 mT/min; line width, 0.5 mT; and amplification, 1000- or 2000-fold depending on ESR signal intensity.

2.2 Transformation of fluorescein derivatives to their triazole forms

DAF-2 and DAF-FM are used to detect the formation of NO under aerobic conditions. The fluorescent yields of these components increase significantly after the transformation to the triazole forms, namely, DAF-2T and DAF-FMT (Kojima et al., 1998, 1999). The excitation wavelengths (495 and 500 nm for DAF-2T and DAF-FMT, respectively) and the emission wavelengths (515 nm for DAF-2T and DAF-FMT) make easy to use these compounds because saliva filtrate and bacterial fraction don't absorb light around 500 nm. The formation of DAF-2T and DAF-FMT can be ascertained by HPLC (Takahama et al., 2005; 2009a).

In addition to the above fluorescent probes, APF is used to detect strong oxidants such as OH radical (OH radical/OH^-, $E^{o\prime}$ = 2.31 V at pH 7), NO_2, ONOOH, and HOCl but not O_2^- (Setsukinai et al., 2003). Because one of the oxidation products is fluorescein, the oxidation of APF can be measured fluorometically. Excitation and emission wavelengths are 490 and 515 nm, respectively. The formation of fluorescein can be ascertained by HPLC (Takahama et al., 2007a).

2.3 Nitration of HPA

HPA and tyrosine are used to detect NO_2 and ONOOH. HPA, which is produced during tyrosine metabolism by *Porphyromonas gingivalis*, is present in the mixed whole saliva (Takahama et al, 2002) and is mainly nitrated by peroxidase/H_2O_2/nitrite systems (Hirota et al., 2005; Takahama et al., 2003a, 2009b). Its nitration product is 4-hydroxy-3-nitrophenylacetic acid (O_2NHPA). This compound has absorption peaks at about 280 and 360 nm, and can be separated from HPA by HPLC (Takahama et al., 2002).

2.4 Oxidation of uric acid

Uric acid, which is present in saliva in the concentration range from 80 to 280 μM (Ferguson, 1989), is an important antioxidant, and this component can be oxidized by NO_2 and

ONOOH (Halliwell & Gutteridge, 1999). The oxidation of uric acid is estimated from the absorbance decrease at 284 nm and the decrease in its concentration by HPLC (Takahama & Hirota, 2010).

3. RNOS production

Around pH 7, RNOS are generated by the autoxidation of NO that is produced by nitrite-reducing bacteria and by the peroxidase-catalyzed oxidation of nitrite. In addition to the above reactions, RNOS is generated by the self-decomposition of nitrous acid and by the reaction of nitrous acid with a salivary component SCN^- under acidic conditions ($pH \leqq 5.3$). The followings deal with the formation of RNOS including NO in bacterial fraction and saliva filtrate.

3.1 Measurement of NO production using $Fe(DTCS)_3$

3.1.1 NO production around pH 7

The formation of NO-$Fe(DTCS)_2$ is not observed in bacterial fraction, but observed when nitrite is added to bacterial fraction (Takahama et al., 2005; Takahama et al., 2007a). The nitrite-induced NO production supports the reduction of nitrite to NO by nitrite-reducing bacteria (Palmerini et al., 2003). Nitrite concentration in the oral cavity increases after the ingestion of nitrate-containing foods (Pannala et al., 2003). The increase in concentration results in the enhanced production of NO that autoxidizes as followings,

$$4NO + O_2 \rightarrow 2N_2O_3 \quad (1)$$

Although NO can inhibit bacterial growth (Benjamin et al., 1994; Dykhuizen et al., 1996; Doel et al., 2004), the increased formation of N_2O_3 may contribute to give nitrosative stresses to tissues in the oral cavity.

3.1.2 Enhancement of NO production by decreasing pH

The pH in the oral cavity, especially dental plaque, rapidly decreases to below 5 after the ingestion of sugar-containing foods (Marsh & Martin, 1999; Lingström et al., 2000). The decrease in pH is due to the production of acid, especially lactic acid and the decreased pH returns slowly to its preingestion value. The frequency of this pH decrease depends on the frequency of ingestion of sugar-containing foods. Frequent and prolonged decrease in plaque pH results in the growth of acid-tolerant bacteria. Nitrite-induced NO production was about 5-fold faster around pH 5 than 7 in bacterial fraction, suggesting the faster production of NO by nitrite-reducing bacteria under acidic conditions (Takahama et al., 2007a, 2009a). In addition to NO production by nitrite-reducing bacteria, self-decomposition of nitrous acid is also possible for NO production under acidic conditions (Oldreive & Rice-Evans, 2001),

$$NO_2^- + H^+ \rightleftarrows HNO_2 \ (pKa = 3.3) \quad (2)$$

$$HNO_2 + H^+ \rightleftarrows H_2NO_2^+ \rightleftarrows H_2O + NO^+ \quad (3)$$

$$2HNO_2 \rightleftarrows N_2O_3 + H_2O \quad (4)$$

$$N_2O_3 \rightleftarrows NO + NO_2 \quad (5)$$

At pH 5, about 2% of nitrite is present as nitrous acid.

3.2 Measurements of RNOS production by fluorescent probes

DAF-2 and DAF-FM can be used to detect NO when pH is higher than 7 and 5, respectively (Kojima et al., 1998, 1999). Because NO is transformed to N_2O_3 under aerobic conditions (reaction 1), N_2O_3 or NO^+ donor can transform of DAF-2 and DAF-FM to DAF-2T (pKa = 6.27) and DAF-FMT (pKa = 4.38), respectively. On the other hand, radicals of DAF-2 and DAF-FM formed by NO_2- and ONOOH-dependent oxidation and peroxidase-catalyzed oxidation can react with NO to produce their triazole forms (Espey et al., 2002; Jourd'heuil, 2002). The above mechanisms of triazole formation suggest that the formation of DAF-2T and DAF-FMT increases with the increase in the concentrations of both NO and oxidants.

3.2.1 RNOS production around pH 7

DAF-2T formation in bacterial fraction is dependent on the concentration of nitrite, suggesting the contribution of NO produced by nitrite-reducing bacteria to DAF-2T formation (Takahama et al., 2005). Ascorbic acid, glutathione, uric acid, SCN^-, and phenolic compounds such as quercetin suppresses its formation (Takahama et al., 2006a). The suppression by ascorbic acid, glutathione, uric acid, and phenolic compounds can be attributed to the scavenging of NO^+, NO_2, and ONOOH, if these RNOS are contributed to the formation of DAF-2 radical and/or DAF-2T. If the DAF-2 radicals are scavenged by ascorbic acid and other antioxidants, DAF-2T formation is also suppressed. Furthermore, the above antioxidants can inhibit peroxidase-catalyzed oxidation of nitrite and DAF-2 to NO_2 and DAF-2 radicals, respectively, to suppress the formation of DAF-2T radical. SCN^- is a substrate of salivary peroxidase and myeloperoxidase around pH 7 (Pruitt et al., 1988; Tenovuo, 1989). Therefore, the inhibition of DAF-2T formation by SCN^- can be attributed to the suppression of the formation of NO_2 and DAF-2 radicals by peroxidases. Oxidation of nitrite by peroxidases proceeds as followings,

$$\text{Peroxidase} + H_2O_2 \rightarrow \text{Compound I} + H_2O \quad (6)$$

$$\text{Compound I} + NO_2^- \rightarrow \text{Compound II} + NO_2 \quad (7)$$

$$\text{Compound II} + NO_2^- + 2H^+ \rightarrow \text{peroxidase} + NO_2 + H_2O \quad (8)$$

SCN^- can react with compound I to suppress the formation of not only NO_2 but also DAF-2 radical producing $OSCN^-$ (Tenovuo, 1989). Phenolic compounds suppress the formation of NO_2 and DAF-2 radicals by reacting with compounds I and II.

Certain bacteria in bacterial fraction produce O_2^- (Marsh & Martin, 1999; Tenovuo, 1989). Leukocytes migrated into the oral cavity also produce O_2^- (Al-Essa et al., 1994; Nakahara et al., 1998; Yamamoto et al., 1991). O_2^- produced in the oral cavity is scavenged by salivary superoxide dismutase to generate O_2 and H_2O_2 (Nagler et al., 2002). H_2O_2 generated from O_2^- is used as a substrate of peroxidases. However, O_2^- can encounter with NO produced by nitrite-reducing bacteria, resulting in the production of $ONOO^-$ in the oral cavity,

$$NO + O_2^- \rightarrow ONOO^- \quad (9)$$

$$ONOO^- + H^+ \rightleftarrows ONOOH \ (pKa = 6.8) \quad (10)$$

$$ONOOH \rightarrow NO_2 + OH \text{ radical} \quad (11)$$

$$ONOOH \rightarrow NO_3^- + H^+ \quad (11a)$$

$ONOO^-$ produced by reaction 9 is protonated to produce ONOOH around pH 7 (reaction 10). Although $ONOO^-$ is unreactive, ONOOH can transform to NO_2 + OH radical as well as nitrate (Goldstein et al., 2005; Halliwell and Gutteridge, 1999). Therefore, ONOOH can give oxidative damages to the oral tissues by itself and by producing NO_2 + OH radical. The possibility of ONOOH formation in the oral cavity is suggested by the result that superoxide dismutase enhanced and inhibited the nitrite-induced formation of DAF-2T and oxidation of APF, respectively, in bacterial fraction (Takahama et al., 2006b, 2007a,b). Superoxide dismutase can prevent the consumption of NO and the formation of $ONOO^-$/ONOOH by reaction 9, leading to the enhancement of DAF-2T formation and the inhibition of APF oxidation. The contribution of ONOOH in the nitrite-induced oxidation of APF is about 30% at pH 7 (Takahama et al., 2007a). $ONOO^-$ reacts with CO_2 producing $ONOOCO_2^-$ that decomposes to nitrate + CO_2 and NO_2 + CO_3^- radical (Goldstein et al., 2005). The concentration of CO_2/HCO_3^- in saliva (10-30 mM) suggests the reaction of $ONOO^-$ with CO_2 in the oral cavity (Ferguson, 1989).

DAF-2T formation has also been studied using saliva filtrate. The formation of DAF-2T in the filtrate is much slower than that in bacterial fraction, and is dependent on the concentration of nitrite added (Takahama et al., 2005, 2007a). This result indicates that although NO is produced by nitrite-reducing bacteria, the formation of DAF-2 radical is inhibited and/or DAF-2 radical is scavenged by certain salivary components. Nitrite-induced oxidative degradation of APF is also much slower in saliva filtrate, implying the presence of scavengers of NO_2 and ONOOH in saliva (Takahama et al., 2007a).

Saliva is collected at 0, 1, 2, 3, and 4 hours after toothbrushing, and five saliva filtrates are prepared. The rate of nitrite-induced formation of DAF-2T in each filtrate increases with the increase in time after toothbrushing (Takahama et al., 2005). The rate of nitrite-induced DAF-2T formation in bacterial fraction obtained from each saliva filtrate also increases with the increase in time after toothbrushing. These results suggest the gradual growth of nitrite-reducing bacteria in the oral cavity after toothbrushing.

3.2.2 Enhancement of RNOS production by decreasing pH

The pH of the oral cavity especially dental plaque, where peroxidase and nitrite are present, decreases to below 5 (Bayindir et al., 2005; Crossa et al., 2001; Marsh & Martin, 1999). Therefore, nitrite-induced transformation of DAF-FM to DAF-FMT has been studied using bacterial fraction in a pH range from 5.3 to 7.2. It is known that the fluorescent yield of DAF-FMT dose not change in the pH range (Kojima et al., 1999). The DAF-FMT formation was about 10 times faster at pH 5.3 than 7.2, suggesting the faster production of NO under acidic conditions as described in section 3.1.2. The faster formation of DAF-FMT also suggests the faster formation of DFA-FM radical, which can be attributed to the enhanced production of NO_2 by peroxidase/H_2O_2/nitrite systems. Contribution of peroxidase/H_2O_2/nitrite systems

to the DAF-FMT formation at pH 5.3 and 7.2 is supported by the result that SCN^- (< 0.2 mM) inhibited the DAF-FMT formation at the pH values (Takahama et al., 2009a), and the enhanced production of NO_2 under acidic conditions is supported by the results that rate of the nitrite-induced oxidation of APF in bacterial fraction is 4-fold faster around pH 5 than 7 (Takahama et al., 2007a). The faster production of NO and NO_2 around pH 5 than 7 can contribute to the much faster formation of DAF-FMT at pH 5.3 than 7.2.

The formation of DAF-FMT is suppressed by various components at pH 5.3 and 7.2. Ascorbic acid (10 μM) (pKa = 4.2, 11.6) suppressed the DAF-FMT formation more than 90% at the pH values, and uric acid (100 μM) (pKa = 5.4 and 10.3) suppressed the DAF-FMT formation by about 60% at pH 7.2 but not at pH 5.3 (Takahama et al., 2009a). Phenolic compounds such as quercetin and cathechin (10 μM) suppressed the formation of DAF-FMT by 95 and 75% at pH 7.2 and by 40 and 10% at pH 5.3, respectively (Takahama et al., 2009a). One of the reasons for the different effects between ascorbic acid and other compounds is the degree of H^+-dissociation; more than 80% of ascorbic acid is present as mono-anion form at pH 5 and 7. On the other hand, about 40 and 83% of uric acid are present as mono-anion form at pH 5 and 7, respectively. The dissociation of phenolic OH groups may increases with the pH increase from 5 to 7; the pKa values of quercetin are 6.6 and 9.7 (Zenkevich & Guschina, 2010), and those of chatechin are 8.2 and 9.2 (El-Hady & El-Maali, 2008).

According to the above mechanism of DAF-FMT formation, ascorbic acid can suppress its formation by scavenging both NO_2 and DAF-FM radical and by inhibiting peroxidase-catalyzed production of the above components around pH 5 and 7. Oxidation rate of quercetin by bacterial fraction at pH 5.3 was about 30% of that at pH 7.2 in the absence of nitrite (Takahama et al., 2009a). This result suggests that the more efficient inhibition of DAF-FMT formation by phenolic compounds at pH 7.2 can be attributed to the more efficient suppression of peroxidase-catalyzed oxidation of nitrite and DAF-FM by quercetin. The greater inhibition of DAF-FMT formation by uric acid at pH 7.2 than 5.3 can also be attributed to more efficient inhibition of peroxidase-catalyzed reactions by uric acid at pH 7.2 than 5.3. Thus, the differences in pKa values among the above components may contribute to the different inhibitory effects between acidic and neutral conditions.

Nitrite-induced formation of DAF-FMT in bacterial fraction is enhanced by SCN^- at pH 5.3 but suppressed at pH 7.2 when SCN^- concentration is higher than 1 mM (Takahama et al., 2009a). SCN^- can react with nitrous acid (Doherty et al., 1997),

$$HNO_2 + SCN^- + H^+ \rightleftarrows ONSCN + H_2O \quad (12)$$

This reaction is possible because about 2% of nitrite is present as nitrous acid at pH 5. ONSCN may contribute to the enhanced formation of DAF-FMT, because SCN^- suppresses peroxidase-catalyzed oxidation of nitrite to NO_2 as described above. ONSCN can dissociate into SCN^- and NO^+ that is a strong oxidant (Licht et al., 1988). Therefore, SCN^--dependent enhancement of DAF-FMT formation can be attributed to the addition of NO^+ to DAF-FM or NO^+-dependent oxidation of DAF-FM to its radical to react with NO. The latter is supported by the faster NO production under acidic conditions (Takahama et al., 2007a, 2009a).

Nitrite-induced oxidative degradation of APF is about 3 and 5 times faster at pH 5.3 than 7.2 in bacterial fraction and saliva filtrate, respectively. The increased oxidation of APF with the decrease in pH may be due to the oxidation of APF by salivary peroxidase/H_2O_2 systems,

NO_2 produced by the systems, and $ONOO^-$/ONOOH. At pH 5.3, ONOOH can be produced by the following reaction in addition to reaction 9.

$$H_2O_2 + HNO_2 \rightarrow ONOOH + H_2O \quad (13)$$

As the contributions of $ONOO^-$/ONOOH are about 10 and 30% at pH 5.3 and 7.2, respectively (Takahama et al., 2007a), it is supposed that peroxidase-dependent oxidation of APF increases with the decrease in pH. Although SCN^- is a good inhibitor of salivary peroxidase at pH 5 (Pruitt et al., 1988), 2 mM SCN^- enhanced nitrite-induced oxidation of APF at pH 5.3 in bacterial fraction. The enhancement of APF oxidation by SCN^- can be supposed to be due to NO^+ produced from ONSCN.

The above results suggest that the production of NO and NO_2 increases in the oral cavity with the decrease in pH. The production of ONSCN accompanies the suppression of peroxidase-catalyzed NO_2 production by SCN^-. The production of NO, NO_2, and ONSCN is also possible in acidic dental plaque. This is supported by the presence of nitrite, SCN^-, and salivary peroxidase in dental plaque (Bayindir et al., 2005; Crossa et al., 2001; Tenovuo, 1989; Tenovuo et al., 1981). The concentration of nitrite in dental plaque is 1.2-2-fold higher than that in saliva (0.05-1 mM) (Bayindir et al., 2005; Crossa et al., 2001). The production of $ONOO^-$/ONOOH in acidic dental plaque is possible because superoxide dismutase enhanced and inhibited the formation of DAF-FMT and the oxidative of APF, respectively, in bacterial fraction at pH 5.3 in the presence of nitrite (Takahama et al., 2007a).

3.3 Nitration

Following reactions are postulated for main pathways of the nitration of HPA in the oral cavity (Hirota et al., 2005),

$$H_2O_2 + 2HPA \rightarrow 2HPA \text{ radical} + 2H_2O \text{ (catalyzed by peroxidase)} \quad (14)$$

$$HPA + NO_2 \rightarrow HPA \text{ radical} + NO_2^- + H^+ \quad (15)$$

$$HPA \text{ radical} + NO_2 \rightarrow O_2NHPA \quad (16)$$

The first step is the oxidation of HPA to its radical, and the second step is the reaction of HPA radical with NO_2. Salivary peroxidase catalyzes the nitration of HPA in the presence of both 1 mM nitrite and 0.5 mM H_2O_2 at pH 5.3 and 7.2, and rate of the nitration at pH 5.3 is similar to that at pH 7.2 (Hirota et al., 2005). During the nitration, nitrite concentration and HPA concentration decrease. The decrease in nitrite concentration has a broad peak around pH 5, whereas the decrease in HPA concentration has a peak around pH 7. The results suggest that the nitration at pH 7.2 is mainly due to the reaction of NO_2 with HPA radicals, both of which are produced by peroxidase-catalyzed oxidation of nitrite and HPA. The contribution of salivary peroxidase on the nitration is supported by SCN^--dependent inhibition of the nitration (50% inhibition, 10 μM) (Takahama et al., 2003a). From the effects of pH on nitrite and HPA consumption, it is deduced that nitration at pH 5.3 mainly proceeds as followings; oxidation of HPA to its radicals by NO_2 and addition of NO_2 to the radical. In contrast to the above result, nitration of HPA is about 3 times faster at pH 5.3 than pH 7.0 when the nitration is induced by peroxidase/glucose oxidase/nitrite systems, which

produce 2 μM H_2O_2/min, and the nitration is nearly completely suppressed by 1 mM SCN^- at pH 5.3 (Takahama et al., 2009b). The above two reports imply that peroxidase-dependent NO_2 production is faster in acidic than neutral dental plaque in the presence of physiological concentration of H_2O_2 in the oral cavity, which is approximately 10 μM (Tenovuo, 1989).

Nitrated HPA has been detected in mixed whole saliva from patients of periodontal diseases who are older than 60 years of age (Takahama et al., 2009b). Increased concentrations of nitrite, HPA, and H_2O_2 and decreased pH in the oral cavity may contribute to the formation of nitrated HPA. In fact, the concentrations of nitrite and HPA tend to be higher in individuals with age of 60-year-old or more. Quercetin (30 μM) suppressed nitrite-induced O_2NHPA formation more than 90% in bacterial fraction at pH 5 (Hirota et al., 2005) and quercetin can stay in the oral cavity for several hours after ingestion of onion soup (Hirota et al., 2001). Chlorogenic acid, which can also scavenge NO_2, stays in the oral cavity for several hours after ingestion of coffee (Takahama et al., 2007b). Therefore, quercetin and chlorogenic acid can function as scavengers of RNOS or electron donors to salivary peroxidase. Flavonoid aglycones and cinnamic acids including chlorogenic acid have been reported to be able to inhibit proliferation of oral cancer cells (Browning et al., 2005; Tanaka et al., 1993; Walle et al., 2005).

3.4 Oxidation of uric acid

Nitrite-induced production of NO_2 has been estimated by measuring the oxidation of uric acid using saliva filtrate. The rate of uric acid oxidation increases with the decrease in pH when the pH is lower than 6, suggesting that nitrous acid contributes to the oxidation of uric acid (Takahama & Hirota, 2010). To simulate dental plaque, oxidation of uric acid has been studied using bacterial fraction. H_2O_2-induced oxidation of uric acid is enhanced by nitrite, suggesting that NO_2 produced by salivary peroxidase/H_2O_2/nitrite systems contributed to the oxidation of uric acid. SCN^- (1 mM) suppresses the uric acid oxidation by about 75%, confirming that peroxidases participate in the oxidation of uric and that even if ONSCN contribute to the oxidation of uric acid, its contribution is small (Pietraforte et al., 2006; Takahama et al., 2003b; Takahama & Hirota, 2010)). The contribution of ONOOH formed by reaction 13 cannot be excluded in the oxidation of uric acid by the systems.

4. Conclusion

With the decrease in pH in the oral cavity from 7 to 5, nitrite-dependent production of not only NO, N_2O_3, NO_2, and $ONOO^-$/ONOOH but also ONSCN seems to be enhanced (Figure 1). If the concentration of nitrite in the oral cavity is increased by ingesting nitrate-rich foods, the increased nitrite concentration results in the increase in formation of NO, N_2O_3, NO_2, $ONOO^-$/ONOOH, and ONSCN under acidic conditions.

Uric acid in saliva can scavenge NO_2 and $ONOO^-$/ONOOH but not ONSCN. Even if NO_2 and $ONOO^-$/ONOOH are scavenged by uric acid, the scavenging will not be complete. Thus, if the concentrations of nitrite and SCN^- increase accompanying the decrease in pH of dental plaque, oral tissues adjacent to the plaque will be injured, because NO, N_2O_3, NO_2, $ONOO^-$/ONOOH, and NO^+ formed in acidic dental plaque can diffuse to the adjacent tissues. Diffused NO can be transformed to N_2O_3 and/or $ONOO^-$/ONOOH. Nitrite (0.05-1

mM) and SCN^- (0.1-2 mM) are always present in the oral cavity (Tenovuo, 1989), therefore it seems to be important to avoid the decrease in pH in the oral cavity to reduce RNOS-induced injuries of oral tissues.

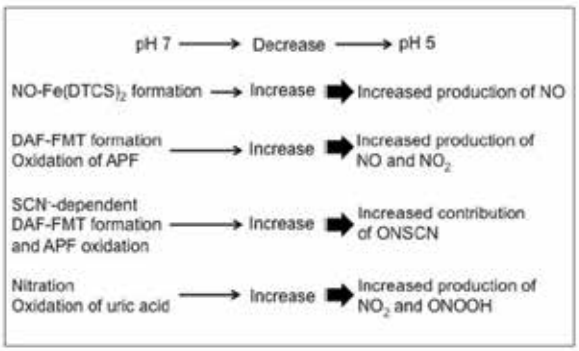

Fig. 1. Increases in RNOS production with the decrease in pH in the oral cavity

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Part 3

Research in Oral Health and Systemic Conditions

14

Dentists and Preventive Oral Health Care

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1. Introduction

Millions of treatment decisions are making by dentists in every day all over the world. Dentists, therefore, have a unique opportunity for delivering updated knowledge on oral health promotion to the public and their decisions regarding disease control results in considerable variation in treatment practices.
Dental caries has been known as the key factor responsible for dental pain and tooth loss in populations all over the world throughout the history of mankind. In spite of preventable nature of dental caries, it is still a main burden of oral diseases in populations even in developed countries.
Practically, avoiding sugar use and applying perfect oral-self care is difficult to be reached on population-level (Marthaler 1990). Therefore, fluoride use is known to be the most important measure for caries prevention in the community level. Regarding the importance of local effect of fluoride, it was recommended to start fluoride use with the erupting first deciduous tooth. Multiple use of various fluoride products provide teeth with increased protection against caries (Zimmer et al. 2003).
Appropriate clinical caries management requires a comprehensive knowledge about caries detection, assessment and diagnosis. Clinicians should have a thorough understanding about the pathogenesis of caries and caries diagnostic level. They should also be able to interpret evidence derived from all sources. Restorative treatment only removes the carious tissues and does not, by itself, cure lesions. Once a restoration is placed, the tooth is subjected to a series of replacement restorations, tending to increase in size, complexity and cost (Pitts 2004).

2. Prevalence and burden of dental caries

Dental caries characterizes by localized dissolution of the hard tissues of tooth due to the production of acids from bacterial metabolism in dental plaque. It has been known as the major cause of dental pain and tooth loss in populations all over the world (Fejerskov and Kidd 2003) throughout the history of mankind and is still a major public health problem worldwide (Selwitz et al. 2007). In most industrialized countries, dental caries affects 60-90% of school-aged children (Petersen 2005a). Dental caries experience of 12-year-old children, based on WHO Global Oral Health Data Bank, is high in Americas (DMFT> 3.5) and in the

European Region (DMFT> 2.5) (Petersen 2003a). Looking at the DMFT data from countries show that there are several countries with fewer than three DMFT but high Sic Index [the Significant Caries (SiC) Index: mean DMFT of the one-third of the group having the highest DMFT in a population) (Bratthall 2000)] values illustrating the hidden caries burden for children (Nishi et al 2002). According to the U.S. Surgeon General's report (U.S. Public Health Service 2000), dental caries is the single most common chronic childhood disease in the United States. About 20% of US population in all age groups has been found to have untreated dental caries (National Center for Health Statistics, 2011). Two recent studies in UK revealed that more than one-third of 5- and 11-year-old children in Great Britain had evidence of caries experience in dentine (Pitts et al. 2006, 2007). In most developing countries, the level of dental caries is tending to rise due to excessive sugar consumption and inadequate exposure to fluoride (Petersen et al. 2005). In adults the situation is more worrisome as dental caries affects almost 100% of the population in the majority of countries (Petersen 2005b). Dental caries is not restricted to children and young adults. The elderly constitute a particular risk population especially regarding root caries (Petersen and Yamamoto 2005). It is worth mentioning, therefore, that dental caries has not been eradicated, but just controlled to a certain degree (Marthaler 2004, Petersen et al. 2005).

Dental caries, in its advanced stages, is associated with considerable pain, anxiety and impaired social functioning. Caries-related tooth loss causes eating disability, reduces self esteem and impair quality of life (Chen et al. 1997). In addition to its burden on individual, dental caries imposes a significant economical burden on communities. Tooth-related diseases have been considered as the forth most expensive to treat in industrialized countries (Petersen 2004). More than 51 million lost school hours per year has been recorded in the USA, due to dental-related illnesses which means approximately 3.1 days per year for 5-17-year-old children (National Center for Health Statistics 1996). There are calculations which show that the budget for restoring the permanent dentition of the child population of low-income nations with amalgam would exceed the available resources for the provision of an essential public health care package for the children of 15 to 29 low-income countries (Robert and Sheiham 2002).

3. Determinants of dental caries

Dental caries has been frequently acknowledged to be a multifactorial disease meaning that it has many causes (Baelum and Fejerscov 2003). Each single factor with a probable role in caries development presents a possible cause. Caries occurrence in different individuals, however, is not due to the operation of all of these possible causes. Different people may have different sets of causes for caries development, which are defined as sufficient causes. Each of these sets, in turn, may consist of many single causes (Rothman 1986). Caries will not develop until all the component causes of a sufficient cause have accumulated (Baelum and Fejerscov 2003).

Tooth (the host), microorganism (the agent) and diet (the environment) (Fejerscov 1997) are major necessary factors in the process of dental caries. By influencing these factors directly or through some intermediates, it is possible to change the route of caries process. From this perspective, it can be stated that dental caries, is a result of complex chains of events which can be proximal or distal. Proximal factors acts directly or almost directly in the causal chain of caries process, while distal factors act indirectly and via several intermediary causes (Petersen 2005a).

Determinants of dental caries can be seen from three different perspectives: tooth level, individual level, and population level. At each of these levels there are some factors which may influence the equilibrium between demineralisation and remineralisation constantly taking place at tooth surface. At tooth level, factors which affect pH fluctuations, such as thickness of microbial deposits, amount and composition of saliva, the diet, and the concentration of fluoride ion in oral fluids will determine the likelihood of mineral loss and rate at which caries occurs. At the individual level, oral health behaviour like frequency of removing dental plaque by tooth brushing or dental floss, frequency of sugar use and fluoride usage will influence factors mentioned in tooth level. At the population level accordingly factors such as socio-economic status, access to oral heath care, and level of education may have controlling effect on the factors in individual level (Baelum and Fejerscov 2003).

A considerable amount of studies over the past decades have shown the linkage between oral health and socio-behavioural factors (Locker 2000, Petersen 2005a, Antunes et al. 2006). Accordingly major oral diseases are primarily considered as behavioural diseases (Petersen 2005a). Dental caries has been found to be more prevalent among children of families in lower social class than those in higher social class (Gratrix and Holloway 1994, Watt and Sheiham 1999), in deprived than affluent families (Prendergast et al. 1997, Antunes et al. 2002, Willems et al. 2005) and also in children with low level of parent's education and family income (Petersen 1992). Miura et al. (1997), analyzing data on oral health and socioeconomic factors of 44 developing countries, found a statistically significant correlation between dental caries of 12-year-olds and socioeconomic factors such as population employed in the service sector, urban population, life expectancy, and school attendance rate. Different dental caries risk has been shown across cultures and ethnic groups even inside a same population (Sundby and Petersen 2003). Tooth loss as an outcome of oral diseases has been shown to have psychosocial causes (Burt et al. 1990). Negative health behaviour such as smoking and infrequent toothbrushing, low income and low level of education (Gilbert et al. 1993, Eklund and Burt 1994) and heavy drinking (Slade et al. 1997, Kressin et al. 2003, Klein et al. 2004, Kida et al. 2006) have been reported to associate with tooth loss. Therefore, to control oral diseases adopting healthy habits including oral self-care (Löe 2000, Axelsson et al. 2002) and regular dental check-ups (Ismail et al. 1994, Richards and Ameen, 2002) are essential. Furthermore, good oral health behaviour will contribute to general health promotion since oral diseases have common risk factors with some other chronic diseases (Sheiham and Watt 2000, Petersen 2003a).

Smoking, as one of the greatest threats to global health, has been considered as a major cause of many oral diseases and unfavourable oral conditions (Reibel 2003) contributing significantly to the global burden of oral disease (Petersen 2003b). The adverse effects of tobacco on oral health range from some harmless to life-threatening conditions such as staining and discoloration of teeth, mouth odor, bad taste and smell, negative effect on wound healing, periodontal disease, and success of dental implants, potentially malignant lesions and oral cancer, and possibly caries and candidosis (Reibel 2003). In a population study in Canada, it has been shown that current smokers are less likely to visit a dentist, more likely to report sensitivity in tooth, tooth ache in previous month, orofacial pain and social limitations due to teeth (Millar and Locker 2007). Strong association between smoking and periodontitis is well documented (Sheiham and Nicolau 2005). Bergström (2004) reported a 5-20-fold higher risk of destructive periodontal disease among smokers than non-smokers.

From the public health point of view, it is essential to consider the whole of the causal chain when assessing health risks. This consideration will also facilitate adopting appropriate policies and strategies for disease prevention. Regarding oral health, in addition to the efforts for modifying the risk behaviours in individual level such as oral hygiene practices, in a broader context, considering socio-environmental factors and the characteristics of available oral health services are needed for effective planning on disease prevention and treatment (Petersen 2005a). A detailed understanding of the factors influencing health – determinants of health– is crucial for effective delivery of health services. Achievement of sustainable improvements in the health of population depends on addressing the underlying causes of disease in a society (Daly et al. 2002, Watt 2007). Assessment of risks to health and focussing on them has a key role in preventing diseases (WHO 2002). Risk assessment in dental public health, however, has still a limited scope; the emphasis mostly being on behavioural risk factors rather than on socio-environmental factors in oral diseases (Petersen 2005a). Oral diseases have some risk factors shared with several chronic diseases, thus adopting a common risk factor approach, aimed at reducing risk factors of a large number of diseases, is suggested for the effective prevention of oral diseases through general health promotion (Sheiham and Watt 2000).

4. Dental caries management

For many years, almost from the beginning of 20th century, caries management has been dealt with tooth restoration as a cure for dental caries and at that time it was considered an improvement in the dental care compared to the previous treatment –tooth extraction (Selwits et al. 2007). New understanding about caries initiation and progression indicated that there are potentials for prevention of dental caries (Daly et al. 2002). Based on this understanding, in some regions like Scandinavia, a preventive approach has been adopted for control of dental caries since many years ago (Heidmann et al. 1987). It should be considered that dental caries is among a group of chronic diseases that are largely preventable by avoiding its risk factors and much more improvements are expected if public health programs established appropriately. (Fejerskov 2004, The Liverpool Declaration 2005).

4.1 Traditional restorative treatment

Traditionally, dental profession has focused on pain relief by restoring damaged teeth or tooth extraction (Kidd and Fejerskov 2003, Anusavice 2005). For many years dental caries in its early or late stages have been treated identically. Early surgical intervention and placement of restoration will, however, result into earlier introduction of teeth in the restoration life cycle (Elderton 1990), which makes the tooth survival time shorter (Anusavice 2005). Therefore, filling damaged tooth with a restoration should not be considered as real treatment since it does not aim at eliminating the fundamental cause of caries i.e. dental plaque (Elderton 1996). Disease control in dental caries concerns influencing biofilm formation and growth, or modifying the dissolution process of tooth enamel, or both (Kidd and Fejerskov 2003), which needs some adjustments in patient's dietary pattern, oral hygiene habits, and fluoride usage as appropriate (Elderton 1996).

Treatment strategies, dominated by restorative approaches, have been shown to be ineffective in diminishing the burden of oral diseases (Elderton 1993, Nadanovsky and Sheiham 1995, Sheiham 1997). In fact restorative treatment, *per se*, does not cure the dental

caries (Elderton 1996, Kidd and Fejerskov 2003, Ericson 2007). Unfortunately, operative intervention has been seen by many patients, dentists, and health decision-makers as the way to manage and control dental caries. But it is well understood that the placement of initial restoration in a tooth will increase the risk of future restorations in that tooth (Elderton 1996, Luan et al. 2000) each being more invasive than the previous one. In this stage the tooth has been entered into the repeat restoration cycle (Elderton 1990). It has been shown that 65% of restorative care of dentists were replacement of previous restorations with the secondary caries being as the most common reason for replacement. (Anusavice 1995, Forss and Widstrom 2004). Research on the longevity of restorations clearly shows that making the first restoration often leads to an irreversible cycle of subsequent restorations (Deligeorgi et al., 2001), which may finally result into tooth removal (Qvist et al. 1990, Mjör et al. 2000; 2005; Tyas 2005).

4.2 Preventive/non-operative caries treatment

Dental caries is the result of mineral loss in tooth tissues due to the bacterial metabolism of plaque biofilm accumulated on tooth surface. A range of factors determine the extent and rate of the mineral loss which include composition of bacterial biofilm, quality and quantity of saliva, the presence of carbohydrate, and the concentrations of minerals (especially fluoride) in oral fluids (Kidd and Fejerscov 2003). By influencing each element of the process, caries initiation and progression can be actively modified and the disease, therefore, be controlled (Baelum and Fejerscov 2003). The following measures may influence caries process: dental plaque removal, chemical modification of plaque, use of fluorides, modification of diet, influencing the composition and flow of saliva (Kidd and Fejerscov 2003).

5. Strategies for caries prevention

Dental caries is a multifactorial disease meaning that it has many risk factors. Since people are different in their risk to dental caries, setting strategies for caries prevention is worthwhile. Preventive strategies attempt to reduce the risk of disease by influencing its determinants (Daly et al. 2002). Strategies for preventing dental caries may be designed at different levels; at the individual level (for patients referring to dental practices) or at the population level (as an oral health care policy for the whole population or some particular subgroups of the population).

5.1 At the individual level

To succeed in caries control at the individual level, there are some aspects to be considered: assessment of the current caries activity and risk of future caries progression, using the information to classify patients in risk groups, selection of the appropriate treatment among the available preventive non-operative treatments, setting follow-up visits.

Caries risk assessment, as a major part of dental practice, will provide valuable information for dentist to focus on treatments according to each patient's need, to recognize particular risk factors for each individual, to define recall interval (since dental care would never complete with one course of treatment), and to inform patients about their relative risk for developing new lesions or progression of current lesions (so that patients get encouragement to keep on recall visits and become active in their preventive care) (Kidd and Fejerskov 2003).

Oral self-care practices have been proved to be effective preventive measures at individual level for maintaining good oral health (Bratthall et al., 1996; Downer 1996; Loe 2000; Axelsson et al., 2002). Moreover, due to common risk factors with general health, oral health behaviours such as oral hygiene practices, limiting sugar use, restricting smoking would help the improvement of general health as well (Sheiham and Watt 2000, Petersen 2003a, Sanders et al. 2005). Preventive measures at the individual level emphasize plaque control, use of fluoride, and diet modification. Selecting each of these measures depends on the particular conditions of each patient and there is no single pre-written caries preventive recommendation suitable for all patients (Kidd and Nyvad 2003).

Plaque control is the cornerstone of preventive caries treatment since carious lesion is the result of metabolic activity of dental plaque at tooth surface. Plaque control includes tooth brushing, interdental cleaning and professional tooth cleaning. For an effective plaque removal, teeth should be brushed at a regular basis at least once a day with fluoridated toothpaste. Twice-a-day tooth brushing, however, have shown to be more effective and, therefore, is more recommended (Adair 2006, Davies 2003). Interdental cleaning is needed especially when there are signs of active proximal lesions. There are different interdental cleaning aids as the form of floss, tape or brush which can be used according to each specific site in the mouth. In case of caries-active patients, it may be necessary to support the patient with additional plaque control in the form of professional tooth cleaning (Kidd and Nyvad 2003).

All individuals should use fluoride toothpaste, containing 1000-1500 ppm fluoride ion, as a basic caries-preventive measure (Kidd and Nyvad 2003, Twetman et al. 2003). Caries-active patients will need additional fluoride therapy in form of home use fluoride moth-wash (Marinho et al. 2003b) or professionally-applied fluoride containing products (American Dental Association Council on Scientific Affairs 2007) until the situation is under the control (Kidd and Nyvad 2003).

Diet change may not be necessary in caries-inactive patients. However, patients must be informed about the role of diet in the process of dental caries. For patients with multiple active lesions, diet analysis is always needed (Kidd and Nyvad 2003) and diet change might be unavoidable.

Recall intervals should be set according to existing caries situation of each individual. Therefore, it may vary widely during the course of treatment. Examining the condition of whole mouth regarding the caries status and quality and flow of saliva, and assessment of patient's compliance at recall visits are of major importance (Kidd and Nyvad 2003).

5.2 At the population level

Strategies employed for the control of dental caries at the population level fundamentally depends on risks, determinants, and distributions of caries in different populations (Sheiham and Fejerskov 2003). These strategies may aim at the whole population which is known as the whole-population approach, or target at certain sections of the population which is named the risk approach. Based on the subdivision of the population identified, the risk approach is known as the directed or targeted approach where a particular subgroup of population are the target group or the high-risk approach where individuals consists the target group (Daly et al. 2002). The goal, in the whole-population approach is to control the determinants of incidence of caries at the whole population while in the risk approach, identifying groups or individuals with high susceptibility to caries in order to protect them

is called for. The advantages and limitations of both high-risk and population strategies are summarized in the following table (Rose 1985):

	High-risk strategy	Population strategy
Advantages	Intervention appropriate to individual Subject motivation Dentist motivation Cost-effective use of resources Benefit: risk ratio favourable	Radical Large potential for population Behaviourally appropriate
Disadvantages	Difficulties and costs of screening Palliative and temporary; not radical Limited potential for both individual and population Behaviourally inappropriate	Small benefit to individual Poor motivation of subject Poor motivation of dentist Benefit: risk ratio worrisome

Table 1. Comparison of high-risk and population strategies

6. Caries-risk assessment

In any preventive program, determining person's risk to develop that kind of disease would help professionals better manage patients preventively. Incorporation of risk assessment, as an important part of clinical decision making, into routine dental practice has been increasingly emphasised in recent years (American Dental Association 1995, Brad Rindal et al. 2006). The information gathered from caries risk assessment will be helpful in directing preventive and curative efforts according to patients' need, identifying the particular risk factors for each patient, and transferring this information to patient in order to encourage him/her for keeping recall appointments (Kidd and Nyvad 2003). Providing preventive measures and recall visits according to each individual's need would ensure appropriate use of resources. Since patients with elevated caries risk require receiving especial preventive regimen to reduce elevated incidence and severity of caries while those with low caries risk needs no additional preventive interventions and should have extended recall intervals. (Brad Rindal et al. 2006). Caries risk assessment covers a variety of factors such as past caries experience, microbiological tests (salivary lactobacilli, mutans streptococci, and yeasts and salivary flow rate and buffer capacity), dietary habits, oral hygiene, and social factors (Hausen 2003).

6.1 How to do caries-activity assessment?

Presence of active caries lesions (cavitated and/or non/cavitated) at the time of examination, is the strongest evidence for the prediction of future caries activity (Zero et al. 2001). There is no consensus on the definition of high caries activity; the following two criteria, however, might be indicative of high rate of caries progression in most populations: 1. Two or more lesion increment annually, and 2. Multiple active lesions in regions of mouth with high and rapid flow of saliva (lower incisors and buccal surfaces of upper molars) (Kidd and Nyvad 2003).

Stage of development of the dentition is another important issue when estimating caries activity status. Risk sites in different stages of dentition over life are as follows: in children, occlusal surfaces of erupting permanent molars; in adolescents, proximal surfaces especially

the distal surface of second premolars and the mesial surface of second molars; in adults and elderly, root surfaces which are difficult to be cleaned (Kidd and Nyvad 2003).

6.2 How to determine the risk factors?

A risk factor is defined as "an environmental, behavioural, or biologic factor confirmed by temporal sequence, usually in longitudinal studies, which if present, directly increases the probability of a disease occurring, and if absent or removed, reduces the probability. Risk factors are part of causal chain, or expose the host to the causal chain. Once disease occurs, removal of a risk factor may not result in a cure." (Beck 1998).

Caries risk factors are usually categorised as biological factors and social and demographic factors. Both of these risk factors can be detected by getting a medical and dental history. The following conditions that contribute to high caries activity should be considered in medical history: Dry mouth due to diseases like Sjögren's syndrome or radiotherapy in head and neck regions, using medications which interfere with salivary flow such as antidepressants or drugs which have sugar in their structure like some syrups or asthma inhalers. The following issues are informative in dental history: 1. A history of multiple restorations with frequent replacements is an important sign of high caries risk. 2. Questions about patient's oral hygiene activities like frequency and time of brushing and flossing, type of toothpaste, method of rinsing after brushing, use of mouthrinse. 3. Patient's diet: frequency of using sugary drinks or snacks. Sometimes asking patients to fill a diet sheet may provide further information than just a verbal enquiry.

Social and demographic risk factors are not involved directly in the process of dental caries (Kidd and Nyvad 2003). Instead, these risk factors such as income, education and social environment will influence dietary and oral health related behaviours (Kidd and Nyvad 2003).

6.3 How to categorise patients based on their caries-activity status?

After the information regarding caries activity gathered, patients will allocate to one of these categories: 1. Caries inactive or caries controlled: no active lesion or at maximum one presents, with no history of recent restoration. 2. Caries active but all relevant risk factors can potentially be changed: in this category, active lesions are present and patients experience two or more new/progressing/filled lesions in each year during past 2-3 years. These patients are able to control caries through changes in risk factors. 3. Caries active but some risk factors cannot be changed (for instance due to dry mouth or using some kind of medications) or risk factors cannot be identified: in this group active lesions are present and there is yearly increment of two or more new/progressing/filled lesions in the preceding 2-3 years. Patients in this category are always at high risk of caries but caries development can be controlled by maximum efforts to control risk factors (Kidd and Nyvad 2003).

Recommendations for controlling disease progression: 1. Caries inactive or caries controlled: these patients only need to keep on careful oral hygiene activities with the use of fluoride toothpaste. 2. Caries active but all relevant risk factors can potentially be changed: in this group, patients should improve their ability for mechanical plaque control. Supplementary fluoride mouthrinse or chair-side fluoride application might be necessary. Diet counselling is needed and diet change may be prescribed in case of presence of multiple active lesions. 3. Caries active but some risk factors cannot be changed or cannot be identified: caries control in this group is the most challenging. All related risk factors must be sought and preventive treatment must be designed individually (Kidd and Nyvad 2003).

High caries risk

- ≤6-year-olds (any of the following situations)
  Any incipient or cavitated primary or secondary carious lesions during last three years
  Presence of multiple factors which may increase caries risk*
  Suboptimal fluoride exposure
  Xerostomia
- >6-year-olds (any of the following situations)
  Three or more incipient or cavitated primary or secondary carious lesions in the last three years
  Presence of multiple factors which may increase caries risk*
  Suboptimal fluoride exposure
  Xerostomia

Moderate caries risk

- ≤6-year-olds
  No incipient or cavitated primary or secondary carious lesions during last three years but presence of at least one factor which may increase caries risk*
- >6-year-olds
  One or two incipient or cavitated primary or secondary carious lesions in the last three years
  No incipient or cavitated primary or secondary carious lesions during last three years but presence of at least one factor which may increase caries risk*

Low caries risk

No incipient or cavitated primary or secondary carious lesions during last three years and no factors which may increase caries risk*

*Factors increasing the risk of caries development:

- Clinical evidence: new lesions, developmental or acquired enamel defects, genetic abnormalities of teeth, presence of exposed root surfaces, premature extractions, anterior caries or restorations, multiple restorations, restoration overhangs and open margins, deep and caries-susceptible unsealed fissures, fixed orthodontic appliances, partial dentures
- Dietary habits: frequent sugar intake, prolonged bottle or breast feeding, drug or alcohol abuse
- Social history: social deprivation, high caries in siblings, low knowledge on dental disease, irregular dental attendance, ready availability of sugary snacks, low dental aspirations
- Fluoride use: no fluoridation of drinking water, no use of fluoridated toothpaste, no use of fluoride supplements
- Plaque control: infrequent and ineffective tooth cleaning, poor manual control
- Saliva: low flow rate, low buffering, high counts of Stereptococus mutans and lactobacillus
- Medical history: medically compromised, physical disability, medication-, radiation-, or disease-induced xerostomia, long cariogenic medications

Table 2. Caries risk criteria for evaluating patients' caries risk (modified from: American Dental Association Council on Scientific Affairs 2006, Preventing Dental Caries in Children at High Caries Risk, SIGN publications 2000)

7. Effectiveness of caries preventive measures

There is a large body of evidence supporting the effectiveness of preventive measures in caries management. We will look at these measures from three different perspectives:

7.1 Community-active measures

These are programs which run for the benefit of whole population. The best example is water fluoridation in which controlled amount of fluoride is added to the public water supply to prevent dental caries in the population using this water. There is substantial amount of evidence representing the effectiveness of water fluoridation in caries prevention (CDC 2001, NHMRC 2007). It has been known as one of the great achievements of public health in 20th century (CDC 2001) and may still be the most cost-effective public health measure to control dental caries in populations with high incidence and prevalence of dental caries (Ellwood and Fejerskov 2003, Pizzo et al. 2007). There are some arguments, however, that the continuation of water fluoridation may be unnecessary especially in industrialized countries (Pizzo et al. 2007) with regard to the following new evidences: 1. Anticaries effect of fluoride mostly exerts from its topical action rather than its pre-eruptive systemic absorption (Hellwig and Lennon 2004), 2. Experiences from some countries have shown that discontinuation of water fluoridation had no negative effect on caries prevalence of the population using that water (Seppa et al. 2000, Kunzel et al. 2000), 3. Substantial decline in caries prevalence has been reported in many European countries where never adopted water fluoridation (Marthaler 2004), and 4. Epidemiologic studies in recent decades have shown an increase in the prevalence of fluorosis in regions with water fluoridation (Cochran et al. 2004, Khan et al. 2005). Confining the consumers' option has also been mentioned as another objection towards water fluoridation (Jones et al. 2005).

Consequently research on alternatives to water fluoridation like salt and milk began in the second half of the 20th century (Petersen and Lennon, 2004). Salt fluoridation has been used as a caries preventive measure in several countries like France, Germany, Switzerland and some South American countries. Caries reduction due to using fluoridated salt has been reported from 14% in Germany (Marthaler 2005) to 84% in Jamaica (Gillespie and Baez 2005). Careful assessment of all fluoride sources available for the population, however, is needed when such program is planning to avoid excessive ingestion of fluoride and probable fluorosis. An increased risk of fluorosis has been reported in Mexico due to nationwide use of fluoridated salt (Vallejos-Sanchez et al. 2006). Switzerland is pioneer in using milk as a vehicle for fluoride since 1962. Milk fluoridation programs have used various channels such as distribution of milk, powdered milk or milk cereal in kindergartens and schools (Jones et al. 2005). Yeung et al. (2005), based on a recent systematic review concluded that sufficient evidence is lacking to show the effectiveness of milk fluoridation in caries reductions. According to the existing studies, the authors, however, suggested that milk fluoridation is beneficial to the permanent dentition of schoolchildren. Other vehicles of fluoride such as fluoridated sugar and beverages, fluoride-rich mineral water seems to be important in caries reduction at the individual rather than population level (Tseveenjav 2004).

7.2 Dental professional-active measures

In order to review the scientific evidence on professionally applied topical fluoride and develop clinical recommendations, the American Dental Association arranged an expert

panel. All publications regarding professionally applied topical fluoride—including gel, foam and varnish forms— were searched through October 2005. The experts were asked to identify any additional systematic reviews or other relevant published trials. After assessing the data from the individual studies which were summarized in the systematic reviews and from the identified clinical studies, the expert panel prepared a document which was resubmitted for more reviewing by other experts in the field of fluoride and caries. The expert panel prepared the clinical recommendations after consideration the comments received. A summary of these evidences and clinical recommendations which were approved by the ADA Council on Scientific Affairs, are presented here (ADA council on scientific affairs 2006):

- Fluoride gel is effective in preventing caries in school-aged children. The best caries reduction effect of fluoride gel is achieved with four minutes or more applications.
- Fluoride varnish is effective in caries prevention in primary and permanent dentition of children and adolescents when applied in six-monthly basis. It is effective in preventing caries of high-risk populations with two or more applications per year.
- Fluoride foam is effective in caries prevention in the primary dentition and newly erupted first molars with four-minute applications every six month.
- Moderate- or high-risk patients younger than 6 years should receive fluoride varnish applications at six-month intervals. The same rule is true for more than 6-year-old moderate- or high-risk patients except that in this age group fluoride gel is applicable as well.
- For patients with lower caries risk, fluoridated water and fluoride toothpaste may provide adequate caries prevention. Application of topical fluoride in this risk category, however, depends on professionals' judgment and patients' preference.

7.2.1 Pit and fissure sealants

Several clinical studies documented the effectiveness of pit and fissure sealant therapy in occlusal caries reduction in the permanent teeth of high-risk children and adolescents (Locker et al. 2003; Davies, 2003), although the quality of many of these studies assessed to be poor (Ahovuo-Saloranta et al. 2004). Various caries preventive effect has been reported for pit and fissure sealants. Rozier (2001), reviewing 24 studies from 1975 to 1990, reported a prevented fraction (the difference between the mean caries increment in the study and control groups divided by the mean increment in the control group [Adair 2006]) of 71% for fissure sealants. This figure was 33% in the review by Mejare et al. (2003) for sealing first permanent molar. Ahovuo-Saloranta et al. (2004) in a review for Cochrane Database of Systematic Reviews reported a range of caries reduction from 86% at 12 months to 57% at 48-54 months follow-up. Accordingly, the authors recommended sealant application in permanent molars for preventing caries in the occlusal surface with considering caries prevalence of both the individual and population. Moreover, cost-effectiveness of sealant therapy has been shown in longitudinal population-based studies (Virtanen et al. 2003) with long-lasting preventive effects (Wendt et al. 2001).

7.2.2 Anti-microbial agents

There are few antimicrobial agents with documented cariostatic effect. This is primarily due to the organization of plaque microorganisms in the form of biofilm. Biofilm, an aggregate of microorganisms in a complex matrix of biopolymers, acts as a barrier which keeps microorganisms out of the reach of antimicrobials and immune response of the host (Scheie 2003). The most comprehensively studied antimicrobial agent is chlorhexidine (Scheie 2003).

Chlorhexidine gel, has been reported to have a caries-preventive effect of 47% (Davies 2003), and is effective in prevention of caries in high-risk children (Rozier 2001). The evidence for the anti-caries effect of the chlorhexidine-containing varnishes has been found to be incomplete in a recent review (Twetman 2004). A wide range of other antimicrobial agents like Cetylpyridinium chloride, Hexetidine, Triclosan, Metal ions, Xylitol, and etc has been studied for their anti-caries effect. Due to the probable deteriorating effect of antimicrobial agents on the ecological balance of the oral flora, the use of these agents, however, should be restricted to situations which conventional prophylactic methods are likely to be ineffective such as handicapped individuals, hyposalivation, intraoral fixation or splinting, orthodontic treatments, prosthetic restorations or implants, and so on (Scheie 2003).

7.3 Individual-active measures

7.3.1 Fluoridated toothpaste

The caries-inhibiting effect of fluoridated toothpaste for permanent dentition is backed up with an established and strong evidence; for primary teeth, the evidence is incomplete (Marinho et al. 2003b; Twetman et al. 2003). Nevertheless no logical reason exists to presume that it is less effective in primary teeth (Adair 2006). In a study with a placebo, the use of fluoridated toothpaste has resulted to a 24.9% prevented fraction in young permanent dentition (Twetman et al. 2003). Higher baseline levels of patients' caries, higher fluoride concentration, higher frequency of use, and supervised brushing have been found to increase the preventive effect of fluoridated toothpaste (Marinho et al. 2003b).

7.3.2 Fluoride supplements

Fluoride dietary supplements have been estimated to have an effectiveness of 20% to 30% for caries reduction. They have primarily been developed for the sake of populations with no access to water-borne fluoride (Adair 2006). They are not, however, considered as a public health preventive measure due to the paradigm shift in the understanding about fluoride's mode of effect from systemic to topical (Fejerskov 2004, Hellwig and Lennon 2004), exposure to other sources of fluoride, and the potential risk of fluorosis in permanent dentition (Adair 2006, Davies 2003), thus their usage are limited in high-risk children (Davies 2003).

7.3.3 Fluoride mouthrinses

Fluoride mouthrinses are available at two forms: 0.2% concentration for weekly and 0.05% concentration for daily use (Adair 2006). Their supervised regular use, with a prevented fraction of 26%, is associated with a clear reduction in caries increment in the permanent dentition of children (Marinho et al. 2003a).

7.3.4 Self-applied fluoride gels

The use of self-applied fluoride gels has been shown to result into 32% caries reduction in fluoride-deficient communities and 7% to 35% in optimally fluoridated areas. There is no systematic review on the effectiveness of purely self-applied gels (Adair 2006).

7.3.5 Self-applied chlorhexidine gels and rinses

A meta-analysis of clinical studies has demonstrated an overall caries- reduction effect of 46% for the chlorhexidine treatment irrespective of application method, frequency, caries risk, caries diagnosis, tooth surface, or fluoride regimen (Van Rijkom 1996).

7.3.6 Slow-release fluoride devices

Such devices would be beneficial to prevent dental caries in high-risk children (Featherstone 2006). In a clinical trial 70% reduction in caries has been reported for high risk children who wore a fluoride-releasing glass device in their mouths comparing to control group (Toumba and Curzon 2005). Evidence for caries-inhibiting effect of slow-release fluoride devices was, however, regarded as weak and unreliable in a recent Chochrane systematic review (Bonner et al. 2006).

7.3.7 Restriction of sugar consumption

There is no doubt that sugars have a fundamental role in the initiation and development of dental caries (Moynihan 2005, Burt and Pai 2001). Although this role seems to be weakened with the nowadays widespread fluoride exposure (Burt and Pai, 2001), there is still a direct relationship between sugar intake and caries in presence of adequate fluoride (Moynihan 2005). Therefore, restriction of sugar consumption remains an essential, if not the most important, aspect of caries prevention (Burt and Pai, 2001). Recommendations in this regard emphasize reducing the frequency and amount of sugar consumption and also limiting sugar use to mealtimes (Moynihan and Petersen 2004, Tseveenjav 2004). The frequency of sugar intake should not exceed than four times per day and the total amount of sugar consumption should be less than 15 kg/year/person (Sheiham 1983).

7.3.8 Non-cariogenic sweeteners

A number of observational studies and clinical trials have shown the caries-protective effect of xylitol, and to a lesser extent sorbitol (Honkala et al. 2006, Burt 2006, Anderson 2003, Hayes 2001). For the first time, comprehensive Finnish "Turku Sugar Study" (Scheinin et al. 1976) revealed an 85% decline in dental caries by total dietary substitution of sucrose with xylitol over a 2-year period. Xylitol also has been shown to reduce the vertical transmission of Streptococcus Mutans from mothers to children (Söderling et al. 2000). Consequently, promotion of the use of xylitol-sweetened gum has been proposed as a caries-preventive measure in public health (Burt 2006, Honkala et al. 1996, Virtanen et al. 1996, Isokangas et al. 1989). Its use may be limited, however, due to high cost and low versatility (Tseveenjav 2004).

7.4 Effectiveness of fluoride in caries prevention in adults

Most of the studies on the effectiveness of fluoride in preventing caries have been conducted among children (National Institutes of Health Consensus Development Conference Statement, 2001). In a systematic review on studies published on the effectiveness of the fluoride in preventing caries in adults, Griffin et al. (2007) found that any fluoride application, self- or professional or water fluoridation averted 0.29 coronal carious and 0.22 root carious surfaces in a year. They found a prevented fraction of 27% for water fluoridation in adults. The authors concluded that fluoride is effective in caries prevention among adults in all ages.

7.5 Effectiveness of non-operative caries management on community level

Practicality and cost-effectiveness of caries preventive measures in managing dental caries on community level have been largely studied. Ekstrand et al. (2000) offered a caries-preventive program including education of the child, parents and teachers on caries disease, training in toothbrushing, and professional plaque removal, applications of sodium fluoride (2%) and sealant applications based on individual needs to a group of children in a district

of Moscow. After 2.5 years the children in study groups had improved their oral health status significantly compared to the children in the control group and the program found to be highly effective in controlling dental caries in the permanent dentition.

Ekstrand and Christiansen (2005) in their study assessed the effectiveness and performance of a non-operative caries treatment program (NOCTP) used since 1987 in the municipality of Nexö in Denmark. Mechanical plaque control was the central focus of the method and the eruption period of molar teeth as a risk factor has been considered. The effectiveness and performance of the NOCTP were both considered high, as very low DMF-S and high percentages of DMF-S = 0 had been achieved by 1999, and 18-year-olds in Nexö had significantly less caries compared to other municipalities. The cost/child/year significantly reduced in the years with the NOCTP compared to that before 1988.

In another study (Axelsson 2006), a needs-related caries preventive program was introduced for all 0-19-year-olds in the county of Varmland, Sweden, in 1979. The goals were set as: not having proximal restorations, occlusal amalgam restorations, and proximal loss of periodontal attachment. Furthermore, motivation and encouragement of individuals to assume responsibility for their own oral health was considered as another goal to be reached. The effect of the program evaluated once every year on almost all 3-19-year-olds from 1979. Most of the individualized preventive program was carried out by dental hygienists or dental assistants at clinics in the elementary schools. During the 20-year period the percentage of 3-year-olds with DMF=0 increased from 51% to 97%. In 1999 as many as 86% of the 12-year-olds diagnosed as being DMF=0. Caries incidence was reduced more than 90% in all age groups. More than 90% did not develop any new caries lesions in 1999. As a consequence, caries prevalence was dramatically reduced. In 12- and 19-year-olds, the mean number of Decayed and Filled Surfaces (DFS) per individual was reduced from 6 to 0.3 and from 23 to 2 respectively. In 19-year-olds the mean number of proximal DFS was <1 and only half of them had to be filled. The mean number of occlusal DFS was less than one.

The above mentioned examples clearly show that preventive programs for the control of dental caries will be successful, if planned and performed based on proper understanding of populations' need and available resources.

Further improvements in oral health and reducing the inequalities in oral health of populations are dependent upon the implementation of public health strategies that give attention to the underlying determinants of oral diseases (Petersen 2003a, Watt 2005, 2007). Despite documented effectiveness of various preventive measures, clinical prevention of oral diseases and health education alone will not result into sustainable improvements in oral health (Watt 2005). Therefore, public health strategies based upon the common risk approach are now suggested for achieving significant oral health gains in both developed and developing countries (Watt 2005). Accordingly, establishment of a comprehensive oral health care system for the control of oral diseases has been set by WHO as a goal to be achieved by the year 2020 (Hobdell et al. 2003).

7.6 Dentists' preventive orientation

7.6.1 Dentists' oral self-care

Due to their professional knowledge of the prevention of oral diseases, dentists hold a key position in providing a positive model of oral self-care for their patients. This highlights the necessity for implementing optimal oral self-care for the dentists themselves. Limited information is, however, available regarding dentists' oral health behavior. In the USA, 73%

of male dentists selected from the basic Health Professionals Follow-Up Study group reported brushing their teeth at least twice daily, and 56%, flossing at least once daily (Merchant et al. 2002). In Mongolia, 81% of dentists reported brushing their teeth twice daily, 62%, using fluoride toothpaste regularly, 52%, eating sugary snacks less than daily, and 75% visiting a dentist for dental check-up (Tseveenjav et al. 2004). Generally, smoking seems to be rare among dentists and it has been reported that they have the lowest smoking rates (from 1% to 23% during years 1979-2005) among all health professionals (Smith and Leggat 2006). Dentists from Jordan (Burgan 2003) and Italy (Lodi et al. 1997) have been found to be exceptions since about one-third of dentists reported to be smokers. In view of the fact that dentists are at the forefront of oral care, it is important that the rate of smoking among dentists even be reduced further.

7.6.2 Dentists' preventive practice

Dentists' clinical decisions influence the oral health (Petersson and Bratthall 1996) and overall health (Dyer and Robinson 2006) of the population. Therefore, dentists are increasingly being expected to apply preventive measures in their routine practice (Pitts 2004). They, however, seem to have underestimated preventive measures and the risk-based approach in their practice (Kawamura et al. 1998, Brennan et al. 1998, Helminen et al. 1999, Varsio et al. 1999).

Due to dentists' knowledge on adverse effects of smoking and their frequent contacts to a wide range of population, their involvement in smoking cessation has been considered as a modern and necessary tool in preventive practice (Warnakulasuriya 2002, Petersen 2003b). Dental professional's advices can effectively motivate smokers to quit smoking (Dolan et al. 1997, Smith et al. 1998, Johnson 2004) even with a brief intervention (Fiore et al. 2000, Warnakulasuriya 2002, Gordon et al. 2005). The great potential benefits of dentists' involvement in smoke cessation for the public health will be more evident when considering that dentists examine a significant number of smokers in each year (Tomar 2001). Dental providers have many opportunities to reduce the prevalence of smoking since dental treatment often necessitates multiple visits that provide a mechanism for initiation, reinforcement, and support of tobacco cessation activities. On the other hand, dental patients (especially those with dental insurance) receive care on a regular basis (Albert et al. 2005). Approximately 50% of smokers have been estimated to visit a dentist annually (Tomar et al. 1996, Tomar 2001), which gives the dental professional the opportunity to associate cessation advice with readily visible changes in oral status. Therefore, the dental office may be ideally suited to help patients quit smoking. Dentists, accordingly, seem to recognize smoking cessation as an important part of their duties and are becoming more concerned in this area of preventive practice (Johnson et al. 2006), although limitations have been reported in dentists' involvement in smoke cessation due to barriers such as lack of training and time constraint (Hu et al. 2006), perceived lack of relevance of smoking cessation to dentistry, patients' not acceptance, and lack of remuneration (Watt et al. 2004).

7.6.3 Dentists' restorative treatment threshold

One of the most important aspects of dentists' practice is their decision as when to treat a caries lesion restoratively. Dentists' restorative threshold can be defined as the point at which they would begin drilling a carious lesion for placement of a restoration. In spite of the progress in understanding the caries process, there is still uncertainty among members of the dental community on clear definition of dental caries (Ismail 2004). During most of

the 20th century, dental caries was detected and managed as if the caries process is equal to 'cavities' and accordingly the practice of dentistry has traditionally focused on developing 'drill and fill' interventions (Ismail 2004). Nevertheless, detecting the early or non-cavitated caries level and preventing these lesions from progressing to the cavitated stage (or being restored) could have a significant impact on the oral health status around the world and certainly also on the costs of treatment (Mjör et al. 2000, Ismail 2004). Making the first restoration leads to an irreversible cycle of subsequent restorations (Elderton 1990, Mjör and Toffentti 2000, Deligeorgi et al. 2001) which may finally result in tooth removal (Mjör et al. 2000). It has been recognized that caries lesions progress at slower rates than previously believed (Pitts 1983, Shwartz et al. 1984, Mejár et al. 1999, Lith et al. 2002) and that caries can be arrested and the affected dental structure remineralized (Elderton and Osman 1991, Verdonschot et al. 1999) so a large proportion of the "iceberg of dental caries" (Pitts and Longbottom 1995) is subject to preventive care (Pitts 2004b). Therefore, dentist's restorative decision making should take into account current knowledge on progression and arresting of caries lesions (Anusavice 1995).

7.6.4 Barriers against providing preventive dental care

The introduction of preventive approach into real practices, however, seems to be challenging since it has not been applied in situations with scientifically approved effectiveness (Horowitz 1995). Furthermore, dentistry as a profession has been recognized to be a technically oriented discipline, dental practice generally follows market principles (Fejerskov and Kidd 2003), and dentists seem to prefer restorative approach (Elderton 1993, Helminen and Vehkalahti 2003). To apply preventive measures in dental care some numerous barriers must be tackled which are categorized as practice-, dentist-, and patient-related barriers (Cohen 1987, Horowitz 1995, Freeman 1999a, 1999b, 1999c).

7.6.5 Dentists' knowledge of and attitudes towards preventive dental care

The major challenges for the future of peoples' oral health will be to translate knowledge and experiences of disease prevention into action programs (Petersen 2003a). Understanding of dental caries initiation and progression has been improved in recent years, which necessitates development of new treatment strategies (Ismail et al. 2001, Featherstone 2004, Fejerskov 2004). Dental professionals are expected to update their practices according to the evidence-based knowledge which emphasize continuous changes in dentists' education (McGlone et al. 2001, Widström 2004). In this process, the central elements to be improved are dentists' preventive knowledge and attitude which acts as a framework for their practice (Brown et al. 2002) and are factors affecting their patients' oral health-related behaviour (Eijkman and de With 1980). Previous studies on dentists' knowledge of and attitudes towards preventive dental care are controversial. Dentists, generally, seem to be knowledgeable in preventive matters (Gonzalez et al. 1988) and have positive attitudes towards prevention (Allard 2000, Kujan et al. 2006); deficiencies in their knowledge, however, have been revealed (Eijkman and de With 1980, Lewis and Main 1996, Moon et al. 1998).

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Inequality of Oral Health in a Life-Course Perspective

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[2]*The Netherlands*

1. Introduction

Viewing health and disease in a life-course perspective has gained scientific interest recently (Kuh & Ben-Shlomo, 1997). Panel studies are scarce but other designs come close to being able to follow health and disease through life (Kuh & Ben-Shlomo, 1997). There are three major perspectives in life-course research: One line emphasizes the importance of life-style and deprivation in childhood for adult chronic disease. This research investigates environmental conditions and experiences through prenatal life, infancy, childhood and adolescence that may make individuals more susceptible to developing adult chronic disease. Pearce et al., 2004 studied the effect of birth-weight, early diet, use of comforter and social status on oral health of young adults, but found only effect of social status in the expected direction. Nicolau and co-workers found a relationship between several biological factors and caries among adolescents (Nicolau et al., 2003, 2007). A second line of research assumes biological programming during critical periods of development either during pregnancy or in early life (Barker, 1994). A third line of research suggests an accumulation of risk through the life course. Accumulation of risk is different from programming in that it does not require the notion of a critical period. This approach explicitly places more emphasis on a greater range of biological and social experiences in childhood, adolescence and in early adulthood than either the life style or programming models. There are reasons to believe that adult oral health is affected through a range of life-course mechanisms. The present work leans on the third perspective arguing that oral health is continuously exposed to environmental and behavioral risks that lead to accumulated plaque in the mouth and diseases in the dental tissues (Fejerskov & Kidd, 2008).

On a population basis the vast majority of children are born with a good oral health. Exposure to different life-styles and nutrional and hygienic conditions appears as a threat to oral health through life (Holst & al., 2007). The global picture of oral health is patterned by variation in living conditions and variation in life-course patterns of oral health (Petersen et al., 2006).

A number of studies have described oral health of populations in repeated cross-sectional studies (Schuller & Holst, 1998, Kelly et al., 2000; Skudutyte-Rysstad &Eriksen 2007, Krustrup et al., 2008). These studies provide valuable information about background related changes in oral health conditions at certain points of time. It has for example been shown

that edentulousness has a much lower incidence now than 30 years ago (Petersen et al., 2004; Holst, 2008). The main explanations for this are improved standard of living, availability of fluoride toothpaste and more accessible dental services. Despite the improvement, social status still affects oral health even though recent research indicates that this relationship has become weaker in some countries (Holst, 2008). There is reason to believe that avoiding edentulousness and maintaining oral health requires a life-long attention to healthy diet, oral health promotion, oral hygiene and preventive dental services.

In this chapter the influence of social status on clinical aspects of oral health is assessed from childhood through adolescence to adulthood in the same birth-cohorts in Norway. This unique possibility was made possible through a careful design of a series of cross-sectional studies in the counties of Trøndelag in Norway (Schuller &Holst, 1998). On a population basis the vast majority of children are born with a good oral health. Exposure to different life-styles and nutrional and hygienic conditions forms a threat to oral health through life (Holst & al., 2007). The global picture of oral health is patterned by variation in living conditions and variation in life-course patterns of oral health (Petersen et al., 2006).

A number of studies have described oral health of populations in repeated cross-sectional studies (Schuller & Holst, 1998, Kelly et al., 2000; Skudutyte-Rysstad &Eriksen 2007, Krustrup et al., 2008). These studies provide valuable information about background related changes in oral health conditions at certain points of time. It has for example been shown that edentulousness has a much lower incidence now than 30 years ago (Petersen et al., 2004; Holst, 2008). The main explanations for this are improved standard of living, availability of fluoride toothpaste and more accessible dental services. Despite the improvement, social status still affects oral health even though recent research indicates that this relationship has become weaker in some countries (Holst, 2008). There is reason to believe that avoiding edentulousness and maintaining oral health requires a life-long attention to healthy diet, oral health promotion, oral hygiene and preventive dental services.

2. Material and methods

The material comprised data from independent random samples of three birth-cohorts living in the counties of Sør- and Nord-Trøndelag in 1983. The birth-cohorts were 1929-1938, 1939-1948 and 1959-1960, and they were 45-54-, 34-44 and 23-24-years old in 1983 (Table 1, sample a). I 2006 two samples were drawn from the 1929-1938 and 1959-1960 birth-cohorts in Nord-Trøndelag only, who were then 67-78-year-old and 46-47-year old (Table 1). The age specific sample size for each of the participating counties were 500 in 1983 and was reduced to 250 in 2006. The sample in the two-year age-group 46-47 was 100 persons.

The methods of data collection comprised standardized clinical measurements and self-administered questionnaires (Bærum et al., 1985; Schuller and Holst, 1998). In 1983 and in 2006 ten and two calibrated dental teams, respectively, collected the data. Two senior researchers (DH and AAS) followed and guided the procedures in order to secure standardized conditions and comparability among the surveys. The first Trøndelag study in 1973 started as part of the first WHO International Collaborative Study survey (Arnljot et al.,

1985). The study was also repeated in 1994 but not reported here. Calibration exercises were conducted each study year. Calibration was performed for paired examiners and intra-examiner variability was high for the DMF index (r>0.92). Inter-examiner agreement was exercised until r> 0.85 between all pairs, and the results otherwise found satisfactory (Bærum et al., 1985; Holst et al., 2007). The examinations took place at the public dental clinics of the South- and Nord-Trøndelag counties. Permission was granted by public authorities and by the participants' informed consent. All necessary permissions were given throughout the study period and by the participants' informed consent. In 2006 the study was approved by the Regional ethical committee Middle of Norway and approved by the Norwegian Council of Research.

		1983 a		1983 b		2006	
Birth-cohort	Age	n	%	n	%	n	%
1959-1960	23-24	1000	84	500	81		
	46-47					100	90
1929-1938	35-44	1000	82	500	80		
	45-54	1000	74	500	72	350	71
	68-77					250	61

1983 a : The sample includes Nord- and Sør-Trøndelag
1983 b: The sample includes Nord-Trøndelag

Table 1. Trøndelagsstudies. Samples in 1983 and 2006 according to birth-cohort and age. Participation in percent

In the present study the outcome variables were number of sound teeth and toothsurfaces (ST, SS) and sound + filled teeth and toothsurfaces (SFT, SFS) and DMFT and DMFS index. DMFT and DMFS are the sums of DT/S, MT/S and FT/S, where DT/S is defined as the number of teeth/toothsurfaces with primary and secondary caries, including root and coronal caries. Only caries with a distinguishable break in the surface was recorded. Missing surfaces is the number of missing tooth surfaces irrespective of cause. FS is the number of surfaces filled, both root and coronal restorations, including all types of filling materials and crowns. The clinical examination comprised recording of the condition of the visible part of the tooth. The analyses were based on 28 teeth excluding third molars.
As part of the study in 1983 twelve questions were asked about social and dental conditions when the sampled persons were ten years old. Social status was measured in two ways: By father's and mother's number of natural teeth in three categories: Many own teeth (2), some own teeth (1) and no own teeth (0). The variables were summed and dummy variables constructed (Table 2, column 4). Eleven other questions were asked about oral health environment at age 10 (Table 2). The questions comprised whether the families had rules for eating sweets, tooth brushing habits, advice about oral health from teachers, school nurse/medical doctor and school dentist, fathers and mothers dental status, visits to a dentist during preschool and school age, parents control of tooth brushing, use of toothpicks

and dental floss. Advice from teachers, school nurse/medical doctor and school dentist were collapsed into an index called advice about oral health (Table 2, column 3). Visits to a dentist during pre-school and school age were summarized to yearly and not yearly. The questions comprising whether the families had rules for eating sweets, tooth brushing habits were combined into parents attention and dummy variables constructed. Sex was included in the meaning of a social construct assuming females to be more engaged in health and oral health behaviors.

Social status in early adulthood was measured as number of years with formal education. Length of education was divided into four quartiles each comprising 25 % of the samples. The first quartile comprised the 25 per cent of the sample with the shortest education, the second quartile the 25 per cent of the sample with the second shortest education, the third quartile the 25 per cent with the second longest education and the fourth quartile comprised the 25 per cent of the sample with the longest education. The quartiles thus represent the distribution of length of education in equally sized groups. Using quartiles eliminates the problem often faced with measuring length of education that the length of education the population changes over time. Length of education was transformed into dummy variables (Table 2, column 4). Four question of oral hygiene practices (1983) were added into oral health behavior index and dummy variables constructed.

Variables	Categories and coding	Additive indices	Analytical categories/dummy variables
Rules for sweet consumption	Yes (1) no (0)		
Toothbrushing habits	Twice a day (1) Once or less (0)		
Advice from teacher	Yes (1) no (0)	**Advice about oral health**	
Advice from doctor/nurse	Yes (1) no (0)	Advice (1-3)	Advice (1)
Advice from school /district dentist	Yes (1) no (0)	No advice (0+0+0)	No advice (0)
Father's dental status	Many teeth (2), few (1) none (0)	**Parents' dental status**	
Mother's dental status	Many teeth (2), few (1) none (0)	Many (4)	Dummy parents' dental status many
		Few (1-3)	Dummy parents'dental status few
		None (0)	Reference category
Visited a dentist pre school	Yearly (2) a few times (1) never (0)	**Dental care at age 10**	
Visited a dentist during school	Yearly (2) a few timel (1) never (0)	Yearly (4)	Yearly (1), Not yearly (0)
		A few times (1-3)	
		Never (0)	
Parents controlled toothbrushing	Often/daily (2) a few times (1) never (0)	**Parents' attention**	
Used toothpicks	Often/daily (2) a few times (1) never (0)	Daily (5-6)	Dummy parents attention daily
Used dental floss	Often daily/ (2) a few times (1) never (0)	A few times (1-3)	Dummy parents attention a few times
		Never (0)	Reference category
Gender	Female (1) Male (0)		
Length of education	Highest quartile (3)		Dummy highest quartile
	Second highest quartile (2)		Dummy second highest quartile
	Second lowest quartile (1)		Dummy second lowest quartile
	Lowest quartile (0)		Reference category
Regular dental visits last three years	Regular each year (1)irregular (0)		
Brushed yesterday	Yes (1) No (0)	**Oral health behaviour**	
Used dental floss yesterday	Yes (1) No (0)	Good (4)	Dummy oral behaviour good
Used toothpicks yesterday	Yes (1) No (0)	Middle (2-3)	Dummy oral behaviour middle
Had sweets yesterday	Yes (1) No (0)	Bad (0-1)	Reference category

Table 2. Variables, categories, indices and analytical categories

2.1 Analysis

In the first part of the analysis social status together with the early oral health environment and sex were related to oral health variables in 1983 by multiple regressions. Since all the dependent variables were measured on the same scale (tooth surfaces, range 1-128), the regression coefficients can be interpreted directly as effects of the independent variables in number of surfaces. For the second part of the analysis the data files from 1983 and 2006 were combined to one data file in order to study whether the impact of social status changed during this period. Multiple regression analysis was used, and the level of significance was p= 0.05. Associations nearly reaching significance (0.07>p>0.05) are shown.

3. Results

The distribution of the independent variables according to age-groups is shown in Table 3. The table provides a picture of how the oral health environment at age ten years varied between the birth-cohorts. The youngest birth-cohort had the best level of oral health environment.

	Age in 1983		
	23-24 year	35-44 year	45-54 year
Oral health environment at age 10			
Had rules for sweet consumption	29.4	20.4	14.4
Toothbrushing twice per day	73.0	64.0	59.4
Got advice about oral health	98.2	70.1	53.8
Parents' many teeth	72.4	47.0	47.4
Dental care yearly	19.3	6.1	3.7
Parents' attention high	34.2	12.4	6.8
Behaviour in 1983			
Regular dental visits	65.8	69.4	63.7
Oral health behaviour good	23.8	15.2	11.0

Table 3. Descriptive statistics for independent variables in 1983. Sample a. Percentage

Table 4 shows the means and standard deviations of the clinical variables. The table provides a clear picture of the variation between the age-groups in the condition of the tooth surfaces. The table also shows how different clinical indicators show very different results. The number of sound tooth-surfaces is absolutely highest in the youngest age group and the number of DMFS and MS highest in the oldest age-group.

Tables 5-7 show how the early oral health environment, the social variables and the oral health behaviours each and combined (R^2) affected oral health in the age-groups in 1983.

			SS		DS		FS		MS		DMFS	
	Age-group	n	Mean	sd	Mean	sd	Mean	sd	Mean	sd	Mean	sd
	23-24	773	84.10	17.41	1.09	2.52	37.89	16.05	4.89	7.34	43.89	17.36
1983*	35-44	773	48.54	21.51	2.25	6.23	48.64	22.86	28.55	30.77	79.45	21.51
	45-54	675	35.11	24.24	2.19	5.38	37.02	27.3	53.66	42.51	92.88	24.24
2006	46-47	96	79.08	21.02	0.80	1.9	38.59	16.73	5.38	7.2	44.77	18.83
	68-77	150	33.02	22.02	1.61	3.31	39.53	25.71	44.16	36.53	85.29	20.17

* Sample a

Table 4. Dental variables in 1883 and 2006. Mean and standard deviation (sd) (basis 124 tooth surfaces, 28 teeth)

3.1 Birth-cohort 1959-1960, 23-24 years in 1983

Table 5 shows the impact of the independent variables on the outcome variables. Having positive oral health behaviors at age ten increased the likelihood of more sound surfaces (SS), more filled surfaces (FS) and more surfaces with caries experience (DMFS) at age 23-24. If parents had many own teeth the 23-24-years-olds had 5.0 more sound surfaces (SS) and 5.0 less surfaces with caries experience (DMFS). Length of education was statistically significantly related to the D-M-F-S variables in the expected direction. Regular dental care was related to mean number of surfaces with untreated decay (DS). Good oral health behavior was statistically significant related to more sound surfaces (SS) and less filled surfaces (FS). The variables in the model explained from 4 -13 % of the variation in the dependent variables.

3.2 Birth-cohort 1939-1948, 35-44 years in 1983

Table 6 shows that parents' dental status and yearly dental visits at age ten had a statistically significant impact on several of the oral health variables. Having parents with many of their own teeth at age ten the 35-44 year olds had more functional surfaces (SFS), less missing surfaces (MS) and surfaces with caries experience (DMFS). Women had less sound surfaces (SS) and more filled surfaces (FS) and DMFS than men when they were 35-44-years-old in 1983. The longer the education, the better the values of the oral health indicators were; the differences between the quartiles of education were big. Dental care last year had a statistical significant influence on DS, SFS, MS and FS. The explained variation varied from 11 – 27 %.

3.3 Birth-cohort 1929-1938, 45-54 years in 1983

Table 7 shows that parents' dental status at age ten years had a statistically significant effect on the oral health variables. In addition tooth brushing and dental care at age 10 had a significant effect on untreated caries (DS). Women had more sound surfaces (SS), less untreated decay (DS), and more filled (FS) and DMFS than men had. Length of education had a significant effect on all oral health variables except untreated caries (DS). Oral health behavior had a similar effect, while regular dental care also affected untreated caries (DS).

Variables	Oral health					Untreated disease					Treated disease				
	SS		SFS			DS		FS			MS		DMFS		
	Coefficient	se	Coefficient		se	Coefficient	se	Coefficient		se	Coefficient	se	Coefficient		se
Intercept	76.13	4.62	118.92		2.11	4.07	0.66	42.79		4.33	4.99	1.95	51.87		4.62
At age 10															
Rules for sweet consumption	2.42	1.53	0.60		0.7	-0.19	0.22	-1.82		1.43	-0.79	0.64	-2.42		1.53
Toothbrushing habits	4.39	* 1.78	-0.71		0.81	0.21	0.25	3.68	*	1.67	0.50	0.75	4.39	*	1.78
Advice about oral health	-0.33	3.69	-1.57		1.68	-0.43	0.52	-1.24		3.46	2.00	1.56	0.33		3.69
Parents dental status few teeth	-0.56	2.77	1.21		1.27	0.03	0.39	1.77		2.60	-1.24	1.17	0.56		2.77
Parents dental status many teeth	5.04	* 2.51	2.14	^	1.15	-0.39	0.36	-2.91		2.35	-1.75	1.06	-5.04	*	2.51
Dental care at age 10	-2.09	1.59	-0.16		0.72	-1.41	0.22	1.93		1.48	0.30	0.67	2.09		1.59
Parents' attention a few times	-1.29	1.62	-0.16		0.74	-0.34	0.23	1.13		1.52	0.50	0.69	1.29		1.62
Parents' attention daily	-0.37	1.96	-0.22		0.9	-0.31	0.28	0.15		1.85	0.53	0.84	0.37		1.98
Early adult age															
Gender	0.06	1.37	-0.56		0.62	-0.57	* 0.19	-6.26		1.28	1.13	* 0.58	-0.06		1.37
Education-second lowest quartile	3.65	* 1.71	2.33	*	0.78	-0.92	* 0.24	-1.32		1.60	-1.41	* 0.72	-3.65	*	1.71
Education-second highest quartile	3.96	* 1.82	1.91	*	0.83	-0.98	* 0.26	-2.05		1.70	-0.93	0.77	-3.96	*	1.82
Education- second highest quartile	8.84	* 1.86	4.04	*	0.85	-1.28	* 0.26	-4.80	*	1.74	-2.76	* 0.78	-8.84		1.86
Last year															
Regular dental care	-1.03	1.33	0.54		0.61	-1.05	* 0.19	1.58		1.24	0.50	0.56	1.03		1.33
Oral health behaviour middle	5.14	* 2.13	1.08		0.97	-0.58	* 0.30	-4.06	*	2.00	-0.50	0.90	-5.14	*	2.13
Oral health behaviour- good	5.77	* 2.44	1.36		0.12	-0.45	0.35	-4.39	*	2.29	-0.93	1.03	-5.77	*	2.44
R^2	0.07		0.05			0.13		0.04			0.04		0.07		
			^p=0.063												

* = p< 0.05
^ =0.05< p< 0.07

Table 5. Relationship between DMFS and life-course variables and indices. Multiple regression. Birth-cohort 1959-60 in 1983

Variables	Oral health				Untreated disease				Treated disease				DMFS	
	SS		SFS		DS		FS		MS					
	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se
Intercept	37.86	2.77	58.28	3.77	7.52	0.81	24.14	2.61	62.96	3.70	90.14	2.77		
At age 10														
Rules for sweet consumption	0.45	2.35	-1.87	3.20	-0.07	0.67	-1.83	2.16	2.01	3.14	-4.53	2.35		
Toothbrushing habits	-0.38	2.08	-3.57	2.84	-0.61	0.60	-2.94	1.93	4.26	2.79	0.38	2.08		
Advice about oral health	1.84	1.66	-0.38	2.26	-0.08	0.47	-2.15	1.53	0.40	2.22	-1.84	1.66		
Parents dental status few teeth	-0.12	2.14	2.59	2.92	1.28 *	0.61	1.84	1.98	-3.99	2.86	0.12	2.14		
Parents dental status many teeth	3.94 *	2.05	6.25 *	2.80	0.63	0.59	1.65	1.89	-6.97 *	2.74	-3.94 *	2.05		
Dental care at age 10	-7.60 *	3.32	-1.06	4.53	0.87	0.93	5.58 ^	3.01	0.07	4.44	7.60 *	3.32		
Parents' attention a few times	-0.59	1.89	2.11	2.58	-0.03	0.54	2.93	1.74	-1.96	2.53	0.59	1.89		
Parents' attention daily	0.21	3.23	1.26	4.40	-0.06	0.92	0.77	2.97	-1.17	4.31	-0.21	3.23		
Early adult age														
Gender	-7.23 *	1.66	-1.06	2.26	-0.79	0.47	6.31 *	1.52	1.87	2.21	7.23 *	1.66		
Education-second lowest quartile	5.49 *	2.06	10.95 *	2.82	-1.06	0.59	4.78 *	1.91	-10.07 *	2.76	-5.49 *	2.06		
Education-second highest quartile	6.78 *	2.14	20.97 *	2.92	-1.65 *	0.61	13.04 *	1.97	-19.54 *	2.86	-6.78 *	2.14		
Education- second highest quartile	11.98 *	2.26	27.80 *	3.08	-1.55 *	0.64	14.60 *	2.07	-26.50 *	3.02	-11.98 *	2.26		
Last year														
Regular dental care	2.58	1.74	17.38 *	2.38	-4.73 *	0.50	12.97 *	1.62	-13.09 *	2.33	-2.58	1.75		
Oral health behaviour middle	6.43 *	2.28	14.05 *	3.11	-0.65	0.66	6.88 *	2.13	-13.60 *	3.05	-6.43 *	2.28		
Oral health behaviour good	3.15	2.86	15.72 *	3.90	-1.11	0.83	12.56 *	2.66	-14.76 *	3.83	-3.15	2.86		
R^2	0.11		0.26		0.17		0.27		0.22		0.11			
							^p=0.064							

* = p< 0.05
^ =0.05< p< 0.07

Table 6. Relationship between DMFS and life-course variables and indices. Multiple regression. Birth-cohort 1939-1948 in 1983

Table 7. Relationship between DMFS-and life-course variables and indices. Multiple regression. Birth-cohort 1929-38 in 1983

Variables	Oral health				Untreated disease		Treated disease					
	SS		SFS		DS		FS		MS		DMFS	
	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se
Intercept	18.46	2.70	17.95	3.99	8.19	0.82	6.61	2.82	104.70	4.03	109.54	2.70
At age 10												
Rules for sweet consumption	-4.20	2.85	-7.65 ^	4.20	1.35	0.79	-1.68	2.72	6.80	4.24	4.20	2.85
Toothbrushing habits	-0.01	2.26	2.41	3.34	-1.51 *	0.65	3.51	2.25	-1.09	3.37	0.01	2.26
Advice about oral health	0.47	1.73	0.91	2.55	-0.30	0.48	0.89	1.65	-6.86	2.57	-0.47	1.73
Parents dental status few teeth	3.45	2.29	5.15	3.38	-0.78	0.65	0.69	2.25	-4.75	3.42	-3.45	2.29
Parents dental status many teeth	5.86 *	2.26	8.53 *	3.34	-0.79	0.64	1.65	2.22	-8.13 *	3.37	-5.86 *	2.26
Dental care at age 10	-7.91	3.59	1.45	5.29	2.06 *	0.94	1.30	3.24	-3.56	5.34	0.79	3.59
Parents' attention a few times	-0.02	2.06	1.94	3.04	0.69	0.56	1.68	1.95	-2.62	3.07	0.02	2.06
Parents' attention daily	0.76	3.78	6.12	5.57	-0.02	1.03	3.95	3.54	-6.47	5.63	-0.76	3.78
Early adult age												
Gender	-8.24 *	1.86	-3.47	2.74	-1.27 *	0.52	7.39 *	1.80	5.50 ^	2.76	8.24 *	1.86
Education-second lowest quartile	3.65	2.23	8.35 *	3.29	-0.76	0.64	5.11 *	2.22	-7.64 *	3.32	-3.65	2.23
Education-second highest quartile	4.68 ^	2.58	19.27 *	3.81	-0.52	0.73	17.50 *	2.51	-18.81 *	3.84	-4.68 ^	2.58
Education- second highest quartile	13.36 *	2.48	32.93 *	3.66	-0.93	0.67	18.53 *	2.32	-32.32 *	3.69	-13.36 *	2.48
Last year												
Regular dental care	10.17 *	1.88	36.16 *	2.78	-3.23 *	0.56	19.92 *	1.92	-34.66 *	2.81	-10.17 *	1.88
Oral health behaviour middle	8.58 *	2.32	15.52 *	3.42	-0.94	0.67	4.45 *	2.32	-15.47 *	3.45	-8.58 *	2.32
Oral health behaviour good	9.10 *	3.16	16.56 *	4.65	-0.46	0.90	4.70	3.09	-16.83 *	4.70	-9.10 *	3.12
R^2	0.191 ^p=0.070		0.434 ^p=0.069		0.135		0.388		0.415 ^p=0.070		0.191 ^p=0.070	

* = p< 0.05
^ =0.05< p< 0.07

3.4 The influence of social status from 1983 to 2006

For this part of the analysis data files from 1983 and 2006 were combined into one datafile. An interaction term between social status measured as length of education and study year was included in order to see if the effect of length of education was important both years or only one of the years.

3.4.1 Birth-cohort 1959-60, age 23-24 and 46-47 in the combined file

Table 8 shows that the interaction between length of education and study year was not significant with the exception of the effect on sound surfaces, where the persons in the second lowest education group had kept nearly 15 more sound surfaces than the lowest group. Gender and regular dental care had an independent effect on mean number of sound surfaces (DS). Oral health behavior had a significant effect on oral health variables.

3.4.2 Birth-cohort 1929-38, age 45-54 and 68-77 in the combined file

Table 9 shows that the effect of social status mesasured as length of education was not dependent upon which year it was measured except that the persons in the second highest education quartile on average had more surfaces with untreated decay compared with persons in the lowest quartile. In this birth-cohort gender and particularly regular dental care had an effect on several of the outcome variables. Functional surfaces increased by nearly 34 surfaces among persons with visits to the dentist compared to those without. Likewise the average number of FS and MS were much higher and lower, respectively, among those with regular dental care.

4. Discussion

This study has shown that social staus and oral health environment in childhood was important for adults' oral health during the most of the 20. century. The attention from parents and the local environment lead to a better oral health outcome in adulthood. Social status measured by length of education was also a personal resource that guided choices leading to better oral health. The longer the education the better the oral health was. Regular dental visits were important especially for the eldest birth-cohort. Good oral health behaviors early and during adulthood were also important for oral health. Effects of more than 30 surfaces were found on indicators like missing and functional tooth surfaces. When the birth-cohorts were followed from 1983 to 2006 social status had an effect in both 1983 and 2006. Judged by the number of tooth surfaces the difference between social status groups had not increased by 2006. The latter observation deserves a critical comment. The cumulative DMFS measure is sensitive to increased levels of risk factors in the sense that more surfaces can be affected, until saturation is reached. When lower risk levels occur, the DMFS figures cannot decline within the same birth-cohort. The Missing, Filled and Sound indicators (the DMF index) cannot reverse. Only the number of decayed surfaces can reverse (Holst and Schuller, 2000). In the present study the average number of decayed tooth-surfaces was significantly reduced and indicated a lower level of recent risk (Holst et al., 2007). This is a serious limitation. With regard to estimating the influence of social status and other explanatory variables, a reduced effect can thus not be shown, and it can only be concluded that the effect of social status did not increase from 1983 to 2006. In a cohort analysis of the relationship between social status and average number of DMFT in 35-44-

Variables	Oral health				Untreated disease				Treated disease					
	SS		SFS		DS		FS		MS		DMFS			
	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se		
Intercept	73.24	2.97	117.84	1.42	4.47	0.42	44.37	2.68	5.92	1.23	54.76	2.86		
Gender	0.36	1.81	-1.23	0.89	-0.68 *	0.26	-1.09	1.63	1.47 ^	0.75	-0.30	1.74		
Regular dental care	-0.61	2.05	-2.24	0.96	-0.74 *	0.29	0.14	1.85	1.01	0.85	0.41	1.97		
Education-second lowest quartile	5.09	2.79	3.16 *	1.30	-1.73 *	0.40	-1.97	2.52	-1.42	1.16	-5.11 ^	2.69		
Education-second highest quartile	1.06	3.00	2.65 ^	1.39	-1.54 *	0.43	1.49	2.71	-1.03	1.25	-1.08	2.89		
Education-highest quartile	11.84 *	2.95	6.40 *	1.37	-2.08 *	0.42	-5.64 *	2.67	-4.21 *	1.22	-11.93 *	2.84		
Oral behaviour middle	5.88 *	2.45	0.91	1.23	-1.12 *	0.35	-4.91 *	2.22	0.12	1.02	-5.91 *	2.36		
Oral behaviour good	6.74 *	2.81	1.22	1.42	-1.30 *	0.40	-4.67 ^	2.54	-0.13	1.17	-6.09 *	2.71		
Year	3.57	4.55	-3.35	2.55	-1.11	0.65	-2.26	4.11	-1.69	1.89	-5.06	4.38		
Interact. Year/second lowest q.	-14.55 *	5.84	-2.55	3.30	1.08	0.83	7.43	5.28	1.66	2.43	10.16	5.63		
Interact. Year/second highest q.	-1.47	6.20	-2.54	3.88	0.22	0.88	-2.57	5.60	-0.91	2.57	3.26	5.97		
Interact. Year/ highest q.	-1.10	6.68	-3.71	3.78	0.66	0.95	-3.40	6.03	3.96	2.77	1.18	6.43		
R^2	0.11		0.12		0.16		0.06		0.05		0.10			
			^p=0.058				^p=0.067		^p=0.051		^p=0.058			

* = p< 0.05
^ =0.05< p< 0.07

Table 8. Relationship between DMFS variables and independent variables. Combined datafile 1983 and 2006. Birth-cohort 1959-1960

Variables	Oral health				Untreated disease				Treated disease					
	SS		SFS		DS		FS		MS		DMFS			
	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se	Coefficient	se		
Intercept	20.45	2.96	23.64	4.42	5.20	0.71	0.02	2.77	101.94	4.28	107.16	2.93		
Gender	-4.31 ^	2.20	1.57	3.30	-1.23 *	0.53	6.03 *	2.06	-5.54	3.18	4.25 ^	2.18		
Regular dental care	12.02 *	2.63	33.84 *	4.05	-1.29 *	0.63	25.55 *	2.46	-35.61 *	3.79	-11.35 *	2.60		
Education-second lowest quartile	1.38	3.30	6.57	4.80	-1.06	0.79	4.79	3.08	-5.17	4.76	-1.44	3.26		
Education-second highest quartile	6.08	3.80	22.72 *	5.54	-1.10	0.91	15.64 *	3.55	-20.72 *	5.49	-6.17	3.76		
Education-highest quartile	10.50 *	4.08	33.98 *	5.98	-9.63	0.98	21.38 *	3.82	-31.21 *	5.89	-10.79 *	4.04		
Oral behaviour middle	6.99 *	2.63	14.31 *	3.96	-0.64	0.63	9.31 *	2.46	-15.42 *	3.79	-6.75 *	2.60		
Oral behaviour good	0.87	3.28	6.98	4.98	-0.63	0.79	8.52 *	3.06	-9.26 ^	4.73	-1.37	3.24		
Year	-6.42	3.87	9.27	6.47	-2.14 *	0.93	2.65	3.62	-6.99	5.59	-6.49	3.83		
Interact. Year/second lowest q.	7.32	5.58	3.03	8.79	1.25	1.34	2.67	5.22	-8.57	8.06	-4.65	5.52		
Interact. Year/second highest q.	5.78	6.29	-12.92	9.58	3.65 *	1.51	-6.91	5.88	3.69	9.08	0.43	6.23		
Interact. Year/ highest q.	9.56	6.79	-12.23	10.63	2.02	1.63	-10.29	6.35	6.83	9.81	-1.44	6.72		
R^2	0.16		0.36		0.06		0.43		0.39		0.17			
	^p=0.050								^p=0.051		^p=0.052			

* = p< 0.05
^ =0.05< p< 0.07

Table 9. Relationship between DMFS- and independent variables. Combined datafiles 1983 and 2006. Birth-cohort 1929-1938

year-olds in 1983 and a new cohort of 35-44-year-olds in 2006 from the same material, the relationship between social status and number of present teeth had disappeared in 2006, and the relationship between social status and average number of DMFT and DMFS was significantly reduced (Holst et al., 2007). This shows that the DMF index can be used in cross-sectional research comparing birth-cohorts of the same age; the index has serious limitations in semi-longitudinal research.

It is important to draw attention to the different dimensions that the chosen oral health indicators reflect. The indicators SS and SFS reflect oral health and function and high and increasing values represent positive expressions of oral health. MF and FS are negative expressions of oral health and high and increasing values show reduced oral health. These treatment indicators have limitations since they do not include repeated treatment in the same teeth. DMFS (or DMFT) are a summarized expression of untreated and treated disease, and the values may be difficult to interpret because the indicators of the index move in contrasting directions over time. It is important that that researchers in oral epidemiology engage in finding new ways measures of disease activity that are different from measures of treatment activity.

There are a number of threats to reliability and validity of the data when surveys are repeated and the same variables are used over time, and different birth-cohorts are exposed to the same procedures. Concepts of behavioral norms and interpretation of clinical symptoms change, and treatment criteria change (Gimmestad& Holst, 2003). Most of the questions in the present surveys, however, were about factual events and clear to the respondents; some memory bias among the respondents with regard to events at age 10 years should be expected. These are measurement errors that increase the variance of the variables and reduce the discriminative ability of the statistical tests. Even though of one of the authors (DH) was present at all the surveys and has acted as the golden standard, it is difficult to avoid flow in the translation of the standardized criteria.

The results from the present study have a limited statistical inference with regard to the size of the population the results may be generalized to. On the other hand when it comes to modeling social processes generalization is based on how validly the model catches the specific underlying social processes. It was not the intention to explain all the variation in the dependent variables. It is interesting to notice that R^2 was high in the oldest cohort. It cannot be settled whether this is a cohort or an age effect. Probably it is both, assuming that age reflects the cumulative exposure to plaque during the life-course, and the later born birth-cohorts have experienced a different environment that will result in a better oral health. There are reasons to believe that our data and the model have caught some of those social processes that were important for oral health and its development over time. Other and nationally representative Norwegian data support the finding of a more equally distributed oral health (Holst et al., 2007; Skudutyte and Eriksen, 2007, Holst & Skau, 2010). The Trøndelag studies started at a time where data on oral health and its determinants were scarce. In hind-sight these studies have provided opportunities for valuable descriptions and explanations of the changes in oral health.

The Norway is considered to have had a homogeneous population compared to many other countries (Krokstad & Westin, 2004). Yet, the demography, the size of the country and the arctic location has resulted in cultural and distributional differences. Living conditions and social disparities have to a large extent affected oral health of the population previously in Norway (Arnljot et al., 1985). During the last decade larger income differences have been

observed that might have lead to increased social inequalities in both oral health and demand for dental services (Krokstad 2004). That seems not to have occurred. Cross-sectional data will typically focus on cross-sectional social differences and discuss these with limited insight over time. Often will the lead time between exposure and result be overlooked. Panel data and data with the present analytical potential can detect whether or not a social problem is increasing or decreasing. It cannot be ignored that the results of this study can be ascribed to welfare policies across a number of living conditions in Norway. The public dental service with a population responsibility and out-reach services in this country is an example of one such public policy that have contributed to increasing public awareness of oral health as a value. A high level of public awareness may be expected to influence both the promotion of oral health and accessible adequate dental care. A life-course perspective provides an opportunity understand oral health over time. The present work supports the assumption that oral health is continuously exposed to environmental and behavioral risks that affect life-time oral health.

5. Conclusion

The purpose of the work was to study the influence of 1) the oral health environment at age 10, 2) of adolescent and adulthood dental behaviors and of 3) social status on oral health in three birth-cohorts later in life (1983) and in 2006 in Norway.

The material comprised data from random samples of three birth-cohorts living in the counties of Sør- and Nord-Trøndelag in 1983. The birth-cohorts were 1929-1938, 1939-1948 and 1959-1960. In 2006 two samples were drawn from the 1929-1938 and 1959-1960 birth-cohort. The data collection comprised standardized clinical measurements and self-administered questionnaires. The early oral health environment and social status and sex were related to oral health in 1983 by multiple regressions. The impact of social status was studied in combined datafiles from 1983 and 2006.

The oral health environment in childhood was important for adults' oral health. The attention from parents and the local environment lead to a better oral health outcome in adulthood. Social status affected choices leading to better oral health. Regular dental visits were important especially for the eldest birth-cohort. Good oral health behaviors early and during adulthood were also important for oral health. Judged by number of tooth surfaces the difference between social status groups had not increased by 2006.

A life-course perspective provides an opportunity to understand oral health over time. The present study supports the assumption that oral health is continuously exposed to environmental and behavioral risks that lead to accumulated diseases in the dental tissues.

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16

The Role of the Oral Health Therapist in the Provision of Oral Health Care to Patients Across All Ages

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1. Introduction

This chapter will describe the role and evolution of the scope of clinical practice of dental hygienists, dental therapists and oral health therapists. These three groups of allied oral health professionals are playing an increasingly important role in the provision of oral health services and it is therefore important to understand how they are utilised as part of the dental team.

Historically, the dental hygiene profession originated in the early 1900s in the US, followed by Norway, 1924; United Kingdom, 1943; Canada, 1947; Japan, 1948; and Australia, 1971 (Johnson, 2009). Dental hygienists predominantly provide health education, preventive, periodontal and orthodontic auxiliary services to people of all ages.

Dental therapists were introduced in New Zealand in 1921 to provide basic preventive and restorative dental care for children in the School Dental Service. Currently more than 50 countries utilise dental therapists (Nash et al., 2008). In Australia and New Zealand, dental therapists have been responsible for examining, diagnosing, and developing plans for the oral health treatment they provide to children and adolescents, and referring patients with treatment needs beyond their scope of practice to dentists (Satur et al., 2009).

Oral health therapists are a relatively new addition to the dental team. They have the combined education and training of both a dental therapist and a dental hygienist. Currently across Australia all oral health therapy education is provided through the tertiary education sector.

An emerging oral health problem in many Western countries is access to dental services by disadvantaged groups, in particular public adult dental patients. Oral health disparities and socioeconomic disadvantage have led to a growing burden of disease amongst sections of the community who at the same time have difficulties accessing appropriate oral health services. There is currently debate in the United States and elsewhere about the need for an oral health practitioner with similar skills to a dental therapist to address the high levels of unmet restorative treatment needs and extend access to oral health care services for lower income groups. This is somewhat different to the situation in countries like Australia, where dental therapists have been long accepted as playing a role in the provision of oral health

care for children and adolescents. In Australia, the debate concerns the expansion of the clinical scope of practice for dental therapists to provide restorative dental treatment to adult patients. One proposed model in some countries is the extension of dental hygiene practice to include these restorative skills. With the advent of a dually-qualified oral health therapist, i.e., combining the clinical skills of a dental hygienist and those of a dental therapist, there is a real opportunity to redefine the way in which the dental team operates. It is important for public health planners to explore a range of models of oral health care that utilise the skills and expertise of all members of the dental team in order to ensure equitable access to oral health services.

To date, there has been very little research conducted on the appropriate utilisation of dental therapists, dental hygienists and oral health therapists as members of the broader dental team. This chapter will explore some of the research relating to models of care and utilisation of members of the dental team, and expanding their scope of practice to improve access to oral health care, with a particular focus on research conducted in Victoria, Australia, the policy implications of that research and the implications that this may have internationally. This research was conducted as a result of changes to the regulatory framework that were introduced in 1999 and 2002 in Victoria designed to expand the scope of practice for dental hygienists and dental therapists. These changes initially allowed dental therapists to provide restorative dental treatment to young adult patients aged 19-25 years, but only on the prescription of a dentist, and encouraged research into the roles and scope of practice for dental therapists and hygienists. In 2009, regulations were further amended to allow dental therapists to provide dental care within their scope of practice to patients across all age groups. These regulations require dental therapists and hygienists to practice the skills in which they have been formally educated and are competent and registered to undertake. The move towards a regulatory framework based on education and competence rather than a defined list of duties, as is common in many jurisdictions, has important implications for the utilisation of the allied oral health workforce.

2. Oral health workforce and utilisation

Dental therapists and dental hygienists were variously introduced into the dental profession around the world to deal with specific issues relating to access to dental care and to work as an adjunct to dentists in the provision of dental care. The continued expansion and evolution of the roles and scope of clinical practice for dental and oral health therapists is seen as an important mechanism in addressing issues relating to workforce shortages and working in underserved communities, where oral health disparities tend to be greater.

2.1 Dental hygienists

In many countries around the world, dental hygienists have traditionally played a much greater role than dental therapists in the provision of oral health care. Eaton et al. (2003) reported that across Canada, the United States of America and Japan, there were a total of 215,435 hygienists for a total population of 421 million people, alongside 253,825 practising dentists. In contrast to this, in 2007, there were a total of 343,922 active dentists and only 30,963 registered dental hygienists in the 30 European Union and European Economic Area (EU/EEA) member states plus Switzerland, with a total population of approximately 500 million people (Widstrom et al., 2010). Over a ten year period from 1997 to 2007, the

population of the EU/EEA plus Switzerland increased by less that 3%, the number of dentists increased by 13% and the number dental hygienists by 42%. The overall ratio of active dentists:dental hygienists changed from 18:1 to 11:1 across Europe, but this was still a long way from the nearly 1:1 ratio across Canada, the United States and Japan.
Although dental therapists have been widely utilised in Australia, it has taken Australia much longer to embrace the dental hygienist profession. In 2006 there were 1045 practising dental hygienists (including 371 dually qualified oral health therapists) and 10,404 practising dentists, a ratio of dentists to dental hygienists of 10:1, for a population of 21 million people. Between 1997 and 2006 there has been 139% increase in the number of practising dental hygienists in Australia, and it is predicted that this growth will continue with a projected increase of 116% to 1,458 dental hygienists by 2025, in addition to an increase in dual trained oral health therapists of 460% to 2,117 by 2025 (Australian Institute of Health and Welfare [AIHW], 2011).

2.2 Dental therapist and oral health therapist workforce

In the United Kingdom there are approximately 5,600 dental hygienists providing mainly periodontal and preventive care; 1,100 dually qualified hygienist-therapists whose remit also includes a wide range of restorative work; and approximately 200 singly qualified therapists (whose training programme ceased some 20 years ago), who traditionally worked mainly in community clinics and with children (Turner et al., 2011). In New Zealand there were 749 registered and practising dental therapists in 2011, with 515 dental hygienists and 2060 dentists, an increase from 640 dental therapists, 377 dental hygienists and 1,640 dentists in 2005 (New Zealand Dental Council, 2005, 2011).
In 2006 the oral health workforce in Australia comprised of 1,171 practising dental therapists and 371 practising oral health therapists (Balasubramanian & Teusner, 2011). In 2006, 98.8% of dental therapists and 94.8% of oral health therapists were female. This pattern of female predominance is similar to that seen for both dental therapists and dental hygienists internationally. This has potential implications for workforce planning, with female practitioners more likely to take time off work and work part-time for child-rearing and family reasons (Hopcraft, 2008). Whilst Australian dentists and dental specialists comprised only 77% of the oral health workforce in Australia, they provide approximately 85 per cent of all dental visits (Teusner & Spencer, 2003). However, whilst the number of practising dental therapists in Australia declined from 1,324 to 1,171 between 1997 and 2006, this was offset by an increase in dual-trained oral health therapists of 371 in 2006 (Balasubramanian & Teusner, 2011).
In Australia, with the majority of training programs now combining dental therapy and dental hygiene to graduate as an oral health therapist, there will be a growing proportion of the oral health workforce who will have clinical skills in both fields, allowing them to play a significantly different role as members of the dental team. Indeed, workforce projections in Australia indicate that the number of oral health therapists will increase 460% to 2,117 by 2025, whilst the number of dental therapists will decline to only 443 over the same period (AIHW, 2011).

3. Oral health therapy education and scope of practice

Oral health education varies across the globe, with the growth in dental schools and graduate numbers dependant on the particular workforce requirements in each country.

There has been enormous change in the oral health education landscape in Australia over the past 20 years, with four new dental schools opening to complement the five existing schools that offer training for dentists. There are also three additional training programs in Australia for dental therapists and dental hygienists that do not concurrently train dentists. In terms of education for dental and oral health therapists, there has been a substantial shift from programs training single qualification graduates (dental therapist or dental hygienist) to Bachelor of Oral Health programs training oral health therapists (dual qualified dental therapists and hygienists).

3.1 Dental therapy, dental hygiene and oral health therapy education

Dental hygiene, dental therapy and oral health therapy education programs have evolved differently around the world, and there is not a common approach to their training. Programs have invariably developed as a response to the particular requirements of a given country, as well as the regulatory environment governing their practice. A number of reviews of dental therapist and dental hygienist education show this significant variation in the duration and nature of educational experiences (Luciak-Donsberger & Aldenhoven, 2004; Johnson, 2003; Nash, 2004; Nash et al., 2008). Interestingly, whilst the roles and functions of dental therapists are reasonably similar internationally, dental hygienists, who practice across many countries, undertake very different clinical duties around the world depending on the legislative environment under which they practice. As a consequence, the education and training requirements also differ considerably. A decade ago, a review of the scope of practice for dental hygienists in nineteen countries investigated eight clinical procedures that hygienists might engage in (Johnson, 2003). In most countries, only four or five of the procedures were within the hygienists' scope of practice, and in only one country did hygienists perform all eight procedures.

3.1.1 Dental hygiene education and scope of practice

The education and training of dental hygienists varies considerably internationally, although there is a trend towards baccalaureate programs in many countries. In the USA in 2002, training programs varied from two to four years, with 78 per cent of graduating dental hygienists awarded an associate degree, 17 per cent a baccalaureate degree, 3 per cent a combined certificate/associate degree and 2 per cent a certificate or diploma (Brown et al., 2005) Dental hygiene education commenced in Australia in 1971, moving from a diploma to a baccalaureate degree in 1998.

Internationally, the practice of dental hygiene has been shifting from traditional models of direct and indirect supervision by a dentist towards a more collaborative approach to practice, where the dentist and hygienist work together to decide on the best approach to patient management and the services required (Johnson, 2003). In Sweden, Denmark, Norway, Finland, the Netherlands and Colorado (USA), dental hygienists are able to practice independently from dentists (Gatermann-Strobel & Perno-Goldie, 2005). Limited independent practice or models of care allowing direct access in restricted practice locations such as nursing homes and public health facilities are permitted in Germany, Latvia, and a number of states in the USA.

In New Zealand, dental hygienists practise in a team situation with clinical guidance provided by a practising dentist or specialist. Clinical guidance means the professional support and assistance provided to a dental hygienist by a dentist/specialist as part of the

provision of overall integrated care to the patient group, and may be provided remotely. Dental hygienists are responsible and accountable for their own clinical practice within their scope of practice but the dentist or specialist is responsible and accountable for the clinical guidance provided. Dental hygiene practice includes – obtaining and reassessing medical and dental health histories; examination of oral tissues and recognition of abnormalities; assessing and provisionally diagnosing diseases of periodontal tissues, and providing appropriate referral; obtaining informed consent for dental hygiene care plans; scaling, debridement and prophylaxis of supra and sub-gingival tooth surfaces (New Zealand Dental Council, 2005).

The Danish *Dental Hygienists Act 1996* permits hygienists to undertake a dental examination and subsequent periodontal management of the patient. Hygienists are able to register to own their practice without the supervision of a dentist, and are required to refer patients with complex treatment requirements, oral pathology which is beyond the scope of practice of a hygienist, complex medical conditions or patients who do not respond to treatment to a dentist. In Finland, dental hygienists work only under the prescribed instructions of a dentist, generally in a team environment. However, they can work independently, and can have their own practice. In Norway, dental hygienists normally work with dentists, although they are able to have their own private practices and are able to diagnose and treat patients. In Sweden, dental hygienists are able to work independently, diagnosing dental caries and periodontal disease and planning appropriate treatment, and providing temporary restorations (Gatermann-Strobel & Perno-Goldie, 2005).

In the Netherlands, dental hygienists have independent status, and predominantly train in special hygiene schools that are not associated with dental schools. Most hygienists are employees in dental practices, however they are able to practice independently from a dentist in a dental hygiene clinic, but all treatment must be referred by a dentist. The first independent practice commenced in 1978 (Gatermann-Strobel & Perno-Goldie, 2005). Approximately 10 per cent of hygienists operate in this manner, and there is pressure from hygienists to acquire the right to initiate their own treatment plans.

In most of the provinces in Canada, the profession of dental hygiene is self regulated, with hygienists and not dentists responsible for registration and licensing (Gatermann-Strobel & Perno-Goldie, 2005). Dental hygienists were first granted self regulation in Quebec in 1975, with other provinces following in the 1990s. In some provinces, hygienists may practice independently, but some treatment may have to be prescribed by a dentist, or the patient must have been seen by a dentist in the previous 12 months. Canadian dental hygienists have expressed a strong interest in expanding their scope of practice and their knowledge base to achieve greater professional independence, expertise and professional respect. However, Canadian dentists believe that hygienists are not adequately trained to practice independently (Adams, 2004).

In the United States of America in 22 states, dental hygienists can initiate treatment and provide dental hygiene services in various settings based on their assessment of the patient need (American Dental Hygienists Association, 2007). This model of dental hygiene is known as direct access, which is defined as a model of practice where the dental hygienist initiates treatment based on their assessment of patient's needs without the specific authorisation of a dentist, treats the patient without the presence of a dentist, and maintains a provider-patient relationship. Independent dental hygiene practice is permitted only in Colorado, and for a short period was also permitted in California. There has been a number

of studies that have examined dental hygienists working in some form of independent practice, examining and treating patients that have not been previously examined by a dentist. In 1986, the Colorado state legislature revised the Colorado Dental Practice Law (DPL) to permit dental hygienists to practice either supervised or unsupervised, and also to allow a dental hygienist to own a dental hygiene practice (Astroth & Cross-Poline, 1998). The Colorado DPL does not require any additional education in order to practice independently. The Colorado study noted that referrals originated from current patients to the independent hygiene practices, implying patient satisfaction with care and treatment received. Hygienists also received referrals from dentists and other health-care professionals, again implying recognition of the value of the dental hygiene services being supplied. The authors noted that this type of referral pattern could signal the establishment of collaborative and respectful working relationships between dentists and dental hygienists engaged in this type of practice. An audit of patient records found a high standard of process of care and management of patient information. The authors concluded that the care provided by the dental hygienists in this study did not exhibit any undue risk to public health and safety. The California Health Manpower Pilot Project 139 (HMPP 139) operated from 1987 until 1990, and various aspects of practice were examined (Kushman et al., 1996; Freed et al., 1997). A total of 16 hygienists established 10 practices, including office-based, home-based and organisational practices. The authors found that all of the practices consistently attracted new patients. Comparisons were made with six dental practices, and this showed that the hygiene practices were superior in several areas, including infection control, follow-ups to medical findings, and updating the medical history and documentation of periodontal and soft-tissue status. A total of 98 per cent of patients were satisfied with their treatment. The authors concluded that, given the methods used in the study, the adequacy of dental care without dentists' supervision was at least as good as hygiene care provided with supervision, and the evidence indicated that independent dental hygiene practice did not increase the risk to the health and safety of the public or pose an undue risk of harm to the public. In both of these studies, the dental hygienists were examining patients and developing oral hygiene care plans, and referring patients to dentists when required.

In Australia, dental hygienists are currently licensed by the Dental Board of Australia, but prior to 2010 they were licensed separately in each State or Territory, with different regulations and scope of practice. In Victoria under the Dentists Act 1972, dental hygienists were licensed to practise within a defined scope of practice listed under the *Dentists Regulations 1992 r.505 Duties of a dental hygienist*, which stated that a dental hygienist may, under the supervision, direction and control of a dentist, perform certain tasks, including the following - measurement and recording of periodontal disease; removal of plaque, extrinsic staining and calculus from teeth; root planing; cleaning and polishing of teeth and restorations; topical application of solutions to teeth or oral tissues; taking of impressions for study casts; limited orthodontic procedures; and taking of periapical and bitewing radiographs. Furthermore, in a dental practice, there had to be one supervising dentist for each dental hygienist employed. In 2002 the Code of Practice for dental hygienists in Victoria removed these words, and their scope changed to include fissure sealants and local analgesia as well as undertake an oral examination, and also altered the supervision requirements so that dental hygienists could work under general supervision – the dentist did not need to be on site for them to practice (Dental Practice Board of Victoria, 2002).

3.1.2 Dental therapy and oral health therapy education and scope of practice

Dental therapy originated in New Zealand, with the recognition of poor oral health of children and the need for a workforce that had an emphasis on prevention (Satur, 2010). After considerable debate over nearly a decade, the Health Department established a dental therapy school in 1921 to train School Dental Nurses to work in the School Dental Service, with the first cohort graduating in 1923. Two further schools were established in 1952 and 1956, however by 1980 with a declining child population and improving oral health these two schools were closed. The training program moved from the control of the Health Department to the Education Department in 1991, and moved to the tertiary sector in 2000 with a Diploma of Dental Therapy at the University of Otago, and later also at Auckland University of Technology. These two programs eventually moved to a dual-outcome Bachelor of Oral Health in 2006 and 2007.

Dental therapy training commenced in 1966 in Australia, following the success of the New Zealand program, and was run under the umbrella of State-based Health Department dental therapy schools (Dunning, 1972; Gussy, 2001; Satur, 2003). In Victoria, the training program was two years in duration and was designed to provide basic dental treatment to children using preventive, educational and reparative measures, under the supervision, direction and control of dentists. The course was upgraded from a Certificate to a Diploma in 1988, and a greater emphasis was placed on preventive care, including the use of fissure sealants, before transitioning to the tertiary education sector in 1996 in Victoria with a Diploma in Oral Health Therapy (Satur, 2010).

Although the first dual-trained Bachelor of Oral Health program did not commence in Australia until 1998 at the University of Queensland and the Queensland University of Technology, in South Australia dental therapists were able to undertake a bridging program since 1980 enabling them to acquire dental hygienist skills and register as both a dental therapist and dental hygienist (Satur, 2010). Other universities in Australia began to offer both add-on programs to allow dental therapists and dental hygienists to upskill and gain dual registration, and eventually they began to combine their training programs into dual-trained Bachelor of Oral Health programs. Currently in Australia there are eight programs that offer dual-trained outcomes in dental therapy and dental hygiene, with two dental hygiene only programs and one dental therapy only program (Satur, 2010).

In the United Kingdom there has been a shift towards dual training as a result of the Nuffield Inquiry in 1993, although there are still many single outcome programs on offer.

There is currently significant debate in the United States about the introduction of dental therapists into the dental workforce, which is seen as a reasonably recent process. However, the history of dental therapists in the United States dates back to 1949, when the state of Massachusetts passed legislation allowing for the training of non-dentists to prepare and restore teeth under the supervision of a dentist (Mathu-Muju, 2011). Strong opposition from the American Dental Association saw the legislation rescinded the following year. Then in 1972 there was a proposal from the University of Southern California to use school dental nurses based on the New Zealand model to address the problems of untreated dental caries in school children (Friedman & Ingle, 1973a, 1973b). Again, strong opposition from two state Dental Associations contributed to the failure of this proposal to gain funding and proceed. In both instances, the dental profession argued that there were significant concerns regarding the quality of care provided by dental therapists.

More recently though, there has been the successful introduction of dental therapists in Alaska and Minnesota, and a growing movement across a number of states to introduce legislation allowing for the creation of a dental therapist model. The Alaska initiative commenced in 2005 with six Alaska Native dental health aide therapists completing a training program in New Zealand and commencing practice in Alaska under Federal authority (Nash & Nagel, 2005). Several studies have subsequently demonstrated that the dental therapists are performing at an acceptable level, with short-term restorative outcomes comparable with those of dentists treating the same populations (Bader et al., 2011; Bolin, 2008). Minnesota enacted legislation that allowed for the establishment of two new groups of dental practitioner – the dental therapist and the advanced dental therapist, with a training program established at the University of Minnesota alongside dental students (Mathu-Muju, 2011). Dental therapists in Minnesota will require direct or indirect supervision from a dentist, whilst the advanced dental therapist (with two years of additional training) will be able to provide treatment without a dentist on-site and also have a broader clinical scope of practice including the extraction of mobile permanent teeth and the limited prescription of medications. Legislation also requires that at least half of the patients treated by dental therapists in Minnesota be from disadvantaged and underserved groups within the community in order to improve access to dental care, and a dentist must complete the initial examination, diagnosis and treatment plan for the patient.

4. Evolving scope of practice

A quarter of a century ago, Barmes and Tala (1987) observed that changing patterns of oral disease were resulting in a polarisation in treatment needs between those requiring minimal simple intervention and those who required more extensive and high technology care. They suggested re-evaluating dentist: auxiliary ratios, with a need to increase the number of auxiliaries (dental therapists and dental hygienists) to provide the low-medium technology dental services, while working in a team environment with dentists who provided the high-technology care.

More recently, Baltutis and Morgan (1998) noted that changes in the epidemiology of dental diseases in Australia had resulted in a significant change in the dental needs in the community. Significant declines in caries experience in children and young adults, decreasing rates of edentulism and an increase in the number of people retaining more teeth into older age had altered the treatment mix. They argued that there was a need to redefine the roles of all members of the dental team, in order to best utilise the skills of each member, so that services are delivered appropriately to the community.

Reports on dental workforce in Australia at the turn of the century suggested a potential crisis in supply and demand, with an ageing workforce nearing retirement impacting on the ability to supply services, and an increasing demand for dental treatment. There is also a significant maldistribution of the dental workforce in Australia, both in terms of geography (rural and urban), and also private and public sector. Approximately 30 per cent of the adult population is eligible for public dental services but less than 10 per cent of dentists work in the public sector, and nearly 80 per cent of dentists working in major cities.(Teusner et al., 2007; Teusner & Spencer, 2003). It was projected that the capacity of the dental workforce in Australia to supply dental services would increase from 28.4 to 29.4 million visits from 2000 to 2010, however the expected demand for services would increase from 23.8 to 33.2 million visits from 1995 to 2010 (Spencer et al., 2003). This was reported as a potential workforce

shortage of 1500 dental care providers by 2010, prompting an expansion in the number of dental schools, and training numbers for dentists and oral health therapists. It also prompted closer consideration of the configuration and roles of members of the dental team, in particular dental hygienists and oral health therapists.

One proposed solution to the problems of access to dental care lies in productivity. Increased productivity in the workforce has driven much of the economy over recent decades, and it is not unreasonable to think that similar gains can be achieved in dentistry, with improvements in dental technology, material and instruments (Spencer et al., 2003). However, it has also been proposed that increases in productivity, that is the number of dental visits or services provided per hour, can be achieved through the substitution of allied dental personnel for a dentist (Spencer et al., 2003). This has been clearly demonstrated in the utilisation of dental hygienists in North America, and also more recently in research in Australia, demonstrating the utilisation of dental hygienists to provide dental care directly to residents of nursing homes without the prescription or supervision of a dentist (Hopcraft et al., 2011b). Spencer et al. (2003) note that any expansion of the dental team role will be a combination of a substitution effect, or more of the same, and a complementary effect with additional new services provided. For example, the addition of a dental therapist to the dental team, with a scope of practice expanded to treat adult patients, would produce the same simple restorative services (substitution), but also additional restorative services (complementarity), as well as additional complex dental services provided by the dentist using the time freed up from previously providing simple restorative procedures.

We will outline here research that has been undertaken to investigate innovative dental therapy and dental hygiene workforce models designed to improve access to dental services.

4.1 Dental hygienists working in nursing homes

The increased utilisation of dental hygienists as part of the multi-disciplinary team has long been recognised as an approach to improve dental service delivery. However, there is still strong opposition from the dental profession to increasing dental hygienists scope of practice, particularly in relation to autonomous or independent clinical practice. Dental hygienists have expressed a willingness to expand their scope of practice to work in underserved areas in order to address workforce shortages or access needs. However many regulatory models for dental hygienists require them to work under the supervision and/or direction of a dentist.

Extensive literature clearly demonstrates that elderly people living in residential aged care facilities display some of the poorest oral health in the community, and with an ageing population in many Western countries and declining rates of edentulism, this group of patients is likely to present significant challenges to the dental profession (Hopcraft et al., 2011a; Hopcraft et al., 2011c). Dentists have also demonstrated low levels of interest and participation in providing dental care for residents of aged care facilities (Hopcraft et al., 2008). Dentists had a strong preference for treating patients at their own practice, and there are a number of significant barriers that appeared to impact on the provision of dental care in nursing homes.

A study was undertaken in Victoria, Australia in 2005 with the aim to determine whether a dental hygienist could undertake dental examinations for residents of aged care facilities,

devise adequate periodontal and preventive treatment plans, and identify and refer patients who require treatment and assessment by a dentist, without the patient first being examined by a dentist. Prior to the commencement of this study under existing legislation, dental hygienists in Australia could only undertake treatment after a patient had an oral examination and a treatment plan devised by a dentist. This is the most common model of care for dental hygienists internationally, with varying levels of supervision the norm. Of course, the problem with this model of care is that it limits access to dental care, particularly because in a nursing home environment, most dentate residents required periodontal and preventive treatment that could be provided by a dental hygienist. This is an inefficient use of resources, requiring a patient to see a dentist for an examination when this aspect of dental treatment could conceivably be provided by a dental hygienist. Therefore, it was important to provide evidence for a model of care where dental hygienists were able to provide dental care without prior examination and referral from a dentist.

A total of 510 residents from 31 nursing homes were examined by a dentist and one of four dental hygienists in 2005-06, with their referral and treatment decisions compared (Hopcraft et al., 2011b). Three of the hygienists had diploma qualifications and one had a bachelor degree, and had graduated between 1988 and 2003. None of them had previously undergone extra training in special needs or gerodontology or had significant experience working in nursing homes. No additional training was undertaken for the dental hygienists prior to commencing this project.

The dentist and hygienist conducted dental examinations of residents in the nursing home in field conditions, with a headlamp, mouth mirror and probe, and were blinded to the others findings until the examination had been completed and documented. The medical history was assessed independently by both the dentist and dental hygienist prior to the dental examination, particularly to determine whether antibiotic prophylaxis for infective endocarditis would be required. No periodontal probing was undertaken for subjects considered at risk. The dental examination measured coronal and root caries for each tooth surface and assessed periodontal disease using the Community Periodontal Index. After completing the dental examination, the dentist and hygienist independently devised a referral plan and an oral hygiene care plan for treatment to be performed by the hygienist, which were then compared for agreement. The referral plan required the clinician to determine whether the subject required treatment that was beyond the permitted scope of practice of a dental hygienist as determined by the Dental Practice Board of Victoria Code of Practice for Dental Hygienists, and therefore, could only be provided by a dentist. The oral hygiene care plan required both the dentist and hygienist to choose what treatment the patient required that should be provided by a dental hygienist from a list of treatment categories: scaling and/or root planing, oral hygiene instruction, denture cleaning, topical fluoride application, dietary advice/counselling, management of dry mouth or no dental hygiene treatment required. In this study, the diagnosis and treatment decisions of the dentist were considered the gold standard, and comparisons were made with the treatment decisions of the dental hygienists.

The treatment needs of residents were high, with most dentate residents requiring preventive and periodontal treatment that could be provided by a dental hygienist, and three-quarters of residents required a referral to a dentist for treatment. Only 4.0% of dentate residents were assessed as requiring a referral to assess for potential oral pathology. There was excellent agreement between the dentist and hygienists regarding the decision to

refer residents to a dentist for treatment, with high sensitivity (99.6%) and specificity (82.9%). Importantly, only 8.0% of residents were referred to a dentist by a hygienist when it was determined that no referral was required. In most cases, these referrals were to check potential soft tissue pathology or for review of inadequately fitting dentures. Nederfors et al. (2000) found that dental hygienists overestimated treatment need for 6.8% of residents. They concluded that it is possible to use an experienced dental hygienist as the professional of the dental team to act as a consultant in long-term care facilities and that this would be preferable from both an economic and pedagogical point of view. The results of this study were similar to those of Nederfors et al. (2000) and demonstrate that dental hygienists can play an important role in the delivery of oral health care to residents of aged care facilities.

One of the key strengths of this study is that the dental hygienists did not require additional education or training prior to undertaking examination of nursing home residents. Sensitivity and specificity of the examination and treatment recommendations were high despite the fact that the four dental hygienists were educated in different jurisdictions, with no prior experience working in nursing homes or with frail and functionally dependent elderly patients. This suggests it is possible to expand the clinical scope of practice for dental hygienists to practise in nursing homes without undertaking specific further education or training.

The increased utilization of dental hygienists as part of the multidisciplinary team has been clearly recognized as an approach to improve dental service delivery. Dental hygienists have been shown to be capable of undertaking a dental examination for residents, correctly identifying the majority of residents who require a referral to a dentist as well as formulating appropriate dental hygiene treatment plans for residents. With a greying population who are retaining more natural teeth, it is important that public dental policy embraces a model of care that places dental hygienists at the frontline of dental service provision in nursing homes. Dental hygienists can be utilized to provide dental examinations for residents on admission to a nursing home, develop an oral hygiene care plan, provide dental hygiene treatment, refer to a dentist and provide ongoing support and oral health education to carers as required. This model of care is likely to improve access to care for residents and has a positive impact on their oral health and quality of life.

More broadly, this study demonstrates that dental hygienists are able to exercise autonomous clinical decision making in the treatment of their patients. In Australia, dental hygienists are trained and educated to diagnose, treatment plan, prevent dental diseases and treat periodontal disease, and their training is often provided alongside dental students in a university setting.

4.2 Dental therapists treating adult patients

In North America, the debate around dental therapists centres on the introduction of a new oral health care provider. Some commentators advocate limiting the scope of practice for dental therapists to children – indeed, this is inherently implied in the preferred terminology of 'pediatric oral health therapist' in the United States (Nash & Nagel, 2005). However, it is important to note the vast differences in the oral health care systems in the United States and other countries that utilise dental and oral health therapists. Dental therapists have a long established role in countries such as New Zealand, Australia and the

United Kingdom, treating children for many decades. With a more 'mature' profession, arguably the push for expansion to treat adult patients makes more sense than in the USA, where the establishment of dental therapy to focus on a particular problem of poor child oral health and access (the same problems that saw the creation of dental therapists in New Zealand nearly a century ago) necessitates restricting their practice to children and adolescents.

Recent legislative changes in Australia have allowed for an expansion in the scope of practice for dental therapists, beginning when the new *Dental Practice Act 1999* enabled dental therapists in Victoria to work in both the public and private sectors, after previously being restricted to working in the public sector only (Satur, 2003). Subsequently, the Dental Practice Board of Victoria developed a new Code of Practice in 2002 allowing dental therapists to expand their patient group to provide dental services to young adults up to the age of 25 years. In 2004, the National Advisory Council for Oral Health (a subcommittee of the Australian Health Ministers conference) called for the use of dental therapists, as members of the oral health team, to assist in addressing workforce and clinical demand issues (Australian Health Ministers' Advisory Council, 2004). In 2002 the Dental Practice Board of Victoria (DPBV) encouraged research aimed at expanding the role of dental therapists and dental hygienists.

In 2006 Dental Health Services Victoria undertook a study to investigate the capacity of dental therapists to provide direct coronal restorative care to adult patients over the age of 25 years on the prescription of a dentist (Calache et al., 2009). This was the first step in the process of determining whether oral health therapists could expand their dental therapy scope of practice to adult patients. This study was followed in 2010 by another study that investigated a pilot educational bridging program designed to provide university trained dental therapists with the requisite knowledge and clinical skills to translate their existing scope of practice to adult patients over the age of 25 years (Calache & Hopcraft, 2011a; Calache & Hopcraft, 2011b).

4.2.1 Capacity for direct restorative care

This project commenced in 2006 at the Royal Dental Hospital of Melbourne (RDHM), and was designed to assess the capacity of dental therapists to provide direct coronal restorations to adults older than 25 years on the prescription of a dentist (Calache et al., 2009). Dental therapists undertook a three day educational program prior to commencement of the study. This program included: infection control measures; demographics of adult patients attending the RDHM; medical problems affecting adult patients' care; psychological issues in care; communication skills; professional and technical skills for the ageing dentition; the impact of partial dentures on the dentition, on dental restorations, and on occlusion; a review of dental materials; periodontology; and health promotion approaches for adult patients. Seven dental therapists participated in the study, placing 356 restorations in 115 patients, with the support of a dentist. The examining dentists undertook the initial examination, and prescribed restorative treatment for the dental therapist to perform. They had to confirm that the procedure and the patient were suitable for management by the dental therapist.

The supporting dentists (separate from the examining dentists) provided support to the therapist as required (rather than "direct supervision"), on issues such as the choice of dental materials and appropriate technique, or if the therapists considered the prescribed

treatment to be beyond their scope of practice. The supporting dentists also undertook an evaluation of each restoration immediately after it had been placed. These restorations were reviewed six-months post placement by reviewing dentists (separate from the examining and supporting dentists) blinded as to which restorations were placed by the dental therapists. Patients' age ranged from 26 to 82 years (82% were >40 years). The supporting dentists and reviewing dentists had extensive experience in clinical teaching and assessment of dental students.

Six months after placement, 94.6% of the direct coronal restorations placed by dental therapists were assessed as meeting all standards, acceptable or satisfactory, with the remaining 5.4% requiring re-treatment. This re-treatment rate was comparable with that reported in the literature for most dental materials at six month of being placed (Sheldon & Treasure, 1999). Glass Ionomer Cement restorations in posterior teeth had the greatest failure rate (12.5%). However, Sidhu (2011) also highlighted that this type of restorative material may have a higher replacement rate, particularly in posterior teeth.

Based on feedback from the therapists and supporting dentists involved in the project, it was proposed that a dental therapist would require approximately 70 hours of additional training (28 hours didactic, 14 hours clinical observation and 28 hours clinical practice) to support their capacity to provide direct coronal restorative services to adults older than 25 years on the prescription of a dentist. This study suggests that dental therapists are capable of providing direct coronal restorations to adult patients on the prescription of a dentist after completing a short educational program.

4.2.2 Pilot educational model

Following the successful study that demonstrated that dental therapists were capable of providing restorative treatment to adult patients on prescription, it was important to further investigate the ability of dental therapists to treat adult patients without the prescription of a dentist, working within their own scope of practice. Models of care that provide substitution of personnel are likely to be more efficient when there are no constraints such as supervision or prescription. Therefore, further research was undertaken to investigate a pilot educational program designed to translate the existing clinical scope of practice for dental therapists in Victoria, Australia to adult patients. Dental therapists have traditionally performed dental examinations, preventive and simple restorative treatment for children without the supervision of a dentist. Translation of these clinical skills to adult patients is seen as one mechanism for improving access to dental care in underserved sections of the community.

An educational bridging program was developed based on educational models shown to be effective in changing clinicians' performance or patient outcomes. The educational program was designed to enable dental therapists with a university qualification to undertake clinical procedures within their existing scope of practice, for patients twenty-six or more years of age. Provision of dental care included the ability to recognise and provide appropriate referral of adult patients if their treatment needs were beyond the scope of clinical practice of the treating dental therapist. The existing scope of clinical practice for dental therapists relevant to management of adult patients is shown in Table 1.

Treatment needs considered outside the scope of clinical practice of dental therapists includes restorative treatment of root caries and carious lesions associated with crowns, bridges, and abutment teeth for removable prostheses; complex restorations extending onto

root surfaces; complex restorations requiring multiple cusp replacement; restorations on teeth affected by advanced periodontal disease; endodontic therapy (apart from pulp capping and pulpotomies) on permanent teeth; indirect restorations; restorative treatment for patients with implants; and extraction of permanent teeth.

Oral Diagnosis	Prevention	Operative Care	Orthodontics	Oral Surgery
Oral examination Intraoral dental radiography Extraoral dental radiography (on prescription) Impression taking (but not for prosthodontics treatment)	Application of therapeutic solutions to teeth (excluding in-surgery bleaching) Fissure sealants Scaling and prophylaxis	Local anaesthesia Restoration of coronal tooth structure (excluding indirect restorations) Pulpotomies	Orthodontic procedures, under the supervision of a dentist (excluding diagnosis; treatment planning; initial fixation of brackets; design, activation and adjustment of orthodontic appliances)	Extraction of deciduous teeth

Table 1. Scope of clinical practice for dental therapists in Australia

The educational program consisted of didactic and interactive workshops (42 hours), clinical observation sessions (14 hours), clinical practicum sessions (42 hours), and clinical experience sessions (105 hours) (Table 2). The clinical observation component consisted of fourteen hours over two days, including observation of public dentists in primary care, general dentistry, and oral medicine providing treatment to adults. This was designed so that participants could observe and discuss various treatments and engage in interactive one-on-one conversation with the dentist, in order to facilitate application of knowledge to practice. Following the clinical observation, the dental therapists then undertook forty-two hours of clinical practicum, providing dental care to adult patients aged 26+ years at the Royal Dental Hospital of Melbourne under the direct supervision of a dentist. These supervising dentists all had extensive experience in clinical teaching of undergraduate students.

This enabled participants to apply new knowledge and skills to their own clinical practice and also facilitated more interactive one-on-one conversation with the supervising dentist. Both the supervising dentist and the participant completed a logbook to provide performance feedback during the clinical practicum sessions. Participants then undertook 105 hours of clinical experience, providing dental care to adults over a period of at least fifteen days, working in close collaboration with a dentist at a local community dental clinic. Again, a logbook was completed by both the supervising dentist and the participant, to provide feedback on the participants' performance. At the completion of the education program, participants undertook a three-hour written examination and an oral examination of thirty minutes (after sixty-minutes to view a clinical case), including one patient case presentation, to assess their ability to provide dental care within their clinical scope of practice to adult patients.

	Hrs	Topics
Self-directed Learning		Pre-reading material on topics in the didactic and interactive workshop component of the program were sent to participants four weeks prior to commencement of the course.
Didactic Workshops		Didactic and interactive workshop activities were delivered by specialist dentists and academics.
Oral examination	3	Medical, dental and social history; extra- and intra-oral clinical examination, including coronal and root caries assessment; periodontal, occlusal and oral mucosal assessment.
Management of older adults	3	Management of attrition, erosion and abrasion, pulpal recession, root caries, xerostomia, oral changes resulting from disease/ medication; management approaches for older adults.
Communication skills	3	Utilisation of appropriate communication skills in specific dental contexts; nature and process of skilled interpersonal communication; record keeping including informed consent.
Medically compromised patients	3	Management of patients with disabilities, cardiovascular disease, endocrine, neurological, haematological and oncological disorders, and poly-medicated patients.
Periodontology	6	Introduction to the periodontium; chronic periodontal disease; periodontal examination including periodontal probing; the importance of periodontium health in treatment planning.
Dental Materials	3	Materials including linings/bases, amalgam, composite resin, glass ionomer cement.
Prosthodontics	3	Identification of appliances used in fixed and removable prosthodontics treatment and the implications of prosthodontics treatment on restorative care and vice versa.
Oral medicine	3	Recognition and identification of oral pathological conditions in the clinical situation; drug interactions; management of dental pain; instigation of appropriate referrals; pharmacology.
Local anaesthesia	6	Techniques for dentate/edentulous patients; appropriate local anaesthetics; maximum safe dose; implications of medical history; local/systemic complications and management.

	Hrs	Topics
Dental emergencies	3	Emergency management of pain associated with acute oral infections (excluding extraction of permanent teeth); instigation of appropriate referrals.
Medical emergencies	3	Principles of emergency care and management of life threatening situations including the unconscious patient, respiratory difficulty, myocardial infarction and allergic reaction.
Case presentations	3	Adult patient case reports for presentation and small group discussion for treatment planning.
Clinical Observation	14	Conducted over two days with observation of public dentists in primary care/general dentistry, and dental specialists (oral medicine) treating adults.
Clinical Practicum	42	Provision of dental care to adult patients under dentist supervision, to apply knowledge and skills learnt in didactic sessions. A logbook completed by the dentist and participant provided feedback.
Clinical Experience	105	Provision of dental care to adult patients over 15 days working in close collaboration with a dentist at their local dental clinic. A logbook completed by the dentist and participant provided feedback.

Table 2. Curriculum content for pilot educational bridging program

The evaluation of this bridging program suggests that it was able to meet its objectives, and was able to successfully prepare university educated dental therapists to translate their existing scope of clinical practice to adult patients 26+ years of age. It was effective in increasing both the knowledge and confidence of the participants to treat adult patients to similar levels they reported for treating children. Confidence is an important educational outcome, and has been linked to increased clinical competence (Lynch et al., 2010; Smith et al., 2006). The success of the education program was also reflected in the high levels of patient satisfaction reported during the clinical practicum and clinical experience sessions in this study. Patient satisfaction is being seen as an increasingly important component of health care, and new models of care must demonstrate patient acceptance if they are going to be effective. Nine participants successfully completed the course assessment, and eight of the participants were deemed clinically competent to treat adult patients without supervision, and were provided with an extended scope of practice by the Dental Practice Board of Victoria. Two therapists required additional assessments before being deemed clinically competent to treat adult patients, and in the end all 10 participants were awarded an extension of scope of practice.

The evaluation of this project resulted in the identification, by participating dental therapists and supervising dentists, of some gaps in the course content. This included additional

clinical observation and didactic content covering cariology and minimal intervention dentistry, prosthodontics, emergency management of oral conditions, and oral medicine/pathology. These recommendations for additional course content were supported by the Dental Practice Board of Victoria in their endorsement of the extended scope of practice for the therapists who completed this pilot education program.
This educational program was specifically designed to extend the scope of practice for dental therapists to treat adult patients, and the evaluation indicated that this program was effective. An analysis of the curriculum content and evaluation by all participants demonstrated that university educated dental therapists were able to gain the necessary knowledge and skills to translate their existing clinical scope of practice to treat adult patients. This study has important implications in enhancing the flexibility of dental team of the future. Broadening the dental therapists scope of practice in this manner would create a more flexible oral health team, potentially allowing dentists to provide more complex procedures for patients most in need. This is significant in the public sector and rural areas where workforce shortages are most acute. However, the economic viability of this model has yet to be tested.

5. Policy developments

The last decade has seen enormous change in the regulatory environment in Australia regarding the clinical scope of practice for allied oral health professionals. Dental therapists have moved from working predominantly in the public sector in most States, to a mix of public and private sector employment. The close supervision and prescriptive requirements for dental therapists and hygienists has also been removed, providing significantly greater autonomy of dental practice. However, complete independent dental practice for dental therapists and hygienists is still not permitted in Australia.

5.1 Policy developments – dental hygienists

Research conducted into the utilisation of dental hygienists working in nursing homes was instrumental in the Dental Practice Board of Victoria amending the 'Code of Practice for the Practice of Dentistry by Dental Hygienists and Dental Therapists' in 2007, allowing dental hygienists to practice in all areas for which they have received formal education, including dental examination and treatment planning. This was the first critical step in increasing the scope of practice for allied oral health personnel, with the emphasis on a clinical scope of practice that was defined by education and competence rather than a defined list of duties. At the time, these changes were considered quite radical in some quarters, and were opposed by the dentist profession in submissions to the Dental Practice Board of Victoria. The changes also highlighted the idiosyncratic nature of dental regulation in Australia, with significant variations in the permitted scope of clinical practice and supervision requirements across other States and Territories. For example, in Queensland, dental hygienists were not permitted to take radiographs, while in New South Wales they were not permitted to perform periodontal probing depth charting. In 2010, a national approach was finally adopted, with the introduction of a national Dental Board, and a single scope of practice registration standard:

> "Dental hygienists, dental therapists and oral health therapists exercise autonomous decision making in those areas in which they have been formally educated and trained.

> They may only practice within a structured professional relationship with a dentist. They must not practise as independent practitioners. They may practise in a range of environments that are not limited to direct supervision."

This national standardised approach to the regulation of the scope of practice for dental hygienists in Australia has the ability to significantly improve access to dental care for underserved population groups such as residents of aged care facilities.

5.2 Policy developments – dental therapists

Until recently, dental therapists in Australia were restricted to treating children (with the exception of Western Australia, where dental therapists were able to treat adult patients under the prescription of a dentist). Each State jurisdiction had its own regulations on clinical scope of practice. In Victoria, the Dental Practice Board of Victoria encouraged research aimed at increasing scope of practice for dental therapists, and improving access to dental care. The research undertaken on expanding the scope of practice for dental therapists treating adult patients provided the evidence which resulted in the Dental Practice Board of Victoria removing, in 2009, the age restriction on dental therapy practice and, in 2010, extending the scope of practice for the dental therapists who successfully completed an educational bridging program designed to enable them to treat adult patient. This research also strengthened the recent approach adopted by the DPBV, that dental therapists are able to work within a clinical scope of practice in which they have been formally educated and trained. The new regulatory framework in Australia from 2010 (under the Dental Board of Australia) now allows dental therapists across Australia to work in this manner, provided they have the appropriate education. The outcomes of this research have resulted in at least one university oral health therapy program introducing a module specifically aimed at the treatment of adult patients. Thus, this research has been pioneering in providing the evidence for both regulatory and educational change. What remains to be seen is the impact that this may have on the future practice of dental and oral health therapy in Australia, and the oral health of the community.

6. Conclusion

Dental therapists, dental hygienists and oral health therapists are increasingly becoming an important part of the dental team internationally, both in the provision of dental services and oral health promotion activities. Broader utilisation of allied dental personnel has the ability to improve access to dental care for many underserved sections of the community.

Recent research in Australia has demonstrated the effectiveness of extending the role of the oral health therapist to target sections of the community with unmet oral health needs. Dental hygienists are able to undertake dental examination, treatment and referral of patients in nursing homes. This model of care is likely to improve access to care, and the preventive focus of dental hygienists is critical in this population.

A 34-day bridging educational program has been shown to be successful in providing dental therapists with the skills required to translate their current scope of clinical practice to adult patients without prescription from a dentist. Dental therapists are competent and safe to provide care to patients across all ages without the prescription of a dentist. Dental therapists are aware of the limits of their abilities, and are likely to err on the side of caution with regard to referring complicated problems to registered dentists. This is important when

the safety and quality of dental services may be questioned in developing new models of care. Importantly, adult patients were satisfied with the restorative treatment services provided by dental therapists, and accepting of dental therapists as a primary health care provider.

7. Acknowledgments

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17

Oral Health & HIV

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1. Introduction

HIV and AIDS continues to ravage developing countries especially those in sub-Saharan Africa three decades into the pandemic. It has eroded social, political and economic health gains and dealing with its consequences is one of the greatest challenges of the new the millennium. There has been a decline in life expectancy in adults, an increase in child mortality rates that has reversed the years of hard won gains achieved in child survival, deepening poverty and exacerbation of food shortages. Susceptibility to HIV AIDS is sustained by the lack of economic, social and political influence, including the capability to effectively inform decision makers and policymakers. The majority of people affected by HIV/AIDS are vulnerable populations who live under conditions of gender-based violence, poor access to health care and inadequate living conditions. There is an urgent need for strategies to remove the barriers that prevent them from voluntary testing and counselling and accessing oral health promotion, prevention and treatment services.

2. Importance & relevance of oral lesions in HIV/AIDS

Oral lesions are a common occurrence in individuals with HIV infection. Oral manifestations include fungal, viral and bacterial infections. Neoplasms, periodontal disease, salivary gland disease and lesions of uncertain origin are also seen. Several studies have emphasised the prognostic significance of oral candidiasis and oral hairy leukoplakia as predictors of immuno suppression and AIDS-defining conditions. Lesions such as oral candidiasis, herpetic ulcers and Kaposi's sarcoma are among the first symptoms of HIV-infection. These conditions, although not life-threatening, impact on the quality of life (Yengopal & Naidoo, 2008) and are often associated with significant pain, discomfort, eating restrictions and consequent diminished nutritional intake. The oral cavity may also be a primary source of infection in any individual, which may spread via the mucosal associated lymphoid tissue or stimulate systemic inflammatory immune responses (Chapple & Hamburger, 2000).

The treatment and management of oral HIV lesions can considerably improve well being. Antiretroviral treatment and improved management of HIV, has been shown to reduce the prevalence of oral manifestations, but there may be an increase in oral warts and salivary gland disease (Greenspan et al., 2001). Oral examination is quick and inexpensive and may have a place, especially in primary health care settings and for screening populations at greater risk of HIV. Early detection of HIV-related oral lesions can be used to diagnose HIV infection, elucidate progression of the disease, indicate a response to antiretroviral therapy

and by predicting immune status can result in timely therapeutic intervention. For HIV infection in women it may be useful in ante-natal screening so that appropriate drug management can be instituted to reduce vertical transmission.

3. Oral lesions: Types and management

3.1 Oral candidiasis

Oral candidiasis is the most common oral lesion with a variable clinical presentation. *Candida albicans* is the most common cause. It is manifested as creamy white pseudomembranous plaques, erythematous patches, non-scrapable hyperplastic plaques or as angular chelitis. Once colonisation and super-infection by *Candida* spp. are established, deeper penetration into submucosal tissue may be facilitated by concomitant mucosal infections caused by bacteria and herpes simplex virus (HSV). In children, lesions are often characteristically of the pseudomembranous and erythematous types. Early presentations are often asymptomatic. Candidiasis may be accompanied by pain and an altered taste sensation, both of which interfere with nutrition and hydration and may be exacerbated by decreased salivary flow.

Pseudomembranous candidiasis is the most common variant and presents as creamy white or yellow, loosely adherent plaques anywhere in the mouth and it can be wiped off to reveal an erythematous surface with or without bleeding (Figures 1 and 2). Erythematous candidiasis presents as multiple, flat, diffuse or discrete red non-removable plaques. It is usually found on the palate, tongue and occasionally on the buccal or labial mucosa (Figure 3). A variant of erythematous candidiasis is median rhomboid glossitis – presenting as a smooth, red, depapilated area in the middle of the tongue (Figure 4).

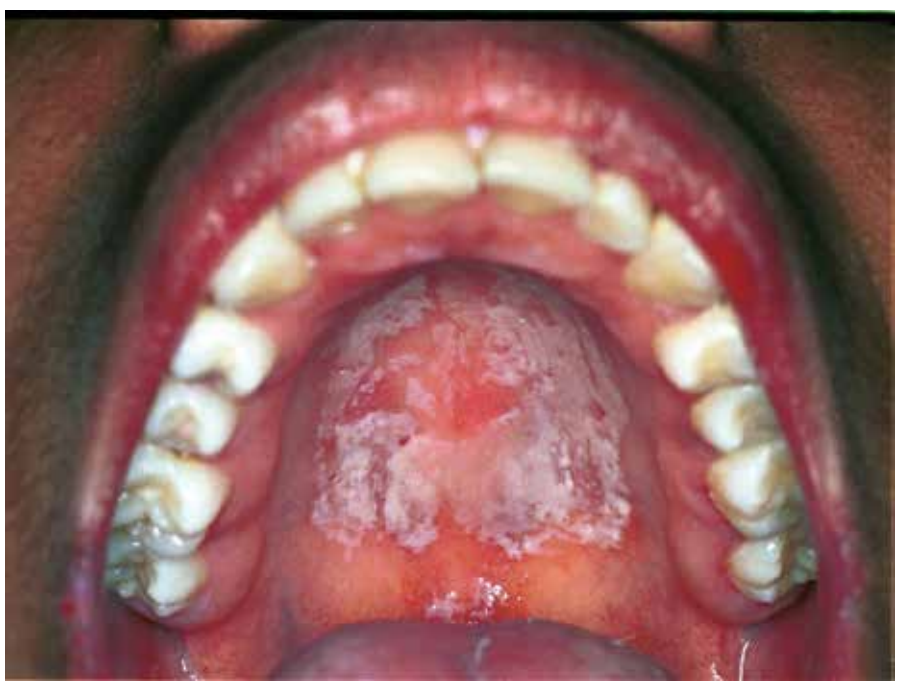

Fig. 1. Pseudomembranous Candidiasis Palate

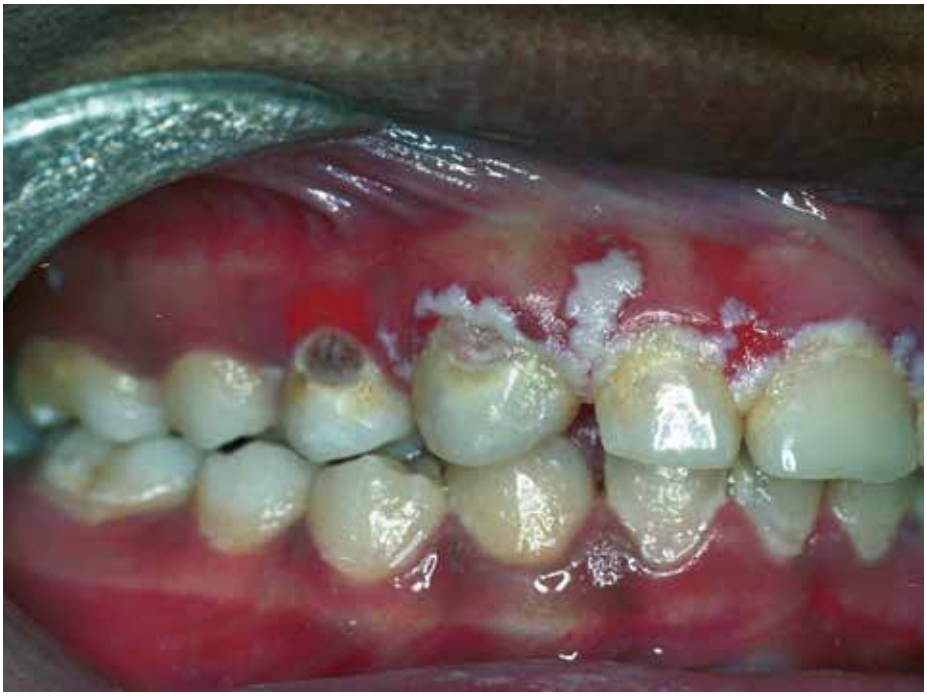

Fig. 2. Pseudomembranous Candidiasis Gingiva (with caries)

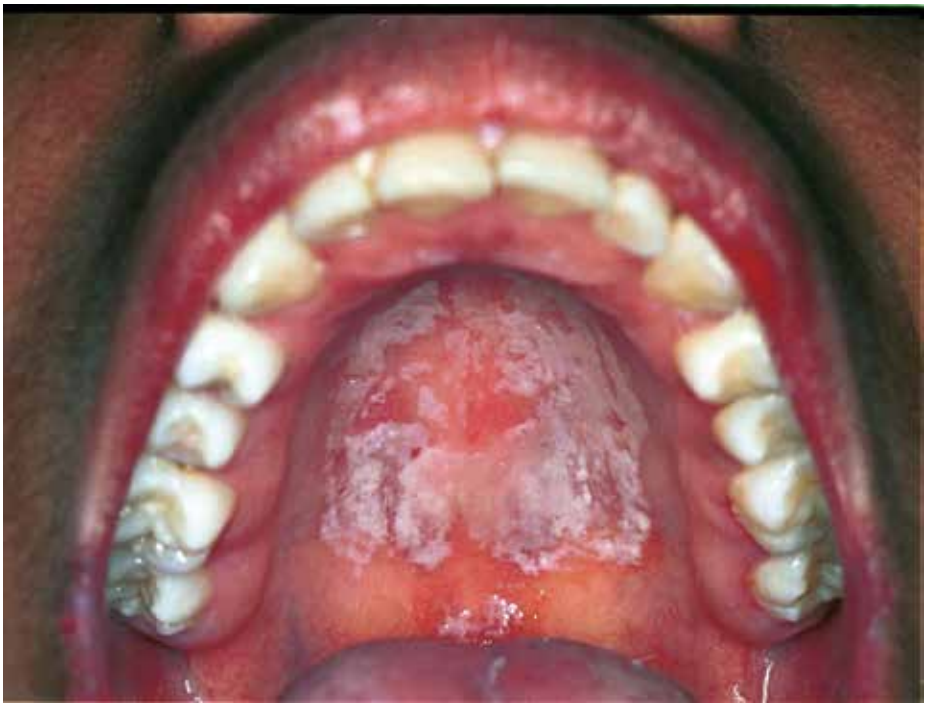

Fig. 3. Erythematous Candidiasis Palate

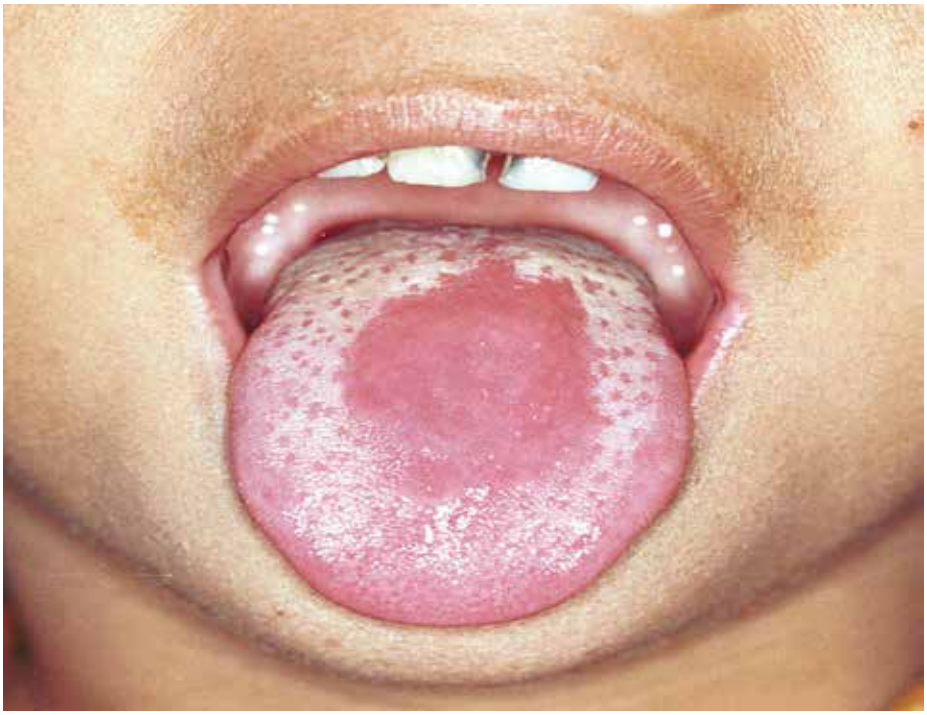

Fig. 4. Median Rhomboid Glossitis Tongue

Hyperplastic candidiasis is usually seen on the buccal mucosa as diffuse, white, adherent lesions (Figure 5). It needs to be distinguished from oral hairy leukoplakia.

Angular cheilitis presents as fissures or linear ulcers at the corners of the mouth, with varying degrees of inflammatory erythema. Hyperkeratosis may be present peripheral to the fissure. Concurrent with angular cheilitis, intraoral candidal involvement is a common clinical finding. The lesions are usually painful and slow to heal because of the repeated opening of the mouth (Figure 6).

Management: Candidiasis should be treated promptly and vigorously and early treatment is warranted, not only because of discomfort, but also because infection may spread to the pharynx and oesophagus. Either topical or systemic antifungal agents may be recommended. Topical treatments include 0.5% gentian violet aqueous solution painted in the mouth three times daily and nystatin suspension 100 000IU/Ml rinse. In severe cases apply 2% micoazole oral gel two or three times daily for ten days and suck amphotericin B lozenges 10mg six hourly for ten days.

Recurrences are common and if there is no response in one or two weeks, systemic agents may be required: Fluconazole 50-100mg daily for seven days, Ketoconazole 200-400mg daily for seven days. Itraconazole 200mg daily for seven days may be useful for azole-resistant *C.albicans* infection. Angular cheilitis is best managed with topical nystatin or for a mixed flora infection miconozole gel.

Due to the high sugar content of some formulations, topical fluoride should be used daily, if frequently prescribed. Dentures should be removed when using medication and local contributory risk factors like continuous denture wear, poor denture hygiene and xerostomia should be eliminated.

Fig. 5. Hyperplastic Candidiasis Buccal mucosa

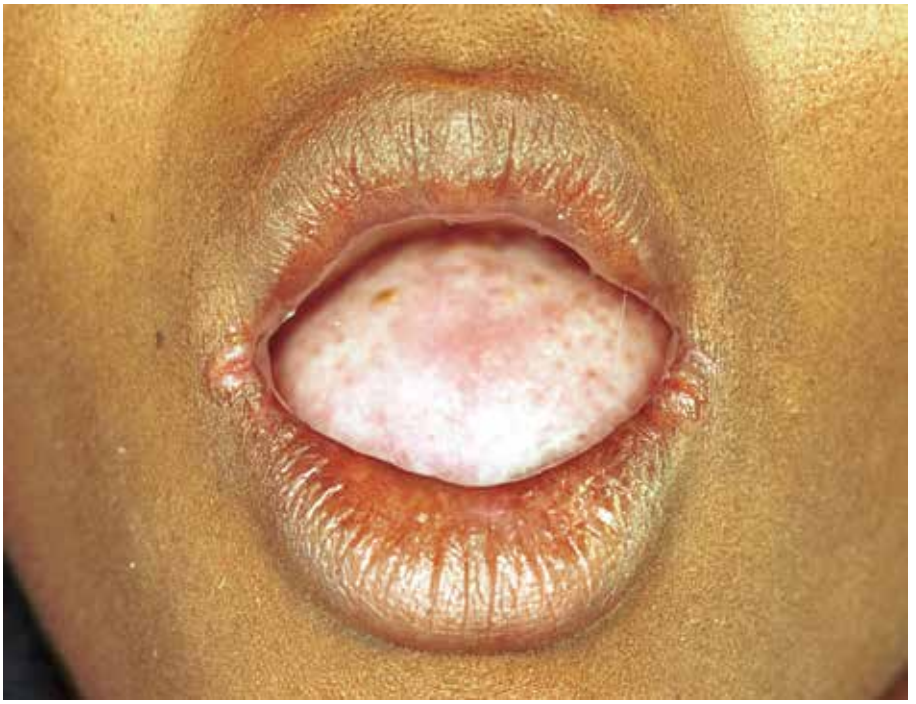

Fig. 6. Angular cheilitis

3.2 Oral hairy leukoplakia

Oral Hairy leukoplakia (OHL) usually presents as white, vertically corrugated projections on the lateral borders of the tongue, unilateral or bilateral and cannot be rubbed off (Figure 7). It is a benign, usually asymptomatic and more common in men. Studies have shown that it is associated with intraepithelial proliferation of the human herpesvirus, the Epstein-Barr virus (EBV) and that multiple strains for the virus are often present in OHL tissues (Ammatuna, 2001). OHL is the only lesions caused by EBV in which the virus replicates and is commnly shed in saliva (Sitki-Green et al., 2002).

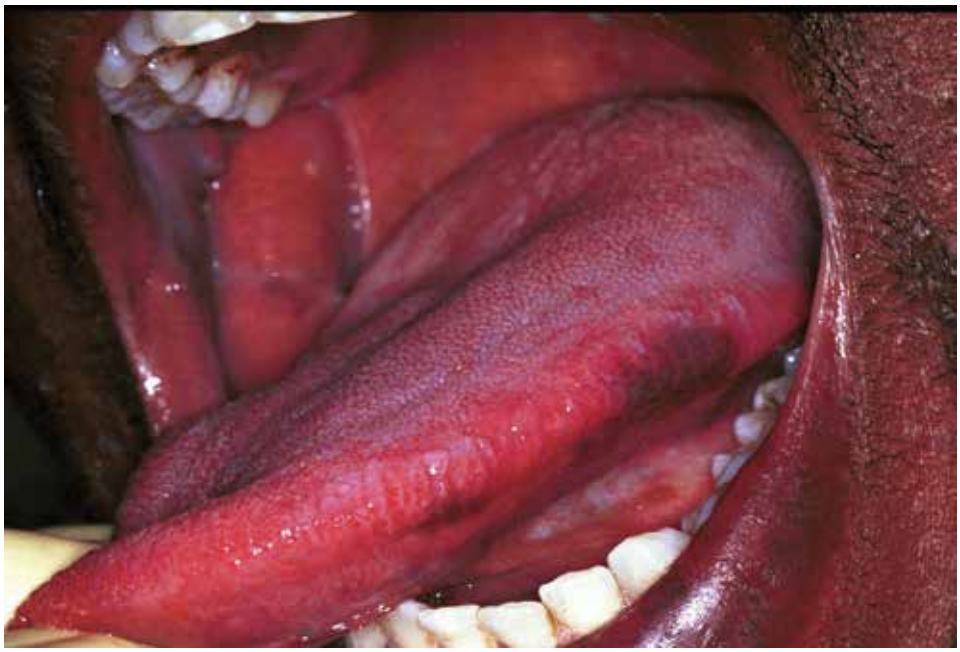

Fig. 7. Oral Hairy Leukoplakia Tongue

Although it may be a source of concern and discomfort to the patient, specific treatment is rarely indicated. Antiretroviral therapy may clear the lesions but the underlying EBV infection is rarely eliminated. Aciclovar 800mg three to five times daily for ten days may be recommended for patients complaining of discomfort. The presence of oral candidiasis and oral hairy leukoplakia in patients receiving antiretroviral medication is indicative of the failure of therapy.

3.3 Oral ulceration

People with HIV present with oral ulcerations of diverse aetiologies. The ulcers may be infectious (viral, bacterial or fungal) or atypical (aphthous or drug-induced) in nature. Herpetic stomatitis caused by the herpes simplex virus 1 (HSV) is commonly seen in HIV-infected patients and has a tendency to recur. Lesions may be seen on the gums, hard palate, vermillion border of the lips and adjacent facial skin (Figure 8). Early vesicles soon rupture to become painful irregular ulcers. In HIV-infected people, the lesions are chronic, recurrent and may progress rapidly to cause extensive mucocutaneous involvement that may persist for several weeks and extend into the oesophagus.

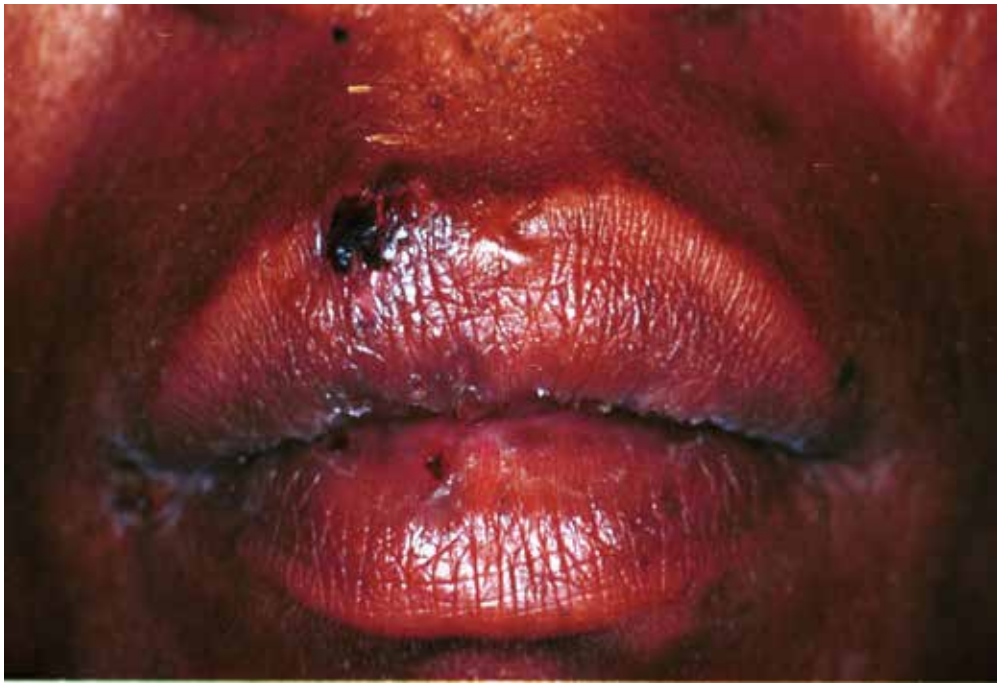

Fig. 8. Herpes Zoster (healing)

It is widely believed that herpes zoster infection (HZI) is a reactivation of latent varicella zoster virus in the dorsal root ganglia. The occurrence of the secondary form of HZI in HIV positive patients, manifests on the skin as localised, disseminated or typical generalised zoster and may herald a poor prognosis.

Aphthous ulcerations can be small or large, single or multiple (minor, major or herpetiform types). Minor aphthous ulcers are painful, round, well-circumscribed with a whitish covering surrounded by an erythematous halo, usually limited to the non-keratinised mucosa of the soft palate, buccal mucosa, tongue or tonsillar area but can occur anywhere in the mouth. Herpetiform ulcers are the least common type and are pinpoint, round and with a perilesional erythema. They are usually found in batches up to a hundred, appearing on nokeratinised mucosa such as the ventral surface of the tongue and soft palate.

Severe recurrent aphthous ulcers (RAU) may occur in the mouth, oropharynx, and oesophagus of untreated HIV/AIDS patients. Aphthous ulcers are deeper than herpetic ulcers and have a well-defined edge, unlike herpetic ulcers, which are shallower with an irregular border. Preceding vesiculation is characteristic of herpetic lesions. Large lesions are progressive, chronic and heal slowly. They often interfere with speech and swallowing and may contribute to inadequate oral intake and rapid weight loss.

Management of oral ulcerations: Early diagnosis and treatment of lesions is important as severe, long-standing, painful lesions may interfere with nutrition and hydration. Treatment is focused on providing symptomatic relief and adequate pain control is essential - paracetamol or paracetamol-codeine with topical 2% viscous lidocaine gel and analgesic mouth rinses are helpful. Herpes simplex lesions often heal spontaneously. A 0.5% gentian violet aqueous solution painted in the mouth three times daily or 1% topical povidone-iodine may be useful for small ulcers. Aciclovir is very useful if administered early – 400mg

eight hourly for five days will effectively treat large ulcers. Intravenous foscarnet has been used to treat acyclovir-resistant HSV infection. Patients sometimes have prolonged bouts and frequent recurrences that are accompanied by severe pain and local tissue destruction. Short courses of topical corticosteroids should be tried, but these ulcers may be resistant to conventional treatment. Thalidomide has been successful in some cases. Viruses may occasionally become resistant and antibiotics may be necessary to limit super-infection.
Treatment for aphthous ulcerations depends on severity of ulcerations. The ulcers respond to topical steroids like triamicinolone acetonide 0.1% in a sodium carboxymethylcellulose base given eight hourly. A 0.2% chlorhexidine digluconate mouth rinse two to four times daily or 1% topical povidone-iodine may also be useful. For large persistent ulcers beclomethasone spray (one or two puffs twice daily on the ulcer), benzydamine hydrochloride mouthwash or betamethasone 0.5mg tablets (dissolved in 15mL water) may be used as a mouthwash for three minutes daily. For longstanding, intractable ulcers, systemic steroids like prednisolone may be used, but it is important to exclude cytomegalovirus (CMV) and herpes, as steroids may exacerbate these ulcers. Recurrences must be treated aggressively. If ulcers persist despite treatment patients should be referred for a biopsy to exclude malignancy or CMV infection.

3.4 Kaposi's sarcoma

Kaposi's sarcoma (KS) is a neoplasm of putative vascular origin. It is a multifocal neoplastic proliferation of endothelail cells. Oral lesions of KS lesions are red, blue and purple and occur commonly on the posterior hard palate and the facial gingiva (Figure 9), with or without ulcerations. Lesions on the palate are associated with pulmonary KS (Pozniak et al., 1992). The African form is characterised by lymph node enlargement. If untreated, they may spread and ulcerate. The human herpes virus 8 (HHV-8) has been identified in all forms of KS and its replication in the oral cavity and viral shedding in saliva are important factors for HHV-8 transmission (Pauk et al., 2000). Recent research has suggested that in certain *in vivo* conditions, oral micoorganisms like *Porphyromonas gingivalis, Fusobacterium nucleatum* and *Prevotella intermedia* can potentially activate HHV-8 to cause disease (Morris et al., 2007).
Lesions begin as flat red macules of variable size and irregular configuration. Although they may appear as a focal lesion, typical oral KS lesions are multifocal, with numerous isolated and coalescing plaques. Eventually the lesions increase in size to become nodular growths and may involve the entire palate (Figure 10).
Nearly two-thirds of patients with oral KS have pain, discomfort or dysphagia, or complain of poor aesthetics and require treatment. In the early stages, the differential diagnosis includes pyogenic granuloma and giant cell granuloma. A biopsy is essential for a definitive diagnosis.
Management: The incidence of oral KS has decreased with the introduction of antiretroviral treatment, but remains the most common oral malignancy in people with HIV. Treatment decisions are made on the basis of the extent of the disease. The early plaque and macular lesions are painless and do not require treatment. Nodular lesions may become unsightly and interfere with mastication. Isolated oral lesions can be treated by laser or surgical excision. Intralesional injections of 1% vinblastine sulphate can cause lesions to regress, however, in some patients it produces pain and may require repeated visits before a response is achieved. Systemic chemotherapy is indicated for patients with widespread progressive disease. Radiation causes mucositis. Benzydamine hydrochloride may cause some relief and is recommended mainly when there are obstructive symptoms. Good oral hygiene and plaque control is essential to prevent secondary infection.

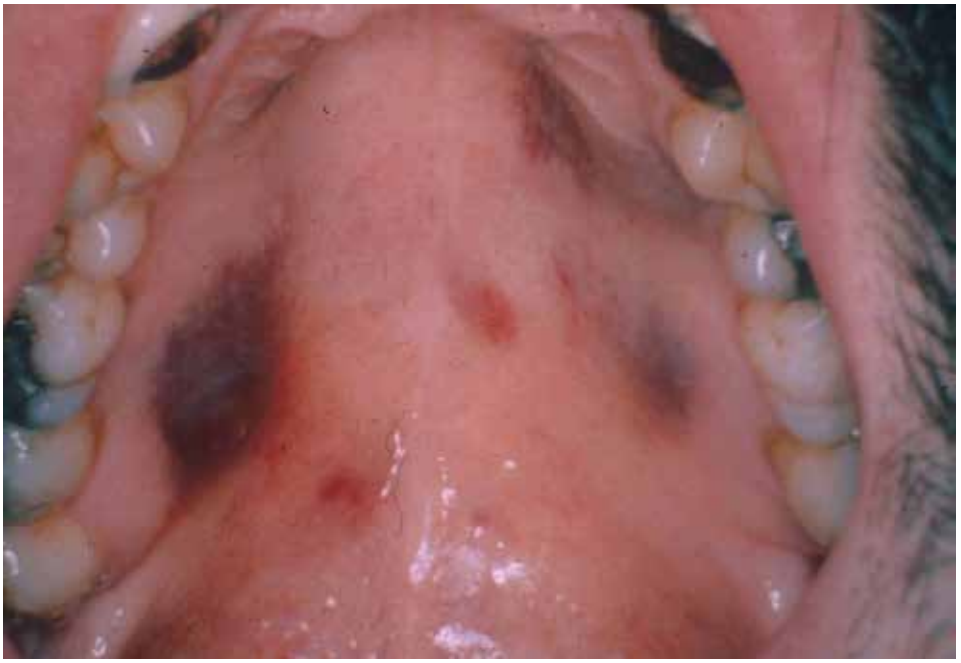

Fig. 9. Kaposi's sarcoma palate

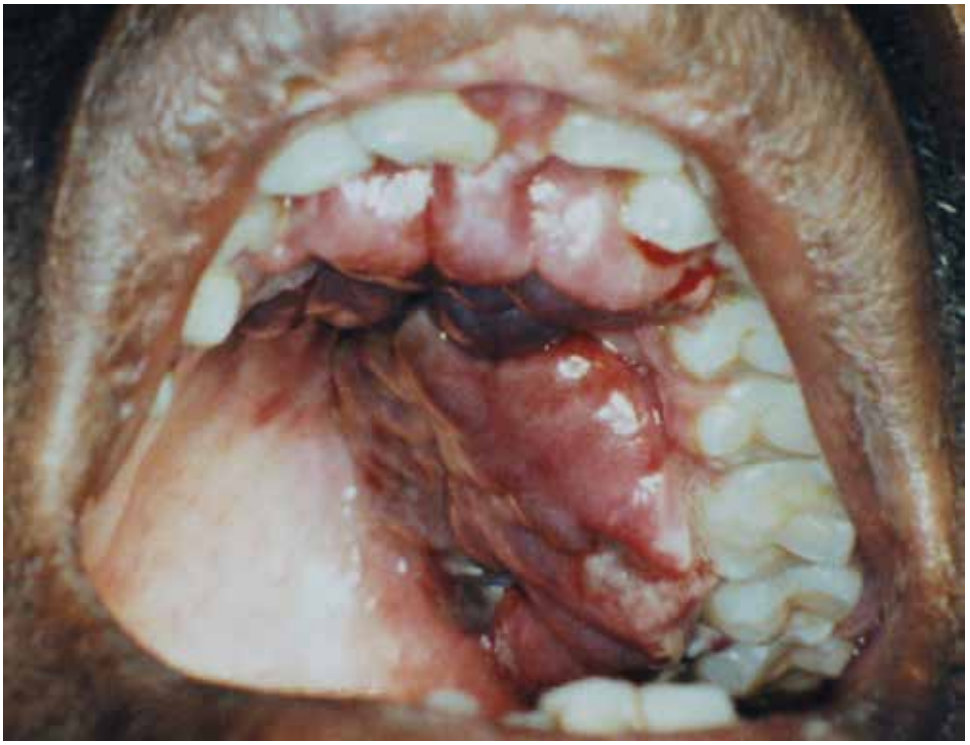

Fig. 10. Kaposi's sarcoma ulcerated

3.5 Non-Hodgkins lymphoma

Non-Hodgkins lymphoma (NHL) is the second most common malignant condition associated with HIV infection. It comprises a group of malignant lymphoproliferative diseases and is an AIDS-defining condition. Lymphomas present as focal soft oral swellings with or without ulceration. They may be red and inflamed and are commonly found on the gingival, palatal or alveolar mucosa (Cattaneo et al., 2005, Iamaroon et al., 2003). The lesions are painful and may progress rapidly. Lesions must be biopsied for a definitive histological diagnosis. Treatment requires systemic combination chemotherapy and occasionally radiotherapy. To reduce pain and interference with chewing and speaking, large exophytic or pedunculated lesions can be surgically removed. Treatment is almost always palliative. For patients with KS and lymphomas, good oral hygiene, plaque control and frequent professional cleaning needs to be encouraged to prevent the lesions becoming infected in the advanced stages. Patients on chemo- and radiotherapy require regular care and maintenance to manage specific oral complications of mucositis and xerostomia and prevent the associated increased risks of bacterial and fungal super-infections. Benzydamine hydrochloride mouth rinse may provide relief and is recommended when there are obstructive symptoms. The immune reconstitution associated with antiretroviral therapy may cause lesions to regress.

4. Gingival and periodontal lesions

The gingival and periodontal lesions associated with HIV infection include linear gingival erythema (LGE), necrotising ulcerative gingivitis (NUG), necrotising ulcerative periodontitis (NUP) and nectrotising stomatitis. Linear gingival erythema is characterized by a profound erythema of the gingival margin especially of the front teeth (Figure 11). In necrotizing ulcerative gingivitis there is destruction of one or more interdental papillae with bleeding, ulceration, necrosis and sloughing. Tissue destruction is limited to the gingival tissues and does not involve the alveolar bone. Necrotising ulcerative periodontitis is characterized by advanced necrotic destruction of the periodontium. There is rapid loss of the periodontal attachment, destruction and sequestration of bone and teeth may become mobile. It is often accompanied by severe pain and halitosis.

Several herpesvirus have been shown to be involved in periodontal disease, particularly human cytomegalovirus and EBV (Slots, 2000) - the latter being associated with destructive periodontal disease. Herpesviruses were shown to be positively associated with elevated levels of periodontopathic bacteria (Slots, 2007).

Management is based on plaque reduction and includes thorough curettage and debridement. Strict oral hygiene measures to be prescribed including meticulous brushing and flossing. A dental referral for professional scaling, local debridement, followed by sub-gingival irrigation and regular long-term maintenance is indicated. Mouth rinses and antibiotic therapy may also be indicated. A regimen of topical antiseptic agents such as 1% povidone-iodine solution and 0.2% chlorhexidine gluconate mouth rinse two or four times daily is often initiated as an adjunct therapy. This regimen should be continued until all the diseased hard and soft tissue has been removed and the patient is no longer symptomatic.

In severe cases, topical antimicrobial treatment should be supplemented by a short course of systemic antimicrobial therapy. Metronidazole 400mg 8 hourly for 5 days may be prescribed

for necrotising lesions. Clindamycin 300mg eight hourly for 7-14 days or co-amoxiclav 375mg eight hourly for five days may be used as alternatives. Mobile teeth may need to be splinted or extracted. Bony sequestrations should be removed under antibiotic cover.

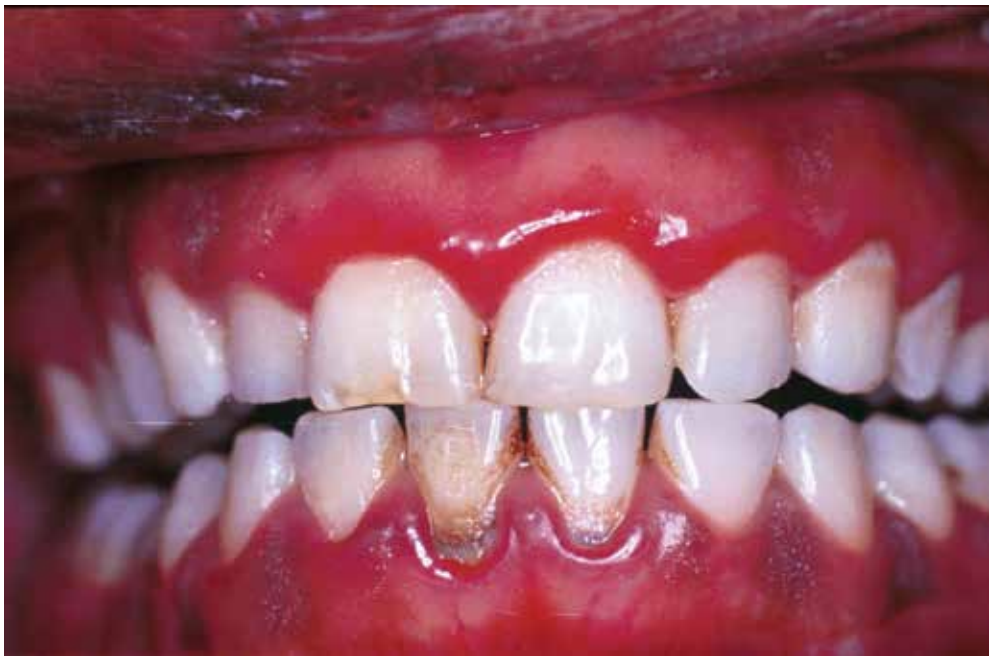

Fig. 11. Linear gingival erythema

5. Salivary Gland Disease (SGD)

Several salivary gland disorders are found in patients with HIV. Parotid gland enlargement often accompanies a syndrome of persistent generalized lymphadenopathy caused by lymphoid proliferation in response to HIV - a condition known as diffuse infiltrative lymphocytosis syndrome (DILS). Patients will DILS are at high-risk of developing lymphoma (Harris, 1999). It is associated with slow progression of the disease. Antiretroviral medication has decreased the prevalence of SGD in adults, but not in children. Parotid gland enlargement may manifest as a unilateral (Figure 12) or bilateral swelling (Figure 13) that may fluctuate in size but commonly persists. Recurrent bacterial parotitis may occur. Salivary gland disease is usually associated with reduced salivary flow and persistent dry mouth and may predispose to the development of dental caries.

Management: No definite treatment is indicated for HIV-related salivary gland disease if there is no super-infection. Oral broad spectrum antibiotics should be used in the treatment of suspected bacterial salivary gland infection. Dry mouth should be treated with salivary substitutes containing methylcellulose. Glycerine may be useful. Sugarless chewing gum should be recommended to stimulate salivary flow. A dry mouth can predispose a patient to dental caries, therefore thorough oral hygiene and the daily use of topical fluoride rinses, varnishes or gels should be recommended to prevent caries. The intake of sugar and sugary foods should be limited.

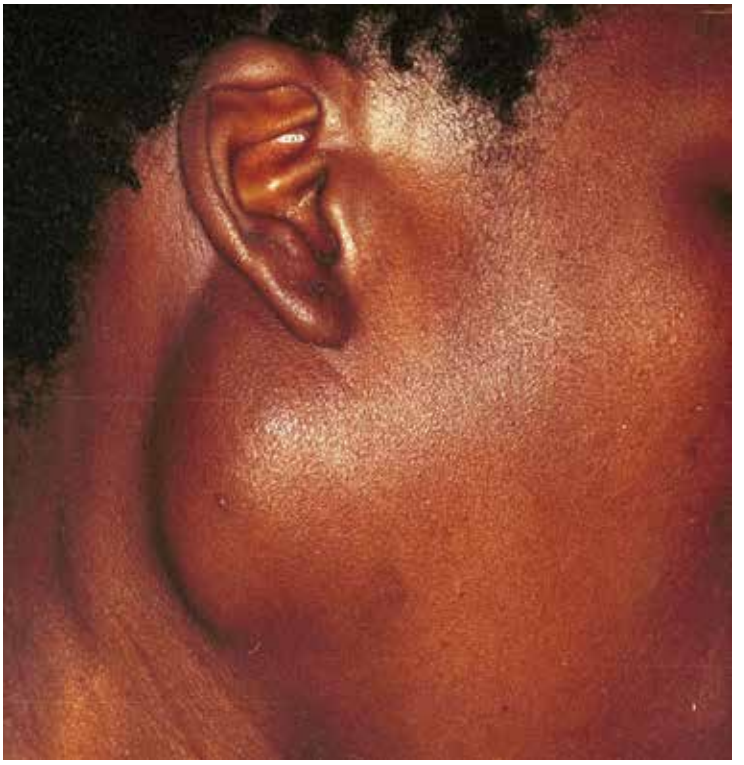

Fig. 12. Parotid gland swelling (adult)

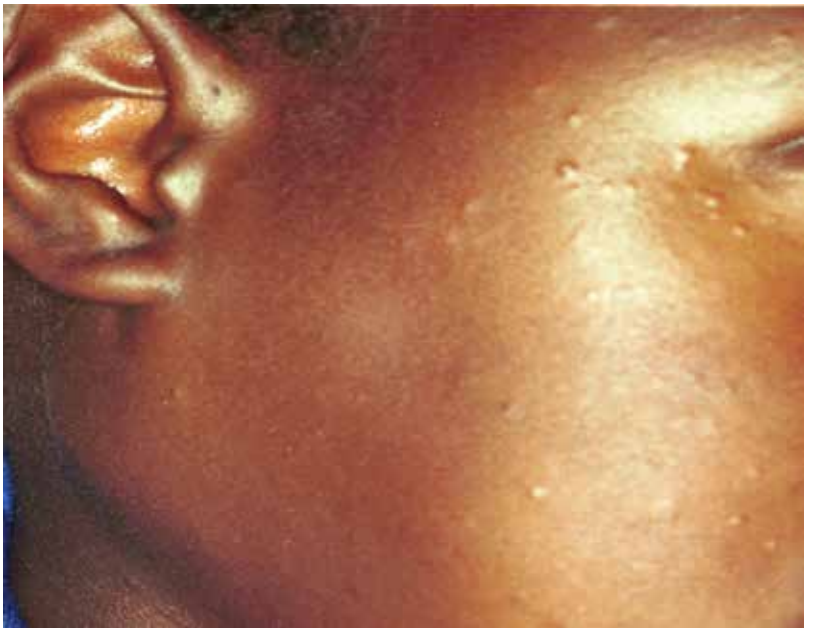

Fig. 13. Parotid gland swelling (child)

6. HPV infection and oral warts

Infections with human papilloma virus (HPV) have distinct appearances and a specific expression of an identified HPV genotype. A few HPV subtypes have been implicated with a subset of oral cancers due to their high-risk oncogenic potential (Nokta, 2008). Most cases of HPV-related oropharyngeal cancers (OPC) are caused by HPV-16 (D'Souza et al 2007) and occurs at higher rates in men who are HIV positive. HPV is particularly associated with head and neck squamous cell carcinomas of the lingual and palatine tonsils. Furthermore, the prevalence of HPV infection in the oral cavity of HIV-positive people without oral cancer was higher than those who were HIV-negative and was strongly associated with HIV infection, immuno-suppression and oro-genital contact (Kreimer et al., 2008).

The increasing prevalence of benign oral warts that has been found in patients on antiretroviral therapy has been associated with HPV-13 and HPV-32 (Greenspan et al., 2001).This was initially thought to be part of the immune reconstitution syndrome, but Lilly et al (2005) reported that the pathology of oral warts was independent of immune reconstitution. Warts are proliferative epithelial lesions and can be found anywhere in the mouth or lips and are cauliflower-like, spiked or raised with a flat surface. Most lesions are asymptomatic, but can interfere with mastication and raise cosmetic concerns. Treatment includes surgical excision, cryotherapy, laser ablation and topical application of keratinolytic agents, but they do tend to recur.

7. Oral health & HIV in children

The oral manifestations of AIDS in children are different from that of adults and can affect them more severely. Studies have emphasised the prognostic significance of oral hairy leukoplakia, Kaposi's sarcoma and Non-Hodgkin's lymphoma as AIDS-defining conditions in adults. Oral candidiasis, parotid gland enlargement, recurrent oral ulcerations and gingival and periodontal disease are the most prevalent oral manifestations commonly seen in children with AIDS.

Molluscum contagiosum is commonly seen on the face. It is caused by the poxvirus that infects the skin and is characterized by clusters of variable sized pearly-white smooth papules, showing characteristic central umbilication. It is usually self-limiting, but in severely immunosuppressed children may be extensive and disfiguring (Figure 14). Management is difficult but repeated topical applications of potassium hydroxide, silver nitrate, liquid nitrogen may be helpful. Dental manifestations include and increased prevalence in dental caries (Naidoo & Chikte, 2004), delayed eruption (Hauk et al., 2001) and over-retention of primary teeth (Flaitz et al., 2001). Children with decreased salivary flow and xerostomia should maintain thorough oral hygiene and use topical fluorides (rinses, gels and varnishes) to prevent caries. Dietary control is essential to limit the intake of sugar and sugary foods. Sugar-based medication should be avoided.

8. Oral lesions in resource poor settings

Many patients may present with any of the lesions described above that are suggestive, but not diagnostic of HIV infection. In resource-poor settings definitive diagnosis may be problematic due to lack of sophisticated diagnostic tests. While oral lesions, may serve as useful indicators not only for disease progression in untreated HIV-positive patients, or

herald failure of treatment in those receiving antiretroviral agents, it should not replace traditional tests for viral loads, CD4 counts and other pathological measurements for positive confirmation.

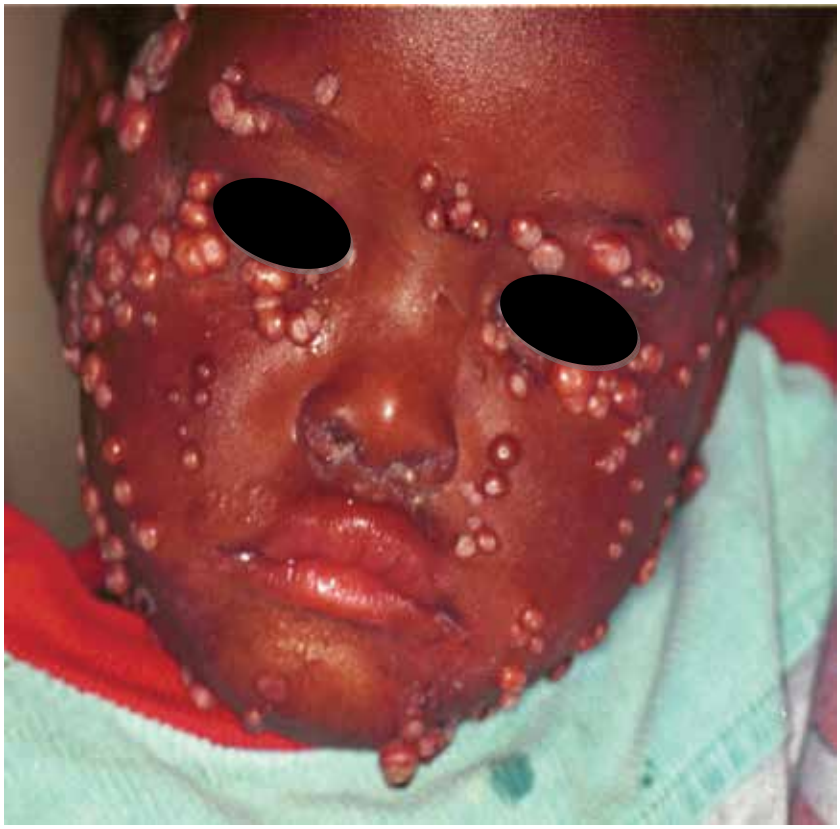

Fig. 14. Molluscum Contagiosum

Saliva has been shown to contain a variety of factors that protects against HIV infection including mucins, secretory leukocyte protease inhibitor, salivary agglutinin, defensins and secretory IgA. Mucosal IgA has been shown to exert antiviral activity by direct neutralization, blocking HIV attachment to epithelial or other target cell receptors and transcytosis of HIV across epithelial cells (Challacombe & Naglik, 2006; Kazmi et al., 2006; Weinberg et al., 2006). Collection of saliva is simple and non-invasive and in resource-poor settings or for large scale population screening, salivary tests may be used to determine HIV serostatus (Chen et al., 2007). More recently, the oral cavity has been viewed as a potentially useful site to initiate a vaccine induced oral mucosal immune response and it is thought that oral mucosal vaccines may induce cellular and humoral immune responses similar to systemic immunization (Stahl-Henning et al 2007).

9. Concluding remarks

Oral health care workers can contribute to the early diagnosis, prevention and treatment of HIV. The oral health management of HIV infected patients should focus on the provision of

dental care and treatment of the oral manifestations of the disease. Despite the fact that significant advances in the pathogenesis and management of the oral manifestations of HIV have been made, more research is required to elucidate the long-term effects of antiretroviral therapy, HPV involvement, the progression and significance of SGD and creative, innovative strategies to reduce the barriers of vulnerable populations seeking oral and general health care.

The health care worker would need to ascertain the patient's overall health status, immune status, prognosis, presence and history of opportunistic infections, risk for developing more serious opportunistic infections, current medications and their long-term survival. Usually no dental modifications are required for patients based on their HIV status. HIV-positive patients should always receive treatment which is standard in its substance (i.e. the same treatment which would be administered to HIV-negative patients) though the treatment may be non-standard in its manner (e.g. slower, more careful treatment, involving greater protective measures). Major concerns are impaired haemostatis, susceptibility to infections, drug interactions and the patient's ability to withstand the stress and trauma of the dental procedure. Treatment planning for HIV-positive patients needs to be carefully thought through and address numerous considerations.

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18

Oral Health of People with Psychiatric Disorders

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1. Introduction

1.1 What are the psychiatric disorders?

Psychiatric disorders are categorized by the Diagnostic and Statistical Manual of Mental Disorders (DSM- IV), which is published by the American Psychiatric Association and covers all mental health disorders for both children and adults. (APA, 1995) It also lists known causes of these disorders, statistics in terms of gender, age at onset, and prognosis in addition to results from some studies concerning the ideal treatment methods. The manual utilizes a multiaxial classification system to formulate the diagnosis of psychiatric patients. The five dimensions for assessment are described in Table 1.

On the fifth axis, the psychiatrist evaluates the patients' level of functioning both at the present time and the highest level within the previous year. This helps the psychiatrist recognize how the above four axes are affecting the patients and what type of changes could be detected.

According to the DSM-IV psychiatric disorders are divided into 17 major categories, including: 1.disorders usually first diagnosed in Infancy, childhood, or adolescence. 2. delirium, dementia, and amnestic and other cognitive disorders. 3.mental disorders due to a general medical condition not elsewhere classified. 4. substance-related disorders. 5. schizophrenia and other psychotic disorders. 6. mood disorders. 7. anxiety disorders. 8. somatoform disorders. 9. factitious disorders. 10. dissociative disorders. 11. sexual and gender identity disorders. 12. eating disorders. 13. sleep disorders. 14. impulse-control disorders not elsewhere classified. 15. adjustment disorders. 16. personality disorders. 17. other conditions that may be a focus of clinical attention.

1.2 Epidemiology of psychiatric disorders

There are evidences of psychiatric disorders being a rising tendency and major health problem for the modern humanity. Studies reported that the prevalence of psychiatric disorders in the Dutch population: those aged under 65 in 1996 had experienced at least one psychiatric disorder in their lifetime, among them 23.3% within the preceding year. (Bijl, Ravelli, & van Zessen, 1998)

Axis	Mean	Description	Examples
Axis I	Clinical Disorders	what we typically think of as the diagnosis	depression, schizophrenia, social phobia
Axis II	Personality Disorders	more long-lasting symptoms and encompass the individual's way of interacting with the world	paranoid, antisocial, borderline personality disorders
Axis III	General Medical Conditions	play a role in the development, continuance, or exacerbation of Axis I and II disorders	brain injury, AIDS resulting in mental illness
Axis IV	Psychosocial and Environmental Problems	events in a person's life that can affect the disorders listed in Axis I and II	death of a loved one, starting a new job, entry to college, unemployment, or marriage
Axis V	Global Assessment of Functioning	the physician's rating of the patient's level of functioning	Global Assessment of Functioning Scale, Social and Occupational Functioning Assessment Scale, Global Assessment of Relational Functioning Scale

Table 1. Five dimensions for assessment of psychiatric disorders (DSM-IV)

The one-year prevalence of major psychiatric disorder, minor psychiatric disorder, and all psychiatric disorder were 1.37 %, 4.26 %, and 5.30 %, respectively in Taiwan in 2000. (Chien, Chou, Lin, Bih, & Chou, 2004)

1.2.1 Schizophrenia

A literature search of schizophrenia-related studies in 2002 showed that 1-year and lifetime prevalence and 1-year incidence of schizophrenia were: 0.34 %, 0.55 %, and 11.1/100,000 persons respectively. (Goldner, Hsu, Waraich, & Somers, 2002)

The cumulative prevalence of psychiatric disorders increased from 0.33 % to 0.64 % from 1996 to 2001 in Taiwan. (I. C. Chien et al., 2004) Another review research indicated that the median incidence was 15.2/100,000 persons and the median lifetime prevalence was 0.72% for schizophrenia. (McGrath et al. 2004)

1.2.2 Eating disorders

Eating disorders are psychiatric disorders, which represent a clinical symptoms to oral health professionals because of their unique psychological, medical, dental patterns, and their unique features. (Aranha et al., 2008) The average prevalence for anorexia nervosa and bulimia nervosa among young females are 0.3% and 1%, respectively. (Hoek, 2006) The incidence of anorexia nervosa in women between 15 and 19 years of age was 270 per 100,000 person-years. (Keski-Rahkonen et al., 2007)

1.2.3 Depression

A systematical review on the prevalence and incidence of perinatal depression from 1980 through 2004 was carried out. The combined prevalence estimates ranged from 6.5% to 12.9% for major and minor depression, and the major depression alone from1.0 to 5.6% at different trimesters of pregnancy and months in the first postpartum year. (Gavin et al. 2005)

Eaton et al. pointed out that there has been a rise in the prevalence of depression among middle-aged females due to increasing chronicity in the U.S. between 1981 to 1993. (Eaton et al. 2007) There has been a rise in the prevalence of depression among middle-aged females in the U.S.. (Eaton, Kalaydjian, Scharfstein, Mezuk, & Ding, 2007)

1.2.4 Dementia and anxiety

The incidence of dementia was 9.2/1000 person-years in aged 65 or over in UK. (Copeland et al., 1992)

A systematic review of literature published between 1980 and 2004 reporting findings of the prevalence and incidence of anxiety disorders in the general population. This study demonstrated that 1-year and lifetime prevalence for total anxiety disorders was 10.6% and 16.6% respectively. (Somers, Goldner, Waraich, & Hsu, 2006)

1.3 The side effects and interaction of drugs for patients with psychiatric disorders

Antipsychotics

The atypical antipsychotics generally produce fewer extra pyramidal side effects than the conventional antipsychotic drugs. However, some atypical antipsychotic drug, such as Clozapine, has an associated risk of agranulocytosis and symptom of tremor at rest. (Jansen 1994; Kane et al. 1988) Clozapine also lead to hypersalivation because of the side effects of cholinergic agonists. (Arranz et al. 2000; Seeman 2004) Some atypical antipsychotics, such as Olanzapine, have not been reported to be associated with agranulocytosis, haemotoxicity, and pose minimal effect on prolactin levels. (Fulton et al. 1997) The atypical antipsychotics raise the risk of diabetes, and cardiovascular disease through antagonism at the H_1, 5-HT_{2A}, or 5-HT_{2C} receptors. The effect of elevation of serum leptin and insulin resistance also cause weight gain. (Lean and Pajonk 2003)

The atypical antipsychotics, such as clozapine, lead to hypersalivation because of the side effects of cholinergic agonists. (Arranz et al. 2000; Seeman 2004)

Anti-seizure drug

Sodium valproate, an anti-seizure drug used for treating patients with a bipolar disorder, can cause thrombocytopenia and reduce platelet aggregation response. (Jeavons et al. 1977)

Tegretol has anticholinergic effects that can cause orthostatic hypotension; thus, the use of vasoconstrictors should be restricted. The use of erythromycin or clarithromycin should be avoided to prevent the risk of Tegretol poisoning. Tegretol poisoning in patients may result in oral ulcers, sore throat, Steven-Johnson syndrome, agranulocytosis, and aplastic anemia. (Dalby 1971; Kimura et al. 1974)

Antidepressant drugs

All tricyclic antidepressants have anticholinergic effects that can cause orthostatic hypotension. (Beckmann and Goodwin 1975; Szabadi and Tavernor 1999)

Selective serotonin reuptake inhibitors (SSRIs) can cause xerostomia. SSRIs also can lead to a reduced platelet aggregation because SSRIs can prevent the resorption of serotonin. (Thase et al. 2001)
Monoamine oxidase inhibitors (MAOIs) have anticholinergic effects that cause orthostatic hypotension. MAOIs also interact with several drugs, thereby causing hypertensive crisis. (El-Ganzouri et al. 1985; Yamada and Yasuhara 2004)

Diseases	Year	Area	Prevalence/accidence	Population
Psychiatric disorders	1996	Dutch	Lifetime prevalence 23.3%	Aged <65
	2000	Taiwan	1-year prevalence: 5.30 %	Population in National Health Insurance
Schizophrenia	2001	System review 1965-2001	1-year incidence: 0.015%	
	2002	Taiwan	1-year incidence: 0.011%	Population in National Health Insurance
Eating disorders	1999	System review 1980-1999	Lifetime prevalence: 0.3 % (anorexia nervosa) Lifetime prevalence: 1% (bulimia nervosa)	Young females
	2004	Finland	Lifetime prevalence: 2.2%; 1-year incidence: 0.27% (anorexia nervosa)	Women aged 15 -19 years
Depression	2004	System review 1980-2004	Prevalence: 12.9% Prevalence: 5.6% (major)	Pregnancy and post amp women
Dementia	1992	British	Lifetime prevalence: 4.3%	Aged >64 years
Anxiety disorders	2006	System review 1980-2004	1-year prevalence: 10.6%; lifetime prevalence: 16.6%.	

(Bijl, et al., 1998; I.-C. Chien, et al., 2004; I. C. Chien, et al., 2004; Copeland, et al., 1992; Gavin, et al., 2005; Goldner, et al., 2002; Hoek, 2006; Keski-Rahkonen, et al., 2007; McGrath, Saha, Chant, & Welham, 2008; McGrath, et al., 2004; Somers, et al., 2006)

Table 2. The prevalence / incidence of psychiatric disorders

Mood stabilizer drugs

Lithium salt leads to polyuria, which often results in dry mouth. The combination of non-steroidal anti-inflammatory drugs (NSAID) increases blood levels of lithium, which may lead to an lithium toxicity.(Corena-McLeod et al. 2008)

Classification	Side effects	Interaction
Antipsychotics		CNS depressant
-Typical	Extrapyramidal symptoms - Acute dystonia - Pseudo parkinsonism - Akathisia - Tardive dyskinesia - Neuroleptic malignant syndrome	
-Atypical	Anticholinergic effect Agranulocytosis Tremor Drowiness	
Antidepressant - Monoamine reuptake inhibitors - Monoamine oxidase inhibitors (MAOI)	Orthostatic hypotension Anticholinergic effect Hyper stimulation Insomnia Anticholinergic effect Impotence or anorgasnia	Hypertensive crisis with tricyclic antidepressants
Mood stabilizer drugs		
-Lithium salt	Polyunia Tremor Weight gain Oedema	Plasma concentration with Erythromycin
Anxiolytic	Drowsiness Excessive somnolence Impaired intellectual function Reduced motor coordination Impaired memory and recall	CNS depressant

Table 3. The side effects and interaction of drugs for patients with psychiatric disorders

1.4 Social stigma of psychiatric disorders

The stigma on people with psychiatric disorders is extensive among this population. Such stigma varies in nature and frequency in different psychiatric disorders. The stigma harms the self-esteem of many people who have serious psychiatric disorders. Negative opinions indiscriminately are likely to overstress the social handicaps together with psychiatric disorders. (Crisp, Gelder, Rix, Meltzer, & Rowlands, 2000) Corrigan et al. reported that two factors that may influence whether a person who might benefit from mental health treatment, such are public stigma and self-stigma. (Corrigan et al. 2003)

1.5 Psychiatric disorders and health-related quality of life (QoL)

Most people with psychiatric disorders can obtain the necessary care services to live normally in the community. They use the outreach support skills provided by institutions to help them in the transition to community living.(A. A. Pinkney, 1991) A poor mental health could result in a poor perception of health-related QoL. A patient-centered, routine assessment of QoL provides a supplemental measure that may help improve the understanding of the effects of psychiatric disease on an individual's life.(Llewellyn, Warnakulasuriya, Llewellyn, & Warnakulasuriya, 2003) Health-related QoL is an important outcome index of mental health. Therefore, a rehabilitation protocol that takes into account the financial situation, family support, and social functioning of patients is essential. (Chan et al., 2007)

2. The oral health status and problems of people with psychiatric disorders

2.1 Prevalence and incidence of oral health problems in patients with psychiatric disorders

The oral health status of people with psychiatric disorders is not desirable in general, but there are also significant variations indicating potential of prevention and improvement. The results of several relevant studies are summarized in table 4.

2.2 Factors associated with poor oral health status among people with psychiatric disorders

There are many factors associated with poor oral health status among people with psychiatric disorders. Gender differences between oral health and psychiatric disorder have been reported. (G. M. Eugenio Velasco, Angel Martinez-Sahuquillo, Vicente Rios, Juan Lacalle, Pedro BulloAn,, 1997) Factors such as age and the length of stay in institutions seem to be associated with the oral health of psychiatric patients. (G. M. Eugenio Velasco, Angel Martinez-Sahuquillo, Vicente Rios, Juan Lacalle, Pedro BulloAn,, 1997; Italo Francesco Angelillo, 1995; Kumar, Chandu, Shafiulla, & Kumar, 2006; Rekha et al., 2002; Tang et al., 2004) Researches also reported that severity of psychiatric disorders was related with oral health. (Italo Francesco Angelillo, 1995; Kumar et al., 2006; Thomas, Lavrentzou, Karouzos, & Kontis, 1996) The typical antipsychotics, which are part of a wide array of medications used for schizophrenia treatment, may cause manifest hypo-salivation by blocking the parasympathetic stimulation of the salivary glands. This is likely to intensify the progression of dental diseases. (Friedlander & Marder, 2002; Thomas et al., 1996) Xerostomia is a significant risk factor which influences the oral health of patients with psychiatric disorders. (Hede, 1995; Locker, 2003)

Country / Area	Samples	CPI*	Oral health Index	Dental treatment needs
Italy (Angelillo et al. 1995)	297, Mean age 55.1	0: 0.9% 1: 4.6% 2: 10.1% 3: 19.6% 4: 64.8%	DMFT# 15.5 Exp@: 100% Ed $: 11.1%	Ext%:80.7%; Con&: 58.3%
South Africa (Rudolph and Chikte 1993)	240 males	0:0 4: 17%	Exp: 88% DMFT: 7.92	Con: All age groups
Spain (Velasco et al. 1997)	565, Mean age 58.0		DMFT: 24.9	
Spain (Velasco and Bullon 1999)	565	0: 8.5% 1:14.2%, 2:43.8% 3:24.6% 4:8.9%	Ed: 31.7%	
India (Kenkre and Spadigam 2000)	128, Mean age 25		Exp: 88% Ed: 3.9%	Con: 88%
UK (Lewis et al. 2001)	326, Mean age 71.1		DMFT:19.1 Ed: 63%	
India (Rekha et al. 2002)			Exp: 75.5%	
Israel (Ramon et al. 2003)	431, Mean age 54.0		DMFT: 26.7	
HK (Tang et al. 2004)	91, Mean age 44.7	4: 28.2%	DMFT>15	Con: 78.8%, Ext: 54%
Israel (Zusman et al. 2010)	254		Exp: 98.4% DMFT: 23.8 Ed: 26%	

* Community Periodontal Index
# No. of teeth with decay, missing, or filling
@ Caries experience
$ Edentulism
% Extraction
& Conservative treatment

Table 4. The oral health status of people with psychiatric disorders

3. Oral health care for people with psychiatric disorders

Oral health programs for people with psychiatric disorders are rare. Researchers have demonstrated the feasibility and efficacy of the combination of mechanical toothbrush, dental instructions and reminders which resulted in additional improvements for the oral health of people with psychiatric disorders. (Almomani et al., 2006) Studies also showed that people with psychiatric disorders receiving motivational interviewing (MI) had significantly better oral health than those receiving oral health education only. Furthermore MI has been shown to be effective for enhancing short-term oral health behavior change for people with severe mental illness. (Almomani, Williams, Catley, & Brown, 2009)

3.1 Barriers to oral health care for people with psychiatric disorders

Most oral health professionals have limited experiences in providing care for people with psychiatric disorders. (Waldman, Perlman, Waldman, & Perlman, 2002) The barriers exist in organization and financing of the care needed as well as in proposing strategies to enhance the delivery of appropriate treatment. (Ridgely, Goldman, & Willenbring, 1990)

General health services are widely utilized by people with psychiatric disorders under psychiatric care in long-term care institutions. However, oral health services remain underutilized, and there is a high prevalence of perceived barriers to receiving dental care in this population. (Dickerson et al., 2003)

3.2 Special requirements of oral health care delivery system for people with psychiatric disorders

Psychiatric disorders have psychopathological characteristics. In particular, there are specific oral health care requirements and management models for patients with psychiatric disorders. (Clark, 1992) These major requirements for people with psychiatric disorders include prophylaxes, calculus removal, and periodontal therapy Patients' dental treatment needs vary depending on several demographic factors, length of stay in institutions and the patient's psychiatric diagnosis. (Barnes et al. 1988)

4. Implications for the oral health policies

Since the psychiatric health care system has not yet been fully established in some countries, patients with psychiatric disorders there are not likely to obtain the necessary care in their communities. Individuals suffering from severe psychiatric disorders may be able to attain a more dignified life if they could avail themselves of personalized, private, and high quality care services in pertinent institutions. To stay in long-term care institutions is, perhaps, the alternative solution to living in the community. Therefore, the reform of institutions, particularly for the provision of relevant services and continued care, can compensate for a little imparity of dental care for these patients, and is a more practical solution than de-institutionalization of patients with psychiatric disorders. (Chu et al. 2010)

Being not life-threatening in most cases, oral diseases have obvious impacts on patients' quality of life. However, patients with psychiatric disorders also suffer from stigma outside and inside themselves. They are vulnerable to oral diseases due to their limited ability/motivation to take care of themselves and also to the side effects of medications

prescribed for treating their psychiatric disorders. Despite of the increased needs for dental prophylaxes and care, oral health care programs for psychiatric patients are rare, underutilized and receiving less attention from the public sectors.

In addition to boost oral health services provided for patients with psychiatric disorders in the community, it is important for the health policy-makers to support oral health promotion programs. The programs will aim at the patients and their families/carers to empower their belief that oral health is essential and attainable through their own efforts. The government should initiate on-the-job education programs for the dental and psychiatric professionals to enhance their capability and motivation to provide proper services to their psychiatric patients' oral health through integrated efforts. Oral health is an essential part of general health, and it is certainly true for patients with psychiatric disorders.

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19

Structural Changes on Human Dental Enamel Treated with Er:YAG, CO_2 Lasers and Remineralizing Solution: EDS Analysis

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1. Introduction

It has been reported that common lasers employed for caries prevention on the enamel surface include CO_2 and Er:YAG types (Ana, et al., 2006); however, CO_2 lasers appear to be more appropriate for preventing dental caries (Rodrigues, et al., 2004). The irradiation of teeth with a laser results in an interaction between the light and the biological constituents of the dental hard substance. In the case of absorption by the specific components of the dental enamel, the irradiated energy is converted directly into heat. This thermal effect is the cause of the structural and chemical changes occurring in the enamel after laser irradiation (Apel, et al., 2002).

The association of laser irradiation with fluoride has demonstrated the best results in the inhibition of caries development. The combined treatment of laser irradiation with fluoride propitiates an expressive fluoride uptake, reducing the progression of caries-like lesions, and this treatment is more effective than laser or fluoride alone. The available data suggest that lasers combined with fluoride are a promising treatment in caries prevention (Ana, et al., 2006). In the same way, the effect of remineralizing solution has been evaluated on caries formation and its progression in the primary tooth enamel. Remineralizing solution has been considered an effective measure for the prevention of white spot lesions because it has the ability to provide mineral sources of calcium (Ca), phosphate and fluoride to demineralized or hypomineralized enamel surfaces, making them less soluble during cariogenic challenges (Westerman et al., 2006). Caries prevention has been evaluated by several techniques, including atomic absorption spectrometry (to obtain Ca and P (phosphorus) concentrations liberated into acid solution), polarized light microscopy (to determine lesion depth) and SEM (to examine morphological changes). However, only minimal research has focused on enamel chemical composition after laser irradiation and acid dissolution. For this purpose, FT-Raman microscopy, X-ray photoelectron spectroscopy (XPS) and energy dispersive spectroscopy (EDS) have been used.

Energy dispersive spectroscopy (EDS) is an analytical technique that allows the detection of the elements present in the studied material. It is very versatile and can be used with any type of solid sample, from metals and ceramics to biological tissues. It is usually coupled with an electron microscope to simultaneously observe the exact area of interest from which the signal will be collected.

EDS analysis provides a specific method to determine the concentration of chemical elements on substratum surfaces, and it has been largely used in engineering and chemistry, but its application has not been widespread in dentistry (Paradella et al., 2008). At first, EDS analysis was introduced into dental research for the basic characterization of restorative dental materials used to repair damaged teeth and/or replace missing teeth (Marshall et al., 1988). More recently, this technique has been used to assess structural changes in tooth surfaces produced by the application of dental materials (Caltabiano, et al., 1996; Papagiannoulis, et al., 2002; Rosin-Grgewt, et al., 2006; Weerasinghe, et al., 2007; Della, et al., 2008; Markovic, et al., 2008; Paradella, et al., 2008; Scougall-Vilchis, et al., 2009; Keinan, et al., 2010) and of laser irradiation (Rodríguez-Vilchis, et al., 2010; Rodríguez-Vilchis, et al., 2011).

The purpose of this chapter is to present the use of EDS as a useful technique for dental research, taking as references previous reports on this area of the knowledge. Additionally, the authors present original research, based on the application of EDS to assess the microstructural changes on the enamel surface achieved through the application of two types of dental lasers and a remineralizing solution, to avoid the development of white spot lesions as a side effect of orthodontic treatment.

2. Enamel structure

To comprehend the nature of the structural changes in human dental enamel treated with Er:YAG and CO_2 lasers and remineralizing solution, it is important to understand the structure of untreated human dental enamel.

Tooth enamel, the hardest mineralized human tissue, (Harris & García-Godoy, 1999; Wang, et al., 2005), is composed almost exclusively (more than 95 wt%) of hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAP) (Pan, et al., 2008), with incorporated trace elements (Reitznwrová, et al., 2000). However, enamel is also porous, with the inorganic component representing only 87% of the total volume. This fact means that approximately 13% of the volume of enamel is composed of organic material (matrix). This organic, protein-rich matrix is mainly water (11 percent of the total volume of enamel) (Harris & García-Godoy, 1999).

Apatite-like crystallites are highly organized hierarchical structures, and scanning electron microscopy (SEM) of enamel surfaces shows well-organized, rod-like apatite crystals, bundled in ordered prisms and elongated in their *c*-axis directions, which lie predominantly parallel to the rod axes. Despite these complex hierarchical structures, the basic building blocks for mineralized tissues are of nanoscale dimensions (Wang, et al., 2005; Pan, et al., 2008).

The hydroxyapatite crystals are oriented by a protein network that makes up the enamel matrix (Harris & García-Godoy, 1999). Amelogenin proteins constitute the primary structural entity of the extracellular protein framework of the developing enamel matrix (Wang, et al., 2005). Although enamel is not considered a living tissue because it has no cells or blood vessels, the overall protein network facilitates the diffusion of fluids, ions and small-sized molecules throughout the enamel (Harris & García-Godoy, 1999). The principal

elements found in enamel are Ca, P, sodium (Na), magnesium (Mg) and chlorine(Cl), and their mean concentrations are 37% Ca, 18% P, 0.4% Mg, 0.7% Na and 0.28% Cl (Reitznwrová, et al., 2000). Other elements reported to be consistently at or above the 1000-ppm level are Zinc (Zn) and silicon(Si), although some 40 other elements are known to be present in small and widely varying amounts (Eanes, 1979).
Ca and P are two biologically abundant elements, and P is an element shared by the collagen that directs biomineral precipitation. Apatite is a "sparingly soluble salt," making it a safe reservoir for Ca and P for use in other biological functions. Apatite's properties can be tailored to some extent through its ability to accept a wide range of chemical substitutions, each of which affects its chemical and physical properties. The most important property is apatite's extensive carbonate substitution, which controls lattice strain, solubility, the nature of substitution, and perhaps apatite's maximum crystal size (Pasteris, et al., 2008).

3. Incipient caries lesions around brackets

One common negative side effect of orthodontic treatment with fixed appliances is the development of incipient caries lesions around the brackets (Behnan, et al., 2010).
The demineralization of enamel adjacent to orthodontic brackets is a significant clinical problem. It has been reported that there is a significant increase in the prevalence and severity of enamel demineralization after orthodontic treatment when compared with untreated control subjects. The overall prevalence of white spot lesions among orthodontic patients has been reported as anywhere between 2 and 96 percent.
Once active orthodontic treatment has been completed, the demineralization process is normally expected to decelerate due to changes in local environmental factors. Some white spot lesions may remineralize and return either to normal or at least to a visually acceptable appearance. However, white spot lesions may also persist, resulting in aesthetically unacceptable results. In severe cases, restorative treatment may be required (Sudjalim, et al., 2006).

3.1 Etiology and development

It usually takes a period of months or even years for a carious lesion to develop; dental caries is not simply a continual, cumulative loss of mineral, but rather a dynamic process, characterized by alternating periods of demineralization and remineralization (Harris & García-Godoy, 1999). White spot lesions develop as a result of a dietary carbohydrate and saliva-modified bacterial infection (*Streptococcus mutans*), resulting in an imbalance between demineralization and remineralization of the enamel (Sudjalim, et al., 2006).
Demineralization is the dissolution of the calcium and phosphate ions from the hydroxyapatite crystals, which are lost into the plaque and saliva. In remineralization, calcium, phosphate, and other ions in the saliva and plaque are redeposited onto previously demineralized areas (Harris & García-Godoy, 1999). This is an interrupted process, with periods of remineralization and demineralization occurring (Sudjalim, et al., 2006). It is possible to have demineralization and remineralization occur without any loss of tooth mass (Harris & García-Godoy, 1999). However, depending on the state of the oral environment in terms of the prolonged accumulation and retention of bacterial plaque on the enamel surface, the standard of individual oral hygiene and the inherent resistance of that person (Sudjalim, et al., 2006), a lesion can result when the cumulative, negative mineral balance

exceeds the rate of remineralization over an extended period (Harris & García-Godoy 1999).

The incipient lesion is macroscopically evidenced by the appearance of an area of opacity – the so-called white spot lesion. During this stage, the carious process can be arrested or reversed (Harris & García-Godoy, 1999). A white spot lesion is the precursor of frank enamel caries (Sudjalim, et al., 2006). The most important fact is that the surface of the enamel is relatively intact, before any physical cavitation requiring clinical intervention has occurred (Harris & García-Godoy, 1999). The white appearance of early enamel caries is due to an optical phenomenon that is caused by mineral loss in the surface or subsurface enamel. Enamel crystal dissolution begins with subsurface demineralization, creating pores between the enamel rods. The resulting alteration of the refractive index in the affected area is a consequence of both surface roughness and loss of surface shine and of alterations in internal reflection, all resulting in greater visual enamel opacity, as porous enamel scatters more light than sound enamel. The demineralization process may encompass the full thickness of the enamel and some of the dentin before the relatively hypermineralized surface layer is actually lost.

It is generally accepted that the insertion of fixed orthodontic appliances creates stagnation areas for plaque and makes tooth cleaning more difficult. The irregular surfaces of brackets, bands, wires and other attachments also limit naturally occurring self-cleansing mechanisms, such as the movement of the oral musculature and saliva. This process, in turn, encourages a lower plaque pH in the presence of carbohydrates and accelerates the rate of plaque accumulation and plaque maturation (Sudjalim, et al., 2006).

The normal formation of a white spot lesion is usually a slower process, which can take 2 years or more. In other cases, such as seen in the xerostomia that follows head and neck radiation, lesions take at least 6 months to develop (Harris & García-Godoy, 1999). However, in patients under fixed orthodontic treatment, demineralized lesions have the potential to develop within 4 weeks of the initiation of the orthodontic treatment (Gorton & Featherstone, 2003; Staud, et al., 2004).

3.2 Prevention of white spot lesions

The development of white spot lesions during fixed-appliance orthodontic treatment can be prevented.

The chosen method or methods for prevention vary from patient to patient, depending on individual needs, available methods and the dentist's clinical criteria. However, the patient's motivation plays a very important role to be considered.

The available methods and techniques have focused primarily on patient education and topical fluoride administration, including the use of fluoride toothpaste, mouth rinses and gels, fluoride varnishes, fluoride in orthodontic bonding agents, fluoride in elastomeric modules and ligature ties. More recently, casein phosphopeptide-amorphous calcium phosphate and laser irradiation on the enamel surface have been introduced for preventive purposes (Schmit, 2002; Sudjalim, et al., 2006; Dun, 2007).

The aim of modern dentistry is the early prevention of tooth decay, rather than invasive restorative therapy (Hannig & Hannig, 2010; Cochrane, et al., 2010). However, despite tremendous efforts to promote oral hygiene and fluoridation, the prevention and biomimetic treatment of early caries lesions are still challenges for dental research and public health, particularly for individuals at high risk for developing caries, which is the most widespread oral disease (Hannig & Hannig, 2010).

The overall management of white spot lesions involves the consideration of methods of preventing desmineralization and also methods of encouraging the remineralization of existing lesions. Preventive measures take precedence, due to the challenging nature of treating patients who do develop significant numbers of white spot lesions. In addition to regular professional oral hygiene visits and the application of appropriate preventive medicaments, successful preventive strategies should involve oral health promotion, patient education and patient compliance (Sudjalim, et al., 2006).

4. Laser technology

4.1 General principles

The word "laser" is an acronym for light amplification by stimulated emission of radiation. Lasers have their basis in certain theories from the field of quantum mechanics, initially formulated during the early 1900s by the Danish physicist Niels Bohr, among others. Einstein's atomic theories on controlled radiation can be credited as the foundation for laser technology. Einstein's article on the stimulated emission of radiant energy, published in 1917, is acknowledged as the conceptual basis for amplified light (Sulewski, 2000).

A beam of light is composed of packets of photons, which are produced by a light bulb or other light sources (Stabholz, et al., 2003). The process of lasing occurs when an excited atom is stimulated to emit a photon before the process occurs spontaneously. Spontaneous emission of a photon by one atom stimulates the release of a subsequent photon and so on (Aoki, et al., 2004).

A laser beam implies stimulated emission of radiation and differs from conventional light source. It has a single wavelength (monochromatic) and is collimated (very low divergence), coherent (photons in phase), and intense. The construction of a light source, based on stimulated emission of radiation, requires an active medium, which is a collection of atoms or molecules. The active medium must be excited to emit the photons by stimulated emission; it may be a gas, liquid, or solid material and may be contained in a glass or ceramic tube (Stabholz, et al., 2003). The photon emitted has a specific wavelength that depends on the state of the electron's energy when the photon is released. The characteristics of a laser depend on its wavelength (Aoki, et al., 2004). When tissue is irradiated, four basic types of laser interaction occur: reflection from tissue, scattering within tissue, absorption by tissue and transmission to the surrounding tissues (Aoki, et al., 2004; Stabholz et al., 2003). Transmission of light passes energy through the tissue without interaction and thus causes no effect or injury. When scattered, light travels in different directions, and energy is absorbed over a greater surface area, producing less intense and less precise thermal effects. Reflection results in little or no absorption and, subsequently, no thermal effect on the tissue. When absorbed by tissue, light energy is converted into thermal energy. A single laser device cannot perform all the required functions because the beam is absorbed or reflected according to its wavelength and the color of the object impacted (Stabholz, et al., 2003).

4.2 Laser technology development

The first laser device was created in 1960 by Maiman, and since then, the laser has been used in various areas of medicine, particularly in ophthalmology, otolaryngology, dermatology and surgery (Sulewski, 2000; Ishikawa et al., 2004).

In 1964, laser was introduced for use in dentistry by Stern, Sognnaes, and Goldman and by Hornby, Meyer and Goldman (Ishikawa et al., 2004). The first laboratory tests in vitro were carried out by Stern and Sognnaes and were limited to the use of ruby laser (Stern & Sognnaes, 1972). Then, due to technological advances, new lasers, such as argon ion, Nd:YAG, and CO_2 lasers, among others, were developed (Parker, 2007a). In time, other laser wavelengths, such as holmium (Ho):YAG and erbium (Er):YAG, were investigated.

Historically, the first lasers to be marketed for intraoral use were generally CO_2 lasers, with otorhinolaryngologic clearances authorized by the US Food and Drug Administration (FDA). During the 1970s and 1980s, intraoral use of CO_2 lasers was confined primarily to specialists, such as ear-nose-throat (ENT) surgeons, oral surgeons, and some periodontists.

It was not until 1990 that the field of laser dentistry began in earnest in the United States, at least in clinical terms. In May 1990, the FDA approved for intraoral soft tissue surgery a pulsed Nd:YAG laser, developed by Myers and Myers and recognized as the first laser designed specifically for general dentistry.

The use of lasers for therapy has become very common in the medical field, and the use of lasers in dentistry is extensive and covers many procedures, such as intraoral soft tissue surgery, hard tissue applications (e.g., caries removal, inhibition and detection, cavity preparation, etching, bleaching, calculus removal, bone ablation, cartilage reshaping, dentin desensitization, analgesia), composite curing, bracket debonding, allow welding, removal of canal debris, performing pulp capping, pulpotomy, and pulpectomy. Other dental applications include laser diagnostic, holography and biostimulation (Sulewski, et al., 2000; Dederich & Bushick, 2004).

4.3 Laser and caries prevention

In the 1960s, Stern et al. reported increased enamel acid resistance after ruby laser irradiation (Stern, et al., 1966). Since then, several studies on caries prevention have been published due to the development of several types of lasers, such as CO_2, (Stern & Sognnaes, 1972; Featherstone, et al., 1998; Hsu, et al., 2000; Tisai, et al., 2002; Kato, et al., 2003; Klein, et al., 2005; Steiner-Oliveira, et al., 2006), argon (Westerman, et al., 2002; Nammour, et al., 2005), Nd:YAG (Bahar & Tagomori, 1994; Hossain, et al., 2001a), and Diodo (Kato, et al., 2006) and more recently with the group of erbium lasers: Er, Cr:YSGG and Er:YAG (Kayano, et al., 1989; Fried, et al., 1996; Hossain, et al., 2001b; Apel, et al., 2004).

There are various theories to explain the reduced acid solubility of dental enamel after heating. For instance, the water permeability of dental enamel has been observed to be lower after heating. More hydroxide and pyrophosphate, but less carbonate, are also generally found, in comparison with unheated enamel (Apel, et al., 2002).

The most accepted theory regarding the mechanism by which laser irradiation enhances enamel acid resistance is the reduction of bound carbonate, when the enamel surface is heated to the range of 100–400°C (Holcom & Young, 1980; Fowler & Kuboda, 1986; Liu & Hsu, 2007). Nevertheless, the modification of organic matter has been reported as one of the mechanisms in laser-induced caries prevention (the organic blocking theory) (Ying, et al., 2004).

In laser therapy, several factors related to exposure need to be considered: the wavelength and energy density of the laser, the irradiation time, the focal distance, and water cooling

(Morioka, et al., 1991; Fried, et al., 1996; Featherstone, et al., 1998; Hossain, et al., 2000; Young, et al., 2000; Hsu, et al., 2000; Tisai, et al., 2002; Kato, et al., 2003; Matson, et al., 2002; Apel, et al., 2002, 2004, 2005; Rodrigues, et al., 2004; Westerman, et al., 2002; Nammour, et al., 2005 Cecchini, et al., 2005; Liu, et al., 2006; Fried, et al. 2006; Castelan, et al., 2007).

Furthermore, to achieve additional prevention, special attention has focused on laser irradiation, topical fluorides and remineralizing solution associations, showing very promising results (Hossain, et al., 2002; Delbem, et al., 2003; Chin-Ying, et al., 2004; Tepper et al., 2004; Rodrigues, et al., 2004; Kwon, et al., 2005; Ana, et al., 2006; Westerman, 2006; Tagliaferro et al., 2007).

4.4 Er:YAG laser

In 1975, Zharicov introduced the erbium-doped: yttrium-aluminum-garnet (Er:YAG) laser. The active medium of this laser is a solid crystal of yttrium-aluminum-garnet that is doped with erbium. This type of laser generates light with a wavelength of 2.94 μm (2.940 nm), in the near- and mid-infrared spectral range and close to the border-infrared and mid-infrared. Furthermore, it is highly absorbed by water because its wavelength coincides with the large absorption band for water. The absorption coefficient of water for the Er:YAG laser is theoretically 10 times higher than that of the CO_2 laser, i.e., 10.6 μm (10.600 nm), and 15.000 to 20.000 times higher than that of Nd:YAG (1.064 nm) (Ishikawa, et al., 2004).

The pulsed Er:YAG laser was approved in 1997 by the FDA for hard tissue treatment, such as caries removal and cavity preparation (Sulewski, 2000). Additionally, other intraoral applications, such as soft tissue surgery, sulcular debridement (1999) and osseous surgery (2004), have been permitted (Aoki, et al., 2004).

The Er:YAG is perhaps the most versatile of all the types of lasers available on the market today because of its many applications in dentistry for both hard and soft tissues. However, one of its limitations is its limited coagulative ability, compared with other types of lasers (Sulewski, 2000).

During Er:YAG laser irradiation, laser energy is absorbed selectively by water molecules and hydrous organic components of biological tissues, causing the evaporation of water and organic components and resulting in thermal effects due to the heat generated by this process (photothermal evaporation). Moreover, in hard tissue procedures, water vapor production induces an increase of internal pressure within the tissue, resulting in explosive expansion, called "microexplosion". These dynamic effects cause mechanical tissue collapse, resulting in "thermomechanical" or "photomechanical" ablation. This phenomenon has also been referred to as 'water-mediated explosive ablation' (Hibst & Keller, 1989; Keller & Hibst, 1989; Aoki, et al., 2004).

Although this laser was introduced into dentistry for the ablation of dental hard tissue (Hibst & Keller, 1989; Keller & Hibst, 1989), an early report (Kayano, et al., 1989) suggested an increase in acid resistance of the enamel adjacent to the ablated area. Later, several in vitro studies (Morioka, et al., 1991; Fried, et al., 1996; Hossain, et al., 2000; Cecchini, et al., 2005; Castelan, et al., 2007) on smooth dental enamel surfaces reported that Er:YAG irradiation promotes caries prevention as well as morphological enamel changes (Matson, et al., 2002; Cecchini, et al., 2005; Apel et al., 2005;). Furthermore, it was reported that both effects depend on the energy density of the laser, among other parameters, including

irradiation time, focal distance, and water cooling (Morioka, et al., 1991; Fried, et al., 1996; Hossain, et al., 2000; Young, et al., 2000; Matson, et al., 2002; Apel, et al; 2002, 2004, 2005; Cecchini, et al., 2005; Liu, et al., 2006; Castelan, et al., 2007).

4.5 CO_2 laser

In 1964, the CO_2 laser was developed at Bell Laboratories in the United States (Parker, 2007a). The active medium of CO_2 laser is a gas, and it emits infrared light at different wavelengths (9,300, 9,600, 10,300 and 10,600 nm) (Aoki, et al., 2004; Ishikawa, et al., 2004; Parker, 2007b). The 10,600 nm CO_2 laser is the most commercially available, and it is used as both a pulsed- and a continuous-wave laser (Rodrigues, et al., 2004). This laser is readily absorbed by water and therefore is very effective for surgery on soft tissues, which have high water content. The primary advantage of CO_2 laser surgery over the scalpel is its strong hemostatic and bactericidal effects. Very little wound contraction and minimal scarring are other advantages of laser surgery, especially for the CO_2 laser. However, the CO_2 laser is also highly absorbed by the principal mineral components of hard tissue, especially the phosphate ions (– PO_4) in carbonated hydroxyapatite. The energy applied is readily absorbed in hard tissues but causes instantaneous heat accumulation in the irradiated inorganic components, resulting in carbonization of the organic components and melting of the inorganic components, instead of the water-mediated physical collapse of hard tissues observed in Er:YAG laser irradiation (Aoki, et al., 2004). The caries-preventive effect produced on the enamel surface due to CO_2 laser irradiation was reported by Stern et al. (Stern, et al., 1972). Subsequently, several studies, both in vitro (Featherstone, et al. 1998; Kantorowitz, et al., 1998; Hsu, et al., 2000; Tsai, et al., 2002) and in vivo (Kato, et al., 2003), have shown increases in enamel acid resistance.

5. General-scope energy dispersive spectroscopy

Energy dispersive spectroscopy (EDS) is an analytical technique that allows the detection of the elements present in the studied material. It is very versatile and can be used with any type of solid sample, from metals and ceramics to biological tissues. It is usually coupled with an electron microscope to observe simultaneously the exact area of interest from which the signal will be collected.

One of the main advantages of EDS is its ability to detect almost all of the elements of the periodic table simultaneously and to quantify the amount of each of those elements present in a sample. Additionally, it is a very attractive technique because of the small amount of time that it takes to analyze a sample, which is typically on the order of minutes. However, when element mapping is needed, the measurements can take as long as several hours, depending on the material and the concentration of the elements of interest.

The main disadvantage of EDS is its inability to detect hydrogen (H), helium (He) and lithium (Li) due to the protecting window used in front of the detector that absorbs low-energy X-rays. This is an important disadvantage, especially for biological samples because many organic compounds and biomaterials are principally composed of carbon (C), oxygen (O) and hydrogen (H) (Williams, et al., 1996).

The main goal of this section is to show the way we use EDS coupled with a scanning electron microscope (SEM) in our research, which involves the chemical characterization of human teeth. For that purpose, we will begin with some fundamental aspects of the

technique that we have found are important to setting the analysis parameters properly and that help with understanding and interpreting the results.

5.1 X-ray production and fluorescence yield

When the incident electron beam reaches the sample, one phenomenon that occurs is that one electron of the inner shells of an atom is excited and ejected from the atom, leaving an electron hole. Another electron from an outer, higher energy shell fills the hole and in the process an X-ray is produced. As the energy of the X-ray is characteristic of the electronic structure of each element and of the differences in energy from one shell to another, this allows knowing from which element the X-ray came from by measuring its energy.

X-ray production is one of several de-excitation processes of an ionized atom. Therefore, it is important to have an idea of the amount of generated X-ray for each atom. The fluorescence yield w for the production of K shell radiation is given by the following equation:

$$\omega_K = \frac{\#K\ photons\ \ produced}{\#K-shell\ \ ionizations}$$

The fluorescence yield is favored for high atomic number atoms. For example, the ω_K for carbon is approximately 0.005, while for germanium, it is approximately 0.5 and near unity for the heaviest atoms. The impact of this number on the analysis of biological samples is obvious: it takes many more beam electrons to produce a significant amount of X-rays from carbon (C), oxygen (O) or nitrogen (N) atoms. In practice, this fact means that a longer analysis time is required to obtain an adequate signal-to-noise ratio.

5.2 Interaction volume

Although it is said that SEM and coupled EDS are surface analytical techniques, this statement is not completely true. Due to the energy of their beam electrons, they are capable of penetrating a sample, interacting with its atoms and therefore generating signals (backscattered electrons, secondary electrons, characteristic X-rays, etc.). The space underneath the sample surface, where these signals are generated, is called the interaction volume (Goldstein, et al., 2003). The shape of the interaction volume varies from a hemisphere, for high atomic number atoms, to a pear, for low atomic number atoms, as seen in Fig. 1.

The dimensions and shape of the interaction volume depend on several factors, such as the energy of the electron beam, the average atomic number of the sample, the density of the material and the incidence angle of the beam.

The energy of the beam has a strong influence on the size of the interaction volume. For example, for iron, the interaction volume size ranges from 0.5 μm at 10 keV to 2 μm at 30 keV. This effect is much more pronounced in low atomic number materials; the interaction volume at 20 keV in a low atomic number target, such as a biopolymer, can be as large as several micrometers, depending on its density.

The next factor affecting the interaction volume is the atomic number Z. The larger the atom is, the higher the probability of interaction with the electron beam will be. Therefore, as Z increases, the interaction volume decreases. For example, at 20 keV, the interaction volume for carbon is approximately 8 μm, while for uranium, it is approximately 0.4 μm.

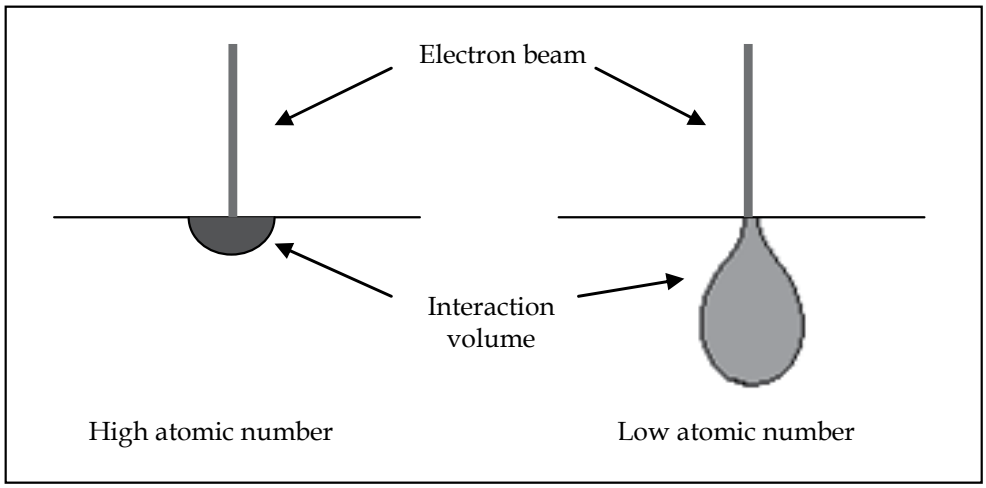

Fig. 1. Interaction volume from samples with different average atomic numbers

In dental research, it is very important to take into account these effects to avoid mistakes in the interpretation of the results. For example, during investigations in which the surface of the teeth are treated and low depths need to be studied, we recommend working with low-beam energy; otherwise, the volume underneath the treated surface will be analyzed together with the space of interest. However, as we decrease the beam energy, the number of generated X-rays also decreases. Thus, care should be taken when choosing the analysis parameters.

5.3 Qualitative analysis

EDS allows us to determine qualitatively the elements present in the specimen. This process is undertaken by analyzing the EDS spectrum and assigning an element to each peak on that spectrum. Today, modern equipment can perform this assignment automatically, although further analysis, done by the researcher, is necessary because many peaks from different elements overlap with the same energies. This fact is most important when analyzing samples, the composition of which is completely unknown.

5.4 Quantitative and semiquantitative analysis

In addition to qualitative analysis, EDS is widely used because of its ability to measure the concentrations of all elements present in samples (except for H, He and Li).. This process is undertaken by a series of measurements, for which the peak intensity from every element is compared with the peak intensity from a reference standard. The minimum detection limit of an EDS analyzer is approximately 0.1% for elements with $Z > 10$ and approximately 1.0 wt. % (weight percentage) for lighter elements (Brundle, et al., 1992).

To perform a true quantitative analysis, several issues must be taken into account. First, the sample and the reference must be flat, such that the surface imperfections do not interfere with the generated X-rays. Second, all the analysis parameters (e.g., accelerating voltage, spot size, time of analysis, etc.) must be the same. Additionally, the reference sample must contain the same elements as the studied specimen.

In practice, it is very difficult to meet all the requirements for a true quantitative analysis for several reasons: our samples are not always flat and free of surface defects, and we do not have a reference standard for each type of sample used (metallic, polymeric, biological, etc.). In such cases, the peaks from the elements in the specimen are compared with the peak of a pure element, usually copper. Some corrections should be made to have reliable results: an atomic number correction, accounting for the fraction of backscattered electrons by the sample within the interaction volume (the Z factor), a correction for the absorption of X-rays inside the sample (the A factor), and a correction for secondary X-ray fluorescence in the sample (the F factor). The most common procedure to take into account these factors is known as the ZAF correction.

In the case of a true quantitative analysis, the expected error is approximately 2% for major concentrations. When using a pure reference element, the error should be expected to be 4-5%. For elements with concentrations of less than 5% the relative error would be approximately 10%. This is why, when using a pure reference element, the process is often called a semiquantitative analysis.

In dental research, due to the inherent changes in morphology and composition of teeth from human to human and from tooth to tooth, it is virtually impossible to carry out a true quantitative analysis. However, a semiquantitative analysis is possible if we are careful during the analysis. The setup parameters of the microscope must always be the same (accelerating voltage, spot size, working distance, etc.). Since we deal with low atomic numbers (mainly O, Ca and P) the spectrum acquisition time should be long in order to have a good signal-to-noise ratio with well-defined peaks and a high number of counts. Calibration with the reference element should be performed every day or even every several hours to account for changes in the electronics of the system due to changes in the room temperature, vacuum, etc. Even with these precautions, as stated previously, we should consider a relative error in the calculations of approximately 10% or more if the concentration of certain elements is less than 5%.

Usually, in the revised literature, people working with teeth have tended to report the concentrations of elements using wt.%, perhaps as a convention. However, we have proposed the use of atomic percentage (at.%) instead, because it is more convenient to consider the difference in the number of atoms, rather than their weight. In this way, we can better correlate any changes in tooth composition directly with the molecular or atomic structure. Therefore, all of our results for tooth composition are presented in atomic percentages. Of course, one can change from one percentage to the other by relating each element composition to its corresponding atomic number.

6. Experimental design

The study protocol was reviewed and approved by the Research and Ethics Committee at the Autonomous University of the State of Mexico. All subjects enrolled in this research signed an informed consent.

6.1 Tooth selection

A total of 48 premolar teeth, extracted for orthodontic reasons, were stored in 0.1% (wt. /vol) thymol solution at 4°C, until the experiment began. The teeth were selected according to the following criteria: intact buccal enamel surfaces without developmental defects,

restorations or fluorosis, not subjected to any pretreatment chemical agents, such as hydrogen peroxide, no cracks and no caries, according to the DIAGNOdent criteria (DIAGNOdent pen, KaVo, Biderach, Germany).

6.2 Sample preparation

All selected teeth were cleaned with a brush and deionized water; subsequently, they were dried with compressed, oil-free air. In the middle third of each root, a mesio-distal perforation was made, and then a fixture of stainless wire was introduced to attach each sample with self-curing acrylic to the top of a polyethylene container. For etching, a 35 percent phosphoric acid gel (Ultra-Etch; Ultradent, UT, USA) was used (15 sec). Then, the teeth were rinsed and dried again, as previously described. On the buccal surface, an orthodontic bracket (slot 0.018 inch standard edgewise premolar bracket, Ormco, CA, USA) was bonded to the enamel with a composite resin (Transbond XT cure, 3 M Unitek, CA, USA, Lot), following the manufacturer's instructions. The position of the orthodontic bracket was parallel to the longitudinal axis of the tooth, at a height of 4.0 mm, using bracket height gauges (Ortho™ Ormco, California, USA)..

6.3 Treatment of the enamel surface

The samples were randomly divided into four groups (n=12): Group 1 no laser irradiation (control group); Group 2 was treated with CO_2 laser; Group 3 was irradiated with Er:YAG laser; and Group 4 was treated with Er:YAG + remineralizing solution (Fig. 2). Each sample was irradiated twice during a time period of 18 sec.

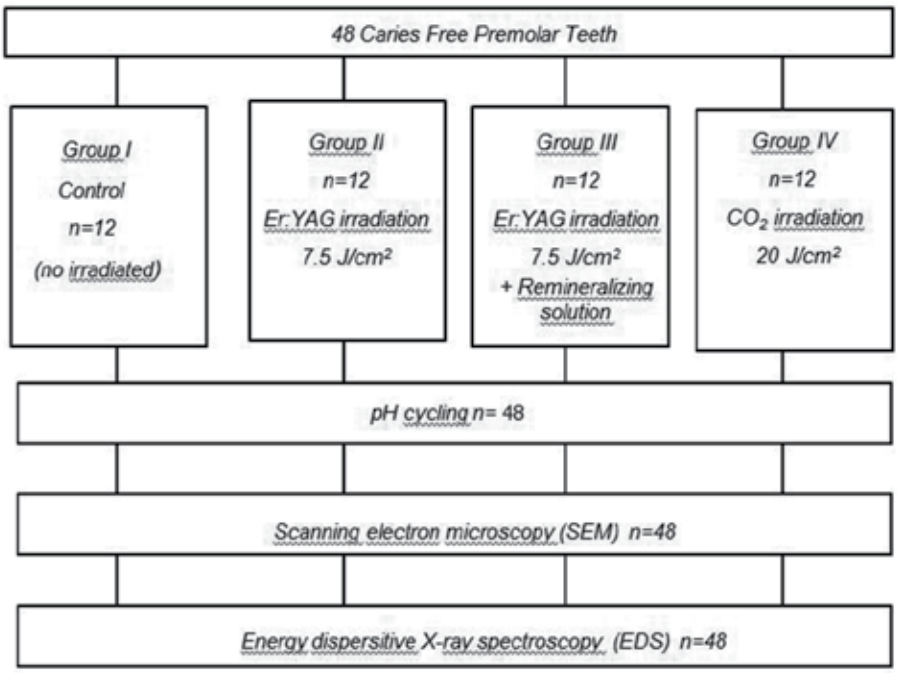

Fig. 2. Experimental design

6.4 pH cycling

After laser irradiation under specific conditions, a pH-cycling model of ten Cate and Duijister, modified by Featherstone (Featherstone, et al., 1998), was used to produce carious lesions, with a demineralization and remineralization period alternating daily over 9 days.

6.5 SEM and EDS

At the conclusion of the pH-cycling process, each tooth was rinsed with deionized water. Finally, the teeth were dried at room temperature and attached to a testing ring, using adhesive carbon paper (SPI Supplies, USA) to be observed by scanning electron microscopy (JEOL, JSM-6510LV, Japan). The atomic percentages (at.%) of calcium (Ca), phosphorus (P), carbon (C) and oxygen (O) on the enamel surface adjacent to the bracket were evaluated by energy dispersive spectroscopy (EDS) (Oxford Instrument, 7582, United Kingdom).

6.6 Statistical analysis

All data were analyzed using the SPSS 13.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA). The measurements were analyzed using the Kruskal-Wallis and Mann-Whitney tests at a $p \leq 0.05$ level of significance.

7. Results

The most significant images obtained for each group are shown. The control group (not irradiated) displayed open enamel prisms (Fig. 3a). In the irradiated samples (Figs. 3b, 3c, 3d), rough areas, craters and cracks were observed.

The experimental data obtained by EDS for all groups regarding the percentages of Ca, P, C and O are displayed in Table 1. A similar content for Ca was observed in all groups; however, additional variations in the content of other elements, especially C, were found in Groups III and IV.

Groups	n	C	O	P	Ca
Group I	12	23.2 A ± 3.5	52.6 A ± 3.2	10.1 A ± 0.9	14.1 A ± 2.0
Group II	12	23.4 A ± 5.4	53.5 A ± 5.1	9.4 A ± 1.1	13.7 A ± 1.7
Group III	12	16.3 B ± 4.9	58.6 B ± 5.2	10.6 A ± 1.2	14.6 A ± 2.6
Group IV	12	14.5 C ± 6.5	57.3 A ± 6.7	11.5 B ± 1.5	16.7 A ± 3.9

*Groups with different letters are significantly different (p≤0.05), based on statistical analysis by element.

Table 1. Mean Values and Standard Deviations of Atomic Percentages for Each Element

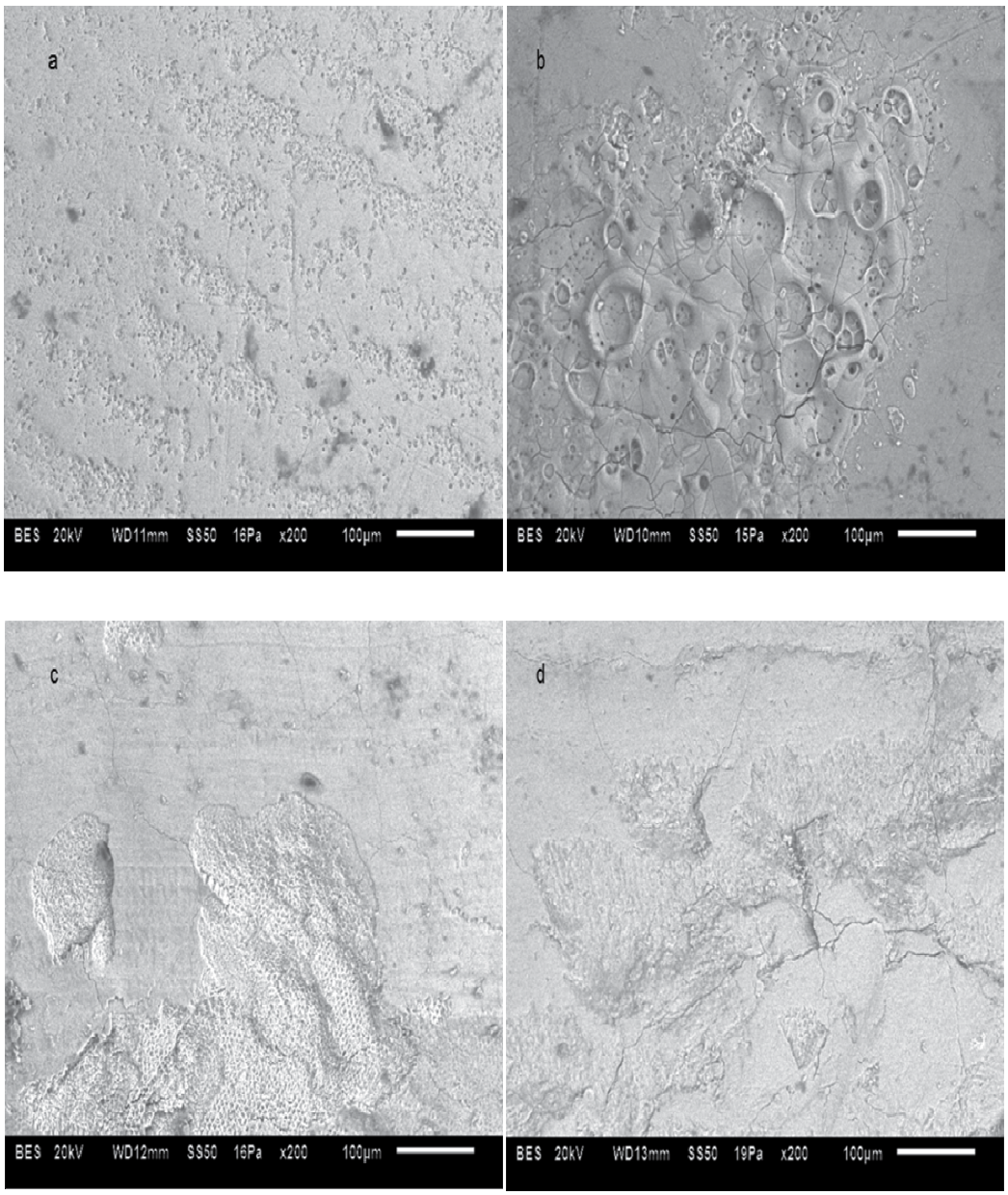

Fig. 3. Representative SEM micrographs of samples from the control group (a) and from experimental groups (b,c,d), showing the typical pattern of a non-irradiated enamel surface with exposed prisms (a), craters and melting produced by CO_2 laser irradiation (b) and craters produced by Er:YAG laser irradiation and evident demineralization due to a pH cycling process (c); also, craters and less demineralization are observed in Group IV (d). Original magnification x 200; scale bar =100 µm

8. Conclusion

The treatment conditions used on dental enamel surfaces for Groups II and IV likely induced changes in the structure of these biological tissues, which could interfere with the development of early lesions of dental caries. However, additional studies are required.

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20

Indigenous Australians and Oral Health

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1. Introduction

Indigenous disadvantage is an ongoing problem in Australia. In terms of health, the situation is critical. Indigenous Australians [1] experience higher rates of chronic disease, the persistence of serious ear and eye infections amongst young children, and often poor access to primary health care facilities (Aboriginal and Torres Strait Islander Social Justice Commissioner, 2005). In the area of oral health, there is also a wide disparity between Indigenous and non-Indigenous Australians. Unfortunately available data on the oral health of Indigenous people is limited, making it all the more difficult to make progress towards eliminating this discrepancy. The reasons for the gap are many, but include the fact that culturally appropriate and timely dental care are often inaccessible, as are appropriate resources on how to maintain good oral health, particularly for those residing in rural and remote areas. Differing understandings of health, as well as the division between medicine and dentistry that has traditionally been so strong in Australia, do nothing to help the situation. Reducing the disparities in oral health between Indigenous and non-Indigenous groups is an immense task that will require a dedicated and coordinated approach – it will depend on improved access to dental care as well as a more holistic approach to oral health, including preventive measures.

In the past, Indigenous Australians enjoyed better oral health than non-Indigenous people Harford et al., 2003). Dental decay and periodontal disease were uncommon in rural and remote Indigenous communities up until recently. Caries was, throughout the 19th and early 20th centuries, regarded as a disease of affluence in Australia – but has now become an 'indicator of deprivation' (Williams et al., 2011). As foods rich in fermentable carbohydrates became more common in rural and remote areas, so did dental decay (Harford et al., 2003). While oral health risk factors are the same for all Australians, many Indigenous people do not enjoy the same access to protection from dental decay afforded by fluoridated water, toothpaste, or easy access to dental care.

This chapter will begin with an overview of the general situation of Indigenous health and disadvantage in Australia, including a discussion of the Close the Gap campaign, and will also delve briefly into Indigenous understandings of health to provide some cultural context. We will then move on specifically to the topic of oral health amongst the

[1] The term 'Indigenous Australians' includes Aboriginal people from across Australia as well as Torres Strait Islanders – the Torres Strait Islands are located between the tip of Cape York, the northernmost point of the state of Queensland, and Papua New Guinea

Indigenous community, including a discussion of the relevant social determinants. Three indicators will be used to assess the levels of Indigenous oral health in comparison to that of non-Indigenous Australians: caries, periodontal disease, and tooth loss. We will provide a brief summary of some of the barriers to attaining better standards of oral health, particularly in remote communities. Finally, we discuss what additional measures might be required if we are to make progress.

2. Closing the Gap: Indigenous disadvantage and health in Australia

In 2000, Commonwealth Minister for Health Dr Michael Wooldridge stated that Australia's 'single most spectacular failure as a nation has been in the area of Aboriginal and Torres Strait Islander health' (Jupp 2001). Such an acknowledgement in itself indicates progress. While the *National Aboriginal Health Strategy* received support from ministers back in 1990, it was never implemented fully (Thomson, 2003). Not until the mid-nineties did the government's involvement in Indigenous health even begin 'to approach the level required to address the persisting health disadvantages experienced by Indigenous people' (Thomson, 2003). As time goes by the issue of Indigenous health is receiving much more attention in politics, the media and the national collective consciousness. This section will first give a brief overview of the current situation of Indigenous health, and will then discuss the social determinants of Indigenous health in Australia. A quick introduction to Indigenous understandings of health will then be followed by a summary of the Close the Gap campaign.

2.1 The situation today

In terms of general health, Indigenous Australians suffer a significantly greater burden of disease than non-Indigenous people, yet they nonetheless have less access to health care than the rest of the population (AIHW, 2011). The Australian Indigenous population is a classic example of a non-Western society being highly susceptible to diabetes upon the introduction of a Western lifestyle (Irvine et al., 2003). They are often diagnosed later, are less likely to receive proper treatment, and are consequently more likely to die from cancer than non-Indigenous Australians (Thomson et al., 2010). Other conditions that impact on Indigenous people's greater burden of disease include kidney and respiratory diseases, rheumatic heart disease, and ear and hearing problems, while inadequate nutrition, alcohol consumption, smoking and the use of other drugs constitute the major risk factors impacting on the quality of life of Indigenous Australians (AIHW, 2011).

2.2 Social determinants

The current health status of Indigenous Australians is linked very closely to the social inequalities that many face (Thomson et al., 2010). These social inequalities are rooted in the experience of 'a history of conflict and dispossession, loss of traditional roles, failed assimilation and passive welfare' (Banks, 2007: 8) shared by many Indigenous groups around the world. The fact that such discrepancies in health status continue to this day, and that they are so overwhelming, is largely attributable to the social determinants of health – current structural and social circumstances (Thomson et al., 2010). Social determinants of Indigenous health include socioeconomic position (incorporating educational attainment, income, and employment), housing, transport (Carson et al., 2007) and racism.

2.3 Indigenous understandings of health

As we see in so many areas concerning Indigenous Australians, there is a lack of data regarding Indigenous understandings of health too, particularly those living in urban areas. We do know, however, that for the most part Indigenous Australians share a holistic understanding of the concept of health, with physical, mental, social, cultural and spiritual health all playing an important part (Commonwealth of Australia, 2007). The Standing Committee on Family and Community Affairs notes that Aboriginal society has 'no word, term or expression for 'health' as it is understood in Western society…The nearest translation in an Aboriginal context would probably be a term such as 'life is health is life'' (National Aboriginal Health Strategy Working Party, cited in Commonwealth of Australia, 2000: vii). As the Committee acknowledges, health disparities between Indigenous and non-Indigenous Australians can in part be attributed to the lack of culturally-appropriate access to health care for Indigenous people - many of the difficulties can be explained by these differing views of health, how to define it, and which services are necessary (Commonwealth of Australia, 2000). This approach differs from Western medicine which tends to separate body, mind and society – but this is not to say that the two approaches are mutually exclusive. It is also important to emphasise the variety of beliefs that occurs between the people of different parts of Australia (Maher, 1999). Health, from an Indigenous perspective, is a concept that incorporates:

> everything important in a person's life, including land, environment, physical body, community, relationships and law. Health is the social, emotional, and cultural well-being of the whole community and the concept is thus linked to the sense of being Indigenous (Queensland Aboriginal and Islander Health Forum, cited in Burns et al., 2010).

2.4 The Close the Gap campaign

The National Indigenous Health Equality Campaign was developed in March of 2006, and the following year launched the name *Close the Gap* for its public awareness campaign. This came in the wake of 2005's Social Justice Report which called for state and national governments to commit to achieving equality for Indigenous people in health and life expectancy within 25 years. To demonstrate the major problem areas for Indigenous disadvantage, the Council of Australian Governments (COAG) set six targets over 2007–2008 towards 'Closing the Gap': it chose to focus on reducing the disparities in life expectancy, young child mortality, reading, writing and numeracy, employment, early childhood education, and secondary school completion (Steering Committee for the Review of Government Service Provision, 2009), so it is clear that health disparities occur within a context of general inequality.

The campaign has brought together many health organisations (both Indigenous and non-Indigenous), including the Indigenous Dentists' Association Australia, as well as human rights groups. Probably the strongest messages conveyed to the public through this campaign include the fact that Indigenous Australians will die up to 17 years earlier than other Australians, and that access to basic health care facilities continues to be very limited (Oxfam Australia, 2010). We are seeing an increased commitment now, with the Federal government signing the Close the Gap Statement of Intent in March 2008, COAG's commitment, and the announcement in late 2008 that the Australian Government would commit the unprecedented sum of AU$1.6 billion towards improving Indigenous health (Oxfam Australia, 2010). This is of course a welcome response, but the National Partnership Agreement makes no mention of oral health, an area that often seems to go ignored.

3. Indigenous oral health

The World Health Organisation defines oral health as 'being free of chronic mouth and facial pain, oral and throat cancer, oral sores, birth defects such as cleft lip and palate, periodontal disease, tooth decay and tooth loss, and other diseases and disorders that affect the mouth and oral cavity' (WHO, 2007). Following on from this, another definition emphasises the fact that a satisfactory standard of oral health will allow an individual to 'eat, speak and socialise without active disease, discomfort, or embarrassment and which *contributes to general wellbeing*' (Dental and Ophthalmic Services Division, 2005, emphasis added). The body of evidence linking oral health to other conditions only continues to grow (Guynup, 2006), demonstrating the importance of oral health as an important public health issue. Unsurprisingly, tooth loss and pain will often restrict eating and can result in weaker nutritional intake, which in turn can be associated with anaemia and gastrointestinal disturbances. Infection and tooth loss often result from poor oral health, and in addition to causing pain they can impede speaking and therefore have an impact on social interaction (Mason et al., 2006). More complex relationships link oral infection to systemic disease, for example arteriosclerosis, cardiovascular disease (Ylöstalo et al., 2006), diabetes (Taylor, Bornakke, 2008), stroke (Joshipura 2003), pre-term and low birth weight babies (Xiong et al., 2006), pulmonary diseases, and disorders such as otitis media and delayed growth and development. Likewise, recent studies have found associations between diseases like arthritis, diabetes, HIV and osteoporosis, and oral, dental and craniofacial diseases and disorders (Slavkin, 2000).

The ramifications of poor oral health can be immense, and are felt much more by Indigenous Australians than non-Indigenous people - Indigenous people have more caries, periodontal disease, and tooth loss than other Australians and, given that problems are more likely to go untreated, are also more likely to have teeth removed (Williams et al., 2011). It is important to note that it is likely that levels of oral disease amongst Indigenous Australians are in fact under-reported (Bazen et al., 2007b).

Many oral health problems suffered by Indigenous Australians share risk factor characteristics with wider general health problems. This means that while a great deal of work needs to be done, we can choose to see this as an opportunity to create positive change – efforts to encourage healthy eating, for example, are likely to have a positive impact not just on the oral health of the community but could also lead to reduced incidence of heart disease, obesity, and anaemia. An oral health campaign around links with drinking alcohol and smoking could have ramifications not just on oral health, but rates of lung cancer and emphysema. Such associations mean that the potential benefits of improvements in Indigenous oral health could extend to have numerous other health benefits, and as we learn more about these links our capacity to improve the situation will only increase. Improved information and understanding of oral health and dental care for this group is absolutely essential for the development and implementation of informed, effective public health policy.

There are numerous challenges arising from the lack of data on Indigenous health, particularly oral health. A large proportion of the available information focuses on specific communities or regions rather than giving an overall picture of the national situation. With wide variations in study design, it is not possible to accurately compare statistics taken in the past to those acquired more recently - before a complete understanding of the oral health status of Indigenous Australians can be attained, there is a great need for further epidemiological information (Williams et al., 2011).

3.1 Experience of oral health impairment

Caries, periodontal diseases and tooth loss all provide visible, quantifiable evidence of oral ill-health, but the experience of pain, oral functioning and quality of life are also very important. People's experience of food avoidance because of dental problems, perceptions of their oral health, and experience of toothache provide additional insights into the oral health of Australians. The *National Survey of Adult Oral Health* (NSAOH) included qualitative questions to assess the experience of oral health impairment.

Poor oral health can cause people to avoid certain foods, which may limit a person's enjoyment of food and their ability to maintain a balanced diet (Slade et al., 2007). Indigenous adults were twice as likely as non-Indigenous adults to report avoiding foods due to oral health problems, with the highest difference in those aged 35-54 years (49% of Indigenous people and 17% of non-Indigenous people).

In responses to the *NSAOH*, Indigenous people were 1.5 times more likely than non-Indigenous people to rate their oral health as 'fair' or 'poor' (the two lowest measures) (Slade et al., 2007). Indigenous adults aged 35-54 years were twice as likely as their non-Indigenous counterparts to provide this rating.

Toothache can be caused by dental diseases, related infections, broken teeth, or nerve sensitivity (largely due to contact with hot or cold food or drinks). Toothache ranges from a short-term mild sensation to persistent, disabling pain. Data on the frequency of toothache collected in the *NSAOH* identified that Indigenous people were 1.8 times more likely than non-Indigenous people to report toothache in the previous year (27% compared with 15%) (Slade et al., 2007). The largest difference was seen for those aged 35-54 years: 39% of Indigenous people and 15% of non-Indigenous people reported toothache.

This section will discuss the current state of Indigenous oral health in comparison to that of non-Indigenous Australians using three main indicators: caries, periodontal disease, and tooth loss. It will also consider other conditions resulting from poor oral health. Caries and periodontal disease are both easily preventable, as well as being curable within the initial stages. We will then move on to present information on some of the barriers to good oral health for Indigenous communities across Australia.

4. Caries

Dental caries (cavities or tooth decay) is caused by acid-producing bacteria that exist in the oral environment. These bacteria proliferate in the presence of sweet and sticky foods (Harford et al., 2003). In the early stages dental caries can be completely reversed, but when left untreated it may cause irreversible damage such as cavitation of tooth enamel. Small cavitations do not generally produce ongoing pain and require small restorations (fillings). Larger carious lesions, however, can completely undermine the structural integrity of the tooth. These often require substantial restorative treatment or extraction, particularly if the lesions extend to the dental pulp, resulting in pulpal infection, pulpal inflammation and pain.

Pulpal inflammation is one of the most common reasons for attendance at the dentist (Williams et al., 2011). It can be reversible up until the carious lesion reaches the pulp, but once it does it is more likely to be irreversible (Abbott & Yu, 2007). The treatment protocol for long-standing irreversible pulpal inflammation is root canal therapy or extraction (Yeng et al., 2007). Long-standing pulpal inflammation will result in pulp necrosis. As pulp necrosis causes loss of the tooth's sensory apparatus, the dental pain associated with the initial inflammation completely subsides. Many patients at this point will assume the

problem has improved or healed itself, but infection of the dental pulp may continue to spread through the apex of the pulp canal/s into the supporting structures, causing periapical periodontitis (Abbott & Yu, 2007). This may result in severe pain and often systemic effects (e.g. fever). Patients with periapical periodontitis require root canal treatment or extraction. If the tooth is to be restored, the remaining decay usually requires substantial extra coronal restoration (i.e. crowns). Both the root canal therapy and the crown are expensive, and this type of treatment from a private practitioner may cost more than one thousand Australian dollars. If specialists are performing the treatment it will likely be more.

Such costs present an insurmountable barrier to many patients, particularly the socially and financially disadvantaged. If the patient is treated in the public sector, whilst the cost is substantially less, the waiting lists are large in some jurisdictions and treatment options are usually restricted by policy. As extractions tend to cost a few hundred dollars in the private sector and tens of dollars in the public sector, it is no surprise that many disadvantaged patients (including Indigenous Australians) opt for extraction, rather than other treatments. Most public dental providers in Australia do not offer root canals or crowns. Whilst extraction may provide quick relief of pain, there are long-term consequences that may need to be addressed later on. For instance, masticatory efficiency diminishes as teeth are lost. If a patient has many extractions they may require dentures. In the private sector dentures may cost upwards of a thousand dollars. In the public sector they cost hundreds of dollars, but there may be a further waiting list. For instance, in 2010, South Australia had approximately a two-year waiting list for treatment in the public dental sector. The waiting list for dentures, however, was about four years.

Caries is a major health concern and if not prevented may have painful and difficult consequences. Regardless of the extent of the disease and the required treatment modality, all of the options will have life-long consequences and require maintenance/treatment even if a tooth is lost. As such, increased policy and interventions aimed at the prevention of dental caries would be cost-beneficial.

Caries experience is measured by the Decayed Missing and Filled Teeth (DMFT) index for permanent (adult) teeth or by the dmft index for deciduous (juvenile) teeth. Both indices measure how many teeth (T/t) are decayed (D/d), missing due to caries (M/s) or filled due to caries (F/f). Neither index differentiates between a tooth with minor problems and one with major problems, nor do they provide a direct indication of the discomfort or dysfunction experienced.

To get a more accurate picture of decay, another index, the Decayed Missing and Filled Surfaces (DMFS) is used. By measuring the number of decayed/missing/filled surfaces on each tooth, rather than the tooth as a whole, the DMFS provides more detail about an individual's caries experience. It is also important to note that the DMFT/dmft and DMFS/dmfs indices are cumulative: once a tooth has experienced caries it is permanently recorded by the index. As a result, these indices provide information about caries experience over a lifetime and cannot account for changes in risk factors or active disease levels.

It should also be noted that these indices do not measure the effect of caries experience on quality of life, which can be significant. It is important to understand this relationship, and so several instruments have been developed to measure the effect oral health has on quality of life. The Oral Health Impact Profile (OHIP) is one such index (Slade & Spencer, 1994). The shortened version, OHIP-14, contains fourteen questions that address the effect of oral health on a subject's life, for instance, recent pain levels or disruptions to sleep.

4.1 Caries among Indigenous children

Indigenous children experience more caries that non-Indigenous children in their deciduous teeth (Jamieson et al., 2007). According to the *Child Dental Health Survey* conducted in 1999, the mean number of decayed, missing, and filled deciduous teeth (dmft) in Indigenous children aged 4–10 years who attended a school dental service clinic was significantly higher than for their non-Indigenous counterparts in NSW, SA and the NT (Armfield et al., 2003). The highest dmft scores were for Indigenous six-year-olds, who experienced 2.4 times the dmft of non-Indigenous children of that age.

Four-year-old Indigenous children had more than three times the dental disease experience of their non-Indigenous counterparts. The highest numbers of missing teeth occurred in five-year-old Indigenous children, with a level more than five times that of non-Indigenous five-year-olds. The highest number of filled teeth occurred in eight-year-old Indigenous children. Taken together, the dmft scores indicated much poorer oral health in the deciduous dentition of Indigenous children aged 4-10 years than of their non-Indigenous counterparts, with the largest differences in the younger age groups.

Poorer oral health for Indigenous children continues among those with permanent teeth: the DMFT[2] was 1.5 times greater for Indigenous children aged 6-15 years than for their non-Indigenous counterparts, with higher DMFTs for each increasing age group. Indigenous children had higher numbers of permanent teeth with untreated decay, with those aged 15 years having almost three times the average number of their non-Indigenous counterparts. Numbers of filled teeth were similarly higher for Indigenous children, with six- year-old Indigenous children experiencing twice the number of filled teeth than non-Indigenous six-year-olds.

Age (years)	Indigenous	Non-Indigenous
6	8	3
7	14	10
8	24	14
9	29	17
10	38	21
11	37	25
12	45	29
13	46	31
14	59	39
15	62	58
16	67	59
17	73	61

Note: 1 Data are for 12-month periods: NSW from 2000; SA from 2003; and the NT from 2002
2 Where children had more than one examination, information from the first examination has been used

Table 1. Proportions (%) of children aged 6-17 years with DMFT>0, by Indigenous status and age, New South Wales (NSW), South Australia (SA) and the Northern Territory (NT), 2000-2003

Source: Jamieson, Armfield & Roberts-Thomson, 2007

[2] The numbers of missing permanent teeth of children aged 6-15 years were negligible

Where children live affects their experience of caries, with caries more common in rural and remote settings than in metropolitan centres (Jamieson et al., 2007a). According to the *Study of Aboriginal and Torres Strait Islander child oral health in remote communities*, Indigenous children living in rural areas had higher dmft and DMFT scores than Indigenous children in metropolitan areas, and non-Indigenous children in both rural and metropolitan areas had similar oral health, with levels of decayed, filled and missing teeth, deciduous and permanent, lower than among Indigenous children. Cariogenic food products are easily available in metropolitan, rural, and remote communities and, as such, consumption patterns can be considered fairly constant.

Fluoridation of water supplies in metropolitan and many rural areas is fairly consistent, however many remote communities do not have access to artificially fluoridated water, although some naturally occurring fluoride may exist. It is likely that differing levels of water fluoridation are implicated in caries levels. Although water fluoridation has been shown to be an effective method for reducing the prevalence of dental caries, patterns of consumption and distribution of fluoridated water vary across Australia. Fluoridation alone cannot totally negate the effects of poor oral hygiene and highly cariogenic diets. Whilst the increase in caries among Indigenous children in remote communities may be associated with decreased water fluoridation, in light of the widespread availability of cariogenic food, it is likely that reduced access to oral care and oral hygiene education may be important factors in the caries rates of remote Indigenous children. Appropriate oral care includes the use of fluoridated toothpaste twice a day. Fluoridated toothpastes are an important part of preventing decay, however in areas without optimally fluoridated water supplies, the use of fluoridated toothpaste becomes more important. The *SDS* provides annual community visits, but many Indigenous children either are not enrolled in schools or are not present on the day of the visit, and miss the professional care benefits offered by this mainstream service.

Rates for hospital dental care were similar for Indigenous and non-Indigenous children living in metropolitan and rural areas, with rates for children living in rural areas 1.3 times higher than those for children living in metropolitan areas (Jamieson et al., 2007a). The higher rates in rural areas reflect the limited oral health services in these locations. The high rate of extractions in rural areas suggests that either more children in rural locations had unsalvageable teeth or that the delay for another appointment would be unreasonable if restorative treatment was unsuccessful.

The age pattern of hospitalisation for dental care was quite different for Indigenous and non-Indigenous children: more than one-half (51%) of Indigenous children were less than five years of age compared with around one-third (34%) of non-Indigenous children (Jamieson et al., 2007a). Only one-tenth of Indigenous children hospitalised for dental care were aged 10-14 years, compared with more than one-quarter (27%) of non-Indigenous children. Hospitalisation for younger children is usually sought when gross caries results in a need for several or many extractions. In these cases it is done under general anaesthesia in one appointment so as to reduce trauma for the child.

The more uniform distribution of the rates and proportions, as well as the age pattern of hospitalisation for dental care suggests that young Indigenous children had more advanced tooth decay in their deciduous teeth, or had a higher number of deciduous teeth that were affected and required extraction, than did young non-Indigenous children (Jamieson et al., 2007a).

Age group	Indigenous		Non-Indigenous		Rate ratio
	Proportion (%)	Rate	Proportion (%)	Rate	
<5 years	51%	907	34%	657	1.4
5-9 years	39%	667	39%	721	0.9
10-14 years	10%	181	27%	501	0.4

Table 2. Proportions and rates of children receiving hospital dental care, by Indigenous status and age group, and Indigenous: non-Indigenous rate ratios, Queensland, Western Australia, South Australia and the Northern Territory, 2002-03
Source: Jamieson, Armfield & Roberts-Thomson, 2007

Note: 1 Rates are per 100,000
2 Rate ratio is the Indigenous rate divided by the non-Indigenous rate

The overall rate of hospitalised dental extractions was slightly higher for Indigenous children than for non-Indigenous children, with the rate for Indigenous children less than 5 years of age more than twice that of their non-Indigenous counterparts (Jamieson et al., 2007). Tooth restoration rates were 1.3 times higher for Indigenous children aged less than 5 years than for their non-Indigenous counterparts, but Indigenous children of all ages were less likely than other children to have pulpal and 'other' treatments.

Increased referral rates for hospitalisation might also be indicative of a lack of cultural awareness amongst dentists treating Indigenous Australians. The experience at Pika Wiya Health Service Inc. in Port Augusta has shown that increased cultural sensitivity has resulted in improved oral health outcomes (Parker et al., 2005). The Western Australia Review has also described oral health services for Indigenous Australians in WA. In light of a decreasing labour market, the Centre for Rural and Remote Oral Health (CRROH) has described sustainable models for servicing rural and remote Indigenous populations that include culturally-sensitive education programs and the training of Aboriginal Health Care Workers (Kruger at al., 2010; Pacza et al., 2001; Bazen et al., 2007). CRROH has also been involved in pre-graduate placements for dental students in the region (Bazen et al., 2007).

4.2 Caries among Indigenous adults

Caries is much more common among Indigenous adults than among non-Indigenous adults (Slade et al., 2007). According to the NSAOH, Indigenous adults were 2.3 times more likely to have untreated caries than the non-Indigenous adult population, and 57% of Indigenous adults had one or more teeth with untreated decay compared with 25% of non-Indigenous adults (Slade et al., 2007).

The severity of decay suffered by Indigenous adults is also notably higher than that experienced by non-Indigenous adults (Slade et al., 2007). According to the NSAOH, Indigenous people 15 years and older had more than three times the number of decayed tooth surfaces than their non-Indigenous counterparts. The greatest difference was in the 35-54 years age group, with Indigenous people experiencing more than five times the decayed tooth surfaces than their non-Indigenous counterparts.

Almost four-fifths (78%) of Indigenous people aged 17-20 years included in the ABC Study were found to have caries, a level 1.2 times that documented for non-Indigenous people of that age group who participated in the NSAOH (Jamieson et al., 2010a).

Data from a large Western Australian retrospective study paints a less favourable picture of the oral health of Indigenous Australians. It calculated an average DMFT score of 8.5, four times higher than the NSAOH DMFT for the general population (Smith et al., 2007).

	Indigenous		Non-Indigenous		Ratio
	Prevalence	Confidence Interval (95%)	Prevalence	Confidence Interval (95%)	
Caries	78	74–82	63	51–73	1.2
Decayed teeth (DT>0)	74	70–79	23	15–34	3.2
Missing teeth (MT>0)	52	47–57	21	12–34	2.5
Filled teeth (FT>0)	23	19–27	49	38–61	0.5

Note: 1 Indigenous data from *ABC* study (2006-2007) and non-Indigenous data from the *NSAOH* (2004-2006)
2 Prevalence is percentage of people with the condition; confidence interval provides an indication of the reliability of the estimated prevalence
3 Ratio is the Indigenous prevalence divided by the non-Indigenous prevalence

Table 3. Prevalence of caries-related conditions, by Indigenous status, and Indigenous-non-Indigenous ratios, Australia, 2004-2007
Source: Jamieson, Sayers & Roberts-Thomson, 2010a

	Indigenous		Non-Indigenous		Ratio
	Prevalence	Confidence interval (95%)	Prevalence	Confidence interval (95%)	
DMFT	4.8	4.3–5.3	2.8	1.8–3.8	1.7
Decayed teeth (DT)	4.1	3.7–4.5	0.5	0.3–.07	8.2
DMFS	8.3	7.2–9.4	3.2	2.1–4.3	2.6
Decayed surfaces (DS)	7.6	6.5–8.7	0.7	0.3–1.0	10.9
Filled surfaces (FS)	0.7	0.5–0.9	2.6	15. –3.7	0.3

Note: 1 Indigenous data from *ABC* study (2006-2007) and non-Indigenous data from the *NSAOH* (2004-2006)
2 Prevalence is percentage of people with the condition; confidence interval provides an indication of the reliability of the estimated prevalence
3 Ratio is the Indigenous prevalence divided by the non-Indigenous prevalence
4 See text for details of DMFT

Table 4. Mean caries scores, by Indigenous status, and Indigenous-non-Indigenous ratios, Australia, 2004-2007
Source: Jamieson, Sayers & Roberts-Thomson, 2010a

Indigenous people aged 17-20 years had 3.2 times the prevalence of decayed teeth and 2.5 times the prevalence of missing teeth than did their non-Indigenous counterparts. On the other hand, the level of fillings was lower among Indigenous people than among non-Indigenous people: the ratio for filled teeth was 0.5 and for filled surfaces was 0.3. Together with their higher decay rates, these ratios suggest that service utilisation was lower – and levels of untreated caries substantially higher – among this Indigenous population than among same-aged non-Indigenous people who participated in the *NSAOH*.

A comparison of the mean number of decayed teeth and surfaces (severity) reveals the same trends. Indigenous people aged 17-20 years experienced 1.7 times the mean number of decayed, missing, or filled teeth than their non-Indigenous counterparts (Jamieson et al., 2010a). When broken down into its components, this group experienced 8.2 times the prevalence of decayed teeth. When using the DMFS compared to DMFT, the mean number of decayed, missing, or filled teeth compared to surfaces increased from 1.7 to 2.6, and the mean number of decayed teeth compared to surfaces increased from 8.2 to 10.9.

4.3 Protective and risk factors for caries

Diet

Caries can largely be prevented by maintaining a healthy diet (Harford et al., 2003). Since the arrival of Europeans in Australia in 1788, there has been a rapid change in diet for many Indigenous people from a fibre-rich, high-protein, low-saturated-fat, traditional diet to a diet high in refined carbohydrates and saturated fats (Australian Bureau of Statistics, 2008; Jamieson et al., 2006). This new diet includes a lot of processed and sugary foods and little fresh produce. This is especially true for people living in remote areas where food can be considerably more expensive than in urban areas (Queensland Health Treasury, 2006). Fresh produce may often be in poor condition after being transported long distances. Many Indigenous people, including children, consume a high level of sugary, cariogenic foods, such as carbonated drinks and confectionary (Jamieson et al., 2006). This non-traditional diet substantially increases the risk of caries.

Water fluoridation

The fluoridation of public water supplies is an effective way to prevent caries (Ehsani & Bailie, 2007). It is considered to be both the most cost-effective and socially equitable way of preventing dental decay and could significantly benefit communities that are socio-economically disadvantaged, such as remote Indigenous communities. National reports have documented that 20 percent of Australians, most of which live in rural areas, currently do not have access to fluoridated water (Australian Health Ministers' Advisory Council, 2001). These reports have recommended that water fluoridation should be extended to small rural communities. *Healthy mouths healthy lives: Australia's national oral health plan 2004-2013* suggests that water fluoridation should be made available to communities with populations less than 1,000 people (National Advisory Committee on Oral Health, 2004), and there is evidence to suggest that fluoridation may be cost effective in larger remote Indigenous communities (Ehsani & Bailie, 2007). Until fluoridation becomes available to all Indigenous people, they will continue to be at increased risk of dental decay. It should be noted that fluoridation of Brisbane's water supply has begun, and that by the end of 2012, 95% of the population will have access to fluoridated water. With the inclusion of Queensland in community water fluoridation statistics, the percentage of Australians lacking access to fluoridated water will continue to decrease (AIHW, 2002).

Oral hygiene

Good oral hygiene is fundamental in preventing caries. Self-care includes frequent tooth-brushing with fluoridated toothpaste and requires an understanding of the value of good oral care, as well as resources available to purchase toothbrushes and toothpaste (Jamieson et al., 2006). There is evidence that oral care practices were not necessary with a traditional

Indigenous diet, and were not part of some Indigenous cultures (Harford et al., 2003). There are also strong ties between socioeconomic status and oral hygiene with those who are more disadvantaged being less likely to practice good oral hygiene (Harford et al., 2003; Slade et al., 2007). Thus, for economic and socio-cultural reasons, Indigenous people are at increased risk of caries.

Professional dental care

Many professional dental services are not affordable for, or available to, Indigenous people (Harford et al., 2003). Few dental professionals work in rural or remote locations, and studies have found that private dental care is too costly for many Indigenous people. Similarly, many dental services are not culturally sensitive, thus creating access barriers for Indigenous people. Without professional dental care, Indigenous people are at increased risk of untreated dental decay.

Hypoplasia

Another important factor for the prevention of caries is having strong teeth from birth (Seow, 1997). Tooth enamel provides a hard, protective surface on the tooth. If the enamel becomes weak, a condition known as enamel hypoplasia may result in increased incidence of caries. Enamel hypoplasia can result from a congenital condition, premature birth, infections during childhood, malnutrition (Pascoe & Seow, 1994) and low birthweight (Lai et al., 1997), many of which occur at higher rates among Indigenous people than in the total population (Australian Health Ministers' Advisory Council, 2008).

5. Periodontal disease

Periodontal diseases are associated with bacterial infection of the periodontal (gum) tissues causing inflammation. Unlike caries, they are specifically attributed to poor oral hygiene as opposed to a poor diet, together with underlying host susceptibility. Like caries, periodontal disease is preventable and treatable. Periodontal diseases range in severity from gingivitis (a mild and completely reversible form) to periodontitis (a severe destruction of the tissues that support the teeth). Gingivitis is characterised by inflammation and bleeding gums and can be completely cured. Symptoms of periodontitis include the loss of tooth-supporting bone and the formation of periodontal pockets (spaces between the gum and tooth), and clinical attachment loss, where bacteria have caused the deterioration of bone and ligament. Periodontitis can result in tooth mobility, partial and total edentulism (loss of all teeth), and halitosis. Most forms of periodontitis do not cause pain, although some forms, namely Acute Necrotising Ulcerative Gingivitis and Acute Necrotising Ulcerative Periodontitis, do cause significant pain. Periodontitis can be localised (to a few teeth) or generalised (to larger areas of the mouth, or the whole mouth). It is predominantly chronic, and may begin in the early 20s age group. However, research suggests that it is typically a disease of ageing and usually occurs later in life (Pihlstrom et al., 2005). Acute forms exist, however these are rare and tend to occur in patients with complicating systemic factors. Acute forms also tend to be localised. Periodontitis risk factors include smoking, diabetes, stress, genetic and epigenetic inherited factors, hormonal imbalance, immunosuppression, maleness, mouth breathing, low socio economic status (SES), poor education, and poor nutrition. As Indigenous Australians are more likely to smoke, have diabetes, have poor nutrition, are typically lower on the SES ladder, and may be at an increased genetic risk (not

yet supported directly by the literature), they are likely to be at an increased risk of developing periodontal disease.
Indices exist to measure periodontal disease, however definitions about what to include in an index are contentious, and the use of different definitions has resulted in a wide range of prevalences within the same populations.
As with caries, these indices do not measure the effect of periodontal disease on quality of life. Once again, measures like OHIP are useful to gauge the effect of disease on quality of life.

5.1 Periodontal disease among Indigenous children

Children rarely develop severe periodontal disease, but gingivitis is relatively common on the gums of Indigenous children around both deciduous and permanent teeth, especially for older children. Although gingivitis in itself does not cause destruction of periodontal structures, it is inflammation nonetheless and should be prevented. Periodontitis is an exacerbation of gingivitis, however the progression from gingivitis to periodontitis is not certain and only occurs in individuals at risk. Furthermore, the prevention of gingivitis, appropriate oral hygiene, decreases the likelihood of developing dental caries. According to the *Study of Aboriginal and Torres Strait Islander child oral health in remote communities*, the prevalence of gingival bleeding, a common symptom of gingivitis, was higher for Indigenous children aged 6-15 years in South Australia than for their non-Indigenous counterparts (Jamieson et al., 2007a). The level of gingival bleeding among Indigenous five-year-olds was almost four times higher than that among non-Indigenous children of the same age. Among 12 year-olds, almost one-half (48%) of Indigenous children had gingival bleeding compared with 23% of non-Indigenous children. The same study found that gingival bleeding was common among Indigenous children in New South Wales. Indigenous children aged 12-14 years had a markedly higher prevalence of bleeding than did their non-Indigenous counterparts, but there was little difference in prevalence between Indigenous and non-Indigenous children 4-12 years. Three-in-five Indigenous children living in remote communities showed some evidence of gingivitis and approximately one-in-five children were at moderate risk of developing gingivitis. More than two-fifths (42%) of Indigenous children aged 15-16 years were at moderate risk of developing gingivitis and 25% were at high risk.

5.2 Periodontal disease among Indigenous adults

Indigenous adults are more likely to suffer from periodontal disease than their non-Indigenous counterparts (Slade et al., 2007). According to the *NSAOH*, almost 27% of Indigenous people 15-74 years had gingivitis; they experienced approximately 1.3 times the prevalence of moderate and severe periodontitis than did their non-Indigenous counterparts. Indigenous people had a slightly higher prevalence of deep (4+mm) periodontal pockets and clinical attachment loss than did non-Indigenous people.
An *ABC-NSAOH* comparison of Indigenous and non-Indigenous people aged 17-20 years demonstrates a more notable difference in periodontal diseases between the two groups: Indigenous people had 1.7 times the prevalence of calculus deposits (a risk indicator of periodontal diseases), 1.2 times the prevalence of gingivitis, 9.5 times the prevalence of moderate or severe periodontal disease, and 11.8 times the prevalence of deep periodontal pockets than did their non-Indigenous counterparts (Jamieson et al., 2010a).

Indigenous people are affected by periodontal diseases at much younger ages than non-Indigenous people (Harford et al., 2003; Armfield et al., 2003; Gracey, 2000). According to the *NSAOH*, Indigenous people aged 15-34 years experienced almost twice the prevalence of moderate or severe periodontitis than their non-Indigenous counterparts (13.5% and 7.3% respectively) (Slade et al., 2007). Compared to non-Indigenous people aged 15-34 years, Indigenous people in the same age group had higher prevalences of deep periodontal pockets (18% compared with 13%), clinical attachment loss (24% compared with 17%), and tooth sites with deep periodontal pockets (1.3% compared with 0.6%).

	Indigenous		Non-Indigenous		Ratio
	Prevalence	Confidence interval (95%)	Prevalence	Confidence interval (95%)	
Calculus deposits	89	86–92	52	41–63	1.7
Gingivitis	89	86–93	74	65–82	1.2
Periodontal pockets 4mm or deeper	61	57–66	5.2	2.3–11.5	11.8
Moderate or severe periodontal disease	27	19–35	2.8	0.8–8.9	9.5

Note: 1 Indigenous data from *ABC* study (2006-2007) and non-Indigenous data from the *NSAOH* (2004-2006)
2 Prevalence is percentage of people with the condition; confidence interval provides an indication of the reliability of the estimated prevalence
3 Ratio is the Indigenous prevalence divided by the non-Indigenous prevalence

Table 5. Prevalence of periodontal risk indicators and periodontal diseases, by Indigenous status, and Indigenous: non-Indigenous ratios, Australia, 2004-2007
Source: Jamieson, Sayers & Roberts-Thomson, 2010a

5.3 Protective and risk factors for periodontal diseases

Smoking

Smoking is a significant risk factor for the development, progression and severity of periodontal diseases (Do et al., 2008). According to the *2004-2005 National Aboriginal and Torres Strait Islander health survey*, one-half of the adult Indigenous population smoked daily or regularly, a level more than twice that of non-Indigenous adults (Australian Bureau of Statistics, 2006).

Diabetes

Diabetes, especially uncontrolled or poorly controlled diabetes, is associated with increased risk of oral infections (Harford et al., 2003). Diabetes/high sugar levels were reported by around 6% of Indigenous people who participated in the *2004-2005 National Aboriginal and Torres Strait Islander health survey* (Australian Bureau of Statistics, 2006). After adjusting for differences in the age structures of the two populations, diabetes/high sugar levels were around 3.4 times more common for Indigenous people than for non-Indigenous people. A 1998-2000 study of periodontal diseases among diabetic and non-diabetic residents of the Anangu Pitjantjatjara lands in South Australia found that Anangu people with diabetes were more than three times as likely as those without diabetes to have 4-5 mm periodontal pockets and almost 10 times as likely to have 6+mm pockets (Endean et al., 2004).

Oral hygiene

Periodontal diseases are also attributed to poor oral hygiene, in which self-care plays an important role. According to the *Study of Aboriginal and Torres Strait Islander child oral health in remote communities*, less than one-fifth of Indigenous children living in remote communities in New South Wales, South Australia and the Northern Territory brushed their teeth at home (20%) or at school (18%), and less than 5% of those younger than five years of age brushed their teeth regularly (Jamieson et al., 2007a). A study in the Top End of the Northern Territory in 2003 found low levels of regular preventive oral health care among remote Indigenous children (Jamieson et al., 2006). The study noted that about 84% of the children in the study used a toothbrush, but only 20% used toothpaste on a daily basis. The use of toothpaste generally started relatively later in life, with the most common commencement age being four years. This may reflect commencement of pre-school and exposure to oral hygiene strategies organised by schools. Children learn their oral self-care habits from seeing what other people do on a daily basis; caregivers who regularly partake in oral self-care habits, such as brushing and/or flossing, are likely to instil such behaviours in the children in their household (Mattila et al., 2001).

Professional dental care

Professional dental care is also important in periodontal health (Pihlstrom et al., 2005). According to the *NSAOH*, fewer Indigenous adults than non-Indigenous adults reported visiting a dentist within the last twelve months (51% compared with 60%) (Slade et al., 2007). Similarly, Indigenous people were more than 20% less likely than non-Indigenous people to visit a dentist annually (43% compared with 53%).

Indigenous people face a number of barriers, including cost, to regular and timely professional dental care (Slade et al., 2007), and the course of periodontitis can be substantially worse for patients without regular access to dental care. Unfortunately, periodontitis and limited dental care (professional and self-care) can establish a 'vicious cycle': the onset of disease makes cleaning more difficult, and, as cleaning becomes more difficult, more acute and deeper bacterial invasion of the tooth surface worsens the level of disease. This cycle eventually results in destruction of the tooth-supporting apparatus and tooth loss.

6. Tooth loss

The main causes of tooth loss are extraction of diseased teeth due to dental caries, periodontal diseases, and trauma (Harford et al., 2003). Complete tooth loss, known as total edentulism, significantly affects oral functioning and quality of life. Tooth loss is overrepresented among Indigenous people and edentulism occurs at younger ages for Indigenous Australians.

6.1 Tooth loss due to injury

Injuries of the head and neck may affect dentition; fractures specifically of the maxilla and mandible are directly related to tooth loss and loss of function (Sclaroff et al., 2000). Fracture of the skull and facial bones, with associated tooth loss, is the third most prevalent head injury in Australia. Tooth loss due to head trauma can markedly reduce quality of life. After adjusting for differences in age, gender and residential location, the rate of hospitalised head

injury due to assault was 21 times higher for Indigenous people living in Queensland, Western Australia, South Australia and the Northern Territory in the six year period 1 July 1999 to 30 June 2005 than for their non-Indigenous counterparts. The rate ratio was especially high among females: 69 for all ages and 93 for the 30–34 years age group. Whilst this statistic is not specific for tooth loss or dental trauma, it is likely that in light of such high rates of facial trauma increased tooth loss also follows.

6.2 Edentulism

Edentulism reflects both extensive dental disease and past surgical approaches to the treatment of oral diseases that relied largely on extractions (Slade et al., 2007). Edentulism leads to poorer oral functioning and often to notable discomfort. Individuals missing all of their teeth must either endure with no teeth, which greatly affects a person's ability to eat, or choose to wear full dentures, which are generally uncomfortable and can lead to complications if not properly cleaned and maintained.

Edentulism is strongly correlated to age; in Australia less than 2% of adults aged 35-54 years have complete tooth loss but this increases to 36% for people aged 75 years or older (Slade et al., 2007). The age distribution of edentulism for Indigenous people is noticeably different from that of the total population. The level of complete tooth loss is almost five times higher among Indigenous people aged 35-54 years than among their non-Indigenous counterparts (7.6% compared with 1.6%). There was also a notable difference for those aged 55-74 years; 21% of Indigenous people suffer from edentulism compared with 14% of non-Indigenous people.

7. Barriers to good oral health among Indigenous people

For many Indigenous Australians there are numerous factors that hinder the maintenance of good oral health. Most of these are linked to socioeconomic disadvantage. They include the cultural and geographical accessibility of oral health services, diet, water fluoridation, living conditions, oral hygiene, the cost of dental care, and lower rates of school attendance for children. Another important issue is the differing understandings of health, as outlined previously. When little of this is understood by mainstream health providers, it is not surprising that this can also constitute a significant barrier. For children, it has been suggested that under-utilisation of the School Dental Service in the Northern Territory may well be a result of low school attendance in some communities, despite the fact the Service provides care to communities regularly (Jamieson et al., 2006).

7.1 Cultural accessibility of oral health services

For the most part, oral health services tend to stipulate certain rules that are not necessarily compatible with Indigenous culture, in addition to the fact that they ignore the Indigenous understandings of health. Barriers can include communication challenges where Indigenous patients do not speak English as their mother tongue, and a general unwillingness to allow patients to visit accompanied by family members or friends, something often important to Indigenous patients. The current lack of Indigenous dentists, dental therapists and other oral health professionals poses a problem given many Indigenous people may be more likely to visit an Indigenous dentist (Jamieson et al., 2008). While in general the staff of oral health services have no training in cultural sensitivity and no support in providing a more

appropriate service for Indigenous patients (Jamieson et al., 2008), efforts at the Oral Health Program at Pika Wiya Health Service in Port Augusta have demonstrated greatly increased acceptance of the service and improved attendance rates after the introduction of a culturally-sensitive oral health care service (Parker et al., 2005).

7.2 Geographical accessibility of oral health services

Australia is geographically one of the world's largest countries, with the vast majority of the relatively small population -89% – living along the coast and the vast interior being very sparsely populated. Considering around a quarter of Indigenous Australians live in remote parts of the country, the distance to the nearest dental clinic can be long, and even when transport is available the roads are often in poor condition (Australian Bureau of Statistics, 2008). For people living in urban areas, transport can also be an issue.

7.3 Diet

Again hinging on Australia's immense area, the transport of healthy foods to remote communities is a major issue and for this reason many Indigenous people can have very limited options in terms of their diet. The availability of many healthier food items (for example wholemeal breads, lean meat, reduced-fat milk, and fresh fruits and vegetables) tends to be erratic in the more rural and remote areas (Williams et al., 2011). Fresh foods in particular, when available, can cost up to 30 percent more than in urban parts of the country (Harrison et al., 2007). With limited range and very high prices, those living in rural and remote Australia are more likely to eat the more affordable foods available, often processed foods high in both sugar and carbohydrates. Such foods of course impact negatively on general and oral health.

7.4 Water fluoridation

The fluoridation of drinking water supplies has been lauded as 'the single most effective public health measure for reducing dental caries across the population, with its most pronounced effects among those who are disadvantaged and most at risk' (Acheson 1998, DHS 2000a) (Government of South Australia, 2004: 16). Fluoridation affords those members of the community lacking in financial resources to buy toothbrushes and fluoridated toothpaste access to fluoride in their water, and this can reduce caries by 20–40% (NHMRC 1991, Ahokas et al., 1999). However, rural and remote communities again tend to miss out here – in excess of 80% of remote-living Indigenous people lack access to fluoridated town-water supplies (Ehsani and Bailie, 2007).

7.5 Living conditions

Many Indigenous Australians live in sub-standard housing (Bailie, 2007), a condition strongly linked to higher levels of poor health and disease (ABS, AIHW, 2008). The factors that impact most on oral health include a lack of safe (let alone fluoridated) drinking water, poor sanitation, and overcrowding. A survey conducted in 2008 found 25% of Indigenous people over the age of 15 years were living in overcrowded housing (Australian Bureau of Statistics, 2009), and this has a direct effect on oral health (Jamieson et al 2010) in that the absence of a clean, safe place to store toothbrushes can discourage their use. Another important factor is the frequent movement between houses that many Indigenous Australians make, meaning they may not always carry oral health care products with them.

7.6 Oral hygiene

Poor oral health results in large part from a lack of oral hygiene. The limited availability of toothbrushes, toothpaste and floss certainly impedes the maintenance of good oral hygiene in some remote communities, but it seems probable that the importance of good oral hygiene is not always recognised by Indigenous people – overall their use of toothbrushes and fluoridated toothpaste is below suggested levels (Jamieson et al., 2006). Given the evidence that the traditional Indigenous diet before colonisation did not necessitate oral self-care, such practice has not featured in many Indigenous cultures (Harford et al., 2003).

7.7 Professional dental care

Medicare is the Australian government's program enabling free treatment for patients of public hospitals as well as free or subsidised treatment by certain medical practitioners. It does not include provisions for any preventive oral health services. While low-income earners are entitled to concessions for public dental treatment, oral health services are often out of reach for many Indigenous people as a result of their expense (Slade et al., 2007). The majority of dental surgeries demand payment on the day, and the National Survey of Adult Oral Health found that Indigenous people were 1.5 times more likely than non-Indigenous people to have difficulty paying even a modest AU$100 dental bill.

7.8 The dental-medical divide

Traditionally, the dental and medical fields have tended to be viewed as completely separate entities. In Australia the two professions have evolved quite separately, and one of the drawbacks of this is 'a general public mostly failing to grasp that the oral cavity relates in dynamic fashion with the rest of our being' (Widdop, 2005). In recent years there has been growing recognition of the links between oral and systemic health, and as a result this disciplinary divide is slowly breaking down (Guynup, 2006). The body of research indicating these links continues to grow, and the connections surely have strong relevance for Indigenous Australians given their poorer health in many different areas, oral and otherwise. While this chapter focuses on improving oral health for Indigenous Australians, it does so with a strong emphasis on the need for an overhaul of Indigenous health in general. It also acknowledges that there may be benefits to be had from an increased awareness amongst the general public of the importance of oral health to general health. The connections between oral health and overall health also give us reason to be optimistic about the broader benefits that could come from effective measures to improve oral health amongst Indigenous Australians.

8. Conclusion

There are many issues contributing to the higher rates of caries, periodontal diseases, and partial and total edentulism experienced by Indigenous Australians, particularly the cultural, economic and geographical factors limiting their access to services. Both the Australian government and the dental sector have a responsibility to address the inequalities in oral health. Today some progress is being made and we are seeing more and more services created with the goal of reducing the gap – so far, however, no program has offered a comprehensive plan targeted at the entire Indigenous population, only certain communities within it. Of course all factors must be considered within the context of the

social determinants of oral health. In order to deliver results, any strategy must deal with the broad range of factors that continue to underlie Indigenous disadvantage in Australia, as well as providing a long-term plan capable of making progress even as the political and economic scenarios change (Thomson et al., 2010). A successful and sustainable approach will also require the input of Indigenous people and health organisations. While the rates of all kinds of diseases, oral and systemic, are on average much higher in the Indigenous community, we can choose to regard this as an opportunity rather than just a miserable state of affairs. Any targeted response to improve oral health for Indigenous Australians is likely to create much broader health benefits for the population, just as initiatives aimed at reducing the rates of diabetes or heart disease will most probably result in improved oral health.

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21

Oral Health Knowledge, Attitude and Practices of Parents/Caregivers

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1. Introduction

Parents usually are the primary decision makers on matters affecting their children's health and health care (Cafferata & Kasper, 1985; Hickson & Clayton, 2002). Moreover, in everyday life, parents function as role models for their children, and therefore, parents' own dental hygiene habits are very meaningful. Parental characteristics and beliefs may also be an important consideration in attempts made to improve children's oral health. Therefore, in attempts to achieve the best oral health outcomes for children, parents should be considered as key persons in ensuring the well-being of young children. This can improve the preventive dental care children receive at home and their use of professional dental services (Inglehart et al., 2002). In addition, appreciating their knowledge, attitude and practices about their children's oral health may help the dental community understand some of the reasons why children do not receive the dental care they need.

It is important to initiate basic good oral health habits in childhood so that the appropriate dental norms are established and then maintained into adult life. The family is the first institution that influences child behavior and development, especially mothers, who are the primary model for developing behavior (Blinkhorn, 1981). Therefore, childhood is an important period of life that needs to be monitored closely so that the child will grow up healthy. However, recent rapid social expansion in many societies creates a negative impact on child-rearing. Parents have to transfer their caring role to caregivers and may compromise the health status of young children including their oral health. This consequence is especially important for preschool children because they are totally dependent on adults.

The most important negative impact to child oral health is Early Childhood Caries (ECC) (Milnes, 1996; Tinanoff & O'Sullivan 1997; Tinanoff, 1998) which may compromise growth and development of affected children (Acs et al., 1992; Ayhan et al., 1996). Several factors could contribute to a high rate of ECC (Seow, 1998; Reisine & Douglass 1998), such as parent health beliefs and attitudes towards their own dental care which is a significant predictor of children's dental care utilization (Amen & Clarke, 2001). Sarnat *et al*. reported that the more positive the mother's attitude regarding her child, the fewer carious teeth were noted, the better the child's oral hygiene, and the more dental treatment the child received (Sarnat et al., 1984). Sasahara *et al*. showed that mothers' oral health behavior was associated with the prevalence and severity of dental caries in their children (Sasahara et al., 1998).

Okada et. al. illustrated that parent oral health behavior could influence their children's gingival health and dental caries directly and/or indirectly through its effect on children's oral health behavior. (Okada et al., 2002).

Even though it has been widely studied, ECC remains a serious public health problem, especially in countries where there is no national program of oral health assessment and no legitimate primary oral health care. Many aspects related to ECC have been investigated including etiology, risk factors, consequences, oral health promotion and preventive measures. Attempts to solve ECC have also been studied intensively. However, there is still no effective program to overcome this problem. A lot of infants and young children around the world, not only in developing countries but also in developed countries (Pitts & Palmer, 1994; Widstrom & Hiiri, 1998), are still facing this severe health problem. There have been many studies focusing on mothers'/caregivers' knowledge, attitude and practices (Kamolmatyakul & Saiong, 2007; Okada et al., 2002; Sarnat et al., 1984; Sasahara et al., 1998). Many studies have shown that good levels of attitude and knowledge did not result in good practice (Benitez et al., 1994; Kamolmatyakul & Saiong, 2007; Tinanoff et al., 1999). Our study demonstrated that despite good levels of knowledge and attitude in oral health, caregivers seem to be unable to apply them to everyday practice (Kamolmatyakul & Saiong, 2007). Therefore, instead of focusing on providing knowledge to mothers/caregivers, more practical programs to let them "do it" in the course will probably result in less carious teeth in young children's mouths. There is no ''magic bullet''. However, this chapter intends to focus on the attempt to generate a universally effective, caries-prevention program which will help improve better oral health for all, starting from a very young age, as a good foundation for a happy smile, as shown in figure 1.

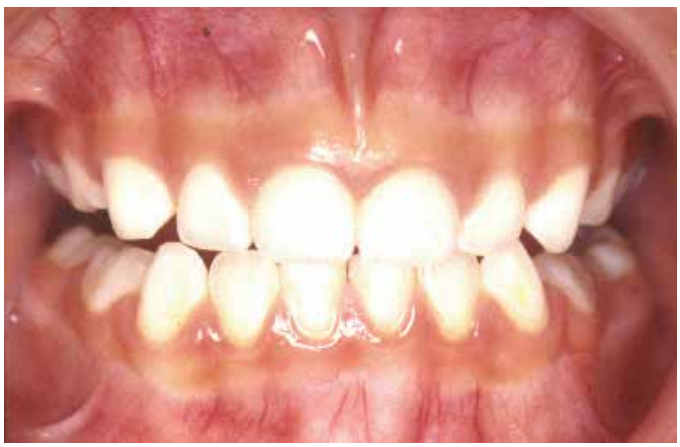

Fig. 1. Soft and hard tissues of a young child's mouth should be seen as the foundation for a lifetime free from preventable oral disease

2. Childhood oral health

Infant oral health care should be seen as the foundation on which a lifetime of preventive education and dental care can be built. In order to help assure optimal oral health in childhood, the American Academy of Pediatric Dentistry (AAPD) recommend that infant oral health care should begin ideally with prenatal oral health counseling for parents. Then

AAPD's recommendations on Infant Oral Health Care. (Revised 1989, 1994, 2001, 2004, 2009)

1. All primary health care professionals who serve mothers and infants provide parent/caregiver education on the etiology and prevention of ECC. Oral health counseling and referral for a comprehensive oral examination and treatment during pregnancy is especially important for the mother.

2. The infectious and transmissible nature of bacteria that cause ECC and methods of oral health risk assessment, anticipatory guidance, and early intervention be included in the curriculum of all medical, nursing, and allied health professional programs.

3. Every infant receives an oral health risk assessment from his/her primary health care provider or qualified health care professional by 6 months of age. This initial visit should consist of the following:
   - assessing the patient's risk of developing oral disease using a caries risk assessment;
   - providing education on infant oral health; and
   - evaluating and optimizing fluoride exposure.

4. Parents or caregivers establish a dental home for infants by 12 months of age. The following should be accomplished at that visit:
   - recording thorough medical (infant) and dental (mother or primary caregiver and infant) histories;
   - completing a thorough oral examination;
   - assessing the infant's risk of developing caries and determining an appropriate prevention plan and interval for periodic reevaluation based upon that assessment;
   - providing anticipatory guidance regarding dental and oral development, fluoride status, non-nutritive sucking habits, teething, injury prevention, oral hygiene instruction, and the effects of diet on the dentition;
   - planning for comprehensive care in accordance with accepted guidelines and periodicity schedules for pediatric oral health;
   - referring patients to the appropriate health professional if intervention is necessary.

5. Health care professionals and all other stakeholders in children's oral health should support the identification of a dental home for all infants at 12 months of age.

6. Legislators, policy makers, and third party payers are educated about the benefits of early interventions in order to support efforts that improve access to oral health care for infants and children.

Table 1. The American Academy of Pediatric Dentistry recommendations on Infant Oral Health Care

an initial oral examination within six months of the eruption of the first primary tooth and no later than twelve months of age should be carried out. The other recommendation is

anticipatory guidance including preventive education and appropriate therapeutic intervention for the infant. These can enhance the opportunity for a lifetime of freedom from preventable oral disease (AAPD, 2011a).

The AAPD also recognizes that infant oral health is one of the foundations upon which preventive education and dental care must be built to enhance the opportunity for a lifetime free from preventable oral disease. The AAPD proposes recommendations for preventive strategies, oral health risk assessment, anticipatory guidance, and therapeutic interventions to be followed by dental, medical, nursing, and allied health professional programs. Table 1 shows AAPD's recommendations for Infant Oral Health Care that have been adopted since 1986 and periodically revised in 1989, 1994, 2001, 2004, and 2009 (AAPD, 2010a).

2.1 What is ECC and its etiology?

A current definition of ECC, adopted by the AAPD, is the presence of 1 or more decayed (noncavitated or cavitated lesions), missing (due to caries), or filled tooth surfaces in any primary tooth in a child under the age of 6 (AAPD, 2011b). ECC has been termed the most prevalent pediatric infectious disease and the most common chronic disease of children in U.S.A. (US Dept of Health and Human Services, 2000). One of the major virulent caries-producing organisms is Mutans streptococci (MS). MS vertical transmission from mothers to infants is the primary source of dental caries (Berkowitz & Jones, 1985; Douglass et al., 2008). However, horizontal transmission between siblings of a similar age or children in a day care center has already been reported (Emanuelsson & Wang, 1998; Mattos-Graner et al., 2001; Mitchell et al., 2009; Van Loveren, 2000). MS can be detected in many locations in the oral cavity. The furrows of the tongue are an important ecological niche in predentate infants (Berkowitz, 2006; Law et al., 2007; Tanner et al., 2002). Transmission of MS may occur from the time of birth. However, significant colonization occurs after dental eruption, as MS can

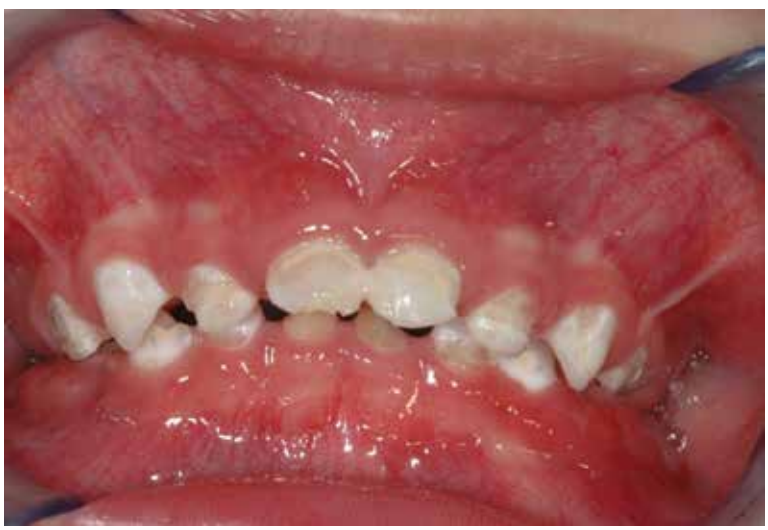

Fig. 2. Caries progression of Early Childhood Caries (ECC) starting from maxillary central incisors and extends gradually to the maxillary lateral incisors, maxillary first primary molars, maxillary canines, and then second primary molar. (Photo courtesy of Dr. Aunwaya Kaewpitak, Prince of Songkla University, Songkla, Thailand)

adhere to non-shedding tooth surfaces. After colonization, they produce acid from sugars which, over time, demineralizes tooth structure (Loesche, 1969). The process normally takes place at the smooth surfaces of upper teeth starting from the central incisors, extending gradually to the lateral incisors, the first primary molars, canines, and then the second primary molars (Edelstein et al., 2009). Figure 2 demonstrates an example of severe ECC in a young child who attended the dental hospital at Prince of Songkla University, Thailand.

2.2 Factors influencing and consequences of ECC?

There are many factors influencing ECC including biological (feeding practices, diet, and MS level of primary caregivers) and social (sociopsychological, socioenvironmental, and socioeconomic status) factors (Edelstein et al., 2009). Starting from the 1990s, these multiple factors have been raised in an attempt to focus attention on, rather than ascribing sole causation to, inappropriate feeding practices (Reisine & Douglass, 1998). Oral health has a significant impact on overall health and well-being. The consequences of ECC, when left untreated, can become painful and cause many alterations including chewing patterns, eating and dietary nutrition, learning, speech and communication, playing, sleeping and, quality of life, in addition to potential growth restriction (Schroth, et al., 2009). Children with ECC have been reported to have a high risk of decay in both primary and permanent dentition. These could cause mal-alignment and crowding of permanent teeth that consequently result in a malocclusion. In addition, early tooth loss may result in speech difficulties as well as associated self-esteem issues due to altered appearance (Schroth et al., 2007b). Therefore, the importance of each influencing factor should be emphasized to all involved agencies and health team personnel.

2.2.1 Biological determinants of ECC

2.2.1.1 Salivary mutans streptococci levels and visible plaque.

The association between the salivary MS level and ECC is well documented (Berkowitz, 2003). The relationship of MS levels between children and their mothers/caregivers has also been evaluated since the mid-1970s (Douglass et al., 2008). Therefore, managing adult reservoirs and interfering with transmission may reduce dental caries onset and experience. Parisotto et al. showed that the higher the levels of maternal salivary MS, the greater the risk of transmission of MS to their infant (Parisotto et al., 2010). Apart from MS salivary levels, the mother's oral hygiene, snack frequency, periodontal disease, and socioeconomic status are also associated with infant colonization (Wan et al., 2001). In addition, the plaque index of young children is a strong predictor of caries (Mattila et al., 1998).

2.2.1.2 Breast- and bottle-feeding

In 2011, the AAPD's recommendations for infant's oral health state that "frequent night time bottle feeding with milk and ad libitum breast-feeding are associated with, but not consistently implicated in, ECC". Not only milk, but bottle feeding with juice/soft drink and repeated use of a sippy cup also increase caries risk (AAPD, 2011b).

2.2.1.3 Diet

Improper diet and nutrition was also reported to be associated with caries in young children; for example, soda or other sugared beverage intakes, greater frequency of

carbohydrate intake, and greater frequency of eating occasions (Mariri et al., 2003). Another important aspect is the quality of fluid intake such as "high-juice group", "high-carbohydrate soft drinks", "high-water group", and "high-milk group". The milk group causes the least caries experience (Sohn et al., 2006). Additionally, normative diet behaviors are correlated with overall caries experience. These include not consuming the recommended five fruits and vegetables on a daily basis and not eating breakfast (Dye et al., 2004). Moreover, the importance of sugar comsumption should also be emphasized. Although toothbrushing has been shown to be essential for prevention of caries, the most important element has to do with the frequency of sugar consumption (Ainamo, 1980). Recently, Kalsbeek and Verrips reported a positive relationship between sweets/snacks consumption and caries occurrence (Kalsbeek & Verrips, 1994).

2.2.2 Social determinants of ECC

Many social determinants affect children's general health as well as oral health. These include personal, cultural, communal and economic factors which influence dental health behaviors and nutritional habits. They are powerful determinants for when or whether families seek dental health care (Waldman, 1995). The maturity of the parents is another important aspect in the family issue; they may be ill-equipped to bring up their children. These habits would show up daily by allowing their children to watch TV for hours, by frequent feeding of unhealthy snacks, and also by using sweets to comfort the child during temper tantrums. All these features should be emphasized in children with caries (Mattila et al., 2000). Therefore, preventive dentistry that concentrates only on the oral health of the child is inadequate. Attention must be focused on the whole family, their dental health habits, and their lifestyles. These strategies need to be emphasized not only by dental staff, but also the involved agents and health team personnel.

2.3 Attempts to solve ECC

ECC is the result of the interplay of substrate, oral bacteria, and the host, as well as the family, social, and economic conditions. Therefore, health-promotion policies that emphasize community empowerment and address the determinants of health are needed along with strategies that focus on disease prevention. Changes in the modern world results in high caries prevalence among young children, not only in developing countries but also in developed countries which used to have a low prevalence of ECC. Both are now facing the problems of ECC consequences (Mattila et al., 2000; AAP, 2011a). Therefore, effective programs to solve ECC problems will benefit all children around the world. Based on ECC influencing factors, the American Academy of Pediatrics (AAP) recommended (AAP, 2011) that ECC prevention should start during the prenatal period, progress through the perinatal period, and then continue with the mother and infant within the context of preschool programs. Since a vertical transmission of cariogenic bacteria usually occurs from mother to child, the approach to create good oral health in children involves first including pregnant women in oral health screening, dental treatment, and oral health hygiene instruction. In addition, their nutrition should be bolstered along with the use of fluoride toothpaste. These strategies can assist in the prevention of ECC. Second, these prenatal visits would also provide an opportunity to build awareness about the importance of oral health for mothers in relation to their infants. Examples of important lessons for mothers include appropriate oral health care during the perinatal period of pregnancy, as it would prevent preterm and

low-birth weight babies. Additionally, women with poor oral health have the chance to infect their babies with cariogenic bacteria and thus increase their children's risk of caries at an early age. Moreover, change of frequent consumption of sugar-containing drinks and sugary snacks should be promoted. These lessons would alter practices through education for pregnant women, mothers/caregivers and school children. Finally, the selection of foods available in the communities should be enabled.

2.4 Mothers'/caregivers' attitude, knowledge and practice

In order to implement effective programs to solve ECC problems, the investigation of knowledge, attitude and practice is essential. Many researchers have tried to assess the relationship between attitude, knowledge and practice on oral health (Ab-Murat & Watt, 2006; Al-Omiri et al., 2006; Smyth et al., 2007). Firstly, they indicated that strong knowledge of oral health exhibits better oral care practice (Smyth et al., 2007). Secondly, people with a more positive attitude towards oral health are predisposed by better knowledge in how to take care of their teeth (Al-Omiri et al., 2006). Thirdly, some researchers showed that appropriate oral health education can help to cultivate healthy oral health practice (Ab-Murat & Watt, 2006). Finally, the change to healthy attitude and practice can be created by providing adequate information, motivation and practice of the procedure with the subjects (Smyth et al., 2007). However, such knowledge that mothers/caregivers know about the concept of the first dental visit before the child's first birthday does not necessarily translate into practices that are likely to prevent ECC (Schroth et al.; 2005; Schroth et al.; 2007a). These data from westernized countries are similar to our study in Thailand. Most parents attending the Prince of Songkla University dental hospital in Thailand had a good level of knowledge and a positive attitude about their children's oral health. However, some of them still could not follow some of the recommendations for preventive pediatric dental care. Therefore, knowledge may not result in appropriate behavior. This discrepancy between dental knowledge and parents oral health care practices indicates a need for oral health education. However, influencing the oral health behavior of parents is difficult. Therefore, we suggested that it may be more practical to offer comprehensive oral health educational programs for children at school (Kamolmatyakul & Saiong, 2007). Based on influencing factors, these programs should involve not only the educational aspect but also aspects of attitude and most importantly, how the practical behaviors can be developed. Therefore, implementation of these programs should involve not only pediatric dentists, allied health professionals, nursery staff, and teachers in kindergarten, but also health policy personnel. However, the most important persons are mothers/caregivers.

2.5 Programs for mothers/caregivers

Infants and toddlers are most susceptible to ECC. Therefore, proper oral care for this age group should be implemented for all persons involved. The first group should be the mothers/caregivers. Since these young children's oral health is totally dependent on their caregivers, a program for these adults is very important. The program should start from the prenatal period. All pregnant women should be scheduled to receive counseling and oral health care during pregnancy. They should also be registered in a dental home program to make sure that their infants undergo oral health assessment by the first birthday. Importantly, the program will help them follow each step of the program without any problem.

2.5.1 Programs related to mothers/caregivers' oral health

Community-based activities should be used to emphasize the importance of oral health for the pregnant woman and her infant(s). In terms of knowledge, they should be educated about the importance of oral health, the transmissible nature of bacteria, and the etiology and prevention of ECC. For example, plaque deposits on tooth surface, improper consumption of snacks, and frequent consumption between meals of sugar-containing snacks or drinks (e.g., juice, milk, formula, soda) are strong caries predictors that increase caries risk. The influences of cariogenicity of certain foods, snacks and beverages and the frequency of consumption of these substances that are related to caries should also be emphasized. Moreover, parents need to be educated regarding other powerful social determinants for children. The most powerful aspects are the issues of being well-equipped to bring up their children. These involve, firstly, avoiding saliva-sharing behaviors (e.g., sharing cups, spoons and other utensils, or cleaning a dropped pacifier or toy with their mouth). Secondly, frequent night time ad libitum breast-feeding, as well as bottle feeding with milk and sugar-containing beverages should be included in educational programs. Finally, repeated use of a sippy or no-spill cup, and frequent consumption between meals of sugar-containing snacks or drinks (e.g., soda, juice, milk, formula) that increase the risk of caries should also be emphasized and discouraged.

The above knowledge should not only be taught in a lecture manner, but also able to be implemented with the possibility of suitable practical methods for them to really apply it. In order to achieve the practical behavior, a good attitude should be implemented, such as good general health depends on good habits (eating, sleeping and routine exercise) and thus dental health also depends on good habits (proper tooth brushing, regular dental visits and a good diet). Parents' self-confidence in bringing up their children in a consistent and logical manner should also be emphasized. Therefore, the programs could build up the parents' attitude that they can be models for their children through a good lifestyle.

In terms of appropriate practical behaviors, the implemented programs should involve oral health services in order to create an impact on the MS reservoir suppresses in mother's/caregiver's mouths, inhibit the MS transmission and decrease the child's caries rate. Oral health services should be provided to pregnant women to get their oral examined and cleaned and to have any needed periodontal and dental work performed before their infant is born. This service would include an oral examination, professional prophylaxis, fluoride treatment, early intervention such as removal of active caries with subsequent restoration, and the use of xylitol chewing gum (AAPD, 2010b).

2.5.2 Programs related to children's oral health

After implementation of knowledge and attitude to mothers/caregivers, the next step is the practical programs to promote appropriate child rearing behaviors instead of improper ones, such as allowing the child to watch TV for hours, frequent feeding of sugar and sweets, and using sweets to comfort during temper tantrums. The most important factor of all that needs to be included is an infant oral health care program because it is one of the foundations upon which promotional education and oral health care must be built to enhance the chance of a lifetime free from preventable oral disease. The program of promotional activity includes promoting teeth cleaning, which is an example that has to be modified according to the age of the child. At first, oral hygiene is the parent's responsibility, then the parent and child must work together, and gradually, the child

assumes the responsibility. This depends on the child's anatomic/physiological development, improving skills, different motivational forces, changing lifestyles and anatomic and physiological changes associated with growing up. The program should facilitate mothers/caregivers to clean their infant's mouth with a clean cloth after each feeding or at least once a day before bed time. Then as soon as the first tooth erupts, they should be cleaned with a soft toothbrush. This will help reduce bacterial colonization. The protocol of activities which should be demonstrated and supervised to mothers/caregivers includes age-appropriate tooth brushing with age-appropriate amount of fluoridated toothpaste twice daily using a soft toothbrush of age-appropriate size, rinsing 0.05% sodium fluoride mouth rinse once a day, and flossing with dental floss to help dislodge food and reduce bacterial plaque levels. Flossing should be initiated around three years of age when adjacent posterior tooth surfaces cannot be cleansed with a toothbrush. The amount of fluoride toothpaste to be used has to be emphasized to mothers/caregivers. According to AAPD guidelines, a 'smear' of fluoridated toothpaste should be used in a child under the age of 2 and a 'pea-size' amount should be used in all children aged 2 to 5 (AAPD 2011b).

2.6 Programs for dentists and allied health professionals

General dentists can provide oral health service to pregnant women/mothers during prenatal, perinatal and postnatal periods, while pediatric dentists can provide oral health services to children starting from infancy through adolescence. Since oral health services for pregnant women/mothers are already discussed above, this section will only deal with children oral health services. Pediatric dentists are the first professionals directly involved in oral health care service for children. They have an opportunity to see children much earlier and thus capture the parents' interest in appropriate oral health milestones and the consequences of improper habits and behaviors. Implementation of an anticipatory guidance to oral health promotional education is an organized way for all oral health providers to enjoy the attention of parents and be more successful in good oral health care for children.

Early access to oral health providers to establish a dental home should be organized no later than when the child reaches 12 months of age. This will ensure that the full range of oral health-promotion and interceptive disease-prevention services will be provided. Oral hygiene measures should be implemented no later than the time of the first primary tooth eruption. However, mothers/caregivers should be taught to clean infants' mouths after each feeding or at least once a day before bed time, as soon as possible, even before tooth eruption. Professionally-applied topical fluoride, such as fluoride varnish and fluoride gel, should be considered for children at risk for caries. Systemically-administered fluoride should be considered for all children with moderate/high caries risk who drink fluoride deficient water (<0.6 ppm), after assessing all other dietary sources of fluoride exposure (AAPD, 2011a).

The AAPD encourages physicians, nurses and other health care professionals to educate pregnant women about perinatal and infant oral health (AAPD, 2011a). Since physicians, nurses, and other health care professionals are far more likely to see new mothers and infants than are dentists, it is important that they be aware of the ECC infectious etiology and associated risk factors, make suitable decisions regarding timely and effective intervention, and assist the establishment of the dental home or merge oral health assessment/intervention as part of a regular holistic child health care clinic program.

Physicians, nurses, physician extenders and child health associates all can intervene at an appropriate point with any child. A similar program in dentistry delivers a well-defined source of information that can be organized by all members of the office team. Regardless, multidisciplinary approaches are needed to promote good oral health in preschool children. These require collaboration among dentists, especially pediatric dentists, allied health professionals, child-care centers personnel, and health policy personnel such as decision-makers, policy-makers, and researchers involved with young children.

2.7 Programs for child-care centers personel

Child-care center personnel comprise of nursery staff and center-based program staff such as staff in day-care centers, pre-kindergartens, nursery schools and teachers in kindergarten. Increasing health promotion in out-of-home child-care settings could improve the oral health of preschool age children. The AAPD encourages child-care centers' staff, early education providers, and parents to implement promotional practices that can decrease the risk of developing ECC in children (AAPD, 2011c). The program could be prepared step by step. First, the health staff, preferably a pediatric dentist, should monitor program practices regarding oral health. Then the individualized recommendations for each program should be carried out at least once a year. Second, the concept of the dental home should be promoted by educating their personnel as well as mothers/caregivers on the importance of oral health and providing assistance with implementation of a dental home no later than 12 months of the child's age. Third, keep oral health records, merging with the child's health report, starting at age 12 months. It should address the child's oral health needs as well as any special instructions given to mothers/caregivers. Fourth, sponsor on-site age appropriate oral health promotion programs for children that will encourage good oral hygiene and dietary practices, injury prevention, and the importance of regular scheduled dental visits. Fifth, provide in-service training programs for the personnel regarding proper nutrition choices, links between diet and tooth decay, oral hygiene concepts, and children's oral health issues including appropriate initial response to traumatic injuries along with complication and dental consequences. Personnel with an understanding of these concepts in their minds are a great benefit in caring for children. Sixth, encourage mothers/caregivers to be active partners in the children's health care process and grant an individualized education plan, one that is responsive to cultural values and beliefs, to meet every family's needs. Written material should be provided and, at a minimum, tackle oral health promotion and disease prevention and the timing of oral health visits. Seventh, integrate oral health activities as part of the daily health care of each child such as oral hygiene practices at least once daily after a meal. Eighth, supply well-balanced diets of low caries-risk, and optimally-fluoridated drinking water accessible for consumption throughout the day. Finally, in terms of general/dental health habits, not permitting infants and toddlers to have bottles/sippy cups in the crib or to carry them while walking, and minimizing saliva-sharing activities (e.g., sharing utensils, orally cleansing a pacifier) help decrease an infant's or toddler's acquisition of cariogenic microbes (AAPD, 2011c).

2.8 Programs for health policy personnel/government

It is important that the oral health needs of infants and young children be addressed as early as possible and as a part of good child-care since dental disease is preventable. Therefore,

the health policy personnel/government should incorporate programs to make sure legislators, policy makers, and third party payers are well-informed regarding the importance of early interventions of ECC. They can then facilitate to support the continuing programs for good oral health in children. The first requirement would be providing knowledge for pregnant women (the most important aspect is education regarding the infectious and transmissible nature of bacteria that causes ECC) to have a good attitude where they can really take care of their own oral health. Moreover, proper oral health services for mothers/caregivers should also be prepared (oral examination, fluoride treatment, professional prophylaxis, early intervention such as removal of active caries with subsequent restoration of remaining tooth structure). Next, health care professionals and all other stakeholders in childrens oral health should support the implementation of a dental home for all infants by 12 months of age. The dental home concept refers to a continuing relationship between health personnel and child, where the child's access to holistic and coordinated oral health care and prevention is the main focus and tailored to the needs of the child. The details of a dental home include, firstly, thorough medical (infant) and dental (parent and infant) histories, a thorough oral examination, performance of an age-appropriate tooth brushing demonstration and prophylaxis. Secondly, fluoride varnish delivered as part of a regular child health clinic program. These procedures can be provided by trained health auxiliaries, community health workers, family physicians, or pediatricians. Alternative health or child care professionals and dental auxiliaries (or trained lay child care workers such as early childhood development workers) should be recruited to ensure access to fluoride-varnish programs. Thirdly, sealant placement on deep grooves and fissures on primary teeth should be delivered by pediatric dentists. Finally, investigating the infant's risk of developing caries and determining a prevention plan and interval for periodic reevaluation should also be scheduled.

In the communities where it is difficult to recruit and retain an adequate number of dentists, health policy personnel should arrange for other oral health and primary health care providers to deliver oral health services and promote an early dental visit within the first year of life. Recent studies, noting that a majority of pediatricians and general dentists were not advising patients to see a dentist by 1 year of age, point to the need for increased infant oral health care education in the medical and dental communities (AAPD, 2011a). It is important to develop oral health information programs to pediatricians. Information on oral health should be included in medical curricula and residency (Balaban et al.; 2011). Therefore, oral health training should be incorporated into pediatric and family medicine residency programs.

For older children, health policy personnel should set a program that facilitates students to take responsibility for their own oral health. This will diminish dependency on oral health personnel. Among teenagers, schools would serve as the best platform for oral health care instruction. The oral health programs should be intensified to promote oral healthcare as a lifelong practice. After incorporation of oral health promotion activities into the school's curriculum, more attempts in the form of educational materials (tooth brushing techniques, healthy food etc.) and general health promotion activities related to oral health need to be carried out. Another important school health policy that needs implementation is healthy eating behavior that bans unhealthy foods and drinks in the school premises. Healthy foods must be made available in the school canteens, while the canteens should be prohibited from selling unhealthy food and drinks such as soda and those with high sugar

levels. Although parents play an important role in influencing their children's eating behavior, a more effective method would be empowering the children to make healthy food choices. At this age, these students are more likely to buy food on their own as compared to primary school children (Cheah et al., 2010).

3. Conclusion

Dental caries is a disease that generally is preventable. Early risk assessment allows for identification of parent-infant groups who are at risk for ECC and would benefit from early preventive intervention. The ultimate goal of early assessment is the timely delivery of educational information to populations at high risk for developing caries in order to prevent the need for later surgical intervention. The most important population is mothers/caregivers. The implementation of systems to promote good oral health for all should be the responsibility of health policy personnel/the government. Combined approaches must be implemented. Strategies should begin with community engagement and always include primary care providers and other community health workers. Arangement programs should involve not only dentists, but also allied health professionals and child-care center personnel. Moreover, these programs should not only be arranged for preventive dentistry which concentrates only on the oral health of the child, but attention must also be focused on the whole family, its dental health habits and lifestyles. A combination of approaches is required to organize these programs. These include recommendations for preventive oral health and clinical care for young infants and pregnant women by primary health care providers, community-based health-promotion initiatives, oral health workforce and access issues, and advocacy for community water fluoridation and fluoride-varnish program access. Further community based research on the epidemiology, prevention, management, and microbiology of ECC would also be beneficial.

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22

Systemic Methods of Fluoride and the Risk for Dental Fluorosis

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1. Introduction

The benefits from ingesting fluoride for controlling dental caries have been suggested more than a century ago. Later in the 1940s, the well conducted water fluoridation program developed in the United States established the potential for delivering fluoride in public water supplies which opened the opportunity for other systemic methods: salt, milk and supplements (Hunstadbraten, 1982; Hoffmann-Axthelm, 1981). Due to its systemic effect, fluoride has been regarded as effective only if ingested for a long period. The low doses proposed were regarded as safe enough to guarantee the most beneficial effect against dental caries with minimal fluorosis.

From a historical perspective, the use of fluoride can be divided into two periods: 1) the earlier era, which goes from 1940s up to 1960s, when water fluoridation was basically the only source of fluoride ingestion and 2) the later era when fluoride could be ingested from multiple sources (soft drinks, infant formulas, vitamins, tablets) (Murray et al., 1991). Hence, due to the widespread of fluoride and the updated knowledge about its mechanisms of action, the general opinion about effectiveness and risk of systemic methods of fluoride are completely different from decades ago. Nevertheless, these methods are still recommended in many countries and receive support from recognized international committees and associations. In contrast, many dental practitioners have conflicting opinions about the safety and benefits of having a water fluoridation program in their city.

In addition to the multiple sources of fluoride, the systemic methods for delivering fluoride are also questioned because several studies have consistently indicated that fluoride's action relies mainly on its post-eruptive effect from topical contact with the tooth structure. The situation gets more obscure when the emerging problem of dental fluorosis can also be attributed to early uncontrolled ingestion of fluoride toothpaste by children as well as other sources (Hellwig & Lennon, 2004; Sampaio & Levy, 2011). This may give the impression that a widely used topical method of fluoride such as dentifrice is the solely contributor for dental fluorosis whereas a systemic method of fluoride such as water fluoridation is ineffective since it is a systemic method to deliver fluoride and most of fluoride effect comes from topical sources. These are points of view which can jeopardize the use of fluoride on an individual basis or in a community level.

One of the main problems when studying fluoride in Dentistry is its paradox of combining beneficial and pathological effects in the same chemical element. Taking other water contaminants such as arsenic, there is no doubt about its deleterious effects on human health. Moreover, no beneficial effect exists when considering an ingestion of low doses of arsenic (Hughes, 2002). For fluoride the situation is different. There is an evident advantageous clinical effect when low doses are used together with the concomitant risk for dental fluorosis. Since the borderline of benefits and risks of fluoride can be rather close, researchers around the world have focused on strategies for controlling the amount of fluoride intake. In addition, other aspects on the use of fluoride must be discussed. For instance, there are many epidemiological and biological evidences that ingestion of high amount of fluoride can result in aesthetically undesirable dental fluorosis; how much of this effect is unacceptable is a matter of debate. As a result of the fluoride debate, more and more clinicians and researchers regard this issue as an important topic for discussion and a challenging problem for dental professionals.
Thus, the aim of this paper is to critically review the current role of systemic methods to deliver fluoride considering the risk for dental fluorosis.

2. The mechanism of action of fluoride

Although the mechanism of action of fluoride is well established today, a series of studies was necessary to recognize its cariostatic effect.
Fluoride is an ion naturally found on soil, air and water due to chemical weathering of minerals that contains this element (Murray at el., 1991). This ion has the capacity of inhibiting and activating enzymatic systems as well as a tendency to fixate on hard tissues (bones and teeth). On the teeth this fixation occurs through the substitution of the hydroxyl ion from the hydroxyapatite by the fluoride ion resulting on fluorapatite during the demineralization–remineralization process of the enamel. One interesting observation is that the fluoride effect on the de-remineralization equilibrium is of outmost relevancy, being more important than the incorporation of fluoride in the dental tissue. Actually, this incorporation is an obvious consequence of the fluoride effect on the demineralization-remineralization process and not the beneficial aspect in itself as it has been thought previously (Fejerskov, 2004). One important study that demonstrated that fluoride incorporated into enamel (structurally bound fluoride) was not effective in inhibiting demineralization of a hard tissue was carried out in Scandinavia (Øggard et al., 1988). The researchers prepared in situ devices and placed human and shark enamel slabs in oral appliances. Why shark enamel? The shark enamel is composed of pure fluorapatite (30,000 ppm) whereas the maximum amount of fluoride in human enamel is much lower (4,800 ppm). The oral removable appliances were used by volunteers that allowed bacterial plaque accumulation (oral biofilms) and the development of carious lesions. Microradiographic analyses showed that carious lesions were present in both types of enamel tissues (human and shark). One first conclusion of this study was that incorporation of fluoride into enamel is not the main mechanism for controlling dental caries development. Moreover, the authors compared the mineral loss data obtained to previous data of enamel exposed to 0.2% of sodium fluoride. The results showed that the mineral loss in human enamel exposed to sodium fluoride was lower than that of shark enamel without any additional treatment. In summary, this work provided evidence that the primary mode of action of fluoride is

topical. The fluoride present in the fluid phases of the oral environment is the most important strategy for controlling dental caries (Buzalaf, 2011).

Since fluoride may inhibit the demineralization or enhance remineralization mainly by topical processes, the most effective fluoride regimens are those when frequent low fluoride concentrations are achieved in the oral environment. As a result, topical methods for delivering fluoride gained a status of most effective ones (Limeback, 1999). However, one must bear in mind that traditional systemic methods such as water fluoridation cannot be excluded because its effectiveness can be also topical though in general it is classified as systemic fluoride method. Another point of remark is that regardless the method (topical or systemic) fluoride treatments do not introduce a new substance but rather increase the concentration of an existing one in the oral environment. It must be pointed out that fluoride may also have some antibacterial effect when high concentrations are maintained in the oral cavity. This effect is mainly achieved in topical applications of very high amount of fluoride incorporated in the formula such as varnishes and gels. Hence, it can be suggested that fluoride has more than one mechanism of action for caries arrestment and these mechanisms can be simultaneously in action when exposure to fluoride takes place. Since dental caries is a multifactorial disease caused by the interplay of different factors of the oral environment the duration and cessation of a fluoride exposure must be considered when searching for its mechanism of action.

The beneficial interference of fluoride in the caries development is directly dependent on a constant and permanent level of fluoride in the oral environment (Fejerskov, 2004). There is no need for a high concentration of fluoride because low concentrations can be sufficient for the control of mineral tooth loss. This is a key point when considering the use of fluoride for caries preventive purposes which is different from caries arrestment (Sampaio & Levy, 2011). According to Buzalaf (2011), a good understanding of the mechanism of action of fluoride can be achieved if you consider five "pools" of fluoride categories in the oral environment: 1) outer fluoride (present outside enamel, in the biofilm or saliva), 2) fluoride in the solid phase (incorporated in the mineral structure, also known as fluorhydroyapatite), 3) fluoride in the enamel fluid, 4) fluoride adsorbed in the crystal surface, also known as loosely-bound and finally 5) calcium fluoride material (Ca_2F, globules that are formed just after the application of high concentrated fluoride products such as varnishes and gels) (Figure 1). Our current understanding about the mechanisms of action of fluoride can be summarized when these categories are evaluated in two aspects: fluoride effect on the inhibition of demineralization and its effect on promoting remineralization. Both are processes of the same chemical reaction and both are equally important for caries control.

2.1 Inhibition of demineralization

The fluoride category known as loosely-bound fluoride is the "pool" that effectively protects the dental enamel from mineral dissolution. Note that the fluoride incorporated in the solid phase has little or no effect. However, the fluoride present in the enamel fluid is also important since this is the fluoride category that can increase the loosely-bound fluoride which protects the enamel crystal by inhibition of demineralization (Arends & Christoffersen, 1990). The calcium fluoride category is also an important source of fluoride and it is formed when there is more than 100 ppm of fluoride in the oral environment. This means that this type of fluoride is available when dental products are used. The mechanism of action of this fluoride category can be explained by the formation of calcium fluoride

(Ca_2F) and its dissolution when there is a pH fall (acidic challenge). During this acid attack, the calcium fluoride material (globules) are dissolved releasing an ionic fluoride, in other words, a fluoride that will be present at the enamel fluid which can be adsorbed by the enamel crystal avoiding the demineralization process. In summary, the loosely bound and calcium fluoride material are sources of fluoride that will protect the enamel from the mineral loss.

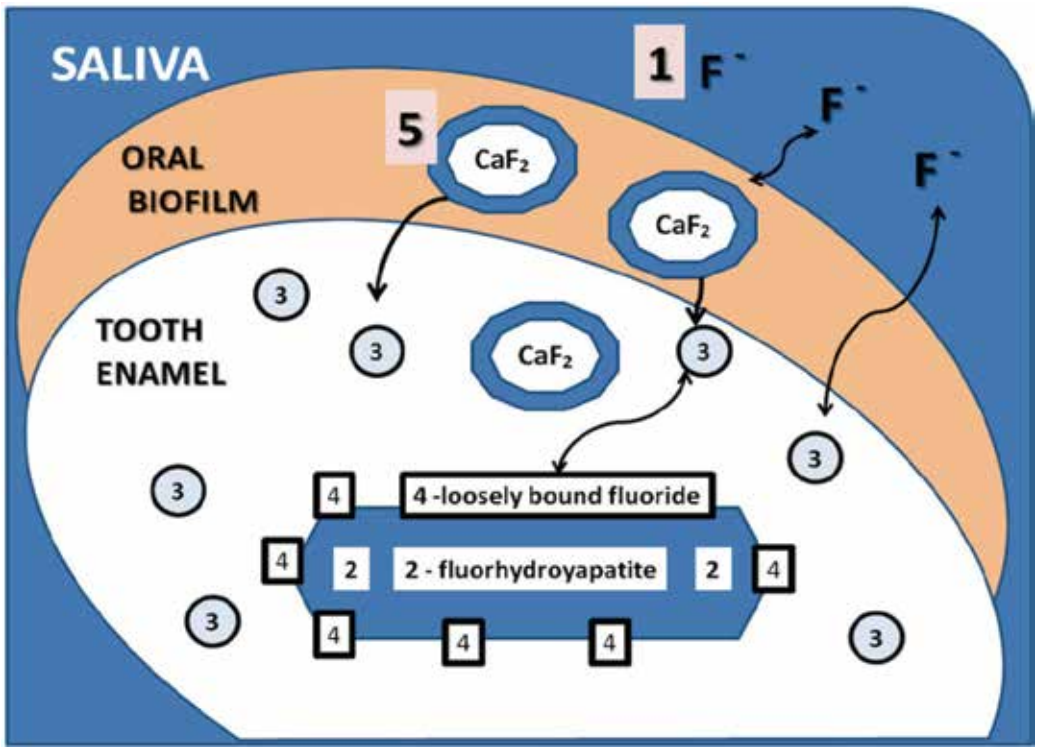

Fig. 1. Schematic representation of fluoride effect on tooth enamel. Note that the numbers represent different categories of fluoride: (1) outer fluoride, (2) fluoride incorporated in the mineral structure, (3) fluoride in the enamel fluid, (4) fluoride adsorbed in the crystal surface, also known as loosely-bound, (5) calcium fluoride material (Ca_2F, globules that are formed just after the application of high concentrated fluoride products)

2.2 Promoting remineralization

When a carious lesion is already present, an acidic challenge is frequently occurring. Under this circumstance, when pH is below 5.5 – a critical pH for dental enamel, the remineralization can naturally take place since saliva is generally supersaturated with respect to dental enamel. If fluoride is present in this acidic medium during dissolution of hydroxyapatite, the solution will be highly supersaturated with respect to hydroxyapatite and all potential mineral loss will actually be preserved in the partially demineralized dental crystals. In other words, traces of fluoride in the fluid phase can control mineral loss. After several cycles of dissolution and reprecipitation, the enamel crystals will be somehow more resistant to future acidic challenges. At this point one may argue that the incorporation of

fluoride will provide a more resistant tissue to dental caries which is not in tune with the actual understanding of fluoride's mode of action (Fejerskov, 2004). However, it must be emphasized that the incorporation of fluoride in this situation is only possible due to the fact that there is a partial dissolved crystal which presents free calcium for fluoride incorporation. Thus, the frequent presence of fluoride in the oral environment during the acidic challenge is as relevant as it is its effect of incorporation. Hence the presence of fluoride at high concentrations is a key strategy for caries control or arrestment of carious lesions (Featherstone, 1999).

2.3 How much fluoride is necessary?

In addition to the understanding of fluoride modes of action, it is also important to observe the concentrations of fluoride used in different methods. The ideal or 'optimal' concentration of fluoride will be the one that will have maximum preventive effect with a minimal risk for dental fluorosis. This is rather difficult to consider since individual variations in fluoride bioavailability and cultural habits may influence the intake of fluoride from systemic methods such as water, salt or milk (Newbrun, 2010).

It must be pointed out that the classification of 'systemic' and 'topic' is related to its way of delivery and not to its mode of action. In other words, the mode of action of water fluoridation for caries control is explained by the topical contact of water fluoride on the teeth when someone is drinking water and eating food prepared with fluoridated water. One additional effect is the redistribution of fluoride in the oral cavity by means of saliva (Whitford, 1996). Hence, as stated before, fluoride acts mainly by its topical effect but this is not an argument to invalidate the systemic methods of fluoride. On the other hand, topical and 'systemic' methods of fluoride delivery may be involved with a high rate of fluoride ingestion. Taking fluoride toothpaste as an example, it is classified as a topical method but there is no guarantee that some ingestion of fluoride may occur when a child is under toothbrushing procedure.

So, if low sustained levels of fluoride is maintained in the oral fluids, some level of loosely bound fluoride will be available and a significantly control of caries progression and also reversal of carious lesions may occur. The low levels of fluoride are those found after many hours on resting dental plaque and saliva, and resulting from the regular use of fluoride toothpastes. Another source of low levels of fluoride are the constant exposure to this substance from water, milk, salt or whatsoever source is available on the oral environment (Lynch et al., 2004).

3. Dental fluorosis

The only recognized side effects of high ingestion of fluoride are dental and skeletal fluorosis (Whitford, 1996). Since skeletal fluorosis occurs only in naturally fluoridated regions where extreme high concentrations of fluoride are found in the water, the focus of this chapter will be on dental fluorosis. In addition to the dose differences for the risk of dental and skeletal fluorosis, one must bear in mind that individuals with dental fluorosis are those who were exposed to fluoride from birth up to 6-7 years of age, exactly the period of tooth formation. For skeletal fluorosis the context is much more complicated. The dose-response outcome is not clear since the different ages reflect different "turn-over" of fluoride in bones. In addition to age and fluoride dose, variables such as gender, calcium intake from the diet, duration of fluoride intake and renal efficiency in fluoride handling are relevant

factors which influence the outcome. The bone lesions are a combination of osteosclerosis, osteomalacia and osteoporosis of varying degrees which can also make diagnosis a difficult task (Krishnamachari, 1996).

Dental fluorosis is an enamel opacity due to a long-term ingestion of fluoride during tooth formation period. The tooth appearance can vary from narrow white lines to "cloudy" white spots or brown areas with pits. Loss of enamel is also frequent in more severe cases (Figure 2).

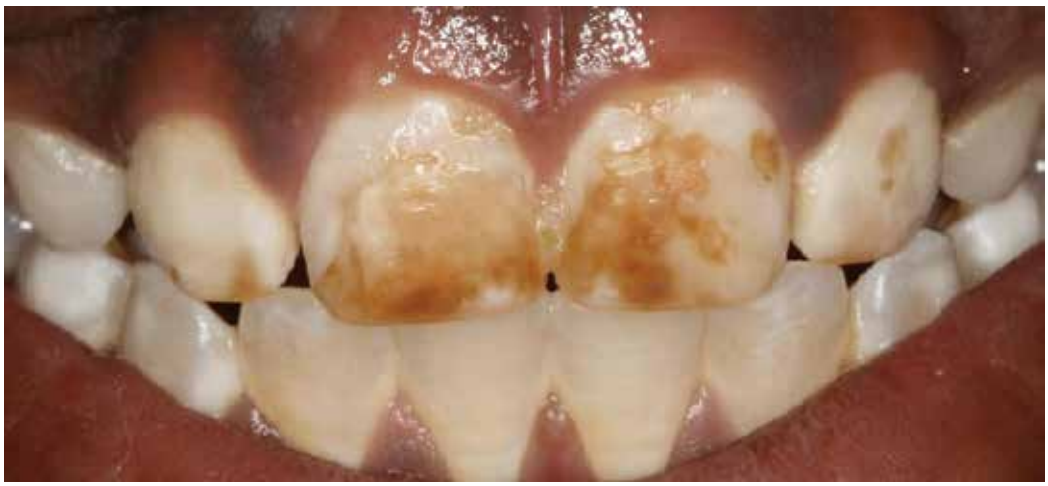

Fig. 2. This is a case of severe dental fluorosis in a 13-year-old child who consumed naturally water fluoride with 4.8 ppm. Note that the dark brown stains are limited to upper incisors. The lower incisors were the less affected teeth

The severity of the disease will depend on several factors such as dosage, duration of exposition, the activity stage of the protein, age and individual susceptibility. Fluorotic enamel is characterized by the retention of amelogenins in the early maturation stage of development and the formation of enamel which have a hypomineralized subsurface and more porous tissue. This is a conflicting point. Since dental fluorosis is related to high consumption of fluoride during tooth development, many dental professionals make the assumption that this tooth condition is related to a high concentration of fluoride in the dental tissues (enamel and dentin). Actually, it is the opposite situation. The white chalk appearance of the enamel is related to the light refraction of this tissue that presents a high porous appearance due the hypomineralized subsurface (Levy, 2003).

There are many individual and environmental variables that may interfere with the severity of dental fluorosis. Malnutrition has been one of these variables (Murray et al., 1991). However, in a study performed in the semi-arid region of Brazil where there was a 20% prevalence of malnutrition the prevalence of dental fluorosis was virtually the same regardless the fluoride level in the drinking water (Sampaio et al., 1999). However, the observation that malnutrition prevalence was not related to dental fluorosis cannot be disregarded since this is an epidemiologic observation for a specific group.

Genetic background appears to have a role in the pathogenesis of dental fluorosis. Moreover, altitude, renal problems and individual cultural habits may also be considered (Buzalaf, 2011).

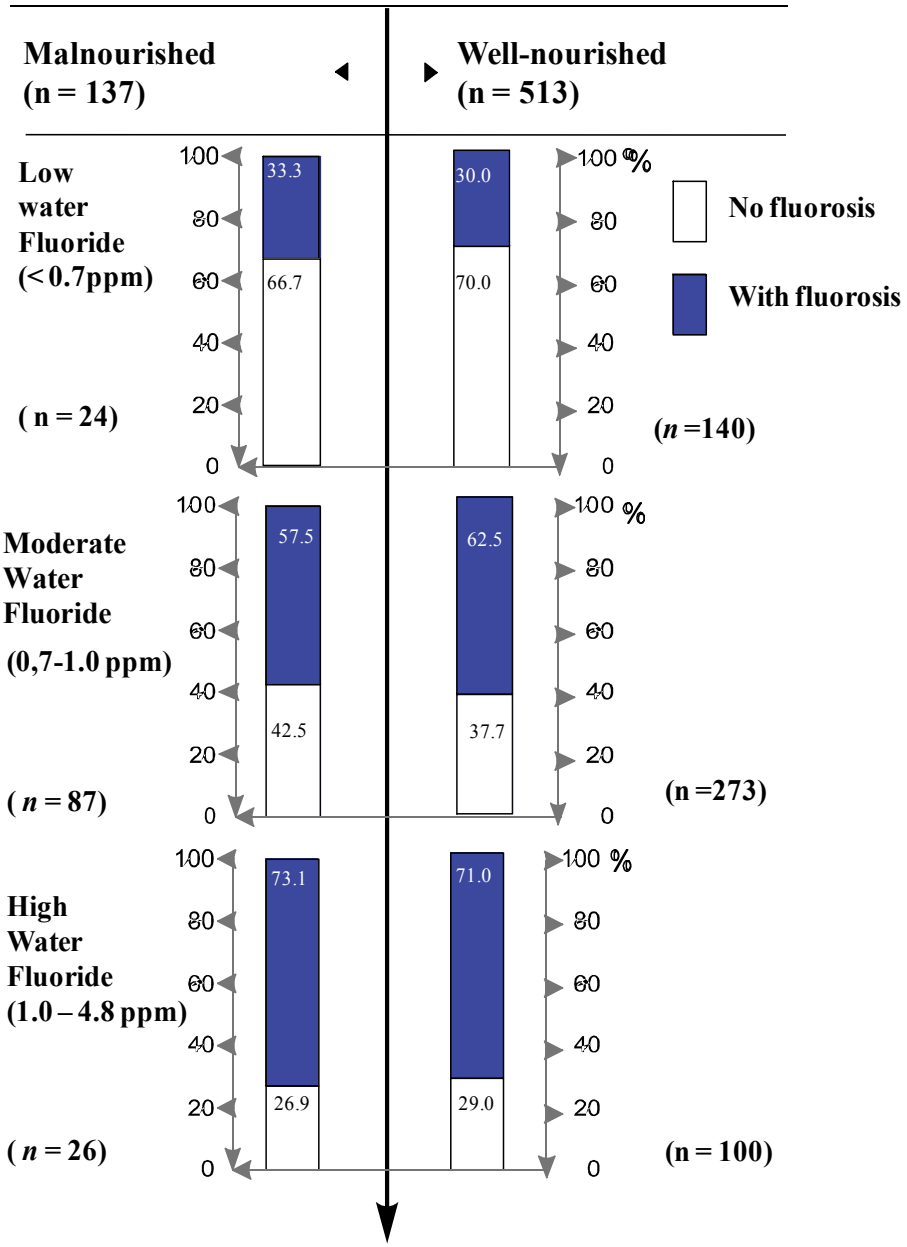

Fig. 3. Distribution of children with and without dental fluorosis in an epidemiologic study assessing the influence of malnutrition on the risk for dental fluorosis. (Source: Sampaio et al., 1999)

There is some consensus that the mechanism by which fluoride interferes with the enamel maturation process that can result in fluorosis is a multi-factorial model (den Besten & Li, 2011). The major theory behind this mechanism is the retention of amelogenin proteins that delay the maturation of the enamel. As a result, the enamel becomes hypomineralized and

porous. The understanding of these events is important because the dental fluorosis diagnosis is sometimes complicated by other enamel defects (Levy, 2003).
Discoloration of the enamel, as seen in figure 2, is due to a secondary uptake of colored substances into the porous enamel. Thus, this is actually a posteruptive condition due to dietary habits and not an indication of fluorosis severity (Sampaio & Levy, 2011).
During the examination for dental fluorosis, the enamel surface must be clean and dry. When the enamel surface is dried, the water in the enamel pores will be replaced by air. Hence, even slight enamel opacities can be observed. This procedure, which is used for scoring fluorosis with a fluorosis index (Dean index or Thysltrup and Fejerskov index), can classify dental fluorosis on different degrees, and differentiate fluorosis from other enamel opacities (Murray et al., 1991).

Fig. 4. The clinical appearance of carious lesions known as white spots. Note the opaque aspect of the lesions, the curved shapes close to the gingival margin. These are some of the points to consider that these white lesions are not related to dental fluorosis. In addition, the lesions are limited to gingival margin. The patient has also gingivitis in a clear indication that these are active carious lesions. The final diagnosis is confirmed by the fact that the patient did not live in areas with water fluoridation systems and avoided the use of fluoride toothpaste since childhood

Enamel hypoplasias are the most common opacity to be confounded with fluorosis. However, hypoplasias are generally enamel lesions of round or oval shapes with marked borders. In addition, hypoplasia may affect a single tooth in contrast to fluorosis that can be observed in contralateral teeth or in the whole dentition. These basic features can help the clinician to differentiate these opacities from fluorosis.
In recent years it has been noticed that the prevalence of enamel fluorosis is increasing in several countries. However less than 40% of dental fluorosis is caused by ingestion of water while the majority is caused by the halo effect that is the addition of the other sources of fluoride such as industrialized food and beverages (Buzalaf, 2011). In Brazil, soft drinks are

beverages consumed less than tap water, but these products can be a source of fluoride. Considering that the highest industrialized part of the country is receiving fluoridated water, a 'halo effect' is likely to be significant. In fluoridated areas, powder milk and infant formulas can be extra sources of fluoride due to the additive effect of the fluoridated water (Sampaio et al., 2010).

Estimates of infant fluoride intake from Brazilian food are considered to be low and seldom more than 0.25 mg daily. However, in a fluoridated city (0.7 ppm), the estimated fluoride intake including the fluoride products (toothpaste and rinse) may increase and possibly reach the threshold for dental fluorosis according to the fluorosis index for the community (Omena et al., 2006).

How much fluoride can result in dental fluorosis? This is a general question that is always present among dentists, patients and health authorities. First it must be pointed out that even individuals with a very low fluoride intake from the water might show some degree of dental fluorosis. Considering the intake solely by water, the amount of fluoride can be directly related to some effect. However, this is not that simple anymore since other sources of fluoride are available nowadays (Levy, 2003). Therefore the 'optimal' fluoride level that would prevent caries without resulting in fluorosis is somehow a theoretical value since bioavailability of fluoride varies among individuals (Sampaio et al., 1999). Nevertheless, the dose that may cause dental fluorosis is within the range of 0.05-0.07 mg F/Kg body weight per day. This means that children who present a fluoride intake above the threshold of 0.07 mg F/Kg per day will probably present some degree of dental fluorosis (Buzalaf, 2011). The upper central incisors are the teeth of more aesthetic concern. The risk period of fluorosis for maxillary central incisor teeth is between 15 and 24 months for males and between 21 and 30 months for females (Bårdsen, 1999).

4. Systemic fluoridation methods and the risk for dental fluorosis

In spite of the safety of most methods of fluoride delivery, an overlap of systemic methods may take place. There is also the risk of a high intake of fluoride due to a combination of water fluoridation and the ingestion of fluoride from toothpastes (Sampaio & Levy, 2011). These are important aspects that a dental professional must consider before establishing a fluoridation program on an individual basis or as an authority in public health office. This is a specific relevant issue regarding systemic fluoride methods. In most circumstances, the dental professionals just follow political decisions about these methods. In many cases the information is scarce and most part of the population is not aware of fluoridation programs. In spite of the general decisions taken by groups or general assemblies, the professional must be aware if a systemic fluoride method is being applied in their own community. For instance, most Brazilian dentists are not aware if there is a water fluoridation program in their hometown in spite of the fact that there is a national program for water fluoridation (Sampaio et al., 2010). This is also valid for countries where salt fluoridation is available and the dentist do not ask if the patient is a fluoride salt consumer. Some authorities consider that systemic fluoride methods are advantageous in comparison to topical methods because the beneficial effect occurs without the evident knowledge of the patient and also the dentist. This is rather disturbing since the lack of knowledge on whether a systemic method is available can create at least two negative interpretations. First, not knowing if someone is drinking fluoridated water or consuming fluoridated salt can jeopardize any community program since most people will not be aware of the beneficial aspect of the measure. Second,

the ignorance can be an opportunity for a problem of overlapping methods. This was the case of Brazil in the 90´s when a national water fluoridation program would overlap with a proposal of salt fluoridation for the majority of the population (Kalamatianos & Narvai, 2006).

Another issue regarding the risk of dental fluorosis is: how much of fluorosis is acceptable? This is a real dilemma that can be solved by accepting that the use of fluoride products may result in mild dental fluorosis in the population. On the other hand, if fluoride is not used at all there is the inconvenience of not preventing the appearance of a disease (caries) that could be prevented if such product was used. This dilemma can be solved by admitting that the use of such products would be reasonable and that its benefit would exceed its damages. Moreover, the mild fluorosis that is produced in most cases has no significance at all for the majority of the population.

In addition to the fact that dentists must be aware of the systemic methods in their places of work, it is also important to know the types of fluoride that are used and the respective concentrations. Table 1 provides some of the fluoride salts that are commonly used for 'systemic method'.

F-methods	**F-compounds**	**F-concentrations**
Water fluoridation	hydrofluorosilicate (FSA), sodium fluorosilicate, sodium fluoride	0.7 - 1.2 mg/L
Salt fluoridation	potassium fluoride , sodium fluoride	250-300 mg/kg
Milk fluoridation	Sodium fluoride or disodium monofluorophosphate	5 mg/L
Dietary F-supplements	sodium fluoride, acidulated phosphate fluoride, potassium fluoride, calcium fluoride	0.25 – 1.0 mg/day

Table 1. Fluoride compounds and concentrations that are usually used in different 'systemic' fluoride methods. (Source: Sampaio & Levy, 2011)

Here we have a review of most important aspects about some community systemic methods.

4.1 Water fluoridation

The water fluoridation is one of the most common delivery methods of fluoride. It presents a lower cost and long range. However for water fluoridation to be effective it has to be a continuous process and the concentration of fluoride has to be well controlled. The recommended concentration varies between 0.7 and 1.2 ppm, depending on the average regional temperature. The lower levels of fluoride are recommended for warmer regions. In these locations the intake of water tends to be higher (Sampaio et al., 2010).

Fluoridation of public water is considered to be one of the ten most important public health measures in the last century being recommended by international health organizations. In addition, there is scientific evidence proving beneficial and safe effects of fluoridation on human health. The inverse relationship between higher fluoride contents of drinking water and lower levels of dental caries experience demonstrated by Dean half century ago is still

true today. A general estimate indicates that over 300 million people in almost 40 countries are exposed to fluoride from adjusted fluoridated water supplies. Most of the individuals of this estimation are located in the United States (195 million people). In spite of being a safe method, recently, the Department of Health and Human Services of the United States proposed a new standardized level of 0.7 ppm fluoride throughout the country as an appropriate level for maximizing benefits while minimizing any risks associated with excessive ingestion (Department of Health and Human Services, 2011). This a precaution measure and must not be interpreted as a limitation of water fluoridation. Actually, the precaution is based on the fact that temperature is no longer a good indicator of fluoride intake. First, most American children in summer live in air conditioning environment most part of their lives. Second, there is an evident raise in the use of dental fluoride products which can result in an increase in the fluoride intake.

In the early seventies several industrialized countries went through a bitter emotional fight about water fluoridation. In some countries, the anti-fluoride people were the winners of the public debate and fluoride was discredited. The fluoride fight did not subside until the people were able to see by themselves the dramatic improvements in their children's dental health and also the decline in their own dental bills due to topical fluoride and fluoride toothpastes. Even though water fluoridation is much more popular in the Americas than in European countries, this method can be regarded as a low cost method to deliver fluoride, particularly for those communities where oral health care and particularly fluoride dentifrices are not available and/or not affordable. Variables that influence the costs per capita of a fluoridation project include: a) the size of the community (the smaller the community, the higher the per capita cost); b) the prevalence of dental caries in the population; c) the number of water sources; d) the type of equipment; e) the fluoride compound and f) the availability of technical support (Sampaio & Levy, 2011). In general, there is a consensus that water fluoridation can be most advantageous for more deprived communities where other health policies are less available, however, at least for the Brazilian situation, water fluoridation is present in most affordable areas of the country whereas the regions where it is most needed it is not available yet (Gabardo et al., 2008).

Water is by large the main source of fluoride intake for human beings (Whitfrod, 1996). In general, the natural fluoride present in the fresh-water do not exceed 0.3 ppm (mg/L). This is a matter of confusion. Most people do not differentiate the natural fluoride from the controlled water fluoridation programs. This is important since most severe cases of dental fluorosis are related to rural areas where the patients have been consuming high amount of fluoride in the water for a long time (Sampaio et al., 1999). On the other hand there is the urban patient who is not exposed to high amounts of fluoride, in general the mother was careful enough to avoid ingestion of fluoride toothpaste and possibly only a mild fluorosis may occur. These are different situations and must be taken under different interpretations because dental fluorosis perception is also different (Murray et al., 1991).

For rural areas or more desert types of climate, one interesting strategy for public health is to monitor water fluoride levels in order to estimate the fluoride intake. Mapping fluoride in areas is very important because in many tropical areas the chances of finding severe cases of dental fluorosis is higher (Levy, 2003).

Finally, it is already evident that the percentage level of effectiveness of water fluoridation in many areas is lower than in others due to the more widespread use of other fluoride modalities. Nevertheless, water fluoridation is still a valuable health measure and must not be underestimated (Sampaio & Levy, 2011).

4.2 Salt fluoridation

This method was introduced in the 1950s following the successful program of iodine against goiter. It was idealized as an option for water fluoridation but reproducing the idea of incorporating fluoride in the tooth (Marthaler, 2005). Today, the aim is to reach communities and regions in the world where oral care prevention measures, and particularly fluoride toothpastes, are not available. This method is successfully implemented in almost all Latin American countries and in some European countries (France, Germany and Switzerland). The levels of 250-300 mg/kg of fluoride in salt are regarded as the ideal range of concentration while the concentration of 200 mg/kg of fluoride is regarded as the minimal acceptable level of fluoride. One positive aspect of salt fluoridation is the very low cost for implementation. However, there is one major point of concern: somehow promoting salt fluoridation could be contraindicated from the perspective of general public health because the greater the salt consumption the greater could be the link to hypertension. On the other hand, most estimates indicate that usually the patients are consuming low salt diets (less than 5 g of NaCl per person per day) and taking this amount of salt, essential hypertension will be uncommon. Moreover, there is no doubt that some salt is required by man, and estimates of normal daily requirements for adults have ranged up to 15 g per day (Dahl, 2005).

Regarding the overlapping of fluoride delivery methods, similar to water fluoridation, some concern has come to a debate. Thus, the simultaneous combination of fluoride ingested from both dentifrice and salt can be a problem? Available data suggest that this combination has not resulted in objectionable enamel fluorosis levels (Menghini, 2005).

In summary, there is no doubt that salt fluoridation is a systemic method of very low cost. Salt fluoridation can be considered as a systemic method of choice when water fluoridation is technically difficult or due to economic or socio-cultural reasons it cannot be implemented (Sampaio & Levy, 2011). Finally, the drawbacks for implementing a salt fluoridation program (such as variation in ingestion, difficulties in maintaining the ideal concentration and concerns with hypertension) are minimal when compared to the advantages of this method.

4.3 Milk fluoridation

The first milk fluoridation experience was developed in Bulgaria, in the cities of Plovdiv and Asenovgrad, in 1988. Then the experience was expanded to other European countries and also to Chile, Peru and China (Bánóczy et al., 2005). Since the amounts of water and milk consumed daily are different, in terms of caries prevention the fluoride concentration should be 1 mg/L and 5 mg/L for water and milk, respectively. These values were considered before the last American resolution of reducing the levels of fluoride in the drinking water (Department of Health and Human Services, 2011). Thus, taking water fluoride as reference new publications are needed for the update of levels of fluoride in milk as well as for other methods. A possible change in fluoride levels in milk is very important since this is the most popular systemic method in some countries. An interesting aspect about milk fluoridation is its use among children. This is the target age group and well conducted school-based programs have been developed (Horowitz, 1982; Rodrigues et al., 2010). As a result, most data available for this method are from studies with children. Milk consumption varies considerably when comparing different regions of the world. The consumption is higher in developed countries (212 kg per person/year) whereas it is lower in developing countries

(45 kg per person/year) (Sampaio & Levy, 2011). Latin America has one of the highest estimates among developing countries with 110 kg per person/year, but this is regarded as low when compared to developed countries. Conversely to salt fluoridation, which can be linked to hypertension, milk fluoridation programs have the appeal of nutrition for children. This is a positive aspect when promoting health. However, the favorable features of milk can be strongly compromised when sucrose is added. In spite of the fact that cow´s milk is essentially non-cariogenic, the addition of sucrose in the milk can promote early caries in young children. Thus, the milk consumption must not increase the sucrose consumption as well. Concerning the effectiveness of fluoridated milk for caries, few randomized clinical studies were conducted. This is also the same for dental fluorosis. However, a recent observation in a Peruvian town with milk fluoridation program showed high consumption of fluoride due to high concentration of fluoride in the drinking water. This is a clear evidence of an overlap of systemic methods that must be avoided (Rodrigues at al., 2010).

5. Risk of fluorosis: What do we know and how to minimize it?

Today, there is clear evidence that fluorosis is increasing worldwide. This concern raises doubts about the beneficial aspects of systemic fluoride methods. But there are clear evidences that these methods have more beneficial effects than risks. For instance, in spite of the potential risk for dental fluorosis, dietary fluoride supplements are regarded as effective in preventing caries and are still available in several countries. This method was not discussed in this paper but this issue is also relevant (Buzalaf, 2011). The recent reduction in fluoride levels in the water communities cannot be interpreted as a limitation of the method. Conversely, this adjustment proves that water fluoridation is still necessary. So, what we know about the risk of dental fluorosis? First, the issue is not as simple as it was before (when water fluoridation started), since today it can involve several sources of fluoride. Second, an 'optimal' dose is a theoretical value, maybe we should work with range of risk and range of concentrations in systemic methods. Third, the classification of systemic x topical methods is no longer valid and might be changed. These major categories might be better classified as: professional methods (varnishes, gels) community methods (salt, water, milk) and individual methods (toothpastes, mouthrinses and supplements). Considering these categories, operational strategies can be more straightforward on the basis of those who are in charge of the method: the dentist, the health authority or the patient.

Other point of concern is that some degree of enamel fluorosis is inevitable with water fluoridation. However, most cases of dental fluorosis are of mild severity. Future studies about fluorosis perception will be valuable for evaluating the level of concern of the population about dental fluorosis. Dean regarded an increased prevalence of fluorosis as an acceptable risk when compared to the preventive benefits.

There are good strategies to minimize the risk of dental fluorosis. The first step is to get the information about the methods of delivering fluoride in a region or town (including toothpastes). Thus, investigating the possible sources of fluoride on an individual basis as well as in a communal basis is important.

The risk of developing fluorosis shows a different trend on urban and rural communities. It is a more common cause of fluorosis on rural communities the high content of fluoride on the drinking water, such as groundwater. On the contrary it is more common on urban

communities the development of fluorosis due to the irrational use of toothpaste by children under 6 years old (Sampaio et al., 2010)

The emerging concern about dental fluorosis must be evaluated in the perspective that systemic methods were already operating when other sources of fluoride were introduced. Thus, the effectiveness of fluoride is not the same for all methods since caries burden is lowering off. It is true that a reclassification to substitute the traditional systemic versus topical methods is necessary. What is not necessary is to simply oppose systemic fluoride methods as long as caries is still the most prevalent disease in many parts of the world.

6. Concluding remarks

- Most studies support the view that the caries-preventive effect of fluoride is mainly post-eruptive. This evidence must not be interpreted as a true limitation of systemic fluoride methods since a topical effect will take place when someone is ingesting fluoride in water, milk or salt or taking a fluoride lozenge.
- Dietary F intake must be considered before any systemic method of fluoridation is implemented. Hence, it is very important to monitor the total fluoride intake of children in the first 3 years of life in order to avoid undesirable aesthetically fluorosis, particularly in central incisors.
- Most systemic methods available are of low cost showing a good cost-benefit relation.
- The overlapping of systemic methods of delivering fluoride must be avoided in order to control caries without the risk of developing dental fluorosis.
- Dental fluorosis related to systemic fluoride methods are of minor concern since mild dental fluorosis is the majority of the cases observed from clinical and epidemiological observations.
- Reclassification to substitute the traditional 'systemic' versus 'topical' methods is necessary. The major categories might be classified as : professional methods (varnishes, gels) community methods (salt, water, milk) and individual methods (toothpastes, mouthrinse and supplements)

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Geriatric dentistry, or gerodontics, is the branch of dental care dealing with older adults involving the diagnosis, prevention, and treatment of problems associated with normal aging and age-related diseases as part of an interdisciplinary team with other healthcare professionals. Prosthodontics is the dental specialty pertaining to the diagnosis, treatment planning, rehabilitation, and maintenance of the oral function, comfort, appearance, and health of patients with clinical conditions associated with missing or deficient teeth and/or oral and maxillofacial tissues using biocompatible materials. Periodontology, or Periodontics, is the specialty of oral healthcare that concerns supporting structures of teeth, diseases, and conditions that affect them. The supporting tissues are known as the periodontium, which includes the gingiva (gums), alveolar bone, cementum, and the periodontal ligament. Oral biology deals with the microbiota and their interaction within the oral region. Research in oral health and systemic conditions concerns the effect of various systemic conditions on the oral cavity and conversely helps to diagnose various systemic conditions.

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