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PERIODONTAL DISEASE IN AN AGED POPULATION,

AND ITS ROLE IN CARDIOVASCULAR MORTALITY

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ACADEMIC DISSERTATION

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1. LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications, referred to in the text by their Roman numerals:

I. Ajwani S, Tervonen A, Närhi T, Ainamo A.
Periodontal health status and treatment needs among the elderly.
Special Care in Dentistry 2001; 21(3): 98-103.

II. Ajwani S, Ainamo A.
Periodontal conditions among old elderly: Five year longitudinal study.
Special Care in Dentistry 2001; 21(2): 45-51.

III. Ajwani S, Mattila KM, Tilvis RS, Ainamo A.
Periodontal disease and mortality in an aged population.
Special Care in Dentistry (In Press)

IV. Ajwani S, Mattila KM, Närhi T, Tilvis RS, Ainamo A.
Oral health, C-reactive protein and mortality – a 10 year follow-up study.
Gerodontology (In Press)

2. ABBREVIATIONS

ANOVA	Analysis of Variance
BMI	Body Mass Index
CHD	Coronary Heart Disease
COPD	Chronic Obstructive Pulmonary Disease
CPITN	Community Periodontal Index for Treatment Needs
CRP	C-Reactive Protein
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
HDL	High Density Lipoprotein
IL	Interleukin
SBP	Systolic Blood Pressure
TNF-α	Tumor Necrosis Factor-α

3. INTRODUCTION

The industrialized world, in recent decades, has seen a steady rise in the number of elderly. Nearly 15% to 18% of the population in the developed countries is above the age of 60 years. Not only has there been an increase in the number of elderly but improvements in social living conditions and medical care have resulted in the extension of the average life span as well. Consequently the proportion of the elderly is expected to increase significantly in the next few decades. The fastest growing segment of this elderly population is going to be of those over the age of 85 years (Ainamo and Österberg, 1992). On the other hand, there has been a rapid decline in edentulism in these countries. (Ainamo and Österberg, 1992; Ettinger, 1993). More number of elderly retaining their natural teeth means more teeth are at risk for dental diseases like periodontal disease.

Periodontal disease is one of the most wide spread chronic diseases world-wide (WHO, 1978). It is an infectious condition that results in inflammatory destruction of the investing and tooth supporting periodontal tissues (gingivae, periodontal ligament and alveolar bone). Epidemiological and clinical research over the last 30 years has transformed our understanding of the etiology, distribution and progression of periodontal disease (Burt, 1993; Burt, 1994; Locker *et al.*, 1998). It is well established that bacterial irritation from the dento-gingival plaque is essential for the development and maintenance of periodontal disease. Dental plaque is a highly complex structured microbial mass in which more than four hundred bacterial types have been identified. Calcification of this dental plaque seen as calculus occurs above and within the gingival sulcus hence, the periodontium is commonly exposed to it for almost the whole of adult life.

However, numerous local oral factors other than bacteria and some systemic factors also contribute to the etiology of periodontal disease. Most frequently mentioned predisposing diseases, conditions, and behaviors for periodontal disease include diabetes, HIV/AIDS, host genetic factors smoking and stress. Osteoporosis is also found to be a risk factor for tooth loss, and oral bone loss (Garcia *et al.*, 1998).

Although, the role of systemic conditions on oral health is known, the role of oral infections, as risk factors for various medical conditions, is not well understood. The hypothesis that oral infections, especially periodontal infections, have potentially serious systemic implications is now gaining credence. Because such a large proportion of the world's population live a lifetime with chronic marginal gingivitis / periodontitis, knowledge regarding any association of dental health with systemic illness is very important.

The role of the "classic" cardiovascular disease (CVD) risk factors like lipids and blood pressure is well understood in middle-aged individuals. These risk factors, however, do not explain all clinical and epidemiological features of CVD. An increasing body of evidence suggests that infections play a role in the pathogenesis of CVD (Mattila *et al.*, 1998), one of these infections being periodontal disease. C-reactive protein (CRP), a classic acute-phase protein is a sensitive objective marker of inflammation, tissue damage and infection. It is recently shown to be associated with cardiovascular disease and mortality (Koenig *et al.*, 1999; Strandberg and Tilvis, 2000) and elevated levels have been observed among middle-aged men with periodontal disease as well, suggesting a possible causal pathway for increased CVD risk among those with periodontal disease (Ebersole *et al.*, 1997; Loos *et al.*,

2000). However, lack of association between periodontal disease and CVD has also been reported (Howell *et al.*, 2001; Hujoel *et al.*, 2000; Hujoel *et al.*, 2002; Joshipura *et al.*, 1996).

At the same time data on the risk for CVD morbidity and mortality in edentulous subjects and their CRP levels are sparse. Most of these subjects are elderly and the combination of factors like systemic diseases, ill-fitting dentures, inability to maintain good oral hygiene, and hyposalivation can result in the growth of many oral microorganisms, and change the oral microflora of the elderly (Loesche *et al.*, 1995; Närhi *et al.*, 1993; Närhi *et al.*, 1998). Consequently, these subjects become vulnerable to various inflammatory mucosal lesions.

Although several studies have looked at the periodontal health of the elderly (Ettinger, 1993), not many are population based and only a few include adequate samples of those 75 years and above. Also, very few longitudinal follow-up studies among this age group have been reported. There are not many studies that have looked at the association of periodontal disease and CV mortality in the elderly, where the relation of the classic risk factors with CVD and mortality seem to reverse (Hakala *et al.*, 1997) and even fewer studies have looked at the association of edentulism, CRP and CV mortality in this elderly population.

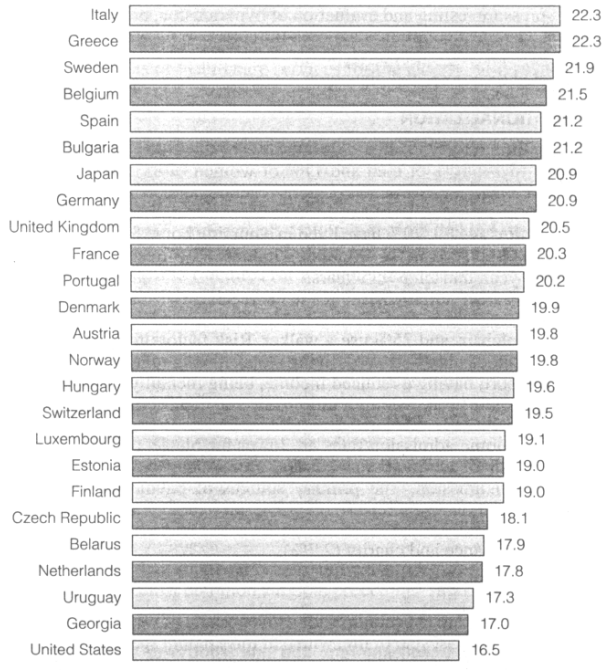
The Helsinki Aging Study for the first time provided a unique opportunity to look at a population-based sample of the community dwelling elderly (aged 75+ years). In this work I have looked at the prevalence of periodontal disease in the elderly **[I]** and the changes in the periodontal conditions over a five-year period **[II]**. As the participants of this study had undergone detailed medical, dental and oral examinations at baseline and their mortality was recorded during the ten year follow-up, I was able to look at the association of periodontal disease **[III]** and edentulism **[IV]** with elevated baseline CRP levels and CVD mortality. The present thesis comprises of the above four studies **[I-IV].**

4. REVIEW OF THE LITERATURE

4.1 The elderly

Aging is a process of gradual and spontaneous change, resulting in maturation through childhood, puberty, and young adulthood and then decline through middle and late age (The Merck Manual of Geriatrics, 2000). Historically the chronologic age of someone defined as elderly involved the age at which someone should be eligible to retire, which was chosen to be at age 65 years. As lifespan has increased, age 65 years as the lower limit is looked upon as being arbitrary. In fact, gerodontologists have found it useful to specify the groups called the 'old elderly', individuals over the age of 75 years and the 'oldest elderly', those age 85 years and older, as groups of special interest. In this study the term elderly often stands for those aged 75 years and above.
However, as chronologic age is associated not only with aging but also with increased prevalence of physical and mental (often) degenerative conditions, decreased level of metabolic function, it is important to consider not only a person's chronologic age but also their "biologic age". Consequently the term elderly realistically and commonly, refers to a group of people who are age 65 and older (although earlier or premature aging also occurs when unusually early functional, medical, physical and mental degeneration occurs).

Figure 1: Percentage of population ≥ 60 years in some of the developed countries in 1996



(*Source*: U.S. Bureau of the Census, International Programs Center, International Data Base, 1996)

Interest in the elderly has grown in recent years because of the increasing proportion of this age cohort in the industrialized society (Figure 1). In 1990, more than 31 million Americans were of age 65 years and above, nearly twice as much as in 1960. This number is estimated to reach around 53 million by 2020, and more than 75 million by 2040 (Day, 1996). One of the fastest growing segments of the U.S. population, the oldest elderly (≥ 85 years), currently accounts for 1.5% of the total population and is projected to account for 3.6% by 2040. As in the U.S., the fastest growing segment of the elderly in Finland is of those over the age of 85. The national population report (Statistics Finland, 1995) has shown that the number of those aged 85 years soared after World

War II. In 1950 they constituted about 0.2% of the total population (n=9,500). By 1994 their proportion was about 1.3% of the total population (n=64,000). According to the population projection their number will grow close to 126,000 by 2030 (2.5%), even though, by then the largest age cohort (those born in 1946-1949) will not have reached the age of 85.
The following topics of the literature review deal mainly with the elderly.

4.2 Edentulism (absence of natural teeth)

As the number of elderly is growing so is of the number of those retaining their natural teeth. There has been a steady decline in the number of edentulous elderly in all the industrialized countries (Ainamo and Österberg, 1992; Ettinger, 1997; Ettinger and Mulligan, 1999). In the United States, the mean number of missing teeth and the percentage of edentulous adults have declined substantially from 1960 to 1980. The percentage of edentulous elderly population (those 65 years and above) dropped from 55% in 1960 to 41% in 1980. Since the 1980s the decline has been less substantial with the number of edentulous elderly dropping to 38% by the early 1990s (White *et al.*, 1995). Data from England and Wales shows a 13% decline in the number of edentulous among those aged 65-74 years. Similar data has been reported in Australia, New Zealand and Japan (Ettinger, 1993). In Scandinavian countries too, a decrease in the number of edentulous elderly have been observed during the 1970s and 1980s. In Sweden, for example, edentulism in the 65-74 year old age group dropped from 52% in 1975 to 29% in 1989. In Finland, no increase or decrease in edentulism was observed among the elderly during the 1970s or the 1980s (Ainamo and Österberg, 1992). A recent study on the prevalence of edentulism among Finnish adults of working age (15-64 years old), however, has reported that the number of edentulous people has fallen significantly in the last 20 years. The prevalence of edentulism decreased from 14% to 6% and at the same the number of people with complete natural dentition has increased from 60% to 80% (Suominen-Taipale *et al.*, 1999). With increasing number of elderly retaining their natural teeth, the demand and use of dental services by the community-dwelling elderly is expected to increase to a rate similar to younger age groups. Therefore, epidemiological data on their oral health and treatment needs is urgently needed for policy planning and developing the necessary health services framework to meet the growing demand.
On the other hand, though the number of subjects without natural dentition is decreasing, edentulism is still widely prevalent, especially, among those aged 75 years and above. As the age advances, oral mucosa becomes more vulnerable to mechanical damage (Pindborg, 1986). Also, a combination of factors like use of dentures, hyposalivation, medications and compromised immune system create an environment favoring microbial growth, which make the elderly subjects highly prone to mucosal changes (Närhi *et al.*, 1993).

4.3 Epidemiology of periodontal disease

Epidemiology can be defined as “the study of the distribution and determinants of disease in human population” (Hennekens and Buring, 1987). One of the fundamental requirements of epidemiological studies designed to estimate prevalence of a disease (like periodontal disease) is that they be population-based. That is, random samples drawn from the general population, population subgroups or population at risk are studied. As a result, these studies are difficult and costly to conduct, especially, if the sample includes the elderly.
With an increased retention of the natural dentition over the last three decades (Ship and II., 1989), there is concern that older persons may have a greater prevalence of periodontal

diseases (Douglass *et al.*, 1993) than the rest. The occurrence of periodontal disease in this population is related to the increase rate of accumulation of plaque during periods of oral hygiene neglect or abstinence (Gluck, 1993). Prevalence of periodontal disease among the adult population has been looked at in numerous studies (Beck, 1996; Hugoson *et al.*, 1992; Locker *et al.*, 1998). These studies have assessed the periodontal status by clinical assessment (Beck, 1996), or clinical and radiographic assessment (Hugoson *et al.*, 1992). They show that the moderate form of periodontal disease is prevalent in large percentage of various populations but the severe form affects only a small percentage. However, not many studies include sufficient number of home-dwelling elders aged 75 years and above. Some of the studies in the United States, which included the old elderly, have shown high prevalence of moderate periodontal disease in this age group (Fox *et al.*, 1994; Gilbert and Heft, 1992; Hunt *et al.*, 1985; Miller *et al.*, 1987). The New England Elders Dental Study (NEEDS) (Fox *et al.*, 1994) revealed that moderate periodontal pocketing (4 to 6 mm) was observed in 66% and severe periodontal pocketing (> 6 mm) was observed in 21% of the study sample (aged 70+). Using the Community Periodontal Index for Treatment Needs (CPITN) method, Galan et al. (Galan *et al.*, 1995) reported similar findings among the community-dwelling older Canadians. High prevalence of deep periodontal pockets (> 4 mm) among the non-institutionalized elderly has also been reported in both the developed and developing countries like China, Japan, Norway, Italy, Australia, India and the Netherlands (Baelum *et al.*, 1988; Grytten *et al.*, 1989; Karsten *et al.*, 1992; Maity *et al.*, 1994; Okamoto *et al.*, 1988; Strohmenger *et al.*, 1991; Yoneyama *et al.*, 1988).

One of the earliest studies among the elderly of Finland was carried out in 1974 in Turku (Mäkilä, 1977). Of the 498 inhabitants of the old people's home examined, all but two women had deepened periodontal pocket ($\geq$ 4 mm). In another study that included 480 inhabitants of 24 Finnish old peoples' home (aged 65 to 100 years), 32% were dentate and 68% of them had periodontal disease (Ekelund, 1983). However, a study looking at the periodontal status of the community-dwelling elderly in Ostrobothnia in northern Finland (Ainamo *et al.*, 1986) showed 37% of the dentate subjects had moderate periodontal disease (4-5 mm periodontal pockets) and 27% had severe or advanced periodontal disease (6mm or deeper periodontal pockets). One of the first national surveys that included those over the age of 65 years was the Mini-Finland Health Survey, carried out from 1977 to 1981. It showed that 77% of the dentate elderly had periodontal pockets of 4 mm or more. However, among the dentate the prevalence of those with $\geq$ 6 mm pockets decreased from 38% in the elderly age group (60-69 years) to 31% in the old elderly group (70 years and above) (Markkanen *et al.*, 1983).

Most of the Finnish studies mentioned above did not include sufficient number of elderly, especially those over the age of 75 years and some of them that did, included elderly subjects from old people's home. There have been no population-based studies, in Finland, looking at the periodontal health of primarily the community-dwelling elderly.

4.4 Progression of periodontal disease in the elderly

Though there have been many cross-sectional and longitudinal epidemiological studies on the prevalence and severity of periodontal disease in adults majority of them give little information about the disease progression in the elderly (aged 75 years and above) largely due to lack of number of subjects with natural teeth. The studies show that the prevalence and severity of periodontal disease increases with age (Axelsson and Lindhe, 1978; Baelum *et al.*, 1988; Bech *et al.*, 1984; Beck *et al.*, 1990b; Bolin, 1986; Douglass *et al.*, 1983; Hakanson, ; Halling and Björn, 1986; Hugoson and Koch, 1979; Hugoson *et al.*, 1992; Löe

et al., 1978; Löe *et al.*, 1986; Okamoto *et al.*, 1988; Palmqvist, 1986). A 10-year retrospective radiographic study of periodontal disease progression in 210 subjects from Gothenburg, Sweden, (Papapanou *et al.*, 1989) demonstrated that the mean annual rate of bone loss among the initially 70-year old subjects was 0.28 mm compared to 0.07 on the 25-year old individuals. Levy et al. (Levy *et al.*, 1990) reported that among 70 years and over Iowans, 35% had at least one site with 2 mm or more of attachment loss over a 2-year period. The Piedmont 65+ study (Beck *et al.*, 1997) showed that 56% of the Blacks and 47% of Whites had experienced 3mm or more bone loss at one or more sites during the 5-year study period. This increased severity of periodontal disease and bone loss with age is probably related to the length of time the periodontal tissues have been exposed to bacterial plaque and is considered to reflect individual's cumulative oral history (Löe *et al.*, 1986).

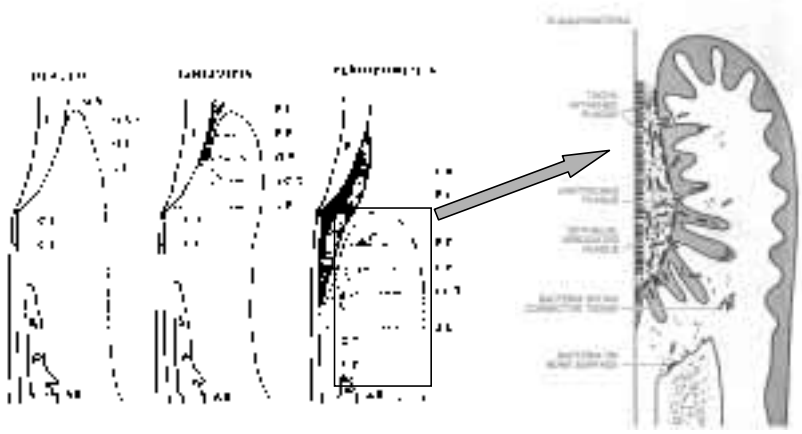
More recent studies carried out in some of the developed countries, show changing patterns of periodontal disease progression. These studies have shown that advanced periodontal destruction and bone loss is seldom seen in individuals under the age of 40 (Brown *et al.*, 1989; Hugoson *et al.*, 1992; Miller *et al.*, 1987; Papapanou *et al.*, 1991). A similar finding has been observed even in the elderly population. Studies among the elderly have shown that advanced periodontal disease affects only a small fraction of this age group (Beck *et al.*, 1990b; Brown *et al.*, 1989; Halling and Björn, 1986; Hunt and Beck, 1990; Miller *et al.*, 1987; Okamoto *et al.*, 1988). However, among those with advanced disease, further breakdown does occur with increasing age. In a 10-year study among the residents of Yonqing county, in China (Baelum *et al.*, 1997), aged 55-69 years at baseline, only those elderly who had more sites with deep pockets and advanced bone loss at baseline, had subsequently shown high tooth mortality. Similar trends were observed in a Swedish study among the residents of Jönköping (Hugoson *et al.*, 1992), where the frequency of younger and middle-aged individuals with moderate to severe marginal loss of alveolar bone did not change overall during the 10-year follow-up period. However, the proportion of individuals with severe bone loss increased considerably among the 60- (from 3% to 26%) and 70-year-olds (from 6% to 38%). High prevalence of advanced periodontal disease in the elderly can probably be explained by increased number of dentate in this age category. The cross-sectional data from the New England Elderly Dental Study (NEEDS) showed that the subjects who retained higher numbers of teeth had more periodontal disease (Joshi *et al.*, 1996). On the other hand, there have been studies that have reported improved or stable periodontal health among the elderly who have retained their natural teeth (Burt, 1994; Ship and Beck, 1996). A 2-year radiographic study in Oslo, Norway (Albandar *et al.*, 1986), demonstrated that the rate of bone loss increased rapidly in people aged 33 to 56 years but did not for younger and older age groups. Another 10-year longitudinal study among healthy adults, aged 29-79 years at baseline (Ship and Beck, 1996) showed only a slight change in the periodontal status of the subjects during the ten-year study period. Recent data has shown that aging as such does not cause attachment loss (Burt, 1994; Fox *et al.*, 1994; Papapanou *et al.*, 1991; Wennström *et al.*, 1993). There have, however, been no long term follow-up studies in Finland to look at the progression of periodontal disease in the elderly.

4.5 Pathobiology of periodontal disease

Periodontitis in moderate to severe forms affects a large segment of the adult population. This refers to hundreds of millions of people world-wide. If periodontitis is associated with increased risk of systemic disease, it is essential to understand its pathogenesis and undertake measures to manage it.

Dental plaque can be defined as the soft deposits that form the biofilm adhering to the tooth surface and other hard surfaces in the oral cavity, including removal and fixed restorations (Bowen, 1976). It primarily consists of numerous bacteria. The pathogenesis of plaque-associated gingivitis occurs as a result of bacterial accumulations (biofilm) on the surface of the teeth close to the gingiva. This in turn initiates vascular changes in the gingival tissues causing migration of polymorphonuclear leukocytes into the tissues and into the sulcus and loss of collagen just apical to the junctional epithelium. The microbial plaque is resistant to normal host response (Page *et al.*, 1997), however, when the bioflm is disrupted as a result of brushing or scaling, the process is reversed and healing occurs (Kornman, 1996). On the other hand if left as it is, the condition may progress to periodontitis.

Figure 2. Histopathology of the periodontium in health and disease



AB = Alveolar bone CA = Calculus CE = Cementum CT = Connective tissue E = Enamel GP = Gingival pocket GS = Gingival sulcus ICT = Inflamed connective tissue JE = Junctional epithelium OE = Oral epithelium OSE = Sulcular epithelium PE = Pocket epithelium PL = Plaque PP = Periodontal pocket

Evidence from numerous epidemiological population-based studies has shown that the pathogenesis and severity of periodontitis is dependent not only on the presence of bacterial plaque but also on the presence of a susceptible host (Offenbacher, 1996). Although, the sub gingival bacterial plaque (comprising of gram negative bacteria) is essential for the initiation of periodontitis the principal signs of the disease such as collagen breakdown and loss of bone are a result of host mediated inflammatory and immune mechanisms that appear to be influenced by genetic and acquired factors. Hence, the progression of periodontal disease varies between individuals (Kornman, 1996).

Periodontitis may relate to susceptibility to systemic disease in three ways (Page, 1998). One, periodontits and systemic diseases like CVD share common risk factors. Therefore factors responsible for increased risk for periodontitis may also be responsible for increased risk of CVD. Two, the sub gingival gram negative bacteria and lipopolysaccahrides (LPS) shed by them can easily pass through the ulcerated pocket epithelium and connective tissue to reach the blood vessels. In sufficient quantities they may induce major vascular responses, including inflammatory cell infiltration in the vessel wall, vascular smooth muscle proliferation, vascular fatty degeneration and intravascular coagulation (Libby *et al.*, 2002).

Three, periodontitis may result in expression of high concentration of proinflammatory mediators like cytokines, TNF-α, IL-1β, PGE_2 and acute phase reactants like CRP and serum amyloid A. They can enter circulation and perpetuate systemic effects (Page, 1998).

4.6 Oral health and systemic health

The effect of various systemic conditions on oral health is now widely understood. Diabetes has been demonstrated to be a risk factor for periodontal disease (Taylor *et al.*, 1998), tobacco use for tooth loss (Krall *et al.*, 1997), attachment loss (Haber *et al.*, 1993), and alveolar bone loss (Grossi *et al.*, 1995), and osteoporosis for tooth loss (Krall *et al.*, 1996) and oral bone loss (Jeffcoat, 1998). The role of oral infections as risk indicators for various medical outcomes, including mortality, is not yet well understood. The hypothesis, that various oral conditions like periodontal disease have severe effects on systemic health, is steadily gaining importance. Gram-negative bacteria found in deep periodontal pockets and furcation lesions, even in sub-clinical and chronic cases (Maiden *et al.*, 1992; Slots and Rams, 1992; Tanner *et al.*, 1992), can multiply readily and disseminate through the blood stream, and are risk factors for coronary heart disease (CHD), pyelonephritis, or brain abscesses (Beck *et al.*, 1996; DeStefano *et al.*, 1993; Grau *et al.*, 1997; Mattila *et al.*, 1989; Navazesh and Mulligan, 1995; Nieminen *et al.*, 1993; Rams and Slots, 1992; Syrjänen *et al.*, 1989; Valtonen, 1991). The severity of coronary atherosclerosis is shown to be directly related to the severity of dental infections (Mattila, 1993; Mattila *et al.*, 1998). Elderly and medically compromised patients with poor oral health are most susceptible to respiratory infections, like pneumonia, resulting from aspiration of oropharyngeal flora into the lower respiratory tract (Bentley, 1984; Christensen *et al.*, 1993; Estes and Meduri, 1995; Finegold *et al.*, 1993; Greenberg *et al.*, 1982; Limeback, 1988; Rams and Slots, 1992; Scannapieco and Mylotte, 1996; Toews, 1986) Periodontal status, assessed radiographically by alveolar bone loss, is associated with an increased risk for chronic obstructive pulmonary disease (COPD) (Hayes *et al.*, 1998). Oral infections with an overreactive immunologic host response can cause "metastatic inflammation", most frequently uveitis or iritis (Brummer and van Wyk, 1987; Kettering and Torabinejad, 1984; Rams and Slots, 1992; Torabinejad *et al.*, 1983). The role of dental infections as risk factors for myocardial infarction and brain infarction, has also been emphasized (Beck *et al.*, 1996; Grau *et al.*, 1997; Mattila, 1993; Syrjänen *et al.*, 1989; Valtonen, 1991).

4.7 Cardiovascular disease (CVD) and mortality in the elderly

Cardiovascular disease (CVD) is the leading cause of death in industrialized countries (Breslow, 1997). Atherosclerotic CVD is one of the major concerns in the elderly American population. Mortality attributable to CVD is about 58% in persons reaching the age of 85 years and the incidence of CVD in persons over the age of 65 years is more than double that of middle aged persons (NIH and NHLBI., 1996). In the United Kingdom, CVD accounts for 30% of total mortality in both men and women (Fletcher *et al.*, 1992). Finland had the highest mortality rate due to CVD in the world in 1950 and though, the rate has reduced over the decades (Vartiainen *et al.*, 1994), CVD is still widely prevalent in both males and females (Table 1).

Table 1. Diseases in elderly Finns

Males		Females	
Cardiovascular disease	45%	Rheumatic disease	47%
Rheumatic disease	37%	*Cardiovascular disease*	39%
Respiratory disease	21%	Respiratory disease	6%

The decline in cardiovascular mortality seen in Finland has also occurred in other developed countries like U.S., Australia, Japan, Canada and New Zealand, and the elderly have shared in the decline (Kannel and D'Agostino, 1995; Sytkowski *et al.*, 1990; Ueshima *et al.*, 1987). Among women, quite large falls in CVD has been observed in almost all the developed countries (Fletcher *et al.*, 1992). This indicates that atherosclerotic cardiovascular mortality may not be an inevitable consequence of aging.

A variety of epidemiological studies have identified innate and acquired cardiovascular risk factors that contribute to the major cardiovascular disease outcomes (Kannel *et al.*, 1988). Cholesterol, blood pressure, smoking and glucose intolerance are some of the major risk factors for CVD among middle-aged subjects (Janghorbani *et al.*, 1993; Jenum *et al.*, 2001; Semenciw *et al.*, 1988). All of the major risk factors tend to increase with age except for cigarette smoking, which declines with advancing age but continues to promote excess CVD in advanced age (Kannel *et al.*, 1997). Recent studies have shown that relation of the classic risk factors with CVD and mortality among the elderly seems to reverse and many of the factors whose importance in CV risk is well accepted in young adults are poor predictors of mortality in the elderly (Casiglia *et al.*, 1993; Casiglia and Palatini, 1998; Galan *et al.*, 1995; Hakala *et al.*, 1997; Kannel *et al.*, 1997). Blood pressure and cholesterol also have a tendency to decline with age. Studies done in the US (Kannel, 1997; Langer *et al.*, 1989) and Finland (Mattila *et al.*, 1988) have reported favorable survival among older people with high blood pressure. Among the participants of the medical component of the Helsinki Aging Study, those with high baseline systolic blood pressure had favorable five-year survival (Hakala *et al.*, 1997). Life style, as in the middle-aged subjects, plays an important role in the development of CVD in the elderly. Lack of exercise, intake of diet high in cholesterol and deficient in fiber and anti-oxidant vitamins, obesity and smoking promote an adverse cardiovascular risk profile and CVD in the elderly (Kannel *et al.*, 1997). Cigarette smoking especially is a significant risk factor for CVD (Bosetti *et al.*, 1999; Castelli, 1990; Tverdal, 1999; Wilhelmsen *et al.*, 1973) and it is also associated with periodontal disease (Axelsson *et al.*, 1998; Bergstrom *et al.*, 2000; Haber *et al.*, 1993). It is therefore, considered as an important cofactor in the relationship between periodontal disease and CVD (Hujoel *et al.*, 2002; Hyman *et al.*, 2002). Blood lipids, on the other hand, have not been consistently found to be related to CVD development in the elderly (LaRosa, 1995).

Although the number of people dying due to CVD is declining, it is still one of the leading causes of death in Finland and all the known risk factors do not explain its incidence. Therefore information about the role of other factors like various infections including dental infection in CVD is needed.

4.8 Periodontal disease and CVD

Many studies in the 1990s have linked dental infections with increased risk of CVD (Beck *et al.*, 1996; Genco *et al.*, 1997; Grau *et al.*, 1997; Mattila *et al.*, 1989; Mattila, 1993; Mattila *et al.*, 1995; Mattila *et al.*, 2000; Mendez *et al.*, 1998; Morrison *et al.*, 1999). One of the first studies was a matched case-controlled study by Mattila et al., where significant positive

associations were observed between myocardial infarction and high dental index score (comprising of sum of scores for number of various lesions, missing teeth, probing depth measures, number of periapical lesions and presence or absence of pericoronitis) (Mattila *et al.*, 1989). In other separate studies the authors reported association between the dental index and atherosclerosis (Mattila, 1993), as well as ischemic events in patients with CHD at entry (Mattila *et al.*, 1995). In their case-controlled study, Grau et al., found positive relationship between the periodontal components of the dental index and stroke (Grau *et al.*, 1997). The National Health and Nutrition Epidemiologic follow-up Study (NHEFS) (DeStefano *et al.*, 1993) demonstrated stronger association of both, periodontal disease and poor oral hygiene, with total mortality than with CHD, particularly among young and middle-aged men (aged 25-49 years). The VA Dental Longitudinal Study (Garcia *et al.*, 1998), on the other hand, found baseline periodontal status as a significant and independent predicator of mortality from all causes. However, the prospective cohort study (Joshipura *et al.*, 1996) involving 44119 male health professionals and the follow-up study (Hujoel *et al.*, 2000) of the same subject population as studied by DeStefano et al. (1993), showed no associations between periodontal disease and CHD, or death. Radiological study (Soikkonen *et al.*, 2000) among the same elderly population as ours, showed radiographic oral foci to be an indicator of death risk among the Helsinki elders, and vertical bone loss judged as advanced infra-bony pockets radiographically was associated with 4-year all-cause mortality.
Most of the above studies have primarily included the young and middle-aged subjects or found association only in these age groups. Not much has been reported about the association of periodontal infections and mortality risk in the elderly (aged 75+ years).

As mentioned earlier the association between periodontitis and atherosclerosis may be because they share many common risk factors like age, male gender, diabetes mellitus, host susceptibility, stress and most importantly smoking (Breivik *et al.*, 1996; Genco, 1996; Genco *et al.*, 1999; Kinane, 1998; Löe *et al.*, 1992). Study on population drawn from the Third National Health and Nutrition Examination Survey (NHANES III) has reported significant association between periodontal attachment loss and CHD only among smokers aged 50 years or less (Hyman *et al.*, 2002). On the other hand periodontal disease and tooth loss were associated with increased risk of ischemic stroke among participants of the Health Professionals' Follow-Up Study (HPFS) who were free of CVD and diabetes at baseline (Joshipura *et al.*, 2003).
Another possible mechanism could be increased levels of inflammatory mediators (like C-reactive protein) as a result of periodontal infections that may induce major vascular responses and in turn contributing to atherogenesis and CVD.

4.8.1 C-Reactive Protein (CRP) and CVD

Cholesterol has long been known to play a crucial part of predicting risk for heart attack in seemingly healthy people. But half of all heart attacks occur in people who don't have high cholesterol. Also, the classical risk factors of CVD cannot account for all the variation in the incidence of CVD cases (No authors listed, 1994; Scannapieco, 1998). As a result there is a growing interest to identify additional markers of coronary risk. One likely candidate is C-reactive protein (CRP). Although, this protein is part of the body's normal response to infection and inflammation, chronically elevated levels are associated with a heightened risk for cardiovascular disease and mortality in both, the middle-aged and the elderly (Danesh *et al.*, 2000; Harris *et al.*, 1999; Kiechl *et al.*, 2001; Koenig *et al.*, 1999; Kuller *et al.*, 1996; Lowe *et al.*, 2001; Ridker *et al.*, 1997; Ridker *et al.*, 1998b; Strandberg and Tilvis, 2000;

Tracy *et al.*, 1997). C-reactive protein is an extremely sensitive, non-specific, acute phase reactant produced in response to inflammatory stimuli such as tissue injury, infection and hypoxia (Pepys, 1995) and is regulated by cytokines including IL-6, IL-1 and TNF-α (Baumann and Gauldie, 1994). Circulating CRP is exclusively produced by hepatocytes (Dong and Wright, 1995; Murphy *et al.*, 1991). The median normal circulating concentration of CRP is 0.8 mg/l and the interquartile range is 0.3 to 1.7 mg/l. In 90% of the apparently healthy people the serum concentration is less than 3 mg/l (Pepys, 1995). Although, this protein is part of the body's normal response to infection and inflammation, the CRP concentration can increase up to a thousand-fold during the acute phase of a disease (Janssen *et al.*, 1986; Kushner, 1991; Raynes, 1994; van Leeuwen *et al.*, 1986).

Increase in CRP concentration in the serum is observed during chronic stages of disease, for example in subjects with chronic bronchitis (Ebersole *et al.*, 1997; Wu *et al.*, 2000). CRP might, also, be indicator of chronic infective processes possibly correlated with risk of coronary heart disease, such as infection by *Chlamydia pneumoniae* or chronic gastric infection with *Helicobacter pylori* (Danesh *et al.*, 1997; Zhu *et al.*, 2000). An association of age, sex, race, smoking, obesity, consumption of coffee and alcohol, stress, physical training, lipid levels, and blood pressure with increased CRP levels has also been reported (Danesh *et al.*, 1999; Danesh *et al.*, 2000; Ershler and Keller, 2000; Gram *et al.*, 2000; Gussekloo *et al.*, 2000; Hutchinson *et al.*, 2000; Koenig *et al.*, 1999; Mendall *et al.*, 1997; Ridker *et al.*, 1998b; Ridker *et al.*, 1999b; Roivainen *et al.*, 2000; Taaffe *et al.*, 2000; Yudkin *et al.*, 1999). A reductase inhibitor (statins) reduces C-reactive protein as well as low-density lipoprotein cholesterol (Bermudez and Ridker, 2002; Wiklund *et al.*, 2002). Increase in CRP levels, on the other hand is known to occur among those on oral contraceptives (Kay *et al.*, 1971; Kluft *et al.*, 2002) and hormonal replacement therapy (Ridker *et al.*, 1999a; Walsh *et al.*, 2000).

The basic process of most of the CVDs such as myocardial infarction (MI), ischemic heart disease (IHD) and stroke is atherosclerosis. It is a progressive degenerative condition involving the large to medium sized arteries. Inflammation is now recognized as a major feature of atherosclerosis (Libby, 1995; Libby and Ridker, 1999; Ross, 1999) and there is significant evidence of an association between systemic inflammation and occurrence of CVD (Blake and Ridker, 2001; Danesh *et al.*, 2000; Rader, 2000). CRP has been shown to be not only a prognostic indicator of acute coronary syndromes (Biasucci *et al.*, 1999; Ferreiros *et al.*, 1999; Morrow *et al.*, 1998), but also, a predictor of future coronary events (Haverkate *et al.*, 1997; Ridker *et al.*, 1998b). Perhaps of greater importance is the demonstration that CRP concentrations predict first MI and stroke (Danesh *et al.*, 2000; Koenig *et al.*, 1999; Kuller *et al.*, 1996; Mendall *et al.*, 2000; Ridker *et al.*, 1997; Ridker *et al.*, 1998a; Ridker *et al.*, 1998b; Ridker *et al.*, 2000; Roivainen *et al.*, 2000; Tracy *et al.*, 1997).
CRP, apart from cytokine activation may also bind and activate the complement, induce expression of several cell adhesion molecules and tissue factor, mediate low-density lipoprotein (LDL) uptake by endothelial macrophages, and induce monocyte recruitment into the arterial wall Therefore, measurement of inflammatory markers such as high-sensitivity C-reactive protein (HSCRP) may provide a novel method for detecting individuals at high risk of plaque rupture. Screening for HSCRP may improve global risk prediction among those with high as well as low cholesterol levels (Ridker *et al.*, 2001).

4.8.2 CRP and Periodontal disease

Not all the established risk factors for elevated CRP like older age, smoking, high blood pressure, obesity and chronic bacterial infections explain raised levels of serum CRP observed in some individuals suggesting that factors and chronic inflammatory conditions other than those above may result in additional stimulus for a systemic inflammatory response. Some of the recent studies have reported elevated CRP levels among those with periodontitis (Fredriksson *et al.*, ; Kiechl *et al.*, 2001; Loos *et al.*, 2000; Noack *et al.*, 2001). Study by Ebersole et al., reported significantly higher levels of CRP among those with adult periodontitis, especially among those having more active sites (Ebersole *et al.*, 1997). The participants of the MI Life Study (Noack *et al.*, 2001) also reported positive association between elevated levels of CRP ($\geq$ 3mg/l) and severity of periodontitis. Periodontitis is an inflammatory reaction of the supporting tissues of the teeth like the periodontal ligament, cementum and alveolar bone to gram-negative anaerobic bacteria. As a response to bacterial endotoxins, the local host inflammatory mediators are activated (Lamster and Novak, 1992; Page, 1991) that in turn initiate localized inflammatory response (Ebersole and Cappelli, 1995; Kinane *et al.*, 1993) and finally result in serum antibody response to the bacteria (Ebersole, 1990; McArthur and Clark, 1993). Bacterial infections may often provide a strong stimulus for a systemic acute phase response that may result in increased production of acute-phase proteins like CRP, α_2- macroglobulin and serum amyloid A (Steel and Whitehead, 1994). Elevation of CRP levels among those with periodontitis indicates that periodontitis may also have systemic cytokine mediated effects that may in turn participate in atherogenesis. This may in turn help to explain conditions where dental infections may stimulate systemic inflammatory response, thereby, placing "apparently healthy" people at increased risk of cardiovascular disease.
Most of the studies looking at levels of CRP among those with periodontitis, however, included primarily the middle-aged subjects and evidence of a similar in the elderly is lacking.

4.9 Salivary microorganisms and denture plaque

Dental plaque can be defined as the soft deposits that form the biofilm adhering to the tooth surface and other hard surfaces in the oral cavity, including removal and fixed restorations (Bowen, 1976). Denture plaque has essentially the same structure as dental plaque on natural teeth (Budtz-Jorgensen *et al.*, 1981; Walter and Frank, 1985) and is primarily composed of microorganisms (Eliasson *et al.*, 1992; Gusberti *et al.*, 1985; Marsh *et al.*, 1992; Theilade *et al.*, 1983; Theilade and Budtz-Jorgensen, 1980). It is known to contain more than 10^{11} organisms per gram in wet weight.
In a study on the composition and ultrastructure of bacterial plaque on the fitting surface of dentures, maxillary denture of 12 edentulous patients were examined (Theilade and Budtz-Jorgensen, 1980), 11 of whom revealed the presence of bacteria on the fitting surface of the denture. Yeast cells (*Candida albicans*) were present in only 5, all of whom suffered from denture stomatitis. Majority of dentures were covered with cocci or short rods and most of them were Gram-positive. Another study by the same authors (Theilade *et al.*, 1983) showed that the predominant cultivable flora in denture plaque of healthy subjects were *streptococci* (0-81 %, median, 41%) with varying proportions of *streptococcus milleri, streptoccus mutans, streptococcus salivarius, streptococcus mitior* and *streptococcus sanguis. Staphylococcus aureus* made up 0-13 % (median, 6%). Gram-positive rods constituted 1-74 % (median, 33%). Among these, *actinomyces israelii, actinomyces naeslundii, actinomyces*

viscosus and *actinomyces odontolyticus* were the most common species. *Lactobacilli*, gram-negative rods and yeasts formed only a small percentage in these subjects. Similar observations were also made by Gusberti and his colleagues (Gusberti *et al.*, 1985).
Shifts in the normal oral flora as a result of systemic diseases, ill-fitting dentures, inability to maintain good oral hygiene, and hyposalivation can result in increased growth of many oral microorganisms (Loesche *et al.*, 1995; Närhi *et al.*, 1993; Närhi *et al.*, 1998) and are suggested to be an important factor for the development of denture stomatitis (Budtz-Jörgensen, 1990). Bacterial and yeast colonization on the palatal mucosa may play an important role in denture stomatitis in this relatively healthy population (Budtz-Jörgensen, 1990; Eliasson *et al.*, 1992). In the edentulous, the altered denture plaque may result in different kinds of chronic oral diseases like denture-associated stomatitis and other mucosal lesions (Budtz-Jorgensen, 1974; Budtz-Jörgensen, 1990; Iacopino and Wathen, 1992; MacEntee, 1985; Stohler, 1984) with systemic consequences (Nikawa *et al.*, 1998).

4.10 Denture related mucosal diseases in the elderly

Saliva has several major functions like cleansing of teeth surfaces, buffering activity against bacterial acids, lubrication, antibacterial action and maintaining tooth integrity. It also aids in various functions like speech swallowing and digestion. At the same time saliva plays an important part in plaque initiation, maturation and metabolism as well as calculus formation, periodontal disease and dental caries among the dentate (Carranza and Bulkacz, 1996) and mucosal lesions associated with dentures among the edentulous. The oral mucosa is known to become more vulnerable to mechanical damage as the age advances (Pindborg, 1986).
In a study among the institutionalized elderly of Denmark (Vigild, 1987), nearly half of the subjects exhibited one or more pathologic conditions of the oral mucosa. The most prevalent finding was denture stomatitis, which manifested in about one third of the elderly and was strongly influenced by the denture hygiene. Denture related traumatic ulcerations were also found in these elderly. In another study among a population of elderly Thai patients (Jainkittivong *et al.*, 2002), the incidence of oral mucosal conditions was 83.6%. Significantly higher prevalence of oral mucosal conditions was observed in denture wearers than subjects who had no dentures. Most common denture-related problems were traumatic ulcer, denture stomatitis and angular cheilitis. Compared with the wearing of partial dentures, wearing complete dentures increased the risk of mucosal lesions (Jainkittivong *et al.*, 2002; Mikkonen *et al.*, 1984). Among the elders of the Helsinki Aging Study, 46% were edentulous and more than half (51%) of the edentulous subjects with complete dentures had mucosal lesions (Nevalainen *et al.*, 1997). The most common denture related mucosal change in these subjects was inflammation under the dentures, especially, the maxillary complete dentures. It was most commonly found among those with subjective symptoms of xerostomia and smokers (data not shown). Mucosal lesions were most common among those wearing complete dentures.
The oral infections in the denture wearers, like the periodontal infections in the dentate, may be responsible for increased production of inflammatory mediators like CRP that are known to be associated with CVD. The NHANES III (Slade *et al.*, 2000) reported significantly higher levels of CRP among the edentulous, as compared to dentate subjects without periodontal disease. There are not many studies looking at the association of denture related mucosal diseases in the edentulous elderly, CRP levels and mortality.

5. AIMS OF THE STUDY

The aims of the present study are:

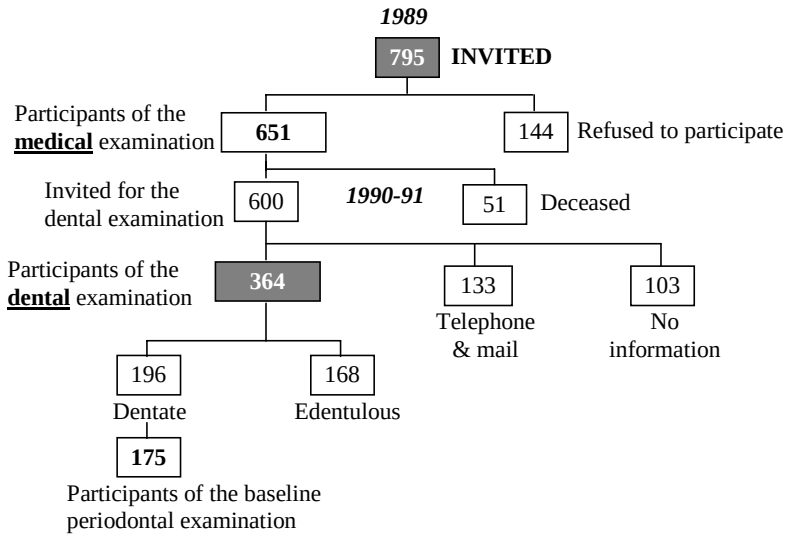
- to determine the periodontal health status and treatment needs of the home-dwelling dentate elderly **[I]**
- to determine the changes in their periodontal health status during the five year follow-up period **[II]**
- to examine the relation of clinical periodontal health, C-reactive protein (CRP) and mortality (all-cause and cardiovascular) among the dentate during the five-year follow-up period **[III]**
- to evaluate the relationship between tooth loss, denture-related chronic mucosal diseases, salivary microorganisms and CRP levels and the influence of these factors as well as of periodontal disease on 10-year all-cause and CV mortality among the dentate and edentulous elderly **[IV]**

6. SUBJECTS AND METHODS

6.1 Subject sample

This study forms a part of a comprehensive longitudinal medical and dental survey, the Helsinki Aging Study (HAS). HAS was a population-based prospective birth cohort study, which was designed to study the prognostic significance of various clinical findings in the elderly population of Helsinki, Finland.

Figure 3: Distribution of the participants in the study (Baseline)

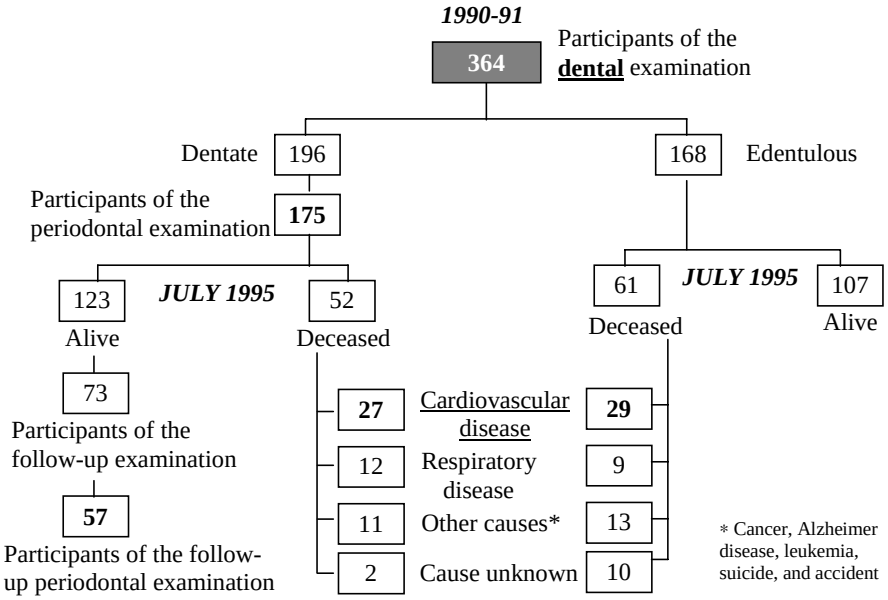


The HAS study sample included a random sample of subjects born in 1904, 1909, and 1914, and living in Helsinki, Finland, on 1st January 1989 (Valvanne, 1992; Vehkalahti *et al.*, 1996). Out of a total subject population of 8035, 900 (300 from each age cohort) were selected for the medical survey. The sample of the two oldest age groups was disproportionate to their share in the general population in order to achieve their sufficient participation. Of the 900 selected, 84 had died before the medical examination, 11 had moved out of Helsinki and 10 could not be located. So the final number of elderly who were invited for the medical examination was 795 (Figure 3).

Between 1989 and 1990, 651 subjects (82%) underwent medical examination and in June 1990, 600 subjects still alive were invited for a comprehensive oral examination. Of the 600 invited, 364 subjects (61% of those invited) (196 dentate and 168 edentulous) aged 76, 81, and 86 years, were examined in 1990-1991. For 133 subjects, information about their dental health was obtained by a phone interview and a mail survey. However, no information could be obtained for the remaining 103 subjects; 3 had died before the dental examinations started, 50 were too ill to participate, 20 refused to participate and 30 could not be found. Of the 364 elderly who underwent dental examination, 293 were examined in a dental clinic at the Institute of Dentistry, University of Helsinki, and 71, who were unable to come to the

Institute of Dentistry either due to poor general health or due to transportation difficulties, were examined in their homes, in old people's homes, or in hospitals. The participation rate was 69% for men and 58% for women. Analysis of the factors related to the non-participation has been published separately (Vehkalahti *et al.*, 1996). Four faculty members performed the clinical examinations and they were calibrated in order to eliminate inter- and intra-examiner errors. In total, 175 subjects, out of the 196 dentate who underwent clinical and radiological examinations, met the Community Periodontal Index of Treatment Needs (CPITN) criteria of having at least one sextant with two or more functioning natural teeth (Ainamo *et al.*, 1982) (Figure 3).

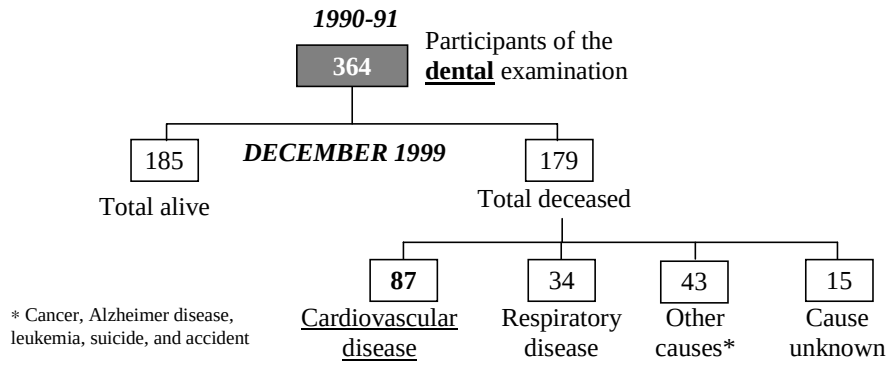
Figure 4: Distribution of the participants in the study (Follow-up)



In July 1995, five years after the medical examination and four years after the dental examination, the baseline participants were invited for a follow-up (Figure 4). Letter describing the follow-up study was mailed to them followed by appointments for clinical and radiological examination over the telephone. To those who could not be contacted by phone, a letter was re-sent. A total of 57 dentate elderly, now aged 81, 86, and 91 years met the CPITN criteria of having at least one sextant with two or more functioning natural teeth and were included for follow-up periodontal examination. Sixteen dentate subjects who attended the follow-up examinations could not be included, as they did not meet the criteria, or required prophylactic antibiotics, or refused clinical examination. Three of the baseline participants were now edentulous.

Prior to the follow-up dental examinations, information about the baseline participants who were now deceased (cause and date of death) was obtained from the Death Registry. Of the 175 participants of the baseline periodontal examination, 52 had died by July 1995. The main causes of death were CVD (48%), followed by respiratory disease (25%), and other causes of death like cancer, leukemia, suicide, and accident (23%). Cause of two deaths (4%) was not known. Among those edentulous at baseline (n=168), 61 had died during this period and the primary cause for 48% of them (n=29) was CVD (Figure 4).

Figure 5: Distribution of the participants in the study (1990-1999)



The Helsinki Aging Study concluded in December 1999, ten years after the baseline medical and nine years after the baseline dental examination. No clinical examinations were conducted in 1999. Only data on mortality was obtained from the Finnish Death Registry. Of the 364 initial participants of the dental study, 185 were alive and 179 died during this study period. As observed in 1995, nearly half the deaths (49%) were due to CVD (Figure 5). The information about the cause and date of all the deaths was obtained from the Finnish Death Register.

6.2 Data collection

6.2.1 Medical examination

The baseline medical evaluation included a postal questionnaire for the subject and for a close informant, structured interview conducted by public health nurses, review of patient records, an examination by a medical practitioner, and laboratory examinations.
Specially trained nurses carried out the measurement of blood pressure between 0800 h and 1000 h, after an overnight fast, but while taking regular medication. High blood pressure was defined on a past diagnosis, with medication, or a current sitting blood pressure greater than 160/95 mm Hg. Diabetes was defined based on a past diagnosis, or as fasting blood sugar of $\geq$ 7.0 mmol / l. Height and weight were measured with light clothing, but without shoes, and the body mass index (kg/m²) was calculated as weight / height ². Serum total cholesterol and triglyceride concentrations were measured enzymatically (Boehringer Mannheim, Germany). High density lipoprotein cholesterol (HDL) was determined after precipitation of very low density lipoprotein (VLDL) and low density lipoprotein cholesterol (LDL) with Mg^{2+} /dextransulphate. Presence of CVD was based on a previous history of myocardial infarction or angina or stroke obtained from earlier hospital records and clinical examination. Information on smoking and alcohol was available from the interview and questionnaire. The subject was accordingly classified as a non-smoker, former smoker or present smoker, and as subject not taking alcohol at all, taking less than once a week, or taking once a week or more, respectively. The social class was judged based on subjects' occupation and years of education.
As a part of the baseline laboratory analyses, blood samples were drawn after an overnight fast. C-reactive protein (CRP) was later measured in 1998 using the frozen (-20° C) baseline

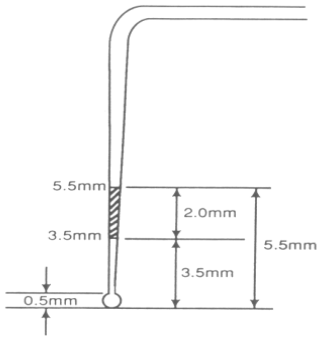
serum samples. A sensitive immunoenzymometric assay that made use of 2 monoclonal antibodies (sensitivity =0.3 mg/l, Medix Diacor) was used for this purpose. Serum concentration of 3mg/l, which is the approximate mean of the reported range for CRP as a risk factor for CVD, peripheral vascular disease, or stroke (1.34 mg/l to 6.45 mg/l) (Koenig *et al.*, 1999; Noack *et al.*, 2001) was used as a cut off point. CRP levels exceeding 3 mg/l were considered elevated.

6.2.2 Dental examination

A comprehensive dental examination carried out for each participant consisted of a questionnaire, full mouth radiological and detailed clinical examination, and laboratory investigations. The examination took an average of two hours per subject.
At the baseline, the clinical examination for those edentulous included evaluation of salivary function and examination of tongue, corners of the mouth, and oral mucosa under and around the dentures. Among the dentate, the examination included assessment of prosthetic condition, periodontal status and dental caries along with evaluation of salivary function. The examinations were carried out in the University Dental Clinic by four faculty members, and the examiners were calibrated for eliminating inter- and intra-examiner errors. Considering the primary aim of a comprehensive oral check-up, and based on the chair-side time reserved for periodontal examination, Community Periodontal Index of Treatment Needs (CPITN) (Ainamo *et al.*, 1982; WHO, 1982) was considered ideal, for such a population-based study.

6.2.2.1 Periodontal examination using the CPITN

International Dental Federation and the World Health Organization jointly developed the CPITN (WHO, 1978). Following extensive testing and after minor modifications, the CPITN was adopted in 1982 (Ainamo *et al.*, 1982). The index is simple, rapid, inexpensive, easily applied, and requires minimum of equipment. The index measures signs of periodontal disease like bleeding, calculus and presence of periodontal pockets, but does not measure the cumulative manifestations of the disease such as attachment loss, recession and alveolar bone loss. Despite this the Index is widely used because of its greatest strength, that is, its simplicity. It is one of the best methods to assess the periodontal conditions among the elderly who are unable to withstand complex examination procedures.



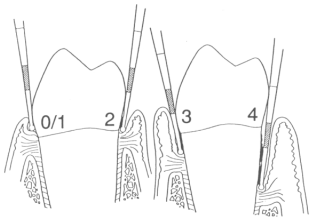
CPITN index uses a specially designed WHO color-coded periodontal probe (Figure 6). The color band of the WHO probe extends from the 3.5 mm line to the 5.5 mm line. The color-coding helps in assessing periodontal pocket depths around the teeth. At the tip of the probe there is a 0.5 mm diameter ball that assists in feeling the sub gingival calculus and also prevents the probe from being pushed through the inflammatory tissue at the base of a pocket.

Figure 6: The CPITN probe

The periodontal examinations involved recordings on *all surfaces of all the teeth* for the presence or absence of any 6 mm or deeper periodontal pockets (Code 4), any 4-5 mm pockets (Code 3), calculus and/or overhanging margins of restorations (Code 2), gingival bleeding on gentle probing (Code 1), and healthy sextants (Code 0) (Table 2). Recordings

were made only for sextants that contained at least two functioning natural teeth. The sextants were scored based on the worst finding. As periodontal treatment needs are influenced by number of edentulous subjects in the population and number of remaining teeth among the dentate subjects, missing sextants were recorded separately, and their number included in the data analysis.

Table 2: CPITN codes and criteria



(*Source*: WHO. Oral health surveys: Basic methods. 3rd ed. Geneva, 1987)

CODES	TREATMENT NEEDS
Code 0: All sextants healthy	*TN 0:* No treatment need
Code 1: One or more sextants with bleeding on probing	*TN I:* Improvement of personal oral hygiene
Code 2: One or more sextants with calculus and/or overhangs	*TN II: I* + scaling and root planing
Code 3: One or more sextants with 4 to 5 mm pockets	
Code 4: One or more sextants with 6mm or deeper pockets	*TN III: I + II* + complex periodontal treatment

To study the need for periodontal treatment, subjects were classified into one of the four treatment needs categories based on their highest CPITN code (Table 2). The total proportion of treatment need per sextant or subject was based on the assumption that those with $\geq$ 4 mm periodontal pockets required oral hygiene instructions along with scaling and root planning and subjects needing complex periodontal treatment required both scaling and root planning and oral hygiene instructions.
To study the association between periodontitis and CV associated mortality, periodontal status was dichotomized and CPITN codes 3 and 4 (periodontal pockets $\geq$ 4 mm) indicated periodontitis.

6.2.2.2 Microbial counts

Salivary microbial (*mutans streptococci and yeast*) counts were analyzed using commercial kits (Närhi, 1994). The methods of collecting saliva and assessing the microbial counts have been reported elsewhere (Närhi *et al.*, 1999). Briefly, estimation of salivary *mutans streptococci* was done by the Dentocult-SM strip mutans® method and salivary *yeast* was done by the Oricult-N® method (Orion Diagnostica, Espoo, Finland). The growth densities of SM, and number of colonies of salivary *yeast* were classified into 4 categories (0 to III) from no growth to $>10^6$ CFUs/mL, and no colonies to >50 colonies per side of the slide, respectively (Närhi *et al.*, 1994; Närhi *et al.*, 1999). In this study, we took the average of *mutans streptococci and yeast* categories for each individual to determine their total microbial count. The microbial count was dichotomized (cut point 2).

6.2.2.3 Mucosal lesions

The examination of the mucosa was carried out by the four faculty members. Details of this examination are given elsewhere (Nevalainen *et al.*, 1997). Briefly, the examinations were carried out in the Dental Clinic under normal light using two mouth mirrors. The dentures were removed prior to the examination and the areas examined included the lips, lower and upper labial/buccal mucosa and sulcus, commissures, alveolar ridges, tongue, floor of the

mouth, and hard and soft palate. The diagnosis was based on clinical examination only and all the mucosal lesions were registered using a modified scheme recommended by the WHO (Kramer *et al.*, 1980). The changes in the mucosa suggesting a yeast infection, such as angular chelitis, plaque like lesion (pseudomembranous or hyperplastic), and erythematous lesions on tongue, mucosa, or hard palate, were recorded and categorized as 'oral candidosis', whereas localized or generalized erythema and/or granular type hyperplasia under the denture was termed as 'Denture stomatitis'. Any and all inflammatory conditions of the mouth, including mucosal lesions and denture stomatitis, were broadly categorized as 'Inflammation of the mouth'.

6.3 Statistical analysis

Statistical evaluations were performed with SPSS for MS (Version 9.0, SPSS Inc., Chicago, IL, USA). Students *t* test was used to determine the statistical significance of the differences in the mean between the ages and sexes **[I]**. Differences in the mean values of the numerical variables between the baseline and 5-year follow-up were analyzed by the paired *t* test **[II]**. Chi-square test was used to test the differences in distribution of treatment needs and to compare the rates and proportions **[I]** & **[II]**. Additionally ANOVA and/or non-parametric tests were also used to calculate the means **[I-IV]**. Any significant association between CV risk factors and periodontal status as well as mortality was determined using Chi square test **[III & IV]**. If the distribution of a variable compared between subgroups of the study population was not normal and could not be made normal by logarithmic transformation, non-parametric tests were used. A p-value less than 0.05, was considered significant.
We used logistic regression to investigate the relationship of various independent dental variables (teeth, mucosal lesions, and microbial count) with the risk of high CRP level and microbial count **[IV]**. Survival estimates were determined using the Kaplan-Meier survival curve **[III]**. A Cox proportional hazards model was then fitted to study the association between periodontal status and all-cause and CV mortality after adjusting for the known CV risk factors. Estimates of odds ratios for those without periodontitis, compared to the ones with the disease or those edentulous were calculated with 95% confidence intervals **[III & IV]**.

6.4 Ethics committee approval

Informed consent was obtained form all subjects prior to the study. The Ethical committees of the Helsinki University Central Hospital, and the Institute of Dentistry, University of Helsinki, Finland approved the protocol of the study.

7. RESULTS

7.1 Natural dentition [I] & [II]

Table 3: Distribution of participants of the periodontal examination at baseline (n=175) and follow-up (n=57)

Age at baseline (follow-up)	Number of subjects							
	Baseline				Follow-up			
	Men		Women		Men		Women	
	n	%	n	%	n	%	n	%
76 (81) yrs	30	54	64	53	12	70	28	70
81 (86) yrs	13	24	35	29	3	18	11	27
86 (91) yrs	12	22	21	18	2	18	1	3
Total	55	100	120	100	17	100	40	100

The baseline included a relatively high proportion of dentate men and women, although, the numbers of retained natural teeth varied greatly. Of the 364 baseline participants, 196 (54%) were dentate and 175 were included in the periodontal examination. Majority of those who participated in the periodontal examination were women both, at baseline (69%) and follow-up (70%) (Table 3).

Nearly 60% (n=73) of the participants who attended the follow-up in 1995 were dentate and 57 were periodontally examined. As at the baseline, this sample also included high proportion of subjects with reduced dentition and the periodontal examination saw the participation of primarily the youngest age group (76 years at baseline) (70%), with only 3 of the 57 follow-up participants belonging to the oldest (86 years at baseline) age group.

Table 4: Mean number of remaining teeth of the baseline participants by age and sex

(Values are Mean ± Standard Deviation (SD))

Age at baseline	Men		Women	
	Mean	SD	Mean	SD
76 years	16.8	7.8	14.8	7.1
81 years	12.9	8.9	12.8	7.5
86 years	13.3	8.1	13.5	8.6
TOTAL	15.1	8.2	14.0	7.4

The mean number of remaining teeth at baseline was 14.4 (SD, 7.7) and mean number of remaining sextants 3.6 (SD, 1.9). The mean number of teeth was highest for 76-year-old male cohort, but the difference between the age groups or sexes was not statistically significant (Table 4). Nearly a third of the dentate participants had 20 or more remaining natural teeth. Among the dentate subjects who participated in both the baseline and the follow-up periodontal examination, a significant decrease in the number of teeth was observed. The mean number of teeth reduced from 15.9 to 15.1 ($p=0.0001$) overall, 17.2 to 15.7 ($p<0.001$) among men and 15.3 to 14.7 ($p<0.001$) among women. The mean number of remaining sextants decreased from 4.0 to 3.6 ($p<0.005$)

during the five-year follow-up period. The decrease in the number of teeth was observed in the group with 10-19 teeth at baseline. Those who had 20 or more natural teeth at baseline seem to retain them. Nearly 41% of the men and 38% of the women still had 20 or more remaining natural teeth.

7.2 Periodontal health status and treatment needs (Baseline) [I]

Overall, of the 175 subjects examined, only 7% had healthy periodontal tissues (code 0). Six percent recorded bleeding on probing (code 1) and calculus and/or overhanging margins of restoration (code 2) was recorded as the worst finding in 41% of the elderly. Deepened periodontal pockets were observed in almost half the participants (46%) with majority of them (35%) having 4 to 5 mm pockets (code 3) as the worst score. Highest score of Code 4 ($\geq$ 6 mm pockets) was observed in only 11%. Periodontal health was better in women than men with 10% (*vs.* 2%, $p<0.05$) having all sextants healthy and only 8% (*vs.* 16%, $p=0.01$) recording the worst finding of 6 mm or deeper periodontal pockets (Table 5).

Table 5: Periodontal status at baseline

CPITN codes	All	Age at baseline			Sex	
	subjects	76 yrs	81 yrs	86 yrs	Men	Women
0 = Healthy	7%	9%	8%	3%	2%	10%*
1 = Bleeding on probing	6%	5%	4%	12%	2%	8%
2 = Supra- or sub gingival calculus and/or overhangs	41%	42%	36%	43%	42%	40%
3 = Pocket depth of 4-5 mm	35%	35%	36%	33%	38%	34%
4 = Pocket depth $\geq$ 6 mm	11%	9%	16%	9%	16%	8%**

Statistical evaluation by Chi square test
* $p<0.05$, ** $p=0.01$

At a sextant level, there was a mean of 3.6 sextants present per person at baseline. Mean number of healthy sextants was 0.4 whereas 1.6 sextants recorded calculus and/or overhanging margins of restoration as the worst finding. At least one sextant on average was found to have a worst finding of 4-5 mm pockets. Women had significantly higher mean number of healthy sextants than men (0.6 ± 1.5 *vs.* 0.1 ± 0.2, $p=0.01$).

Treatment needs

Determining the treatment need using the CPITN is based on the presumption that finding of calculus assumes that there will also be bleeding on probing. Consequently those who had the worst finding of Code 2 (or 3) not only required scaling and root planing but also had to be given oral hygiene instructions. Similarly those undergoing complex periodontal treatment required scaling and root planning as well as oral hygiene instructions,
Our results showed that 93% of all the dentate participants required oral hygiene instruction and 87% of then needed either scaling and root planning or removal of overhanging margins of restorations. Only 11% of our subjects required any kind of complex periodontal treatment; at the same time, only 7% had no treatment need. Men had higher treatment need

than women with only one male (compared to 12 female) participant requiring no periodontal treatment ($p<0.05$).

7.3 Periodontal health status and treatment needs (1995) [II]

The changes in the periodontal status of the 57 subjects who underwent baseline and follow-up periodontal examination are shown in Table 6. At baseline 5 of the 57 subjects had all sextants healthy (Code 0) compared to 4 during the follow-up and only 1 of them had Code 0 both at baseline and follow-up. Worst score of Code 1 (bleeding on probing) was found in 3 subjects at baseline and in 2 at follow-up. There was an increase in the number of subjects with the worst finding of calculus and/or overhanging margins (Code 2) (from 24 to 33), and a decrease in those with 4-5 mm periodontal pockets (Code 3) (from 22 to 13) during the 5-year period. This decrease was significant among those with 4-6 sextants (from 50 to 22, $p<0.05$). Marginal increase was observed in the number of subjects with 6 mm or deeper pockets (Code 4) (from 3 to 5). In short the periodontal status worsened for 9% of the subjects, improved for 5% but remained almost unchanged for nearly 86% of the subjects.
At a sextant level, there was an overall improvement during the 5-year period. Mean number of sextants with Code 0 increased from 0.63 to 0.78 and with Code 1 decreased from 0.35 to 0.29. There was also a significant decrease in mean number of sextants with worst score of Code 3 from 1.08 to 0.38 ($p=0.001$). Although, the mean number of sextants with highest score of Code 2 and Code 4 increased, the change was not statistically significant. As seen at baseline, women at the follow-up had more number of healthy sextants and fewer sextants with deep periodontal pockets than did men.

Table 6: Changes in the CPITN score for the 57 subjects during the 5-year period

		Follow-up (n)					
Highest CPITN score		0	1	2	3	4	Highest score at baseline
Baseline (n)	0	1	-	4	-	-	5
	1	-	-	3	-	-	3
	2	3	2	13	5	1	24
	3	-	-	13	7	2	22
	4	-	-	-	1	2	3
Highest score at follow-up		4	2	33	13	5	**57**

Status		
	Same (unchanged/changed by 1 code)	49
	Improved (decreased by 2 codes)	3
	Deteriorated (increased by 2 codes)	5

Treatment needs

During the follow-up period an increase was observed in the number of subjects with Code 2, but at the same time there was a decrease in the number of elderly with Code 3. As a result, the treatment need for the 57 participants of the baseline and follow-up periodontal examination remained almost the same.
Comparing the overall treatment need of the participants of baseline (n=175) and follow-up (n=57), except for a marginal decrease in proportion of those requiring complex periodontal

treatment (11% to 7%) and an equivalent increase in those needing scaling and root planning (87% to 90%), the need remained unchanged.

7.4 Periodontal disease and cardiovascular (CV) mortality (1995) [III]

To look at the association of periodontal disease with mortality, especially CV mortality, the baseline periodontal status was dichotomized. Of the 175 elderly who underwent periodontal examination at baseline, 80 were classified as having periodontitis (CPITN code = 3 or 4).

Table 7: Association of various CV risk-factors with periodontal status, baseline data

Baseline characteristics	Periodontitis		
	Yes n=80	No n=95	*p*
Age:			
76 y	41 (51%)	53 (56%)	
81 y	25 (31%)	23 (24%)	
86 y	14 (18%)	19 (20%)	ns
Women	49 (61%)	71 (75%)	0.056
Social class:			
Class I	12 (15%)	12 (13%)	
Class II	18 (23%)	30 (32%)	
Class III	35 (44%)	36 (38%)	
Class IV	10 (13%)	14 (15%)	ns
Current smoker	5 (6%)	3 (3%)	ns
Alcohol (once a week or more)	10 (13%)	9 (10%)	ns
Diabetics	12 (15%)	15 (16%)	ns
Hypertensives	23 (29%)	36 (38%)	ns
Number of teeth †	15.3 (8.1)	13.6 (7.3)	ns
Body mass index (kg/m²) †	25.5 (3.5)	25.6 (3.7)	ns
Systolic blood pressure (mm Hg) †	155 (24.9)	160 (24.8)	ns
Diastolic blood pressure (mm Hg) †	80 (12.1)	85 (13.9)	<0.05
Serum cholesterol (mmol/L) †	6.3 (1.2)	6.6 (1.3)	ns
Serum HDL (mmol/L) †	1.5 (0.4)	1.5 (0.5)	ns
Serum triglyceride (mmol/L) †	1.2 (0.6)	1.5 (0.9)	ns*
Serum C-reactive protein (mg/L) †	2.4 (4.3)	2.1 (2.3)	ns*

†Values are mean (SD).
Statistical evaluation by Chi square test and ANOVA
* Statistical evaluation by Kruskal-Wallis Test

Table 7 shows the association of various baseline CV risk factors with baseline periodontal status. The univariate analyses showed that males and those with lower BP were more likely

to have periodontal disease. Interestingly, factors like age, smoking, social class, diabetes and alcohol use were not associated with baseline periodontitis. Apart from lower diastolic blood pressure, periodontal disease was not significantly correlated to any other CV risk factor in this study population (Table 7). On the other hand those who were alive in 1995 had significantly higher BMI ($p<0.05$), systolic ($p<0.005$) and diastolic ($p<0.05$) blood pressure and cholesterol ($p<0.005$) at baseline than the deceased. The association of periodontitis with five-year total mortality was of borderline significance ($p=0.08$). Cumulative survival for CV mortality was significantly lower in subjects with periodontitis ($p=0.05$). When the model was adjusted for age, sex and history of CVD, periodontitis was associated with a 60% increase in the risk of death from all causes (p=ns) and almost 2.4 fold (CI 1.07-5.18) increase in CV mortality. On adjusting for diastolic blood pressure, the only potential confounder found in the univariate analyses in this study population, the result remained almost unchanged (HR 2.33, CI 1.0-5.42). Further adjustment for other relevant risk factors for CV mortality like smoking, cholesterol, HDL, BMI and history of hypertension, did not affect the magnitude of the hazards ratios (HR 2.28, CI 1.03-5.05).

7.5 Periodontal disease, edentulism and CV mortality (1999) [IV]

By December 1999, 179 participants of the baseline dental study had died. As observed at the first follow-up (in 1995) the deceased were significantly older, were diabetic, and had lower BMI, systolic and diastolic blood pressure and serum cholesterol level (Table 8). However, after adjusting for age (which strongly correlated with the above variables) only diabetes status and serum cholesterol level remained significantly associated with mortality (data not shown). Among the deceased 73 subjects had undergone periodontal examination at baseline and 49% of those with periodontal disease at baseline had died during the study period.

The edentulous differed more from all dentate individuals. They were significantly older, predominantly females, of lower social class, they smoked more often, consumed more alcohol and had higher CRP than the dentate. Higher percentage of those who were edentulous died by 1999 compared to those with 20 or more remaining teeth ($p<0.01$), or those without periodontal disease at baseline ($p<0.01$).

ALL-CAUSE MORTALITY

To look at the association of periodontal status (i.e. no periodontitis, periodontitis and edentulous) with all- cause mortality, we included the known risk factors associated with mortality in the Cox model. These included age, sex, social class, body mass index, smoking status, blood pressure and serum cholesterol. Although edentulism was associated with almost 60% increase in risk for all-cause mortality after adjusting for age and sex (HR 1.57, CI 1.03 – 2.41), the association lost significance on adjusting for other risk factors (HR 1.48, CI 0.95 – 2.31). Periodontal disease was associated with increased mortality from all causes but the association was not statistically significant (HR 1.58, CI 0.96 – 2.61).

CV MORTALITY

After adjusting for age, sex and other CV risk factors like social class, body mass index, smoking status, blood pressure, serum cholesterol level and history of cardiovascular disease the risk for CV mortality was almost double among those with periodontitis than those

without periodontitis (HR 1.97, CI 1.01 – 3.85). Edentulism was, however, not associated with CV mortality in the adjusted Cox model.

Table 8: Association of various baseline CV risk-factors with status in 1999

Baseline characteristics	Status in 1999		
	Dead (n=179)	Alive (n=185)	*p*
Age:			
76 years	54 (30%)	111 (60%)	
81 years	57 (32%)	49 (26%)	
86 years	68 (38%)	25 (14%)	<0.0001
Women	125 (70%)	137 (74%)	ns
Social class:			
Class I	15 (8%)	24 (13%)	
Class II	30 (17%)	49 (27%)	
Class III	68 (38%)	74 (40%)	
Class IV	43 (24%)	27 (15%)	<0.05
Current smoker	17 (10%)	15 (8%)	ns
Alcohol (≥ once a week)	23 (13%)	22 (12%)	ns
Diabetics	36 (20%)	19 (10%)	<0.05
Hypertensives	64 (36%)	63 (34%)	ns
BMI (kg/m²) †	25.2±3.6	26.1±3.8	<0.05
Systolic blood pressure (mm Hg) †	154±26.0	159±24.9	<0.05
Diastolic blood pressure (mm Hg) †	81±11.6	83±11.9	0.05
Serum cholesterol (mmol/L) †	6.3±1.2	6.7±1.3	0.001
Serum HDL (mmol/L) †	1.5±0.5	1.5±0.5	ns
Serum triglyceride (mmol/L) †	1.4±0.8	1.4±0.8	ns*
Serum CRP protein †	3.3±4.7	3.2±6.2	ns*

† Values are mean±SD.
Statistical evaluation by Chi square test and ANOVA
* Statistical evaluation by Kruskal-Wallis Test

7.6 C-Reactive protein and salivary microorganisms [III & IV]

Those who had all the sextants healthy (CPITN = 0) at baseline had significantly lower mean baseline CRP (0.58 mg/l) than those with gingivitis (CPITN = 1 or 2) (2.72 mg/l) or periodontitis (CPITN = 3 or 4) (2.05 mg/l) (p=0.01). A CRP level exceeding 3 mg/l was significantly more common among those dying between 1991 and 1995, and this association was observed only among those with periodontitis. Also, a significant linearly increasing trend in the risk of death was observed when moving from the category no periodontitis-low CRP to periodontitis combined with elevated CRP (p<0.05). Over 70% of subjects with low

CRP and no periodontal disease at baseline were alive in 1995, in comparison to only 40% with elevated CRP and periodontal disease. This association was not seen at 10 years.

After adjusting for age and sex, significantly higher percentage of edentulous subjects had elevated CRP levels ($\geq$ 3 mg/L) than those with 20 or more teeth or dentate without periodontal disease or dentate without dentures. Among the edentulous, those with mucosal lesions or any inflammation in the mouth had significantly higher CRP ($p<0.01$ and $p<0.05$ respectively, data not shown). This relation was not significant among the dentate. Of all participants (n=364), a high percentage of those with denture stomatitis had elevated CRP ($p<0.05$). More subjects with complete dentures and having denture stomatitis had elevated CRP than did those without complete dentures and not having stomatitis ($p<0.05$). A similar trend was observed for salivary microbial counts, which were significantly higher in the edentulous, and those with denture stomatitis, oral candidosis or inflammation in the mouth.

The multivariate associations between dental variables (like number of teeth, microbial counts and mucosal lesions) and elevated CRP were determined using a logistic regression model. The outcome in the model was presence of elevated CRP ($\geq$ 3 mg/L). The model was adjusted for age, sex, history of smoking, alcohol consumption, blood pressure, social class and presence of established risk factors for elevated CRP like emphysema or chronic bronchitis or asthma or muscle and joint disease. There was a two-fold odds of elevated CRP associated with the presence of mucosal lesions (OR 2.18, CI 1.03 – 4.61) and high salivary microbial counts (OR 2.31, CI 1.06 – 5.05). The odds of elevated CRP reduced with increase in number of teeth (OR 0.95, CI 0.90– 1.00). High salivary microbial count was strongly associated with the presence of mucosal lesions (OR 2.13, CI 1.11 – 4.11).

8. GENERAL DISCUSSION

8.1 Subjects and methods

The Helsinki Aging Study included a representative sample of the general home-dwelling elderly population of Helsinki City. The participants underwent in-depth medical examination in 1989-90 and were invited for dental examinations one year later. Majority of the participants who attended the baseline dental examinations belonged to the youngest age group (76 years), were in generally good state of health and mobile enough to attend the clinical examinations at the University dental clinic. After controlling for other factors, the strongest factors for non-participation in the dental study at baseline were older age, limited mobility, dementia and edentulism (Vehkalahti *et al.*, 1996).

In Finland, women outnumber the men in the general population, especially in the older age groups (75+). The male to female ratio for the 77-year age group is 1:2, and increases with age (Statistics Finland, 1995). As our study sample was representative of the community-dwelling elders of Helsinki, Finland, women formed a high percentage in this sample. Not many studies have been undertaken on the community-dwelling elderly (aged 75+ years) before.

The follow-up dental examinations five years later included only a third of the baseline participants (n=121). They principally comprised of that segment of the baseline study sample that were the healthiest and were mobile enough to get to the dental office and participate in the clinical and radiological examinations in 1995-96. One of the disadvantages of longer follow-up periods is the greater likelihood that subjects would be lost from the study (Ismail *et al.*, 1990). This is primarily because of high attrition rate, especially in the older people because of the deterioration of general health conditions. Almost a third of the participants of our study died during the follow-up period. As at the baseline, the participants of the follow-up were mostly women belonging to the youngest age group (now 81 years). The study sample is therefore unique and very few similar follow-up studies have ever been done. All the participants of the HAS were followed up until December 1999.

The dental examination conducted at the School of Dentistry (Helsinki, Finland) included full mouth radiological examination, in-depth clinical examination that included assessment of dental caries, prosthetic condition, salivary function and periodontal status, and comprehensive laboratory investigations. The clinical examination on average took approximately two hours. Since comprehensive oral evaluation was the primary aim of the clinical examination and considering the age of the participants, a simple, rapid but comprehensive periodontal index was required. Community Periodontal Index for Treatment Need (CPITN) index (Ainamo *et al.*, 1982; WHO, 1982) was selected as the preferred option considering the study design and the chair-side time reserved for the periodontal examination.

8.2 Dental status

More than half the participants (54%) of the baseline dental examination were dentate and majority of them were men (60%). More than third of our dentate population (aged 76 years and above) had 20 or more remaining natural teeth, a WHO suggested marker for acceptable periodontal health in the elderly (aged 65 to 75 years). These findings suggest that there

were more dentate Helsinki elders than in previous studies from Finland, Sweden or Denmark (Ainamo *et al.*, 1986; Kalsbeek *et al.*, 1991; Kirkegaard *et al.*, 1986; Vehkalahti *et al.*, 1991; Willemsen *et al.*, 1991). The mean number of remaining teeth in the dentate elderly of our study was 14.4 (n=175) and was higher than that reported in the elderly of the Mini-Finland study (1978-80) (mean, 11) (Markkanen *et al.*, 1983) and the study in Ostrobothnia, Finland (1985) (mean, 12) (Tervonen, 1988). These findings show an increase in the number of dentate elderly since the seventies, a trend observed in other western countries (Hugoson *et al.*, 1988; No authors listed, 1987; Nordenram and Böhlin, 1985; Nordström *et al.*, 1995). The mean number of teeth was higher in men than in women, in the mandible than in maxilla and in anterior sextants than in posterior. This is in accordance with many of the previous studies (Ahlqwist, 1989; Hiidenkari *et al.*, 1996; Nordström *et al.*, 1995; Takala *et al.*, 1994).
On the other hand 46% of the elderly participants were edentulous and edentulism was more frequent in women than men (60% vs. 40%). This finding was similar to that reported in the national survey in 1990 (Ainamo and Murtomaa, 1991). It is, however, possible that the number of edentulous subjects in Helsinki, Finland, may have been under-represented in this study as being edentulous was one of the reasons for not participating in the dental study (Vehkalahti *et al.*, 1996).

Five years later, more dentate subjects than the edentulous participated in the follow-up examination (60% vs. 40%). However, among the participants of both the baseline and follow-up periodontal examination, there was a decrease in the number of teeth as well as the number of remaining sextants. This may be mainly due to the extraction of teeth, after the baseline examination, which had poor prognosis. Each of the dentate participants was given a copy of their orthopantamographs and explained their treatment needs, which they reportedly informed their dentists. Another possible reason can be the deterioration in their general health and inability to maintain oral hygiene resulting in the loss of teeth due to dental caries or periodontal disease. Nonetheless, among the participants of the baseline and follow-up examination, there was very little change, during the five years, in the number of elderly who had 20 or more natural teeth at baseline. It seemed these subjects were highly motivated and maintained their oral health, hence, retaining their teeth. Almost 40% of the dentate elderly who attended the follow-up periodontal examination had 20 or more teeth. The mean number of teeth observed in this study sample was higher than observed in some of the other studies (Baelum *et al.*, 1997; Papapanou *et al.*, 1989).

8.3 Periodontal disease

Periodontal disease is common in the older age groups and this has been reported in numerous studies (Beck, 1996; Hugoson *et al.*, 1992; Locker *et al.*, 1998). Age has been shown to be related to periodontal disease after controlling for the various risk factors (Grossi *et al.*, 1994; Grossi *et al.*, 1995; Locker and Leake, 1993; Papapanou *et al.*, 1991). However, other studies have shown that age is not a risk factor for periodontal disease; instead factors that are associated with periodontal disease etiology are also associated with aging hence, the relation. In a study on the national sample of the U.S. population Abdellatif and Burt showed that oral hygiene was a stronger predictor of periodontal disease than age (Abdellatif and Burt, 1987). This finding is supported by many other studies that have shown a range of factors like dental visits, education level, socioeconomic status, systemic health and oral microorganisms are related more to the periodontal status than the age of the individual (Beck *et al.*, 1990a; Fox *et al.*, 1994; Hunt and Beck, 1990). Elderly of our study

reported high prevalence of periodontal disease with almost all of them having either gingivitis or supra/sub gingival calculus or periodontal pockets (≥ 4mm). However, the percentage of Helsinki elders with periodontal disease was less than that observed in earlier Finnish studies. The Mini-Finland study and the study among the adults of Ostrobothnia, Finland, reported higher percentage of elderly with deep periodontal pockets than observed among the elderly of our study though the elderly subjects in these studies were younger than participants of our study (65+ years *vs.* 75+ years) (Ainamo *et al.*, 1986; Markkanen *et al.*, 1983). Several factors may contribute to lower prevalence of periodontal disease found in our study relative to previous studies. The elderly of our study were mainly urban-dwellers and had reported regular use of dental services. Majority of them were well educated and were in relatively good state of health (data not shown). As mentioned previously these factors, and not age alone, may be responsible for the lower prevalence of the periodontal disease. Most of the studies on the epidemiology of periodontal disease have reported greater periodontal breakdown among men than women (Brown *et al.*, 1996; Diamanti-Kipioti *et al.*, 1995; Fox *et al.*, 1994; Hunt and Beck, 1990; Miller *et al.*, 1987; Papapanou *et al.*, 1988). In our study, though women had lesser mean number of teeth they had more healthy sextants and fewer deep pockets than men.

In the CPITN system the highest score of an individual is derived from the highest score of one or more sextants. Therefore, it is possible that an individual may have a highest CPITN score of code 2 or 3 but may have only one sextant with that score. Therefore, we also looked at the periodontal status at the sextant level and found that there were more sextants with code 1 and 2 than the number of individuals with that score. It is likely that individuals who had periodontal pockets in some sextants (codes 3 or 4) also had calculus and/or overhangs and bleeding in some of the other remaining sextants. Hence, overestimation of periodontal disease and treatment needs, though possible may not be severe in these elderly subjects. The clinical study did not record attachment loss or bone loss, both of which indicate past history of periodontal disease. These parameters were assessed in a radiological study (Soikkonen *et al.*, 1998) that included majority of the subjects of clinical examination and the baseline radiographic periodontal findings including bone loss have been reported elsewhere (Soikkonen *et al.*, 1998). The radiological study like the clinical study concluded that periodontal disease was highly prevalent in this elderly population.

Another important factor associated with periodontal disease, especially in the elderly is the number of natural teeth. As the number of elderly increases so do those who retain their natural teeth. Retention of teeth in older age may contribute to an increase in risk of periodontal disease (Papapanou, 1999). In a study of risk indicators and markers for periodontal disease in independently living older adults (aged 50 year and above) of Ontario, Canada (Locker and Leake, 1993), age, education, smoking status, and number of teeth present had the most consistent and significant independent effects in multivariate analyses. Among the elders of the New England Elders Dental Study (NEEDS) (Fox *et al.*, 1994) higher prevalence of moderate to severe periodontal disease was observed in subjects having teeth in both the arches than having teeth in only one arch. Among the same participants the extent of bleeding on probing, pocket depth, and loss of attachment all increased as numbers of teeth increased (Joshi *et al.*, 1996). A Swedish study (Hugoson *et al.*, 1992) revealed that increase in periodontal disease among the 70-year-olds between 1973 and 1983 increased considerably due to growing number of dentate individuals in this age group. In a recent study, which is a continuation of the previous studies among the individuals of the Jönköping county in Sweden (Hugoson *et al.*, 1998), those with severe periodontal disease had more teeth in 1993 than in 1983. On average they had 4 more teeth per subject in the group exhibiting bone loss of up to two-third the normal alveolar bone height.

Despite high prevalence of periodontal disease in the elderly, recent studies in the western countries have shown that severe form of periodontal disease affects only a minority of subjects in the industrialized countries (Beck *et al.*, 1990b; Brown *et al.*, 1989; Halling and Björn, 1986; Hunt and Beck, 1990; Miller *et al.*, 1987; Okamoto *et al.*, 1988), at proportion not exceeding 10-15% of the population (Papapanou, 1999). These studies also show that the distribution of advanced periodontal disease in the general population as well as among the elderly is fairly uneven. The percentage of subjects with advanced periodontal breakdown it seems increases considerably with age and appears to reach its peak at the age of 50-60 years. The increased tooth loss occurring after this age appears to account for the subsequent decline in prevalence. In our study only 11% of our subjects had deep periodontal pockets ($\geq$ 6mm). This may probably be due to high number of missing teeth in these individual that were lost either due to periodontal disease or caries.

Given the increasing number of elderly with more retained teeth, dentists should expect greater amount of periodontal disease in older adults. This will influence the estimates of treatment needs in the future and an increase in demand for professional health care services may be likely. Elderly in our study had high treatment need with almost 90% of them requiring scaling and root planning or removal of overhangs at baseline and follow-up. Thompson and Lewis (Thompson and Lewis, 1994) have reported a dramatic increase in periodontal provision from 1978-79 (3% of total services) to 1992-92 (22% of total services) as more teeth were being retained. The new cohorts of elders will consider good oral health as an essential part of attaining an improved quality of life. Therefore, emphasis should be given not only to the treatment of periodontal disease in these subjects but also to the prevention of the disease by means of regular mechanical oral hygiene measures like scaling and oral hygiene instructions.

8.4 Progression of periodontal disease

The current knowledge on the progression of periodontal disease suggests that periodontal disease does not progress linearly with age but may progress in bursts of disease activity which are random with respect to time and initial disease state is followed by long periods of remission and healing if the periodontal health is maintained, or occur as repeated bursts of activity during short periods of time if no care is provided (Albandar, 1990). The rate of progression is slow hence, longitudinal studies extending over a long time period are essential to monitor the change in periodontal status.

There are many factors that are associated with the progression of periodontal disease. These include age, sex, tobacco use, systemic conditions like diabetes and osteoporosis, oral hygiene, specific bacteria and deep periodontal pockets (Baelum *et al.*, 1997; Beck, 1996; Beck *et al.*, 1997; Machtei *et al.*, 1999; Norderyd *et al.*, 1999; Ogawa *et al.*, 2002). However, only bacterial plaque has been shown experimentally to induce gingivitis in humans (Löe *et al.*, 1965), indicating that it is one of the etiological factors for periodontal disease and risk factor for progression of the disease. Another important risk factor consistently reported in many studies that increases the odds of further periodontal breakdown is smoking and the extent and severity of the periodontal disease has also been shown to be dose-dependent (Ogawa *et al.*, 2002; Tonetti, 1998). A possible mechanism for rapid periodontal destruction in smokers is alteration of host response in general and neutrophil function in particular (Quinn *et al.*, 1996). Smoking has been shown to impair oral neutrophil chemotaxis and phagocytosis and this may be responsible for increased

periodontal destruction. Increased probing depth at baseline is one of the important factors predicting future periodontal disease regardless of the age or smoking status of an individual. The Piedmont 65+ Dental study (Beck *et al.*, 1997), the study among elders of the Yonqing county in China (Baelum *et al.*, 1997) and Nigata city in Japan (Ogawa *et al.*, 2002) showed that sites with deep periodontal pockets were at higher risk of further periodontal breakdown as age advanced, though, shallow sites should not be considered risk free. In our study majority of the participants were non-smokers/ex-smokers. During five years, there was a marginal increase in number of subjects with periodontal pockets $\geq$ 6mm but the increase was not statistically significant. However, there was a significant decrease in number of subjects with highest score of Code 3 ($\geq$ 4mm periodontal pockets). This may be because many of these pockets would have healed as a result of regular periodontal treatment and maintenance. Each participant was given a copy of their orthopantamogram and explained about their periodontal status, which they reportedly told their dentists. Another possible reason may be that some of these pockets would have deepened and were 6mm or deeper at follow-up or were extracted during the follow-up period. The effect of regular use of dental services or visits to the dentists can have an effect on the progression of periodontal disease. The Piedmont 65+ study (Beck *et al.*, 1997) showed that sites among the white study population who used the dental services regularly were less likely to experience attachment loss. In general, the periodontal status among the dentate participants of the baseline and follow-up, at the sextant level, was stable and there was almost no change in their treatment need. Periodontal disease progression in the elderly with relatively good general health is, therefore, not related to age.

8.5 Periodontal disease, CRP and cardiovascular mortality

In our study, periodontal disease was associated with cardiovascular mortality and the association remained after controlling for the known CV risk factors. This finding disproves the theory that periodontal disease is associated with CVD due to shared risk factors. As for the "classic" risk factors for cardiovascular disease, higher BMI, systolic and diastolic blood pressure, serum cholesterol levels were associated with lower mortality. This inverse relation between the risk factors and survival has been reported in several earlier studies (Langer *et al.*, 1989; Mattila *et al.*, 1988). An earlier study on blood pressure and mortality in the entire study population of HAS reported the inverse relationship between SBP and DBP and mortality (Hakala *et al.*, 1997). Factors like age, smoking, social class, diabetes and alcohol that have been shown to be associated with periodontitis did not have any significant relation with the periodontal status of the study subjects. It is possible that subjects with serious medical conditions or conditions associated with smoking and alcohol had died before the study commenced. Hence, the study sample is more likely to represent those home-dwelling elderly who were in relatively in good state of health. This may be one of the reasons for very few smokers and regular alcohol consumers in our study and may explain why the known risk factors for CVD were not associated with CV mortality. There was significant correlation observed only between periodontal disease and diastolic blood pressure. Therefore the association between periodontal disease and CV mortality as a result of a confounding effect is unlikely.

The NHEFS (DeStefano *et al.*, 1993) and VA Dental Longitudinal Study (Garcia *et al.*, 1998), reported strong association between periodontal disease total mortality in middle aged men. In our study, periodontal disease was not significantly associated with total mortality in the general population. On the other hand, the risk of CV mortality was significantly higher among those with periodontal disease. The Dental Longitudinal Study

(DLS) (Beck *et al.*, 1996) comprising of Normative Aging Study cohort of adult men also reported significant association between clinical periodontal status and total CHD events (fatal and non fatal), as well as radiologically assessed high bone loss and fatal coronary heart disease. A retrospective cohort study using participants in the 1970-1972 Nutrition Canada Survey (NCS) (Morrison *et al.*, 1999) concluded that poor dental health was associated with an increased risk of CV mortality after controlling for various risk factors. However, lack of association has also been reported (Christensen *et al.*, 1993; Howell *et al.*, 2001; Hujoel *et al.*, 2000; Joshipura *et al.*, 1996). In the Health Professional Follow-up Study (HPFS) (Joshipura *et al.*, 1996), self reported dental health among 44119 male health professionals aged 40 to 75 years was obtained. The study found no overall association between periodontal disease and coronary heart disease. Similar findings were reported from the first National Health and Nutrition Examination Survey (NHANES) Epidemiologic follow-up Study (Hujoel *et al.*, 2000), which was a follow-up of the same subject population as studied by DeStefano *et al.* (1993). It included dentate adults from the general population aged 25 to 74 years at baseline and followed them up for 10 years.

Type of lifestyle, smoking habits, diet, level of education, and regular health care play an important role in the maintenance of general health, and are behavioral risk factors and possible confounding factors when looking at the cause of death. As mentioned earlier, most of our participants, who were primarily home-dwelling women, were reportedly active, non-smokers with a good level of basic education, and under regular medical care (unpublished data). Therefore, the role of these confounding factors was limited, and the association between mortality and periodontal status studied, almost independent.

Various potential mechanisms linking dental infections and cardiovascular disease have been hypothesized. Bacteria from dental infections can enter the blood stream after dental procedures like tooth brushing or scaling and directly trigger thrombotic events. Bacteria like *Streptococcus sanguis* for example have been known to directly aggregate human platelets (Herzberg *et al.*, 1983). At the same time bacteria found in dental plaque like *Actinibacillus actinomycetemcomitans* and *porphyromonas gingivalis* along with other oral bacteria like *Chlamydia pneumoniae* and herpes viruses have been found in human atherosclerotic plaques (Prasad *et al.*, 2002). Beck at al hypothesized (Beck *et al.*, 1996) that subjects with genetically determined strong monocytic response to bacterial antigens could be at high risk for developing both periodontal disease and atherosclerosis. Another possible hypothesis is that a susceptibility to strong inflammatory response (indicated by high leveld of inflammatory mediators like CRP) could increase the risk of both periodontitis and cardiovascular event. Inflammation in the vessel wall plays an essential role not only in the initiation and progression of atherosclerosis but also in the erosion or fissuration of plaques and eventually in the rupture of plaques (Ross, 1999).

CRP has been shown to predict CV mortality in some of the recent studies (Danesh *et al.*, 1998; Folsom, 1999; Koenig *et al.*, 1999; Ridker *et al.*, 1998a) and elevated CRP levels have been observed in middle-aged patients with periodontits (Ebersole *et al.*, 1997; Loos *et al.*, 2000). The subjects included in these studies have been clearly younger than in the present study. Periodontitis had an interesting relation to baseline CRP in our study. Those with elevated CRP at baseline had increased risk of mortality between 1991 and 1995 and this association was significant only among those with periodontitis at baseline. When the subjects were divided into four categories according to whether they had periodontitis and elevated CRP or not, an increasing, significant linear trend was observed in mortality when going from the group no periodontitis and normal CRP to the group with both of these

factors present. This is in good agreement with some earlier studies in supporting the hypothesis that infections are a risk factor for CVD mostly in individuals who react to the infection with a systemic inflammatory reaction which reflected in elevated CRP (Kiechl *et al.*, 2001; Roivainen *et al.*, 2000). Due to unavailability of serum samples, CRP value for many subjects (n=53) was missing, and the number of subjects in each category were low. The earlier report that was based partly on the same subjects as our present study, showing that elevated levels of CRP increased mortality, included all those individuals of the whole Helsinki Aging Study material for whom the was the baseline serum sample available (Strandberg and Tilvis, 2000), whereas the present study included the study subjects who were still alive and dentate (and for whom CRP was available) in June 1990; 51 individuals had died before reaching this point. It seems likely that individuals who had died before June 1990 were mostly the ones with the highest CRP levels at baseline. This view is supported by the fact that the average CRP levels (which were determined using the same laboratory and measurement techniques for all HAS cohort), 1.6 mg/l, were clearly lower than the ones in the earlier study (3.2 and 5.2 mg/l in survivors and nonsurvivors, respectively). Furthermore 9% of the study subjects in the first report had CRP exceeding 10 mg/l, as compared with only 1.7% individuals in the present study. Thus, our present material may reflect only "remnants" of the association between CRP and increased mortality.

The likelihood of potential biases in this study would be small. Firstly, the dental examinations were performed prior to the follow-up for death, eliminating any bias in the periodontal health assessment. Secondly, determining if periodontal disease is associated with increased risk of mortality was not planned when conducting the baseline examinations. The possibility of information bias is, therefore, remote. Due to decreased number of subjects participating in the dental examinations, however, there may be a possibility of a selection bias. This is often, inevitable among the elderly due to compromised general health and high annual attrition rate.

8.6 Mucosal lesions and C-reactive protein

Most of the studies on dental infections and CRP have mainly involved dentate individuals. The NHANES III (Slade *et al.*, 2000) was one of the few studies that included the edentulous. The study showed that the age standardized prevalence of elevated CRP was significantly higher among the edentulous than in those with no pockets. There was no significant difference in the CRP levels between those edentulous and those with extensive periodontal pockets. In our study, after adjusting for age and sex, a higher percentage of subjects who were edentulous at baseline had elevated baseline CRP level, as compared with the dentate with or without periodontal disease. Also, more elderly subjects with complete dentures and denture stomatitis had elevated CRP levels than those without complete dentures and not having stomatitis. Among the edentulous, those with mucosal lesions or any inflammation in the mouth had significantly more often elevated CRP levels.

As the age advances oral mucosa becomes more vulnerable to mechanical damage (Pindborg, 1986). In large population studies it has been shown that most mucosal changes are related to the use of dentures in the elderly (Vehkalahti *et al.*, 1991). This is, most often, either due to their inability to maintain optimal oral hygiene because of various handicaps or hyposalivation/ xerostomia as a result of medication. In today's urban society, edentulism is no longer acceptable, and almost all edentulous wear complete dentures. However, if not

removed and cleaned properly, denture surfaces harbour similar plaque as is seen on tooth surfaces. The upper denture especially acts as an incubator for numerous anaerobic microbes because of its close adherence to the palate and lack of cleansing action by the saliva. The adherence of *Candida* cells on saliva-coated surfaces like prosthetic devices coupled with less than optimum immune response play a key role in the pathogenesis of oral candidosis (Nikawa *et al*., 1993). Among the participants of the HAS, 51% of the edentulous subjects wearing complete dentures had mucosal lesions (Nevalainen *et al*., 1997) and 67% had high salivary microbial counts. In a regression model presence of mucosal lesions and high salivary microbial counts were significantly associated with elevated CRP levels. Importantly, those having clinical signs of oral candidosis or denture stomatitis also showed elevated levels of CRP and microbial counts. These inflammatory changes in the oral cavity along with increased microbial growth may explain elevated CRP levels in these edentulous subjects. It is likely that a combination of factors like poor immune response, lack of oral hygiene, hyposalivation and intake of medications make the oral infections equally if not more important risk factors than periodontal disease in the elderly.

9. CONCLUSIONS

The following conclusions were drawn from this study:

1. The baseline and the five-year follow-up dental examinations included a high proportion of elderly subjects with reduced dentition **(I & II)**.

2. At baseline there were a high proportion of elderly who had calculus and/or overhanging margins of restoration (code 2) or shallow periodontal pockets (code 3) as the worst finding. Consequently the need for oral hygiene instruction as well as scaling and root planning and/or removal of overhangs was also high **(I)**.

3. At the five-year follow-up in 1995 the periodontal status scores remained almost the same for nearly 85% of the participants who had attended both the periodontal examinations. There was no change in their treatment need during the follow-up period **(II)**.

4. After adjusting for all the relevant risk factors, periodontitis more than doubled the risk for CV mortality between 1990 and 1995. The highest mortality was observed in dentate subjects having both periodontitis and elevated CRP at baseline **(III)**.

5. High microbial counts and mucosal lesions were associated with elevated CRP levels and more of the edentulous subjects had elevated ($\geq$ 3 mg/L) CRP levels, high salivary microbial counts and mucosal lesions than those with at least 20 teeth **(IV)**.

6. The edentulous had higher CV mortality than the dentate without periodontal disease both at the end of five-year and ten-year period but the difference was not statistically significant in this study **(III & IV)**.

7. In 1999, as observed in 1995, CV mortality was higher among the dentate with periodontal disease when compared to dentate without periodontal disease **(IV)**.

8. There were no significant differences in all-cause mortality among those dentate without periodontal disease, those dentate with periodontal disease and those edentulous at the end of both the 5- and 10-year follow-up periods **(III & IV)**.

10. SUMMARY

Rapid growth in the elderly population in Western countries, decreased edentulism, and increased number of retained teeth has raised serious concerns about the oral health of elderly population. More number of retained teeth in turn relate to increased risk for dental diseases like periodontal disease. Recent studies have shown an association between dental infections and systemic conditions like cardiovascular disease (CVD) among the middle-aged subjects. However, the role of oral infections as risk indicators for various medical outcomes, including mortality, is not yet well understood. C-reactive protein (CRP), a sensitive systemic marker of inflammation, has been shown to predict cardiovascular events among middle-aged and elderly subjects. Elevated levels of CRP have been observed in middle-aged dentate subjects with chronic dental infections, especially periodontitis.

The Helsinki Aging Study (HAS) a population-based study included a random sample of subjects born in 1904, 1909, and 1914, and living in Helsinki, Finland, on 1st January 1989. In 1990-91, 364 subjects (196 dentate and 168 edentulous) aged 76, 81, and 86 years, participated in the dental examination. Periodontal examination (using CPITN index) was carried out for 175 dentate subjects at baseline and 57 dentate subjects at the follow-up in 1995. Those edentulous underwent detailed oral examination. Information about cause and date of death of the deceased subjects was registered continuously with the Death Registry. The study ended in December 1999. Nearly half the subjects had died due to CVD.

At baseline healthy periodontal tissues (code 0) were found in only 7% of the subjects. Gingival bleeding (code 1) was recorded in 6%, and calculus and/or overhanging restorations (code 2) in 41% of the subjects, as the worst finding. Nearly half the dentate subjects (46%) had one or more periodontal pockets. Healthy periodontal tissues were more frequently found in women ($p<0.05$); they also had fewer deepened periodontal pockets than did men ($p=0.01$). Over 90% of all the dentate subjects needed oral hygiene instruction, 87% needed scaling and/or removal of overhanging margins, and 11% complex periodontal treatment.
Between 1990 and 1995, there was a decrease in the mean number of teeth (15.9 to 15.1) and mean number of remaining sextants (4.2 to 3.7). However, 41% of men and 38% of women had 20 or more remaining natural teeth. Minor changes were seen in the number of subjects with healthy periodontium (code 0), or with highest score of code 1. There was, however, an increase in subjects with the code 2 (from 43% to 58%), and decrease in percentage of subjects with highest score of code 3 (from 38% to 25%). Subjects with $\geq$6 mm periodontal pockets (Code 4) increased slightly, from 5% to 7%. However, the periodontal treatment needs, during the five years, remained almost unchanged.

In the univariate analyses among the dentate, male subjects and those with lower diastolic blood pressure were more likely to have periodontal disease. Of note, factors like age, smoking, social class, diabetes and alcohol use were not associated with baseline periodontitis. On the other hand edentulous participants comprised of mainly older women belonging to the lower social class who smoked more often, consumed more alcohol and had higher CRP than the dentate subjects. Edentulous subjects had more often elevated CRP levels ($\geq$ 3 mg/L) than those with 20 or more teeth or dentate without periodontal disease or dentate without dentures. More subjects with complete dentures and denture stomatitis had elevated CRP levels than those without complete dentures and not having stomatitis. Presence of mucosal lesions (RR 2.18, CI 1.03 – 4.61) and high salivary microbial count (RR 2.31, CI 1.06 – 5.05), significantly more common in the edentulous, showed independent association with baseline elevated CRP. Among dentate, a CRP level exceeding 3 mg/l was significantly

more common among those dying during the five-year follow up, and this association was observed only among those with periodontitis.

After adjusting for the known risk factors, the risk for CV mortality among dentate with periodontal disease at baseline, was more than double (CI 1.03-5.05) in 1995, and was almost two-fold in 1999 (CI 1.01 – 3.85) than dentate without periodontal disease at baseline. However, no significant differences in overall mortality were observed among dentate without periodontal disease, dentate with periodontal disease and those edentulous at the end of both five-year and ten-year follow-up periods.

This study is one of the few that have reported an association between elevated levels of CRP and clinical periodontal disease as well as oral mucosal lesions among those aged 75+ years. This finding emphasizes the fact that maintaining good periodontal hygiene and oral health in general, in the elderly, is very important for their overall health. As periodontal disease usually begins in early adulthood, emphasis should, therefore, be paid to the life long maintenance of periodontal health.

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