CHAPTER 1: NATURAL HISTORY OF PERIODONTAL DISEASES

1.1 EPIDEMIOLOGY OF PERIODONTAL DISEASES

1.1.1 Methodological issues

1.1.1.1 Epidemiology—fundamental aspects

Epidemiology, according to general definition, deals with the study of determinants of the occurrence of health-related conditions with the scope to identify the alterable causes and apply findings to control the problem (MacMahon & Trichopoulos, 1996). A central theme of epidemiology is the distinction between causal and non-causal statistical association between categories of events.

The concept of causes and causal inference is fundamental to epidemiology. A causal factor of a disease is ‘an event, condition, or characteristic that plays an essential role in producing an occurrence of the disease’ (Rothman, 1986). Modern epidemiology has come to a conclusion that a disease can have more than one cause and a factor may be a causal factor for several diseases or conditions. Therefore, in order to fulfil the scope of epidemiology, that is to prevent disease by identifying determinants of the disease, it is necessary to have a much more comprehensive model of disease causation than the model presented by the concept of a single necessary cause.

A number of different criteria have been used to distinguish causal statistical associations from non-causal ones. The most frequently used by epidemiologists is a set of criteria developed by Bradford Hill (1965) based on Henle-Koch postulates and discussed in detail by Lilienfeld (1967). These criteria are as follows:

- **Consistency of association.** A factor is more likely to be causal if studies involving different populations, methods and time periods produce similar results of the relationship.
- **Strength of association.** The stronger the association, the more likely it is not entirely owing to error.

- **Time sequence correct.** The factor must precede the occurrence of the disease.

- **Specificity of the association.** If the factor is related to other diseases, the association is less likely to be causal. This criterion may be applied less stringently today because of multifactoriality of cause.

- **Degree of exposure (dose-response effect).** The risk of developing the disease should be related to the degree of exposure to the factor. This criterion is considered as quite significant.

- **Biological plausibility.** The association should make sense in the light of current knowledge.

- **Experimental evidence.** Laboratory studies and randomised clinical trials testing interventions provide strong evidence in identifying causality of the factor.

These criteria bear on the view of causal inference, which is a matter of well-informed judgement of the credibility of all available evidence and current knowledge. The more evidence provided on a factor, the more precise the inference about the causality of the factor which can be made.

Different types of epidemiological studies satisfy different criteria of causality. Cross-sectional studies are unable to answer questions about time sequence and cannot conclude the causality of the association. However, this type of study can provide strong evidence concerning criteria of consistency, strength and degree of exposure. Hence, cross-sectional studies can set the fundamental knowledge of the epidemiology and sometimes can replace longitudinal studies, which can be difficult to conduct. This
is relevant in the study of association between smoking and periodontal diseases where temporal sequence cannot be determined and intervention involving random assignment is difficult owing to ethical considerations.

### 1.1.1.2 Epidemiological assessment of periodontal diseases

The fundamental essence of any epidemiological study is a precise definition of the disease under investigation. However, at present periodontal research does not have uniformly established epidemiological criteria for periodontal disease assessment. Periodontal studies have employed numerous signs including bleeding on probing, presence of calculus, probing depths, clinical attachment level and radiographic assessment of alveolar bone to assess periodontal disease and they have been applied inconsistently. Moreover, a number of different indices have been developed and used during several decades of periodontal research reflecting the body of knowledge at a particular time.

During the 1980s a composite index, Community Periodontal Index of Treatment Need (CPITN) (Ainamo et al., 1982), was employed as the major epidemiological instrument of periodontal research. This index was based on the firm belief that poor oral hygiene was the only alterable identified cause of the disease, periodontitis was universal and gingivitis without treatment inevitably progressed into periodontitis. This belief, however, has been strongly challenged in the light of current knowledge of the natural history of the disease.

The partial recording and hierarchical scoring systems used in CPITN can affect assessment of periodontal disease status by assuming bleeding and presence of calculus when pockets are present. However, these relationships may differ between populations, resulting in distorted estimates of calculus and bleeding among populations. Recording pocket depth only may lead to underestimating disease severity among older population
when gingival recession is prevalent. Baelum, Fejerskov & Wanzala (1993a) and Baelum & Papapanou (1996) assessing the validity of CPITN have found that the index is of very limited use for expressing the prevalence and severity of periodontal destruction. Other studies (Schürch et al., 1988) also found similar limitations of the CPITN in epidemiological study of periodontal diseases. Therefore, the CPITN is not a reliable epidemiological index for periodontal study and should not be used in epidemiological research (Baelum, 1998). However, this index is still in use as the main instrument in most of epidemiological studies, even in risk assessment studies conducted in developing countries (Lembariti, Frencken & Pilot, 1988; Songpaisan & Davies, 1989; Mumghamba, Markkanen & Honkala, 1995; Taani, 1997). Consequently, there is still an unfilled gap in the body of knowledge of periodontal disease patterns in two-thirds of the world population. More research is required in these populations using more accurate and reliable disease measurement.

Findings relating to initiation and progression of periodontal diseases have recommended assessment of attachment levels and pocket depth separate from that of gingival inflammation (Löe et al., 1967). The need of this separate recording system has risen from the desire not to merge qualitative and quantitative recording. Thus, it is necessary to quantify actual destruction of the periodontal attachment in millimetres as internationally recognised measure. Also, this reflects the challenging of the previous concept of inevitable progress of gingivitis into periodontitis over time. The clinical measurement of periodontal attachment and radiographic assessment of alveolar bone heights have proven to fulfil these requirements.

Measurement of loss of periodontal attachment (LOA) has contributed most of valuable information in studies of the natural history of periodontal diseases and it has been employed as the key method since the 1970s (Löe et al., 1978a; 1978b; Axelsson & Lindhe, 1978; Anerud et al., 1983; Ismail et al., 1987; Baelum, Fejerskov & Karring, 1986; Baelum, 1987; Baelum et al., 1988; Beck et al., 1990; Brown, Oliver & Löe,
1990; Machtei et al., 1992; Papapanou & Lindhe, 1992; Slade & Spencer, 1995; Albandar, Brunelle & Kingman, 1999; Thomson, Hashim & Pack, 2000). This measurement fulfils criteria of being directly related to periodontal destruction, hypothesis-free and objectively measurable. This measurement, moreover, has been shown to be strongly correlated with the other main method of assessing periodontal destruction, radiographic assessment of alveolar bone heights (Papapanou & Wenstrom, 1989).

On the other hand, LOA measurement has been criticised for recording the area destruction of periodontal attachment as a linear measurement at several points (Theil & Heaney, 1991). Some suggestions had been made to solve this problem by developing a statistical model for calculating the area of LOA by combining the linear clinical attachment level with gingival and radiographic assessment (Hujoel, Bollen & Schork, 1989; Hujoel, Bollen & DeRouen, 1992). However, this model has so far not been implemented in practical situations. It therefore remains unknown to what extent this model may, in fact, be useful in improving the validity of LOA measurement.

1.1.1.3 The prevalence, extent and severity scores

Considerable variation exists in the definition of pocket depths (or loss of attachment) as deep or pathological, which reflect true periodontal destruction. In addition, the number of affected sites required for a subject to be considered as a case also varies to a large extent. More uniform criteria are needed in epidemiological studies of periodontal diseases to enable better understanding and comparisons.

The prevalence, extent and severity scores are the three main instruments used to describe periodontal disease destruction in a population. The prevalence is a percentage in a population of individuals having disease, which satisfies a specific case definition of the disease. For instance, extent is the proportion of teeth or sites with LOA
exceeding defined discrete amount of measurement in millimetres, for example 2, 3, 4, 5, 6 mm or more. The third score, severity is normally a mean of LOA of all sites with LOA more than or equal to 2 mm. Extent and severity scores are defined in the most consistent manner in most studies. However, all three scores can be dependent on the number of teeth examined per mouth and the number of sites measured per tooth (Diamanti Kipioti et al., 1993). Besides, the prevalence score is totally dependent on case definition employed in a particular study, which is most inconsistent in epidemiological research of periodontal diseases.

A case-definition for established periodontitis needs to show the attachment level that constitutes evidence of disease activity and the number of such sites needed to establish disease presence. A number of case definitions have been employed in assessing the prevalence of periodontitis in epidemiological studies. These case definitions have depended on the authors’ school of thought, methodology used, purpose of the study and sometimes age of concerned population. No one case definition, however, has shown clear pre-eminence over another. Some case definitions are combinations of gingival conditions, attachment levels and alveolar bone levels (Hugoson & Jordan, 1982). Other studies used the mean of periodontal attachment loss of all sites in defining cases (Grossi et al., 1994) or percentage of sites with LOA or pocket depth (PD) more than a particular threshold (Locker & Leake, 1993). Beck et al. (1990) defined cases with periodontitis as having four or more sites with LOA≥5 mm and one or more sites with PD≥4 mm in a study of the elderly. This case definition combines true LOA with gingival margin dependent pocket depth indicating treatment needs. This can be considered as reasonable in defining disease in descriptive and risk assessment studies; however, the thresholds used may not be relevant to use among the younger age groups.
The inconsistency in the definition of the cases of epidemiological studies has not made comparisons between studies readily feasible. Uniform criteria for defining established periodontitis seem desirable in periodontology today. However, establishment of these criteria would demand tremendous efforts and would not be possible in the near future. Therefore, it is wise to use several case-definitions to enable comparison between studies.

1.1.2 Distribution of periodontal diseases

1.2.2.1 The prevalence, extent and severity of periodontal diseases

The prevalence of periodontitis in adult populations has been measured by means of clinical assessment of periodontal attachment (Brown, Oliver & Löe, 1990; Beck et al., 1990; Löe, Anerud & Boysen, 1992; Locker & Leake; 1993, Soder et al., 1994; Slade & Spencer, 1995; Thomson, Hashim & Pack, 2000) assessment of alveolar bone level (Papapanou, Wennstrom & Grondahl, 1988; Salonen et al., 1991) or a combination of the two (Papapanou et al., 1990). Some studies were cross-sectional, while others were designed as longitudinal or risk assessment studies.

Table 1.1 summarises epidemiological studies of the distribution of periodontal disease in different populations. Owing to the scope of this project, only major studies using probing depth and/or probing attachment levels were included.

These major studies have presented characteristic patterns of periodontal diseases in various populations of different age groups. It is obvious that the criteria for defining disease cases are far from identical and make direct comparisons between studies difficult. However, it is evident that the prevalence of severe periodontitis is confined within a minority of a population studied. Moreover, this minority bears the main burden of the disease in a population. That is, the concept of universality of periodontitis within a population is no longer supported. Furthermore, the paradigm that
destructive periodontitis is the main cause of tooth loss among adults is being questioned. Our current understanding of periodontitis from findings of previous studies has led naturally to identification of factors that may play a role in determining disease initiation and progression on an individual or group level. Further, the next targeted level is tooth and site level, which is of great interest in periodontal research.
Table 1.1: Periodontal disease distribution among different populations revealed by studies with various methodologies and assessing instruments. (*Abbreviations are defined at the end of the Table*).

<table>
<thead>
<tr>
<th>Authors and date</th>
<th>Methodology</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Hugoson &amp; Jordan, 1982 Sweden</td>
<td>Cross-sectional. Random sample of 600 subjects aged 20–70 years. Assessment of gingivitis, PD, full mouth radiographic assessment of bone levels. 5 groups by severity.</td>
<td>Most subjects had gingivitis, its prevalence increased with age. Severe periodontitis was at most 8% of subjects.</td>
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<tr>
<td>Yoneyama et al., 1988 Japan</td>
<td>Cross-sectional. Random sample of 319 subjects aged 20–79. Mean value, frequency distribution and percentile of PD and LOA at three sites per tooth.</td>
<td>Practically all subjects had one or more sites with LOA or PD≥1 mm. Small group aged 20–59 had advanced disease. Molar teeth expressed more disease. Recession increased with age.</td>
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<tr>
<td>Brown, Oliver &amp; Löe, 1990 United States</td>
<td>Cross-sectional. 15,132 employed United States adults aged 18–84. NIDR probe. Half-mouth assessment of PD and GR at mesial and buccal sites. BOP.</td>
<td>BOP: 44% of subjects. PD 4–6 mm: 13.4% of subjects or 0.6 site per person and at 1.3% of all sites. PD 7+ mm: 0.6% of subjects or 0.01 site per person and at 0.03% of all sites. LOA≥3 mm: from 16-80% subjects. 3.4 sites per person LOA≥5 mm: from 2-35% subjects. 0.7 sites per person.</td>
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### Table 1.1 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Designation</th>
<th>Description</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Beck et al., 1990</td>
<td>Cross-sectional.</td>
<td>690 community dwelling older adults aged 65+. Full mouth probing at two sites per tooth.</td>
<td>Mean Extent and Severity in blacks: 78%, 4 mm; in whites: 65%, 3.1 mm. Severe disease in 46% of blacks and 16% of whites.</td>
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<tr>
<td>United States</td>
<td></td>
<td>Severe cases: 4+ sites with LOA ≥ 5 mm and 1+ site with PD ≥ 4 mm. BANA test</td>
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<td>Ismail et al., 1990</td>
<td>Longitudinal.</td>
<td>Total of 165 subjects re-examined. Four sites per tooth; whole mouth recording.</td>
<td>13.3% of subjects had mean LOA increment of 2+ mm 3.0% of subjects had mean LOA increment of 3+ mm Age, smoking and tooth mobility at baseline were associated with attachment loss.</td>
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<tr>
<td>United States</td>
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<tr>
<td>Papapanou et al., 1990</td>
<td>Cross-sectional.</td>
<td>192 subjects in four age strata. Full mouth series of intra-oral radiographs. PD, probing attachment level, BOP.</td>
<td>3.1% of approximal sites radiographic bone loss more than the critical limits. 70% of sites exhibited BOP. Sites had BOP combined with PD ≥ 4 mm and ≥ 6 mm were 27% and 4.1% respectively.</td>
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<tr>
<td>Sweden</td>
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<tr>
<td>Söder et al., 1994</td>
<td>Cross-sectional.</td>
<td>1,681 subjects aged 31–40. Full mouth, 6 sites per tooth assessment for PD.</td>
<td>5% had 1 tooth with PD ≥ 5 mm. 7%, 2–5 teeth. 2%, 6–9 teeth. 3%, 10+ teeth. Calculus, smoking and frequency of dental visits were related to the number of teeth with PD ≥ 5 mm.</td>
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<tr>
<td>Sweden</td>
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<tr>
<td>Slade &amp; Spencer, 1995</td>
<td>Cross-sectional.</td>
<td>Total 801 subjects 60+ years of age randomly selected in South Australia. NIDR protocol. Full mouth. PD and GR measured at three sites per tooth.</td>
<td>LOA 4+ mm at 1+ sites in 89.1% of subjects. Mean Extent: 78.1%. Severity: 3.09 mm. Extent identical for mesiobuccal and distolingual sites. Severity identical for buccal and distolingual sites. LOA highest at maxillary molars. PD is higher than GR in maxilla and equal to GR in mandibular. Men had more LOA than women.</td>
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<tr>
<td>Australia</td>
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Table 1.1 (continued)

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Study Design</th>
<th>Sample Description</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baelum et al., 1988 Kenya</td>
<td>Cross-sectional. 1131 Kenyan adults aged 15–65. LOA and PD at 4 sites per tooth of all teeth. Oral hygiene, tooth mobility. Examinations under natural light.</td>
<td>Poor oral hygiene increasing with age. PD ≥ 2 mm on &lt;20% of sites irrespective of age. Skewed distribution of LOA and PD ≥ 4 mm and ≥ 7 mm. Highest Extent of LOA at maxillary molars and mandibular incisors.</td>
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<tr>
<td>Mumghamba, Markkanen &amp; Honkala, 1995 Tanzania</td>
<td>Cross-sectional. 1764 subjects aged 3-84 years. GR and PD at buccal surface of ten index teeth. Plaque, calculus. SES, oral hygiene behaviour, smoking.</td>
<td>PD ≥ 4 mm in 8%; PD ≥ 6 mm in 0.5%. GR ≥ 4 mm in 13%. Age, plaque and calculus were significantly related to PD and GR in multivariate models.</td>
<td></td>
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<tr>
<td>Baelum et al., 1997 China</td>
<td>Longitudinal. 398 dentate Chinese adults remained at follow-up. Low access to care. LOA and PD at 4 sites per tooth. Oral hygiene, tooth mobility.</td>
<td>Extent of LOA ≥ 3 mm and ≥ 4 mm in 10 years was positively skewed. 21.8% of sites lost 3+ mm, 9% 4+ mm. Highest Extent of LOA at maxillary molars and mandibular incisors. No significant difference in attachment loss with other populations from developed countries.</td>
<td></td>
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<tr>
<td>Albandar, Brunelle &amp; Kingman, 1999 United States</td>
<td>NHANES III. Cross-sectional. 9,689 adults 30–90 years old. NIDR methodology. Half-mouth; two sites per tooth.</td>
<td>Prevalence of LOA ≥ 3 mm: 53.1% of subjects. 19.6% of teeth per person. PD: 63.9% and 19.6% of teeth. 21.8% of population have mild form, 12.6% have moderate to severe forms of periodontitis. Male; blacks and Mexican Americans have more LOA.</td>
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</table>

LOA: loss of periodontal attachment
PD: pocket depth
GR: gingival recession
BOP: bleeding on probing

B/R: bone/root ratio
NIDR: The United States National Institute of Dental Research
NHANES III: The United States National Health and Nutrition Survey III
BANA test: hydrolysis of benzoyl-DL-arginine naphthylamide
1.1.2.2 Tooth and site specificity of periodontal attachment loss

The classic study by Löe et al. (1978b) examined different populations and observed different levels of LOA between teeth and sites among individuals irrespective of the populations studied. These differences were clearer with increased age. Mean LOA was highest on maxillary molars and mandibular incisors. Buccal and mesial sites appeared to have different rates of LOA as well. Recent studies in developing countries have confirmed the unequal or specific distribution between sites on the teeth and between different teeth in a mouth (Baelum et al., 1988; 1997). These studies have also reported highest loss of clinical attachment level on molars in the maxilla and incisors in the mandible.

Several studies using the United States National Institute of Dental Research (NIDR) methodology in populations from developed countries had confirmed the site and tooth specificity of PD, GR and LOA. Slade and Spencer (1995) found among 60+ years old South Australians the lowest mean LOA in mandibular incisors while confirming that maxillary molars have the highest mean LOA and differences between sites of the extent and severity scores of LOA. A study of the United States employed population (Brown, Oliver & Löe, 1990) also had similar findings. A recent study in a younger population (Thomson, Hashim & Pack, 2000), which investigated site and tooth specificity of LOA and its components showed differences between site and teeth. Thomson, Hashim and Pack did not find higher extent and severity scores in mandibular incisors as compared to lower molars, in contrast to findings from developing populations.

An important issue to consider when comparing between sites is the distribution of tooth loss by tooth type. Different tooth groups tend to be lost at different frequencies, thus making the comparison of periodontal destruction components sometimes difficult.
Molar teeth, which may accumulate more caries and/or periodontal disease, are more likely to be lost than other teeth. Therefore, a significant proportion of heavily diseased sites of those teeth may be lost. In this case, remaining teeth may be recorded as having more severe disease compared to missing teeth when it may not be true.

A further question which arises is that some proportion of destruction recorded may not be true disease; it may be owing to other non-disease factors such as dehiscence of bone or habits causing gingival recession. The proportion of this destruction may not be equally distributed across the mouth. This issue may contribute to the unequal distribution of disease between teeth and sites.

Previous findings suggested the site- and tooth-specificity of patterns of periodontal loss of attachment. However, no inferential testing of statistical significance between these differences had been done. Furthermore, some discrepancies in comparison between sites have been reported in findings of several studies referred to above. It is not clear yet whether these inconsistencies were owing to chance alone or to differences in methodologies, the discrepancies in distribution of tooth loss or to real differences between populations studied. This question needs to be further investigated.

1.1.2.3 Distribution of periodontal diseases in developed and developing populations

The previously held belief that higher prevalence and severity of periodontitis existed among populations of developing nations where living standards are lower and less access to health care services compared to that of developed nations has not been confirmed by most studies. Studies in the 1960s using composite indices had come to the conclusion that developing nations had poorer oral hygiene status and, consequently, more periodontitis (Russell, 1963; Russell et al., 1965). That conclusion was a result of the previously dominant concept of a necessary and sufficient role of
oral hygiene in the disease initiation and progression and the scarcity of studies conducted among developing populations.

However, Anerud et al. (1983), comparing groups of United States, Norwegian and Sri Lankan young adults found strikingly similar rates of periodontal breakdown, despite the last group having much poorer oral hygiene conditions. Furthermore, Baelum et al. (1996) raised very interesting issues by recalculating and comparing findings from several studies in various countries. Their meta-analysis had shown similarities in the disease patterns in six out of the eight samples, irrespective of oral hygiene conditions and levels of access to dental care.

Loss of periodontal attachment data (mostly from developed countries) and the more superficial CPITN data from many developed and developing countries have presented similarities in the prevalence and severity of periodontitis. There are few exceptions from some studies of Sri Lankan tea workers (Löe et al., 1978b) and South Pacific Islands (Cutress, Powell & Ball, 1982). However, it is obvious that there are no clear differences in the prevalence of severe stages of periodontitis between developed and developing populations irrespective of methodologies and indices used. Clear differences are only apparent in poorer oral hygiene and greater calculus accumulation in even a young age group in populations of developing countries. Thus, the prevalence and severity of the disease can be considered far more similar between populations and are confined to small groups at high risk in each population. Different populations, however, may differ in the number of risk factors or in level of exposure to a particular risk factor or may have different resistance to risk factors. This area in periodontology requires further research.
1.1.2.4 Periodontal disease patterns in Vietnam

Data on oral disease patterns among the Vietnamese population are scarce. The available studies were conducted as pathfinder studies or with a small sample only. In the 1960s, when investigating oral health among South Vietnamese (Russell et al., 1965) had found poor oral hygiene and high PI score across the sample.

The first National Oral Health Survey (NOHSV) conducted in 1989 was the first combined effort at describing the prevalence and severity of oral disease in Vietnam (Ngo et al., 1995; Le, 1998). It was conducted in 12 sites with a sample of 300 conveniently selected subjects for each of the following age groups: 12 years old, 15 years old and 35–44 years old. It was designed as a pathfinder study and there was no social survey conducted to describe the population or to draw any inferential statistics. The World Health Organisation (WHO) CPITN methodology was used as the assessing instrument of periodontal destruction.

Periodontal diseases were prevalent in all age groups as described in table 1.2 as mean number of sextants with CPITN scores and table 1.3 as mean percentage of persons affected.

Table 1.2: Mean sextants with CPITN scores

<table>
<thead>
<tr>
<th>Age</th>
<th>N</th>
<th>Mean number of sextants</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Score 0</td>
</tr>
<tr>
<td>12</td>
<td>300</td>
<td>1.37</td>
</tr>
<tr>
<td>15</td>
<td>300</td>
<td>1.35</td>
</tr>
<tr>
<td>35-44</td>
<td>300</td>
<td>0.39</td>
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</tbody>
</table>

Source: NOHSV 1989 (Ngo et al., 1995)
Table 1.3: Mean percentage of persons with worst CPITN scores

<table>
<thead>
<tr>
<th>Age</th>
<th>N</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
<th>Score 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>300</td>
<td>1.7</td>
<td>3.3</td>
<td>95.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>300</td>
<td>2.7</td>
<td>1.6</td>
<td>93.7</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td>35–44</td>
<td>300</td>
<td>0.7</td>
<td>1.1</td>
<td>67.0</td>
<td>29.9</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Source: NOHSV 1989 (Ngo et al., 1995)

Overall, the studied population showed poor to very poor oral hygiene, with almost all examined subjects presenting with gingival bleeding and calculus. Furthermore, some 30% of 35–44-year-old subjects had detectable periodontal pockets more than or equal to 4 mm.

Despite the limitations of the sampling and examination scheme, the NOHSV 1989 had presented an overview of the patterns of periodontal diseases among the study sample and provided a background for further research which might use more precise methodology of assessing the disease.

1.1.2.5 Summary

To summarise, it is evident that the periodontal disease distributions among different populations share some specific characteristics as follows:

1. Loss of periodontal attachment is virtually universal among adult population and it may be age-related.

2. There are no uniform criteria for defining the moderate and severe forms of the disease. The prevalence of periodontitis is dependent on used definitions
of the disease. Scientific research would benefit from uniform definitions of the disease, which could be used in descriptive and risk assessment studies.

3. The LOA is characterised by site and tooth specificity. Some teeth and sites are more affected than the others.

4. The distribution of LOA and alveolar bone loss are positively skewed within any age group. It means that only a small fraction of the population demonstrates severe and widespread periodontal destruction and carries the major burden of the disease in that population.

5. All these characteristics are found not only in populations with high oral hygiene standards and high access to care but also in populations with poor oral hygiene and low or virtually no formal oral care.

Thus, the questions left to be answered are to understand possible pathways through which some sites, teeth, individuals or groups of individuals are affected by the disease process. These individuals or groups of interest may differ from the general population by some particular factors or conditions that may influence the causal chain. A new era in periodontology—risk assessment research—in which the existence of risk factors and indicators that may cause the disease in susceptible groups of the population or may expose individuals to the causal chain is highly desirable.

1.1.3 Risk assessment in periodontology—a new perspective

Recent research in periodontology has confirmed the chronic nature of periodontitis and has changed the previous paradigm of aetiology and pathogenesis of the disease. The old paradigm was based on the firm belief that the destructive periodontitis was universal and there was only one causal factor, which had been already identified. Under those circumstances, risk assessment had no basis and seemed to be impractical.
However, under the new paradigm the prevalence of periodontitis is known to be lower and some individuals or groups of individuals experience more disease than others. Therefore, as with other chronic medical conditions, risk assessment will have an increasing role in periodontal research.

In 1996, the World Workshop on Periodontics adopted the following working definition of the term ‘risk factor’ that can be applied in periodontology:

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

(American Academy of Periodontology, 1996a)

This definition reflects the temporality of causality and indicates the relationship of risk factors with the causal chain. Nevertheless, this definition seems to be too broad to describe factors that may contribute to the disease. Moreover, identification of the temporal evidence is not always possible owing to cost, time and ethical issues associated with longitudinal research design. Thus, numerous efforts have been made to propose a working model or scheme for risk identification, assessment and elimination.

The extensive collaborative research publications—for example, the ‘Risk markers for oral diseases’ Volume 3 Periodontal diseases by Johnson (1991)—have provided the scientific evidence, rationale, methodology and perspective of risk assessment in periodontology. The studies were based on periodontal data from industrialised (Burt, 1991), non-industrialised countries (Baelum, Manji & Fejerkov, 1991) and worldwide prevalence of severe forms of periodontal diseases (Page, 1991) and concluded that high-risk groups and individuals for the disease do exist in populations. Numerous
factors were classified as associated with the disease initiation and progression, showing the multi-factorial nature of periodontal diseases. Also, the implications of risk assessment of periodontal diseases as a major public health problem were reviewed (Pilot, 1991).

Many other recent publications have reviewed and emphasised the importance of risk assessment in dentistry as a whole and in periodontology in particular (Stamm et al., 1991; Genco, 1996). Four rationales for the prediction of future oral disease occurrence have been considered. First, the disease is relatively low in prevalence rate. Second, new technology allows the implementation of risk assessment activities. Third, risk assessment is to target appropriate levels of prevention and care for individuals at high risk. And the fourth rationale is the attraction of risk assessment in increasing the efficacy and efficiency of prevention (Stamm et al., 1991).

Beck (1994; 1998) and Page and Beck (1997), summarising the current understanding of periodontal diseases, have put a further fundamental step in risk assessment for the disease. A practical useful classification of risk factors has been implemented in relation to causality. According to this classification, a risk factor must be a part of the causal chain or expose the subject to the cause, and it must fulfil the criteria of causality-Bradford Hill’s criteria, for example. It is similar to the above criteria by the World Workshop in Periodontology 1996. Nevertheless, these criteria of identifying a risk factor are to be met only in longitudinal studies. Consequently, variables that are thought to be risk factors are often identified from findings in cross-sectional studies. To assist the definition of risk, the authors suggested the use of term risk indicator to name a putative risk factor detected in cross-sectional studies but that has not yet been confirmed through longitudinal studies. Demographic risk factors (or named as background characteristics by Genco (1996)) are to meet the criteria of risk factors, but they are immutable to change. The third level of variables is risk marker or risk predictor that is not a part of the causal chain but that can be associated with an
increasing level of risk. These variables can be used to identify individuals at risk but cannot be used in interventions to reduce the disease.

Owing to the cross-sectional nature of the study, variables associated with the periodontal disease occurrence are named as risk indicators (or putative risk factors). The findings are used to provide information about consistency, strength and dose response effect characteristics of the putative risk factors and support the identification of variables as risk factors for periodontitis in populations.

1.2 PATHOGENESIS OF PERIODONTAL DISEASES

Extensive research during the last two decades has led to several coherent concepts that explain the underlying chains of events in the pathogenesis of periodontitis. Different forms of periodontitis have very similar, if not identical, histopathological, ultrastructural features and pathways of periodontal tissue destruction, as well as regenerative processes. Today, understandings of the disease can characterise disease development with their specific features and factors, which can play a main role.

Owing to the scope of this research, the pathogenesis of periodontal disease is briefly discussed with only some main points, which can help to explain the biological plausibility of the risk factors investigated.

1.2.1 The microbial factors for periodontal disease

The recognition that periodontal disease is an infectious disease has been widely accepted and serves an important role in understanding the natural history of the disease (Socransky, 1977; Socransky & Haffajee, 1990). Bacteria that accumulate in dental plaque are primary causative agents of gingivitis (Löe, Thelaide & Jensen, 1965; Löe et al., 1967) and various forms of periodontitis (Haffajee & Socransky, 1994; Listgarten, 1994; Moore & Moore, 1994). However, the cause-effect relationship has both common
and distinctive features for the two processes. Unlike gingivitis, which is closely related with bacteria colonisation and level of plaque accumulation, periodontitis has much more specific and complicated bacterial aetiology.

Previously, it was widely accepted that gross accumulation of dental plaque would be necessary and sufficient to cause periodontitis (Schei et al., 1959). However, recent research has led to the concepts of micro-bacterial specificity in the aetiology of periodontitis (Lösche, 1976; Socransky, 1977). This concept has emerged from epidemiological, clinical, animal studies and laboratory assays of bacterial species inhabiting oral cavity.

Numerous studies based on criteria developed by Socransky (1977) have concluded a putative pathogenic role of a dozen bacteria, mainly Gram-negative species. These species include *Actinobacillus actinomicetemcomitans*, *Bacteroides forsythus*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Campylobacter rectus*, *Fusobacterium nucleatum*, and *Treponema denticola* (Zambon, 1996). The first four bacteria most consistently comply with the above criteria in numerous studies. Risk assessment studies have also demonstrated a relationship between these bacteria and clinical signs of disease (Beck et al., 1992; Grossi et al., 1994; 1995).

Research has shown that colonisation of virulent bacteria is necessary, but not sufficient for the disease (Beck et al., 1990; 1992; Offenbacher, 1996). Rather, there is an interaction of bacterial factors with other host and environmental factors which may dramatically modify the disease expression.

1.2.2 Host response and periodontal tissues metabolism in disease

There are several models developed to describe the pathways by which the periodontal lesion is initiated and progresses under the attack of virulent bacteria and their products. Models considering the necessity of the presence of pathogenic bacteria to initiate the
disease process have put more emphasis on the importance of the host responses and other factors such as smoking and some general diseases. The latter factors are even thought to outweigh the essence of bacterial pathogens in the pathogenesis of the disease. Also, connective tissues of the periodontium and their regulators play role in balancing tissue repair and destruction (Bartold, Walsh & Narayanan, 2000).

In the susceptible host or under the influence of environmental or acquired factors, the host defence systems may be overcome in a number of ways. Tissue destruction may be initiated and progressed by both direct and indirect effects of bacteria plus the effects of the altered host defence system. Direct effects of bacteria are important in the early stage of the disease and characterised by production of enzymes (proteases, collagenase, fibrinolysin, phospholipase A) that could degrade the surrounding tissues of the superficial layers of the periodontium (Holt & Bramanti, 1991).

Indirect effects of bacteria are initiated after neutrophil clearance fails to prevent bacterial penetration into periodontal tissues. The monocyte/lymphocyte system is activated as a response to bacterial products and antigens. The activation of this cellular stage of the immune system stimulates production of both catabolic cytokines and inflammatory mediators such as prostaglandins E2 (PGE2), which in turn promote the release of enzymes destructive to the extracellular matrix and bone (Offenbacher, 1996). During the phagocytosis, polymorphonuclear neutrophils (PMNs) themselves can release some enzymes that may cause degradation of collagen and contribute to tissue damage.

Some main cytokines and inflammatory mediators that have been found to be related with the presence of periodontitis are as follows:

1. Interleukin 1 (IL-1): a pro-inflammatory, multifunctional cytokine which stimulates bone resorption and production of PGE2 and matrix metalloproteinases (MMP) that
degrade extracellular matrix. Found in elevated levels in diseased tissues and gingival crevicular fluid (Tatakis, 1993).

2. Tumour necrosis factor alpha (TNF-α): a similar mediator in many biological activities as compared with IL-1. Its production by monocytes and fibroblasts is stimulated by bacterial lipopolysaccharides.

3. Prostaglandin E2 (PGE2) released by monocytes is found to induce bone resorption and matrix metalloproteinases production (Offenbacher, Heasman & Collins, 1993).

To summarise, bacterial pathogens of high enough concentration in a susceptible host or susceptible sites of a susceptible host can break through local defence mechanisms and propagate into tissues and activate cellular mechanisms of the immune response. The components of the latter, including monocytes and fibroblasts, are capable of inducing number of cytokines destructive to the surrounding tissues. These components can stimulate inflammatory responses such as bone resorption and collagen destruction. This chain of events seems to be consistent in most of types of periodontal destruction. However, other known risk factors can play important role in determining the susceptibility of the host and, consequently, the course and outcomes of the process.

1.2.3 Putative risk factors

According to current understanding of the pathogenesis of periodontal disease, it is essential to look at factors that may play a role in the initiation and progression of the disease. Several factors can be considered as potential risk factors (or risk indicators) for periodontal destruction, such as tobacco smoking, demographic factors such as age, sex, race, socio-economic status, several general diseases and conditions and psychological stress (Tonetti, 1993). Tobacco smoking as a main focus of this project is considered in more detail in chapter 2.
1.2.3.1 Demographic factors

1.2.3.1.1 Age

Earlier reports on periodontal destruction among various populations have suggested age as an unchangeable risk factor for the disease (Løe et al., 1986). There is little doubt that the prevalence, extent and severity of periodontal disease increase with age, and it is expected that more disease will be found in the older population. More recently, the question has been raised as to whether age is only a marker for the accumulation of bone and attachment loss, or whether the destruction is actually a part of the physiology of aging. There is not enough evidence to conclude a higher prevalence of the disease among older adults after controlling for other factors. Furthermore, as age is an unmodifiable factor that does not allow any intervention, it cannot be considered as a risk factor but remains a demographic factor (Beck, 1998) (or background characteristic) for the disease, which must be controlled for in assessing other potential risk factors.

1.2.3.1.2 Sex

Numerous studies reported higher periodontal destruction among males compared to the female population (Brown, Oliver & Løe, 1990; Slade & Spencer, 1995). The reasons for these sex differences are not clear, but it is thought to be related to poorer oral hygiene level, which is usually observed among males (Slade & Spencer, 1995; Albandar & Kingman, 1999). However, the relationship observed between sex and the disease is not apparent and is not considered as strong and consistent. Thus, sex may be a demographic factor, which may interfere with the effects of other factors and it must be controlled for in investigating the disease.
1.2.3.1.3 **Socio-economic status (SES)**

The possible relationship between periodontal disease and socio-economic status was found in several studies (Beck et al., 1990; Locker & Leake, 1993; Dolan et al., 1997). Gingival condition is clearly related to lower SES, but the relationship between SES and periodontitis is less direct. It can be certain that gingival health is better among individuals with higher education and with more secure income. SES is a modifiable factor and it can be examined in multivariate models for the disease.

1.2.3.1.3 **Race**

Several studies involving different racial populations have found some difference in the expression of periodontal disease (Beck et al., 1990). Once again, race is not a modifiable factor, and some discrepancies in disease expression may be explained by the difference in other risk factors between populations.

1.2.3.2 **General diseases and conditions**

1.2.3.2.1 **Diabetes Mellitus**

The association between diabetes and periodontal breakdown was found to be inconsistent in a number of studies. Some studies have found no, or little, correlation between the two diseases (Barnett et al., 1984; Hayden & Buckley, 1989), whereas other studies, including some large-scale population studies, have shown a greater risk for periodontal disease among diabetics (Cianciola et al., 1982; Dennison, Gottsegen & Rose, 1996; Grossi et al., 1996). The above studies often controlled for different types of diabetes, method and level of metabolic control, duration and onset of complications in analyses. The level of the metabolic control may have an impact on periodontal disease expression (Miller et al., 1992; Seppala & Ainamo, 1994). On the other hand, periodontal interventions, which improve periodontal condition, may improve the metabolic control among diabetics, as measured by blood glucose level or glycosylated
haemoglobin levels (Grossi et al., 1996; Mealey, 1996). Thus, these studies may suggest that diabetes mellitus may increase the susceptibility to periodontal destruction and serve as a risk indicator for the disease.

1.2.3.2.2 **Osteoporosis**

Studies of the relationship between osteoporosis and periodontal diseases have not confirmed osteoporosis as a true risk factor for periodontal destruction (Salvi et al., 1997). There is still a question whether osteoporosis can cause periodontitis or simply is a risk factor for alveolar bone loss, leading to tooth mobility and tooth loss.

1.2.3.2.3 **Rheumatoid arthritis**

The possible interrelation between periodontal disease and rheumatoid arthritis was evaluated in several studies (Tolo & Jorkjend, 1990; Mercado et al., 2000). The findings were still conflicting; however, these efforts encourage further detailed investigation of the association between these two common conditions.

1.2.3.3. **Psychosocial stress**

The role of psychosocial factors in the initiation and development of periodontal disease has been examined in a number of recent studies. Psychosocial factors are thought to adversely change the host response in favour of putative periodontal pathogens. Already in the first half of the 20th Century the link between stress and acute necrotising ulcerative gingivitis (ANUG) had been described emphasising the importance of the level of stress adaptation as a contributing factor in the occurrence of the disease (Murayama et al., 1994).

Besides ANUG, the pathological link between stress and periodontal destruction, however, has not yet been established. It can be suggested that people with lower coping ability encountering stressful events may change their lifestyle and behaviour to such an extent as to have adverse consequences on their periodontal health. Such
changes in the lifestyle and behaviour may include neglecting oral hygiene, taking up smoking or changes in diet. People with stress may have reduced salivary flow, altered gingival fluid circulation and even immunological imbalance. These factors per se can influence periodontal inflammatory processes. Several studies have found some periodontal disease indicators such as tooth loss and gingival bleeding to be associated with work stress (Marcenes & Sheiham, 1992) and financial strains (Moss et al., 1996). Nevertheless, the evidence is not sufficient to assume a causal relationship between these two conditions. Further prospective studies are required to confirm or refute the nature of this interaction.

1.2.3.4 Oral factors

The role of oral factors in the initiation and progression of periodontal disease is evident. Plaque as a primary etiological factor is discussed elsewhere in this chapter. Owing to the scope of this project, only several clinical factors for the disease are considered, one of which is calculus.

The evidences of calculus as a risk factor for periodontal disease seem less pronounced and somewhat controversial. Several epidemiological studies indicated that calculus is significantly related to poorer periodontal status (Mandel & Gaffar, 1986; Albandar, Rise & Abbas (1987); Albandar et al., 1998; Van Palenstein et al., 1998; Albandar & Kingman, 1999). Some other studies reported a negative association between calculus and the disease activity (Baelum et al., 1993b). A review of studies showed that plaque can have pre-eminence over its mineralised formation-calculus (Mandel & Gaffar, 1986). Subgingival calculus is rather a secondary factor in gingival pockets already formed by other factors. On the other hand, calculus formation may be dependent on several other factors (Christersson et al., 1992) indicating the possibility of multiple effects between calculus and the disease. The biological plausibility of the possible relationship between calculus and periodontitis is not clear. Evidence may suggest that
calculus is a risk marker for the disease, which may be associated with the chronicity and progression but not the initiation of the disease. This issue can be of some importance in populations with low level of oral hygiene and low access to dental care.

1.3 PERIODONTAL DISEASES AND GENERAL HEALTH

Periodontitis, a chronic infectious disease with manifestations of a local and systemic host response, appears to have influences on general health and the expression of some systemic diseases or conditions. There is an increasing interest over recent years in the relationship between periodontal and systemic health. Periodontitis can have significant effects on general health, and a number of systemic diseases and conditions can be potential risk factors for periodontitis as discussed in the previous section. Therefore, it is essential to look at the effects of periodontal disease as a possible risk for other systemic diseases and conditions.

1.3.1 Periodontal disease and cardiovascular diseases (CVD)

A number of studies that examined the potential of periodontal infection as a risk factor for CVD have shown a positive association between presence of periodontitis and myocardial infarction and stroke (Mattila et al., 1989; 1993; 1995; Beck, 1991; DeStefano et al., 1993; Beck et al., 1996). Periodontal infection appears to have the degree of risk similar to other well-known risks for CVD, such as smoking, age and diabetes. More recent studies have also pointed to a possibility of an association between periodontitis and a wide range of cardiovascular diseases (Grau et al., 1997; Beck, Slade & Offenbacher, 2000).

A clear explanation of the association between the two pathogenic processes has not yet been uncovered. The oral infection may be the source of many inflammatory products like lipopolysaccharides and biological mediators such as prostaglandins and tumour necrosis factors alpha (TNF-α), which can exert effects on the vascular system.
However, it is also hypothesised that the two processes may have some shared events in the pathogenesis, such as smoking and diabetes (Beck, Slade & Offenbacher, 2000).

1.3.2 Periodontal disease and respiratory disease

The association between periodontal infection and diseases and conditions of the respiratory tract, such as pneumonia, chronic bronchitis and chronic obstructive pulmonary disease (COPD), is still hypothetical. However, it is becoming apparent that periodontal infection may be the source of respiratory pathogens. Some Gram-negative bacilli commonly associated with pneumonia have been observed in cultures from the subgingival tissues of patients with periodontitis (Slots, Rams & Listgarsten, 1988; Slots, Feik & Rams, 1990). Evidence also exists about adverse influence of periodontitis on chronic bronchitis and COPD (Murphy & Sethi, 1992).

1.3.3 Periodontal disease and pregnancy

Several studies have suggested an adverse influence of periodontal disease on the course of pregnancy. It has been suggested that periodontal disease may increase the risk of having preterm low birth weight (PLBW) infants (Collins et al., 1994). This outcome is thought to be the effect of biologic mediators of inflammatory processes such as prostaglandins E2 and TNF-α. The common bacterial product lipopolysaccharide also may have a triggering role in adverse change of the course of pregnancy. Offenbacher et al. (1996) found significantly more periodontal attachment loss among mothers of PLBW infants compared with mothers of normal-term infants.