Position Paper

Epidemiology of Periodontal Diseases*

This paper was prepared by the Research, Science and Therapy Committee of the American Academy of Periodontology and is intended for the information of the dental profession. It represents the position of the Academy in regard to the current state of knowledge about the epidemiology of periodontal diseases. This paper, with issues examined from the epidemiological viewpoint, is intended to give practitioners an epidemiological perspective on issues of interest to them. It replaces the version published in 1996. *J Periodontol 2005;76:1406-1419.*

Epidemiology is the study of health and disease in populations and of how these states are influenced by heredity, biology, physical environment, social environment, and personal behavior. Analytical epidemiology seeks to identify the risk factors associated with a disease, to quantify the strength of those associations, and to estimate whether an association is causal. An understanding of risk factors can lead to theories of causation and then to treatment protocols for clinicians to use with their patients. The essential features of epidemiology as a method of research, when compared to clinical research and case studies, are that 1) groups rather than individuals are the focus of study and 2) persons with and without a particular disease (e.g., periodontal diseases), and with and without the exposure of interest are included, rather than just patients. The study of population groups rather than individuals is to allow for valid estimates while accounting for normal biological variation (e.g., some individuals form plaque readily, others do not). Broadening a study to include those without disease, as well as those with it, provides a reference point against which to quantify risk.

Advances in research over recent years have led to a fundamental change in our understanding of the periodontal diseases. As recently as the mid-1960s, the prevailing model for the epidemiology of periodontal diseases included these precepts: 1) all individuals were considered more or less equally susceptible to severe periodontitis; 2) gingivitis usually progressed to periodontitis with consequent loss of bony support and eventually loss of teeth; and 3) susceptibility to periodontitis increased with age and was the main cause of tooth loss after age 35.[1-4] Advances in our understanding of periodontal diseases since that time have led to this old disease model being reevaluated.

This review concentrates on recent research in the epidemiology of chronic periodontitis. It will assess current knowledge on prevalence, incidence, severity, risk factors, and predicting disease risk. The review does not directly address microbial infection and host response mechanisms, modes of disease progression (i.e., bursts or linear), links between periodontitis and systemic diseases, the specifics of less common clinically-recognized conditions such as aggressive periodontitis, and conditions associated with hematological or genetic disorders.

GINGIVITIS: PREVALENCE AND DISTRIBUTION

National survey data show that gingivitis is found in early childhood, is more prevalent and severe in adolescence, and then tends to level off in older age groups.[5] The prevalence of gingivitis among schoolchildren in the United States has ranged from 40% to 60% in national surveys.[6,7] In the national survey of employed adults in 1985-86, 47% of males and 39% of females aged 18 to 64 exhibited at least one site which bled on probing.[8] The mean number of bleeding sites per person was higher in older than in younger males, but this was not seen in females. In the first U.S. national survey of adults in 1960-62, which scored gingivitis visually, 85% of men and 79% of women were found to have some degree of gingivitis.[9] In the third National Health and Nutrition Examination Survey (NHANES III, 1988-94), 50% of adults were found to have gingivitis on at least three or four teeth.[10] Even allowing for the differences in measurement techniques between the two surveys, there appears to have been an improvement in gingival health over that 25-year period.

Plaque deposits are closely correlated with gingivitis, a relationship long considered one of cause-and-effect. Longitudinal studies among Norwegian professionals and students, among whom oral hygiene was excellent, found no increase in prevalence and severity of gingivitis between the late teen years and age 40.[11] In a related study among Sri Lankan tea workers, both oral hygiene and the gingival condition were poorer at all ages.[12] Studies among other populations in developing

* This paper was revised under the direction of the Research, Science and Therapy Committee and approved by the Board of Trustees of the American Academy of Periodontology in May 2005.

countries show that gingivitis, associated with extensive plaque and calculus deposits, is the norm among adults.[13-15]

Research dating back to the 1980s has shown that relatively few sites with gingivitis go on to develop periodontitis.[16-21] Even so, prevention of gingivitis, in the individual patient or in populations, is still the first step toward preventing periodontitis. On the question of why some gingival sites make the transition from being periodontally healthy to those which bleed on probing, there are indications that more than just plaque accumulations are involved.[22] There may be an age relationship; a more pronounced inflammatory response to the same plaque challenge has been reported in older than in younger people.[23] A genetically determined response has also been suggested, with non-smoking or former-smoking interleukin (IL)-1 genotype-positive individuals having greater risk of bleeding on probing (BOP) than non-smoking and former-smoking IL-1 negatives.[24] For example, in the study just described, when the association between the IL-1 genotype and BOP was tested in a large population which included smokers, the significant associations disappeared because of what the authors called "the overriding effects of smoking." Smokers also appear to be at higher risk than non-smokers of making the transition from gingiva that do not bleed on probing to those that do.[25] There are some differences among researchers about the effects of smoking on gingival bleeding, a subject that will be visited later in this report. Stress has also been associated with increasing IL-1β levels.[26] Oral contraceptives have long been considered a risk factor for gingival bleeding[27] and some still are.[28] But with the lower dosages now generally used, that risk has diminished, and modern oral contraceptives may not affect the inflammatory response of the gingiva to dental plaque.[29]

MEASUREMENT OF PERIODONTITIS

The basic clinical measures for periodontitis, apart from gingival bleeding and radiographic assessment of bone loss, are clinical attachment loss (CAL) and probing depth (PD). The standard protocol used today for measuring CAL and PD with a manual probe was first described more than 45 years ago[30] and has not changed much since. Various scaled indexes have been used in the past, but these were "composite" indexes which scored gingivitis and periodontitis on the same scale. Composite indexes are now considered invalid and have thus been discarded. Although CAL, a measure of accumulated past disease at a site rather than current activity, remains a diagnostic "gold standard" for periodontitis,[31] the absence of consensus on how best to incorporate CAL and PD into a case definition of periodontitis continues to hamper clinical and epidemiological research. Studies have measured CAL and PD on all teeth, all teeth in two quadrants, the worst teeth in each sextant, and selected index teeth. Measurements have been made on six, four, two, and one sites per tooth. As one illustration of the problems that follow this lack of uniformity, it has been suggested[32] that the 1985-86 National Survey of Oral Health in U.S. Employed Adults and Seniors[8] may have underestimated the national prevalence of periodontitis because it measured only two sites per tooth (mesiobuccal and mid-buccal) in one maxillary and one mandibular quadrant. Furcation and lingual areas, the places where disease is considered most likely to develop, were not included in the survey protocol.

A case definition for periodontitis needs to establish 1) what depth of CAL at any one site constitutes evidence of disease processes; 2) how many such sites need to be present in a mouth to establish disease presence; and 3) how to include probing measurements and BOP in the case definition. The first issue also has to make allowance for examiner variation, which can confuse efforts to measure CAL progression. Even though measurements of probing depth are repeatable to within 1 mm more than 90% of the time,[33] the standard deviation of repeated CAL measurements of the same site by an experienced examiner with a manual probe is around 0.8 mm.[34] Accordingly, change in attachment level in a clinical study needs to be at least 2 mm (i.e., two to three times the standard deviation) before the investigators can be confident that they are seeing real change rather than measurement error.[35,36] CAL progression of at least 3 mm over a given time period has been the criterion for change in other studies.[37,38]

A high proportion of even young adults have at least one site with 2 mm CAL.[39] Because this level of CAL is so common it is not satisfactory to use it to define periodontitis in a cross-sectional study. An approach like the Extent and Severity Index,[40] in which "extent" refers to the number of teeth in the mouth with CAL of ≥1 mm and "severity" is the mean CAL for those teeth, might be appropriate in some circumstances, although the CAL cutoff limit of 1 mm needs to be increased for the reasons of examiner reliability discussed above. Some consensus on age-related case definitions for "serious" and "moderate" disease would also assist research. A number of studies have used their own case definitions for "serious" disease, mostly based on combinations of CAL and PD or extent of bone loss,[12,41-46] but no uniformity has yet emerged.

The inherent measurement problems have led researchers to look for markers of periodontitis which, if valid and reliable, would decrease our dependence upon clinical measures based on probing for diagnosing disease. As our understanding of periodontitis etiology has deepened, some markers have emerged as likely candidates. The most promising are the inflammatory cytokines that are expressed in gingival crevicular fluid (GCF) as part of the host response to inflammation, a number of which have been associated with active disease.[47,48] These cytokines include prostaglandin E_2 (PGE_2), tumor necrosis factor-alpha (TNF-α), IL-1 alpha (IL-1α), IL-1 beta (IL-1β), and others. While it has been documented for some time that these and other constituents of GCF are associated with inflammatory response, actually quantifying these associations and determining the sensitivity of the measures (i.e., the extent to which the quantity of expressed cytokine goes up or down as inflammation goes up and down) is proving more difficult. One cross-sectional study found greater quantities of PGE_2 expressed by persons with gingivitis only than by those with gingivitis plus untreated periodontitis.[49] The researchers attributed this finding to the chronic gingivitis present, which, if true, would diminish the value of this test for periodontitis. The enzyme aspartate aminotransferase (AST), which has been identified as present in the GCF of periodontitis patients, also has been studied. Initial tests have been promising,[50] and AST can be identified by a simple chairside test. To date, however, these approaches to measure periodontitis by means of inflammatory cytokines in GCF are still being tested. It will be a distinct help to both clinicians and researchers if one or more of them can become established as valid and reliable measures of active periodontitis.

THE PREVALENCE OF PERIODONTAL DISEASES

Prevalence is the number of cases of a disease in a designated population at a given point.[51] Our best information on the prevalence of numerous conditions, including periodontal diseases, comes from the results of national surveys of representative samples conducted by the National Center for Health Statistics and the National Institute of Dental and Craniofacial Research, with additional data from smaller scale surveys of specific, non-representative groups. Any prevalence information must be interpreted in light of the population studied and the periodontitis case definition applied.

The old model of periodontal diseases, described earlier, held that susceptibility to periodontal diseases was virtually universal. Today, however, it is well documented that only some 5% to 15% of any population suffers from severe generalized periodontitis, even though moderate disease affects a majority of adults.[8,39,52] This clustering of serious disease in a subset of the population has been recorded among well-treated patients[20,53-55] as well as in epidemiologic studies of populations which do not receive modern dental care.[13-15,56] What epidemiology has demonstrated is that the majority of just about any adult population has chronic periodontitis to some degree, but that mild attachment loss, as measured by CAL of 2 mm or so, is compatible with good health and function for many years.

Periodontitis, viewed for years as primarily the outcome from infection, is now seen as resulting from a complex interplay between bacterial infection and host response, often modified by behavioral factors.[57] The host response is now seen as a key factor in the clinical expression of periodontitis,[58] with only some 20% of periodontal diseases now attributed to bacterial variance.[57] Some 50% of periodontal diseases have been attributed to genetic variance and more than 20% to tobacco use,[57] although the role of tobacco has also been estimated as higher.[59]

Determining the prevalence of periodontitis in the U.S. population, seemingly a straightforward issue, in fact is complicated by the various case definitions used. If periodontitis is defined as the identification of at least one site with CAL of ≥2 mm, around 80% of all adults are affected, and around 90% of those aged 55 to 64.[8,39] When the case definition is at least one site with CAL of ≥4 mm, the prevalence in those aged 55 to 64 drops to around 50%. When it is CAL of ≥6 mm, prevalence is less than 20%.[39] Using pockets of ≥4 mm as a case definition, 30% of adults had met that criterion on at least three to four teeth.[52] When measured at population level and without adjustment for possible confounders, prevalence is greater in African-Americans[60] and in Native Americans.[61]

These national data make it clear that the milder forms of periodontitis are close to universal. The more severe manifestations of the disease, meaning those that lead to tooth loss or at least threaten it, are less prevalent. Even just these few data demonstrate that any prevalence data need the reference markers of the relevant case definition and the age group to which they apply.

INCIDENCE OF PERIODONTITIS

Incidence is defined as the number of new cases in a population over a given time period.[51] In public health practice, "cases" means people, so that when applied to a tuberculosis outbreak, for example, it will mean the

number of new people diagnosed with the condition during a stated time period. In periodontitis, "incidence" is often taken to mean new sites that meet a definition of periodontitis, even if these occur in people who already have other diseased sites. The term is also applied to an increase in CAL or bone loss in a site that has already been recorded as diseased. As with prevalence, measures of periodontitis incidence will vary according to the case definition of the disease. The more severe the extent of CAL or bone loss that is defined as incidence, the lower will be the incidence of periodontitis recorded.[62]

Longitudinal studies are logistically and intellectually demanding, but are required if incidence is to be measured. Some longitudinal studies have confirmed the results of cross-sectional studies in identifying age as a risk factor for progression of CAL,[63,64] although others[37,65] concluded that progression of CAL is more closely related to the extent of baseline CAL than to age. Healthy older people in the Baltimore Longitudinal Study of Aging did not show much attachment loss even over a 10-year period.[66]

In the Piedmont study in North Carolina, which followed a population sample aged 65 to over 80 for 3 years, baseline findings were that CAL was much more extensive in study participants than it was in younger groups.[43] These and subsequent reports from the Piedmont study[38,67,68] have made a substantial contribution to our understanding of the natural history of periodontitis. Using 3 mm as an estimate of CAL, it was found that African-Americans were more likely to experience incident CAL than whites, and about half of the whole group experienced at least one site with 3 mm CAL over the first 18 months.[38] After 3 years of observations, it was found that only 12% experienced CAL in each of the two 18-month periods.[67] It was also found that CAL during the first 18 months was related to subsequent CAL at the subject level, although not at the individual site level, a finding which supports the episodic, randomized model of periodontitis. Past disease predicted subsequent CAL, although not usually at the same site, and a previous disease episode did not put a site at higher risk for a subsequent episode.[68] As would be expected, persons with greater degrees of attachment loss at baseline were also more likely to lose teeth over the next 5 years.[68]

A 15-year longitudinal study of 480 tea workers in Sri Lanka demonstrated a wide range of susceptibility to periodontitis.[12] The group studied had virtually no dental treatment, so the data reflected the natural history of periodontitis. Based on tooth loss and interproximal CAL, it was concluded that about 8% demonstrated rapid progression of periodontitis, 81% showed moderate progression, and the remaining 11% showed no progression beyond gingivitis. In the rapid- and moderate-progression groups, periodontitis progressed with age (much more rapidly in the first group), whereas in the non-progressing group age was not a factor. This Sri Lanka study, like the Piedmont study, demonstrated that loss of CAL became severe over time only for a small group of susceptible individuals.

DETERMINANTS OF PERIODONTITIS

A *risk factor* is an environmental exposure, aspect of behavior, or an inherent characteristic which is associated with a disease.[51] The association may or may not be causal, though the use of the term increasingly implies known or suspected causality. The term *determinant* is often used synonymously with *risk factor* in the literature, but for clarity is best reserved for risk factors that cannot be modified (e.g., age, previous disease experience). The term *risk indicator* describes plausible correlates of disease identified in cross-sectional studies, while *risk factor* is best applied to those correlates confirmed in longitudinal studies. The term *risk factor* implies a modifiable condition (e.g., smoking, plaque deposits). Risk indicators identified in cross-sectional studies are not always confirmed as risk factors in longitudinal studies.[69] The term *risk marker* is used more in the predictive sense, a factor associated with increased probability of future disease but where causality is usually not implied.

Age

The prevalence and severity of CAL is invariably related directly to age in cross-sectional surveys. Taking the 1985-86 NIDR national survey of employed adults, the proportion of adults with at least one CAL site of ≥2 mm exceeded 70% even in adults aged 35 to 44 years, and was more than 90% in those aged 55 to 64.[8] For ≥4 mm loss of attachment, prevalence was 13.8% of 25- to 34-year-olds and 53.6% of 55- to 64-year-olds. PD is also related to age, although less directly. The 1985-86 national survey found that pockets of 4 to 6 mm were present in 13.4% of all adults and were more frequent in older age groups.[70] Pockets of ≥7 mm were found in only 0.6% of those examined and were not related to age.

The older assumption that periodontitis is a disease of aging is no longer tenable.[71-75] The current view sees the greater periodontal destruction in the elderly as reflecting lifetime disease accumulation rather than an age-specific condition. A relatively low prevalence of severe (as opposed to moderate) CAL among the

elderly was first shown in Sweden[76] and has since been demonstrated elsewhere. Surveys of older people in the United States, Canada, and Australia have found that CAL or PD of 6 mm or more was prevalent in 15% to 30% of persons examined.[44,77-79] In all of these studies, CAL of 4 to 6 mm was common. Higher estimates of periodontal destruction came from a cross-sectional New England study of community-living elderly people.[80,81] The New England study was of persons aged 70 to 96, older than those in the 1985-86 national survey, and the results could reflect cohort effects (i.e., results specific to the generation studied and which may not be seen in subsequent generations). All of these reports agree that CAL increases with age, but most did not find extensive loss of function in the affected teeth.

Periodontitis seen in youth and early adulthood can probably be classified as aggressive periodontitis,[82] and some degree of CAL in youth is well documented in population studies.[83-92] These findings are from well-treated populations as well as those where modern dental care does not exist. It can be hypothesized that the more susceptible members of the population are those in whom periodontitis begins in youth. If that is so, then the relatively low prevalence of severe CAL among many dentate elderly could be partly a survival phenomenon, meaning that those most susceptible to severe periodontitis have already lost teeth. The most rapid disease progression is seen in that relatively small number of persons in whom the disease starts young, and there is some evidence that these individuals have some genetic predisposition to periodontitis.[89,93,94]

It is uncommon for elderly people with reasonably intact dentition to exhibit sudden bursts of periodontitis.[73] Tooth retention, good oral hygiene, and periodontal health (exhibited by little gingival inflammation and few deep pockets) are closely associated, regardless of age.[95,96]

Gender

CAL of all levels of severity is generally more prevalent in males than in females. This has been a consistent finding in all national surveys[8,9,97] in the United States since the first such survey in 1960-62. Males usually exhibit poorer oral hygiene than females, whether measured as calculus or soft plaque deposits.[8,95,97,98]

The reasons for these gender differences have not been explored in detail, but are thought to be more related to poorer oral hygiene, less positive attitudes toward oral health, and dental-visit behavior among males than to any genetic factor. There are, of course, certain gender-related temporary syndromes related to hormonal conditions, such as pregnancy-associated gingivitis, as well as puberty-associated gingivitis which can affect children of both sexes.

Socioeconomic Status (SES)

A multitude of disease conditions are associated with socioeconomic status, and cause/effect (e.g., social stress as a contributory cause of heart disease) is plausible.[99] Generally, those who are better educated, wealthier, and live in more desirable circumstances enjoy better health status than the less educated and poorer segments of society. Periodontal diseases are no different[100,101] and historically have been related to lower SES.[9,97] The ill effects of living in deprived circumstances can start early in life.[102]

Gingivitis and poor oral hygiene are clearly related to lower SES, but the relationship between periodontitis and SES is less direct. For example, the 1985-86 national survey[8] found that the prevalence of CAL at all levels of severity was not closely related to household income. On the other hand, CAL of ≥4 mm and ≥7 mm in at least one site were both closely correlated with educational levels.

It is likely that the widely observed relation between SES levels and gingival health is a function of better oral hygiene among the better educated, more positive attitudes toward oral hygiene, and a greater frequency of dental visits among the more dentally aware and those with dental insurance (who are more likely to be white-collar employees; i.e., those with more education). While racial/ethnic differences in periodontal status have been demonstrated many times, it is thought unlikely that these represent true genetic differences. It is more likely that SES, a complex and multifaceted variable that can include a variety of cultural factors, is confounding these relationships.

Genetics

Our understanding of the genetic role in periodontal diseases has grown remarkably in just a few years; the first report identifying a genetic component in periodontitis appeared as recently as 1997.[103] Most of the research relating to the strength of genetics as a determinant of disease has been laboratory and clinical studies rather than epidemiology, but that research should still be briefly reviewed here.

The original 1997 report,[103] using data from patients in private practices, found that a specific genotype of the polymorphic IL-1 gene cluster was associated with more severe periodontitis. This relationship could be demonstrated only in non-smokers, which suggested right away that the genetic factor was not as strong a

risk factor as smoking. The IL-1 gene cluster has received a lot of research attention since then. This is appropriate, given that the proinflammatory cytokine IL-1 is a key regulator of the host response to microbial infection,[104] although IL-1 is unlikely to be the only genetic factor involved.[105] IL-1 has been identified as a contributory cause of periodontitis among some patient groups[106-109] and in one epidemiological study.[110] However, not all studies exploring a possible genetic link have found one.[111,112]

While there seems to be little doubt about a genetic component in periodontitis, the strength of that component is still being determined. At one end, a study among 169 twin pairs concluded that about half of the variance in periodontitis was attributable to heritability.[113] At the other end, there were no differences in tooth loss attributable to IL-1 variation over 10 years in a non-smoking, well-maintained population.[114] A combination of IL-1 genotyping and smoking history may provide a good risk profile for patients[104] and a smoking–genetic interaction may be a contributory factor in severity of periodontitis.[93,115] The role of IL-1 in regulating host response to infection has been described as clearly present, but not essential.[106,109] Further research, especially epidemiological studies of people with and without disease, will be necessary before the genetic contribution to the initiation and progression of periodontitis can be specified. With current knowledge, inducing periodontal patients to stop smoking would be a higher priority than genetic testing.

RISK FACTORS FOR PERIODONTITIS

Plaque, Microbiota, and Oral Hygiene

While there is a clear causal relationship between poor oral hygiene and gingivitis, the relationship of oral hygiene to periodontitis is less straightforward. Oral hygiene can favorably influence the ecology of the microbial flora in shallow-to-moderate pockets, but it does not affect host response. Oral hygiene alone has little effect on subgingival microflora in deep pockets[116] and personal oral hygiene practices among health professionals have been shown to be unrelated to periodontitis in these individuals.[117] The conclusion from older studies, mostly cross-sectional, in populations with poor oral hygiene is that plaque and supragingival calculus accumulations correlate poorly with severe periodontitis.[12-15,18,118-121] Results from other well-controlled studies also concluded that the quantity of plaque accumulation was, at best, only weakly correlated with periodontitis.[17,19,122-125] Clinical findings from the Karlstad studies in Sweden,[126,127] however, concluded that CAL in susceptible adults can be halted almost completely when meticulous self-performed plaque control is combined with professional prophylaxis three to six times per year. The prophylaxis in these studies included sub- and supragingival scaling, and root planing.[126,127]

Studies using qualitative measures of plaque (i.e., microbiota), rather than just plaque quantity, have historically produced mixed results, although modern molecular techniques have clarified the picture more in recent years. Cross-sectional associations between putative periodontopathogens and clinical periodontitis have been reported[128,129] and their presence in subgingival plaque samples from susceptible patients has predicted CAL over the short term.[45] On the other hand, the presence of specific microbiota could not predict the development or progression of periodontitis in clinical longitudinal studies for up to 3 years.[130-132] It has long been thought that Gram-negative anaerobes were the primary pathogens in periodontal pockets, but for many years efforts to identify specific causative microorganisms have been unsuccessful. More recently it has become clearer that in the broad Gram-negative profile found at diseased sites there are several putative pathogens that are consistently found. The predominant group includes *Actinomyces actinomycetemcomitans (Aa), Bacteroides forsythus (Bf)* (now *Tannerella forsythensis*), *Porphyromonas gingivalis (Pg), Prevotella intermedia (Pi), Fusobacterium nucleatum, Campylobacter rectus*, and *Treponema denticola*.[133-140] The presence of different clonal types of these bacteria is recognized, and it is not known whether all clonal types are pathogenic. If they are not, that could well account for some of the inconsistent associations found between the bacterial presence in the periodontal crevice and clinical disease.[57]

Some of these putative pathogens can become established in young children.[141-143] While these organisms in the periodontal crevice are closely associated with periodontitis, an important finding is that supragingival plaque can serve as a natural reservoir for them.[144-146] When the bacterial insult is strong enough to overwhelm host defense, bacteria in supragingival plaque migrate subgingivally to form a subgingival biofilm.[57] Frequent professional supragingival cleaning, added to good personal oral hygiene, has been shown to have a beneficial effect on subgingival microbiota in moderately deep pockets.[116,147] These findings collectively form an evidence base for close control of supragingival plaque as part of periodontal therapy.

Tobacco

Smoking is clearly a risk factor for periodontal diseases, with the risk of periodontitis attributable to

tobacco, compared to its non-use, in the order of 2.5 to 6.0 or even higher.[148] Exactly how it acts in the causal chain, however, is still a subject for research. Smoking was first identified as a risk factor from an analysis of data from the 1971-75 National Health and Nutrition Examination Survey in the United States (NHANES I), which showed an association between smoking and periodontal diseases, independent of oral hygiene, age, or other factors.[149] The evidence to identify smoking as a risk factor for periodontitis has continued to mount since then[63,122,150-156] and assessments of randomly chosen patient groupings invariably show a higher prevalence of periodontitis among smokers.[157-159] It has been stated that 90% of persons with refractory chronic periodontitis are smokers,[160] and healing following mechanical treatment is slower in smokers.[161,162] Slower healing could come from the inhibition of growth and attachment of fibroblasts in the periodontal ligament of smokers[163] and in their slower post-therapy reduction of white blood cells and neutrophils.[164] Evidence for a non-effect of smoking on periodontitis is thin, although one study was found that reported smokers responding to mechanical treatment just as positively as non-smokers.[165]

Experimental studies on plaque accumulation in smokers give mixed results, with some showing no difference,[154,157,166] while others find more plaque and calculus in smokers.[167,168] Evidence on whether smoking promotes the growth of periodontal pathogens is mixed. Earlier studies showed no difference in prevalence of these bacteria subgingivally,[169,170] but more recent evidence suggests that smokers may have higher prevalence, rather than counts or proportions, of pathogenic species subgingivally.[171,172] Smoking appears to promote a favorable habitat for these species in shallow pockets.[171,173,174]

When discussing gingival bleeding earlier in this report, it was stated that smokers were more at risk of making the transition from non-bleeding to bleeding sites on probing.[25] However, there is actually more evidence to support the view that smoking suppresses the vascular reaction which follows gingivitis, as well as compromising host response to infection in other ways. In experimental plaque-induced gingivitis, despite the rate of plaque accumulation being equal in smokers and non-smokers, the increase in gingival vascularity in smokers was only half of that seen in the non-smokers.[175] In effect, this is a masking effect on the signs of inflammation[148] and may be related to one reported finding of no difference in the risk of gingival recession between smokers and non-smokers with minimal disease.[176] Further studies have confirmed that smoking suppresses hemorrhagic response as measured by BOP.[177,178] Others have found no difference in the extent of BOP between smokers and non-smokers despite the smokers having deeper pockets[179] or more plaque and calculus.[167] In both instances more gingival bleeding in the smokers would have been expected. While none of this weakens the evidence that smoking is a major risk factor for periodontitis, further study on how smoking affects gingival bleeding is needed.

In other aspects of host response, smoking inhibits granulocyte function[180] and interactions between smoking and the IL-1 gene cluster have also been indentified.[181] In that interesting study, no difference in mean CAL could be detected between smokers and non-smokers in those who were genotype-negative, but for those who were genotype-positive, the smokers had considerably greater CAL than non-smokers. Smoking aggravates all tissue-destructive diseases, periodontitis included, by priming the production of TNF-α,[182] and it also causes the release of cytokines.[183] Smoking has been shown to be a stronger risk factor for periodontitis than insulin-dependent diabetes mellitus.[184] The evidence is clear that smoking is a major risk factor for periodontitis.

PREDICTING THE RISK OF PERIODONTITIS

Attempts to identify markers of future disease go back some years. The aim is to identify the presence of some easily measured entity, one that clinicians can readily test for in a patient, that would predict with high reliability the risk of future disease. The research design has to be longitudinal, where participants have measures of suspected predictors measured at baseline (e.g., plaque, subgingival calculus, tobacco use, diabetes, SES, specific cytokines in GCF, psychic stress), and development of new periodontal lesions or progression in existing lesions is noted over a period of time. Cross-sectional assessments are limited in their usefulness. In a longitudinal design, the disease outcome can then be related to the baseline measures. There are many complications in this type of research given the complexity of the host response to periodontal infections, both in conceptualizing the research questions and measuring hypothesized predictors. Models that fit past data often cannot be accurately extended to present conditions.[185]

The presence of visible plaque and calculus, as one example of a hypothesized marker, was long assumed to predict future CAL or bone loss, but studies have shown that clinical measures of plaque and calculus by themselves do not predict future disease to any useful extent.[125,186-189] Models that have included the

subgingival presence of specific pathogens such as *Aa, Pi, Pg*, and *Tf* with other indicators have shown a moderate degree of predictability.[134,190-192] Host response needs to be worked into the equation, and it is now recognized that smoking and genetic predisposition are major players in this regard. When smoking and IL-1 genotype status (positive or negative) are included in a predictive model, none of the baseline clinical indicators added significantly to the model for subsequent tooth loss. The baseline clinical indicators performed much better in a model that included IL-1 genotype status in non-smokers.[193] What this body of research has demonstrated is that multiple predictors work better than any one single predictor by itself, although the nearest we come to a universal predictor is tobacco use.[21,190,194,195]

Studies have investigated the mind–body connection and measured the role of psychosocial stress in terms of adverse life events or a history of clinical depression. Stress does seem to be associated with progressive periodontitis, whether assessed in a case-control study,[196] cross-sectionally,[197] or in a longitudinal design.[198] Since psychosocial distress is a well-documented risk factor for a number of different diseases,[99] the identification of its predictive role in periodontitis strengthens the hypothesis that periodontitis is related to systemic diseases.

While risk prediction is still not a precise science in periodontology, enough advances in our knowledge of risk factors have been made to permit development of a risk calculator that is offered to practitioners to help assess a patient's risk of disease.[199] Refinement of risk prediction models in the future will give practitioners an ever improving evidence base upon which to select treatment.

SUMMARY

1) Data on the prevalence of periodontitis are dependent on how the disease is defined and the age group from which they were taken. Some 5% to 20% of any population suffers from severe, generalized periodontitis, although mild to moderate periodontitis affects a majority of adults. For those who are most susceptible, periodontitis becomes evident in teenage and early adult years rather than the later years.
2) Risk factors for periodontitis include smoking, genetic predisposition, probably psychosocial stress, diabetes, and several uncommon systemic diseases.
3) Improved molecular biology techniques for measuring bacteria and inflammatory cytokines have aided recent research in both epidemiology and clinical studies, and in the future are likely to permit more precise diagnosis in the clinic.

ACKNOWLEDGMENTS

The primary author of this paper is Dr. Brian Burt. Members of the 2003-2004 Research, Science and Therapy Committee include: Drs. Henry Greenwell, Chair; Joseph Fiorellini; William Giannobile; Steven Offenbacher; Leslie Salkin; Cheryl Townsend, Board Liaison; Phillip Sheridan, Board Consultant; and Robert Genco, ex-officio.

REFERENCES

1. Belting CM. A review of the epidemiology of periodontal diseases. *J Periodontol* 1957;28:37-46.
2. Kreshover SJ, Russell AL. Periodontal disease. *J Am Dent Assoc* 1958;56:625-629.
3. Russell AL. Epidemiology of periodontal disease. *Int Dent J* 1967;17:282-296.
4. Waerhaug J. Epidemiology of periodontal disease: Review of literature. In: Ramfjord SP, Kerr DA, Ash MM, eds. *World Workshop in Periodontics*. Ann Arbor, MI: University of Michigan; 1966:181-211.
5. Stamm JW. Epidemiology of gingivitis. *J Clin Periodontol* 1986;13:360-370.
6. U.S. Public Health Service, National Center for Health Statistics. Periodontal disease and oral hygiene among children, United States. Washington, DC: Government Printing Office; 1972. DHEW publication number (HSM) 72-1060, Series 11 No. 117.
7. Bhat M. Periodontal health of 14- to 17-year-old US schoolchildren. *J Public Health Dent* 1991;51:5-11.
8. U.S. Public Health Service, National Institute of Dental Research. *Oral Health of United States Adults; National Findings*. Bethesda, MD: National Institute of Dental Research; 1987. NIH publication number 87-2868.
9. U.S. Public Health Service, National Center for Health Statistics. Periodontal disease in adults, United States 1960-1962. Washington, DC: Government Printing Office; 1965. PHS publication number 1000, Series 11 No. 12.
10. Oliver RC, Brown LJ, Löe H. Periodontal diseases in the United States population. *J Periodontol* 1998;69:269-278.
11. Anerud A, Löe H, Boysen H, Smith M. The natural history of periodontal disease in man; changes in gingival health and oral hygiene before 40 years of age. *J Periodontal Res* 1979;14:526-540.
12. Löe H, Anerud A, Boysen H, Morrison E. Natural history of periodontal disease in man. Rapid, moderate and no loss of attachment in Sri Lankan laborers 14 to 46 years of age. *J Clin Periodontol* 1986;13:431-445.
13. Baelum V, Fejerskov O, Karring T. Oral hygiene, gingivitis, and periodontal breakdown in adult Tanzanians. *J Periodontal Res* 1986;21:221-232.
14. Baelum V, Wen-Min L, Fejerskov O, Xia C. Tooth mortality and periodontal conditions in 60- to 80-year-old Chinese. *Scand J Dent Res* 1988;96:99-107.
15. Baelum V, Fejerskov O, Manji F. Periodontal diseases in adult Kenyans. *J Clin Periodontol* 1988;15:445-452.

16. Listgarten MA, Schifter CC, Laster L. 3-year longitudinal study of the periodontal status of an adult population with gingivitis. *J Clin Periodontol* 1985;12:225-238.
17. Haffajee AD, Socransky SS, Dzink JL, Taubman MA, Ebersole JL, Smith DJ. Clinical, microbiological and immunological features of subjects with destructive periodontal diseases. *J Clin Periodontol* 1988;15:240-246.
18. Okamoto H, Yoneyama T, Lindhe J, Haffajee A, Socransky S. Methods of evaluating periodontal disease data in epidemiological research. *J Clin Periodontol* 1988;15:430-439.
19. Lindhe J, Okamoto H, Yoneyama T, Haffajee A, Socransky SS. Longitudinal changes in periodontal disease in untreated subjects. *J Clin Periodontol* 1989;16:662-670.
20. Kornman KS. Patients are not equally susceptible to periodontitis: Does this change dental practice and the dental curriculum? *J Dent Educ* 2001;65:777-784.
21. Machtei EE, Hausmann E, Dunford R, et al. Longitudinal study of predictive factors for periodontal disease and tooth loss. *J Clin Periodontol* 1999;26:374-380.
22. Muller HP, Heinecke A, Eger T. Site-specific association between supragingival plaque and bleeding upon probing in young adults. *Clin Oral Investigations* 2000;4:212-218.
23. Fransson C, Mooney J, Kinane DF, Berglundh T. Differences in the inflammatory response in young and old human subjects during the course of experimental gingivitis. *J Clin Periodontol* 1999;26:453-460.
24. Lang NP, Tonetti MS, Suter J, Sorrell J, Duff GW, Kornman KS. Effect of interleukin-1 gene polymorphisms on gingival inflammation assessed by bleeding on probing in a periodontal maintenance population. *J Periodontal Res* 2000;35:102-107.
25. Muller HP, Stadermann S, Heinecke A. Longitudinal association between plaque and gingival bleeding in smokers and non-smokers. *J Clin Periodontol* 2002;29:287-294.
26. Deinzer R, Forster P, Fuck L, Herforth A, Stiller-Winkler R, Idel H. Increase of crevicular interleukin 1-beta under academic stress at experimental gingivitis sites and at sites of perfect oral hygiene. *J Clin Periodontol* 1999;26:1-8.
27. Jenkins WM, Papapanou PN. Epidemiology of periodontal disease in children and adolescents. *Periodontol 2000* 2001;26:16-32.
28. Tilakaratne A, Soory M, Ranasinghe AW, Corea SM, Ekanayake SL, de Silva M. Effects of hormonal contraceptives on the periodontium, in a population of rural Sri-Lankan women. *J Clin Periodontol* 2000;27:753-757.
29. Preshaw PM, Knutsen MA, Mariotti A. Experimental gingivitis in women using oral contraceptives. *J Dent Res* 2001;80:2011-2015.
30. Ramfjord SP. Indices for prevalence and incidence of periodontal disease. *J Periodontol* 1959;30:51-59.
31. Goodson JM. Diagnosis of periodontitis by physical measurement: Interpretation from episodic disease hypothesis. *J Periodontol* 1992;63(Suppl.):373-382.
32. Baer PN, Lester ML. Oral health survey of U.S. adults: NIDR 1985 national survey. [Editorial]. *Periodontal Case Rep* 1988;10:7.
33. Jeffcoat MK, Reddy MS. Advances in measurements of periodontal bone and attachment loss. *Monogr in Oral Sci* 2000;17:56-72.
34. Haffajee AD, Socransky SS. Attachment level changes in destructive periodontal diseases. *J Clin Periodontol* 1986;13:461-475.
35. Haffajee AD, Socransky SS, Goodson JM, Lindhe J. Intraclass correlations of periodontal measurements. *J Clin Periodontol* 1985;12:216-224.
36. Lindhe J, Haffajee AD, Socransky SS. Progression of periodontal disease in adult subjects in the absence of periodontal therapy. *J Clin Periodontol* 1983;10:433-442.
37. Haffajee AD, Socransky SS, Smith C, Dibart S. Relation of baseline microbial parameters to future periodontal attachment loss. *J Clin Periodontol* 1991;18:744-750.
38. Brown LF, Beck JD, Rozier RG. Incidence of attachment loss in community-dwelling older adults. *J Periodontol* 1994;65:316-323.
39. Third National Health and Nutrition Examination Survey, 1988-94. Hyattsville, MD: Centers for Disease Control; 1997. Public use data file no. 7-0627.
40. Carlos JP, Wolfe MD, Kingman A. The extent and severity index: A simple method for use in epidemiologic studies of periodontal disease. *J Clin Periodontol* 1986; 13:500-505.
41. Machtei EE, Christersson LA, Grossi SG, Dunford R, Zambon JJ, Genco RJ. Clinical criteria for the definition of "established periodontitis." *J Periodontol* 1992;63:206-214.
42. Hugoson A, Laurell L, Lundgren D. Frequency distribution of individuals aged 20-70 years according to severity of periodontal disease experience in 1973 and 1983. *J Clin Periodontol* 1992;19:227-232.
43. Beck JD, Koch GG, Rozier RG, Tudor GE. Prevalence and risk indicators for periodontal attachment loss in a population of older community-dwelling blacks and whites. *J Periodontol* 1990;61:521-528.
44. Locker D, Leake JL. Periodontal attachment loss in independently living older adults in Ontario, Canada. *J Public Health Dent* 1993;53:6-11.
45. Haffajee AD, Socransky SS, Lindhe J, Kent RL, Okamoto H, Yoneyama T. Clinical risk indicators for periodontal attachment loss. *J Clin Periodontol* 1991;18:117-125.
46. Page RC. Severe forms of periodontitis in children, juveniles and adults: Worldwide prevalence. In: Johnson NW, ed. *Risk Markers for Oral Diseases, vol. 3. Periodontal Diseases*. Cambridge: Cambridge University Press; 1991: 76-106.
47. Offenbacher S, Collins JG, Yalda B, Haradon G. Role of prostaglandins in high-risk periodontitis patients. In: Genco R, Hamada S, Lehner T, McGhee J, Mergenhager S, eds. *Molecular Pathogenesis of Periodontal Disease*. Washington, DC: American Society for Microbiology; 1994:203-213.
48. Page RC. Host response tests for diagnosing periodontal diseases. *J Periodontol* 1992;63(Suppl.):356-366.
49. Heasman PA, Lauffart BL, Preshaw PM. Crevicular fluid prostaglandin E_2 levels in periodontitis-resistant and periodontitis-susceptible adults. *J Clin Periodontol* 1998;25: 1003-1007.
50. Magnusson I, Persson RG, Page RC, et al. A multi-center clinical trial of a new chairside test in distinguishing between diseased and healthy periodontal sites. II. Association between site type and test outcome before and after therapy. *J Periodontol* 1996;67:589-596.
51. Last JM, ed. *A Dictionary of Epidemiology*, 4th ed. New York: Oxford University Press; 2001:91,140,160.

52. Oliver RC, Brown LJ, Löe H. Periodontal diseases in the United States population. *J Periodontol* 1998;69:269-278.
53. Baelum V, Chen X, Manji F, Luan WM, Fejerskov O. Profiles of destructive periodontal disease in different populations. *J Periodontal Res* 1996;31:17-26.
54. Lindhe J, Nyman S. Long-term maintenance of patients treated for advanced periodontal disease. *J Clin Periodontol* 1984;11:504-514.
55. Tonetti MS, Muller-Campanile V, Lang NP. Changes in the prevalence of residual pockets and tooth loss in treated periodontal patients during a supportive maintenance care program. *J Clin Periodontol* 1998;25:1008-1016.
56. Baelum V. Pattern of periodontal breakdown in adult Tanzanians. *Scand J Dent Res* 1987;95:221-228.
57. Page RC, Offenbacher S, Schroeder HE, Seymour GJ, Kornman KS. Advances in the pathogenesis of periodontitis: Summary of developments, clinical implications and future directions. *Periodontol 2000* 1997;14:216-248.
58. Darveau RP, Tanner A, Page RC. The microbial challenge in periodontitis. *Periodontol 2000* 1997;14:12-32.
59. Hujoel PP, Bergstrom J, del Aguila MA, DeRouen TA. A hidden chronic periodontitis epidemic during the 20th century? *Community Dent Oral Epidemiol* 2003;31:1-6.
60. Taylor GW. Exploring interrelationships between diabetes and periodontal disease in African Americans. *Compendium Contin Educ Dent* 2001;22:42-48.
61. Skrepcinski FB, Niendorff WJ. Periodontal disease in American Indians and Alaska Natives. *J Public Health Dent* 2000;60(Suppl. 1):261-266.
62. Oringer RJ, Fiorellini JP, Reasner DS, Howell TH. The effect of different diagnostic thresholds on incidence of disease progression. *J Periodontol* 1998;69:872-878.
63. Ismail AI, Morrison EC, Burt BA, Caffesse RG, Kavanagh MT. Natural history of periodontal disease in adults: Findings from the Tecumseh Periodontal Disease Study, 1959-87. *J Dent Res* 1990;69:430-435.
64. Nelson RG, Shlossman M, Budding LM, et al. Periodontal disease and NIDDM in Pima Indians. *Diabetes Care* 1990;13:836-840.
65. Papapanou PN, Wennstrom JL. A 10-year retrospective study of periodontal disease progression. Clinical characteristics of subjects with pronounced and minimal disease development. *J Clin Periodontol* 1990;17:78-84.
66. Ship JA, Beck JD. Ten-year longitudinal study of periodontal attachment loss in healthy adults. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;81:281-290.
67. Beck JD, Koch GG, Offenbacher S. Attachment loss trends over 3 years in community-dwelling older adults. *J Periodontol* 1994;65:737-743.
68. Beck JD, Sharp T, Koch GG, Offenbacher S. A 5-year study of attachment loss and tooth loss in community-dwelling older adults. *J Periodontal Res* 1997;32:516-523.
69. Beck JD. Methods of assessing risk for periodontitis and developing multifactorial models. *J Periodontol* 1994; 65(Suppl.):468-478.
70. Brown L, Oliver R, Löe H. Evaluating periodontal status of U.S. employed adults. *J Am Dent Assoc* 1990;121: 226-232.
71. Johnson BD, Mulligan K, Kiyak HA, Marder M. Aging or disease? Periodontal changes and treatment considerations in the older dental patient. *Gerodontol* 1989;8:109-118.
72. Johnson NW. Detection of high-risk groups and individuals for periodontal diseases. *Int Dent J* 1989;39:33-47.
73. Page RC. Periodontal diseases in the elderly: A critical evaluation of current information. *Gerodontol* 1984;3: 63-70.
74. Van der Velden U. Effect of age on the periodontium. *J Clin Periodontol* 1984;11:281-294.
75. Burt BA. Periodontitis and aging: Reviewing recent evidence. *J Am Dent Assoc* 1994;125:273-279.
76. Hugoson A, Jordan T. Frequency distribution of individuals aged 20-70 years according to severity of periodontal disease. *Community Dent Oral Epidemiol* 1982; 10:187-192.
77. Hunt RJ, Levy SM, Beck JD. The prevalence of periodontal attachment loss in an Iowa population aged 70 and older. *J Public Health Dent* 1990;50:251-256.
78. Gilbert GH, Heft MW. Periodontal status of older Floridians attending senior activity centers. *J Clin Periodontol* 1992; 19:249-255.
79. Slade GD, Spencer AJ, Gorkic E, Andrews G. Oral health status and treatment needs of non-institutionalized persons aged 60+ in Adelaide, South Australia. *Aust Dent J* 1993;38:373-380.
80. Douglass CW, Jette AM, Fox CH, et al. Oral health status of the elderly in New England. *J Gerodontol* 1993;48: 39-46.
81. Fox CH, Jette AM, McGuire SM, Feldman HA, Douglass CW. Periodontal disease among New England elders. *J Periodontol* 1994;65:676-684.
82. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999;4:1-6.
83. Anerud KE, Robertson PB, Löe H, Anerud A, Boysen H, Patters RM. Periodontal disease in three young adult populations. *J Periodontal Res* 1983;18:655-668.
84. Clerehugh V, Lennon MA. A two-year longitudinal study of early periodontitis in 14- to 16-year-old schoolchildren. *Community Dent Health* 1986;3:135-141.
85. Hoover JN, Ellegaard B, Attstrom R. Radiographic and clinical examination of periodontal status of first molars in 15- to 16-year-old Danish schoolchildren. *Scand J Dent Res* 1981;89:260-263.
86. Kallestal C, Matsson L, Holm A-K. Periodontal conditions in a group of Swedish adolescents. I. A descriptive epidemiologic study. *J Clin Periodontol* 1990;17:601-608.
87. Latcham NL, Powell RN, Jago JD, Seymour GJ, Aitken JF. A radiographic study of chronic periodontitis in 15-year-old Queensland children. *J Clin Periodontol* 1983; 10:37-45.
88. Mann J, Cormier PP, Green P, Ram CA, Miller MF, Ship II. Loss of periodontal attachment in adolescents. *Community Dent Oral Epidemiol* 1981;9:135-141.
89. Thomson WM, Edwards SJ, Dobson-Le DP, et al. IL-1 genotype and adult periodontitis among young New Zealanders. *J Dent Res* 2001;80:1700-1703.
90. Timmerman MF, Van der Weijden GA, Abbas F, et al. Untreated periodontal disease in Indonesian adolescents. Longitudinal clinical data and prospective clinical and microbiological risk assessment. *J Clin Periodontol* 2000; 27:932-942.
91. Van der Velden U, Abbas F, Van Steenbergen TJ, et al. Prevalence of periodontal breakdown in adolescents and

presence of *Actinobacillus actinomycetemcomitans* in subjects with attachment loss. *J Periodontol* 1989;60: 604-610.
92. Wolfe MD, Carlos JP. Periodontal disease in adolescents: Epidemiologic findings in Navajo Indians. *Community Dent Oral Epidemiol* 1987;15:33-40.
93. Parkhill JM, Hennig BJ, Chapple IL, Heasman PA, Taylor JJ. Association of interleukin-1 gene polymorphisms with early-onset periodontitis. *J Clin Periodontol* 2000;27:682-689.
94. Colombo AP, Eftimiadi C, Haffajee AD, Cugini MA, Socransky SS. Serum IgG2 level, Gm(23) allotype and FcgammaRIIa and FcgammaRIIIb receptors in refractory periodontal disease. *J Clin Periodontol* 1998;25: 465-474.
95. Abdellatif HM, Burt BA. An epidemiological investigation into the relative importance of age and oral hygiene status as determinants of periodontitis. *J Dent Res* 1987; 66:13-18.
96. Burt BA, Ismail AI, Eklund SA. Periodontal disease, tooth loss, and oral hygiene among older Americans. *Community Dent Oral Epidemiol* 1985;13:93-96.
97. U.S. Public Health Service, National Center for Health Statistics. Basic data on dental examination findings of persons 1-74 years; United States, 1971-1974. Washington, DC: Government Printing Office; 1979. DHEW publication number (PHS) 79-1662, Series 11 No. 214.
98. U.S. Public Health Service, National Center for Health Statistics. Oral hygiene in adults, United States 1960-1962. Washington, DC: Government Printing Office; 1966. PHS publication number 1000, Series 11 No. 16.
99. Marmot M, Wilkinson RG, eds. *Social Determinants of Health*. New York: Oxford University Press; 1999:291 p.
100. Astrom AN, Rise J. Socio-economic differences in patterns of health and oral health behaviour in 25-year-old Norwegians. *Clin Oral Investig* 2001;5:122-128.
101. Thomson WM, Locker D. Dental neglect and dental health among 26-year-olds in the Dunedin Multidisciplinary Health and Development Study. *Community Dent Oral Epidemiol* 2000;28:414-418.
102. Schou L, Wight C. Does dental health education affect inequalities in dental health? *Community Dental Health* 1994;11:97-100.
103. Kornman KS, Crane A, Wang HY, et al. The interleukin-1 genotype as a severity factor in adult periodontal disease. *J Clin Periodontol* 1997;24:72-77.
104. McDevitt MJ, Wang HY, Knobelman C, et al. Interleukin-1 genetic association with periodontitis in clinical practice. *J Periodontol* 2000;71:156-163.
105. Mark LL, Haffajee AD, Socransky SS, et al. Effect of the interleukin-1 genotype on monocyte IL-1beta expression in subjects with adult periodontitis. *J Periodontal Res* 2000;35:172-177.
106. Diehl SR, Wang Y, Brooks CN, et al. Linkage disequilibrium of interleukin-1 genetic polymorphisms with early-onset periodontitis. *J Periodontol* 1999;70: 418-430.
107. Laine ML, Farre MA, Gonzalez G, et al. Polymorphisms of the interleukin-1 gene family, oral microbial pathogens, and smoking in adult periodontitis. *J Dent Res* 2001;80:1695-1699.
108. Lang NP, Tonetti MS, Suter J, Sorrell J, Duff GW, Kornman KS. Effect of interleukin-1 gene polymorphisms on gingival inflammation assessed by bleeding on probing in a periodontal maintenance population. *J Periodontal Res* 2000;35:102-107.
109. Cullinan MP, Westerman B, Hamlet SM, et al. A longitudinal study of interleukin-1 gene polymorphisms and periodontal disease in a general adult population. *J Clin Periodontol* 2001;28:1137-1144.
110. Thomson WM, Edwards SJ, Dobson-Le DP, et al. IL-1 genotype and adult periodontitis among young New Zealanders. *J Dent Res* 2001;80:1700-1703.
111. Kinane DF, Hodge P, Eskdale J, Ellis R, Gallagher G. Analysis of genetic polymorphisms at the interleukin-10 and tumour necrosis factor loci in early-onset periodontitis. *J Periodontal Res* 1999;34:379-386.
112. Hodge PJ, Riggio MP, Kinane DF. Failure to detect an association with IL1 genotypes in European Caucasians with generalised early onset periodontitis. *J Clin Periodontol* 2001;28:430-436.
113. Michalowicz BS, Diehl SR, Gunsolley JC, et al. Evidence of a substantial genetic basis for risk of adult periodontitis. *J Periodontol* 2000;71:1699-1707.
114. Cattabriga M, Rotundo R, Muzzi L, et al. Retrospective evaluation of the influence of the interleukin-1 genotype on radiographic bone levels in treated periodontal patients over 10 years. *J Periodontol* 2001;72:767-773.
115. Meisel P, Timm R, Sawaf H, Fanghanel J, Siegmund W, Kocher T. Polymorphism of the N-acetyltransferase (NAT2), smoking and the potential risk of periodontal disease. *Arch Toxicol* 2000;74:343-348.
116. Westfelt E. Rationale of mechanical plaque control. *J Clin Periodontol* 1996;23(3 Pt. 2):263-267.
117. Merchant A, Pitiphat W, Douglass CW, Crohin C, Joshipura K. Oral hygiene practices and periodontitis in health care professionals. *J Periodontol* 2002;73: 531-535.
118. Cutress TW, Powell RN, Ball ME. Differing profiles of periodontal disease in two similar South Pacific island populations. *Community Dent Oral Epidemiol* 1982;10: 193-203.
119. Ismail AI, Eklund SA, Striffler DF, Szpunar SM. The prevalence of advanced loss of periodontal attachment in two New Mexico populations. *J Periodontal Res* 1987; 22:119-124.
120. Lembariti BS, Frencken JE, Pilot T. Prevalence and severity of periodontal conditions among adults in urban and rural Morogoro, Tanzania. *Community Dent Oral Epidemiol* 1988;16:240-243.
121. Löe H, Anerud A, Boysen H. The natural history of periodontal disease in man: Prevalence, severity, and extent of gingival recession. *J Periodontol* 1992;63:489-495.
122. Grossi SG, Genco RJ, Machtei EE, et al. Assessment of risk for periodontal disease. II. Risk indicators for alveolar bone loss. *J Periodontol* 1995;66:23-29.
123. Machtei EE, Norderyd J, Koch G, Dunford R, Grossi S, Genco RJ. The rate of periodontal attachment loss in subjects with established periodontitis. *J Periodontol* 1993;64:713-718.
124. Peretz B, Machtei EE, Bimstein E. Changes in periodontal status of children and young adolescents: A one year longitudinal study. *J Clin Pediatr Dent* 1993;18:3-6.

125. Badersten A, Nilveus R, Egelberg J. Scores of plaque, bleeding, suppuration and probing depth to predict probing attachment loss. 5 years of observation following nonsurgical periodontal therapy. *J Clin Periodontol* 1990;17:102-107.
126. Axelsson P, Lindhe J. The significance of maintenance care in the treatment of periodontal disease. *J Clin Periodontol* 1981;8:281-294.
127. Axelsson P, Lindhe J, Nystrom B. On the prevention of caries and periodontal disease. Results of a 15-year longitudinal study in adults. *J Clin Periodontol* 1991;18: 182-189.
128. Socransky SS, Haffajee AD, Smith C, Dibart S. Relation of counts of microbial species to clinical status at the sampled site. *J Clin Periodontol* 1991;18:766-775.
129. Beck JD, Koch GG, Zambon JJ, Genco RJ, Tudor GE. Evaluation of oral bacteria as risk indicators for periodontitis in older adults. *J Periodontol* 1992;63:93-99.
130. Listgarten MA. Microbiological testing in the diagnosis of periodontal disease. *J Periodontol* 1992;63(Suppl.): 332-337.
131. Listgarten MA, Slots J, Nowotny AH, et al. Incidence of periodontitis recurrence in treated patients with and without cultivable *Actinobacillus actinomycetemcomitans, Prevotella intermedia*, and *Porphyromonas gingivalis*: A prospective study. *J Periodontol* 1991;62: 377-386.
132. Wennström J, Dahlen G, Svensson J, Nyman S. *Actinobacillus actinomycetemcomitans, Bacteroides gingivalis* and *Bacteroides intermedius*; predictors of attachment loss? *Oral Microbiol Immunol* 1987;2: 158-163.
133. Albandar JM, Brown LJ, Löe H. Putative periodontal pathogens in subgingival plaque of young adults with and without early-onset periodontitis. *J Periodontol* 1997; 68:973-981.
134. Machtei EE, Dunford R, Hausmann E, et al. Longitudinal study of prognostic factors in established periodontitis patients. *J Clin Periodontol* 1997;24:102-109.
135. Haffajee AD, Cugini MA, Tanner A, et al. Subgingival microbiota in healthy, well-maintained elder and periodontitis subjects. *J Clin Periodontol* 1998;25:346-353.
136. Haraszthy VI, Hariharan G, Tinoco EM, et al. Evidence for the role of highly leukotoxic *Actinobacillus actinomycetemcomitans* in the pathogenesis of localized juvenile and other forms of early-onset periodontitis. *J Periodontol* 2000;71:912-922.
137. Papapanou PN, Baelum V, Luan WM, et al. Subgingival microbiota in adult Chinese: Prevalence and relation to periodontal disease progression. *J Periodontol* 1997;68: 651-666.
138. Riggio MP, Lennon A, Roy KM. Detection of *Prevotella intermedia* in subgingival plaque of adult periodontitis patients by polymerase chain reaction. *J Periodontal Res* 1998;33:369-376.
139. Ximenez-Fyvie LA, Haffajee AD, Socransky SS. Comparison of the microbiota of supra- and subgingival plaque in health and periodontitis. *J Clin Periodontol* 2000;27:648-657.
140. Hamlet SM, Cullinan MP, Westerman B, et al. Distribution of *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis* and *Prevotella intermedia* in an Australian population. *J Clin Periodontol* 2001;28:1163-1171.
141. Okada M, Hayashi F, Nagasaka N. PCR detection of 5 putative periodontal pathogens in dental plaque samples from children 2 to 12 years of age. *J Clin Periodontol* 2001;28:576-582.
142. Tanner AC, Milgrom PM, Kent RJ, et al. The microbiota of young children from tooth and tongue samples. *J Dent Res* 2002;81:53-57.
143. Yang EY, Tanner AC, Milgrom P, et al. Periodontal pathogen detection in gingiva/tooth and tongue flora samples from 18- to 48-month-old children and periodontal status of their mothers. *Oral Microbiol Immunol* 2002;17:55-59.
144. Gmur R, Marinello CP, Guggenheim B. Periodontitis associated bacteria in supragingival plaque of dental hygienists: Stability of carrier state and clinical development. *Eur J Oral Sci* 1999;107:225-228.
145. Sakellari D, Belibasakis G, Chadjipadelis T, Arapostathis K, Konstantinidis A. Supragingival and subgingival microbiota of adult patients with Down's syndrome. Changes after periodontal treatment. *Oral Microbiol Immunol* 2001;16:376-382.
146. Ximenez-Fyvie LA, Haffajee AD, Socransky SS. Microbial composition of supra- and subgingival plaque in subjects with adult periodontitis. *J Clin Periodontol* 2000;27:722-732.
147. Hellstrom MK, Ramberg P, Krok L, Lindhe J. The effect of supragingival plaque control on the subgingival microflora in human periodontitis. *J Clin Periodontol* 1996;23:934-940.
148. Bergstrom J, Preber H. Tobacco use as a risk factor. *J Periodontol* 1994;65(Suppl.):545-550.
149. Ismail AI, Burt BA, Eklund SA. Epidemiologic patterns of smoking and periodontal disease in the United States. *J Am Dent Assoc* 1983;106:617-621.
150. Grossi SG, Zambon JJ, Ho AW, et al. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol* 1994;65:260-267.
151. Bergstrom J, Floderus-Myrhed B. Co-twin control study of the relationship between smoking and some periodontal disease factors. *Community Dent Oral Epidemiol* 1983;11:113-116.
152. Locker D. Smoking and oral health in older adults. *Can J Public Health* 1992;83:429-432.
153. Gonzalez YM, De Nardin A, Grossi SG, Machtei EE, Genco RJ, De Nardin E. Serum cotinine levels, smoking, and periodontal attachment loss. *J Dent Res* 1996; 75:796-802.
154. Chen X, Wolff L, Aeppli D, et al. Cigarette smoking, salivary/gingival crevicular fluid cotinine and periodontal status. A 10-year longitudinal study. *J Clin Periodontol* 2001;28:331-339.
155. Haffajee AD, Socransky SS. Relationship of cigarette smoking to attachment level profiles. *J Clin Periodontol* 2001;28:283-295.
156. Amarasena N, Ekanayaka AN, Herath L, Miyazaki H. Tobacco use and oral hygiene as risk indicators for periodontitis. *Community Dent Oral Epidemiol* 2002; 30:115-123.
157. Haber J, Wattles J, Crowley M, Mandell R, Joshipura K, Kent RL. Evidence for cigarette smoking as a major risk

factor for periodontitis. *J Periodontol* 1993;64:16-23.
158. Horning GM, Hatch CL, Cohen ME. Risk indicators for periodontitis in a military treatment population. *J Periodontol* 1992;63:297-302.
159. Jette AM, Feldman HA, Tennstedt SL. Tobacco use: A modifiable risk factor for dental disease among the elderly. *Am J Public Health* 1993;83:1271-1276.
160. Johnson GK, Slach NA. Impact of tobacco use on periodontal status. *J Dent Educ* 2001;65:313-321.
161. Grossi SG, Zambon J, Machtei EE, et al. Effects of smoking and smoking cessation on healing after mechanical periodontal therapy. *J Am Dent Assoc* 1997; 128:599-607.
162. Kinane DF, Radvar M. The effect of smoking on mechanical and antimicrobial periodontal therapy. *J Periodontol* 1997;68:467-472.
163. James JA, Sayers NM, Drucker DB, Hull PS. Effects of tobacco products on the attachment and growth of periodontal ligament fibroblasts. *J Periodontol* 1999;70: 518-525.
164. Christan C, Dietrich T, Hagewald S, Kage A, Bernimoulin JP. White blood cell count in generalized aggressive periodontitis after non-surgical therapy. *J Clin Periodontol* 2002;29:201-206.
165. Pucher JJ, Shibley O, Dentino AR, Ciancio SG. Results of limited initial periodontal therapy in smokers and non-smokers. *J Periodontol* 1997;68:851-856.
166. Danielsen B, Manji F, Nagelkerke N, Fejerskov O, Baelum V. Effect of cigarette smoking on the transition dynamics in experimental gingivitis. *J Clin Periodontol* 1990;17:159-164.
167. Paidi S, Pack AR, Thomson WM. An example of measurement and reporting of periodontal loss of attachment (LOA) in epidemiological studies: Smoking and periodontal tissue destruction. *NZ Dent J* 1999;95: 118-123.
168. Muller HP, Stadermann S, Heinecke A. Bleeding on probing in smokers and non-smokers in a steady-state plaque environment. *Clin Oral Investig* 2001;5:177-184.
169. Preber H, Bergstrom J, Linder LE. Occurrence of periopathogens in smoker and non-smoker patients. *J Clin Periodontol* 1992;19(9 Pt. 1):667-671.
170. Stoltenberg JL, Osborn JB, Pihlstrom BL, et al. Association between cigarette smoking, bacterial pathogens, and periodontal status. *J Periodontol* 1993;64:1225-1230.
171. Haffajee AD, Socransky SS. Relationship of cigarette smoking to the subgingival microbiota. *J Clin Periodontol* 2001;28:377-388.
172. Zambon JJ, Grossi SG, Machtei EE, Ho AW, Dunford R, Genco RJ. Cigarette smoking increases the risk for subgingival infection with periodontal pathogens. *J Periodontol* 1996;67(Suppl.):1050-1054.
173. Eggert FM, McLeod MH, Flowerdew G. Effects of smoking and treatment status on periodontal bacteria: Evidence that smoking influences control of periodontal bacteria at the mucosal surface of the gingival crevice. *J Periodontol* 2001;72:1210-1220.
174. van Winkelhoff AJ, Bosch-Tijhof CJ, Winkel EG, van der Reijden WA. Smoking affects the subgingival microflora in periodontitis. *J Periodontol* 2001;72: 666-667.
175. Bergstrom J, Persson L, Preber H. Influence of cigarette smoking on vascular reaction during experimental gingivitis. *Scand J Dent Res* 1988;96:34-39.
176. Muller HP, Stadermann S, Heinecke A. Gingival recession in smokers and non-smokers with minimal periodontal disease. *J Clin Periodontol* 2002;29:129-136.
177. Bergstrom J, Bostrom L. Tobacco smoking and periodontal hemorrhagic responsiveness. *J Clin Periodontol* 2001;28:680-685.
178. Biddle AJ, Palmer RM, Wilson RF, Watts TL. Comparison of the validity of periodontal probing measurements in smokers and non-smokers. *J Clin Periodontol* 2001;28:806-812.
179. van der Weijden GA, de Slegte C, Timmerman MF, van der Velden U. Periodontitis in smokers and non-smokers: Intra-oral distribution of pockets. *J Clin Periodontol* 2001;28:955-960.
180. Soder B, Jin LJ, Wickholm S. Granulocyte elastase, matrix metalloproteinase-8 and prostaglandin E_2 in gingival crevicular fluid in matched clinical sites in smokers and non-smokers with persistent periodontitis. *J Clin Periodontol* 2002;29:384-391.
181. Meisel P, Siegemund A, Dombrowa S, Sawaf H, Fanghaenel J, Kocher T. Smoking and polymorphisms of the interleukin-1 gene cluster (IL-1α, IL-1β, and IL-1RN) in patients with periodontal disease. *J Periodontol* 2002;73:27-32.
182. Gustafsson A, Asman B, Bergstrom K. Cigarette smoking as an aggravating factor in inflammatory tissue-destructive diseases. Increase in tumor necrosis factor-alpha priming of peripheral neutrophils measured as generation of oxygen radicals. *Int J Clin Lab Res* 2000;30:187-190.
183. Fredriksson M, Bergstrom K, Asman B. IL-8 and TNF-α from peripheral neutrophils and acute-phase proteins in periodontitis. *J Clin Periodontol* 2002;29:123-128.
184. Moore PA, Weyant RJ, Mongelluzzo MB, et al. Type 1 diabetes mellitus and oral health: Assessment of periodontal disease. *J Periodontol* 1999;70:409-417.
185. Yang MC, Marks RG, Clark WB, Magnusson I. Predictive power of various models for longitudinal attachment level change. *J Clin Periodontol* 1992;19:77-83.
186. Haffajee AD, Socransky SS, Goodson JM. Clinical parameters as predictors of destructive disease activity. *J Clin Periodontol* 1983;10:257-265.
187. Claffey N, Nylund K, Kiger R, Garrett S, Egelberg J. Diagnostic predictability of scores of plaque, bleeding, suppuration and probing depth for probing attachment loss. 3-1/2 years of observation following initial periodontal therapy. *J Clin Periodontol* 1990;17:108-114.
188. Lang NP, Joss A, Orsanic T, Gusberti FA, Siegrist BE. Bleeding on probing: A predictor for the progression of periodontal disease? *J Clin Periodontol* 1986;13: 590-596.
189. Persson RE, Persson GR, Kiyak HA, Powell LV. Oral health and medical status in dentate low-income older persons. *Spec Care Dent* 1998;18:70-77.
190. Albandar JM. Global risk factors and risk indicators for periodontal diseases. *Periodontol 2000* 2002;29: 177-206.
191. Timmerman MF, Van der Weijden GA, Arief EM, et al. Untreated periodontal disease in Indonesian adoles-

cents. Subgingival microbiota in relation to experienced progression of periodontitis. *J Clin Periodontol* 2001;28: 617-627.
192. Tran SD, Rudney JD, Sparks BS, Hodges JS. Persistent presence of *Bacteroides forsythus* as a risk factor for attachment loss in a population with low prevalence and severity of adult periodontitis. *J Periodontol* 2001; 72:1-10.
193. McGuire MK, Nunn ME. Prognosis versus actual outcome. IV. The effectiveness of clinical parameters and IL-1 genotype in accurately predicting prognoses and tooth survival. *J Periodontol* 1999;70:49-56.
194. Alpagot T, Bell C, Lundergan W, Chambers DW, Rudin R. Longitudinal evaluation of GCF MMP-3 and TIMP-1 levels as prognostic factors for progression of periodontitis. *J Clin Periodontol* 2001;28:353-359.
195. Norderyd O, Hugoson A, Grusovin G. Risk of severe periodontal disease in a Swedish adult population. A longitudinal study. *J Clin Periodontol* 1999;26:608-615.
196. Croucher R, Marcenes WS, Torres MC, Hughes F, Sheiham A. The relationship between life-events and periodontitis. A case-control study. *J Clin Periodontol* 1997;24:39-43.
197. Genco RJ, Ho AW, Grossi SG, Dunford RG, Tedesco LA. Relationship of stress, distress and inadequate coping behaviors to periodontal disease. *J Periodontol* 1999; 70:711-23.
198. Elter JR, Beck JD, Slade GD, Offenbacher S. Etiologic models for incident periodontal attachment loss in older adults. *J Clin Periodontol* 1999;26:113-123.
199. Page RC, Krall EA, Martin J, Mancl L, Garcia RI. Validity and accuracy of a risk calculator in predicting periodontal disease. *J Am Dent Assoc* 2002;133:569-576.