DENTAL SCIENCE, MATERIALS AND TECHNOLOGY

PERIODONTAL DISEASE: SYMPTOMS, TREATMENT AND PREVENTION

SHO L. YAMAMOTO
EDITOR

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Preface

Periodontal disease is a chronic bacterial infection characterized by persistent inflammation, connective tissue breakdown and alveolar bone destruction. The chronic inflammation associated with periodontal disease represents the host response to bacterial plaque, mediated by the environment in which the response occurs. This book presents topical research data in the study of periodontal disease, including aesthetic periodontal therapy and root coverage techniques; clinical features of periodontal diseases in children and adolescents; biomechanics and the perioprosthetic patient; maternal periodontitis and perinatal outcomes; identifying patients with enhanced disease susceptibility in periodontal disease; and inflammatory mediators and oxidative stress in periodontal disease.

Chapter I - Aesthetic considerations have influenced the management of dental maladies in varying degrees for many years. For many years the goals of periodontal surgery have been determined by functional aspects only. During recent years periodontal surgery has shifted its focus from achieving more functional goals toward a combination of both good functional and esthetic results. While accomplishing the best possible functional result, esthetics should not only be maintained, but also enhanced. Sometimes the esthetic outcome is the only important factor and function becomes secondary (e.g. treatment of recessions or the creation of papillae). Predictability becomes the key word in this type of periodontal surgery. Patient awareness and expectations have increased recently to the point that less than optimal esthetics is no longer an acceptable outcome. Periodontal plastic surgery would accordingly be defined as "surgical procedures performed to prevent or correct anatomic, developmental, traumatic or disease induced defects in the gingiva, alveolar mucosa or bone". The present chapter is presenting and discussing the clinical outcomes of several root coverage techniques: pedicle soft tissue grafts, rotational flaps, coronally advanced flap, semilunar flap, free soft tissue graft, nonsubmerged grafts, submerged grafts etc.

Chapter II - The clinical features of periodontal diseases in children and adolescents differ from those in adults. Periodontitis is extremely rare in children, except those complicated with certain kinds of systemic diseases, whereas gingivitis is commonly encountered. Childhood gingivitis can be reversed by professional mechanical tooth cleaning in combination with tooth brushing instruction. On the other hand, gingivitis becomes increasingly prevalent with age through the adolescent period, and early diagnosis and appropriate interventions are necessary to prevent the onset of marginal periodontitis during adolescence. Since most children with periodontitis possess a background of abnormal immune responses, they have a lower likelihood of good prognosis,even though diligent interventions are performed. Other types of periodontal diseases include gingival recession,

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which is mainly caused by traumatic occlusion, and gingival overgrowth, which has a hereditary background and is associated with specific medication such as antiepilepticphenytoin. In addition, cases with a rapid loss of gingival attachment and alveolar bone due to mechanical injury at the periodontal sulcus, termed "acute periodontitis," are also encountered. Furthermore, an unintentional attachment loss, when materials such as small plastic tubes being fitted to the teeth are inserted, is a unique type of periodontitis in young children. It should be noted that periodontitis associated with anatomical anomalies, which are derived from fragile periodontal attachment, is also encountered.

Considering the etiology of periodontitis, it is important to identify periodontitis-related bacterial species, since the disease is generally known to be caused by specific bacteria. However, most of those belong to the obligate anaerobic group, and it is difficult and time-consuming to isolate them. On the other hand, recent developments in molecular biological techniques have enabled rapid identification of species using bacterial DNA extracted from various kinds of clinical specimens. Such approaches do not require isolation of viable bacteria and even small amounts of DNA can be detected using PCR techniques. With such modern techniques, the author have evaluated the distribution of periodontal bacterial species in children, changes of species in the same subjects over a long interval, combinations of species simultaneously detected, and mother-to-child transmission. In addition, the distributions of bacterial species in children with Down's syndrome and other developmental disabilities have been analyzed. The authors' results have provided valuable information regarding bacterial profiles in clinical specimens, which should lead to further beneficial methods for clinical use in the near future.

Chapter III - In advanced perioprosthetic cases where the periodontium's integrity is severely compromised and the dental barrier's function is extremely disrupted, the biomechanical response to the extrinsic mechanical stimuli of the system including the prosthetic restoration supported by the biological tissues is quite altered. The differentiated altered experience of the functional loading due to the lowered periodontium's threshold along with the apical shift of the system fulcrum due to the periodontium's structure reduction require a modified design of the restoration's metal framework as a critical factor in the system's survival in order to secure the expected longevity of both the restorative and biological structures, capturing the failure initiation of either progressive tissular or technical collapse. So, the purpose of the present study was to: a. analyze the way by which the periodontium reacts to the developing forces and how its integrity is related to the experience of the stress field on the perioprosthetic patient; b. determine the parameters defining the tooth prognosis in the perioprosthetic patient and how the restoration type is involved; c. report the clinical significance of tooth splinting by cantilever cross arch fixed partial denture applied on the perioprosthetic patient and the way it is related to the response of the reduced periodontium and finally d. investigate the clinical significance of the specific design of the metal framework in cantilever cross-arch fixed partial dentures via a theoretical finite element model.

Chapter IV - Periodontal disease is a chronic bacterial infection characterised by persistent inflammation, connective tissue breakdown and alveolar bone destruction. The chronic inflammation associated with periodontal disease represents the host response to bacterial plaque, mediated by the environment in which the response occurs. Periodontitis is both site-specific and episodic in nature and thus biomarker development could prove

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invaluable in identifying sites with active disease, predicting sites that may develop disease, monitoring response to therapy or identifying patients with enhanced disease susceptibility.

In periodontal disease gingival crevicular fluid (GCF) flows from the gingival microcirculation into the periodontal pockets and the volume increases in proportion to the severity of the local inflammatory process. The study of GCF samples, from defined sites of chronic periodontal inflammation, allows non-invasive access to an inflammatory exudate that could be used for biomarker discovery. GCF contains proteins synthesised and secreted in the inflamed gingival tissues and carried by the GCF to the gingival crevice/pocket. Here, they are augmented by proteins released from bacteria and host cells, particularly polymorphonuclear leukocytes (PMNs), present in the periodontal pocket. The constituents of GCF are therefore derived from a number of sources including microbial plaque, host inflammatory cells, serum and tissue breakdown products. Saliva has also been studied in the search for biomarkers of periodontal disease. Saliva is a more complex fluid, comprising glandular secretions, components of GCF, components of serum and also particles (including bacteria) from a variety of oral and airway sources. Although saliva has the advantage of being easily collected, its biochemical complexity may hinder detection of biomarkers specific for periodontal disease. Furthermore the fact that saliva bathes the whole mouth negates the use of salivary biomarkers for site-specific identification or monitoring of periodontal disease.

Despite an impressive list of possibilities, biomarkers have yet to reach routine clinical use as reasonable predictors of periodontal status. This chapter reviews the analysis of GCF and saliva for monitoring periodontal health and disease. Potentially important biomarkers of disease in both GCF and saliva are highlighted and their merits are described in further detail. Putative biomarkers from both host and bacterial sources are considered and the use of multiple biomarkers is discussed. Following the technological revolution in both genomic and proteomic analysis over the last decade it is tempting to speculate that the next decade could bring much waited progress in the field of biomarker identification and application in the field of periodontal disease.

Chapter V - Periodontal disease represents today the main cause of teeth loss after the third decade of life. About 60% of dental extractions are due to etiopathogenetic periodontal factors. After 35 years, the frequency of marginal periodontal disease varies from 80% to 100% of world population, depending on statistical method used and the demographic areas considered, showing a similar frequency in both sexes, slightly higher in female.

Two important and interrelated factors are involved in its physiopathological progression: 1) the activation of immune system and the release of inflammatory mediators, such as IL-1β, IL-6 and TNF-α, which could overflow into the blood system and induce a systemic inflammatory response; 2) the production of oxygen radicals and their related metabolites.

A recent focus of the dental research is the individuation of biomarkers, which can be easily used as diagnostic tools. Among them, metalloproteinases (MMPs) and heat shock proteins (HSPs) could provide potential biomarkers, which could be useful for evaluating both the periodontitis development and the incidence of the related cardiovascular diseases. Recent studies, in fact, have shown a direct correlation between periodontal and cardiovascular diseases: in particular, both diseases have systemic and local causes, and the constant bacterial contamination of oral cavity could be linked not only to periodontopathy but also to the development of cardiovascular diseases.

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To date, the periodontal disease therapy available is based on the individuation and the elimination of the causing factors. Nevertheless, new innovative surgical and pharmacological therapies could be developed.

The aim of this work is to review the literature data focusing on the role of inflammatory mediators and oxidative stress in periodontal disease and related factors.

Chapter VI - Periodontal disease results from complex interactions between infectious agents and host factors. The disease expression can be modified by environmental, acquired, and genetic risk factors. Tobacco usage, especially smoking, is considered a major modifiable risk factor for periodontal disease. In addition to periodontal disease, tobacco usage is also a risk factor for oral cancer and its recurrence, dental cariesand congenital defects in children from mothers who smoke while pregnant. In periodontal disease, smokers have deeper probing depths, more gingival recession, more alveolar loss and more furcation involvement than non-smokers. They also show less favorable responses to various kinds of periodontal treatments including non-surgical, surgical, regenerative procedures and dental implants. It is clear from epidemiology studies that tobacco usage is correlated with periodontal disease. This chapter reviews the evidence for the association between periodontal disease and tobacco, and describes what is currently known about how tobacco and its components affect the periodontal tissues that result in tissue damage.

Chapter VII - A topical issue in periodontology is to find objective diagnostic methods which may be combined with the classical clinical inspection parameters to yield a reliable grading of the severity and extent of periodontal disease. This study deals with a novel cytodiagnostic fluorescence test, performed on exfoliation samples taken from periodontal/oral tissues, useful to assess the severity of periodontal disease. Twenty-one patients with different degrees of periodontitis were subjected to clinical and histopathological grading and the results compared with those obtained from the cytodiagnostic fluorescence assay. The author found that the amount of blood cells (polymorphonuclear and mononuclear leukocytes, erythrocytes), the occurrence of morphologically abnormal epithelial cells, and the number of spirochetes showed a statistically significant correlation with the clinical and histopathological diagnostic parameters, the latter being considered as the most reliable predictors of the severity of periodontal disease. On these grounds, the author suggest that this cytodiagnostic method may greatly help dental practitioners to achieve a chair-side, reliable and objective evaluation of the degree and activity of periodontitis at first dental visit, and to perform a targeted treatment and an accurate follow up of the patients during supportive periodontal therapy.

Chapter VIII -Differentiation of health from disease is central to understanding diagnosis and treatment of periodontal diseases. It is logical to begin with an in-depth examination of the structure and physiology of the healthy periodontium.

Chapter IX - Objectives: The purpose of this study was to compare the short-term clinical effects of a single intrasulcular injection of 2% chlorhexidine gluconate gel (CG) and placebo gel (PG) in orthodontic patients with fixed appliances and established gingivitis aged from 12 to 20 years.

Methods and Materials: 50 patients (31 females, 19 males) were divided into two groups (CG and PG) of 50 subjects. This study was single blind randomized split mouth clinical trial. As randomly assigned by coin toss, the first permanent molars on the right or left side of the mouth received either CG or PG. Probing depth (PD) was measured with a Michigan 0 probe. The gingival index (GI) of Löe and SILNESS and papilla bleeding index (PBI) of

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MÜHLEMANN were recorded on the first permanent molars. These indices were measured at baseline, and in treatment on second, fourth, eighth, and the twelfth weeks. T-test and chi-square test were used to analyze the data.

Results: T-test showed that PD was reduced in experimental group in comparison with the control group in the 4th week and following intervals ($p<0.001$). Chi-square showed that PBI was improved in experimental group in comparison with the control group in the 2nd week and following intervals ($p<0.001$). The same test showed that GI was improved in experimental group in the 2nd week and following intervals ($p<0.001$).

Conclusion: The data indicate that the use of a single application of 2% CG was effective in reducing gingivitis related to banded first permanent premolars in adolescents undergoing orthodontic treatment in short time.

Chapter X - The focal infection theory, which for almost half a century justified indiscriminate extraction of teeth to cure focal infections, since the end of the 1940s has become progressively a discarded concept. In parallel with the declining importance assigned to pulp and periapical infections in the pathogenesis of focal diseases, over the last decade there has been increasing interest in the possible relationship between periodontal infection and systemic diseases. Periodontal pathogens and their products, as well as inflammatory mediators produced in gingival tissue, might enter the bloodstream through ulcerated pocket epithelium, causing systemic effects (focal diseases).

On the basis of this mechanism, chronic periodontitis has been implicated as risk factor for cardiovascular diseases associated to atherosclerosis, bacterial endocarditis, diabetes mellitus, respiratory disease preterm delivery, rheumatoid arthritis, and more recently osteoporosis, pancreatic cancer, metabolic syndrome, renal diseases and neurodegenerative diseases such as Alzheimer's disease. Numerous hypotheses, including common susceptibility, systemic inflammation, direct bacterial infection and cross-reactivity, or molecular mimicry, between bacterial antigens and self-antigens, have been postulated to explain these relationships. In this context, the association of periodontal disease with systemic diseases has introduced the concept of "periodontal medicine", which ultimately guides the medical community in therapeutic approaches to improve not only the patient oral health but also systemic health.

This chapter summarizes the pathophysiology of periodontal disease and presentsan update on interrelationships and interactions between periodontal disease and systemic diseases. Moreover, this chapter reviews the published literature that describes the effects of periodontal treatment on cardiovascular diseases, adverse pregnancy outcomes, diabetes mellitus, and respiratory disease.

Chapter XI - Obesity, diabetes and oral diseases (dental cariesand periodontal diseases), largely preventable chronic diseases, are described as global pandemic due their distribution and severe consequences. WHO has called for a global action for prevention and promotion of these diseases as a vital investment in urgent need.

Diabetes and obesity, showing an increasing trend, lead to disabilities and negatively impacts on the quality of life through life course along with oral diseases. WHO projects that the prevalence of diabetes and deaths/year attrituble to diabetes complications will double worldwide by 2030. Globally, more than 1 billion adults are overweight; almost 300 million of them are clinically obese. Being obese/overweight raises steeply the likelihood of developing DM2. Approximately 85% of people with diabetes are DM2, and of these 90% are obese or overweight. Obesity increases the likelihood of periodontitis which is one of the

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most common chronic diseases worldwide, described as pandemic, and closely related to DM2. Promoting good oral health is significantly essential for prevention and reducing the negative consequences of periodontal diseases, DM2 and obesity, and to maintain good health, as proposed by European health goals by WHO.

Chapter XII - Periodontitis is one of the predominant polymicrobial infections of humans. Since periodontitis results from complex interactions of multiple microorganisms, it is important to investigate interactions between different periodontal bacteria and host cells. Porphyromonas gingivalis, a gram-negative anaerobe, is a major colonizer of gingival tissues and has been etiologically implicated in periodontal as well as cardiovascular diseases. Cellular invasion by periodontal pathogens including P. gingivalis has been proposed as a possible virulence factor, affording protection from the host immune responses and contributing to tissue damage. In recent periodontal research, polymicrobial infection models have been used to study host response profiles. However, data on the potential of host cell invasion by periodontal pathogens in polymicrobial infection are scarce. The author investigated the ability of periodontal pathogens to modulate invasion of human gingival epithelial cells and aortic endothelial cells by P. gingivalis. Among the pathogens, Fusobacterium nucleatum was shown to significantly enhance the P. gingivalis invasion. The author describe the complex interaction between periodontopathogens and host cells, with a particular focus on the co-infection by P. gingivalis and F. nucleatum.

Chapter XIII -Periodontitis is a major chronic inflammatory disease that destroys periodontal tissue and eventually results in tooth loss. Although periodontitis is a local disease, its chronic status triggers systemic inflammatory diseases including severe type 2 diabetes, heart disease, cancer and atherosclerosis. Therefore, the development of new treatments for periodontitis contributes to the effective inhibition of systemic inflammatory diseases.

High Mobility Group Box-1 (HMGB1), a primarily nuclear protein, is present in many eukaryotic cells and is highly conserved between species. HMGB1 appears to have distinct functions in cellular systems. It acts as an intracellular regulator of transcription and plays a crucial role in the maintenance of DNA function. Extracellular HMGB1 released by various cell types (i.e. macrophages/monocytes, endothelial cells and pituicytes), or necrotic cells, stimulated by lipopolysaccharide (LPS) or tumor necrosis factor- ,TNF-[] acts as a proinflammatory cytokine through the multi-ligand receptor for advanced glycation end-products (RAGE) and toll-like receptors (TLRs) 2 and 4. Extracellular HMGB1 plays a critical role in the progression of chronic inflammatory diseases, such as septic shock, rheumatoid arthritis, diabetes and atherosclerotic lesions. Recent studies show that HMGB1 is continuously released from gingival epithelial cells modulated by TNF- and expressed in epithelial tissues of patients with periodontitis. HMGB1 may be involved in the progression of periodontitis as a novel inflammatory mediator. Therefore, understanding the mechanisms underlying the functions of HMGB1 may lead to novel therapeutic approaches for chronic periodontitis and help to prevent systemic inflammatory diseases.

This review summarizes the current knowledge on HMGB1, including its correlation with disease and preventive medicine.

Chapter XIV - Chronic periodontal diseases include a group of inflammatory diseases that affect periodontal supporting tissues of the teeth and encompass destructive and nondestructive conditions. Periodontal diseases are multifactorial and the role of dental biofilm in their initiation is primary. However, whether dental biofilm affects a particular

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subject, what form the disease takes and how it progresses, are all dependent of a wide variety of factors. Therefore, the objective of this chapter is to outline the risk factors described for the most prevalent chronic periodontal diseases (plaque induced gingivitis and chronic periodontitis) and to explain some basic concepts related to the current understanding of the role of these risk factors based on in vitro, animal and human studies. The review will focus on the factors that may be associated with a direct increase in the likelihood of occurrence of disease or an increase in its severity. The following factors will be discussed: 1) host characteristics, such as age, gender and race; 2) social and behavioral factors (socioeconomic status, cigarette smoking and emotional stress); 3) systemic factors, e.g. diabetes mellitus and osteoporosis; 4) genetic factors; 5) tooth-level factors (root grooves, tooth position, caries, occlusal discrepancies, iatrogenic restorations, root abnormalities and periodontal parameters); and 6) the microbial composition of dental biofilm. Finally, this chapter will also present literature-based evidence on predictive factors associated with patients and tooth susceptibility for recurrence of periodontitis after the end of the active periodontal therapy and will examine the use of some prognostic models which may be useful for clinicians in the identification high-risk groups of patients.

Chapter XV - The oral cavity is a warm, moist environment, in which a number of microorganisms colonize and live in harmony as a community, a so-called biofilm. In this environment, antimicrobial peptides may play a critical role in maintaining normal oral health and controlling innate and acquired immune systems in response to continuous microbial challenges in periodontal disease. Two major families of antimicrobial peptides, found in the oral cavity, are defensin and cathelicidin. Members of the defensin family are cysteine-rich peptides, synthesized by plants, insects, and mammals. These peptides vary in length and in the number of disulfide bonds, and have a beta-sheet structure. In the oral cavity, four alpha-defensins are synthesized and stored in neutrophil granules, which are converted into active peptides by proteolytic processing, while three human beta-defensins (hBDs), hBD-1, hBD-2, and hBD-3, are predominantly produced by oral epithelial cells. The only member of the cathelicidin family found in humans is LL-37, an alpha-helical peptide that contains 37 amino acids and begins with two leucines at its NH3-terminus. LL-37 is derived from enzymatic cleavage of a precursor peptide, namely, human cationic antimicrobial peptide-18. Clinically, differential expression of antimicrobial peptides has been reported in specific types of periodontal disease, and their presence has been shown in saliva and gingival crevicular fluid. Current evidence suggests that alpha-defensins, beta-defensins, and LL-37 have distinct, but overlapping, roles in antimicrobial and pro-inflammatory activities. Several studies have shown antimicrobial activities of hBD-2, hBD-3, and LL-37 against several periodontal pathogens, suggesting their potential role as antimicrobial agents for periodontal disease. The clinical significance of antimicrobial peptides in periodontal disease has recently been demonstrated in morbus Kostmann syndrome, a severe congenital neutropenia, in which chronic periodontal infection in young patients, resulting from a deficiency of neutrophil-derived antimicrobial peptides, causes early tooth loss. Although researchers initially focused their attention on antimicrobial activities, it is now becoming evident that defensins and LL-37 are multifunctional molecules that mediate various host immune responses, and may thus represent essential molecules of innate immunity in periodontal disease. In this chapter, basic knowledge and the clinical importance of antimicrobial peptides in periodontal disease will be discussed in detail.

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