

Reaching a better understanding of non-oral disease and the implication of periodontal infections

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The last decade has witnessed a spectacular increase in the awareness of the association between chronic periodontitis and systemic diseases. Published studies have focused on the statistical relationship between periodontitis and systemic diseases and on patho-physiologic aspects of periodontitis having the potential to aggravate systemic disease. Today, a declining number of physicians attempt to manage the entire range of medical disorders that can affect infants, children or adults, but those who do must have available a broad spectrum of current and accurate information. Likewise, general dentists and periodontists, as medical sub-specialists, must be cognizant of medical topics in order to manage patients with medical conditions that may alter periodontal treatment and prognosis. Keeping up with the most recent advances in cellular and molecular biology, molecular genetics, and medical technology is more challenging than ever. With that in mind, this volume of *Periodontology 2000* concentrates on those medical diseases that are most important in relationship to periodontal treatment. The authors have placed emphasis on disease etiology, symptoms, diagnostic tests, diagnoses, and treatment regimens of the current best practice. It is hoped that this volume will be a welcome aid to the readers, addressing the need for current information of medical diseases and worthy of frequent reference.

Age-related medical diseases

With the increasing age of the population seeking periodontal care and the accumulation of drug-trea-

ted ailments in aging patients, several pharmaceutical agents can have a major impact on periodontal management. This volume starts with an examination at key drug interactions that can play a role in periodontal therapy (37). Older patients are more than twice as susceptible to adverse drug reactions as younger patients. Changes with aging in body composition, and in drug distribution, metabolism, excretion, and response, make the older patient more vulnerable to adverse reactions. Drug complications in elderly compared to younger individuals are also likely to be more serious and to require extended hospitalization for a longer period of time (31). In the USA, older adults at home consume nearly 3 times as many drugs as the general population, with women taking twice as many drugs as men (17). The average post-retirement aged person receives 18 prescriptions annually. Also, the aged patients often bear the brunt of reflexive prescribing for uninvestigated symptoms (43). More than 50% of older patients do not take their drugs as prescribed, and about 25% of them make errors likely to result in drug-induced illness (6). The remaining non-compliance is often referred to as intelligent non-compliance in which patients alter the dose of medications in order to decrease adverse reactions. Older patients are also more likely to be the ones in need of periodontal therapy to preserve or replace lost teeth. This puts an increased obligation on the dentist to have the most complete knowledge possible of pharmaceuticals and their impact on periodontal therapy.

The significance of the aging population is also highlighted in the second manuscript of this volume as it continues with a look at osteoporosis (12). Three

decades ago osteoporosis was a curiosity in medicine, but today it is a major health care concern, yet too few dentists understand the disease and its impact on periodontitis. Osteoporosis is a generalized, progressive diminution in bone tissue mass per unit volume, causing skeletal weakness, even though the ratio of mineral to organic elements is unchanged. Histologically, there is a reduction in cortical thickness and in the number and size of trabeculae of cancellous bone. Bone formation appears to be normal but bone resorption is increased. If one considers chronic and aggressive periodontitis to be bone-resorptive diseases, then the imbalance between osteoporosis-related bone resorption and formation becomes important in terms of periodontal disease. Moreover, with periodontal regeneration and dental implants being mainstay therapies in current periodontics, the balance in bone homeostasis comprises a crucial treatment consideration. Between the ages of 51–70 years osteoporosis is six times more common in women than in men (8). Past the age of 70 years men catch up significantly but osteoporosis remains twice as prevalent in women. Studying the relationship between osteoporosis, chronic periodontitis and tooth loss is particularly difficult because of the slowly progressive nature of periodontitis. The problem is further compounded by risk factors that are shared by both osteoporosis and periodontitis, such as endocrine disorder (diabetes mellitus) or drug-induced (corticosteroids, tobacco, ethanol) bone wasting.

The need for understanding osteoporosis is also underscored by the benefits and risks associated with osteoporotic medicine. While amino-bisphosphonates are important bone-sparing agents in osteoporosis treatment, case reports have described the potential of these therapies to induce osteonecrosis of the jaw (44).

As the average age of the population increases and the survival rate of cancer patients continues to improve, there has been a major increase in the number of individuals receiving cancer therapeutics. As described in this volume (3), the expanding range of cancer therapeutic options has presented the dentist with a new and ever challenging risk of oral complications. Some cancer chemotherapeutic drugs can cause stomatitis, the severity of which may be related to the degree of periodontal disease. Proper periodontal treatment prior to cancer chemotherapy can minimize gingival hemorrhage, tissue sloughing, oral pain and consequently poor food intake (34). Radiation therapy to the head and neck places patients at high risk for xerostomia and at risk for osteonecrosis

if teeth subsequently need to be extracted (23). Professional periodontal prevention and a life-long attention to strict oral hygiene are key measures to avoid the need for oral and periodontal surgery in cancer survivors.

Immuno-compromising human diseases

Human immunodeficiency virus (HIV) infection is caused by one of several related retroviruses that become incorporated into host cell DNA and result in a wide range of clinical presentations, varying from an asymptomatic carrier state to severely debilitating and fatal disorders. Acquired immunodeficiency syndrome (AIDS) is a secondary immunodeficiency syndrome resulting from HIV infection and characterized by opportunistic infections, malignancies, neurologic dysfunction, and other syndromes. However, advances in HIV therapy have significantly improved the quality and duration of life. The variability in clinical presentation compels the dentist to be knowledgeable about HIV-related diseases and treatment. Yin et al. (46) have reviewed topics of HIV infections, which are relevant for the dentist.

As a result of HIV infection, the number and function of T-cells, B-cells, natural killer cells, and monocytes-macrophages are subverted (11). Knowledge of the extent of host immune impairment is important in the management of periodontal disease, as it is related to increased risk of progressive periodontitis. The single best predictor of the onset of opportunistic infections is the number of circulating CD4+ lymphocytes (38). As periodontitis may comprise a serious opportunistic infection in the immunocompromised host, diligent periodontal preventive measures are of utmost importance.

Cell and organ transplant patients constitute another group of immunosuppressed patients, who have increased in number due to improved long-term treatment outcomes (40). This volume of *Periodontology 2000* develops a basis for periodontal treatment of transplant patients. Sixty years ago, researchers had some success transplanting organs in animals, and there had even been a few failed attempts at human organ transplants. Numerous studies showed that human organ transplantation was feasible, and that it would potentially be beneficial to thousands of patients, but nobody had been able to perform a successful transplantation (19, 30). Success finally came in the early 1950s, when several organ

transplants within a few years gave new hope of life to ailing patients (24). In the following decades, physicians learned how to transplant a variety of organs with markedly improved success. Today, most organ transplants are relatively safe, routine procedures, and transplantation is considered the best treatment option for thousands of cases of end-stage diseases every year. Transplant patients are now routinely seeking oral health care, requiring the dentist to have a solid working understanding of transplantation and subsequent therapy.

Periodontal biofilm and immuno-inflammatory contributory risks to major human diseases

The concept that oral infections are linked to the overall health of patients has been the focus of much research in the past decade. Knowledge about virulence factors of periodontal pathogenic bacteria and protective host immune responses has provided significant insights into the etio-pathogenesis of periodontal diseases and into the potential for periodontal disease to contribute to medical pathosis.

Despite advances in neonatology and significant decreases in infant mortality, the rate of spontaneous premature birth has remained relatively stable over the years. Premature delivery and low birth-weight babies are leading determinants of neonatal mortality and serious morbidity, often leading to neurologic and developmental restrictions in early childhood (21). Multiple lines of evidence exist to strongly support a role for maternal infection and inflammation of the genital tract as well as inflammation from sites distant from the pelvis, in the etiology of preterm birth (1, 2, 13, 16, 42). The role of maternal periodontitis as a potential maternal-fetal stressor having detrimental effects on pregnancy outcome is a relatively new area of investigation. This volume presents the current understanding of high risk pregnancy and explores the potential contribution of maternal periodontitis to prematurity (26).

Cardiovascular disease remains a leading cause of death in developed nations. Two of the major independent risk factors for cardiovascular diseases are high blood pressure and altered lipid metabolism. A key strategy for addressing these risk factors is to educate the public and health-care practitioners about the importance of prevention and proper intervention. Inflammation in the blood vessel wall

may play a fundamental role in all stages of atherosclerosis, and in precipitating heart attacks and other acute cardiovascular events (39). In addition, a hyperinflammatory state or trait may be an important characteristic for cardiovascular disease as well as for periodontitis (4, 33). The potential association between cardiovascular disease and chronic periodontitis, and the dentist's possible role in preventing cardiovascular disease are presented here (29).

Diabetes mellitus is a heterogenous group of endocrine disorders in which hyperglycemia results from both impaired insulin secretory response to glucose and from decreased insulin effectiveness. Diabetes mellitus has reached epidemic proportions in many populations and therefore requires dentists to have first-hand, up-to-date knowledge of the risks, management and complications of the disease. This volume of *Periodontology 2000* discusses current concepts of diabetes mellitus and the potential benefits of reducing periodontal bacterial and inflammatory loads on glycemic control (25).

The increase in the prevalence of diabetes is partly due to a dramatic increase in obesity in the general population. This volume explores obesity as a significant health condition, and the possibility that adipose tissue involves more than simply being a storage site of triglycerides-containing cells (35). Current data indicate the adipose tissue may play a role in vascular and inflammatory regulation (15, 45). Additionally, adipose tissue, acting as an inflammatory end organ, may have a contributory role in the pathogenesis of periodontitis. This further shows the importance of understanding the pathology of obesity and the risks to oral and general health and well-being.

Aspiration pneumonia is the pathologic consequence of an abnormal entry of fluids, particulate matter or secretions into the lower airways. Healthy persons commonly aspirate, but the inoculum is usually cleared without disease sequelae by normal host defense mechanisms. The thought of pneumonia as a bacterial infection is an obvious concept to dentists. However, the possibility that oral biofilms and periodontal inflammatory disease is a potential contributor to acquired pneumonia is not fully appreciated. Common pathogens in aspiration pneumonia are anaerobic bacteria that colonize the gingival crevice and periodontal pockets (27). Patients who aspirate outside a hospital setting usually experience an anaerobic infection, whereas nosocomial aspiration pneumonia tends to involve a more complex mixture of microorganisms (10, 36). This microbial difference can greatly affect the outcome

of aspiration pneumonia and the choice of treatment. This volume considers the dentist's role in preventing periodontal microorganisms from entering the lower airways of individuals in nursing homes, and in ventilator acquired respiratory infections (32).

Acquired and environmental risks to periodontal health

The risk of tobacco use to general health is commonly known and represents a significant burden on patients, health care providers, and society. In addition to the systemic health problems, tobacco use is associated with loss of periodontal attachment and alveolar bone beyond what can be expected from bacterial infection alone. Smoking is associated with a relative immunosuppression exhibited by an altered T-cell ratio (28). Osteoblast function may be impaired leading to a reduction in bone mineral density similar to the risks associated with osteoporosis. Tobacco use is also linked to impaired neutrophil functions and thus a decreased ability to fight infection (14). In addition, the oral cavity is exposed to high concentrations of cytotoxic and vasoactive substances, such as nicotine, that locally may contribute to periodontal diseases. Despite the multiple mechanisms by which smoking may lead to periodontal destruction, smoking may be the most readily modifiable risk factor, other than the microbial biofilm, in a patient's risk profile for periodontal disease.

The role of smoking in several major systemic diseases and in periodontitis makes unraveling the confounding effect of tobacco in oral and systemic health interactions a challenging area of clinical research. This volume of *Periodontology 2000* focuses on the increased risk for periodontitis and the altered outcome of periodontal treatment in patients who are tobacco users (20). Further, given the etiologic role of smoking as an acquired risk factor in maintaining or restoring periodontal health, this volume underscores the potential role of dentists in tobacco cessation programs.

The influence of stress on human diseases is not well understood. Stressors that provoke physiologic response episodes can be psychological or biological. Life events such as separation from family can commonly precede physiologic stress response episodes. Acute necrotizing ulcerative gingivitis is a type of periodontal disease that is associated with stress episodes, yet stress is not often considered significant in the etiology or exacerbations of other types of periodontal disease (9,18). The procedures and sur-

geries associated with therapeutic management of periodontitis are stressful for many patients and may also, at least temporarily, aggravate ongoing periodontal disease. This volume explores the evidence for stress as a risk factor for periodontal disease and its influence on wound healing associated with periodontal treatment (5).

Hemostasis requires the combined activity of vascular, platelet, and plasma factors counterbalanced by mechanisms to limit the accumulation of platelets and fibrin to the area of injury. There are numerous patients with a relative impairment of hemostasis, such as patients with cardiovascular disease, who have been treated with thrombolytic agents (7,22). Dentists manage an increasing number of patients with innate and acquired bleeding disorders. People with bleeding disorders should be scrupulous about oral hygiene to prevent or decrease the need for invasive periodontal therapy or tooth extraction. This volume of *Periodontology 2000* describes disorders characterized by tendency to bleed and reviews methods to arrest bleeding from injured blood vessels (41). The therapeutic challenges during periodontal treatment of patients with bleeding disorders are also presented to aid the dentist in proper management decisions.

Conclusion

Chronic periodontitis is a multifactorial disease with a microbial primary etiology. The medical status of the patient may significantly influence the development of periodontal disease. Systemic health aspects can also determine the approach to and outcome of periodontal treatment. For example, routine periodontal treatment may not achieve the desired outcome when healing is inhibited by corticosteroid drugs, immunosuppressive agents used in organ transplantation, or cytotoxic cancer medication. Likewise, osteoporosis and especially smoking can significantly compromise the prognosis following periodontal therapy. Proper knowledge of major medical diseases and their relationship to periodontitis will allow for better patient care and a more complete understanding of the evidence associating oral and systemic health.

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