

Practical Osseous Surgery in Periodontics and Implant Dentistry

Serge Dibart and Jean-Pierre Dibart



PRACTICAL OSSEOUS SURGERY IN PERIODONTICS AND IMPLANT DENTISTRY

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Edited by

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Foreword

I am delighted to be asked to write the forward for this new book on practical osseous surgery. This book is greatly needed in dentistry and, quite frankly, is overdue. I am especially glad that Serge Dibart and Jean-Pierre Dibart decided to undertake this work and to provide the dental profession with a much-needed resource in the management of intraoral bone.

I cannot help but smile when I see the words “bone” or “alveolar bone” or “osseous.” I am reminded of long ago at the start of my graduate training program in periodontology at Harvard under the mentorship of Paul Goldhaber. I did not realize until I arrived in Boston that Paul was a world authority on bone and that he would begin to teach my fellow residents and me all of the intricacies and exciting mysteries of bone. Quite frankly, I thought I was at Harvard to study “periodontal pockets.” I remember that in the first month of the residency program, my classmates and I rotated through orthopedic surgery at Massachusetts General Hospital. Paul wanted us to see the management of bone up close and firsthand. And so we watched as hips, knees, and elbows were repaired or replaced or tumors removed from legs and arms and subsequent osseous defects grafted. It was an amazing introduction to osseous surgery. And soon thereafter, upon returning to the dental school, we were given new Ochsenbein chisels and Schluger files and shown how to remove and contour the alveolar bony defects associated with periodontitis. We were also taught the initial steps in bone regeneration using allograft material and later, tissue-guiding membranes. It was a phenomenal time of being “immersed” in the training of the surgical management of bone.

Osseous surgery has clearly come a very long way since I was a resident in periodontics. It is extraordinary what has been introduced to dentistry in the last 30 years, and quite frankly, there is no looking back. Resective osseous surgery, while not as popular as it once was, is nonetheless an essential part of managing bony defects in the treatment of periodontitis and placing dental implants. Sophisticated instruments such as the Piezotome have been introduced to make bone cutting and resection easier and with much fewer complications. Bone regeneration for both periodontal disease management and implant placement management has come a very long way. We now have at our disposal signaling molecules such as growth and differentiation factors that can greatly enhance our ability to regenerate bone. Even

as we are adopting specific signaling molecules into our practice, new molecules are being developed that may prove to be more efficacious.

The subsequent introduction of guided bone regeneration principles and techniques has taught us that we can in fact regenerate bone where it is critically needed prior to implant placement. And this new ability to regenerate bone where needed ushered in the era of “prosthodontically driven” implant placement. Guided bone regeneration, coupled with bone grafts, signaling molecules, and tissue excluding/guiding membranes have allowed the clinician to dictate where bone will be regenerated. No longer does the mere presence of bone dictate where an implant will be placed. Moreover, extraction sockets are now carefully managed during tooth removal, using a combination of atraumatic techniques, bone grafts, and membranes to ensure maximal preservation of the site.

And now, with no end in sight, osseous surgery has also advanced orthodontic tooth movement. Several years ago the Wilcko brothers brought periodontally accelerated osteogenic orthodontics to the forefront through a series of intriguing cases presented in publications and at meetings. It became clear that the manipulation of bone through osseous surgery, combined with bone regeneration techniques, could foster quicker tooth movement. A more minimally invasive surgical technique introduced will likely make this approach to tooth movement even more acceptable to orthodontists and patients.

All told, I say “lucky us”. Serge and Jean-Pierre Dibart have provided us with a first-rate book that provides current concepts and techniques for managing “bone” in periodontics, orthodontics, and implant dentistry. Realizing how far and how quickly dentistry’s management of osseous conditions has advanced, I look forward to the future and the continual development of this aspect of patient management in dentistry, knowing that clinicians such as the Dibarts will help advance this very exciting area of dentistry.

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Section 1

Body-Mouth Connection: Relevant Pathologies Affecting Dental Treatment, Guidelines, Prevention, and Necessary Precautions

Chapter 1 Body Weight, Diet, and Periodontitis

Jean-Pierre Dibart, MD

BODY WEIGHT

Introduction

The body mass index relates body weight to height. Body mass index, or BMI, is defined as the weight in kilograms divided by the height in meters squared. Obesity is defined as a body mass index greater than 30 kg/m²; BMI between 25 kg/m² and 30 kg/m² defines overweight people, the normal weight being between 19 kg/m² and 25 kg/m². Obesity is a chronic disease with many important medical complications. The main cause of obesity is an imbalance between energy intake and energy expenditure.

The necessary treatment includes

- a calorie-restricted diet,
- increased physical activity, and
- nutritional modifications, with reduction of fat and sugar intake

The prevalence of obesity has increased in Western countries. It is a metabolic disease that predisposes to many medical complications such as cardiovascular disease, cancer, arthrosis, and diabetes, and it has also been implicated as a risk factor for chronic health conditions such as periodontitis. Obesity is associated with periodontal disease because the adipose tissues secrete some cytokines and hormones that are involved in inflammatory process. A high body mass index is associated with a systemic low-grade inflammatory state. Tumor necrosis factor- α , a proinflammatory cytokine, is produced in adipose tissues and is responsible for lowered insulin sensitivity, called insulin resistance which is responsible for elevated plasma glucose levels.

Periodontitis is characterized by alveolar bone loss, which is the consequence of bone resorption by the osteoclasts. Bone-forming cells (osteoblasts) and bone-resorbing cells (osteoclasts) are under hormonal control; the bone formation is negatively regulated by the hormone leptin, produced from adipocytes.

Health education should encourage better nutritional habits to reach normal weight and prevent obesity, and also to promote better oral hygiene to prevent periodontal disease (Alabdulkarim et al. 2005; Dalla Vecchia et al. 2005; Ekuni et al. 2008; Khader et al. 2009; Lalla et al. 2006; Linden et al. 2007; Nishida et al. 2005; Reeves et al. 2006; Saito et al. 2001; Saito et al. 2005; Wood, Johnson, and Streckfus 2003; Ylostalo et al. 2008).

Body Mass Index

High body mass index is a risk factor for periodontitis. There is a 16% increased risk for periodontitis per 1 kg/m² of increased body mass index. Body mass index is also significantly associated with the community periodontal index score (Ekuni et al. 2008). Total body weight is associated with periodontitis. Adolescents aged 17 to 21 years old have a 1.06 times increased risk for periodontal disease per 1 kg increase in body weight (Reeves et al. 2006). There is a significant correlation between body mass index and periodontitis, with a dose-response relationship (Nishida et al. 2005). Obesity is a risk factor for periodontitis; there is an association between high body weight and periodontal infection (Ylostalo et al. 2008). High body mass index is significantly associated with periodontitis, with an odds ratio of 2.9 (Khader et al. 2009). Obesity with a body mass index greater than 30 kg/m² is significantly associated with periodontitis, with an odds ratio of 1.77 (Linden et al. 2007).

Obese patients are 1.86 times more likely to present periodontitis according to the following groups:

- For patients older than 40 years of age, the odds ratio is 2.67.
- For females, the odds ratio is 3.14.
- For nonsmokers, the odds ratio is 3.36 (Alabdulkarim et al. 2005).

There is a positive correlation between body mass index and periodontitis, with a significantly higher prevalence in females. Obese females are significantly (2.1 times) more likely to have

periodontitis (Dalla Vecchia et al. 2005). Obesity is also associated with deep probing pockets. High body mass index and body fat are significantly associated with the highest quintile of mean probing pocket depth (Saito 2005). There is a positive and significant association between high body mass index and the number of teeth with periodontal disease; this may be explained by obesity being responsible for a systemic low-grade inflammatory state (Lalla et al. 2006). People with higher categories of body mass index and upper body abdominal fat have a significantly increased risk of presenting with periodontitis (Saito et al. 2001).

There are significant correlations between body composition and periodontal disease. Body mass index and abdominal visceral fat are significantly associated with periodontitis (Wood, Johnson, and Streckfus 2003). Only 14% of normal-weight people have periodontitis; although 29.6% of overweight people and 51.9% of obese people present with periodontitis. High percentage of body fat, which is a person's total fat divided by that person's weight, is significantly associated with periodontal disease, with an odds ratio of 1.8 (Khader et al. 2009).

Physical Activity

There is an inverse linear association between sustained physical activity and periodontal disease: increased physical activity induces an improvement in insulin sensitivity and glucose metabolism. Periodontitis risk decreases with increased average physical activity. Compared with men in the lowest quintile for physical activity, those in the highest quintile have a significant 13% lower risk of periodontitis. Physically active patients present with significantly less average radiographic alveolar bone loss (Merchant et al. 2003).

Waist-to-Hip Ratio and Waist Circumference

High waist-to-hip ratio is a significant risk factor for periodontitis. Upper-body obesity as measured by the waist-to-hip ratio or the waist circumference is related to visceral abdominal adiposity. Because of induced systemic inflammation and insulin resistance by adipose tissue, it represents a risk factor for type 2 diabetes and cardiovascular diseases. Patients with a high waist-to-hip ratio present a significantly increased risk for periodontitis (Saito et al. 2001). Periodontitis is more frequent among patients with high waist circumference and high waist-to-hip ratio; high waist circumference is significantly associated with periodontitis with an odds ratio of 2.1 (Khader et al. 2009). Adolescents aged 17 to 21 years old have an 1.05 times increased risk of periodontal disease per 1-cm increase in waist circumference (Reeves et al. 2006). Waist-to-hip ratio, which characterizes abdominal visceral fat, is statistically significantly associated with periodontitis. There

are significant correlations between body composition and periodontal disease, waist-to-hip ratio being the most significant element associated with periodontitis (Wood, Johnson, and Streckfus 2003). High waist-to-hip ratio is also significantly associated with the highest quintile of mean probing pocket depth (Saito et al. 2005).

Adipokines

Adipocytes produce cytokines, or adipokines, which are responsible for the association between obesity and other disease. Adipocytes in the adipose tissues of obese people produce large quantities of leptin, which regulates energy expenditure and body weight (Nishimura et al. 2003). Adiponectin and resistin are adipokines, which are responsible for systemic inflammation and insulin resistance in obese people. Serum resistin levels are higher in patients with periodontitis than in healthy subjects. Periodontitis patients with at least one tooth with a probing pocket depth greater than 6mm have two times higher serum resistin levels than subjects without periodontitis (Furugen et al. 2008). Periodontitis is significantly associated with increased resistin levels. Resistin and adiponectin are secreted from adipocytes, and resistin plays an important role in inflammation (Saito et al. 2008).

Experimentation

Experimental calorie-restriction diet may have anti-inflammatory effects. A low-calorie diet results in a significant reduction in ligature-induced gingival index, bleeding on probing, probing depth, and attachment level. Periodontal destruction is significantly reduced in low-calorie-diet animals (Branch-Mays et al. 2008). After oral infection with *Porphyromonas gingivalis*, mice with diet-induced obesity present a significantly higher level of alveolar bone loss, with 40% increase in bone loss 10 days after inoculation. Accompanying the increase in bone loss, obese mice show an altered immune response with elevated bacterial counts for *P. gingivalis* (Amar et al. 2007).

The Metabolic Syndrome

Metabolic syndrome is characterized by the following:

- Central visceral obesity
- Hypertriglyceridemia and low levels of high-density lipoprotein cholesterol
- Hypertension
- Insulin resistance

Abdominal visceral obesity is characterized by an increased waist circumference.

Atherogenic dyslipidemia is defined by raised triglycerides and low concentrations of high-density lipoprotein cholesterol, elevated apolipoprotein B, small high-density lipoprotein cholesterol particles, and small low-density lipoprotein cholesterol particles.

Hypertension is characterized by chronic elevated blood pressure.

Insulin resistance or lowered insulin sensitivity is associated with high risk for cardiovascular disease and diabetes.

A proinflammatory state is generally present with the elevation of serum C-reactive protein because adipose tissues release inflammatory cytokines, inducing the elevation of C-reactive protein.

Prothrombotic state is characterized by raised serum plasminogen activator inhibitor and high fibrinogen (Grundt et al. 2004). The metabolic syndrome is associated with severe periodontitis; these patients are 2.31 times more likely to present with the metabolic syndrome. The prevalence of the metabolic syndrome is

- 18% among patients with no or mild periodontitis,
- 34% among patients with moderate periodontitis, and
- 37% among patients with severe periodontitis (D'Aiuto et al. 2008).

NUTRITION

Omega-3 Polyunsaturated Fatty Acids

Sources of omega-3 polyunsaturated fatty acids (eicosapentaenoic acid and docosahexaenoic acid) can be found in animals and especially in fish such as salmon, tuna, and mackerel. They are also present in many vegetables and nuts (alpha-linolenic acid), such as walnuts and almonds. They are capable of reducing proinflammatory cytokine levels (Enwonwu and Ritchie 2007).

Fish oil rich in omega-3 polyunsaturated fatty acids, especially eicosapentaenoic acid and docosahexaenoic acid, may protect from bone loss in chronic inflammatory diseases, such as rheumatoid arthritis or periodontitis.

A fish oil-enriched diet inhibits alveolar bone resorption after experimental *P. gingivalis* infection. *P. gingivalis* infected rats fed omega-3 polyunsaturated fatty acids have the same alveolar bone levels as do the healthy animals. Omega-3 polyunsaturated fatty acid dietary supplementation can modulate inflammatory reactions leading to periodontitis, with reduction of the alveolar bone resorption (Kesavalu et al. 2006).

Free Radicals, Reactive Oxygen Species, and Antioxidants

Free radical-induced tissue damage and antioxidant defense mechanisms are important factors present in inflammatory diseases. High levels of reactive oxygen species activity combined with low antioxidant defense can lead to inflammatory diseases such as periodontitis.

Oxidative stress is an imbalance between excess production of reactive oxygen species and low antioxidant defense. The reactive oxygen species are

- superoxide anions,
- hydroxyl radicals, and
- peroxyl radicals (Nassar, Kantarci, and van Dyke 2007).

P. gingivalis induces the release of inflammatory cytokines such as interleukin-8 and tumor necrosis factor- α , leading to an increased activity of polymorphonucleocytes. After the stimulation by bacterial antigens, activated polymorphonucleocytes produce the reactive oxygen species (Sculley and Langley 2002).

Systemic inflammation accelerates the consumption of antioxidants such as vitamins and minerals. Increased production of reactive oxygen species necessitates more antioxidant elements such as zinc, copper, and selenium. Selenium has oxidation-reduction functions, and selenium-dependent glutathione enzymes are necessary for reduction of damaging lipids (Enwonwu and Ritchie 2007). In periodontitis, oxidative stress is present either locally and in the serum. Low serum antioxidant concentrations are associated with higher relative risk for periodontitis. Low serum total antioxidant concentrations are inversely associated with severe periodontitis (Chapple et al. 2007).

Lycopene is an antioxidant carotenoid contained in vegetables, particularly in tomatoes. In periodontitis patients, there is a significant inverse relationship between serum lycopene levels and C-reactive protein, and between monthly tomato consumption and white blood cell count. There is also an inverse relationship between monthly tomato consumption and congestive heart failure risk. For moderate monthly tomato consumption, the risk ratio for congestive heart failure is 3.15; for low monthly tomato consumption, the risk ratio is 3.31; and for very low monthly tomato consumption, the risk ratio is 5.1. For people without periodontitis and with moderate serum lycopene level, the risk ratio for congestive heart failure is 0.25 (Wood and Johnson 2004). Peri-implant disease is caused by bacteria infection associated with inflammation and tissue destruction, which is induced by free radicals and reactive oxygen species. In saliva of patients with peri-implant

disease, the total antioxidant status and the concentrations of antioxidants such as uric acid and ascorbate are significantly decreased. On the contrary, total antioxidant status and concentrations of uric acid and ascorbate are higher in healthy people (Liskmann et al. 2007). The total antioxidant capacity of the gingival crevicular fluid and plasma is significantly lower in chronic periodontitis. Successful periodontal therapy increases significantly the total antioxidant capacity of gingival crevicular fluid (Chapple et al. 2007). Gingival crevicular fluid antioxidant concentration is significantly lower in periodontitis. Total antioxidant capacity of plasma is also lower in periodontitis, which can result from excessive systemic inflammation or may induce the periodontal destruction (Brock et al. 2004).

Fusobacterium-stimulated polymorphonucleocytes induce the release of reactive oxygen species, which are responsible for a high degree of lipid peroxidation (Sheikhi et al. 2001). Imbalance between oxidative stress and antioxidant capacity may be responsible for periodontal disease. Lipid peroxidation is significantly higher in periodontitis patients. On the contrary, total antioxidant capacity in saliva is significantly lower in periodontitis patients (Guentsch et al. 2008). Reactive oxygen species are responsible for the destruction of periodontal tissues because of the imbalance between oxidant and antioxidant activity.

In periodontitis, gingival crevicular fluid presents a significantly higher lipid peroxidation level. Saliva shows lower antioxidant glutathione concentration and higher lipid peroxidation level. Periodontal therapy induces a significant decrease of lipid peroxidation and a significant increase in glutathione concentrations (Tsai et al. 2005). Gingival crevicular fluid total antioxidant capacity is significantly decreased in periodontitis patients, presenting lower mean plasma antioxidant capacity. Concentrations of glutathione, which has antioxidant activity, are lower in gingival crevicular fluid because of decreased glutathione synthesis and increased local degradation. In periodontitis plasma and gingival crevicular fluid contain a lower mean total antioxidant capacity (Chapple et al. 2002). Total salivary antioxidant concentrations are significantly lower in periodontitis because of the enhanced action of the reactive oxygen species, which may also predispose to increased effects of reactive oxygen species on periodontal tissues (Chapple et al. 1997).

Superoxide dismutases are antioxidant enzymes that neutralize superoxide radicals. Copper, zinc, and superoxide dismutase are antioxidants that play a protective role against oxidation caused by infections (Balashova et al. 2007).

After stimulation by bacterial antigens, polymorphonucleocytes produce superoxide radicals. The increased number and activity of leukocytes induce an important reactive oxygen species release, with damage to periodontal tissues and to

alveolar bone. Ascorbate, albumin, and urate are antioxidant elements of plasma; although urate is the main antioxidant of saliva (Sculley and Langley-Evans 2002). Reactive oxygen species are produced by leukocytes during an inflammatory response. Periodontal destruction is secondary to the imbalance in the antioxidant and oxidant activity in periodontal pockets. Reactive oxygen species are responsible for extracellular matrix proteoglycan degradation because of their oxidant action (Waddington, Moseley, and Embery 2000).

Nutritional Status

Nutrition

Malnutrition impairs phagocytic function, cell-mediated immunity, complement system, and antibody and cytokine production. Protein energy malnutrition is responsible for impaired immunity and multiplication of oral anaerobic pathogens.

Inflammation necessitates the use of increased quantities of vitamins and minerals. Adequate energy and nutrients are necessary for the production of acute phase proteins, inflammatory mediators, and antioxidants.

Calcium and Vitamin D

Calcium and vitamin D are two important elements for bone metabolism. Women with hip osteoporosis have more than three times the alveolar bone loss around posterior teeth than do women without hip osteoporosis. Calcium and phosphorus are major minerals in hydroxyapatite crystals, and vitamin D regulates calcium and phosphorus metabolism and intestinal absorption. Calcium and vitamin D dietary intake is essential for bone health in periodontitis. Calcium and vitamin D medical supplementation is always necessary for osteoporosis treatment and prevention (Kaye 2007).

Whole Grain

Periodontitis may decrease with higher dietary whole-grain intake; four whole-grain servings per day may decrease the risk. Men in the highest quintile of whole-grain intake are 23% less likely to have periodontitis than are those in the lowest (Merchant et al. 2006).

Diet

Patients with metabolic syndrome who undergo 1 year of a nutritional program show the following significant changes in gingival crevicular fluid:

- Reduction of clinical probing depth
- Reduction of gingival inflammation
- Reduced levels of interleukin-1 β
- Reduced levels of interleukin-6 (Jenzsch et al. 2009)

Cranberry

A treatment with a cranberry antioxidant fraction prepared from cranberry juice inhibits *Aggregatibacter actinomycetemcomitans*-induced interleukin-6, interleukin-8, and prostaglandin E2 inflammatory mediators production, as well as cyclooxygenase-2 inflammatory enzyme expression (Bodet, Chandad, and Grenier 2007).

Green Tea

Catechins are antioxidants derived from green tea; they are able to reduce collagenase activity and tissue destruction. Collagenase activity in gingival crevicular fluid of highly progressive periodontitis patients is inhibited by green tea catechins. Among green tea catechins, epicatechin gallate and epigallocatechin gallate have the most important inhibitory effect (Makimura et al. 1993). Green tea catechins may help in the treatment of periodontal disease. Green tea catechins show a bactericidal effect against Gram-negative anaerobic bacteria such as *P. gingivalis* and *Prevotella* spp. After a mechanical treatment and the local application of green tea catechins, pocket depth and proportion of Gram-negative anaerobic rods are significantly reduced (Hirasawa et al. 2002).

Garlic

Garlic has antimicrobial properties against periodontal pathogens and their enzymes. Periodontal pathogens present among the lowest minimal inhibitory concentrations and the lowest minimum bactericidal concentrations of garlic. Garlic inhibits trypsin-like and total protease activity of *P. gingivalis* (Bakri and Douglas 2005).

Onion

Onion extracts may possess a bactericidal effect on some oral pathogens such as *Streptococcus mutans*, *Streptococcus sobrinus*, *P. gingivalis*, and *Prevotella intermedia* (Kim 1997).

Vitamins

Vitamin C

There is a significant association between low vitamin C levels and periodontal attachment loss. Patients with vitamin C deficiency show more attachment loss than subjects with normal serum vitamin C levels (Amaliya et al. 2007). Serum vitamin C level is inversely correlated to attachment loss; clinical attachment loss is 4% greater in patients with lower serum vitamin C level (Amarasena et al. 2005). Low serum vitamin C is inversely associated with periodontitis, especially in severe disease. Higher serum vitamin C concentrations are associated with less-severe periodontitis, with an odds ratio of 0.5 (Chapple, Miward, and Dietrich 2007). Chronic peri-

odontitis patients present significantly reduced plasma vitamin C levels; after 2 weeks of dietary vitamin C intake as grapefruit consumption, the plasma levels rise significantly and the sulcus bleeding index is reduced (Staudte, Sigush and Glockmann 2005). *P. gingivalis* infection is associated with low levels of serum vitamin C; there is a highly significant inverse association between plasma vitamin C and *P. gingivalis* antibody levels. High antibody titers to *A. actinomycetemcomitans* and *P. gingivalis* are inversely correlated with low levels of vitamin C, especially for vitamin C concentrations lower than 4 mg/L (Pussinen et al. 2003).

Vitamin B

Chronic periodontitis patients supplemented with multiple vitamin B medications, show significantly lower mean clinical attachment levels (Neiva et al. 2005).

Alcohol Consumption

There is a significant positive linear relationship between high alcohol consumption and periodontal parameters such as mean clinical attachment loss and mean probing depth (Amaral, Luiz, and Leao 2008).

Deep probing depth is significantly associated with high alcohol consumption with an odds ratio of 7.72 (Negishi et al. 2004). Alcohol consumption is significantly associated with increased severity of clinical attachment loss, with the following odds ratios:

- 1.22 for 5 drinks per week
- 1.39 for 10 drinks per week
- 1.54 for 15 drinks per week
- 1.67 for 20 drinks per week (Tezal et al. 2004)

Alcohol consumption is significantly associated with probing depth and attachment loss. For 15–29.9g alcohol per day, patients have a significantly higher odds ratio (2.7) of having more than 35% of their teeth with probing depth greater than 4 mm (Shimazaki et al. 2005). People who drink alcohol have a higher risk of getting periodontal disease: it is an independent risk factor for periodontitis.

- For 0.1–4.9g per day, the relative risk is 1.24.
- For 5–29.9g per day, the relative risk is 1.18.
- For more than 30g per day, the relative risk is 1.27 (Pitiphat et al. 2003).

Gamma-glutamyl transpeptidase enzyme serum levels are elevated in case of liver damage by chronic alcohol intake. Severe alcohol use with plasma gamma-glutamyl transpeptidase level greater than 51 IU/L is significantly associated with periodontal parameters such as plaque index, gingival margin

level, gingival index, probing depth, and attachment loss (Khocho et al. 2003).

Elevated levels of reactive oxygen species following chronic alcohol consumption induce an increased periodontal inflammation, high oxidative damage, and elevated tumor necrosis factor- α concentrations. In rats with ligature-induced periodontitis, ethanol feeding decreases the ratio of reduced oxidized glutathione. Alcohol intake increases polymorphonuclear leukocyte infiltration, tumor necrosis factor- α production, and gingival oxidative damage (Irie et al. 2008).

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Chapter 2 Diabetes and Periodontitis

Jean-Pierre Dibart, MD

INTRODUCTION

Definitions

The characteristic metabolic disorder in diabetes is hyperglycemia. Diabetes mellitus is characterized by chronic elevated levels of glucose in the blood. The diagnosis of diabetes is made with fasting plasma glucose levels of 126 mg/dL or greater. Diabetes mellitus results from a dysregulation of glucose metabolism due to the decreased production of insulin by the β cells of islets of Langerhans in the pancreas.

Diabetes is a chronic disease of adults and children and is of two types:

1. diabetes mellitus type 1, which occurs predominantly in youth, although it can occur at any age, and
2. diabetes mellitus type 2, which is the most prevalent type of diabetes and which occurs predominantly in overweight people.

High levels of glycosylated hemoglobin (HbA1c) are the result of elevated blood glucose levels over a period of a few months before the day of blood analysis. HbA1c is a good measure of long-term glucose levels. The normal serum levels of glycosylated hemoglobin are between 4% and 6% (Ship 2003). Severely elevated levels are greater than 9%, and mildly elevated levels are between 7% and 9% (Madden et al. 2008).

Glycemic control is based on following factors:

- better nutrition
- weight loss
- self-monitoring of blood glucose levels
- prevention and treatment of infections (Madden et al. 2008)

Complications

Poorly controlled blood glucose level is the principal cause of vascular complications. There are two types of cardiovascular complications in diabetes:

1. Macrovascular pathology or macroangiopathy, with increased risk of myocardial infarction, peripheral arterial disease, and stroke.
2. Microvascular pathology or microangiopathy, with
 - retinopathy and vascular damage of the retina;
 - nephropathy, with renal failure, renal insufficiency, and end-stage renal disease;
 - neuropathy of peripheral nerves;
 - poor wound healing;
 - enhanced risk of infection; and
 - periodontal disease.

Diabetic microangiopathy is responsible for compromised delivery of nutrients to tissues and poor elimination of metabolic products. Diabetes induces most of its complications on blood vessels, on large vessels with macroangiopathy, and on small vessels with microangiopathy.

Uncontrolled diabetes with poor glycemic control is a risk factor for severe periodontitis. The treatment of periodontitis improves glycemic control (Boehm and Scannapieco 2007). Mean advanced alveolar bone loss is significantly associated with eye vascular complication or retinopathy, with an odds ratio of 8.86 (Negishi et al. 2004). *Porphyromonas gingivalis* is capable of invading endothelial cells causing vascular damage; infection worsens glycemic control inducing hyperglycemia and increases the severity of microvascular and macrovascular pathology (Grossi et al. 2001).

Patient Management

Periodontitis may influence the severity of diabetes because of inflammation and uncontrolled glucose levels, and treatment of periodontal disease may be beneficial to diabetes control. Health education to encourage better oral care is necessary to reduce the prevalence of the diabetic disease and its complications.

For dentists, knowledge of the general and oral signs of diabetes are necessary. Dentists must be prepared to manage diabetic emergencies:

- low blood glucose levels or hypoglycemia (the most frequent complication)
- high blood glucose levels or hyperglycemia, with possible ketoacidosis or coma.

Dentists should be aware of circumstances that can induce hyperglycemia, such as infections, corticosteroids, surgery, stress, and medications, or circumstances that can induce hypoglycemia, such as an inappropriate diet or treatment and associated medications (Ship 2003).

Diabetes care should include personal glucose monitoring with blood tests. Regular care should also include laboratory information regarding levels of blood glucose, glycosylated hemoglobin for glycemic control, leukocyte count for infections, C-reactive protein for inflammation, and creatinine for renal failure. Before any oral procedure, fasting glucose and glycosylated hemoglobin must be checked (Taylor 2003).

In case of surgery, antibiotic therapy may be used to prevent or treat oral infections, because opportunistic infections are more frequent with uncontrolled diabetes.

Endodontic and periodontic lesions of teeth are associated with hyperglycemia and may necessitate a sudden increase in insulin demand in order to normalize glucose levels. But after dental and periodontal treatment, the insulin need returns to baseline (Schulze, Schonauer, and Busse 2007).

Diabetes and Periodontitis

Periodontitis is twice as prevalent in diabetic patients than in healthy subjects (Grossi et al. 2001). Diabetes is a modifying and aggravating factor in the severity of periodontal disease. Periodontitis results from an interplay of bacterial infection and host response. Severe periodontitis often coexists with diabetes mellitus; periodontitis increases the severity of diabetes and complicates metabolic control. Infection and advanced glycation end products–mediated cytokine response is responsible for periodontal tissue destruction. The host response to infection is an important factor in extension and severity of periodontal disease; periodontitis severity and prevalence are increased in diabetes. Diabetes and periodontitis can both stimulate chronic production of inflammatory cytokines. These cytokines are elevated in periodontitis and may in turn predispose to diabetes. Cytokines can promote insulin resistance and cause the destruction of pancreatic beta cells, inducing diabetes (Duarte et al. 2007; Grossi 2001; Iacopino 2001; Kuroe et al. 2006; Nassar, Kantarci, and van Dyke 2000; Nibali et al. 2007; Nishimura et al. 2003; Novak et al. 2008). Oral diseases are associated with diabetes. Periodontitis is a risk factor for poor glycemic

control and complications of diabetes. Sometimes periodontitis may be the first clinical manifestation of diabetes (Lamster, Lalla, and Borgnakke 2008). Periodontal indices, such as probing depth, attachment loss, and tooth loss, are significantly higher in diabetes family members (Meng 2007). There is a significant association between diabetes and deep probing depths and severe alveolar bone loss (Negishi et al. 2004). Periodontal infection is responsible for chronic inflammation, periodontal tissue destruction, and impaired tissue repair (Iacopino 2001).

Periodontal Therapy

Successful anti-infectious periodontal therapy has a beneficial effect on metabolic control of type 2 diabetes and glucose regulation. Proinflammatory cytokines, such as tumor necrosis factor- α (TNF- α), produced from excess amount of adipocytes, are responsible for lowered insulin sensitivity, called *insulin resistance*, and hyperglycemia. Diabetes can affect the periodontal tissues and the treatment of periodontal disease. Successful antimicrobial periodontal therapy may then result in improved insulin resistance and better glycemic control (Grossi et al. 1997; Katz 2005; Lalla, Kaplan et al. 2007; Madden 2008; Navarro-Sanchez, Faria-Almeida, and Bascones-Martinez 2007; O Connell 2008). Diabetes and periodontitis are secondary to chronic inflammation, altered host response, or insulin resistance. Periodontitis is associated with an elevated systemic inflammatory state and increased risk of hyperglycemia. Periodontal therapy that causes the decrease of oral bacterial load and reduction of periodontal and systemic inflammation can improve blood glucose control (Mealey and Rose 2008).

TYPE 2 DIABETES MELLITUS

Periodontal Treatment

Preventive periodontal therapy should be intense enough to reduce periodontal inflammation and glycosylated hemoglobin levels. Periodontitis treatment should include scaling, root planing, oral hygiene instruction, and chlorhexidine rinse treatment (Madden et al. 2008). After nonsurgical periodontal therapy, significant probing depth reduction is observed after full-mouth scaling and root planing, with improvement in glycemic control and reduction in glycosylated hemoglobin levels (Rodrigues, Taba, and Novaes 2003). After full-mouth subgingival debridement in diabetic patients, many subgingival bacterial species are reduced, such as *P. gingivalis*, *Tannerella forsythensis*, *Treponema denticola*, and *Prevotella intermedia*. *P. gingivalis* is detected more frequently in patients with increased glycosylated hemoglobin levels and worse glycemic control (Makiura et al. 2008). After periodontal therapy, including scaling, root planing, and doxycycline, there is a significant reduction of 1.1 mm in probing depth, a reduction of 1.5% in glycosylated hemoglobin levels, and reduction in

serum inflammatory mediators such interleukin-6 (IL-6) and granulocyte colony-stimulating factor (O'Connell et al. 2008). After subgingival scaling and root planing, patients show significant reduction in total gingival crevicular fluid volume and levels of IL-1 β and TNF- α . There is an improvement in metabolic glycemic control, with significant reduction in glycosylated hemoglobin, at 3 and 6 months after treatment (Navarro-Sanchez, Faria-Almeida, and Bascones-Martinez 2007). Periodontitis can contribute for poorer glycemic control in diabetes. IL-6, IL-1 β , and TNF- α are produced in response to periodontopathic bacteria and can modify glucose metabolism. Periodontal therapy has a beneficial effect on glycemic control. Diabetic patients should receive regular oral examination for periodontitis prevention and periodontal treatment (Taylor 2003). After full-mouth subgingival debridement, the percentage of macrophages releasing TNF- α decreases significantly by 78%, high-sensitivity C-reactive protein decreases significantly by 37%, and soluble E selectin decreases by 16.6% (Lalla, Kaplan, et al. 2007). After periodontal therapy including doxycycline, there is great reduction in probing depth and subgingival *P. gingivalis* concentrations. Treatment can improve glycemic control. Patients receiving periodontal treatment show a reduction of periodontal inflammation and significant reduction in mean glycosylated hemoglobin levels about 10% (Grossi et al. 1997). In diabetics local minocycline administration in every periodontal pocket once a week for a month significantly reduces the serum TNF- α levels, with an average reduction of 0.49pg/mL (Iwamoto et al. 2001).

Advanced Glycation End Products

Nonenzymatic reaction of glucose with amino acids in proteins leads to accumulation of irreversible molecules called *advanced glycation end products*. They promote inflammatory response and the production of reactive oxygen species. Tissue destruction is associated with oxidative stress due to the imbalance between reactive oxygen species and antioxidant defense. Oxidative stress can damage proteins, lipids, and DNA. Glycation end products can interact directly or indirectly by reacting with receptors for advanced glycation end products. Hyperglycemia causes the production of advanced glycation end products and reactive oxygen species, which are responsible for oxidative damage leading to vascular complications. Inflammatory response is secondary to the action of advanced glycation end products, which induce production of reactive oxygen species and inflammatory mediators (Nassar, Kantarci, and van Dyke 2007). In diabetes, glycation and oxidation of proteins and lipids lead to the formation of advanced glycation end products and promotion of oxidative stress in periodontal tissues. There is an increased immunoreactivity for advanced glycation end products in the gingiva of diabetics, with increased oxidant stress in periodontal tissues (Schmidt et al. 1996). Elevated levels of blood glucose lead to the production of irreversible advanced glycation end products, which are partly respon-

sible for development of diabetic vascular complications. They induce the production of inflammatory mediators and tissue-destructive enzymes. Activation of receptors for advanced glycation end products causes enhanced inflammation and tissue destruction. Chronic accumulation of advanced glycation end products is responsible for the destruction and inflammation in diabetic periodontium (Lalla et al. 2000). Diabetes promotes degenerative vascular changes in gingival tissues. Vascular degeneration worsens with poor glycemic control and duration of diabetes. Hyperglycemia induces alteration of gingival collagen by amino-acid nonenzymatic glycation and formation of advanced glycation end products, with production of modified collagen and poor wound healing. Advanced glycation end products induce oxidant stress and interact with receptors for advanced glycation end products, with production of enzymes, cytokines, and inflammatory mediators (Ryan et al. 2003). Serum advanced glycation end products are significantly associated with aggravation of periodontitis (Takedo et al. 2006). Advanced glycation end products and their receptors are involved in the pathogenesis of periodontitis. Receptors for advanced glycation end products are expressed in gingival tissues from diabetic patients with periodontitis. The expression of receptors for advanced glycation end products is positively correlated with TNF- α levels (Meng 2007). Receptors for advanced glycation end products are present in human periodontium. Advanced glycation end products, through interaction with their receptors, have destructive effects on gingival tissues in patients with periodontitis and diabetes (Katz et al. 2005).

Impaired Glucose Tolerance

Impaired glucose tolerance after an oral glucose tolerance test may be the symptom of a prediabetic state. Impaired glucose tolerance is significantly associated with periodontitis and alveolar bone loss. Having deep pockets is significantly associated with past glucose intolerance. The proportion of subjects with impaired glucose tolerance increases significantly in patients in the higher tertiles of alveolar bone loss (Saito et al. 2006). A significant 3.28 times increase of alveolar bone loss is present among patients with newly diagnosed diabetes, compared with people with normal glucose tolerance (Marugame et al. 2003). Experimentally high-fat-fed periodontitis rats develop more severe insulin resistance, and they present earlier impaired glucose tolerance (Watanabe et al. 2008). Prediabetic rats with periodontitis present increased impaired glucose tolerance. Periodontitis in prediabetic rats is associated with increased fasting glucose and increased insulin resistance (Pontes Andersen et al. 2007).

Glycated Hemoglobin

Periodontitis patients with diabetes present significantly higher glycated hemoglobin levels (Jansson et al. 2006).

Periodontitis is associated with high values of glycated hemoglobin (greater than 9%), with an odds ratio of 6.1. Mean advanced alveolar bone loss is also significantly associated with high glycated hemoglobin levels, with an odds ratio of 4.94. High values of glycated hemoglobin are significantly associated with advanced periodontitis, presenting more than 50% mean alveolar bone loss and two or more teeth with probing depth greater than 6mm (Negishi et al. 2004). Hyperglycemia induces inflammatory cytokine production and periodontal inflammation. Glycated hemoglobin level greater than 8% is significantly associated with gingival crevicular fluid IL-1 β levels. Probing depth, attachment levels, bleeding on probing, and random glucose are significantly associated with gingival crevicular fluid IL-1 β levels (Engebretson et al. 2004). Patients with glycated hemoglobin levels greater than 9 percent have a significantly higher prevalence of severe periodontitis, with an odds ratio of 2.9 (Tsai, Hayes, and Taylor 2002). Periodontal therapy may improve HbA1c levels. After full mouth scaling and root planing, there is a significant reduction in glycated hemoglobin levels (Rodrigues et al. 2003). Local minocycline administration in every periodontal pocket significantly reduces serum glycated hemoglobin levels, with an average reduction of 0.8% (Iwamoto et al. 2001).

Systemic Inflammation

In periodontal inflammation, IL-1 β , IL-6, IL-8, and interferon gamma levels are higher in gingival tissues. IL-1 β and IL-6 are elevated in cases of diabetes and periodontitis (Duarte et al. 2007). In diabetes hyperglycemia is associated with higher levels of inflammatory cytokines, TNF- α , IL-1 β , and IL-6. They are responsible for initiation and progression of inflammation and periodontal disease severity (Nassar, Kantarci, and van Dyke 2007). Circulating TNF- α is produced by adipocytes in adipose tissue of obese patients and is responsible for insulin resistance. TNF- α concentrations are significantly correlated with periodontitis severity, attachment loss, and gingival crevicular fluid IL-1 β levels (Engebretson et al. 2007). TNF- α is produced by adipocytes, macrophages, and monocytes. It is elevated in obese patients and decreases with weight loss. It is responsible for hyperglycemia due to insulin resistance (Nishimura et al. 2003). Persistent elevation of TNF- α , IL-1 β , and IL-6 levels is responsible for damage to the liver cells, release of acute-phase proteins, dyslipidemia, and damage to pancreatic β cells (Grossi 2001). People with diabetes have dyslipidemia with elevated levels of low-density lipoprotein cholesterol and triglycerides. Periodontitis may also lead to increased low-density lipoprotein cholesterol and triglyceride levels. Periodontitis causes systemic bacteremia with elevated serum IL-1 β and TNF- α levels, which are responsible for metabolic disorders and dyslipidemia (Iacopino 2001). TNF- α produced by periodontal inflammation is responsible for altered glucose regulation and insulin resistance (Iwamoto et al. 2001).

Clinical Parameters

Diabetes is associated with significantly more calculus formation, tooth loss, and increased severity of periodontitis. Patients have three times higher mean attachment levels and frequency of probing depth greater than 6mm than non-diabetic patients. There is also a significantly higher frequency of sites with attachment levels greater than 3mm (Novak et al. 2008). Diabetes patients show a

- significant increased prevalence of periodontitis
- significant lower number of teeth
- significant increase in probing depths greater than 4 mm and pocket depths greater than 4 mm
- significant association with bleeding on probing
- significant association with plaque
- significant association with the presence of *P. gingivalis* and *T. forsythensis* (Campus et al. 2005).

Severe generalized periodontitis is associated with low-grade systemic inflammation, and with significantly increased blood leukocyte counts.

The metabolic modifications include dyslipidemia with significantly lower high-density lipoprotein cholesterol and higher low-density lipoprotein cholesterol, and significantly increased non-fasting glucose levels (Nibali et al. 2007). Diabetic patients present a positive association between the severity of periodontal infection and serum lipids. Especially high low-density lipoprotein cholesterol levels are significantly associated with antibody titer to *P. gingivalis* (Kuroe et al. 2006).

TYPE 1 DIABETES MELLITUS

Clinical Parameters

Patients with type 1 diabetes mellitus are predisposed to periodontitis. Children and adolescents with type 1 diabetes mellitus present significantly more plaque and more gingival inflammation. Periodontitis is associated with type 1 diabetes, with an odds ratio of 2.78. The severity of periodontal destruction is significantly associated with mean glycated hemoglobin and duration of diabetes. Periodontal disease prevalence depends on duration of diabetes, glycemic control, and importance of gingival inflammation (Dakovic and Pavlovic 2008). From 6 to 11 years old, and more so after 12, periodontal destruction is increased in type 1 diabetes. Diabetes is a significant risk factor for periodontitis, especially for 12- to 18-year-old children. Children with type 1 diabetes present significantly more dental plaque, gingival inflammation, and attachment loss (Lalla, Cheng, et al. 2006). Periodontal destruction is related to the level of glycemic metabolic control. there is a significant positive association between

mean glycated hemoglobin levels and periodontal disease, with an odds ratio of 1.31 (Lalla, Cheng, et al. 2007). Periodontal disease is significantly associated with mean duration of type 1 diabetes. Diabetes is significantly associated with a higher prevalence of *P. gingivalis* and *P. intermedia* presence in subgingival plaque samples. Serum immunoglobulin G antibody levels against *P. gingivalis* are significantly elevated in periodontitis patients with diabetes (Takahashi et al. 2001). Type 1 diabetic pregnant women present significantly higher plaque index, gingival inflammation, mean probing depth, and mean clinical attachment level (Guthmiller et al. 2001).

Chronic Inflammation

Hyperglycemia induces glycation of amino acids with production of advanced glycation end products, promoting inflammatory response with release of TNF- α and IL-6. People with diabetes have significantly higher gingival crevicular fluid, prostaglandin E₂, and IL-1 β levels. Type 1 diabetes patients have abnormal monocyte inflammatory secretion in response to lipopolysaccharide of *P. gingivalis*. Monocytes of diabetic patients secrete more prostaglandin E₂, TNF- α , and IL-1 β (Salvi, Beck, and Offenbacher 1998). Diabetic patients present a significantly higher TNF- α monocyte secretion in response to *P. gingivalis* lipopolysaccharide. These patients present an upregulated monocyte TNF- α secretion phenotype, which is associated with a more severe periodontal disease (Salvi et al. 1997).

Periodontal Therapy

Periodontal therapy has a beneficial effect on glycemic control in type 1 diabetes. Periodontitis treatment and prevention are necessary for a good metabolic control in type 1 diabetic patients (Taylor 2003). Young patients with diabetes should have regular periodontitis treatment and prevention in order to stop periodontitis progression and periodontal destruction (Lalla et al. 2006). Full-mouth disinfection applied every 3 months significantly improves periodontal status and glycemic control. After full-mouth disinfection, type 1 diabetes adult periodontitis patients present significantly lower plaque index, less bleeding on probing, less probing depth, and gain of clinical attachment (Schara, Medvesck, and Skaleric 2006).

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