

Diagnostic and Therapeutic Strategies for the Management of the Diabetic Patient

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ABSTRACT

The bridge between oral and systemic health exists and becomes more concrete as data continue to emerge in support of this relationship. The medical management of diabetes is affected by the presence of chronic infections, such as periodontitis. This article reviews the pathogenesis of periodontal disease as it relates to diabetes. The author discusses patient susceptibility in terms of risk and recommends risk assessment to determine optimal treatment strategies. Patients with poorly controlled diabetes are at greater risk for developing periodontitis. The opportunity for systemic exposure to periodontal pathogens and pro-inflammatory mediators associated with periodontitis is discussed relative to their specific effects on patients with diabetes. The importance of good metabolic control in terms of risk for developing long-term complications of diabetes is presented and the impact of periodontitis on achieving adequate metabolic control is described. Special considerations for the management of patients with diabetes in the dental office are reviewed, including the signs and symptoms of diabetes, risk assessment for diabetes, and the challenges of “tight control” with insulin and oral agents with regards to hypoglycemia. It is recommended by the author that a thorough medical history of the patient be obtained, that the patient’s medications are known, that the dentist consults with the patient’s physician to assess the patient’s glycemic control, and that the patient’s blood glucose levels and dietary intake be monitored before treatment. Finally, the author reviews the long-term complications of diabetes, particularly the oral complications that can affect overall health. The author concludes with the belief that the treatment of periodontal diseases should not be considered optional or elective but, instead, should be a necessary and integral part of a patient’s overall health care program.

The bridge between oral and systemic health has been reinforced during the past decade by multiple publications describing this important connection in both dental and medical journals. The oral focus of these publications has been on periodontal diseases, which are the most common dental conditions. It is known that a number of systemic diseases, including diabetes, can increase an individual’s risk for developing periodontitis, which is a chronic and progressive disease with no known cure.

However, periodontal disease is certainly treatable and may even be prevented by appropriate risk assessment and risk reduction strategies. Conversely, untreated periodontal disease has been linked to an increased risk for developing certain systemic conditions as well as difficulties in managing certain systemic conditions. The medical management of diabetes is affected by the presence of chronic infections, such as those seen in patients with periodontitis. These links between oral and systemic health have led to the

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belief that the treatment of periodontal diseases should not be considered optional or elective but, instead, should be a necessary and integral part of a patient's overall health care program.

THE PATHWAY TO PERIODONTAL DISEASE

Understanding the pathway to periodontitis is essential because it enables clinicians, researchers, and patients to consider the possible mechanisms by which oral-systemic connections occur (Figure 1).¹ It is a microbial challenge to the host or person with poor oral hygiene that initiates the cascade of events that can result in periodontal breakdown. The presence of bacterial endotoxins, antigens, and other virulence factors stimulate the host immuno-inflammatory response. Neutrophils are recruited to the site of the infection to address the pathogenic microbes, which then invoke an antibody response. In more resistant individuals,

these events lead to the development of localized reversible inflammation, known as gingivitis. In more susceptible individuals, very high levels of pro-inflammatory mediators—known as cytokines, prostanoids, and matrix metalloproteinases—will be produced by the host, leading to connective tissue breakdown and bone metabolism changes associated with the bone loss that is pathognomonic to periodontitis. In the clinical setting, this cascade of events presents as the signs of disease: increases in probing depth, loss of clinical attachment, and radiographic evidence of bone loss. So the question becomes, “Who are these susceptible individuals?”

Genetics plays a significant role in who may be susceptible. Studies have shown that at least 50% of all cases of periodontal disease have some genetic component.² In addition, there are a number of environmental and acquired risk factors that put patients at greater risk (Table 1). Risk assessment is impor-

tant because it has been recognized that the more risk factors a patient has, the more likely he or she is to develop the disease. There is often more than an additive effect, there is a synergistic effect between these risk factors.

Identification and consideration of these risk factors is critical to successful periodontal treatment because they can affect the onset, the rate of progression, and the severity of periodontal disease. In addition, these risk factors may determine treatment strategies and explain variability in the therapeutic responses of patients. Risk factor assessments can alter the way patients are viewed by the practitioner, leading to a decision process based on risk. The primary goal of the practitioner would be risk reduction. A simple example of this would be improvements in oral hygiene since it has long been known that poor oral hygiene increases the risk of disease. A clinician may proceed with caution if a patient presents with multiple risk factors. In

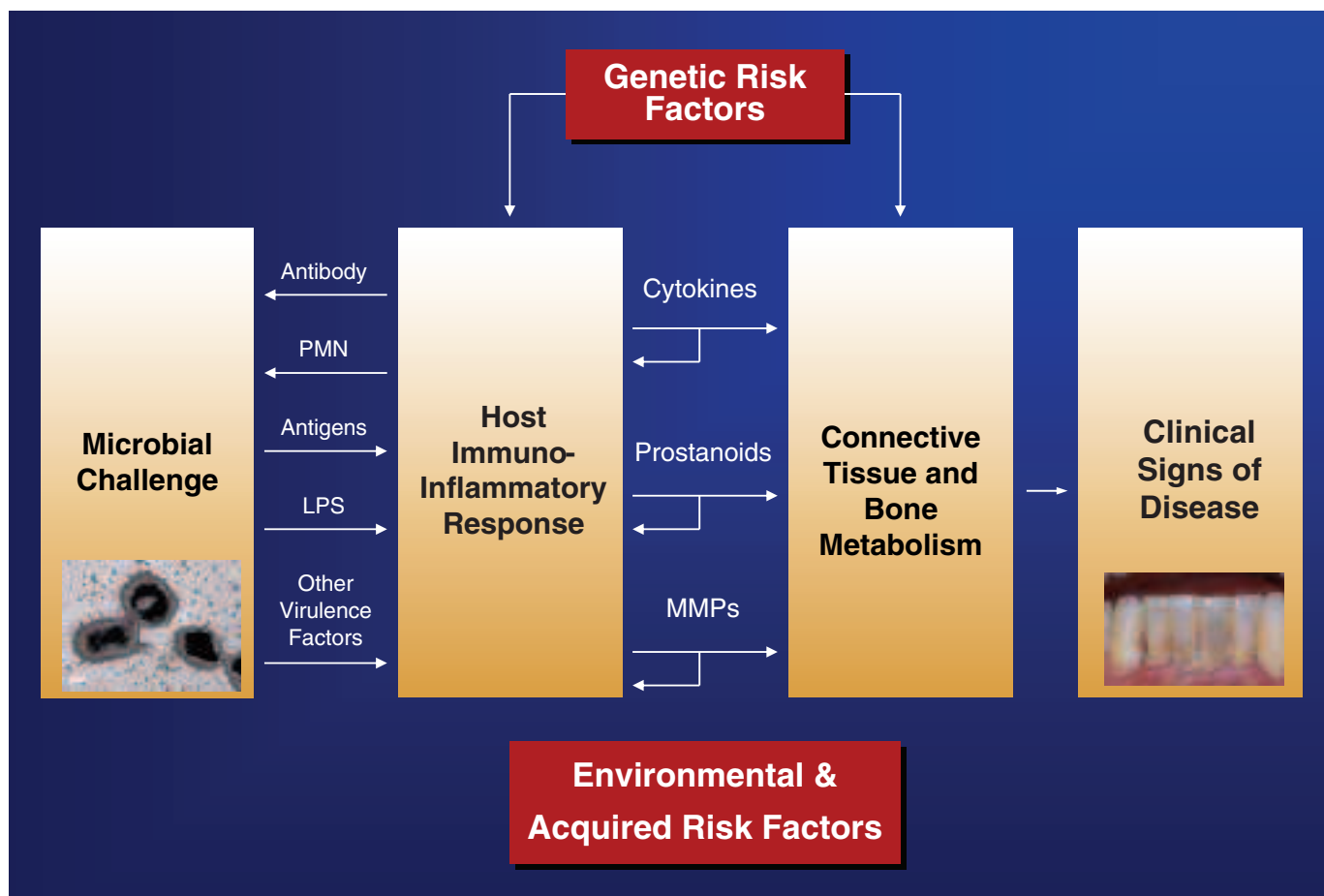


Figure 1 The pathway to periodontal disease through which clinicians consider how oral-systemic connections occur.

PMN = polymorphonuclear leukocytes. LPS = lipopolysaccharides. MMPs = matrix metalloproteinases.

addition, patients begin to be viewed in terms of risk when considering how treatment should proceed. Depending on the type of risk (eg, the presence of a systemic condition such as diabetes), the clinician will interact more with our medical colleagues in an attempt to reduce the risk.

Ultimately, as part of a risk assessment, risk reduction for periodontal disease needs to be considered. Risk reduction strategies are listed in Table 2. Obviously, the more risk factors a patient has, the more frequent his or her dental visits should be, including more intensive periodontal therapy and follow-up maintenance. Certain risk factors can be modified while others cannot (eg, heredity). Once this is determined, the appropriate therapeutic regimens can be utilized, including the use of adjunctive medications that may be administered to the patients that have been referred to as “perioceutics” in the past.³ Locally applied or systemically delivered antimicrobials may be one choice; host modulatory agents are another, which may be ideal for patients who cannot reduce their risk (such as patients who have a genetic predisposition). For smokers, smoking cessation is the obvious first step, but what if the patient will not stop smoking? Cutting back on tobacco use may help, but other strategies would need to be considered in those patients who cannot or will not stop smoking. In diabetic patients, the patient’s physician should be consulted to help the patient achieve better metabolic control of his or her diabetes to facilitate an optimal response to periodontal therapy. Patients who are unable to control their diabetes will be much more difficult for the oral health care provider to manage and may require the use of adjuncts to traditional mechanical therapy, such as antimicrobials and host modulatory therapy as part of their treatment regimen.

ORAL–SYSTEMIC EXPOSURE

The presence of periodontitis can present a significant challenge to the entire body. The surface area of the pocket epithelium is estimated to be the equivalent to the surface area of the palm of

TABLE 1:
Risk Factors for Periodontal Disease

Heredity
Family history PST-test
Smoking
Frequency (current, past)
Diabetes
Duration, control
Stress
Reported by patient
Medications
Calcium channel blockers Dilantin Cyclosporin Known to cause dry mouth
Nutrition
Poor oral hygiene
Plaque and calculus
Faulty dentistry
Overhangs Subgingival margins
Hormonal variations
Pregnancy Increased estradiol and progesterone Menopause Decreased estrogen Osteoporosis
Immunocompromise
Human immunodeficiency virus Neutropenia
Connective tissue diseases
Previous history of periodontitis

one or even two hands, depending on the severity of the periodontal disease. If a patient had an equivalent challenge anywhere else on the body, it certainly would be of concern. The problem is that many people do not have any signs or symptoms of periodontal disease,

TABLE 2:
Risk Management for Periodontal Disease

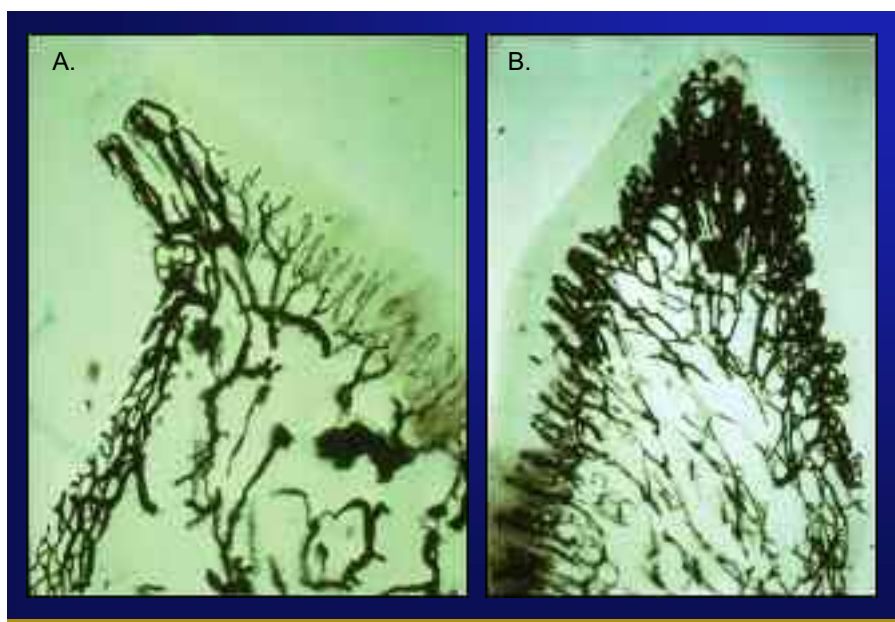
Heredity
Perioceutics
Smoking
Cessation Perioceutics
Diabetes
Improved control Work with medical doctor Perioceutics
Stress
Management Perioceutics
Medications
Change in medications Work with medical doctor Perioceutics
Nutrition
Supplements
Poor oral hygiene
Improved oral hygiene Perioceutics
Faulty dentistry
Corrective dentistry
Hormonal variations
Consult with medical doctor Perioceutics
Immunocompromise
Consult with medical doctor Perioceutics
Connective tissue diseases
Consult with medical doctor Perioceutics

resulting in an often silent disease. In addition, the presence of deep inflamed pockets is not directly visible to those who have periodontal disease; therefore, they do not recognize the challenge that exists in the oral cavity. It is important for dental practitioners to express this

not only to their patients but also to physicians because many physicians are often unaware of the significant challenge that oral infection and inflammation can present to the entire body. If the periodontitis is not treated, these bacteria will eventually enter into the bloodstream, attracting platelets and putting patients at greater risk for a number of systemic diseases, including cardiovascular disease, which is the number one cause of mortality among people with diabetes.

The systemic exposure to periodontal pathogens is a result of the loss of the epithelial integrity within the periodontal pockets in people with periodontal disease, allowing for bacterial penetration into the tissues and eventually the bloodstream, resulting in a bacteremia. If periodontal disease is left untreated, every time the patient eats, he or she will have a recurrent transient bacteremia. Oral pathogens have been found throughout the body, in fetal cord blood, and in atheromatous plaques.⁴ Endotoxins can

also penetrate into these tissues resulting in endotoxemia. Many of the pro-inflammatory mediators present in patients with periodontitis can be found not only within the gingival crevicular fluid flowing out of their pockets but also within the gingival tissues and alveolar bone and eventually in the bloodstream, resulting in elevated levels of Interleukin-1 and 6, tumor necrosis factor, and prostanooids. Figures 2A and 2B demonstrate the differences in the vascularity of healthy versus inflamed gingival tissue.⁵ When there is inflammation, there is much more vascularity, a greater chance for bacteremias and endotoxemias to occur, and more chances for the inflammatory mediators to enter into the system. Once in the system, all of these factors can have a profound effect on the patient, particularly the diabetic patient, leading to insulin resistance and resulting in difficulties in achieving metabolic control of the diabetes.



Figures 2A and 2B The differences in the vascularity of (A) healthy gingival tissue versus (B) inflamed gingival tissue.

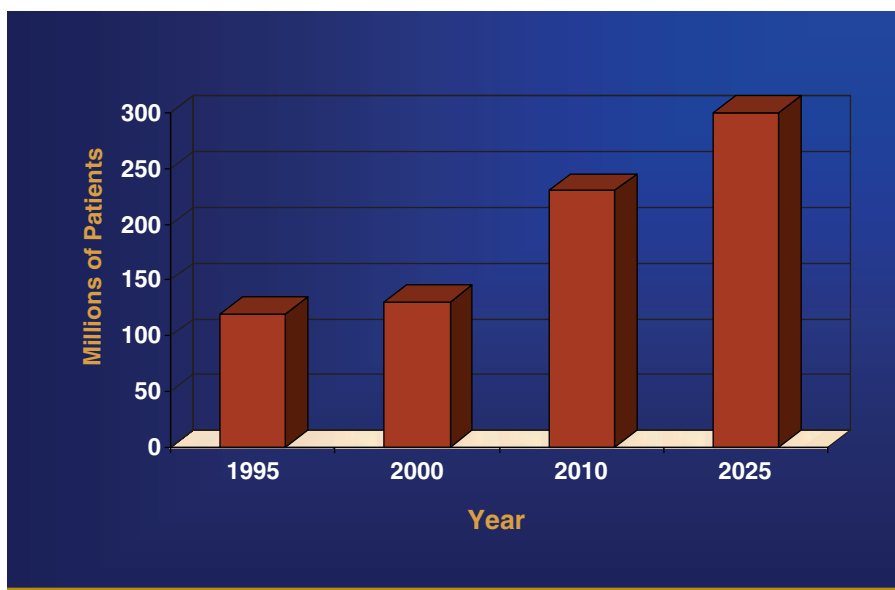


Figure 3 It is estimated that by the year 2025, the number of people in the world with diabetes will approximate 300 million, which is considered a global epidemic.

DIABETES

The link between periodontal and systemic health is a two-way street, particularly when it comes to periodontitis and diabetes mellitus. There are a number of systemic diseases and conditions that can increase a patient's susceptibility to periodontitis, and top on the list is diabetes mellitus. Conversely, periodontal infections can have an impact on systemic health, and diabetes tops the list once again in that if you have untreated periodontitis, it can impede the metabolic control of diabetes.

In 1995, there were approximately 110 million people with diabetes worldwide. However, if the numbers are projected to the year 2025, it is estimated that the number of people in the world with diabetes will approximate 300 million, which is considered a global epidemic (Figure 3).⁶ In the United States in 1995, there were approximately 12 million people with diabetes, and it is estimated that in 2025 the numbers will reach more than 20 million (Figure 4).⁶ In China, the estimated rise is much more rapid, going from the same 12 million in 1995 to nearly 40 million people with diabetes by the year 2025. In Europe,

the numbers of people with diabetes fall somewhere between those reported in the United States and China. The greatest numbers of people with diabetes in the world is expected in India, where by the year 2025 it is estimated that more than 55 million people will have diabetes. It is believed that the greatest growth of patients will be in Asia where it is predicted by the year 2010, more than 60% of all patients suffering from diabetes will live.

Why is there such a rise? The reasons include increasing longevity, change in demographics, and genetic predispositions. Rising urbanization and changes in lifestyle play a role as well as an increased prevalence of obesity. In the United States, obesity is known to play a role, where more than 60% of the adult population is considered to be either overweight or obese. There are approximately 18 million people with diabetes currently in the United States, with 798,000 new cases diagnosed yearly.⁷ In addition, 90% to 95% of all cases in the United States are type 2. This presents a substantial health care problem in light of the long-term complications of the disease. Diabetes is the leading cause of blindness in adults. End-stage renal disease, cardiovascular complications, and nontraumatic amputations are additional complications, and the health care costs are immense: \$98.2 billion annually.⁸

The Diabetes Control and Complications Trial (DCCT) found that improved control of blood glucose reduces the risk of a number of long-term complications, particularly retinopathy, nephropathy, and neuropathy (Figure 5).⁹ Data for reductions in cardiovascular disease are emerging as well.¹⁰ According to the DCCT trial, the risk of sustained retinopathy progression (gauged by glycosylated hemoglobin [HbA1c]) in years of follow-up is in those patients with higher HbA1c levels (Figure 6).¹¹ As a result of these findings, the major objective of physicians is reducing and maintaining low levels of HbA1c, which is a long-term marker of control (unlike blood glucose which fluctuates daily as we eat). HbA1c levels of 4% to 6% are normal, <7% is considered good diabetes control, 7% to 8% is moderate control, and with >8% action is suggested to

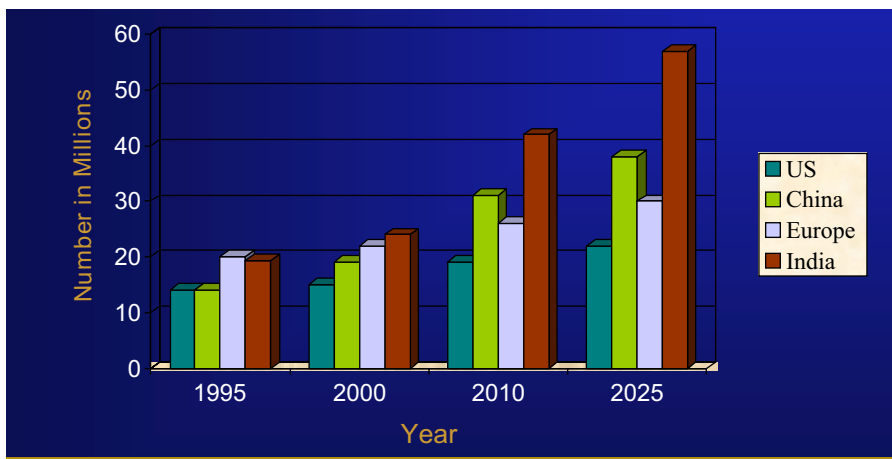


Figure 4 The projected number of diabetics to the year 2025 worldwide. The greatest number of diabetic people in the world will be in India.

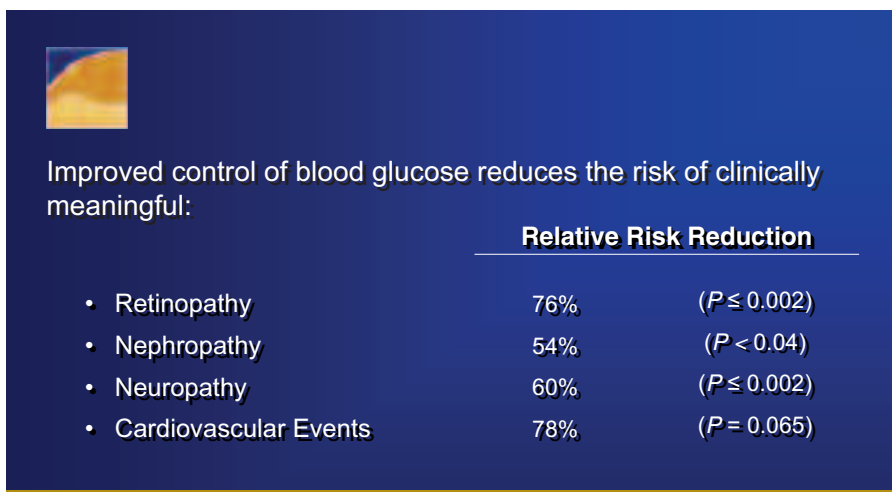


Figure 5 Results from the Diabetes Control and Complication Trial found the improved control of blood glucose reduces the risk of some long-term complications.^{9,10} (Figure 2006 © Thomson Professional Postgraduate Services®. All rights reserved.)

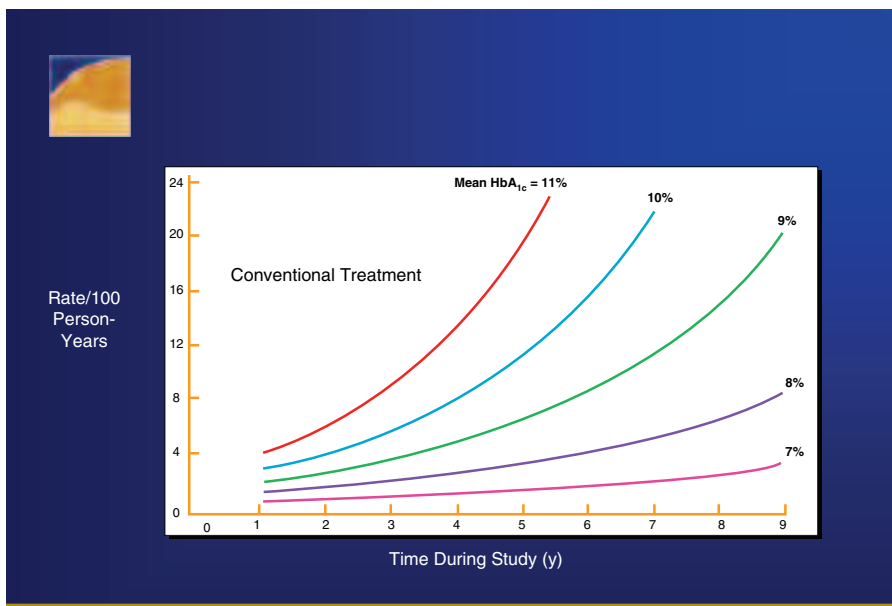


Figure 6 The risk of sustained retinopathy progression in years of follow-up is in those patients with higher HbA1c levels.¹¹ (Figure 2006 © Thomson Professional Postgraduate Services®. All rights reserved.)

TABLE 3:**Classic Signs and Symptoms of Diabetes Mellitus**

- Polydipsia, polyuria, nocturia, polyphagia
- Unexplained weight loss
- General fatigue
- Increased infections
- Leg cramps
- Numbness in the extremities
- Impotence
- Blurred vision

improve control. Currently, blood levels of glucose and HbA1c can be determined chairside. Glycated serum protein levels are an emerging intermediate marker of control, but HbA1c levels are most commonly used today to determine long-term control in the diabetic patient. It is the primary objective of most physicians to keep these levels low to prevent long-term complications.

DENTISTS AND DIABETES

How does this relate to the practicing dentist? Every dentist will encounter patients with diabetes. In the United States, where 6% to 7% of the population is diabetic, a dental practice of 2500 patients will most likely have 150 to 175 diabetic patients, and 50% of those patients may not even be aware they have the disease. It may be the dentist who picks up certain signs of diabetes and refers the patient to the physician. Dentists and physicians need to work together to better manage their patients with diabetes. In developing relationships with the physicians, the dentist may find that through referrals their practice will grow and they may be treating many more patients with diabetes.

Signs and Symptoms/Risk Assessment

It is important for dentists to recognize the classic signs and symptoms of diabetes, which should be taught as an

TABLE 4:**Laboratory Diagnostic Criteria for Diabetes Mellitus****Laboratory Methods (to be confirmed on subsequent day)**

- Classic symptoms and casual (nonfasting) plasma glucose ≥ 200 mg/dL
- Fasting plasma glucose ≥ 126 mg/dL
- Two-hour postprandial glucose ≥ 200 mg/dL during an oral glucose tolerance test
- Test performed with 75 g of anhydrous glucose dissolved in water

Categories of fasting plasma glucose (FPG)

- FPG < 110 mg/dL = normal fasting glucose
- FPG ≥ 110 mg/dL and < 126 mg/dL = impaired fasting glucose
- FPG ≥ 126 mg/dL = provisional diagnosis of diabetes (confirmed on next day)

Categories of two-hour postprandial glucose (2hPG)

- 2hPG < 140 mg/dL = normal glucose tolerance
- 2hPG ≥ 140 mg/dL and < 200 mg/dL = impaired glucose tolerance
- 2hPG ≥ 200 mg/dL = provisional diagnosis of diabetes (confirmed on next day)

integral part of the dental education process. Once diagnosed, it is equally important for the dentist to know how the diabetic patient should be appropriately managed in the dental office. Classic signs and symptoms include polydipsia, polyuria, nocturia, polyphagia, unexplained weight loss, general fatigue, and increases in infections (Table 3). Other symptoms are leg cramps, numbness in the extremities, impotence, and blurred vision. In a risk assessment for diabetes, age is a factor with most diabetics > 45 years of age (because most patients are type 2). However, the number of overweight adolescents with type 2 diabetes is growing rapidly, which is associated with the risk factor of obesity. There is a very strong genetic predisposition that occurs with type 2 diabetes; therefore, a family history of the patient is important. Other indicators include racial descent, gestational diabetes or a history of delivering a baby > 9 pounds, a history of impaired glucose tolerance and impaired fasting glucose, hypertension, and dyslipidemia. Gestational diabetes is a concern because many of the women who develop gestational diabetes will eventually develop type 2 diabetes. Of patients who have gestational diabetes, 30% to 50% will develop type 2 diabetes within 10 years. Once it is determined that a patient may be diabetic, he or she should be referred to the physician, and laboratory diagnostic criteria (Table 4)

will be conducted in the physician's office for a definitive diagnosis.

In an undiagnosed patient, particularly a type 1 diabetic, a life-threatening incident, such as ketoacidosis, can occur, which may be precipitated by systemic infection or stress. Therefore, dentists also need to know the signs and symptoms of ketoacidosis: nausea, vomiting, abdominal pain, dehydration, changes

TABLE 5:**Precipitants, Signs, and Symptoms of Hypoglycemia****Precipitants**

- Missed meals and snacks
- Excessive insulin dose
- Intensive treatment regimens or "tight control"
- Inattention to warning symptoms
- Recent exercise
- Alcohol and drugs

Signs and Symptoms

- Confusion
- Shakiness, tremors
- Agitation
- Anxiety
- Sweating
- Dizziness
- Tachycardia
- Feeling of "impending doom"
- Seizures
- Loss of consciousness

in respiration, altered mental status, and possible coma. These patients require immediate medical attention and additional laboratory findings to confirm ketoacidosis.

Insulin and Hypoglycemia

The only hormone that lowers blood glucose is insulin. As previously mentioned, physicians work diligently to reduce hyperglycemia to prevent the long-term complications of diabetes. An unfortunate event associated with intensive medical treatment regimens or “tight control” is low blood glucose or hypoglycemia. There are a number of hormones that can raise blood glucose, including: glucagon, catecholamines (epinephrine), glucocorticoids (cortisol), and growth and thyroid hormones. Many emergency kits in the dental office contain glucagon for the management of extreme cases of hypoglycemia. The important thing for the dentist to know about the different types of insulin is the time of peak activity after administration, because this is when patients are more prone to develop hypoglycemic episodes. Patients on insulin are susceptible to hypoglycemia as are patients on certain oral agents, especially the second generation sulfonylureas, which produce a relatively high incidence of hypoglycemia.

Some of the precipitants of hypoglycemia include missed meals and snacks (it is important to ask patients if they have eaten), intensive treatment regimens, an excessive insulin dose, inattention to warning symptoms, recent exercise, alcohol use, and drug use (Table 5). If the signs and symptoms of hypoglycemia (Table 5) are known to the dentist, he or she can detect it early and treat it very rapidly.

What preventative measures can be taken to help avoid this? A thorough medical history, consideration of the patient’s medications, the avoidance of visits at the peak activity periods of insulin and oral medications, consultation with the physician to assess the patient’s glycemic control, and of monitoring the dietary intake and blood glucose levels with a glucometer before treatment. In addition, it is important to recognize the signs and symptoms of low blood glucose and to administer a carbo-

TABLE 6:

Emergency Treatment of Hypoglycemia

Establish blood glucose level with glucometer (if possible)

In awake patient, give 15 g of carbohydrate orally as either:

- 120–180 mL (4–6 oz) fruit juice or sugared soda
- 3–4 teaspoons of table sugar
- hard candy
- cake frosting in a tube

In patient unable to use oral route with IV in place either:

- 25–30 mL of 50% dextrose (D50)
- 1 mg glucagon

In patient unable to use oral route without IV in place:

- 1 mg glucagon subcutaneously or intramuscularly

Monitor patient for 1 hour after recovery

Seek emergency medical assistance if patient does not respond

hydrate source in a timely manner. One major problem experienced with diabetic patients is that the greater the number of hypoglycemic events, the more likely it is that the patient will develop a condition known as hypoglycemia unawareness. Basically, this means that the patient will not experience the early signs and symptoms of hypoglycemia and may experience seizures and loss of consciousness fairly rapidly. Table 6 lists the steps for emergency treatment of the patient with hypoglycemia. Because a dentist may treat many people with diabetes, he or she should be prepared to manage the hypoglycemic patient.

Complications Compound Complications

The classic complications of diabetes (angiopathy, nephropathy, retinopathy, neuropathy, and wound healing problems) are of major concern to physicians and they should be to dentists as well. In the assessment of the diabetic patient, the dentist needs to know of any long-term complications of the disease because the more complications a diabetic patient has, the more likely the patient is to develop additional complications. Once the patient’s complications are determined, his or her medical and dental treatment can center on preventing the development of additional complications.

Periodontitis—The Sixth Long-Term Complication of Diabetes

There exists a two-way street between diabetes and periodontal disease in that diabetics are at a greater risk for developing infections and these infections can impair a diabetic’s metabolic control.¹² There are a number of periodontally relevant host-response abnormalities that occur in diabetic patients, which increases their risk for developing periodontitis such as vascular abnormalities, imbalances in lipid and collagen metabolism, and neutrophil dysfunction. In particular, the presence of glycated proteins such as advanced glycation end products (AGEs) can put a patient at higher risk for developing periodontitis as well as other long-term complications of diabetes. These altered proteins develop through a nonenzymatic process; as proteins bathe in blood with very high glucose levels they actually become glycated. These AGEs then interact with receptors on a number of different cells known as receptors for AGEs, or RAGEs, which results in an increase in pro-inflammatory mediators that can lead to the connective tissue breakdown seen in periodontitis. In addition, a number of growth factors are produced, which can result in the proliferation of cells and matrix known to play a role in retinopathy.



Figure 7 Paper strips may be used to measure the levels of the pro-inflammatory mediators.



Figure 8 Dentition of an adolescent girl with type 1 diabetes, poor metabolic control, and severe periodontitis.



Figure 9 This 55-year-old man with type 2 diabetes has obvious recession and loss of attachment.



Figure 10 A type-2 diabetic patient who has significant periodontitis, which may never be picked up by a cursory oral examination.



Figure 11 There can be very significant inflammation leading to abscess formation in patients with diabetes.



Figure 12 The enlargement of the parotid glands can lead to xerostomia, which contributes to the development of candidiasis, burning mouth and tongue, and caries.

Salvi and colleagues analyzed the gingival crevicular fluid of diabetic patients and found a fourfold increase of pro-inflammatory mediators compared with nondiabetic control subjects.¹³ This was believed to be a result of the hypersecretion of these factors by monocytes in the diabetic subjects. The subjects in this study were determined to be at risk for periodontitis because of excessive inflammation with an equivalent bacterial burden. Because of the major role these mediators play in the progression of their periodontal disease, future dental diagnostics may include measuring the levels of the pro-inflammatory mediators, which could particularly benefit diabetic patients. This test may take the form of paper strips placed into the periodontal pockets (Figure 7) from which the levels of cytokines, prostanoids, and enzymes in the gingival crevicular fluid can be measured; or the collective levels from all of the sites present in a patient may be measured using a mouth rinse technique.

In the future, dentists will most likely develop a closer relationship with physicians to monitor patients for changes in oral health. Figures 8 through 10 show examples of diabetic patients in whom periodontal disease is present. For the type 1 adolescent diabetic patient in Figure 8, the physician could most likely view the gingival inflammation during a cursory oral examination and refer the patient to the dentist for therapy. In Figure 9, the 55-year-old man with type 2 diabetes has obvious recession and loss of attachment. However, the patient in Figure 10 exemplifies a type 2 diabetic patient who has significant periodontitis, which may never be picked up by a cursory oral examination. In this case, probing depths and radiographs would be necessary for the detection of periodontitis. However, improvements in biochemical diagnostics for periodontitis might allow physicians, nurses, and even patients to send samples to a centralized laboratory for evaluation and preliminary detection of perio-

dontal inflammation and breakdown with subsequent referral to the oral health care provider for a complete oral evaluation and treatment.

Diabetic patients can also develop oral conditions other than periodontitis, including candidiasis and caries. It is often found that the level of disease does not correlate with the levels of bacteria or plaque (Figure 11). There can be very significant inflammation leading to abscess formation in patients with diabetes. Also, the enlargement of the parotid glands can lead to xerostomia or dry mouth, which contributes to the development of candidiasis and burning mouth and tongue as well as caries (Figure 12). The administration of antifungal agents may be necessary for the management of candidiasis. The management of oral burning symptoms can include the maintenance of adequate oral hydration and restrictions on the intake of caffeine and alcohol. In addition, preventive measures for infection and delayed wound healing need to be taught at all levels, because diabetics

are at greater risk for infection and delayed wound healing. The preventive measures involve frequent dental visits to assess plaque control, risk assessment profiles to identify risk, preoperative and postoperative antibiotic therapy if necessary, and the avoidance of compounding risk factors such as smoking.

MANAGING PERIODONTAL DISEASE IN THE DIABETIC

Periodontal health is particularly important in people with diabetes because it is known that bacterial infections decrease insulin-mediated glucose uptake by the skeletal muscle leading to whole-body insulin resistance. The presence of bacterial endotoxins and host-derived cytokines induce insulin resistance and decrease insulin action. Untreated periodontal disease results in chronic inflammation that leads to increased insulin resistance, reduced glucose tolerance, and an increased risk of diabetic complications. Two studies have demonstrated that diabetic subjects with severe periodontitis are at greater risk for developing nephropathy and cardiovascular disease, which can both affect mortality in this patient population.^{14,15} In an 11-year follow-up of subjects, Thorstensson and colleagues demonstrated that diabetics with severe periodontitis had a greater prevalence of proteinuria indicative of nephropathy and a greater number of cardiovascular complications.¹⁴ These oral-systemic connections in diabetics have been confirmed most recently by Saremi and colleagues,¹⁵ who reported that periodontal disease is strongly predictive of mortality from ischemic heart disease and diabetic nephropathy in a population of Pima Indians with type 2 diabetes. In an 11-year follow-up, the age- and sex-adjusted death rates of the type 2 diabetics increased with the severity of their periodontitis. There is no doubt that optimal oral health is essential to the medical management of the diabetic patient.

CONCLUSION

Important factors to consider in assessing the periodontal status of patients with diabetes are the patient's degree of

metabolic control, the duration of the disease, the presence of other long-term complications, and concurrent risk factors. Patients with more than one risk factor have an even greater risk for developing periodontitis. Nonmicrobial risk factors amplify the host response, which is most evident in individuals with diabetes and can be compounded by concurrent risk factors such as smoking and genetics. Therapeutic strategies should include reduction of bacterial infection, modulation of the host response, and risk reduction to help improve therapeutic outcomes in the susceptible diabetic patient. Improving diagnostics is important for early detection and intervention. In addition, for improved patient care, treatment plans should be individualized, patient education and motivation are paramount, and routine maintenance is necessary.

In conclusion, diabetes mellitus has a significant impact on the tissues throughout the body, including the oral cavity. Poorly controlled diabetes increases the risk for periodontitis. Periodontal infection and the treatment of periodontal disease can alter glycemic control. Early intervention and treatment of periodontitis may help to prevent the development of long-term complications of diabetes, such as nephropathy and cardiovascular disease thereby having an impact on mortality. The future will include a greater need for dental and medical practitioners to communicate and partner. The group practice of the future will most likely be the dentist and the physician working very closely together. Periodontal treatment may eventually be covered by medical insurance, which would include consultations, diagnostics, and therapeutics. The data emerging from studies of diabetic patients are important for establishing the absolute necessity for periodontal health. The treatment of periodontal disease should not be considered an option or elective and the demand for preventive care will increase. There is an urgent need for knowledge transfer, which will be facilitated by the integration of the emerging data and concepts into both dental and medical school curriculum at all levels.

REFERENCES

1. Page RC, Kornman KS. The pathogenesis of human periodontitis: an introduction. *Periodontol* 2000. 1997;14:9-11.
2. Michalowicz BS, Diehl SR, Gunsolley JC, et al. Evidence of a substantial genetic basis for risk of adult periodontitis. *J Periodontol*. 2000;71(11):1699-1707.
3. Ryan ME. Clinical applications for host modulatory therapy. *Compend Contin Educ Dent*. 2002;23(11A):1071-1082.
4. Haraszthy VI, Zambon JJ, Trevisan M, et al. Identification of periodontal pathogens in atheromatous plaques. *J Periodontol*. 2000; 71(10):1554-1560.
5. Novak MJ, Donley TG. Using host response modifiers in the treatment of periodontal disease. *Pract Proced Aesthet Dent*. 2002; 14(9):suppl 3-10.
6. World Health Organization. *Diabetes: Incidence and Prevalence Data*. Ref Type: Report; 1999.
7. Economic consequences of diabetes mellitus in the U.S. in 1997. American Diabetes Association. *Diabetes Care*. 1998;21(2): 296-309.
8. US Department of Health and Human Services, Centers for Disease Control and Prevention. *National Diabetes Fact Sheet: National estimates and general information on diabetes in the United States*. Atlanta, GA: NIH Publication No. 98-3926. Ref Type: Report; 1997.
9. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *N Engl J Med*. 1993;329(14):977-986.
10. Effect of intensive diabetes management on macrovascular events and risk factors in the Diabetes Control and Complications Trial. *Am J Cardiol*. 1995;75(14):894-903.
11. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. *Diabetes* 1995;44(8):968-983.
12. Loe H. Periodontal disease. The sixth complication of diabetes mellitus. *Diabetes Care*. 1993;16(1):329-334.
13. Salvi GE, Beck JD, Offenbacher S. PGE2, IL-1 beta, and TNF-alpha responses in diabetics as modifiers of periodontal disease expression. *Ann Periodontol*. 1998;3(1):40-50.
14. Thorstensson H, Kuylensstierna J, Hugoson A. Medical status and complications in relation to periodontal disease experience in insulin-dependent diabetics. *J Clin Periodontol*. 1996;23(3 Pt 1):194-202.
15. Saremi A, Nelson RG, Tulloch-Reid M, et al. Periodontal disease and mortality in type 2 diabetes. *Diabetes Care*. 2005;28(1):27-32.