

## Dentists, diabetes and periodontitis

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### Abstract

This review updates the relationship between diabetes mellitus and periodontitis. A checklist has been included to assist the general dental practitioner identify individuals with undiagnosed diabetes. The literature indicates a similar incidence of periodontitis exists between well-controlled diabetics and non-diabetics. However, a greater incidence and severity of periodontitis is observed in both Type 1 and 2 long-term diabetics with poor metabolic control. There is an undeniable link between diabetes mellitus and periodontitis with complex interactions occurring between these diseases. A critical review of the literature fails to support the notion that periodontal therapy has a beneficial effect on the long-term control of diabetes. We have explored the associations between periodontitis and diabetes in the hope of providing the general dental practitioner with the knowledge to support the diabetic patient with the best possible dental care and advice.

**Key words:** Diabetes mellitus, periodontitis, diagnosis.

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### INTRODUCTION

The links between diabetes and periodontitis have been extensively investigated and it is clear that poorly controlled diabetics have an increased susceptibility to periodontitis. This article provides an overview of diabetes mellitus and periodontitis and highlights the importance of the general dental practitioner in the detection of diabetes.

Diabetes mellitus is the most common endocrine disorder, characterized by an inability of the body's cells to utilize glucose. The cardinal feature of this condition is increased blood glucose level, resulting from decreased production of insulin, insulin dysfunction or lack of insulin receptor responsiveness at target organs, such as the skeletal muscles and liver. The prevalence of diabetes is not easy to determine because many diabetics remain undiagnosed, as up to

half of affected individuals remain unaware of their disease status.<sup>1</sup> In South Australian adults, the prevalence of Type 1 diabetes is 0.5 per cent and that of Type 2 diabetes is 3.2 per cent. Type 2 diabetes is the most common form of the disease and accounts for 86 per cent of all cases.<sup>2</sup> Diabetes is a current health priority for two reasons. Firstly, the ageing of the population will result in more people succumbing to the disease, with an estimated 25 per cent increase in the number of cases of diabetes.<sup>2</sup> Secondly, the prevalence is estimated to increase from 4.1 per cent in 1998 to 5.7 per cent in 2006, irrespective of the ageing of the population. Consequently, a substantial increase in the number of people with diabetes is anticipated in the near future.<sup>2</sup>

When considering risk factors, (factors which directly increase the probability of the disease occurring), it is well recognized that systemic diseases such as poorly controlled diabetes are significant contributors to the development of periodontitis.

### Diabetes – classification and epidemiology

The American Diabetes Association suggests the use of the terms Type 1 and 2 when classifying diabetes and further suggests the dropping of the terms 'insulin-dependent diabetes mellitus' and 'non insulin-dependent diabetes mellitus' and their acronyms IDDM and NIDDM as these terms may cause confusion and lead to the classification of patients based on treatment rather than aetiology.<sup>3</sup>

Type 1 diabetes mellitus commonly develops in individuals less than 30 years old and often presents in childhood and adolescence. Insulin therapy is required for all patients with Type 1 diabetes because the beta cells of the islets of Langerhans in the pancreas have been destroyed and, as a result, no insulin is produced. Without insulin to assist with the transport of glucose into cells, glucose accumulates in the tissue fluids and blood.<sup>4</sup> Type 2 diabetes is the most common form of the disease. It occurs because of a decreased responsiveness to insulin (or insulin resistance) at target organs. It typically begins at around middle age (40 years) and may be treated by dietary modification, oral hypoglycaemic agents or may require insulin therapy in uncontrolled cases.

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Patients with long standing diabetes frequently experience pathologic changes in many tissues and organs and the extent of diabetic complications is related to the degree of metabolic control. The major complications of diabetes, which include retinopathy, nephropathy, neuropathy, and vascular degeneration, are the result of hyperglycaemia.<sup>3</sup> Both types of diabetes are risk factors for periodontitis, which is now a recognized complication of diabetes mellitus.<sup>5</sup>

### Risk factors for the development of diabetes

The risk of developing diabetes is significant if there is a family history; 23.9 per cent of people without diabetes and 52.5 per cent of people with diabetes had a first degree relative (mother, father, sister, brother, grandfather, grandmother) with diabetes.<sup>2</sup> The prevalence of diabetes increases with age, with people over 50 years experiencing prevalence rates that are significantly higher than the expected rate. People from specific ethnic backgrounds (China, the Indian sub-continent and Pacific Islands) are more likely than other Australians to develop diabetes. Indigenous Australians have more than twice the diabetes prevalence rates than have other Australians. These high rates have been attributed to a genetic predisposition (thrifty gene), accompanied by an increasingly western lifestyle and the associated factors of a low-fibre, high fat diet and lack of physical activity.<sup>6</sup>

Obesity is a well established risk factor for Type 2 diabetes and is expressed in terms of Body Mass Index (BMI). A BMI greater than 30 indicates obesity and a BMI between 25 and 30 indicates overweight. A South Australian study revealed that 67.6 per cent of the diabetic population are either overweight or obese.<sup>7</sup> Physical inactivity together with obesity contribute to the 'lifestyle' components of risk for Type 2 diabetes. Exercise increases the sensitivity of insulin, improving its ability to moderate blood glucose levels.

The following check list is a useful incorporation into a medical history screen in order to identify patients at risk of Type 2 diabetes (Table 1).<sup>8</sup> If patients respond positively to one or more items, they may be at risk for diabetes. They should be encouraged to visit their doctor for diagnostic assessment.

### Diagnosis and monitoring of diabetes

The primary methods used to diagnose diabetes are fasting venous plasma glucose levels and oral glucose tolerance tests. Oral glucose tolerance tests used in the

**Table 1. Screening criteria for diabetes mellitus Type 2<sup>8</sup>**

Age >50 years	Previous abnormality of glucose tolerance, including diabetes during pregnancy
Obesity/overweight	Heart disease
First degree family history of Type 2 diabetes	Age >35 in Aborigines and Torres Strait Islanders
High blood pressure	Age >35 with ethnic predisposition (Chinese, Indian, Pacific Islanders)

**Table 2. Diagnostic criteria for diabetes mellitus<sup>8</sup>**

Classical symptoms of thirst and polyuria, plus Fasting venous plasma glucose level of $\geq 7.0$ mmol/L
or
Random or two-hour post glucose loading (75g) venous plasma glucose level of $\geq 11.1$ mmol/L (oral glucose tolerance testing)

past tended to give false positive results because of stress-induced adrenaline release that impairs the response to glucose loading.<sup>2</sup> As a result, the test is now used less frequently and a diagnosis can be made from a simple fasting venous plasma glucose level. Diagnostic criteria for diabetes mellitus are shown in Table 2.<sup>8</sup> Diabetes is monitored by two blood tests, the venous plasma glucose level (a short-term measure) and Glycosylated Haemoglobin (HbA1c), which measures the amount of glucose-bound haemoglobin. As the blood glucose level increases, the proportion of haemoglobin molecules binding glucose increases with time. Measurement is taken from a fasting sample of blood and provides information on the level of control of diabetes throughout the 30 to 90 day half-life of red blood cells.<sup>9</sup>

### Medical treatment of diabetes

Treatment of diabetes aims to lower blood glucose levels and prevent the complications associated with the disease. Diet control is the first step in individuals with Type 2 diabetes, reducing the intake of refined sugar and foods high in fat. Weight loss and exercise may also be advocated in order to reduce body fat. Oral hypoglycaemic agents such as metformin hydrochloride, glipizide, glicizide and glibenclamide are used when dietary measures prove unsuccessful. These aim to promote insulin release from the pancreas, encourage insulin uptake in the target organs and suppress appetite. Insulin therapy is required in Type 1 diabetes, severely uncontrolled Type 2 patients and for Type 2 patients with decreased insulin production. Modern insulin therapy combines the use of short acting, rapid onset insulin with a longer acting form, so that glucose levels are maintained with minimal peaks and troughs through the day.

### Infections and diabetes mellitus

Diabetics have impaired immune defence mechanisms, are more susceptible to infection and infections in diabetics are more severe when compared with non-diabetics.<sup>10</sup> Bacterial infections decrease the effectiveness of insulin receptors on target tissue cells, reducing the ability of the body to utilize glucose. Poor metabolic control of diabetes results with a consequent increased risk of developing diabetic complications.<sup>10</sup>

Many specific infections are more common in diabetic patients, and some occur almost exclusively in them. Other infections occur with increased severity and are associated with an increased risk of complications in patients with diabetes.<sup>11</sup>

Common infections in patients with diabetes include, respiratory tract infections, urinary tract infections,

pyelonephritis, cystitis, otitis media, sinusitis, cholecystitis, and candidiasis.<sup>11</sup>

The risk of oral infections, particularly periodontitis, among patients with diabetes needs to be considered and may be higher compared to non-diabetic individuals.<sup>12</sup> Although periodontitis rarely causes death, it can lead to more serious oral infections such as fascial space infections and may be a major factor in bacteraemia.<sup>13</sup>

### Periodontitis

The various forms of periodontitis are characterized by inflammation of the supracrestal tissues and destruction of alveolar bone and the periodontal ligament. The multifactorial model for the aetiology of periodontitis proposed by Clarke and Hirsch<sup>14</sup> incorporates the role of personal, environmental and systemic factors along with the agent (bacteria) to explain peoples' varying susceptibility to periodontitis. Some risk factors for periodontitis are smoking, diabetes, stress, neutrophil dysfunction, hyperlipidaemia, hormonal, health care, socio-economic status, oral hygiene, diet, and alcoholism. The combination of risk factors which confer susceptibility to periodontitis vary between individuals and also vary in their 'power' at different times through a person's life.

### Links between diabetes and periodontitis

There is general agreement that poorly controlled diabetes is a risk factor for the development of periodontitis. While many studies have found an association between diabetes and periodontitis, others have failed to establish this link. Much of the confusion in the literature can be attributed to a number of variable factors such as small sample sizes, the varying measurements and indices used for periodontal disease between studies. In addition to this, controls are often assumed to be non-diabetic without documentation to establish this and the types of diabetes have frequently been mixed in the populations studied. To further add to the confusion in the literature a varying number of statistical methods have been used to analyse the information.<sup>15</sup>

### Periodontal conditions in Type 1 diabetes

The literature for Type 1 diabetes is less clear than for Type 2. Results vary between studies, with some failing to establish a link.<sup>16,17</sup> However, many of these studies included very young subjects in whom one would not expect to see the development of periodontitis.<sup>4</sup> Studies performed on adult populations show there is a definite relationship between Type 1 diabetes and periodontitis.<sup>18-21</sup> Firali found significantly greater levels of attachment loss in insulin dependent diabetics.<sup>20</sup> Susceptibility to and severity of, periodontitis in the diabetic group increased with the duration of diabetes. Subjects with poorly controlled diabetes showed more attachment and bone loss compared to well-controlled diabetics.<sup>19</sup>

### Type 2 diabetes

Many of the reports on Type 2 diabetes and periodontitis are based on studies of Pima Indians in Arizona. This community has the highest recorded incidence and prevalence of Type 2 diabetes in the world. The following study is representative of the results of the majority of studies performed on Pima Indians. Emrich *et al.*<sup>22</sup> studied the relationship between Type 2 diabetes and periodontal disease in 1342 Pima Indians: there was a higher prevalence of periodontitis in diabetic subjects at all age groups under 55 years. There were no significant differences in plaque and calculus scores between the three groups. Emrich *et al.*<sup>22</sup> concluded that diabetics were approximately three times more likely to develop periodontitis than non-diabetics. Unfortunately, this study gave no information about the subjects' level of diabetic control. Taylor *et al.*,<sup>23</sup> who carried out a longitudinal study on 100 Pima Indians, found that poorly controlled diabetics had more severe periodontitis than controlled diabetics, and that subjects with Type 2 diabetes and periodontitis had increased risk of poor glycaemic control, the first report of this in the literature. However, when evaluating the studies on Pima Indians, one needs to consider that this population is not representative of other groups.

Diabetics with poor metabolic control have a higher prevalence of, and more severe, periodontal destruction and individuals with longer duration diabetes have a greater degree of periodontal destruction.<sup>19,20,22,24</sup> Oliver and Tervonen<sup>25</sup> stated that if there were a large number of poorly controlled diabetics in a study group, they were likely to have more periodontitis than the control group. Conversely, if the study group contained mainly well-controlled diabetics, the differences in periodontal status between the two groups were likely to be minimal.

### Mechanisms of action

The main mechanisms by which diabetes and periodontitis are related are via alterations in host responses and collagen metabolism. The primary factor responsible for the development of diabetic complications is prolonged tissue exposure to hyperglycaemia, which results in the production of advanced glycation end products (AGEs). This leads to an increase in collagen cross-linking and the generation of reactive oxygen intermediates, such as free radicals.<sup>26</sup> The modified collagen fibres accumulate in the tissues, resulting in thickening of the basement membrane. This impairs oxygen diffusion, waste elimination, leukocyte migration and the diffusion of immune factors and may thereby contribute to the pathogenesis of periodontitis.<sup>27</sup>

There may be an increase in the local production of cytokines that enhance the inflammatory response, leading to connective tissue damage, bone resorption and delayed wound repair. Significantly higher cytokine levels have been found in the gingival crevicular fluid of diabetics when compared with non-diabetics, with both groups demonstrating periodontitis.<sup>26,28,29</sup>

Hyperglycaemic conditions result in decreased cellular proliferation and growth of periodontal ligament (PDL) fibroblasts and collagen synthesis. Patients with diabetes have an increase in gingival crevicular fluid collagenase activity when compared with non-diabetics.<sup>25</sup> This greater collagenase activity would suggest an increased degree of collagen breakdown in the tissues of diabetics.

Polymorphonuclear leukocytes (PMNs) are the primary defence cells of the periodontium. Poorly controlled diabetes is associated with abnormalities in PMN functions such as impaired adherence, chemotaxis and phagocytosis, all of which render the host more susceptible to infections. Abnormalities in PMN function can be markedly improved with insulin therapy and meticulous control of the disease.<sup>4,19,25,26,30</sup> This may explain why well-controlled diabetics are not at increased risk for periodontitis.

### Microbiology

Many different species of subgingival micro-organisms are associated with the various forms of periodontitis; the subgingival microflora of diabetics and non-diabetics with periodontitis has been the subject of numerous studies.<sup>10</sup> La Farge found that no specific microflora has been associated with periodontitis in the presence of diabetes mellitus.<sup>31</sup> This was confirmed by Oliver and Tervonen, who suggested that periodontitis in poorly controlled diabetics was not caused by an increased pathogenicity of the microflora in these individuals, but by other factors.<sup>25</sup> No significant differences were detected between prevalence of five different micro-organisms studied in Type 2 diabetics and non-diabetics.<sup>32</sup> Similar bacterial species were recovered in diabetic patients as well as non-diabetics in another study.<sup>33</sup> To date, the evidence is that the microflora of pockets in diabetics and non-diabetics is similar.

### Periodontal treatment and metabolic control of diabetes

Does periodontal treatment affect the metabolic control of diabetes? The consensus of opinion at present is that there may be a relationship, but that it is not well defined. Several studies, including controlled clinical trials, have shown that control of a periodontal infection through a combination of mechanical and chemical therapy may improve glycaemic control. Unfortunately, these studies are limited and unconvincing.

Grossi *et al.*<sup>34</sup> conducted a controlled investigation of 113 Type 2 diabetics who were randomly divided into five groups. At baseline, each group received thorough ultrasonic cleaning and root planing. The groups then received one of the following antimicrobial regimes: topical water and systemic doxycycline, topical 0.12 per cent chlorhexidine (CHX) and systemic doxycycline, topical povidone-iodine and systemic doxycycline, topical 0.12 per cent CHX and placebo, and topical water and placebo (control group). The

dose of doxycycline was 100mg twice daily (BD) for two weeks. Glycosylated haemoglobin and serum glucose levels were recorded at the commencement of the study and at three and six months. Although an improvement was seen in all groups, only those treated with doxycycline showed statistically significant improvement in HbA1c levels at the three month interval ( $p < 0.04$ ). The authors concluded that the use of doxycycline, in addition to mechanical therapy, improved glycaemic control. However, the decrease in HbA1c levels was transient, with all groups showing similar results comparable to baseline after six months. The adjunctive use of doxycycline in periodontal therapy to improve long-term metabolic control of diabetes cannot be justified from the results of this study.

The level of diabetic control in Type 1 diabetics with periodontitis was investigated during and after mechanical periodontal therapy.<sup>35,36</sup> The studies were performed because previous uncontrolled studies had suggested a beneficial effect of periodontal treatment on metabolic control. Although there was a reduction in HbA1c levels in some cases, the differences from baseline were not significant. In these controlled, single-blind studies, the period of testing the HbA1c was under two months. This was probably too short because the metabolic response half life for HbA1c is 28 days.<sup>10</sup> In a pilot study by Miller *et al.*<sup>37</sup> the effects of mechano-chemical periodontal therapy on the metabolic state of nine poorly controlled diabetic patients was evaluated. A control group was not included in the study. Each subject was treated by mechanical therapy followed by a 14 day course of doxycycline (100mg BD). The study duration was two months, after which time HbA1c levels were not significantly different from baseline. In five of the nine subjects, there was a statistically significant reduction in HbA1c, but there were no changes in gingival inflammation or bleeding on probing.

None of these studies have conclusively shown that periodontal therapy improves the metabolic control of diabetes and yet, this concept has gained prominence in both the periodontal literature and in the public domain. Longer-term studies are needed to clarify the effects of periodontal therapy on metabolic control of diabetes. The important issues that require clarification are the choice of biochemical tests and monitoring intervals after treatment, whether periodontitis has an effect on metabolic control of diabetes and the degree of improvement in periodontal health that needs to occur before metabolic control is affected. It is also important to establish which aspect of therapy (mechanical, chemical or both) affects diabetic control. Finally, changes in blood glucose levels attributed to periodontal treatment need to be differentiated from the effects of conventional management of diabetes.

### The dentist's role in the detection of diabetes

The dentist can be pivotal in the diagnosis of diabetes by recognizing tell-tale features of gingivitis and



**Table 3. Signs of gingivitis and periodontitis in diabetic patients<sup>38,39</sup>**

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Enlarged velvety-red gingival tissues that bleed easily (Fig 1).
Vascular changes that can give the gingivae a distinct purple /bluish hue (Fig 2).
Multiple periodontal abscesses.
Mobile teeth indicating bone loss.
Proliferative tissue at the gingival margin.
Inflammation spreading through the attached gingiva.
Lack of resolution of gingival signs after conventional treatment.
Severe, aggressive periodontitis relative to patient's age.
Delayed wound healing following oral surgical procedures.

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periodontitis that are consistent with diabetes-related conditioning of periodontal responses to plaque. Dentists should be suspicious of patients presenting with multiple periodontal abscesses, unusual gingival reddening or abnormal responses to plaque that persist after tooth debridement and plaque control. The oral manifestations listed in Table 3,<sup>38</sup> while not pathognomonic for diabetes, may result from uncontrolled hyperglycaemia. Oral symptoms reported



**Fig 1.** Unusually intense gingival response to dental plaque in a 38-year-old female. The gingivae are bright red, have a glossy surface and bleed profusely on probing. The inflammation extends throughout the attached gingiva of the affected areas. Diabetes mellitus was diagnosed on subsequent referral to the patient's general medical practitioner.



**Fig 2.** Localized gingival swelling and inflammation extending through the attached gingiva of teeth 23 and 24 in a 32-year-old uncontrolled diabetic. The bluish tinge of the gingival tissues is a common, although not an exclusive sign of diabetes-conditioned gingival inflammation. Another feature is that the severe gingival inflammation does not necessarily affect all gingival areas.

by diabetic patients may include burning mouth, dry mouth and altered taste. These symptoms relate to neuropathy associated with diabetes.<sup>39</sup>

A recent study conducted by Beikler *et al.* found glucose levels in blood sampled after bleeding on periodontal probing had a high correlation with blood samples taken from fingertips.<sup>40</sup> This work suggests that the general dentist could use gingival blood samples in glucose self monitoring devices as a simple screening method to detect undiagnosed diabetics and identify patients with poor metabolic control.

## CONCLUSION

Well-controlled diabetics have a similar incidence of periodontitis as do non-diabetics. However, a greater incidence and severity of periodontitis is observed in both Type 1 and 2 long-term diabetics with poor metabolic control. Although there is weak evidence that control of periodontitis can contribute to better metabolic control of diabetes, many of the studies have had flawed designs, indicating that better designed investigations are required. In conclusion, there is an undeniable link between diabetes mellitus and periodontitis with complex interactions occurring between these diseases. The well-informed dentist has the opportunity to be at the forefront of diagnosing diabetes. We have explored the associations between diabetes mellitus and periodontitis in the hope of arming the clinician with the knowledge to provide the diabetic patient with the best possible dental care and advice.

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