Bidirectional Interrelationships Between Diabetes and Periodontal Diseases: An Epidemiologic Perspective

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This review evaluates evidence for a bidirectional relationship between diabetes and periodontal diseases. A comprehensive Medline search of the post-1960 English language literature was employed to identify primary research reports of relationships between diabetes and periodontal diseases. Reports included in the review on the adverse effects of diabetes on periodontal health (DM→PD) were restricted to those comparing periodontal health in subjects with and without diabetes. Review of adverse affects of periodontal infection on glycemic control included reports of periodontal treatment studies and follow-up observational studies in which changes in glycemic control could be assessed. Observational studies reporting DM→PD provided consistent evidence of greater prevalence, severity, extent, or progression of at least one manifestation of periodontal diseases in the large majority of reports (supportive evidence in 44/48 total reviewed; 37/41 cross-sectional and 7/7 cohort). Additionally, there were no studies reviewed with superior design features to refute this association. Treatment studies provided direct evidence to support periodontal infection having an adverse, yet modifiable, effect on glycemic control. However, not all investigations reported an improvement in glycemic control after periodontal treatment. Additional evidence to support the effect of severe periodontitis on increased risk for poorer glycemic control comes from 2 follow-up observational studies. The evidence reviewed supports viewing the relationship between diabetes and periodontal diseases as bidirectional. Further rigorous, systematic study is warranted to establish that treating periodontal infections can be influential in contributing to glycemic control management and possibly to the reduction of the burden of complications of diabetes mellitus. *Ann Periodontol 2001;6:99-112.*

KEY WORDS

Diabetes mellitus/prevention and control; periodontitis/complications; risk factors; literature review.

Diabetes mellitus and chronic periodontitis are common chronic diseases in adults in the U.S. population. Diabetes mellitus is disease of metabolic dysregulation characterized by hyperglycemia due to defects in insulin secretion, insulin action, or both. Dysregulation of protein and lipid metabolism also occurs. Particularly susceptible individuals or those with chronic poor metabolic control may experience one or more commonly recognized complications in the eyes, heart, blood vessels, kidney, and nervous system. These complications are associated with a significant burden for the individual and society in terms of increased morbidity and premature mortality. This increased burden includes direct costs of medical care and indirect costs such as lost productivity.[1]

There are 2 major types of overt diabetes in the U.S., Type 1 (formerly classified as insulin-dependent) and Type 2 (formerly classified as non-insulin-dependent).[2] Additional types of diabetes include gestational diabetes mellitus, which affects approximately 3% to 5% of all pregnancies, and diabetes associated with or secondary to other conditions, comprising 1% to 2% of individuals with diabetes in the U.S.[1,2] Type 2 diabetes is most prevalent; approximately 90% to 95% of people diagnosed with diabetes in the U.S. have Type 2, and almost all people ages 45 years and older diagnosed with diabetes have Type 2. Over

the past 35 years, diabetes prevalence has increased 3-fold.[3] Several factors associated with this increase in prevalence include aging of the U.S. population, reduction in mortality of persons with diabetes, changes in criteria used to diagnose diabetes, and an increase in the prevalence of risk factors for diabetes such as obesity and physical inactivity.[3]

Prevalence of Type 2 diabetes is positively associated with age and minority status. Among people 65 years or older, diabetes prevalence is approximately 3.5 times greater than prevalence for people of all ages.[3] Several minority ethnic populations are 2 to 3 times more likely to have diabetes than non-Hispanic white individuals of similar age in the U.S.[4]

The 2 most common periodontal diseases are gingivitis and chronic periodontitis. Gingivitis is prevalent, with approximately 50% of the U.S. population in all age groups exhibiting reversible gingival inflammation.[5] Chronic periodontitis is a potentially progressive bacterial infection resulting in inflammation and destruction of tooth-supporting tissues. However, moderate or severe chronic periodontitis, with destruction of periodontal attachment tissues, is much less common than gingivitis, affecting approximately 13% of the entire U.S. population.[6]

The biologic mechanisms important in diabetes adversely affecting periodontal health are likely to be multifactorial. Mechanisms such as microangiopathy, alterations in gingival crevicular fluid, alterations in collagen metabolism, altered host inflammatory response, altered subgingival microflora, and genetic predisposition have been proposed as contributory.[7-12]

The purpose of this report is to review the evidence for a bidirectional, adverse interrelationship between diabetes mellitus and periodontal diseases.

DIABETES: EFFECTS ON PERIODONTAL HEALTH

Current evidence supporting the link between diabetes mellitus and periodontal diseases comes from a review of English language literature published since 1960. This review was conducted using a Medline search, as well as reviewing reference lists of relevant papers obtained from the search to identify primary research reports on investigations of relationships between diabetes and periodontal diseases. The reports with information on the effects of diabetes on periodontal health included in the review were restricted to those that compared periodontal health in subjects with and without diabetes.

To summarize the evidence on the effects of diabetes on periodontal health, studies were broadly classified by age group and type of diabetes (Table 1). Using this classification scheme, there were 10 reports focusing principally on children and adolescents with Type 1 diabetes;[13-22] all except 1[13] reported greater prevalence, extent, or severity of at least one measure of periodontal disease. Another set of studies of subjects between the ages of 15 and 35 years with Type 1 diabetes all reported greater prevalence, extent, or severity of at least one measure or index of periodontal disease.[23-28] A third set of studies of Type 1 diabetes (or with subjects reported as being insulin-dependent without actual diabetes type specified) included adults between 20 and 70 years old.[29-33] All 5 of these reports also noted greater prevalence, extent, or severity of at least one measure or index of periodontal disease.

There are a smaller number of studies on the relationship between Type 2 diabetes and periodontitis. The review identified 8 reports limited to subjects with Type 2 diabetes. Three of the reports[34-36] included only adults. The remaining 5 reports are from an epidemiologic study in the Pima Indians of the Gila River Indian Community, Arizona and include subjects ages 5 and older[37] or 15 and older.[38-41] These 8 studies all reported significantly poorer periodontal health in subjects with diabetes. A subset of these reports provided additional epidemiologic parameter estimates of association and risk. Emrich et al.[39] reported that the odds were approximately 3 times greater for people with diabetes to have destructive periodontal disease after controlling for other important factors. Nelson et al.[38] found a 2.6-fold greater risk of advanced periodontal disease incidence, and Taylor et al.[41] reported that subjects with Type 2 diabetes had a 4-fold greater risk for more severe alveolar bone loss progression.

Several reports consist of analyses in which subjects with Type 1 and Type 2 diabetes were not distinguished. All of the studies in this subset were cross-sectional and included adult subjects, although 2 studies in this group included children or adolescents as well.[42,43] Eight of these 10 studies reported greater prevalence, extent, or severity of periodontal disease for at least one measure or index of periodontal disease.[42,44-50] Hove and Stallard[51] and Benveniste et al.[43] did not find significant differences in periodontal disease between subjects with and without diabetes.

Finally, there is a set of cross-sectional studies in which the type of diabetes was not specified and was not easily determined from other information provided. Five of the 8 reports in this set included only adults.[27,52-55] The other 3 reports included subjects with ages ranging from childhood to older adulthood.[56-58] All of these studies found subjects with diabetes to have increased prevalence, extent, or severity of periodontal disease. Two of the population-based surveys, Grossi et al.[53] and Dolan et al.,[55] provide epidemiologic estimates of association for diabetes and attachment loss severity, with diabetic individuals being approximately twice as likely to have more severe attachment loss than those without diabetes, after controlling for other variables.

Table 1.

Summary of Studies on the Association Between Diabetes and Periodontal Diseases, Classified by Strength of Evidence, Diabetes Type, and Age

Reference	Country	Study Design	Diabetes Type*	N Subjects a. Diabetics b. Controls	Ages† a. Diabetics b. Controls	Periodontal Measure: Diabetes Effect‡	Other Diabetes-Related Variables Considered	Evidence Level§
Firatli, 1997[16]	Turkey	Prospective	1	a. 44 b. 20	a. 12.2 (mean) b. 12.3 (mean)	Ging: 0s Pd: 0s Lpa: 1s	Glycemic control Duration of diabetes	II-2
Cohen et al., 1970[23]	USA	Prospective	1‖	a. 21 b. 18	a. 18, 35 b. 18, 35	Ging: 1s Lpa: 1r, 1s	None	II-2
Tervonen and Karjalainen, 1997[32]	Finland	Prospective	1	a. 36 b. 10	a. 24, 36 b. 24, 36	Ging: 0e Pd: 1r Lpa: 1e	Glycemic control Duration of diabetes Diabetes complications	II-2
Novaes et al., 1996[34]	Brazil	Prospective	2	a. 30 b. 30	a. 30, 77 b. 30, 67	Pd: 1s, 1r Lpa: 1s, 1r	Glycemic control	II-2
Nelson et al., 1990[38]	USA	Prospective	2	a. 720 b. 1,553	a. 15, 55+ b. 15, 55+	XRBL: 1i, 1p	None	II-2
Taylor et al., 1998[41]	USA	Prospective	2	a. 24 b. 338	a. 15, 57 b. 15, 57	XRBL: 1i, 1r	None	II-2
Taylor et al., 1998[40]	USA	Prospective	2	a. 21 b. 338	a. 15, 49 b. 15, 49	XRBL: 1i, 1r	Glycemic control	II-2
Goteiner et al., 1986[13]	USA	Cross-sectional	1	a. 169 b. 80	a. School ages b. 5, 18	Ging: 0s Lpa: 0p, 0s PDI: 0s	None	III
Harrison and Bowen, 1987[14]	USA	Cross-sectional	1	a. 30 b. 30	a. 4, 19 b. 4, 19	Ging: 1s Lpa: 1p	Glycemic control	III
Novaes et al., 1991[22]	Brazil	Cross-sectional	1	a. 30 b. 30	a. 5, 18 b. 5, 18	Ging: 1s Pd: 0s XRBL: 1s	None	III
Cianciola et al., 1982[18]	USA	Cross-sectional	1	a. 263 b. 208	a. <10, >19 b. <10, >19	Ging: 1p Lpa: 1p XRBL: 1p, 1s JPS: 1p,1s	Duration of diabetes	III
de Pommereau et al., 1992[15]	France	Cross-sectional	1	a. 85 b. 38	a. 12, 18 b. 12, 18	Ging: 1e Lpa: 0e, 0p, 0s XRBL: 0e, 0p, 0s	Glycemic control Duration of diabetes	III

* Diabetes type: 1 = Type 1 diabetes mellitus; 2 = Type 2 diabetes mellitus; 1,2 = subjects with both Type 1 and Type 2 diabetes mellitus included; 9 = diabetes type not specified and not clearly ascertainable from other information in the report.

† Ages: subjects' ages presented as minimum, maximum reported for those with diabetes (a) and controls (b) unless otherwise specified.

‡ Measure of periodontal disease status. Measures used include: Ging = gingivitis or gingival bleeding; Pd = probing depth; Lpa = loss of periodontal attachment; XRBL = radiographic bone loss; JPS = juvenile periodontal score; MGI = modified gingival index; PI = Russell's periodontal index; PDR = periodontal disease rate (proportion of teeth affected by periodontal disease). The number following the measure corresponds to greater disease in those with diabetes (1) or no difference between those with diabetes and controls (0). The letters following the number correspond to the parameter(s) assessed in the study: e = extent; i = incidence; p = prevalence; s = severity; r = progression.

§ Hierarchy of evidence based on classification scheme used by U.S. Preventive Services Task Force[99]: I = evidence obtained from at least one properly randomized controlled trial; II-1 = evidence obtained from well-designed controlled trial without randomization; II-2 = evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group; II-3 = evidence obtained from multiple time series with or without the intervention; dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence; III = opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

‖ Diabetes type not specified but ascertained by reviewer from other information in the report.

Table 1. (continued)

Summary of Studies on the Association Between Diabetes and Periodontal Diseases, Classified by Strength of Evidence, Diabetes Type, and Age

Reference	Country	Study Design	Diabetes Type*	N Subjects a. Diabetics b. Controls	Ages† a. Diabetics b. Controls	Periodontal Measure: Diabetes Effect‡	Other Diabetes-Related Variables Considered	Evidence Level§
Ringelberg et al., 1977[19]	USA	Cross-sectional	I	a. 56 b. 41	a. 10, 16 b. 10, 12	Ging: 1s MGI: 1s	None	III
Firatli et al., 1996[20]	Turkey	Cross-sectional	I	a. 77 b. 77	a. 12.5 (mean) b. 12.6 (mean)	Ging: 0s Pd: 1s Lpa: 1s	Duration of diabetes	III
Pinson et al., 1995[17]	USA	Cross-sectional	I	a. 26 b. 24	a. 7-18 b. 7-18	Ging: 1s Pd: 0s Lpa: 0s	Glycemic control Duration of diabetes	III
Faulconbridge et al., 1981[21]	England	Cross-sectional	I	a. 94 b. 94	a. 5, 17 b. 5, 17	Ging: 1s	Duration of diabetes	III
Kjellman et al., 1970[25]	Sweden	Cross-sectional	I‖	a. 105 b. 52	a. 15, 24 b. 15, 24	Ging: 1e Pd: 0s XRBL: 0s	Glycemic control Diabetes complications	III
Güven et al., 1996[24]	Turkey	Cross-sectional	I	a. 10 b. 52	a. 18, 27 b. 19, 22	Ging: 1e	None	III
Rylander et al., 1987[26]	Sweden	Cross-sectional	I	a. 46 b. 41	a. 18, 26 b. 19, 25	Ging: 1e, 1p Pd: 0e Lpa: 1e, 1p XRBL: 0p	Diabetes complications	III
Sznajder et al., 1978[27]	Argentina	Cross-sectional	I‖	a. 20 b. 26	a. 9, 29 b. 9, 29	Ging: 1s Lpa: 0s	None	III
Galea et al., 1986[28]	Malta	Cross-sectional	I‖	a. 82 b. Unknown	a. 5, 29 b. 5, 29	Pd: 1p	Glycemic control Duration of diabetes Diabetes complications	III
Hugoson et al., 1989[30]	Sweden	Cross-sectional	I	a. 154 b. 77	a. 20, 70 b. 20, 70	Ging: 1e Pd: 1e, 1p, 1s XRBL: 1s	Duration of diabetes	III
Glavind et al., 1968[29]	Denmark	Cross-sectional	I‖	a. 51 b. 51	a. 20, 40 b. 20, 40	Ging: 0s Pd: 0s Lpa: 1s XRBL: 1s	Duration of diabetes Diabetes complications	III
Thorstensson and Hugoson, 1993[31]	Sweden	Cross-sectional	I	a. 117 b. 99	a. 40, 70 b. 40, 70	Ging: 0e Pd: 1e, 1s XRBL: 1s	Duration of diabetes Onset age	III
Tervonen et al., 2000[33]	Finland	Cross-sectional	I	a. 35 b. 10	a. 29.7 (mean) b. 29.0 (mean)	XRBL: 1e	Glycemic control Duration of diabetes Diabetes severity based on presence of complications	III

Table 1. (continued)

Summary of Studies on the Association Between Diabetes and Periodontal Diseases, Classified by Strength of Evidence, Diabetes Type, and Age

Reference	Country	Study Design	Diabetes Type*	N Subjects a. Diabetics b. Controls	Ages† a. Diabetics b. Controls	Periodontal Measure: Diabetes Effect‡	Other Diabetes-Related Variables Considered	Evidence Level§
Morton et al., 1995[35]	Mauritius	Cross-sectional	2	a. 24 b. 24	a. 26, 76 b. 25, 73	Ging: 1p Pd: 1s Lpa: 1s	None	III
Shlossman et al., 1990[37]	USA	Cross-sectional	2	a. 736 b. 2,483	a. 5, 45+ b. 5, 45+	Lpa: 1p XRBL: 1p	None	III
Emrich et al., 1991[39]	USA	Cross-sectional	2	a. 254 b. 1,088	a. 15, 55+ b. 15, 55+	Lpa: 1p, 1s XRBL: 1p, 1s	None	III
Sandberg et al., 2000[36]	Sweden	Cross-sectional	2	a. 102 b. 102	a. 64.8 (mean) b. 64.9 (mean)	Ging: 1e Pd: 1e XRBL: 1p	Glycemic control Duration of diabetes	III
Wolf, 1977[42]	Finland	Cross-sectional	1,2	a. 186 b. 156	a. 16, 60 b. 16, 60	Ging: 1s Lpa: 1s XRBL: 1s	Glycemic control Duration of diabetes Diabetes complications	III
Benveniste et al., 1967[43]	USA	Cross-sectional	1,2‖	a. 53 b. 71	a. 5, 72 b. 5, 72	Ging: 0s Pd: 0p, 0s	None	III
Finestone and Boorujy, 1967[44]	USA	Cross-sectional	1,2‖	a. 189 b. 64	a. 20, 79 b. 20, 79	PI: 1s	Glycemic control Duration of diabetes Diabetes complications	III
Belting et al., 1964[48]	USA	Cross-sectional	1,2‖	a. 78 b. 79	a. 20, 79 b. 20, 79	PI: 1s	Diabetes severity	III
Oliver and Tervonen, 1993[45]	USA	Cross-sectional	1,2	a. 114 b. 15,132	a. 20, 64 b. 20, 64	Pd: 1e, 1p Lpa: 1e, 0p, 0s	None	III
Yavuzyilmaz et al., 1996[49]	Turkey	Cross-sectional	1,2	a. 17 b. 17	a. 25, 74 b. 19, 29	Pd: 1s	None	III
Bridges et al., 1996[46]	USA	Cross-sectional	1,2	a. 118 b. 115	a. 24, 78 b. 24, 78	Ging: 0s Pd: 0s Lpa: 1s	Glycemic control Duration of diabetes	III
Sandler and Stahl, 1960[50]	USA	Cross-sectional	1,2‖	a. 100 b. 3,894	a. 20, 69 b. 20, 69	PDR: 1e	None	III
Bacic et al., 1988[47]	Yugoslavia	Cross-sectional	1,2	a. 222 b. 189	a. <20, 60+ b. <20, 60+	Pd: 1e, 1p, 1s	Glycemic control Duration of diabetes Diabetes complications	III
Hove and Stallard, 1970[51]	USA	Cross-sectional	1,2‖	a. 28 b. 16	a. 20, 40+ b. 20, 40+	Ging: 0s Pd: 0s XRBL: 0s	Duration of diabetes Diabetes severity	III

Table 1. (continued)

Summary of Studies on the Association Between Diabetes and Periodontal Diseases, Classified by Strength of Evidence, Diabetes Type, and Age

Reference	Country	Study Design	Diabetes Type*	N Subjects a. Diabetics b. Controls	Ages† a. Diabetics b. Controls	Periodontal Measure: Diabetes Effect‡	Other Diabetes-Related Variables Considered	Evidence Level§
Mackenzie and Millard, 1963[52]	USA	Cross-sectional	9	a. 124 b. 92	a. 32, 78 b. 32, 78	XRBL: 0s	None	III
Sznajder et al., 1978[27]	Argentina	Cross-sectional	9	a. 63 b. 39	a. 30, 49 b. 30, 50	Ging: 1s Lpa: 1s	None	III
Dolan et al., 1997[55]	USA	Cross-sectional	9	Weighted a. 107 b. 554	a. 45, 75+ b. 45, 75+	Lpa: 1e, 1p, 1s	None	III
Grossi et al., 1994[53]	USA	Cross-sectional	9	a. 1,426 b. 69	All: 25, 74; unknown for diabetics	Lpa: 1s, 1p	None	III
Tervonen and Knuuttila, 1986[54]	Finland	Cross-sectional	9	a. 50 b. 53	a. <30, 40+ b. <30, 40+	Ging: 1e Pd: 1e, 1p XRBL: 0s	Glycemic control	III
Campbell, 1972[56]	Australia	Cross-sectional	9	a. 70 b. 102	a. 17, 39 b. 17, 39	Pl: 1p, 1s	None	III
Albrecht et al., 1988[57]	Hungary	Cross-sectional	9	a. 1,360 b. 625	a. 15, 65+ b. 15, 65+	Ging: 1s Pl: 0s	None	III
Szpunar et al., 1989[58] (NHANES I)	USA	Cross-sectional	9	a. 474 b. 15,174	a. 6, 65+ b. 6, 65+	Pl: 1s	None	III
Szpunar et al., 1989[58] (HHANES)	USA	Cross-sectional	9	a. 322 b. 8,040	a. 15, 65+ b. 12, 65+	Pl: 1s	None	III

As with other complications of diabetes, current evidence also supports poorer glycemic control contributing to poorer periodontal health. Primary research reports in the literature investigating relationships between glycemic control level and periodontal disease have been predominantly studies where subjects either had Type 1 diabetes, a combination of both Type 1 and Type 2 diabetes, or where the diabetes type was not specified (Table 2). There have been only 5 reports published on the association between glycemic control and periodontal disease specifically in Type 2 diabetes.[34,36,40,59,60] Four of these studies found poorer glycemic control to be a significant factor associated with poorer periodontal health.[34,40,59,60] Among the studies providing information on differences in periodontal health classified by glycemic control status, most have been cross-sectional, with 19/34 reporting more frequent or severe periodontal disease in those with poorer glycemic control[14,16,25,28,32-34,40,44,45,54,59-66] and 15 reporting no differences.[15,17,26,36,42,46,47,51,57,67-72] Among the follow-up studies in this body of literature, 8/9 reported poorer periodontal health in subjects with poorer glycemic control.[16,32,34,40,60,63,64,66] Additionally, among reports published before 1990, 6/16 reported more frequent or severe periodontal disease in subjects with poorer glycemic control,[14,25,28,44,54,61] whereas 13/18 papers published since 1990 reported results supporting poorer glycemic control associated with or contributing to more severe or frequent periodontal disease.[16,32-34,40,45,59,60,62-66]

Although the preponderance of studies included in this review of the adverse effects of diabetes on periodontal health are cross-sectional and describe findings of convenience samples, principally from outpatients in hospitals and clinics, the smaller subset of longitudinal and population-based studies also strongly supports the association between diabetes and increased occurrence and severity of periodontal diseases. While limitations on causal inference must be considered, the literature provides consistent evidence of greater prevalence, severity, or extent of at least

Table 2.

Summary of Reports With Information on Effects of Glycemic Control on Periodontal Status, Sorted by Strength of Evidence, Diabetes Type, and Age

Reference	Country	Study Design	Diabetes Type*	Age	Effect†	Non-DM Comparison Group‡	Evidence Level§
Seppälä, Seppälä, Ainamo, 1993[63]	Finland	Prospective	1	Adults	1	N	II-2
Tervonen and Karjalainen, 1997[32]	Finland	Prospective	1	Adults	1	Y	II-2
Karjalainen and Knuuttila, 1996[66]	Finland	Prospective	1	Children	1	N	II-2
Firatli, 1997[16]	Turkey	Prospective	1	Children	1	Y	II-2
Seppälä and Ainamo, 1994[64]	Finland	Prospective	1, 2	Adults	1	N	II-2
Wolf, 1977[42]	Finland	Prospective	1, 2	Mixed ages	0	Y	II-2
Novaes et al., 1996[34]	Brazil	Prospective	2	Adults	1	Y	II-2
Taylor et al., 1998[40]	USA	Prospective	2	Mixed ages	1	Y	II-2
Sastrowijoto et al., 1989[71]	Netherlands	Cross-sectional	1	Adults	0	N	III
Moore et al., 1999[72]	USA	Cross-sectional	1	Adults	0	N	III
Tervonen et al., 2000[33]	Finland	Cross-sectional	1	Adults	1	Y	III
Gusberti et al., 1983[61]	USA	Cross-sectional	1	Children	1	N	III
Barnett et al., 1984[68]	USA	Cross-sectional	1	Children	0	N	III
Harrison and Bowen, 1987[14]	USA	Cross-sectional	1	Children	1	Y	III
Sandholm et al., 1989[70]	Finland	Cross-sectional	1	Children	0	Y	III
de Pommereau et al., 1992[15]	France	Cross-sectional	1	Children	0	Y	III
Pinson et al., 1995[17]	USA	Cross-sectional	1	Children	0	Y	III
Galea et al., 1986[28]	Malta	Cross-sectional	1	Children and young adults	1	Y	III
Kjellman et al., 1970[25]	Sweden	Cross-sectional	1	Children and young adults	1	Y	III
Rylander et al., 1987[26]	Sweden	Cross-sectional	1	Mixed ages	0	Y	III
Safkan-Seppälä and Ainamo, 1992[62]	Finland	Cross-sectional	1	Mixed ages	1	N	III
Finestone and Boorujy, 1967[44]	USA	Cross-sectional	1, 2	Adults	1	Y	III
Bacic et al., 1988[47]	Yugoslavia	Cross-sectional	1, 2	Adults	0	Y	III
Oliver and Tervonen, 1993[45]	USA	Cross-sectional	1, 2	Adults	1	N	III
Tervonen and Oliver, 1993[65]	USA	Cross-sectional	1, 2	Adults	1	N	III

* Diabetes type: 1 = Type 1 diabetes mellitus; 2 = Type 2 diabetes mellitus; 1,2 = subjects with both Type 1 and Type 2 diabetes mellitus included; 9 = diabetes type not specified and not clearly ascertainable from other information in the report.

† 1 = Subjects with poorer glycemic control had poorer health than the comparison group(s); 0 = no difference in the periodontal health status between subjects with poorer glycemic control and comparison group(s).

‡ Y = the report included subjects without diabetes as well as subjects with diabetes classified by glycemic control status.

§ Hierarchy of evidence based on classification scheme used by U.S. Preventive Services Task Force.[99] I = evidence obtained from at least one properly randomized controlled trial; II-1 = evidence obtained from well-designed controlled trial without randomization; II-2 = evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group; II-3 = evidence obtained from multiple time series with or without the intervention; dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence; III = opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

Table 2. (continued)

Summary of Reports With Information on Effects of Glycemic Control on Periodontal Status, Sorted by Strength of Evidence, Diabetes Type, and Age

Reference	Country	Study Design	Diabetes Type*	Age	Effect†	Non-DM Comparison Group‡	Evidence Level§
Bridges et al., 1996[46]	USA	Cross-sectional	1, 2	Adults	0	Y	III
Ainamo et al., 1990 [60]	Finland	Prospective (case report)	2	Adults	1	N	III
Unal et al., 1993[59]	Turkey	Cross-sectional	2	Adults	1	Y	III
Sandberg et al., 2000[36]	Sweden	Cross-sectional	2	Adults	0	Y	III
Hove and Stallard, 1970[51]	USA	Cross-sectional	9	Adults	0	Y	III
Nichols et al., 1978[67]	USA	Cross-sectional	9	Adults	0	N	III
Tervonen and Knuuttila, 1986[54]	Finland	Cross-sectional	9	Adults	1	Y	III
Albrecht et al., 1988[57]	Hungary	Cross-sectional	9	Mixed ages	0	Y	III
Hayden and Buckley, 1989[69]	Ireland	Cross-sectional	9	Mixed ages	0	N	III

one manifestation of periodontal disease in the large majority of studies. Additionally, there are no studies reported in the literature with superior design features to refute this assessment. The studies were conducted in distinctly different settings with subjects from different ethnic populations, different age mixes, and with a variety of measures of periodontal status (i.e., gingival inflammation, pathologic probing depth, loss of periodontal attachment, or radiographic evidence of alveolar bone loss). The studies also used various parameters to summarize periodontal disease occurrence (prevalence, incidence, extent, severity, or progression). Hence, this inevitable variation in methodology and study populations limits the possibility that the same biases or confounding factors apply in all the studies and provides support for concluding that diabetes is a risk factor for periodontal disease incidence, progression, and severity. Further, there is substantial evidence to support a "dose-response;" i.e., as glycemic control worsens, the adverse effects of diabetes on periodontal health become greater.

PERIODONTAL INFECTION: EFFECTS ON GLYCEMIC CONTROL

While there is substantial evidence to support considering diabetes as a risk factor for poor periodontal health, there is also evidence for periodontal infection adversely affecting glycemic control in diabetes, although this has been less extensively studied. Indirect evidence comes from investigations of relationships between insulin resistance and active inflammatory connective tissue diseases,[73,74] other clinical diseases,[73-76] and acute infection.[77,78] Due to the high vascularity of the inflamed periodontium, this inflamed tissue may serve as an endocrine-like source for tumor necrosis factor-α (TNF-α) and other inflammatory mediators.[12,79] Because of the predominance of Gram-negative anaerobic bacteria in periodontal infection, the ulcerated pocket epithelium could constitute a chronic source of systemic challenge for bacterial products and locally produced inflammatory mediators. TNF-α, interleukin (IL)-6, and IL-1, all mediators important in periodontal inflammation, have been shown to have important effects on glucose and lipid metabolism, particularly following an acute infectious challenge or trauma.[12,80,81] TNF-α has been reported to interfere with lipid metabolism and to be an insulin antagonist.[82,83] IL-6 and IL-1 have also been reported to antagonize insulin action.[81,84,85] To date, all reports on an infection-related alteration of the endocrinologic-metabolic status of the host have been with acute infections. There is a compelling need to evaluate these relationships in the chronic infection context applicable to periodontal infection.

More direct evidence regarding the effects of periodontal infection on glycemic control in diabetes comes from treatment studies[42,63,64,86-93] and observational studies[94,95] (Table 3). There is evidence to support periodontal infection/severe periodontitis having an adverse, yet modifiable, effect on glycemic control.[42,63,87,88,92] However, not all investigations report an improvement in glycemic control after periodontal treatment.[64,89-91,93] There are major variations in the design, conduct, and results of these studies as

Table 3.

Effects of Periodontal Disease and Its Treatment on Glycemic Control: Clinical and Epidemiological Evidence

Reference	Study Design	Diabetes Type	N Subjects a. Treatment (ages) b. Control (ages)	Follow-Up	Periodontal Therapy	Metabolic Control Outcome Measure	Effects on Metabolic Control	Evidence Level*
Aldridge et al., Study 1, 1995[89]	RCT	1	a. 16 (16-40) b. 15 (16-40)	2 months	Treatment group: OHI, scaling, adjustment of restoration margins, and reinforcement after 1 month. Control group: no treatment.	Glycated hemoglobin, fructosamine	Periodontal treatment had no effect on change in glycated hemoglobin.	I
Aldridge et al., Study 2, 1995[89]	RCT	1	a. 12 (20-60) b. 10 (20-60)	2 months	Treatment group: OHI, scaling and root planing, extractions, root canal therapy. Control group: no treatment.	Glycated hemoglobin	Periodontal treatment had no effect on change in glycated hemoglobin.	I
Grossi et al., 1996,[86] 1997[92]	RCT	2	a. 89 (25-65) b. 24 (25-65)	12 months	Treatment groups received systemic doxycycline or placebo and ultrasonic bactericidal curettage with irrigation using either H_2O, chlorhexidine, or povidone-iodine. Controls received ultrasonic bacterial currettage with H_2O irrigation and placebo	Glycated hemoglobin	The 3 groups receiving doxycycline and ultrasonic bacterial curettage showed significant reductions ($P \leq 0.04$) in mean glycated hemoglobin at 3 months.	I
Smith et al., 1996[90]	Treatment study, non-RCT	1	a. 18 (26-57) b. 0	2 months	Scaling and root planing with ultrasonics and curets, OHI.	Glycated hemoglobin	No statistically or clinically significant change in glycated hemoglobin.	II-1
Westfelt et al., 1996[91]	Treatment study, non-RCT	1 and 2	a. 20 (45-65) b. 20 (45-65)	5 years	Baseline oral hygiene instruction, scaling and root planing followed by periodic prophys, OHI, localized subgingival plaque removal, and surgery at sites with bleeding on probing and PD >5 mm.	Glycated hemoglobin	The mean value of HbA1c between BL-24 months was not significantly different from that between 24-60 months.	II-1
Christgau et al., 1998[93]	Treatment study, non-RCT	1 and 2	a. 20 (30-66) b. 20 (30-66)	2 months	Scaling and root planing, subgingival irrigation with chlorhexidine, OHI, extractions.	Glycated hemoglobin	No effect on glycated hemoglobin.	II-1
Taylor et al., 1996[94]	Historical prospective cohort	2	†49 (severe periodontitis) 56 (less severe periodontitis)	2-4 years	Not applicable	Glycated hemoglobin	Those with severe periodontitis were ~6 times more likely to have poor glycemic control at follow-up.	II-2

* Hierarchy of evidence based on classification scheme used by U.S. Preventive Services Task Force.[99] I = evidence obtained from at least one properly randomized controlled trial; II-1 = evidence obtained from well-designed controlled trial without randomization; II-2 = evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group; II-3 = evidence obtained from multiple time series with or without the intervention; dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence; III = opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.
† No treatment or control groups.
‡ No subjects received treatment.
§ Not specified.
‖ Thirty-eight subjects were followed for 1 year and 22 subjects for 2 years. PIDD: poorly controlled insulin-dependent diabetes; CIDD: controlled insulin-dependent diabetes.

Table 3. (contined)

Effects of Periodontal Disease and Its Treatment on Glycemic Control: Clinical and Epidemiological Evidence

Reference	Study Design	Diabetes Type	N Subjects a. Treatment (ages) b. Control (ages)	Follow-Up	Periodontal Therapy	Metabolic Control Outcome Measure	Effects on Metabolic Control	Evidence Level*
Collin et al., 1998[95]	Retrospective cohort	2	‡25 with diabetes (58-76) 40 without diabetes (59-77)	2-3 years	Not applicable	Glycated hemoglobin	HbA1c level significantly increased in those with advanced periodontitis, but not in those without	II-2
Williams and Mahan, 1960[87]	Descriptive clinical study	§	a. 9 (20-32) b. 0	3-7 months	Extractions, scaling and curettage, gingivectomy, systemic antibiotics	Insulin requirement; diabetes control (not operationally defined)	7/9 subjects had "significant" reduction in insulin requirements	III
Wolf, 1977[42]	Treatment study, non-RCT	1 and 2	a. 117 (16-60) b. 0	8-12 months	Scaling and home care instructions, periodontal surgery, extractions, endodontic treatment, restorations, denture replacement or repair	Blood glucose; 24-hour urinary glucose; insulin dose	Compared 23 subjects with improved oral infection with 23 who had no improvement after treatment for oral infection and inflammation. Subjects with improved oral inflammation and infection tended to demonstrate diabetic control improvement (P <0.1). Discussion states "treatment of periodontal inflammation and periapical lesions...does little to improve the control of diabetes."	III
Miller et al., 1992[88]	Treatment study, non-RCT	1	a. 10 (not given) b. 0	8 weeks	Scaling and root planing, systemic doxycycline	Glycated hemoglobin, glycated albumin	Found decrease in glycated hemoglobin and glycated albumin in patients with improvement in gingival inflammation (P <0.01); patients with no improvement in gingival inflammation had either no change or increase in glycated hemoglobin post-treatment.	III
Seppälä et al., 1993,[63] 1994[64]	Treatment study, non-RCT	1	a.‖ 38, 1 year; 22, 2 years 26 PIDD, 1 year (48 ± 6) 12 CIDD, 1 year (43 ± 5) 16 PIDD, 2 years 6 CIDD, 2 years b. 0	2 years	Scaling and root planing, periodontal surgery, extractions	Medical history for baseline control status; glycosylated hemoglobin A1 and blood glucose for assessing response to treatment	Reported an improvement of the HBA1 levels of the PIDD and CIDD subjects (P <0.068; t test).	III

described in recent detailed reviews.[12,96] Perhaps most notable are the identification of only 3 published controlled clinical trials;[86,89,92] with 1 trial specifically designed for periodontal treatment in patients with Type 2 diabetes,[86,92] and potential limitations in length of follow-up time to assess changes in glycated hemoglobin in studies reporting no improvement of glycemic control.

Despite the variation in the literature, there is a distinction in the effect of periodontal treatment on glycemic control related to the mode of therapy.[12] Studies involving mechanical periodontal treatment alone[64,89,90,91,93] reported improvement in periodontal status only (i.e., no change in glycemic control), while studies including systemic antibiotics accompanying mechanical therapy reported an improvement in both periodontal status and glycemic control.[87,88,92] It has been hypothesized that these differential results due to antibiotic use (especially doxycycline) may involve several mechanisms, including an antimicrobial effect, modulation of host response, and possibly inhibition of the non-enzymatic glycosylation process.

Additional evidence to support the effect of severe periodontitis on increased risk for poorer glycemic control comes from 2 longitudinal observational studies. In a longitudinal epidemiological study of the Pima Indians in Arizona, Taylor et al.[94] found that subjects with Type 2 diabetes in good to moderate control and with severe periodontitis at baseline were approximately 6 times more likely to have poor glycemic control at approximately 2-years follow-up than those without severe periodontitis at baseline. In another observational study of 25 adults with Type 2 diabetes, aged 58 to 77 years, Collin et al.[95] also reported an association between advanced periodontal disease and impaired metabolic control.

The clinical and epidemiological evidence reviewed provides support for the concept that periodontal infection contributes to poorer glycemic control in people with diabetes mellitus. However, further rigorous, controlled trials in diverse populations are warranted to firmly establish that treating periodontal infections can be influential in contributing to glycemic control management and possibly to the reduction of the burden of complications of diabetes mellitus.

CONCLUSION

The evidence supports viewing the relationship between diabetes and periodontal diseases as bidirectional; that is, diabetes is associated with increased occurrence and progression of periodontitis, and periodontal infection is associated with poorer glycemic control in people with diabetes. While treating periodontal infection in people with diabetes is clearly an important component in maintaining oral health, it may also have an important role in establishing and maintaining glycemic control. Additional rigorous clinical investigations in diverse populations are warranted to support and extend existing evidence that treating periodontal infections can be influential in contributing to glycemic control management and possibly to the reduction of the burden of complications of diabetes mellitus.

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REFERENCES

1. Harris MI. Summary. In: *National Diabetes Data Group. Diabetes in America,* 2nd ed. NIH Publication No. 95-1468. Washington, DC: Government Printing Office; 1995:1-13.
2. Gavin JR, Alberti KGMM, Davidson MB, et al. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [see comments]. *Diabetes Care* 1997;20:1183-1197.
3. Kenny SJ, Aubert RE, Geiss LS. Prevalence and incidence of non-insulin-dependent diabetes. In: *National Diabetes Data Group. Diabetes in America,* 2nd ed. NIH Publication No. 95-1468. Washington, DC: Government Printing Office; 1995:IV47-IV68.
4. Centers for Disease Control and Prevention. *National Diabetes Fact Sheet: National Estimates and General Information on Diabetes in the United States,* revised ed. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 1998.
5. Albandar JM, Kingman A. Gingival recession, gingival bleeding, and dental calculus in adults 30 years of age and older in the United States, 1988-1994. *J Periodontol* 1999;70:30-43.
6. Albandar JM, Brunelle JA, Kingman A. Destructive periodontal disease in adults 30 years of age and older in the United States, 1988-1994. *J Periodontol* 1999;70:13-29.
7. Salvi GE, Lawrence HP, Offenbacher S, Beck JD. Influence of risk factors on the pathogenesis of periodontitis. *Periodontol 2000* 1997;14:173-201.
8. Wilton JMA, Griffiths GS, Curtis MA, et al. Detection of high-risk groups and individuals for periodontal diseases. Systemic predisposition and markers of general health. *J Clin Periodontol* 1988;15:339-346.
9. Murrah VA. Diabetes mellitus and associated oral manifestations: A review. *J Oral Pathol* 1985;14:271-281.
10. Manouchehr-Pour M, Bissada NF. Periodontal disease in juvenile and adult diabetic patients: A review of the literature. *J Am Dent Assoc* 1983;107:766-770.
11. Oliver RC, Tervonen T. Diabetes—a risk factor for periodontitis in adults? *J Periodontol* 1994;65:530-538.
12. Grossi SG, Genco RJ. Periodontal disease and diabetes mellitus: A two-way relationship. *Ann Periodontol* 1998; 3:51-61.
13. Goteiner D, Vogel R, Deasy M, Goteiner C. Periodontal and caries experience in children with insulin-dependent diabetes mellitus. *J Am Dent Assoc* 1986;113:277-279.
14. Harrison R, Bowen WH. Periodontal health, dental caries, and metabolic control in insulin-dependent diabetic children and adolescents. *Pediatr Dent* 1987;9: 283-286.

15. de Pommereau V, Dargent-Paré C, Robert JJ, Brion M. Periodontal status in insulin-dependent diabetic adolescents. *J Clin Periodontol* 1992;19:628-632.
16. Firatli E. The relationship between clinical periodontal status and insulin-dependent diabetes mellitus. Results after 5 years. *J Periodontol* 1997;68:136-140.
17. Pinson M, Hoffman WH, Garnick JJ, Litaker MS. Periodontal disease and Type I diabetes mellitus in children and adolescents. *J Clin Periodontol* 1995;22:118-123.
18. Cianciola LJ, Park BH, Bruck E, Mosovich L, Genco RJ. Prevalence of periodontal disease in insulin-dependent diabetes mellitus (juvenile diabetes). *J Am Dent Assoc* 1982;104:653-660.
19. Ringelberg ML, Dixon DO, Francis AO, Plummer RW. Comparison of gingival health and gingival crevicular fluid flow in children with and without diabetes. *J Dent Res* 1977;56:108-111.
20. Firatli E, Yilmaz O, Onan U. The relationship between clinical attachment loss and the duration of insulin-dependent diabetes mellitus (IDDM) in children and adolescents. *J Clin Periodontol* 1996;23:362-366.
21. Faulconbridge AR, Bradshaw WC, Jenkins PA, Baum JD. The dental status of a group of diabetic children. *Br Dent J* 1981;151:253-255.
22. Novaes AB Jr., Pereira, ALA, de Moraes N, Novaes AB. Manifestations of insulin-dependent diabetes mellitus in the periodontium of young Brazilian patients. *J Periodontol* 1991;62:116-122.
23. Cohen DW, Friedman LA, Shapiro J, Kyle GC, Franklin S. Diabetes mellitus and periodontal disease: Two-year longitudinal observations. Part I. *J Periodontol* 1970;41: 709-712.
24. Güven Y, Satman I, Dinccag N, Alptekin S. Salivary peroxidase activity in whole saliva of patients with insulin-dependent (Type-1) diabetes mellitus. *J Clin Periodontol* 1996;23:879-881.
25. Kjellman O, Henriksson CO, Berghagen N, Andersson B. Oral conditions in 105 subjects with insulin-treated diabetes mellitus. *Svensk Tandlakaretidskrift* 1970;63: 99-110.
26. Rylander H, Ramberg P, Blohmé G, Lindhe J. Prevalence of periodontal disease in young diabetics. *J Clin Periodontol* 1987;14:38-43.
27. Sznajder N, Carraro JJ, Rugna S, Sereday M. Periodontal findings in diabetic and nondiabetic patients. *J Periodontol* 1978;49:445-448.
28. Galea H, Aganovic I, Aganovic M. The dental caries and periodontal disease experience of patients with early onset insulin dependent diabetes. *Int Dent J* 1986;36: 219-224.
29. Glavind L, Lund B, Löe H. The relationship between periodontal state and diabetes duration, insulin dosage, and retinal change. *J Periodontol* 1968;39:341-347.
30. Hugoson A, Thorstensson H, Falk H, Kuylenstierna J. Periodontal conditions in insulin-dependent diabetics. *J Clin Periodontol* 1989;16:215-223.
31. Thorstensson H, Hugoson A. Periodontal disease experience in adult long-duration insulin-dependent diabetics. *J Clin Periodontol* 1993;20:352-358.
32. Tervonen T, Karjalainen K. Periodontal disease related to diabetic status. A pilot study of the response to periodontal therapy in Type 1 diabetes. *J Clin Periodontol* 1997;24:505-510.
33. Tervonen T, Karjalainen K, Knuuttila M, Huumonen S. Alveolar bone loss in Type 1 diabetic subjects. *J Clin Periodontol* 2000;27:567-571.
34. Novaes AB Jr., Gutierrez FG, Novaes AB. Periodontal disease progression in Type II non-insulin-dependent diabetes mellitus patients (NIDDM). Part I—Probing pocket depth and clinical attachment. *Braz Dent* 1996;7: 65-73.
35. Morton AA, Williams RW, Watts TLP. Initial study of periodontal status in non-insulin-dependent diabetics in Mauritius. *J Dent* 1995;23:343-345.
36. Sandberg GE, Sundberg HE, Fjellstrom CA, Wikblad KF. Type 2 diabetes and oral health. A comparison between diabetic and non-diabetic subjects. *Diabetes Res Clin Pract* 2000;50:27-34.
37. Shlossman M, Knowler WC, Pettitt DJ, Genco RJ. Type 2 diabetes mellitus and periodontal disease. *J Am Dent Assoc* 1990;121:532-536.
38. Nelson RG, Shlossman M, Budding LM, et al. Periodontal disease and NIDDM in Pima Indians. *Diabetes Care* 1990;13:836-840.
39. Emrich LJ, Shlossman M, Genco RJ. Periodontal disease in non-insulin-dependent diabetes mellitus. *J Periodontol* 1991;62:123-131.
40. Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M. Glycemic control and alveolar bone loss progression in Type 2 diabetes. *Ann Periodontol* 1998;3:30-39.
41. Taylor GW, Burt BA, Becker MP, et al. Non-insulin dependent diabetes mellitus and alveolar bone loss progression over 2 years. *J Periodontol* 1998;69:76-83.
42. Wolf J. Dental and periodontal conditions in diabetes mellitus. A clinical and radiographic study. *Proc Finn Dent Soc* 1977;73(4-6 Suppl.):1-56.
43. Benveniste R, Bixler D, Conneally PM. Periodontal disease in diabetics. *J Periodontol* 1967;38:271-279.
44. Finestone AJ, Boorujy SR. Diabetes mellitus and periodontal disease. *Diabetes* 1967;16:336-340.
45. Oliver RC, Tervonen T. Periodontitis and tooth loss: Comparing diabetics with the general population. *J Am Dent Assoc* 1993;124(12):71-76.
46. Bridges RB, Anderson JW, Saxe SR, Gregory K, Bridges SR. Periodontal status of diabetic and non-diabetic men: Effects of smoking, glycemic control, and socioeconomic factors. *J Periodontol* 1996;67:1185-1192.
47. Bacic M, Plancak D, Granic M. CPITN assessment of periodontal disease in diabetic patients. *J Periodontol* 1988;59:816-822.
48. Belting CM, Hiniker JJ, Dummett CO. Influence of diabetes mellitus on the severity of periodontal disease. *J Periodontol* 1964;35:476-480.
49. Yavuzyilmaz E, Yumak O, Akdoganli T, Yamalik N, Ozer N, Ersoy F. The alterations of whole saliva constituents in patients with diabetes mellitus. *Aust Dent J* 1996;41: 193-197.
50. Sandler HC, Stahl SS. Prevalence of periodontal disease in a hospitalized population. *J Dent Res* 1960;39:439-449.
51. Hove KA, Stallard RE. Diabetes and the periodontal patient. *J Periodontol* 1970;41:713-718.
52. Mackenzie RS, Millard HD. Interrelated effects of diabetes, arteriosclerosis and calculus on alveolar bone loss. *J Am Dent Assoc* 1963;66:191-198.
53. Grossi SG, Zambon JJ, Ho AW, et al. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol* 1994;65:260-267.
54. Tervonen T, Knuuttila M. Relation of diabetes control to periodontal pocketing and alveolar bone level. *Oral Surg Oral Med Oral Pathol* 1986;61:346-349.
55. Dolan TA, Gilbert GH, Ringelberg ML, et al. Behavioral risk indicators of attachment loss in adult Floridians. *J Clin Periodontol* 1997;24:223-232.

56. Campbell MJA. Epidemiology of periodontal disease in the diabetic and the non-diabetic. *Aust Dent J* 1972; 17:274-278.
57. Albrecht M, Bánóczy J, Tamás G Jr. Dental and oral symptoms of diabetes mellitus. *Community Dent Oral Epidemiol* 1988;16:378-380.
58. Szpunar SM, Ismail AI, Eklund SA. Diabetes and periodontal disease: Analyses of NHANES I and HHANES *J Dent Res* 1989;68(Spec. Issue):383(Abstr. 1605).
59. Ünal T, Firatli E, Sivas A, Meric H, Oz H. Fructosamine as a possible monitoring parameter in non-insulin dependent diabetes mellitus patients with periodontal disease. *J Periodontol* 1993;64:191-194.
60. Ainamo J, Lahtinen A, Uitto V-J. Rapid periodontal destruction in adult humans with poorly controlled diabetes. A report of 2 cases. *J Clin Periodontol* 1990;17: 22-28.
61. Gusberti FA, Syed SA, Bacon G, Grossman N, Loesche WJ. Puberty gingivitis in insulin-dependent diabetic children. I. Cross-sectional observations. *J Periodontol* 1983; 54:714-720.
62. Safkan-Seppälä B, Ainamo J. Periodontal conditions in insulin-dependent diabetes mellitus. *J Clin Periodontol* 1992;19:24-29.
63. Seppälä B, Seppälä M, Ainamo J. A longitudinal study on insulin-dependent diabetes mellitus and periodontal disease. *J Clin Periodontol* 1993;20:161-165.
64. Seppälä B, Ainamo J. A site-by-site follow-up study on the effect of controlled versus poorly controlled insulin-dependent diabetes mellitus. *J Clin Periodontol* 1994;21: 161-165.
65. Tervonen T, Oliver RC. Long-term control of diabetes mellitus and periodontitis. *J Clin Periodontol* 1993;20: 431-435.
66. Karjalainen KM, Knuuttila MLE. The onset of diabetes and poor metabolic control increases gingival bleeding in children and adolescents with insulin-dependent diabetes mellitus. *J Clin Periodontol* 1996;23:1060-1067.
67. Nichols C, Laster LL, Bodak-Gyovai LZ. Diabetes mellitus and periodontal disease. *J Periodontol* 1978;49:85-88.
68. Barnett ML, Baker RL, Yancey JM, MacMillan DR, Kotoyan M. Absence of periodontitis in a population of insulin-dependent diabetes mellitus (IDDM) patients. *J Periodontol* 1984;55:402-405.
69. Hayden P, Buckley LA. Diabetes mellitus and periodontal disease in an Irish population. *J Periodont Res* 1989; 24:298-302.
70. Sandholm L, Swanljung O, Rytömaa I, Kaprio EA, Mäenpää J. Periodontal status of Finnish adolescents with insulin-dependent diabetes mellitus. *J Clin Periodontol* 1989;16:617-620.
71. Sastrowijoto SH, Hillemans P, van Steenbergen TJM, Abraham-Inpijn L, de Graaff J. Periodontal condition and microbiology of healthy and diseased periodontal pockets in Type 1 diabetes mellitus patients. *J Clin Periodontol* 1989;16:316-322.
72. Moore PA, Weyant RJ, Mongelluzzo MB, et al. Type 1 diabetes mellitus and oral health: Assessment of periodontal disease. *J Periodontol* 1999;70:409-417.
73. Svenson KLG, Lundqvist G, Wide L, Hällgren R. Impaired glucose handling in active rheumatoid arthritis: Relationship to the secretion of insulin and counter-regulatory hormones. *Metabolism* 1987;36:940-943.
74. Hällgren R, Lundquist G. Elevated serum levels of pancreatic polypeptide are related to impaired glucose handling in inflammatory states. *Scand J Gastroenterol* 1983;18:561-564.
75. Beck-Nielsen H. Clinical disorders of insulin resistance. In: Alberti KGMM, Defronzo RA, Keen H, Zimmet P, eds. *International Textbook of Diabetes Mellitus*. New York: Wiley; 1992:531-568.
76. Beisel WR. Metabolic response to infection. *Annu Rev Med* 1975;26:9-20.
77. Drobny EC, Abramson EC, Baumann G. Insulin receptors in acute infection: A study of factors conferring insulin resistance. *J Clin Endocrinol Metab* 1984;58:710-716.
78. Sammalkorpi K. Glucose intolerance in acute infections. *J Intern Med* 1989;225:15-19.
79. Offenbacher S, Katz V, Fertik G, et al. Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol* 1996;67:1103-1113.
80. Feingold KR, Soued M, Serio MK, Moser AH, Dinarello CA, Grunfeld C. Multiple cytokines stimulate hepatic lipid synthesis in vivo. *Endocrinol* 1989;125:267-274.
81. Ling PR, Istfan NW, Colon E, Bistrian BR. Differential effects of interleukin-1 receptor antagonist in cytokine- and endotoxin-treated rats. *Am J Physiol* 1995;268(2 Pt 1):E255-E261.
82. Feingold KR, Grunfeld C. Role of cytokines in inducing hyperlipidemia. *Diabetes* 1992;41(Suppl. 2):97-101.
83. Grunfeld C, Soued M, Adi S, Moser AH, Dinarello CA, Feingold KR. Evidence for two classes of cytokines that stimulate hepatic lipogenesis: Relationships among tumor necrosis factor, interleukin-1 and interferon-alpha. *Endocrinol* 1990;127:46-54.
84. Michie HR. Metabolism of sepsis and multiple organ failure. *World J Surg* 1996;20:460-464.
85. Pickup JC, Mattock MB, Chusney GD, Burt D. NIDDM as a disease of the innate immune system: Association of acute-phase reactants and interleukin-6 with metabolic syndrome X. *Diabetologia* 1997;40:1286-1292.
86. Grossi SG, Skrepcinski FB, DeCaro T, Zambon JJ, Cummins D, Genco RJ. Response to periodontal therapy in diabetics and smokers. *J Periodontol* 1996;67:1094-1102.
87. Williams RC Jr, Mahan CJ. Periodontal disease and diabetes in young adults. *JAMA* 1960;172:776-778.
88. Miller LS, Manwell MA, Newbold D, et al. The relationship between reduction in periodontal inflammation and diabetes control: A report of 9 cases. *J Periodontol* 1992;63:843-848.
89. Aldridge JP, Lester V, Watts TLP, Collins A, Viberti G, Wilson RF. Single-blind studies of the effects of improved periodontal health on metabolic control in Type 1 diabetes mellitus. *J Clin Periodontol* 1995;22:271-275.
90. Smith GT, Greenbaum CJ, Johnson BD, Persson GR. Short-term responses to periodontal therapy in insulin-dependent diabetic patients. *J Periodontol* 1996;67:794-802 (erratum: 1996;67:1368).
91. Westfelt E, Rylander H, Blohmé G, Jonasson P, Lindhe J. The effect of periodontal therapy in diabetics. Results after 5 years. *J Clin Periodontol* 1996;23:92-100.
92. Grossi SG, Skrepcinski FB, DeCaro T, et al. Treatment of periodontal disease in diabetics reduces glycated hemoglobin. *J Periodontol* 1997;68:713-719.
93. Christgau M, Palitzsch KD, Schmalz G, Kreiner U, Frenzel S. Healing response to non-surgical periodontal therapy in patients with diabetes mellitus: Clinical, microbiological, and immunologic results. *J Clin Periodontol* 1998;25:112-124.
94. Taylor GW, Burt BA, Becker MP, et al. Severe peri-

odontitis and risk for poor glycemic control in patients with non-insulin-dependent diabetes mellitus. *J Periodontol* 1996;67:1085-1093.
95. Collin H-L, Uusitupa M, Niskanen L, et al. Periodontal findings in elderly patients with non-insulin dependent diabetes mellitus. *J Periodontol* 1998;69:962-966.
96. Taylor GW. Periodontal treatment and its effects on glycemic control: A review of the evidence. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999;87:311-316.
97. U.S. Department of Health and Human Services. *Oral Health in America: A Report of the Surgeon General.* Rockville, MD: U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health; 2000.
98. Taylor GW, Loesche WJ, Terpenning MS. Impact of oral diseases on systemic health in the elderly: Diabetes mellitus and aspiration pneumonia. *J Public Health Dent* 2000;60:313-320.
99. U.S. Preventive Services Task Force. *Guide to Clinical Preventive Services,* 2nd ed. Washington, DC: Government Printing Office; 1996.

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