Dental Conditions and Periodontal Disease in Adolescents with Type 1 Diabetes Mellitus

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1. Introduction
The importance of type 1 (diabetes mellitus) DM lies in the function it plays in dentition and oral health for children and adolescents. The consequences of DM concerning oral health are in connection with the systemic changes caused by the disease, though the results are in certain cases conflicting. Oral manifestations related to DM may have a strong inclination to periodontal disease, as well as an increased incidence of dental caries, mucosal lesions and dry mouth (xerostomia). However, as mentioned before, the results are not entirely in accord. Children and adolescents with type 1 DM are more susceptible to infections in the dental connective tissues than those without type 1 DM. The dentist’s liability is to evaluate the dangers and maintain adequate oral hygiene to prevent the occurrence of disfunctional oral effects of type 1 DM.

2. Periodontal disease
Periodontitis is a chronic multifactorial plaque induced Gram-negative anaerobic infection of the periodontium that results in the destruction of periodontal tissues and loss of alveolar bone. Periodontitis is to be treated by the mechanical removal of supra- and subgingival bacterial plaque with scalers, curettes or ultrasonic devices (scaling and root planing [SRP]), and by instructing the parient about oral hygiene. The development of new dental plaque deposits and re-infection of the subgingival tissues can only be prevented in case of a near-ideal oral hygiene. For the improvement of clinical periodontal status the regular use of systemic or local antibiotics as an adjunctive therapy to SRP is still concerned problematic. Deep residual periodontal lesions can usually be reduced or eliminated by surgery.

2.1 Diabetes and periodontal disease
There is an extensive debate on the influence of DM on the risk of periodontal disease. According to most of the experts, patients suffering from diabetes mellitus are highly susceptible to develop periodontal disease. In 1993, periodontal disease was termed as the sixth complication of diabetes, while in the report of the Expert Comittee on the Diagnosis and Classification of Diabetes Mellitus issued in 1997, periodontal disease was mentioned as a disease of very high incidence in case of patients with diabetes. Many papers on the subject have outlined that the inclination, extent, severity and development of
Periodontal disease are significantly increased in case of patients with diabetes. Impaired immune response, different bacterial microflora and collagen metabolism are involved in the pathogenesis of diabetic periodontal disease. This is especially true if the diabetes is poorly controlled and there is a lasting periodontal disease in case of type 1 DM individuals.

Gingival bleeding is a sign of inflammation. Vascular changes in diabetes mellitus may result in increased gingival bleeding. If however the diabetes is adequately treated, there are fewer vascular changes. Gingival bleeding is in positive correlation with the accumulation of plaque and calculus. Diabetics showed more plaque and higher calculus index scores than the control groups. Calcium concentration was high in both the parotid and submandibular saliva of patients with type 1 DM. This result may explain the regularly experienced increase in calculus formation in the case of these patients. Individuals with a decreased glucose tolerance showed a higher rate of pocket formation, presence of calculus, increased tooth mobility and tooth loss. Variable models have been developed to give reason to this correlation such as periodontal chronic inflammation which results in increased circulating cytokines and inflammatory mediators, autoimmune response to the chronic periodontal infection that gives way to endothelial dysfunction, or the presence of certain factors that leads to increased inclination both to periodontal disease and diabetes vascular diseases at the same time.

Statistically significant relation has been detected between the HbA1C levels of the patients and the biomass, haemolysin activity and protease activity. The biofilm formation is likely to have an effect on the pathogenicity of oral candidosis.

There is, however, a minority of experts who are sceptical about the high risk of type 1 DM. Today Glickman’s theory is the most widely accepted one. According to Glickman, the father of modern periodontology, diabetes are not the direct cause, but a predisposing condition for periodontal disease. There is a bidirectional relationship between diabetes and periodontal diseases. Diabetic adolescents have more prevalence and more severe gingival inflammation than healthy control persons of the same age, despite similar plaque scores. Metabolic imbalances in the tissues may reduce the resistance of diabetics to infection, and thus affect the initiation, development and progression of periodontal disease. Adolescents with type 1 DM develop an earlier and higher gingival inflammatory response to a similar bacterial challenge than non diabetics. In accordance with this fact, extended studies have shown that severe periodontal disease in diabetic patients is primarily related to poor metabolic control and other diabetes complications occurring during the follow-up process. Still, long-duration diabetics resulted in more severe periodontitis than short-duration diabetics. It has been proposed that fine periodontal treatment of diabetic patients may lead to the lowering of diabetic complications. Chronic Gram-negative infections and chronic endotoxaemia, which arise in case of periodontal disease, may also increase insulin resistance and reduce metabolic control in case of diabetic patients. This entails the hypothesis that elimination or control of periodontal infection may improve the metabolic control of diabetes. It has been proposed that a microbiological imbalance in the gut may increase the gram-negative bacterial load, which would also increase the systematic inflammatory burden through the lipopolysaccharides leakage into the circulation. Increased inflammation leads to insulin resistance. According to a study, insulin requirements were lowered following periodontal treatment and reduction of inflammation in diabetic patients. It has been demonstrated that the interaction of periodontal bacterial byproducts with mononuclear phagocytic cells and fibroblasts induces the chronic release of cytokines (IL-1β, IL-6, TNF-α), PGE2 and CRP.
Recently many studies have proposed that periodontal disease is a substantial aggravating factor in restoring the health of patients with diabetes.\textsuperscript{56} It is mainly due to the fact that it maintains a chronic systemic inflammatory process. However, the causality between periodontitis and altered glycaemic control can only be justified epidemiologically with prospective interventional studies.\textsuperscript{57} The control of periodontal disease could be an essential part of the overall treatment of diabetic patients: the periodontal therapy may improve glycaemic control, and could lead to a significant lowering of HbA1c values.\textsuperscript{40}

Concerning the adolescents, the oral hygiene seems to be better in case of the diabetic patients than in case of the other group of young patients who have shown highly variable work shifts leading to poor oral hygiene. The difference is reflected by a lesser bacterial plaque among the diabetics. This is in conflict with the results of other authors who observed similar oral hygiene status and plaque indexes in the two groups, or even comparatively increased plaque accumulation among the diabetics.\textsuperscript{58} The reason for this may be the following: although the diabetics were controlled, they showed a high gingival response to the irrigation caused by bacterial plaque retention.\textsuperscript{59} Regularly diabetics have a greater incidence regarding periodontal disease than healthy individuals,\textsuperscript{60,61} though other studies have not detected such relation between periodontal disease and diabetes.\textsuperscript{62,63,64} They didn’t confirm any association between diabetes and periodontal disease in adolescents. They believe that there is no difference between on the one part type 1 DM adolescents and children, and on the other healthy individuals regarding clinical periodontal status. However Fructosamine value, used to diagnose and monitor diabetes, was observed to be in correlation with the gingival index score in case of type 1 DM adolescents and children, but not in case of healthy control subjects.\textsuperscript{65} Bay et al.\textsuperscript{34} found no difference in the degree resolution of gingivitis following scaling and root planning between young diabetics and healthy control group. Barnett et al.\textsuperscript{35} studied periodontitis prevalence in young diabetics but none of the individuals showed radiographic sign of periodontitis. Despite the comparatively better control of bacterial plaque among the diabetics, a change in their periodontal response was detected. Therefore it seems that local immune response may possibly change among these patients, and the lesions caused by microbial agents in case of periodontal disease, which can be associated with a lesser tissue repair capacity, might be the reason for the increased deterioration of periodontal structures shown in the diabetic group.\textsuperscript{4}

It is possible, that the diversities observed by the different authors result from local health care habits. In an area with a tradition of good oral hygiene, the oral hygiene habits of diabetes are not better than those of healthy people. Therefore in case of similar oral hygiene habits, diabetical patients show lower periodontal values than healthy persons because of the above mentioned immune response. In areas where the dental treatment habits of the population are poorer, the greater attention of well-controlled DM patients to oral hygiene results in higher values than those of healthy individuals.

### 2.2 Prevalence of gingivitis, periodontitis in adolescents with type 1 DM

Since there are conflicting reports in the literature, the aim of this study was analyse the periodontal disease in adolescents with type 1 diabetes mellitus.\textsuperscript{66} Characterization of risk factors, local such as oral hygiene-, general (duration of DM, age, degree of metabolic control of DM) and contributory factors-, such as toothbrushing, have been identified that determining the risk factors place people enhanced risk in development and progression of periodontal diseases.
A dental clinical cross-sectional examination was carried out on 259 adolescents of ages 14-19 with type 1 DM in comparison with a non-DM group as control group. Children who had been under the age of eight at the onset of DM were excluded, as where those with any additional disease or taking other chronic medication. The control group comprised of metabolically healthy individuals. The DM patients were classified according to the categories recommended by the World Health Organisation (1999). The Greene-Vermillion OHI-S index was used to determine the level of oral hygiene. Periodontal changes were rated by the Russell's periodontal index (PI), which estimates the degree of periodontal disease occurring in the mouth by measuring both bone loss around the teeth and gingival inflammation. This method is regularly used in the epidemiological investigation of the disease. Alveolar bone loss was tested according to Schei et al (1959), and Hirschman et al (1994) with panoramic radiograph and vertical or posterior bitewings radiographs.

The DM subjects were characterised according to the following criteria: mean postprandial blood glucose level during the period of 6 months prior to the dental examination; glycosylated haemoglobin (HbA1C) level; duration of the DM; the age at the onset of DM. The ADA (2005) criteria were used concerning the DM control. Diabetes mellitus was well-controlled (in 210 cases), if six months before the dental examination the mean postprandial blood glucose level of the patients was normal or near normal (below 7.5 mmol/l), there was no glycosuria HbA1C≤ 6.5%, and severe hypoglicaeia did not occur. Control was taken to be poor when the postprandial blood sugar was ≥ 7.5 mmol/l and/or haemoglobin was > 6.5%, or in case of patients with asymptomatic hypoglicaeia.

The incidence of gingivitis and periodontitis was much higher in case of diabetic adolescents than in case of metabolically healthy persons (p< 0. 0001) and especially in case of girls ( p< 0. 001). Healthy periodontium was only found in case of 2.6% of the DM adolescents and the rest of DM patients had either gingivitis (61.03%) or periodontitis (39%), while a high rate of metabolically healthy persons (80.5%) has shown a healthy periodontium. Gingivitis and periodontitis was experienced in case of 18.4% and 1.1% of the patients. (Fig.1.)

With the fall of oral hygiene (OHI-S) index (p< 0. 0001) the intensity of gingivitis and periodontitis (PI) has become more severe. (Fig.2.)

An important positive correlation has been shown between the control level of the disease and the intensity of gingivitis and periodontitis. In case of well-controlled 'Type 1' diabetic adolescents the PI mean value was lower than in case of patients with poor glycemic control ( p< 0. 0001).

In the diabetic group the periodontal disease was detected to be severe in case of those who had a lasting DM (>5 years) (p<0.001).

The majority of the control persons showed no alveolar bone loss (83% had intact alveolar bone) and those who had alveolar bone loss, had primarily that of horizontal type. In case of diabetic adolescents prevalence of intact alveolar bone was lower (61.8%) than in case of the control group. Therefore higher degree of alveolar bone resorption (both horizontal and horizontal+vertical type) was experienced in case of diabetic patients than in case of the control group (p<0.001).

The mean values of alveolar bone resorption were higher in case of diabetic boys than in case of diabetic girls (p<0.0001).
Prevalence of Gingivitis and Periodontitis

Fig. 1. Prevalence of gingivitis and periodontitis

Oral Hygiene and PI

Fig. 2. The mean value of PI according to oral hygiene (OHI-S)
The intensity of gingivitis and periodontitis, as well as the increased alveolar bone loss was more prevalent and more severe in diabetic adolescents than in healthy individuals. Several authors suggested a correlation between diabetes mellitus and periodontal diseases. According to them periodontal disease is one of the most prevalent and rapidly progressive complications of DM in case of adults.

Sappala et al. (1993) has shown that adults with Type 1 diabetes mellitus have higher degree of attachment loss and bone loss than control subjects under similar dental plaque conditions. The authors received the same results for diabetic adolescents. The oral hygiene (OHI-S), especially the debris index was worse in case of diabetic individuals than in case of the control persons and correlation was found between on the one part the intensity of gingivitis and periodontitis and on the other the oral hygiene. However De Pommereu et al. found more serious gingivitis in diabetics than in control persons, although plaque scores were the same in both groups. Interestingly, according to the present study diabetic adolescents, especially boys have more severe alveolar bone destruction than non-diabetics.

The present study demonstrates that severity of periodontal disease increases with the duration of diabetes mellitus, in agreement with the results in case of adults measured by Pavez and Greene Vermillion (1964), Rosenthal et al. (1988), and Lopey et al. (2002). This study shows that the poorly controlled type 1 DM with elevated blood glucose and glycosylated hemoglobin (HgA1c) levels have more incipient and serious periodontal diseases with alveolar bone loss in case of adolescents with lasting diabetes mellitus. Adequate metabolic control of diabetes mellitus lowers inclination to infection. This is also crucial for the prevention of periodontal disease in case of adolescents with diabetes mellitus. In case of adult diabetic patients with poorly controlled diabetes mellitus, increased metabolic control may improve periodontal condition (Miller et al. 1992, Yki-Jarvinen 1989, Harris 1995, RST/AAP 1999).

Periodontitis is a complex multifactorial disease. It can especially cause a problem for adolescents with DM. Inadequate oral hygiene is responsible for high oral debris in case of diabetic adolescents, being in correlation with the status of periodontium. Several other characteristics such as long duration, early onset (under 14 years), and degree of metabolic control, have been determined as factors increasing the risk of disease. In case of diabetic girls the monthly hormonal level alterations of the gingival may play a role in the development and progression of gingivitis, periodontitis and alveolar bone resorption.

Frequent dental treatments may help maintain good oral health. Treatment is especially crucial at the onset of the disease. Dental care at the early stages of the disease, reducing susceptibility to infection, is also significant for the prevention of periodontal disease in case of adolescents with type 1 diabetes mellitus. Children should also be checked regularly for bleeding gums or inflammation for to prevent the alveolar bone loss, which leads to irreversible changes of periodontium.

The education of youngsters on proper home oral care is the basic method for periodontal treatment and prevention. In most cases the gingivitis can be resolved by plaque control.

3. Caries

Dental caries is a chronic bacterial disorder where bacterial processes damage hard tooth structure (enamel, dentin, and cementum). The tissues break down progressively, resulting in dental caries (cavities, holes in the teeth). The basic factors are the causal microorganism, the host (tooth), the substrate (diet), and the immune capacity of the patient.
Two groups of bacteria may cause caries: *Streptococcus mutans* and *Lactobacillus*. Bacteria gather around the teeth and gum in a sticky, creamy-coloured mass called plaque, which serves as a biofilm. Bacteria in an individual's mouth transform glucose, fructose, and most regularly sucrose into acids such as lactic acid through a glycolytic process called fermentation. In direct relation with the tooth, these acids may lead to demineralization, i.e. the dissolution of its mineral content. However the process is dynamic. If the acid is neutralized by saliva or mouthwash, remineralization may arise. Fluoride toothpaste or dental varnish can help remineralization. If the demineralization process is continuous, enough mineral content could be lost so that the soft organic material left behind disintegrates, forming a cavity or hole. Caries is one of the most common diseases of the world at present.

### 3.1 Diabetes and caries

Epidemiological studies do not seem to be in accord on the characteristics of diabetes mellitus (DM) concerning the incidence of dental caries in case of both children and adults. Although adolescents may be more caries-prevalent than individuals of other ages, only few studies deal with this age group. In case of type 1 diabetics an increased prevalence was detected, located particularly in the root or dental neck regions. However studies differ whether control of DM or sucrose-free diet of DM patients is more likely to promote or inhibit the development of dental caries. Opinions do not match concerning the dental condition for patients with DM or the outcome of early DM manifestation regarding the dental condition. Cross-sectional studies have reported a low prevalence of caries in case of children and adolescents with type 1 DM, and this has mainly been explained by the sucrose-restricted diet, which is a part of the lifelong treatment. According to Wegner, the frequency of caries in DM children is at least not lower than in non-DM children. Wegner also observed that, directly after the diagnosed onset of their disease, some young DM patients displayed a higher activity of caries than healthy subjects of the same age, but the frequency of caries gradually diminished in association with dietary restriction and treatment with insulin. Other researchers proposed a relationship between the development of caries and the level of metabolic control. These researches showed a higher prevalence of caries in case of poorly controlled DM than in case of well-controlled disease. The reason is that higher glucose content in oral fluids adds to bacterial proliferation, enhancing the formation of dental plaque. It has been shown for all concerning age groups that children with DM have less caries than non-diabetic children. However, these experiments also demonstrated that the result was due to an abundance of sites where teeth were lost without replacement. The complications were not symptoms of type 1 DM, they might be caused by poor medical and dental care. Some studies proposed that salivary secretion rates should be substantially lowered in case of children with type 1 DM when compared to healthy children. Reduced salivary secretion increases the probability of caries, although adequate metabolic control prevents the most dangerous salivary alterations such as high glucose content and low pH, while a fine diabetic diet, rich in fiber and poor in simple carbohydrates, can decelerate the development of plaque and the proliferation of acidogenic bacterial microflora. Individuals at ages of adolescence generally clean their teeth less frequently than persons at ages after adolescence. Behavioral factors such as dental self-efficacy are in relation with DM self-efficacy and adherence. Adequate oral health habits may lead to lower incidence of caries. On the other hand, Moore et al. observed similar regularities concerning the use of dentifrice and dental floss between diabetics and non-diabetics. However other studies demonstrated that diabetic patients used dental floss more frequently than non-diabetics. It seems that there are contradicting studies on the dental condition in case of patients with DM as well as on the effect of early DM manifestation on the dental condition.
3.2 Dental caries in adolescent with type 1 DM
Since there are conflicting reports regarding the dental condition in patients with DM or the effect of early DM manifestation on dental condition, the aim was to analyse the dental status DMF-T and the prevalence of dental caries in adolescents with type 1 DM and compare the findings with those from metabolically healthy individuals, in an effort to determine the risk factors play a role in the development of dental caries in DM adolescents.91

A dental clinical cross-sectional examination was carried out on 259 adolescents aged 14-19 years with type 1 DM in comparison with a non-DM group as control. Children who had been under the age of eight at the onset of DM were excluded, as were those with any additional disease or taking other chronic medication. The control group comprised metabolically healthy individuals. The DM patients were classified according to the categories recommended by the World Health Organisation (WHO). Caries was assessed by the DMF-T index. Within this index, F was used for the filled teeth, D denoted the number of untreated carious teeth without regard to whether the lesion was enamel or of root. Extractions for orthodontics or periodontal reasons were excluded. The Greene-Vermillion OHI-S index was used to determine the level of oral hygiene. The DM subjects were characterised according to the following criteria: mean postprandial blood glucose level and during the period of 6 months prior to the dental examination; glycosylated haemoglobin (HbA1C) level; the duration of the DM; and the age at the onset of DM: Concerns by DM control, the ADA (2005) criteria were offered. Diabetes mellitus was well-controlled (210 cases) if six months before the dental examination the mean postprandial blood glucose level of the patients was normal or near normal (below 7.5 mmol/l) there was no glycosuria HbA1C ≤ 6.5% and severe hypoglicaeia is did not occur. Control was taken as poor when the postprandial blood sugar was ≥ 7.5 mmol/l and/ or haemoglobin was > 6.5%, or in cases of patients with asymptomatic hypoglicaeia.

The DM adolescents had a slightly higher mean DMF-T score than the control subjects. The difference was found to be statistically significant (p<0.001).

When the components of DMFT were considered, there were more filled (F) (p<0.001) and fewer decayed teeth (D) (p<0.0001) among the DM adolescents than in the healthy controls. When the number of missing teeth was considered, there were no significant differences between the DM patients and the healthy controls.

The DM boys had a slightly higher mean DMFT score than the DM girls (p<0.001). More decayed (D) (p<0.001) and filled (F) teeth were found among the DM boys than among the DM girls (p<0.001). As regard the number of extracted (M) teeth, there were no significant differences between the boys and the girls.

The age of the patient at the onset of DM was correlated to the caries condition (D). This suggested that the early onset of DM (before the age of 14) was related to significantly fewer decayed and filled teeth compared with the patients in whom the DM had developed after age 14 years (p< 0.01). (Fig.3.)

However the adolescents with good oral hygiene (OHI-S=0), there was a significant differences (P<0.0001). (Fig.4.) A positive correlation was found between of the level of control of the DM and the dental condition. In the well-controlled DM adolescents the mean number of decayed (D) teeth was lower (p< 0.0001), but the number of filled (F) teeth was higher than in patients with poorer glycemic control(P<0.001). (Fig.5.)
Fig. 3. The mean number of the DMF-T and D+F according to the age of the patient at the onset of type 1 DM in patients with good oral hygiene (OHI-S=0)

Fig. 4. The mean number of the DMF-T and D+F according to the age of the patient at the onset of type 1 DM in patients with good oral hygiene (OHI-S=0)
This study of adolescents with type 1 DM demonstrated that none of the subjects has intact dentitions. Poor glycaemic control and the early onset of DM may increase the risk of dental caries but appropriate oral hygiene together with satisfactory metabolic control may prevent the development of dental caries in adolescents with type 1 DM.

4. Tooth eruption

Eruption is the physiological process of tooth development and growth during which the teeth enter the mouth and become visible. Normally they cut themselves through the oral mucosa without any inflammation.

Mixed dentition starts when the first permanent molar appears in the mouth, usually at five or six years, and ends when the last primary tooth is lost, usually at ten, eleven, or twelve years. Afterwards the permanent dentition begins and lasts as long as the person lives or until all of the teeth are lost (edentulism).

4.1 Diabetes mellitus and accelerated eruption

It has been demonstrated that diseases containing metabolic instabilities, such as diabetics, weaken the resistance to inflammation. As a result, the gingival inflammation accompanies eruption in the diabetic patients at an increased rate as compared to the non-diabetic individuals.

Information on dentition concerning the age group from 5 to 9 is limited to about 60 type 1 DM children. Ziskin et al. detected a small and insubstantial affect of diabetes on dental development. Studies concerning accelerated dental development in case of diabetic children who are less than 11.5 years old are not in accord. Older diabetic children manifested delayed dental development. The edentulous interval was longer in case of diabetic children than in case of the control population.
Adler et al. proposed that metabolic disorders cause the acceleration and delay experienced in dentition. A biphasic effect of the diabetic state on dental development was detected: on the one hand acceleration in the early diabetes, and on the other retardation in lasting diabetes. The result conflicted with common knowledge: acceleration was observed in dentition until the age of 10 and delay after the age of 10 (especially for the eruption of canine and the premolars). This may be in correlation with diseases containing metabolic instabilities, such as diabetes.

Other studies showed that children with diabetes in the late mixed dentition period (ages 10-14) had a higher inclination for advanced tooth eruption than those without diabetes. Alterations in tooth eruption were not detected in the early mixed dentition group (ages 6-10). Individuals with higher height showed higher propensity for expedited tooth eruption. The expedited eruption among patients with higher height was more characteristic in the older group than in the younger one.

5. Diabetes and dental, periodontal prevention in adolescents

Diabetes is a chronic metabolic disease which affects the entire organism, disturbing especially the oral health. Health habits are substantial for preventing dental and periodontal diseases and maintaining oral health in a population of patients with type 1 DM.

It is a vital task for dentists to foster good oral health habits, executing periodic dental examinations and ensuring sufficient oral hygiene. These conditions significantly affect the diabetic patients’ oral health. Dentists must minimize the risk factors of periodontal disease, caries and oral soft tissue pathologies. Dentists should continually instruct and motivate the patient concerning oral hygiene.

Dental practice showed that health promoting methods reduce the patient’s smoking habits. It is possible to use pharmacological and behavioral strategies in a private practitioner’s office to help patients quit smoking. However inadequate undergraduate dental education and practitioner continuing education threaten to be an obstacle for the daily use of these practices. There are positive signs concerning the improvement of educational opportunities, nevertheless the incorporation of these technics in the clinical practice must still be highlighted.

There are two kinds of professional oral hygiene promotion: active and sustaining procedure. The initial or causal promotion is to eliminate the plaque and the plaque retentional factors and to remove the supra- and subgingival calculus, as well as the root planing and the curettage and to eliminate the carious lesions. The goal of these procedures is to terminate the inflammation of the gingiva and to stop further development of the gingival recession, thus eliminating the bacterial elements responsible for inflammation. The most important condition of efficient private oral hygiene is the smooth cleanable tooth surface. For it is useless to instruct the patient even on the most refined tooth brushing technique or on the use of dental floss if the teeth are covered with calculus or there are overfilled interdental spaces. Dental practice should include dental check within one or two months, oral hygiene treatment, repeated fixing of gingival and periodontal indexes, as well as their comparison with the initial values, and in certain cases causal surgical periodontal interventions. Nonetheless, further instructions and motivations are also essential.
6. References


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This book is a compilation of reviews about the complication of Type 1 Diabetes. T1D is a classic autoimmune disease. Genetic factors are clearly determinant but cannot explain the rapid, even overwhelming expansion of this disease. Understanding etiology and pathogenesis of this disease is essential. The complications associated with T1D cover a range of clinical obstacles. A number of experts in the field have covered a range of topics for consideration that are applicable to researcher and clinician alike. This book provides apt descriptions of cutting edge technologies and applications in the ever going search for treatments and cure for diabetes.

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