Journal of Clinical Periodontology
Official Journal of The European Federation of Periodontology
Founded by the British, Dutch, French, German, Scandinavian, and Swiss Societies of Periodontology

J Clin Periodontol 2009; 36: 100–105 doi: 10.1111/j.1600-051X.2008.01350.x

Role of serum cytokines tumour necrosis factor-α and interleukin-6 in the association between body weight and periodontal infection

Tuomas Saxlin[1], Liisa Suominen-Taipale[2], Jaana Leiviskä[2], Antti Jula[2], Matti Knuuttila[3] and Pekka Ylöstalo[1]

[1]Institute of Dentistry, University of Oulu, Oulu, Finland; [2]National Public Health Institute (KTL) of Finland, Helsinki, Finland; [3]Oral and Maxillofacial Department, Oulu University Hospital, Oulu, Finland

Saxlin T, Suominen-Taipale L, Leiviskä J, Jula A, Knuuttila M, Ylöstalo P. Role of serum cytokines tumour necrosis factor-α and IL-6 in the association between body weight and periodontal infection. J Clin Periodontol 2009; 36: 100–105 doi: 10.1111/j.1600-051X.2008.01350.x.

Abstract

Aim: To study the role of serum cytokines tumour necrosis factor α (TNF-α) and interleukin 6 (IL-6) as potential mediators in the association between body weight and periodontal infection among an adult population.

Material and Methods: This study was based on a subpopulation of the Health 2000 Health Examination Survey, which included dentate non-diabetic, non-rheumatic subjects, aged between 45 and 64 years, who had never smoked and whose serum levels of TNF-α and IL-6 were analysed and whose periodontal status was clinically determined (effective $n = 425$). The number of teeth with periodontal pockets of 4 mm or more and the number of teeth with periodontal pockets of 6 mm or more were used as outcome variables. Relative risks and 95% confidence intervals were estimated using Poisson regression models.

Results: Serum IL-6, but not TNF-α associated with teeth with deepened periodontal pockets. Multivariate models showed that IL-6, but not TNF-α, could mediate the effect of body weight on periodontium.

Conclusion: In this population of non-diabetic and non-rheumatic subjects, who had never smoked, serum IL-6 was associated with periodontal infection. The results suggest that serum IL-6 could be one mediating factor that connects body weight and periodontal infection.

Key words: body weight; IL-6; periodontal infection; TNF-α

Accepted for publication 23 October 2008

Cytokines, essential parts in the regulation of inflammation, play a role in wound repair and in transient inflammations, as they activate defence mechanisms but may also give rise to considerable tissue damage in more severe inflammations. Cytokines have been suggested to have a role in the pathogenesis of several diseases, such as diabetes mellitus (Stumvoll et al. 2005), rheumatoid arthritis (Park & Pillinger 2007) and also in the pathogenesis of periodontitis (Page 1991, Gemmell et al. 1997, Graves 1999). Moreover, it has been suggested that cytokines are important mediators in the cross-susceptibility of periodontitis with diabetes mellitus (Preshaw et al. 2007) and rheumatoid arthritis (Mercado et al. 2003, Bartold et al. 2005).

Obesity is characterized as a state of low-grade systemic inflammation (Fantuzzi 2005). It is known that adipose tissue cells – adipocytes, preadipocytes and macrophages – secrete cytokines, including, for example, tumour necrosis factor α (TNF-α) and interleukin 6 (IL-6), among over 50 other bioactive substances collectively known as adipokines (Ritchie 2007). This concurs with the findings which have shown that obese individuals have elevated levels of circulating TNF-α and IL-6 compared with normoweight subjects and also that the levels of these cytokines decrease after weight loss (Ziccardi et al. 2002).

Conflict of interest and sources of funding statement

The authors declare that there are no conflicts of interest in this study.
The present study is part of the Health 2000 Health Examination Survey, organized by the National Public Health Institute (KTL) of Finland (http://www.ktl.fi/health2000), and partly supported by the Finnish Dental Society Apollonia and the Finnish Dental Association.

In recent years, it has been found that obesity is associated with periodontitis (Saito et al. 2001, Al-Zahrani et al. 2003, Wood et al. 2003, Dalla Vecchia et al. 2005, Genco et al. 2005, Reeves et al. 2006) and has been suggested to be second only to smoking as the strongest risk determinant for periodontitis (Nishida et al. 2005). However, the nature of the association between body weight and periodontal infection is not known and the mechanisms how body weight might affect periodontium are also unclear. Earlier studies have suggested that cytokines produced by adipose tissue could be one mechanism mediating this association (Saito & Shimazaki 2007), although the evidence is still somewhat ambiguous. The presence of such a mediating mechanism would support the conception that the association between body weight and periodontal infection is causal, and conversely the lack of evidence suggests that the association is not a causal one.

The aim of this study was to investigate the role of serum cytokines TNF-α and IL-6 as potential mediators in the association between body weight and periodontal infection among an adult population.

Material and Methods

Study design

The nationally representative Health 2000 Health Examination Survey was carried out in 2000 and 2001 by the National Public Health Institute of Finland. The study population comprised 8028 subjects aged 30 or older living in continental Finland. The data for this survey were collected from clinical oral and health examinations, from laboratory measurements, from self-administered questionnaires and by interviews. Informed consent was obtained from the participants. The study protocol was approved by the ethical committee of Helsinki University Hospital. Additional information about the Health 2000 Health Examination Survey is available in the published report at: http://www.ktl.fi/terveys2000/julkaisut/baseline.pdf.

A subsample of the original Health 2000 Health Examination Survey was invited to take further examinations in 2001 and 2002 (the average time span to the original study was 481 days) consisting of persons aged between 45 and 74 years living near five central university hospitals ($n = 1526$). Blood samples were collected including serum cytokines TNF-α and IL-6. For this study, we used a subpopulation of dentate non-rheumatic, non-diabetic subjects who were 45–64 years old, who had never smoked and whose serum levels of TNF-α and IL-6 were analysed and periodontal health clinically determined (effective $n = 425$). Rheumatoid arthritis was determined on the basis of information obtained from the health interview. The question posed was ''Do you have rheumatoid arthritis diagnosed by a physician?'' with the answer options being yes/no. Diabetes was determined on the basis of the health interview and the health examination. Only subjects who had not been diagnosed with diabetes by a physician and who had no indications of the disease were included in the study population.

Outcome variables

Five calibrated dentists performed clinical oral examinations in a dental chair using a headlamp, mouth mirror and a WHO periodontal probe in line with the WHO instructions. The clinical oral examinations included assessment of the condition of periodontium and teeth. Periodontal pocket depth on probing was measured on four surfaces of each tooth (distobuccal, mid-buccal, mid-oral, mesio-oral), and the deepest measurement on each tooth was recorded. Third molars were excluded from the periodontal examination. The percentual agreement between the examiners and the reference examiner in periodontal pockets was 82% (κ 0.32) (Vehkalahti et al. 2004, p. 30). We used existing periodontal infection, defined as the number of teeth with deepened periodontal pockets (4 mm or more) as an outcome variable. We also used the number of teeth with deep periodontal pockets (6 mm or more) as an outcome variable. The distributions of the outcome variables are presented in Fig. 1.

Explanatory variables

Serum levels of TNF-α and IL-6 were analysed by solid phase, enzyme-labelled chemiluminescent immunometric assay using an analyzer Immulite (Siemens Healthcare Diagnostics, Deerfield, IL, USA). The inter-assay coefficient of variation (CV) of TNF-α varied from 2.5% (high-level control, 500 ng/l) to 11.0% (low-level control, 7 ng/l). The inter-assay CV of IL-6 varied from 5.0% (high-level control, 500 ng/l) to 7.0% (low-level control, 21 ng/l). The detection limits of the assays were 1.5 ng/l for TNF-α and 0.5 ng/l for IL-6. Serum levels of TNF-α and IL-6 were used in the multivariate analyses as continuous variables.

Body weight was assessed using body mass index (BMI), which is a measure of body weight in relation to height (kg/m^2). Information about height and weight were primarily obtained from the clinical examination, but where this information was missing, other sources were used, namely interviews and questionnaires. BMI (assessed at the time of the original Health 2000 Health Examination) was used in the analyses as a continuous variable.

Confounding variables

Age was included into the analyses as a continuous variable. Education was

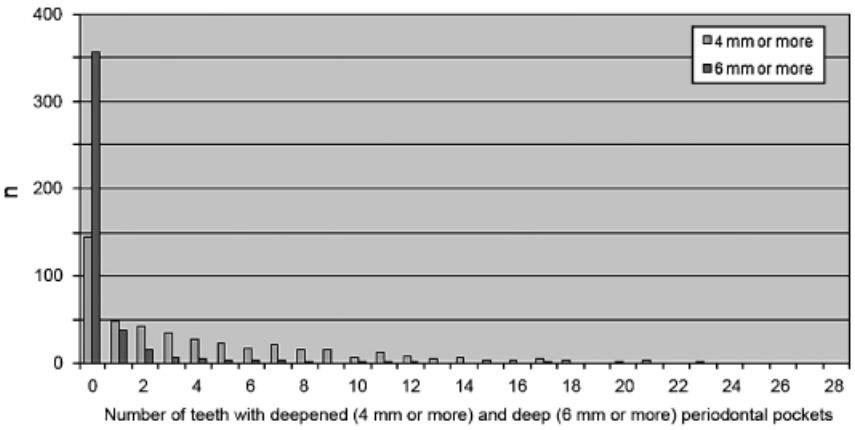

Fig. 1. Number of subjects with teeth with deepened (4 mm or more) and deep (6 mm or more) periodontal pockets.

Table 1. Basic characteristics of the study population

	n	Minimum–Maximum	Mean (SD*)/proportion
Age	430	45–64	53.8 (5.7)
Gender (%)			
Males	153		35.6
Females	277		64.4
Number of teeth	430	1–32	23.0 (7.0)
Number of teeth with periodontal pockets ⩾4 mm	430	0–23	3.7 (4.5)
Number of teeth with periodontal pockets ⩾6 mm	430	0–17	0.5 (1.6)
Education (%)			
Low	125		29.1
Intermediate	132		30.7
High	173		40.2
Presence of plaque (%)			
No plaque	168		39.5
Plaque in gingival margins	226		53.2
Plaque also elsewhere	31		7.3
Missing information	5		
Body mass index			
Original survey	430	19.0–45.5	26.7 (4.2)
Further examinations	427	19.1–47.7	26.7 (4.4)
Serum tumour necrosis factor α (TNF-α), (ng/l)	430	1.4–126	5.7 (6.1)
Serum interleukin 6 (IL-6), (ng/l)	430	0.4–12.9	1.5 (1.2)

*SD, standard deviation.

categorized into three categories. The lowest level consisted of those who had less than a high school education and did not have formal vocational qualifications; the second level comprised those who had graduated from high school and the highest level subjects with a university degree or who had graduated from polytechnics. The presence of dental plaque was measured from three teeth at one surface each as follows: buccal surface from the most posterior tooth on the upper right side, lingual surface from the most posterior tooth on the lower left side and buccal surface from tooth 33. The presence of plaque was categorized into three categories as follows: no visible plaque, visible plaque at gingival margins, visible plaque elsewhere. The highest value was recorded. Percentual agreement between the examiners and the reference examiner in the presence of dental plaque was 57% (κ 0.22) (Vehkalahti et al. 2004, p. 30). The number of teeth (as a continuous variable) was treated as the offset variable in the regression models.

The selection of covariates was based on current knowledge of the potential risk factors of periodontal infection. We estimated relative risks (RR) with 95% confidence intervals using Poisson regression models. Logarithmic transformations of serum TNF-α and IL-6 were made to normalize the skewed distributions of serum TNF-α and IL-6 before the analyses. The basic characteristics of the study population are presented in Table 1 (Fig. 1).

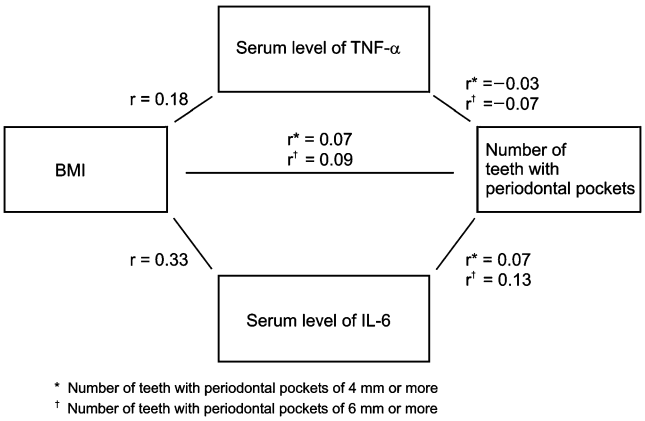

Fig. 2. Spearman's correlation coefficients (r) between the number of teeth with deepened (4 mm or more) and deep (6 mm or more) periodontal pockets, body mass index (BHI) and serum levels of cytokines tumous necrosis factor alpha (TNF-α) and interleukin 6 (IL-6).

Results

Spearman's correlation coefficients between the number of teeth with deepened (4 mm or more) and deep (6 mm or more) periodontal pockets, BMI and the serum levels of cytokines TNF-α and IL-6 are presented in Fig. 2.

In these data, we found an association between serum levels of IL-6 and the number of teeth with deepened (4 mm or more) and deep (6 mm or more) periodontal pockets (Table 2) after controlling for confounding factors such as gender, age, education and presence of plaque. We found no consistent association between serum levels of TNF-α and the number of teeth with deepened periodontal pockets (Table 2).

There was an association between BMI and the number of teeth with deepened and deep periodontal pockets in this population of subjects aged 45–64 years (Table 3). Adding TNF-α into the regression models did not have an essential effect on the strength of these associations, whereas adding IL-6 slightly weakened the strength of the association between BMI and the number of teeth with periodontal pockets of 6 mm or more, but not the association between BMI and the number of teeth with periodontal pockets of 4 mm or more (Table 3).

Table 2. The relation of serum tumour necrosis factor α (TNF-α) and interleukin 6 (IL-6) levels to the number of teeth with periodontal pockets [unadjusted and adjusted* relative risks (RR) with 95% confidence intervals (CI)]

	Teeth with periodontal pockets ⩾4 mm		Teeth with periodontal pockets ⩾6 mm	
	unadjusted RR (95% CI)	adjusted RR (95% CI)	unadjusted RR (95% CI)	adjusted RR (95% CI)
TNF-α†	0.89 (0.43–1.86)	0.79 (0.40–1.54)	1.41 (0.17–11.6)	1.08 (0.08–13.8)
IL-6†	1.60 (1.04–2.45)	1.20 (0.78–1.86)	3.94 (1.73–8.95)	2.42 (0.94–6.24)

*Adjusted for gender, age (continuous variable), education, presence of plaque and number of teeth (offset variable).
†Log-transformed value.

Table 3. The relation of body mass index (BMI) to the number of teeth with periodontal pockets [adjusted relative risks (RR) with 95% confidence intervals (CI)]

	Teeth with periodontal pockets ⩾4 mm		Teeth with periodontal pockets ⩾6 mm	
	RR	95% CI	RR	95% CI
Model 1* BMI	1.03	1.00–1.06	1.04	0.94–1.14
Model 2† BMI	1.03	1.00–1.06	1.04	0.94–1.14
Model 3‡ BMI	1.03	1.00–1.06	1.02	0.93–1.13

*Adjusted for gender, age (continuous variable), education, presence of plaque and number of teeth (offset variable).
†Adjusted for gender, age (continuous variable), education, presence of plaque, number of teeth (offset variable) and serum tumour necrosis factor α (TNF-α) level (continuous variable, log-transformed value).
‡Adjusted for gender, age (continuous variable), education, presence of plaque, number of teeth (offset variable) and serum interleukin 6 (IL-6) level (continuous variable, log-transformed value)

Discussion

In these data IL-6, but not TNF-α, associated with the number of teeth with deepened (4 mm or more) and deep (6 mm or more) periodontal pockets. This means that IL-6, but not TNF-α, could be one potential mediating factor in the association between body weight and periodontal infection. This interpretation is also supported by the fact that adding IL-6 into the multivariate model slightly attenuated the association between BMI and the number of teeth with periodontal pockets of 6 mm or more.

Obesity, a state of low-grade systemic inflammation, has been suggested to associate with periodontal infection in several studies (Saito et al. 2001, Genco et al. 2005). The mechanisms how obesity has an effect on periodontium are not known, but there are several possible biological explanations. For example, adipose tissue is known to secrete several types of substances, including cytokines TNF-α and IL-6 (Ritchie 2007), which has been suggested to mediate the effect of body weight on periodontium (Saito & Shimazaki 2007). This view is supported by the findings of Lundin et al. (2004), who reported a significant positive correlation between the levels of TNF-α in gingival crevicular fluid (GCF) and high BMI (over 40). In their study, the level of TNF-α in GCF was positively associated with high BMI in subjects without periodontal disease, which suggests that the TNF-α in GCF is partly originated from adipose tissue. In addition, systemic TNF-α may play a part in the development of insulin resistance (Nishimura & Murayama 2001), which is also suggested to be a mediating mechanism between obesity and periodontitis (Genco et al. 2005). However, it must be pointed out that diabetics and subjects with any indication of the disease were excluded from our study sample, so we cannot draw any conclusions about the possible role of insulin resistance (and the role of TNF-α in insulin resistance) in the aetiology of periodontal infection.

In this study population of non-diabetic and non-rheumatic subjects, serum TNF-α showed no association with periodontal infection. This may be related to the fact that serum TNF-α did not show as strong a correlation with BMI in this population as for instance in the previously mentioned study by Ziccardi et al. (2002). In contrast, serum IL-6 associated with the number of teeth with deepened periodontal pockets (4 mm or more) and deep periodontal pockets (6 mm or more). This suggests that systemic IL-6 may have some detrimental effects on periodontium or alternatively that periodontal infection causes systemic elevation of IL-6 levels. Naturally, the latter possibility cannot be excluded due to the cross-sectional study design.

Other possible explanations

Our group has recently studied the role of another suggested mediating mechanism – namely elevated levels of serum lipids. Interestingly, these results suggest that none of the serum lipids (triglycerides, HDL–cholesterol or LDL–cholesterol) separately seem to be an important mediating factor in the association between body weight and periodontal infection, at least among normoweight subjects (Saxlin et al. 2008). However, based on the said study, the possibility that different lipid fractions in combinations have some effects on periodontium cannot be excluded.

There are also other possible mechanisms that could mediate the effect of body weight on periodontium. These include for example the effect of other adipokines produced by adipose tissue, such as leptin and plasminogen activator inhibitor-1 (PAI-1). The biological mechanisms how these substances might affect the pathogenesis of periodontal infection is quite poorly understood to date. Leptin is thought to regulate adipose tissue mass and it has been reported that leptin concentrations in gingival tissues and in GCF are negatively correlated with periodontal disease progression (Johnson & Serio 2001, Karthikeyan & Pradeep 2007).

PAI-1 is a regulatory protein of the coagulation cascade and it prevents the dissolution of clots by inhibiting extracellular matrix degradation and fibrinolysis. PAI-1 is strongly expressed in visceral fat in obese subjects

(Shimomura et al. 1996). The plasminogen activator system has been reported to be active in gingival tissues (Kinnby et al. 1999). Although the exact mechanisms are not known, one possible mechanism is that PAI-1 reduces the blood flow in the periodontium of obese subjects and therefore promotes the development of periodontal disease (Saito & Shimazaki 2007).

The nature of the association between body weight and periodontal infection has not been confirmed yet. It is possible that this association is confounded by factors that are difficult, unless impossible to control for. Moreover, previous studies on this association, to our knowledge, have been cross-sectional in nature, which means that any conclusions about the directions of the causal relations cannot be made. To truly clarify the direction of the association between body weight and periodontal infection, longitudinal studies are needed.

Strengths and limitations

Using the number of teeth with periodontal pockets as an outcome variable provides many advantages. Perhaps the most important aspect is that, this way the study focuses on the extent of the infection at the time of the survey and does not incorporate the disease history. The use of a continuous variable also reduces the effect of misclassification of periodontal infection compared with a situation where the outcome is dichotomous. An additional advantage is that risk estimates, that is RR, can be interpreted in a probabilistic manner. Probing depths of 4 and 6 mm were used as cut-off values, because they are widely used boundary values for pathologically deepened periodontal pockets. However, when interpreting the results, it must be noted that the number of teeth with deep periodontal pockets (6 mm or more) was low, so the results are subject to large random variation.

We restricted the analysis to never smokers, because smoking is known to be a strong risk factor for periodontal disease, preventing the detection of weaker determinants. Our decision to restrict the analysis to never smokers was based on suggestions in earlier studies that have shown that control for smoking is otherwise insufficient (Hujoel et al. 2002).

The limitations of the present study include the cross-sectional study design. Hence, as mentioned above, we cannot draw any definite conclusions about the relation between cause and effect. Another limitation is that we only studied the effect of cytokines TNF-α and IL-6. We cannot therefore exclude the possibility that there are other cytokines or substances produced by adipose tissue that could mediate the association between body weight and periodontal infection.

Serum samples of TNF-α and IL-6 were collected for more than 1 year after the original health examination (mean 481 days). However, because the aim of this study was to examine the possible mediating effects of elevated levels of serum TNF-α and IL-6 on the association between body weight and periodontal infection, we do not consider this time span to be a major obstacle due to the stability of body weight. For example, in this study population mean BMI was 26.68 at the time of the original health examination, and later, at the time of the follow-up examinations, which included the serum samples of TNF-α and IL-6, the mean BMI was 26.71.

Conclusions

When interpreting the results, it must be kept in mind that the disease mechanisms leading to periodontal infection might be different in subgroups such as diabetics, rheumatics and among morbidly obese subjects, for instance. In this study population consisting of non-diabetic and non-rheumatic subjects, we found that serum IL-6, but not TNF-α, may mediate the possible inflammatory effect of body weight on periodontium. Despite these suggestive findings, the mechanisms how body weight has an effect on periodontium need to be further investigated.

References

Al-Zahrani, M. S., Bissada, N. F. & Borawski, E. A. (2003) Obesity and periodontal disease in young, middle-aged, and older adults. *Journal of Periodontology* **74**, 610–615.

Bartold, P. M., Marshall, R. I. & Haynes, D. R. (2005) Periodontitis and rheumatoid arthritis: a review. *Journal of Periodontology* **76**, 2066–2074.

Dalla Vecchia, C. F., Susin, C., Rösing, C. K., Oppermann, R. V. & Albandar, J. M. (2005) Overweight and obesity as risk indicators for periodontitis in adults. *Journal of Periodontology* **76**, 1721–1728.

Fantuzzi, G. (2005) Adipose tissue, adipokines and inflammation. *Journal of Allergy and Clinical Immunology* **115**, 911–919.

Gemmell, E., Marshall, R. I. & Seymour, G. J. (1997) Cytokines and prostaglandins in immune homeostasis and tissue destruction in periodontal disease. *Periodontology 2000* **14**, 112–143.

Genco, R. J., Grossi, S. G., Ho, A., Nishimura, F. & Murayama, Y. (2005) A proposed model linking inflammation to obesity, diabetes and periodontal infections. *Journal of Periodontology* **76**, 2075–2084.

Graves, D. T. (1999) The potential role of chemokines and inflammatory cytokines in periodontal disease progression. *Clinical Infectious Diseases* **28**, 482–490.

Hujoel, P. P., Drangsholt, M., Spiekerman, C. & DeRoen, T. A. (2002) Periodontitis-systemic disease associations in the presence of smoking – causal or coincidental? *Periodontology 2000* **30**, 51–60.

Johnson, R. B. & Serio, F. G. (2001) Leptin within healthy and diseased human gingiva. *Journal of Periodontology* **72**, 1254–1257.

Karthikeyan, B. V. & Pradeep, A. R. (2007) Leptin levels in gingival crevicular fluid in periodontal health and disease. *Journal of Periodontal Research* **42**, 300–304.

Kinnby, B., Lindberg, P., Lecander, I. & Matsson, L. (1999) Localization of plasminogen activators and plasminogen activator inhibitors in human gingival tissues demonstrated by immunohistochemistry and in situ hybridization. *Archives of Oral Biology* **44**, 1027–1034.

Lundin, M., Yucel-Linberg, T., Dahllöf, G., Marcus, C. & Modeer, T. (2004) Correlation between TNFa in gingival crevicular fluid and body mass index in obese subjects. *Acta Odontologica Scandinavica* **62**, 273–277.

Mercado, F. B., Marshall, R. I. & Bartold, P. M. (2003) Inter-relationships between rheumatoid arthritis and periodontal disease. *Journal of Clinical Periodontology* **30**, 761–772.

Nishida, N., Tanaka, M., Hayashi, N., Nagata, H., Takeshita, T., Nakayama, K., Morimoto, K. & Shizukuishi, S. (2005) Determination of smoking and obesity as periodontitis risks using the classification and regression tree method. *Journal of Periodontology* **76**, 923–928.

Nishimura, F. & Murayama, Y. (2001) Periodontal inflammation and insulin resistance – lessons from obesity. *Journal of Dental Research* **80**, 1690–1694.

Page, R. (1991) The role of inflammatory mediators in the pathogenesis of periodontal disease. *Journal of Periodontal Research* **26**, 230–242.

Park, J. Y. & Pillinger, M. H. (2007) Interleukin-6 in the pathogenesis of rheumatoid arthritis. *Bulletin of the NYU Hospital for Joint Diseases* **65** (Suppl. 1), S4–S10.

Preshaw, P. M., Foster, N. & Taylor, J. J. (2007) Cross-susceptibility between periodontal disease and type 2 diabetes mellitus: an immunobiological perspective. *Periodontology 2000* **45**, 138–157.

Reeves, A. F., Rees, J. M., Schiff, M. & Hujoel, P. P. (2006) Total body weight and waist circumference associated with chronic periodontitis among adolescents in the United States. *Archives of Pediatrics and Adolescents Medicine* **160**, 894–899.

Ritchie, C. S. (2007) Obesity and periodontal disease. *Periodontology 2000* **44**, 154–163.

Saito, T. & Shimazaki, Y. (2007) Metabolic disorders related to obesity and periodontal disease. *Periodontology 2000* **43**, 254–266.

Saito, T., Shimazaki, Y., Koga, T., Tsuzuki, M. & Ohshima, A. (2001) Relationship between upper body obesity and periodontitis. *Journal of Dental Research* **80**, 1631–1636.

Saxlin, T., Suominen-Taipale, L., Kattainen, A., Marniemi, J., Knuuttila, M. & Ylöstalo, P. (2008) Association between serum lipid levels and periodontal infection. *Journal of Clinical Periodontology*, **35**, 1040–1047.

Shimomura, I., Funahashi, T., Takahashi, M., Maeda, K., Kotani, K., Nakamura, T., Yamashita, S., Miura, M., Fukuda, Y., Takemura, K., Tokunaga, K. & Matsuzava, Y. (1996) Enhanced expression of PAI-1 in visceral fat: possible contributor to vascular disease in obesity. *Nature Medicine* **2**, 800–803.

Stumvoll, M., Goldstein, B. J. & van Haeften, T. W. (2005) Type 2 diabetes: principles of pathogenesis and therapy. *Lancet* **365**, 1333–1346.

Vehkalahti, M., Knuuttila, M. & Hausen, H. (2004) Kliinisten mittausten laadun varmistaminen (Quality assurance of clinical examinations). In: Suominen-Taipale, L., Nordblad, A., Vehkalahti, M. & Aromaa, A. (eds). *Suomalaisten Aikuisten Suunterveys, Terveys 2000 – Tutkimus (Oral Health of Finnish Adults, Health 2000 Health Examination Survey)*, pp. 24–32. Helsinki: Publications of the National Public Health Institute.

Wood, N., Johnson, R. B. & Streckfus, C. F. (2003) Comparison of body composition and periodontal disease using nutritional assessment techniques: third National Health and Nutrition Examination Survey (NHANES III). *Journal of Clinical Periodontology* **30**, 321–327.

Ziccardi, P., Nappo, F., Giugliano, G., Esposito, K., Marfella, R., Cioffi, M., D'Andrea, F., Molinari, A. M. & Giugliano, D. (2002) Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. *Circulation* **105**, 804–809.

Address:
Tuomas Saxlin
Institute of Dentistry
University of Oulu
PO Box 5281
90014 Oulu
Finland
E-mail: tuomas.saxlin@oulu.fi

Clinical Relevance

Scientific rationale: It has been suggested in a number of cross-sectional studies that there might be an association between body weight and periodontal infection. To date, the nature of this association has not been confirmed. Cytokines TNF-α and IL-6 produced by adipose tissue have been suggested to be one possible biological mechanism explaining this association.

Principal findings: Serum IL-6 may mediate the effect of body weight on periodontium.

Practical implications: Longitudinal, preferably randomized, studies are needed to clarify the true nature of the association between body weight and periodontal infection.