J Clin Periodontol 2007 ; 34: 390–396 doi: 10.1111/j.1600-051X.2007.01068.x

Journal of Clinical Periodontology

Association of height with inflammation and periodontitis: the Study of Health in Pomerania

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Meisel P, Kohlmann T, Kocher T. Association of height with inflammation and periodontitis: the Study of Health in Pomerania (SHIP). J Clin Periodontol 2007; 34: 390–396. doi: 10.1111/j.1600-051X.2007.01068.x.

Abstract

Aim: Short stature in adulthood has been associated with increased risk of health problems. Predisposition to inflammatory diseases might be associated with impaired length growth and impose a lifelong inflammatory burden. We tested this hypothesis in a cross-sectional population-based study with respect to periodontitis.

Material and Methods: In 4290 randomly selected subjects from the normal population , we determined anthropometric measures and diagnostic periodontal parameters. Behavioural and environmental risk factors were assessed by interviews and questionnaires.

Results: In regression analyses adjusted for age, gender, smoking, diabetes, education, and dental appointments, an inverse association was observed between height and clinical attachment loss. The magnitude of the association was higher in presence of risk factors smoking or diabetes. Odds ratios for smoking were 3.5 (2.2–5.7%, 95% confidence interval) and 2.6 (1.5–4.3%) with the shortest and tallest height quartile, respectively. Figures for diabetes were 1.37 (1.04–1.80%) and 0.97 (0.67–1.39%), respectively. Stratification for age and gender revealed that taller subjects had less periodontitis and decreased concentrations of markers of systemic inflammation than their shorter counterparts.

Conclusion: This study is the first to associate height with periodontitis concluding that individuals born with a high susceptibility to infectious and inflammatory diseases may suffer from such diseases in childhood whereby the length growth could be impaired. Reaching adulthood, growth comes to a halt but the individual remains susceptible to inflammatory sequelae. Thus, smaller persons pertain a tendency to more severe periodontitis.

Key words: height; inflammation; periodontitis; population study

Accepted for publication 28 January 2007

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

This work is part of the Community Medicine Research (CMR) net of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (grant no. ZZ9603), the Ministry of Cultural Affairs and the Social Ministry of the Federal State of Mecklenburg-West Pomerania. The CMR gathers several research projects which share data from the population-based Study of Health in Pomerania (SHIP; http://www.medizin.uni-greifswald.de/cm).

Short stature in adulthood has been associated with increased risk of health problems (Tuvemo et al. 1999). Recently, a pathophysiological model was suggested linking infectious exposure at earlier ages and environmental factors to inflammation, height, morbidity, and mortality at older ages (Crimmins & Finch 2006). The authors argued that early-life infections impose a lifelong inflammatory burden, presumably leading eventually to the development of atherosclerotic and thrombotic conditions. This may explain the widely discussed association of periodontal diseases with various systemic diseases which have in common an inflammatory background (Kantarci & van Dyke 2005). Genetic predisposition and intrauterine imprinting in addition to a high-infectious environment and possible nutritional restrictions may interact in producing a condition which is now widely discussed as a ''hyper-reactive type'' of the innate immune system. Individuals reacting with an exaggerated response to inflammatory stimuli could suffer from more infectious or inflammatory diseases in their childhood during which most of the growth spurt occurs. Besides the lifelong enhanced morbidity, it was also shown that such a

condition could result in a reduced body height (Crimmins & Finch 2006). If so, we can hypothesize that subjects suffering from lifelong inflammatory diseases were delayed in their growth and a reduced height should be detectable in their later life.

Indeed, inflammatory diseases frequently impair linear growth during childhood (Preece et al. 1986). Such diseases influencing the growth of children include inflammatory intestinal diseases (Hildebrand et al. 1994, Burnham et al. 2004), juvenile rheumatoid arthritis (Bacon et al. 1990), atopic dermatitis (Baum et al. 2002), and cystic fibrosis (Rosenfeld et al. 2001).

Periodontitis is a chronic inflammatory disease affecting more or less most adults. The inflammation leads to pocket formation in the gingival tissue, attachment loss, bone destruction, and eventually to tooth loss. This local inflammation hardly occurs during childhood. The severest cases of periodontitis in adulthood could be the consequence of a ''hyper-reactive'' individual predisposition. Therefore, detecting reduced height in subjects suffering from periodontitis could be a hint of inflammatory susceptibility during the growth period in childhood. Periodontal disease offers the unique possibility of tracing their natural history in each individual as the diagnostic measures accumulate during lifetime and are easy to assess.

In industrialized nations, periodontitis affects 30–50% of the adults, 10% of them with severe symptoms (Albandar 2002). Periodontitis is a multifactorial disease modified by numerous risk factors. Such risk factors influencing susceptibility to extent, severity and course of the disease are age, sex, socio-economic status, smoking, diabetes, and also inherited factors (Genco 1996, Heitz-Mayfield 2005). Although bacteria are necessary for periodontal disease to occur, a susceptible host is also required (Kinane & Lappin 2002).

With respect to the model mentioned above, one may speculate that the predisposition with hyper-reactive inflammatory susceptibility makes an individual prone to both the reduced length growth and an exaggerated inflammatory response to infectious challenges. This might be revealed in exaggerated periodontitis.

In a cross-sectional health study comprising 4290 randomly selected subjects, we tested if the hypothesis could be supported in our data set. To do so, we searched for a possible relationship between the height of the subjects studied and their periodontal state.

Material and Methods

Study population

Four thousand two hundred and ninety subjects were selected by a two-stage cluster sampling method from a population of 210,000 inhabitants of the north-eastern German region of Pomerania designated as SHIP study. From 32 communities in the region a random sample was drawn from residence registries, stratified by gender and age. Finally, 7008 subjects were sampled, with 292 persons of each gender in each of twelve 5-year age strata (age range 20–80 years). The net sample (without migrated or deceased persons) consisted of 6267 eligible subjects. The final SHIP sample comprised 4310 participants (response 68.8% of eligible subjects). Owing to incomplete data, finally 4290 data sets were included in the analysis. The design of the study, the recruiting of participants and the scope of this population-based cross-sectional health survey was reported elsewhere (Hensel et al. 2003). The participants gave their written informed consent and the study was approved by the local ethics committee. Table 1 lists characteristics of the subjects which were relevant to the objective of the study.

Anamnestic and periodontal examinations

Periodontal status was assessed by specially trained and calibrated dentists. For attachment loss, double examinations (full-mouth, four-point measurement) of four periodontally diseased test patients yielded an intra-class correlation of 0.82–0.91, and the inter-rater correlation was 0.84 (Hensel et al. 2003). Assessment included probing depth, clinical attachment loss (CAL), plaque, bleeding on probing, and the number of teeth. The periodontal examination was carried out on either the left or right side quadrants and the examination side was changed from subject to subject. All fully erupted teeth were assessed excluding third molars. A maximum of 14 teeth per subject was examined. Attachment loss and probing depth were assessed with a periodontal probe (PCP 11, HuFriedy, Chicago IL, USA) at mesiobuccal, distobuccal, midbuccal, and midlingual aspect on each selected tooth. Attachment loss is represented by the distance from the cemento-enamel junction to the bottom and probing depth by the distance from the gingival margin to the bottom of the periodontal pocket. The measurements were made in whole millimetres. Smoking behaviour and socio-economic status were assessed with an extensive questionnaire and an interview.

Statistics and clinical chemistry

ANOVA or the Mann–Whitney or Kruskal–Wallis tests were used to assess the significance of the height effects on periodontal or inflammatory markers. We used logistic regression analyses to adjust the effects for confounding variables. To avoid arbitrary disease criteria, attachment loss measures were divided in tertiles and comparisons between the first and third were made. Statistical significance was assumed for odds ratios whose confidence intervals did not cross a value of 1.0. Stratification was performed to adjust measures in subgroups for age and sex.

The statistical software STATVIEW® 5.0 (SAS, Cary, NC, USA) was used.

Clinical chemistry data were determined by standard laboratory methods. In blood samples drawn by venipuncture, white blood count, fibrinogen according to Clauss, and LDL/HDL cholesterol were determined.

Table 1. Characteristics of the study population: sex: male/female (%); smoking: never/ever (%); education: less than 10th grade/otherwise (%), diabetes: subjects treated with antidiabetic drugs or with HbA_{1C} >7% (%)

Age group	*N*	Sex	Smoking	Education	Diabetes
20–⩽30	594	46/54	52/48	11/89	1.0
>30–⩽40	766	47/53	45/55	9/91	0.5
>40–⩽50	753	47/53	44/56	21/79	4.6
>50–⩽60	791	47/53	55/45	47/53	9.5
>60–⩽70	792	53/47	55/45	76/24	16.3
>70	614	55/45	58/42	79/21	21.8

Results

It was a prerequisite of the present study to avoid the confounding of age on body height and on disease parameters as well. Figure 1 shows the age effects which are consistent with common knowledge. Dividing the study population into 12 age cohorts of 5 years each, we estimated the height quartiles separately for male and female participants in every age cohort. Figure 2 gives a comparison of attachment loss between short and tall persons showing less periodontitis in the tallest ones. In systemic inflammation parameters as white blood count the same effect was seen. The impact of body height on the difference is detectable for periodontitis and WBC in all age cohorts. The differences are significant except for the oldest cohort. The differences were also detected with the disease-causing signs (gingival plaque index, $p = 0.0025$) as well as with the outcome of the disease, i.e. the number of teeth ($p = 0.0052$). In this population, the mean difference in height between subjects in the tallest quartile and those in the shortest quartile was 16.1 and 15.5 cm in males and females, respectively.

Therefore, we compared the periodontal parameters among the tallest persons with those belonging to the shorter quartiles. The results are given in Table 2. There is a small but consistent difference in all parameters assessed. Even though the effect is rather small, it is detectable for different definitions and thresholds of attachment loss but not for probing depth. Subjects in their age and sex-specific fourth quartile of height have on average less attachment loss (extent and severity), less plaque and more teeth than their counterparts in the lower quartiles with a continuous trend. Moreover, markers of systemic inflammation measured in blood show the same trend to be decreased in the taller subjects compared with their shorter counterparts.

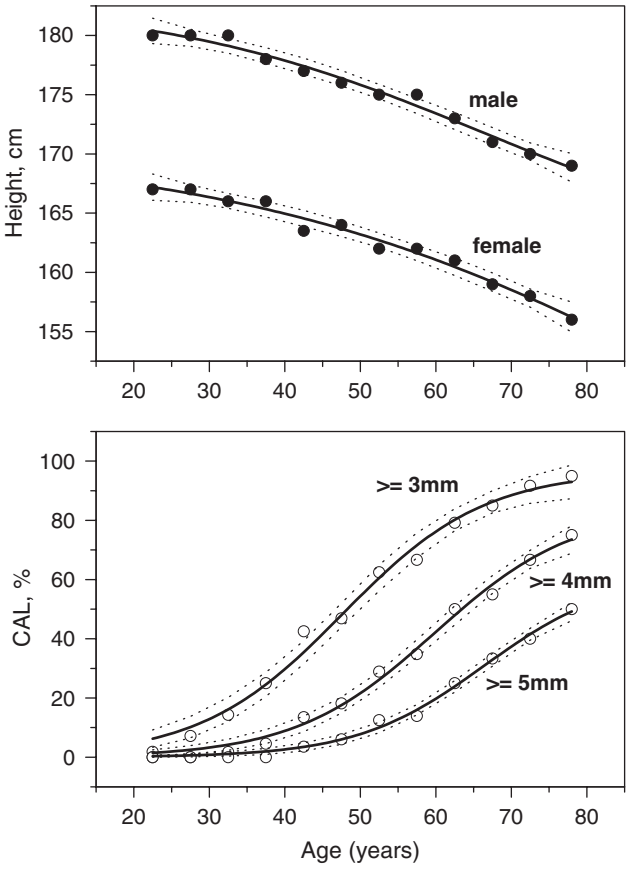

Fig. 1. Age dependency of body height in male and female subjects of the the Study of Health in Pomerania study (top) and of extent of periodontitis expressed as percentage of all sites assessed exceeding 3, 4, or 5 mm attachment loss (bottom). Shown are the fitted curves to the medians in each of 12 age cohorts (solid lines) and the 95% confidence bands (dotted lines).

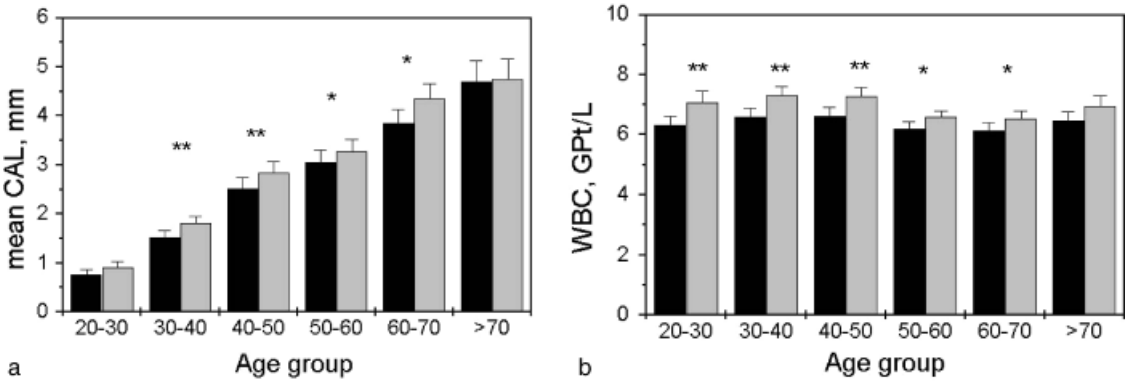

Fig. 2. Comparison of mean attachment loss (a) and white blood cell count (b) in six age groups of 10 years each. Compared are the measurements between subjects in the fourth quartiles (black columns) of their age-and sex-specific height percentiles with those in the first height quartiles (grey columns) including the 95% confidence intervals. Differences significant $p < 0.05$ (*) or $p < 0.01$ (**). Attachment loss ANOVA: Age groups $p < 0.0001$, height first *versus* fourth quartile $p = 0.0003$, no interaction ($p = 0.625$). WBC count ANOVA: Age groups $p < 0.0001$, height first *versus* fourth quartile $p < 0.0001$, no interaction ($p = 0.667$). Quartiles were estimated age-specifically and separately in twelve 5-year cohorts, combined in six groups for better clarity.

Table 2. Periodontal measures and markers of systemic inflammation compared between the smallest and the tallest subjects

Parameter	Height ⩽25th percentile	Height ⩽75th to >25th	Height >75th percentile	p^*
% CAL⩾3 mm median (IQR)*	48.7 (67.8)	41.7 (67.5)	40.5 (64.3)	0.0018
% CAL⩾4 mm median (IQR)	16.7 (53.2)	12.8 (48.8)	11.1 (45.0)	0.0012
% CAL⩾5 mm median (IQR)	5.9 (34.4)	2.9 (25.0)	2.3 (21.9)	0.0004
CAL mean, mm ± SD	2.81 ± 1.91	2.60 (1.92)	2.47 ± 1.80	0.0002
No. of teeth, mean ± SD	16.9 ± 9.9	17.7 (9.6)	18.1 ± 9.3	0.0233
White blood count, mean ± SD	6.96 ± 2.11	6.73 (2.08)	6.39 ± 1.73	< 0.0001
Fibrinogen, mean ± SD	3.07 ± 0.76	2.97 (0.69)	2.97 ± 0.69	0.0059
Ever smokers, % (95% CI)	49.6 (46.8–52.4)	47.9 (45.8–50.0)	49.7 (46.6–52.9)	0.5126
Packyears smoked, mean ± SD	9.1 ± 14.3	8.6 ± 14.3	8.3 ± 13.8	0.5285
Low work grade of spouse, %	39.5 (35.8–43.3)	35.4 (32.7–38.2)	30.9 (27.0–35.0)	0.0100
Education < 10th grade, %	44.9 (42.1–47.8)	41.0 (38.9–43.1)	33.8 (30.9–36.8)	<0.0001

Body height percentiles were determined separately for males and females in each of the twelve 5-year age cohorts.
*Kruskal–Wallis test.
IQR, interquartile range; SD, standard deviation; CAL, clinical attachment loss.

Table 3. Logistic regression of third *versus* first tertile of % attachment loss ⩾4 mm on periodontal risk factors stratified in quartiles of body height (first quartile the shortest, fourth quartile the tallest)

Parameter	Odds ratios (95% confidence intervals)		
	height ⩽25th percentile	height >25th to ⩽75th	height >75th percentile
Age	1.18 (1.15–1.21)	1.17 (1.16–1.19)	1.21 (1.18–1.24)
Sex	0.72 (0.46–1.14)	0.75 (0.54–1.05)	0.51 (0.30–0.84)
Dental appointment	1.14 (0.56–2.31)	1.59 (0.96–2.62)	1.75 (0.78–3.92)
Education	1.81 (1.08–3.05)	2.34 (1.57–3.48)	1.43 (0.76–2.69)
Diabetes	1.37 (1.04–1.80)	1.03 (0.84–1.26)	0.97 (0.67–1.39)
Smoking	3.50 (2.16–5.68)	3.84 (2.71–5.43)	2.55 (1.51–4.32)
White blood count	2.49 (1.18–5.26)	1.54 (0.78–3.05)	1.46 (0.38–5.64)

Shown are the odds ratios [95% confidence intervals (CI)]. Independent variables age: continuous in years; sex: male 0, female 1; diabetes continuous as $\%HbA_{1C}$; last dental appointment: >1 year, within last 6 months (reference); smoking: ever *versus* never; education level less than 10th grade 1, otherwise 0; WBC: white blood count >10). $N = 3475$ (edentulous subjects not included).

Indicators of socio-economic status tend to be better in taller persons.

As various risk factors of periodontitis are associated with age, viz. smoking, diabetes, number of dental treatments, etc., we performed a logistic regression analysis adjusting for all these confounding variables. Table 3 shows the adjusted odds ratios for the association of these factors with periodontitis calculated separately for each height stratum. For all the periodontal risk factors, i.e. diabetes, smoking, and increased white blood count, height modifies their impact in such a way that the tallest are affected the slightest. Thus, there is evidence of effect modification as the odds ratios of having periodontitis in the presence of a risk factor is lower in the tallest height stratum as compared with the shortest one.

In Fig. 3, we present stratification according to smoking status and diabetes. Obviously, in either case there is more attachment loss if the risk factor is present, while the effect of height on the extent of attachment loss is significant in the strata with and without the risk factor. For CAL the Kruskal–Wallis *p*-values were 0.020 and 0.005 for never and ever smokers, respectively. The figures for diabetes were $p = 0.009$ and 0.080 for non-diabetics and diabetics, respectively. For the latter, the number of subjects was too low to reach statistical significance. However, even though the impact was more pronounced when the risk factor was present, the interaction term was not significant. Interaction was also included in the logistic regression analyses shown in Table 4. These show a remarkable correspondence in risk factor associations between inflammatory markers and periodontitis, in height impact and the lacking significance of the interaction term (at least for smoking with height interaction). We analysed the data files for the most significant predictors of markers of systemic inflammation, which are above the cut-off thresholds of clinical significance (Table 4). Beside risk factors of systemic diseases such as cholesterol, diabetes, and smoking we found attachment loss and again body height as a significant factor. With increasing height the probability of belonging to the subjects having inflammation markers above the clinically relevant cut-off thresholds decreases. This probability decreases by 30–60% for subjects in the fourth quartile compared with those in the first quartile, i.e. the shortest (odds ratios between 0.68 and 0.44, $p < 0.01$).

Discussion

For nearly one decade, there has been an ongoing research activity for genetic risk factors in periodontitis to clarify the background of the known individual predisposition to the disease. This was encouraged by the understanding that the periodonto-pathogenic infection is the prerequisite of the disease but host factors contribute considerably to the extent, severity and duration of the disease (Kinane & Lappin 2002).

Moreover, the insight into associations between periodontitis and systemic diseases leads to the assumption of a common underlying inflammatory trait. The innate immune system may be activated by low-grade inflammation in utero or during infant life. This bundle of factors increases or worsens in later life symptoms of inflammation of periodontitis and systemic diseases as well, e.g. cardiovascular or diabetic complications (Rosenfeld et al. 2001, D'Aiuto

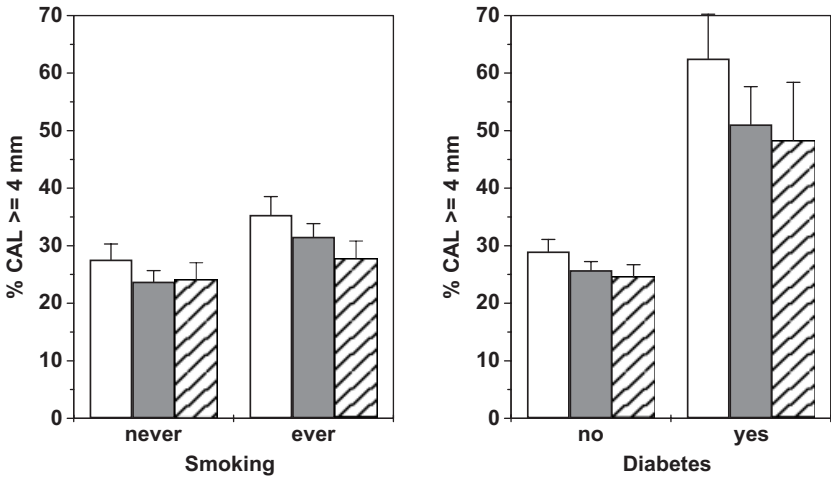

Fig. 3. Stratified analysis of the relationship between clinical attachment loss (CAL) $\geqslant 4$ mm according to smoking status or diabetes and the age- and sex-specific height quartiles (first quartile the smallest, second and third quartiles together, fourth quartile the tallest). Smoking: ANOVA smoking $p<0.0001$, height $p=0.0006$, interaction $p=0.265$. Diabetes: ANOVA diabetes $p<0.0001$, height $p=0.0026$, interaction $p=0.174$.

et al. 2004). Golub et al. (2006) suggested that systemic diseases provide a systemic inflammatory response co-affecting periodontal diseases when induced by periopathogenic bacteria. This chain of events may also act in the opposite direction, i.e. worsening of systemic diseases by periodontitis-born inflammation. Coexistence or mutual intensification of these diseases is a matter of individual predisposition. There is evidence that such pathognomic combinations even increase mortality (Abnet et al. 2005, Hamalainen et al. 2005).

In the present population-based study we have shown that there is a significant relationship between body height and periodontal measures, i.e. tooth loss and attachment loss. From the analyses, we concluded that the height effects are most pronounced in the individuals with the shortest stature. This is most obvious from the attachment loss, whereas the number of teeth may be subject to influences other than inflammation. Besides age, gender, and education, we found that mainly those variables are negatively associated with height which are related to inflammation. These variables are white blood count and high-fibrinogen levels, and, in addition, periodontal attachment loss. The latter may be considered as a measure of the lifelong accumulation of inflammatory episodes or even chronic inflammation.

Taken together, these findings and the references cited support the hypothesis suggested by Crimmins & Finch (2006). As shown in their paper, height is linked to infections and the inflammatory response. Chronic infection and chronic inflammation as typical of periodontal diseases are associated with high levels of circulating inflammation markers, viz. CRP, fibrinogen, and cytokines. Especially, interleukin (IL)-6 seems to play a crucial role in the relationship in inflammation-induced growth retardation. Treatment with anti-TNFα antibodies of paediatric patients with Crohn's disease does not only lower the disease activity index, it also promotes growth (Borelli et al. 2004). Likewise, this treatment is effective in children with growth retardation due to juvenile arthritis (Tynjala et al. 2006). Treatment with etanercept or infliximab did not only suppress the inflammation in these patients, it also restored growth velocity. The relationship to inflammation markers is also obvious from the data shown in our study.

If there exist individuals who are prone to a hyper-reactivity to inflammatory stimuli, this could be manifested already during childhood. At this time, when the growth spurt occurs, susceptibility to infectious and/or inflammatory diseases may be increased and slow down the length growth. Such individuals are then most probably also vulnerable to inflammatory diseases in their adulthood. In this way, the association between body height and periodontitis may be explained. Albeit many more factors determine growth, the associations between systemic diseases, the local chronic inflammation of periodontitis and height strongly support the idea of a special hyper-reactive type of vulnerability. It should be kept in mind that such an inborn or acquired predisposition acts as a disease modifier rather than a cause. In periodontitis, the causative factor is the infection-induced formation of gingival plaque.

Even malnutrition as an important growth-affecting factor shows interrelationships to inflammation (Finch & Crimmins 2004). In experimental intestinal disease in rats it was calculated that 40% of growth retardation is attributable to inflammation, with the rest being due to under-nutrition (Sawczenko et al. 2005). The inflammation-related reduction in growth is independent of nutritional intake (Koniaris et al. 1997). This may not only be associated with reduced body height or increased morbidity but also with an increased mortality rate. On the other hand, babies born small for gestational age due to intra-uterine growth retardation show diminished final height, present with an elevated neutrophil count and may be vulnerable to illness acquired later in life (Ibanez et al. 2005). Likewise, there is a negative association between birthweight and CRP levels (Sattar et al. 2004) or fibrinogen concentrations (Tuya et al. 2005). The latter study on twins is compatible with the hypothesis that genetic factors play an important role in these associations (Ijzerman 2005). The effects of low birthweight on disease risk are increased by slow infant growth in childhood (Barker et al. 2002). On the other hand, in a recently published large twin study relating height and coronary heart disease, environmental factors (intra-uterine or postnatal) were found to affect height and the disease (Silventoinen et al. 2006). These findings may be important in interpreting the results presented here. Because of the inflammatory background of both periodontitis and cardiovascular diseases the assumption of a direct link between these diseases is much discussed (Kinane & Lappin 2002, Meurman et al. 2004). It was hypothesized that taller stature may represent resilience against adult exposures that are risks of cardiovascular diseases (Osika et al. 2006). Our results suggest that also for periodontal diseases an individual's fate during childhood as reflected by height could affect his or her resilience against the various risk factors.

Table 4. Logistic model for dependent variables white blood count >10 Gpt/l ($N = 4167$), fibrinogen >3.5 g/l ($N = 4158$) and % attachment loss $\geqslant 4$ mm (fourth *versus* first quartiles, $N = 3445$)

	White blood count		Fibrinogen		CAL $\geqslant 4$ mm	
	odds ratios (95% CI)	*p*	odds ratios (95% CI)	*p*	odds ratios (95% CI)	*p*
Age	0.97 (0.96–0.98)	<0.001	1.025 (1.02–1.03)	<0.001	1.18 (1.17–1.19)	<0.001
Sex	1.40 (1.04–1.89)	0.026	1.72 (1.45–2.05)	<0.001	0.84 (0.66–1.08)	0.175
HbA_{1C}	1.37 (1.21–1.55)	<0.001	1.11 (1.02–1.21)	0.012	1.09 (0.94–1.27)	0.260
LDL/HDL	1.16 (1.06–1.28)	0.002	1.21 (1.14–1.29)	<0.001	1.19 (1.08–1.32)	<0.001
Smoking	1.04 (1.01–1.06)	<0.001	1.02 (1.01–1.04)	<0.001	1.05 (1.02–1.09)	0.003
Height, second to third	0.65 (0.47–0.90)	0.010	0.84 (0.69–1.01)	0.068	0.67 (0.50–0.90)	0.007
Height, fourth quartile	0.44 (0.27–0.73)	0.001	0.68 (0.52–0.88)	0.004	0.60 (0.41–0.88)	0.009
Smoking × Height	1.00 (0.99–1.01)	0.589	1.00 (0.99–1.01)	0.858	1.01 (0.99–1.03)	0.308

Independent: age continuous in 1 year increments; sex: male 0, female 1; diabetes continuous as percent HbA_{1C}; LDL/HDL continuous; smoking: continuous as packyears; height quartiles with the smallest as reference.

Owing to the cross-sectional setting, the study has some limitations. A causative sequence cannot be deduced from the interacting relationships between periodontitis, markers of systemic inflammation, and height. The data analysis regarding the height of the participants is complicated by secular trends in the population as nearly four generations are included (Cole 2003). Age effects on height originate from secular trends, increased height in the younger generations and a shrinking spinal column at older ages. Periodontal parameters tend to be increased at older ages, especially CAL is an accumulating measure. In this respect, the age dependency reflects the natural history of the disease. From these cross-sectional data it is impossible to decide how much of the height changes with age (Fig. 1) is due to acceleration or to shrinking spine columns in the older. Nevertheless, the relationship between periodontal measures and height is still detectable and significant within the different 10-year age cohorts (Fig. 2). Another point of concern is the central role of smoking in the aetiology of periodontal attachment loss (Hyman & Reid 2003). Albeit the height effect is detectable in never as well as in ever smokers, it is more pronounced in subjects who were smokers during their lifetime. In our study, the proportion of smokers were identical in all height strata. Thus, it is to be assumed that height acts as an risk indicator modifying the effects of periodontal risk factors (Ylöstalo & Knuuttila 2006).

Parental health and genetic endowment together with intra-uterine, childhood, and early adult exposures may all influence an individual's health. Furthermore, height is associated with socio-economic differences (Heineck 2006), which are also important risk indicators in periodontal diseases. For all these influences, height might be a biomarker accessible during lifetime (Gunnell 2002). Subnormal growth during any growth phase is associated with an increased risk of adult shortness (Luo & Karlberg 2000).

In conclusion, we postulate the following sequence of events to explain the association between height and periodontal disease. An individual can be born with a special susceptibility to infectious and inflammatory diseases caused by genetic predisposition and/or by intra-uterine imprinting. In childhood, when such exaggerated diseases occur, the length growth could be impaired. Reaching adulthood, growth comes to a halt but the individual remains susceptible to inflammatory sequelae. Thus, smaller persons pertain a tendency to develop more severe periodontitis and, probably, also other diseases with an inflammatory background.

References

Abnet, C. C., Qiao, Y. L., Dawsey, S. M., Dong, Z. W., Taylor, P. R. & Mark, S. D. (2005) Tooth loss is associated with increased risk of total death and death from upper gastrointestinal cancer, heart disease, and stroke in a Chinese population-based cohort. *International Journal of Epidemiology* **34**, 467–474.

Albandar, J. M. (2002) Global risk factors and risk indicators for periodontal diseases. *Periodontology 2000* **29**, 177–206.

Bacon, M. C., White, P. H., Raiten, D. J., Craft, N., Margolis, S., Levander, O. A., Taylor, M. L., Lipnick, R. N. & Sami, S. (1990) Nutritional status and growth in juvenile rheumatoid arthritis. *Seminars in Arthritis and Rheumatism* **20**, 97–106.

Barker, D. J. P., Eriksson, J. G., Forsen, T. & Osmond, C. (2002) Fetal origins of adult disease: strength of effects and biological basis. *International Journal of Epidemiology* **31**, 1235–1239.

Baum, W. F., Schneyer, U., Lantzsch, A. M. & Kloditz, E. (2002) Delay of growth and development in children with bronchial asthma, atopic dermatitis and allergic rhinitis. *Experimental and Clinical Endocrinology and Diabetes* **110**, 53–59.

Borelli, O., Bascietto, C., Viola, F., Bueno de Mesquita, M., Barbato, M., Mancini, V., Bosco, S. & Cucchiara, S. (2004) Infliximab heals intestinal inflammatory lesions and restores growth in children with Crohn's disease. *Digestive and Liver Diseases* **36**, 342–347.

Burnham, J. M., Shults, J., Semeao, E., Foster, B., Zemel, B. S., Stallings, V. A. & Leonard, M. B. (2004) Whole body BMC in pediatric Crohn disease: independent effects of altered growth, maturation, and body composition. *Journal of Bone and Mineral Research* **9**, 1961–1968.

Cole, T. J. (2003) The secular trend in human physical growth: a biological view. *Economics and Human Biology* **1**, 161–168.

Crimmins, E. M. & Finch, C. E. (2006) Infection, inflammation, height, and longevity. *Proceedings of the National Academy of Scences USA* **103**, 498–503.

D'Aiuto, F., Parkar, M., Andreou, G., Brett, P. M., Ready, D. & Tonetti, M. S. (2004) Periodontitis and atherogenesis: causal association or simple coincidence? *Journal of Clinical Periodontology* **31**, 402–411.

Finch, C. E. & Crimmins, E. M. (2004) Inflammatory exposure and historical changes in human life-spans. *Science* **305**, 1736–1739.

Genco, R. J. (1996) Current view of risk factors for periodontal diseases. *Journal of Periodontology* **67** (Suppl.), 1041–1049.

Golub, L. M., Payne, J. B., Reinhardt, R. A. & Nieman, G. (2006) Can systemic diseases coinduce (not just exacerbate) periodontitis? A hypothetical ''two-hit'' model. *Journal of Dental Research* **85**, 102–105.

Gunnell, D. (2002) Commentary: Can adult anthropometry be used as a ''biomarker'' for prenatal and childhood exposures? *International Journal of Epidemiology* **31**, 390–394.

Hamalainen, P., Meurman, J. H., Kauppinen, M. & Keskinen, M. (2005) Oral infections as predictors of mortality. *Gerodontology* **22**, 151–157.

Heineck, G. (2006) Height and weight in Germany, evidence from the German Socio-Economic Panel 2002. *Economics and Human Biology* **4**, 359–382.

Heitz-Mayfield, L. J. (2005) Disease progression: identification of high risk groups and individuals for periodontitis. *Journal of Clinical Periodontology* **32** (Suppl. 6), 196–206.

Hensel, E., Gesch, D., Biffar, R., Bernhardt, O., Kocher, T., Splieth, C., Born, G. & John, U. (2003) Study of Health in Pomerania (SHIP), a health survey in an east German region. Objectives and design of the oral health section. *Quintessence International* **34**, 370–378.

Hildebrand, H., Aronson, S. & Selvik, G. (1994) Growth as a parameter of inflammation in Crohn's disease, using roentgen stereophotogrammetric analysis. *Acta Paediatrica* **3**, 1070–1075.

Hyman, J. J. & Reid, B. C. (2003) Epidemiologic risk factors for periodontal attachment loss among adults in the United States. *Journal of Clinical Periodontology* **30**, 230–237.

Ibanez, L., Fucci, A., Valls, C., Ong, K., Dunger, D. & de Zegher, F. (2005) Neutrophil count in small-for-gestational age children: contrasting effects of metformin and growth hormone therapy. *Journal of Clinical Endocrinology and Metabolism* **90**, 3435–3439.

Ijzerman, R. G. (2005) Genetic and environmental origins of the association between birth weight and cardiovascular risk factors. *Journal of Thrombosis and Haemostasis* **3**, 1141–1142.

Kantarci, A. & van Dyke, T. E. (2005) Resolution of inflammation in periodontitis. *Journal of Periodontology* **76**, 2168–2174.

Kinane, D. F. & Lappin, D. F. (2002) Immune processes in periodontal disease. *Annals of Periodontology* **7**, 62–71.

Koniaris, S. G., Fisher, S. E., Rubin, C. T. & Chawla, A. (1997) Experimental colitis impairs bone growth independent of nutritional factors. *Journal of Pediatric Gastroenterology and Nutrition* **25**, 137–1341.

Luo, Z. C. & Karlberg, J. (2000) Critical growth phases for adult shortness. *American Journal of Epidemiology* **152**, 125–131.

Meurman, J. H., Sanz, M. & Janketm, S. J. (2004) Oral health, atherosclerosis, and cardiovascular disease. *Critical Reviews in Oral Biology and Medicine* **15**, 403–413.

Osika, W., Ehlin, A. & Montgomery, S. M. (2006) Does height modify the risk of angina associated with economic adversity? *Economics and Human Biology* **4**, 398–411.

Preece, M. A., Law, C. M. & Davies, P. S. (1986) The growth of children with chronic paediatric disease. *Clinical Endocrinology and Metabolism* **15**, 453–477.

Rosenfeld, M., Gibson, R. L., McNamara, S., Emerson, J., Burns, J. L., Castile, R., Hiatt, P., McCoy, K., Wilson, C. B., Inglis, A., Smith, A., Martin, T. R. & Ramsey, B. W. (2001) Early pulmonary infection, inflammation, and clinical outcomes in infants with cystic fibrosis. *Pediatric Pulmonology* **32**, 356–366.

Sattar, N., McConnachie, A., O'Reilly, D., Upton, M. N., Greer, I. A., Davey Smith, G. & Watt, G. (2004) Inverse association between birth weight and C-reactive protein concentrations in the MID SPAN family study. *Arteriosclerosis Thrombosis Vascular Biology* **24**, 583–587.

Sawczenko, A., Azooz, O., Paraszczuk, J., Idestrom, M., Croft, N. M., Savage, M. O., Ballinger, A. B. & Sanderson, I. R. (2005) Intestinal inflammation-induced growth retardation acts through IL-6 in rats and depends on the -174 IL-6 G/C polymorphism in children. *Proceedings of the National Acadademy of Sciences USA* **102**, 13260–13265.

Silventoinen, K., Zdravkovic, S., Skytthe, A., McCarron, P., Herskind, A. M., Koskenvuo, M., de Faire, U., Pedersen, N., Christensen, K. & Kaprio, J.GenomEUtwin Project. (2006) Association between height and coronary heart disease mortality: a prospective study of 35,000 twin pairs. *American Journal of Epidemiology* **163**, 615–621.

Tuvemo, T., Cnattingius, S. & Jonsson, B. (1999) Prediction of male adult stature using anthropometric data at birth: a nationwide population-based study. *Pediatric Research* **46**, 491–495.

Tuya, C., Mutch, W. J., Broom, I. & McNeill, G. (2005) The effect of birth weight on clottable and intact fibrinogen levels: a twin study. *Journal of Thrombosis and Haemostasis* **3**, 1143–1148.

Tynjala, P., Lahdenne, P., Vahasalo, P., Kautiainen, H. & Honkanen, V. (2006) Impact of anti-TNF therapy on growth in severe juvenile idiopathic arthritis. *Annals of Rheumatic Diseases* **65**, 1044–1049.

Ylöstalo, P. V. & Knuuttila, M. L. (2006) Confounding and effect modification: possible explanation for variation in the results on the association between oral and systemic diseases. *Journal of Clinical Periodontology* **33**, 104–108.

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Clinical Relevance

Scientific rationale for the study: Body height is a biomarker of early life events, which has intensively been studied with respect to cardiovascular disease (CVD). It was shown, that it is predictive of CVD events. It may also prime a subject for further chronic diseases such as periodontitis.

Principal findings: In 4300 subjects we found body height to be consistently associated with periodontal disease and markers of systemic inflammation.

Practical implications: In the multifactorial pathogenesis of periodontal diseases, the clinician ''should'' be aware not only of actual risk factors as smoking or diabetes but also of modifying factors dating from early childhood. This may help to better understand the individual dispositions for the disease.