Lead exposure and periodontitis in US adults

M. C. P. Saraiva[1], R. S. Taichman[2], T. Braun[3], J. Nriagu[4], S. A. Eklund[5], B. A. Burt[5]
[1]Department of Paediatrics and Social Dentistry, School of Dentistry of Ribeirão Preto, University of São Paulo, SP, Brazil, [2]Department of Periodontics and Oral Medicine, Prevention, Geriatrics, School of Dentistry, University of Michigan, Ann Arbor, MI, USA and Departments of [3]Biostatistics, [4]Environmental Health Science, and [5]Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, USA

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Background and Objective: Lead is known to have significant effects on bone metabolism and the immune system. This study tested the hypothesis that lead exposure affects periodontitis in adults.

Material and Methods: This study used the data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–94). It analyzed data from 2500 men and 2399 women, 20–56 yr old, who received complete periodontal examination. Periodontitis was defined as the presence of > 20% of mesial sites with ≥ 4 mm of attachment loss. Lead exposure was grouped into three categories: < 3; 3–7; and > 7 µg/dL. Covariates were cotinine levels, poverty ratio, race/ethnicity, education, bone mineral density, diabetes, calcium intake, dental visit, and menopause (for women). All analyses were performed separately for men and women and considering the effect design. Univariate, bivariate, and stratified analysis was followed by multivariable analysis by estimating prevalence ratios through poisson regression.

Results: After adjustment for confounders, the prevalence ratios, comparing those with a lead blood level of > 7 µg/dL to those with a lead blood level of < 3 µg/dL was 1.70 (95% confidence interval (CI): 1.02, 2.85) for men and 3.80 (95% CI: 1.66, 8.73) for women.

Conclusion: The lead blood level was positively and statistically associated with periodontitis for both men and women. Considering the public health importance of periodontitis and lead exposure, further studies are necessary to confirm this association.

Maria da Conceição P. Saraiva, Avenue Do Café s/n, CEP 14040–904, Ribeirão Preto, São Paulo, Brazil
Tel: + 55 16 3602 3995
Fax: + 55 16 3633 0999
e-mail: mdsaraiv@umich.edu

Despite the decline of environmental and occupational lead contamination in the past few decades, sources of lead exposure are still found in some neighborhoods, especially in the more underprivileged areas (1,2). Moreover, it has been accepted that there is no threshold for the deleterious health effects of lead (3,4). These facts strengthen the importance of continued investigation into the effects of lead on human health.

In the past two decades, increasing evidence has been gained to support the fact that chronic lead exposure may affect bone metabolism (5,6) and possibly the immune system (7,8). This evidence makes lead a potential risk factor for periodontitis – a complex multifactorial disease that affects bone – which is initiated by an imbalance of the host defense system and the pathogenicity of microorganisms (9).

Lead affects bone metabolism by interfering with calcium metabolism, which directly affects bone cells and bone matrix synthesis (6). Physiological mechanisms that control calcium levels affect the absorption, retention, and distribution of lead in a similar manner. As calcium regulates many cell functions, such as the response to hormonal and electrical stimuli, the interference of calcium metabolism by lead might also affect such cellular functions (6,10).

The direct effect of lead on osteoblasts includes the impairment of bone matrix synthesis, the process of initiation of mineralization, and the regulation of bone resorption (6). Impairment of bone matrix is mostly caused by interference with the collagen and noncollagen protein synthesis (11,12). Lead also displaces calcium

ions from synthesized osteocalcin, which in turn inhibits its binding to hydroxyapatite, disturbing bone formation (13,14). *In vitro*, lead stimulates the proliferation of osteoclast-like cells from the bone marrow of rats, and also the production of prostaglandin E2 (15).

Clinical evidence of the deleterious effect of lead exposure on bone metabolism in humans is reduced child growth (16–18). Development of osteopenia and osteoporosis (6) has also been proposed, but the evidence from human studies is still debatable. Osteopenia has been reported in rats exposed to low levels of lead in a dose-dependent interaction with calcium intake (19,20).

The effect of lead on the immune system has been attributed mostly to downregulation of a cell-mediated immune response (21). In *in vitro* and animal studies, lead exposure has been associated with imbalances of T-helper cell (Th1/Th2) activity (22), decreases in interferon-γ, and increases in tumor necrosis factor (23) and interleukin-12 (24). The effects of lead in humans are still controversial, mostly because of lack of control of confounders and small sample sizes of the majority of the studies. Among the effects of lead exposure in humans are the decreased percentage of monocytes, an increase in the percentage of CD4$^+$ cells (25,26), and impaired polymorphnuclear neutrophil functions (27,28).

Several of the cellular and immunologic responses to chronic lead exposure have also been described for periodontitis (29–31). We propose that the direct effect of lead on bone matrix formation has the potential to interfere with the progression of periodontitis, because bone is constantly remodeling and periodontitis is a relatively slow progressive disease characterized by periods of activity and quiescence. A recent study demonstrated that lead might impair the bone-healing process (32). Similar immunologic alterations associated with lead exposure, such as impaired chemotaxis and phagocytosis of polymorphnuclear neutrophils (29), imbalance of Th1/Th2 cells (31), and an increase in prostaglandin E2 production

(9), have also been reported for periodontitis. In fact, the causal association between lead exposure and periodontitis has already been proposed (33,34). However, these studies had some limitations, such as lack of control of confounders and inappropriate control groups. Recently, an analysis of the Third National Health Examination Survey (NHANES III) data (35), using blood lead levels as the outcome variable, proposed that periodontal bone loss would contribute to the delivery of lead into the bloodstream. It is possible that periodontal attachment and bone loss might contribute to increased lead blood levels; however, given the episodic nature of periodontitis, it seems hardly likely that the association found was solely the result of periodontal breakdown tissue. The association found in that study might, in part, be attributed to lack of control of some confounders, such as osteopenia/osteoporosis (30), menopause (36), and calcium intake (37). Thus, the objective of this study was to assess the association between lead blood levels and periodontitis in the United States population, using data from a representative national sample.

Material and methods

Data source and study population

The data source for this study was the NHANES III, a cross-sectional survey of a complex, multistage, stratified clustered sample intended to be representative of the civilian noninstitutionalized US population older than 6 mo (38). Oral examinations were performed in a mobile examination center by six trained and calibrated examiners. Clinical evaluation of periodontal tissues was performed in two diagonally opposite quadrants – one superior and another inferior – chosen at random for each individual. Quadrants did not include third molars, and only two sites (mesial-buccal and buccal) per tooth were examined. Detailed information of examination procedures have been reported previously (39).

NHANES III had an original sample size of 39,695 individuals, of whom

33,994 were interviewed. This study included only individuals from 30 to 55 yr old. Individuals over 55 yr old were excluded to avoid inclusion of survivors who predominate in elderly samples, resulting in an artificial stabilization of average attachment loss (or prevalence of periodontitis) according to age in a population. The cut-off point of 55 yr was based on the point of stabilization of average attachment loss (which ranged from 52 to 55 yr old) using a median-smoothing curve plotted for all individuals and stratified by gender and race/ethnicity.

Only individual Whites, African-Americans, and Mexican-Americans with a complete periodontal examination and information on lead blood levels were included in this study. Because of increased bone metabolism resulting in significant increase in lead blood levels, pregnant (*n* = 253) and breastfeeding (*n* = 81) women were excluded from this study. The analyses thus proceeded with a total of 2399 women and 2500 men.

Outcome variables

The case-definition of periodontitis was at least 10% of mesial sites with at least 4 mm of clinical attachment loss (40). Clinical attachment loss was calculated by subtracting the distance from the gingival margin to the cemento–enamel junction from pocket depth (41). Only the information on attachment loss from mesial sites was included, avoiding any influence of gingival recession from buccal sites, which may not represent periodontitis.

Exposure variable

Lead exposure was measured as the total lead blood level (μg/dL). The lead blood level was categorized into three levels: < 3 μg/dL; 3–7 μg/dL; and > 7 μg/dL. For this population, 3 μg/dL represents the 50th percentile and 7 μg/dL represents approximately the 90th percentile of the distribution of lead.

Covariates

The following factors were used as covariates in the regression analysis:

age, gender, presence of diabetes, cotinine blood levels, education, economic level (poverty), dental caries, tooth loss, and race/ethnicity (whites, African-Americans and Mexican-Americans). Diabetes was defined from a question included in the personal interview: 'have you ever been told by a doctor you had diabetes?'. Women who reported to have had diabetes only during pregnancy were not considered as diabetic. Cotinine levels were used to define tobacco smoking as well as smoking status (current, former, and never smokers). Cotinine levels (ng/ml) were categorized into five levels representing the 60th, 70th, 80th and 90th percentile, respectively: < 1.53, 1.54–63.3, 63.4–202.39, 202.40–305.8, and > 305.9. Education was defined in three levels as < 12, 12 and > 12 yr of education. Poverty ratio (family income divided by the poverty threshold for the year in which the family was interviewed) was categorized into three levels: ≤ 1.301; 1.301–3.500; and > 3.500 (38). Serum calcium was categorized according to the median level.

Levels of bone mineral density (BMD) were calculated separately for men and women, based on the standard deviation of the distribution of bone mineral density for non-Hispanic whites from 20 to 29 yr old (42). Very low levels of BMD (osteoporosis) refers to more than 2.5 standard deviations below the mean; low levels of BMD (osteopenia) refers to scores from 1 to 2.5 standard deviations below the mean; high levels refers to 1 standard deviation below the mean up to the mean; and very high levels refers to BMD scores above the mean. The number of teeth present in the mouth was also used as covariate in order to take tooth loss into consideration (41).

Age of the participant's house was included in the models in an attempt to control for factors associated with current exposure to lead in paint. Time of construction of the house was available from NHANES III in three categories: house built before 1946; house built between 1946 and 1973; and house built after 1973. Menopause status was defined as women not having periods in the past 12 mo (excluding those reporting to be pregnant or breastfeeding during the past 12 mo). Current pregnancy information that was used to exclude individuals was assessed by the question 'are you pregnant now?' with the confirmation of a pregnancy test.

Statistical analysis

The statistical analysis was performed separately for men and women. This was because women are submitted to hormonal influences on bone metabolism during menopause (43), pregnancies, and breastfeeding (44). All analyses took into consideration the sampling design by using the survey procedures on the STATA 8.0 statistical program. Prevalence ratio was used as measurement of association calculated through poisson regression (45). Univariate and bivariate analysis was performed followed by stratified analysis and modeling. Multivariate poisson regression models were built backwards, keeping known confounders in the model, even if they were not significant (alpha = 0.05). As there was a significant drop in lead blood levels from the phase I to the phase II of NHANES III, a variable identifying the survey phase was forced into the model. Systematic bias from examiners was also handled by considering a variable specific to each examiner. Some covariates, such as menopause and osteoporosis, were forced into the model in an attempt to control the increased delivery of lead stored in bones. Also, age of residence was forced into the model in an attempt to control for recent exposure to lead. Plausible interactions of the second order were also tested ($p < 0.10$).

Results

The average attachment loss on mesial tooth sites for women and men were, respectively, 1.1 mm [standard error (SE) = 0.05] and 0.93 mm (SE = 0.04). Among men, the prevalence of individuals with at least 10% of their mesial sites showing attachment loss of at least 4 mm was 12.3% (SE = 1.0) and among women the prevalence was 7.2% (SE = 0.61).

Table 1 shows the bivariate analysis for lead blood levels among women and men. The unadjusted prevalence ratio for lead blood level was statistically associated with periodontitis for both men and women.

Table 2 shows the adjusted prevalence ratio (sequential analysis) as the confounders are added to the model. After adjustments for socio-economic factors, the lead blood level prevalence ratio showed the highest drop when cotinine levels were added to the model. After the addition of cotinine levels, only small changes were observed in the adjusted prevalence ratio for lead blood level, both for men and for women. We tested the interaction between smoking status and lead blood level and no significant interactions were found (Table 3). The interaction between cotinine levels and lead blood level was also studied, but no interaction for men was found. The very small number of women (cells containing only one individual) with moderate cotinine levels and high lead blood levels precluded from testing the interaction of cotinine and lead blood level among women. Independent of smoking status, the prevalence ratio for high lead blood levels is > 1, even for never smokers to whom the prevalence for periodontitis is very small. Among nonsmoker women, only 1.21% (SE = 0.43) had a lead blood level of > 7 µg/dL and among men this proportion was 6.2% (SE = 1.4). Moreover, the trend analysis was significant for men ($p = 0.0373$) and for women ($p = 0.0230$). No significant interactions were observed between lead blood level and the other covariates evaluated (serum calcium, poverty, race/ethnicity, osteoporosis, and education).

Discussion

This study showed a significant positive association between lead and periodontitis for both men and women. The prevalence ratio, comparing those with a lead blood level of > 7 µg/dL to those with a lead blood level of < 3 µg/dL, was lower for men (prevalence ratio = 1.73, 95% confidence interval (CI: 1.02, 2.92) than for

Table 1. Characteristics of 30–55-yr-old men (n = 2500) and women (n = 2399) of the US population [data were obtained from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–94)]

	Men					Women				
	n^*	%†	SE‡	PR¶	95% CI§	n^*	%	SE	PR	95% CI
Race/ethnicity										
White	873	10.1	1.3	1.00		853	5.3	0.9	1.00	
African-American	771	24.2	1.6	2.39	1.78, 3.21	811	12.4	1.3	2.34	1.59, 3.45
Mexican-American	856	12.4	1.2	1.23	0.90, 1.67	735	7.8	1.1	1.47	0.95, 2.26
p-value				< 0.0001					< 0.0001	
Poverty ratio										
> 3.500	699	9.0	1.3	1.00		536	1.9	0.7	1.00	
1.301–3.500	716	10.8	1.5	1.18	0.83, 1.70	677	6.6	1.2	3.57	1.61, 7.93
< 1.301	904	19.8	1.8	2.16	1.61, 2.91	1000	13.3	1.8	7.21	3.41, 15.27
p-value				< 0.0001					< 0.0001	
Education (years)										
> 12	915	5.7	0.9	1.00		818	2.3	0.7	1.00	
= 12	769	15.3	1.8	2.67	1.81, 3.94	851	8.7	1.3	3.72	1.97, 7.02
< 12	750	26.4	2.6	4.61	3.29, 6.46	686	15.0	2.3	6.43	3.37, 12.26
p-value				< 0.0001					< 0.0001	
Dental visit										
Every year/2 yr	1052	7.4	1.0	1.00		1263	2.7	0.6	1.00	
Whenever need/never	1333	18.1	1.6	2.46	1.83, 3.32	1084	12.7	1.6	5.08	3.13, 8.25
p-value				< 0.0001					< 0.0001	
Bone mineral density**										
Very high	1102	12.3	1.5	1.00		1230	7.1	1.2	1.00	
High	863	11.2	1.7	0.91	0.63, 1.30	646	5.1	1.2	0.72	0.41, 1.27
Low and very low	385	12.9	2.2	1.04	0.68, 1.61	326	7.9	1.8	1.11	0.68, 1.79
p-value				0.7912					< 0.0001	
Menopause										
No	–	–	–	–	–	1946	5.1	0.7	1.00	
Yes	–	–	–	–	–	453	12.7	2.4	2.49	1.63, 3.81
p-value									< 0.0001	
Cotinine level										
< 1.53	1321	5.9	0.9	1.00		1600	3.0	0.6	1.00	
1.5 3–63.39	300	11.4	2.7	1.92	1.14, 3.23	235	11.3	3.0	3.79	2.03, 7.09
63.40–202.39	285	19.4	3.2	3.27	2.05, 5.21	177	7.7	3.2	2.58	1.07, 6.22
202.40–305.89	247	20.8	4.1	3.50	2.03, 6.04	138	15.5	3.9	5.18	2.46, 10.90
> 305.89	297	25.9	3.9	4.36	2.74, 6.95	201	18.2	4.4	6.11	3.14, 11.90
p-value				< 0.0001					< 0.0001	
Smoking status										
Never	888	4.1	0.7	1.00		1439	3.7	0.6	1.00	
Former	707	10.2	1.7	2.50	1.70, 3.66	392	4.6	1.7	1.23	0.57, 2.67
Current	905	22.4	2.6	5.47	3.50, 8.57	568	13.2	2.5	3.54	2.25, 5.57
p-value				< 0.0001					< 0.0001	
Calcium intake (mg)										
≥ 760	1385	9.5	0.9	1.00		924	4.6	1.0	1.00	
< 760	1114	15.7	2.0	1.66	1.24, 2.23	1475	7.8	0.9	1.69	1.07, 2.67
p-value				0.0011					0.0247	
Diabetes mellitus										
No	2402	11.5	1.0	1.00		2296	5.9	0.7	1.00	
Yes	98	22.8	6.2	1.98	1.13, 3.48	103	25.3	6.2	4.31	2.64, 7.05
p-value				0.0182					< 0.0001	
Lead blood level (µg/dL)										
< 3	773	5.5	1.1	1.00		1713	4.1	0.7	1.00	
3–7	1268	13.5	1.4	2.45	1.53, 3.93	596	11.5	2.0	2.76	1.67, 4.56
> 7	459	25.6	3.1	4.64	2.91, 7.40	90	39.5	10.5	9.54	5.24, 17.34
p-value				< 0.0001					< 0.0001	

*The number of individuals may very from variable to variable because of missing values of covariates.
†Weighted percentage.
‡Standard error.
¶Prevalence ratio.
§95% confidence limit.
**Levels of bone mineral density (BMD) were calculated separately for men and women, based on the standard deviation of the distribution of bone mineral density for 20–29 yr-old non-Hispanic whites. Very low level of BMD (osteoporosis) refers to < 2.5 standard deviations from the mean; low level of BMD (osteopenia) refers to scores from 1 to 2.5 standard deviations; high levels refers to 1 to lower than the mean; and very high levels refers to scores above the mean.

women (prevalence ratio = 3.88, 95% CI: 1.71, 8.77). However, this difference may be explained by the different distribution of lead exposure between the two groups, which was higher among men. While the majority of women were categorized as having a lead blood level of < 3 µg/dL, the majority of men were exposed to higher levels (3–7 µg/dL) (Table 1).

Although significant, the association found in this study needs to be discussed carefully. We began this study with the premise that, in the absence of bias, our results would tend to be an underestimation of the true association, if the association was true. This premise had the argument that current lead blood levels occur partially from recent exposure to lead and partially from accumulated lead in bones, resulting in a large variance of lead exposure. As lead blood levels have been declining in the USA, it can be argued that current lead blood levels among Americans would reflect mostly recent exposure because the turnover of lead in bones may take years, or even decades (2). The decline in lead blood levels was significant during the interval between data collection for the NHANES II survey and the NHANES III survey (46), but only 13 yr had elapsed between introduction of the major regulations to control lead in the USA [control of lead in gasoline (1973) and in paint (1977)] to when NHANES III was conducted (47). It is possible that the contribution of lead from bones, as a result of past exposure, was still a valid assumption in the early 1990s, especially for those people previously exposed to high levels of lead. Considering that bone turnover contributes partially to current lead blood levels, we controlled for factors that can momentarily increase the delivery of lead into the bloodstream, such as menopause and osteopenia/osteoporosis, as well as recent exposure to lead, such as cotinine levels and living in old houses. Moreover, we excluded woman who were pregnant and those who were breast-feeding. If the current levels of lead actually do not reflect past lead exposure, there are two possible interpretations for the association found. As in any cross-sectional study,

the current level of one factor can be considered as a surrogate of past exposure. Another possibility is that the lead blood levels reflect an unappreciated variable or residual confounder, in particular something derived from socio-economic level and smoking. Lead exposure and periodontitis are known to be associated with socio-economic status and lifestyle (48). The standard measurements of socio-economic status (income levels and education) have been questioned as valid measurements of the social

environment and social class (49). It is possible that with the decline of environmental lead in the USA, lead blood levels has become a better marker for individuals living in unfavorable social environments, and those having deleterious health habits, such as poor nutrition, smoking, or living in old houses in poor neighborhoods. Living in poor and lower-educated neighborhoods per se has been considered as a risk indicator of health effect and also as a predictor of deleterious health behavior, such as a smoking habit and

Table 2. Sequential analysis showing the effect of confounders on the prevalence ratio (PR) for periodontitis (≥ 10% of mesial sites with attachment loss ≥ 4 mm) among men (n = 2500) and women (n = 2399) of the 30–55 yr US population [data were obtained from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–94)]

Variables	Lead blood level (µg/dL)	Men		Women	
		PR-adj.†	95% CI‡	PR-adj.	95% CI
Crude analysis	< 3	1.00		1.00	
	3–7	2.45	1.53, 3.93	2.76	1.67, 4.56
	> 7	4.69	2.91, 7.40	9.53	5.24, 17.34
Age + examiner	< 3	1.00		1.00	
	3–7	2.26	1.43, 3.60	2.46	1.46, 4.16
	> 7	3.91	2.50, 6.13	7.64	4.59, 12.73
+ NHANES phase + region + house + number of teeth lost + menopause (only for women)*	< 3	1.00		1.00	
	3–7	1.68	1.08, 2.61	1.77	0.98, 3.19
	> 7	2.73	1.72, 4.33	7.02	4.26, 11.56
+ Povert ratio*	< 3	1.00		1.00	
	3–7	1.68	1.05, 2.69	1.52	0.77, 3.01
	> 7	2.58	1.63, 4.11	5.01	2.76, 9.07
+ Education*	< 3	1.00		1.00	
	3–7	1.65	1.04, 2.63	1.57	0.79, 3.12
	> 7	2.22	1.32, 3.73	4.68	2.49, 8.78
+ Race/ethnicity*	< 3	1.00		1.00	
	3–7	1.63	1.02, 2.61	1.54	0.77, 3.06
	> 7	2.16	1.28, 3.66	4.54	2.50, 8.25
+ Cotinine*	< 3	1.00		1.00	
	3–7	1.44	0.89, 2.34	1.14	0.58, 2.23
	> 7	1.74	1.02, 2.95	3.74	1.85, 7.55
+ Smoking status*	< 3	1.00		1.00	
	3–7	1,44	0.88, 2.30	1.12	0.56, 2.23
	> 7	1.70	1.01, 2.84	3.73	1.83, 7.63
+ Diabetes*	< 3	1.00		1.00	
	3–7	1.42	0.88, 2.31	1.15	0.58, 2.26
	> 7	1.72	1.02, 2.90	3.80	1.87, 7.73
+ Calcium intake*	< 3	1.00		1.00	
	3–7	1.38	0.85, 2.23	1.11	0.56, 2.22
	> 7	1.68	1.01, 2.80	3.75	1.84, 7.65
+ Dental visit*	< 3	1.00		1.00	
	3–7	1.42	0.88, 2.30	1.10	0.53, 2.26
	> 7	1.71	1.01, 2.87	3.50	1.57, 7.81
+ Osteoporosis*	< 3	1.00		1.00	
	3–7	1.37	0.84, 2.23	1.15	0.55, 2.37
	> 7	1.70	1.02, 2.85	3.80	1.66, 8.73

*This variable is added to the model containing the all the variables in previous row.
†Adjusted prevalence ratio, except for the first row, which shows the crude prevalence ratio.
‡95% confidence limit.

Table 3. Interaction between smoking status and lead blood levels, with and without cotinine, in the model

Variables	Lead blood level (µg/dL)	Men		Women	
		PR-adj.†	95% CI‡	PR	95% CI
Interaction with cotinine level in the model					
Never smokers	< 3	1.00		1.00	
	3–7	1.19	0.51, 2.77	1.01	0.37, 2.81
	> 7	1.25	0.43, 3.61	2.59	0.85, 7.90
Past smokers	< 3	1.44	0.59, 3.53	0.49	0.10, 2.33
	3–7	1.83	0.77, 4.36	1.67	0.55, 5.01
	> 7	3.17	1.24, 8.09	9.04	2.41, 33.94
Current smokers	< 3	1.79	0.70, 4.56	0.69	0.18, 2.57
	3–7	2.72	1.08, 6.83	0.71	0.14, 3.52
	> 7	3.07	1.22, 7.71	1.79	0.38, 8.41
p-value*			0.8253		0.3514
Interaction without cotinine level in the model					
Never smokers	< 3	1.00		1.00	
	3–7	1.25	0.55, 2.83	1.04	0.40, 2.69
	> 7	1.36	0.48, 3.88	2.49	0.70, 8.84
Past smokers	< 3	1.69	0.71, 4.03	0.51	0.09, 3.01
	3–7	1.92	0.83, 4.44	2.16	0.83, 5.61
	> 7	3.27	1.29, 8.29	8.28	2.16, 31.75
Current smokers	< 3	2.29	0.94, 5.61	2.65	1.28, 5.46
	3–7	3.57	1.61, 7.95	3.02	1.22, 7.51
	> 7	4.10	1.77, 9.51	7.18	3.12, 16.55
p-value*			0.8360		0.5243

*p-value for the interaction between smoking status and lead blood level.
†Adjusted prevalence ratio.
‡95% confidence limit.

lower physical activity (50). It is possible that oral hygiene and willingness to access dental treatment, which is associated with periodontitis (51), may also be predicted by the neighborhood environment. Moreover, there is some evidence that negative life events and psychosocial stress may be associated with periodontitis (52). Another possibility is that sustained hardship for long periods of time may also characterize individuals living in the deprived and contaminated areas. Elreedy *et al.* (1), reported that even after controlling for traditional individual indicators of socio-economic status, residence in a more deprived geographical area was a modifier of cumulative lead exposure in bone. Although the mechanism is not well understood, the contextual effect of living in a deprived area has been reported as an independent risk factor for several diseases (53), including dental caries (54). It is possible that contamination with lead and other toxicants may, in part, explain this contextual effect. There is also some evidence that lead is highly absorbed in individuals with poor nutrition, and who have low calcium and vitamin D intake, conditions that are more likely to be observed in poor neighborhoods (1,55,56). We tested interaction between calcium intake and iron intake in our study (data not shown) but neither calcium nor iron was an effect modifier. However, the lack of evidence of interaction in a cross-sectional study does not rule out the possibility of a past interaction. Therefore, we cannot rule out that the association found in this study between lead blood levels and periodontitis might be a residual confounder of socio-economic status, which was represented in this study only by poverty level and education. However, some other variables that could, to a certain extent, reflect other characteristics of social position were also used in this study, such as frequency of dental visity and age of the house. Nevertheless, it is is not known by how much these variables actually reduced the influence of residual confounders.

Residual confounder from smoking is another potential threat to the validity of any study of risk factors for periodontitis (57). Associations of periodontitis with systemic diseases have been attributed mostly to residual confounding from smoking (57).

Despite theoretical explanations for the association found in this study, it is important to point out that the association between lead blood levels and attachment loss was moderate and very stable, independently of confounders.

A major limitation of this study is its design, facing the constant decline of lead exposure in the USA and its unequal decline associated with socio-economic position. Moreover, the low levels of lead, and the consequently relatively small sample size of people with high exposure, preclude us from testing interactions that could be important in understanding the association. None of the interactions tested were statistically significant.

In spite of some weaknesses, the strength of this study is that NHANES III is a complex random sample representative of the US population, and thus selection bias common to occupational studies is not expected to be responsible for our results.

By contrast with a recent analysis of NHANES III (35), in which attachment loss was evaluated as a possible source of lead delivered into the bloodstream, we failed to observe an interaction between smoking and lead blood levels. One possible reason is that we excluded individuals over 56 yr old to avoid a survivorship influence. In spite of better oral health, the inclusion of individuals older than 55 yr old increases the proportion of individuals with possible confounders such as osteopenia, osteoporosis, and menopause. These conditions are associated with increased bone turnover, resulting in an increase of lead blood levels (36,43), and are also associated with periodontitis. In that study there were no adjustments for such conditions, or even adjustment for the number of teeth present in the mouth (57).

This study showed a positive statistically significant association between PbB and periodontitis after adjusting for major known risk factors. In spite of relatively low levels of exposure to lead among the US population, the persistence of lead contamination among areas of underprivileged segments of society, as well as a higher prevalence of periodontitis among the poorest, further studies are necessary to confirm this association. Studies using cumulative measures of lead, as well as studies using populations or occupational groups exposed to high levels of lead, may give us a more complete picture of the statistical association found in this study.

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