

Blood lead concentration, renal function, and blood pressure in London civil servants

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Abstract

Blood lead concentration was measured in 398 male and 133 female London civil servants not subject to industrial exposure to heavy metals. The relation between blood lead and serum creatinine concentrations and blood pressure were examined. Blood lead concentration ranged from 0.20 to 1.70 $\mu\text{mol/l}$ with a geometric mean concentration of 0.58 $\mu\text{mol/l}$ in men and 0.46 $\mu\text{mol/l}$ in women ($p < 0.001$). In women blood lead concentration increased with age ($r = +0.27$; $p = 0.002$). In the two sexes blood lead concentration was positively correlated with the number of cigarettes smoked a day (men $r = +0.17$ and women $r = +0.22$; $p \leq 0.01$), with the reported number of alcoholic beverages consumed a day (men $r = +0.34$ and women $r = 0.23$; $p < 0.01$), and with serum gamma-glutamyltranspeptidase (men $r = +0.23$ and women $r = +0.14$; for men $p < 0.01$). Blood lead concentration was not correlated with body weight, body mass index, and employment grade. In men 14% of the variance of blood lead concentration was explained by the significant and independent contributions of smoking and alcohol intake and in women 16% by age,

smoking, and alcohol consumption. In men serum creatinine concentration tended to rise by 0.6 $\mu\text{mol/l}$ (95% confidence interval from -0.2 to +1.36 $\mu\text{mol/l}$) for each 25% increment in blood lead concentration. In men and women the correlations between blood lead concentration and systolic and diastolic blood did not approach statistical significance. In conclusion, in subjects not exposed to heavy metals at work gender, age, smoking, and alcohol intake are determinants of blood lead concentration. At a low level of exposure, lead accumulation may slightly impair renal function, whereas blood pressure does not seem to be importantly influenced. Alternatively, a slight impairment of renal function may give rise to an increase in blood lead concentration.

Lead is a trace metal which during life accumulates in the human body¹ and which has been implicated in the pathogenesis of renal tubular dysfunction² and of hypertension.³ The lead burden on the environment showed an explosive growth during the past century in industrialised as well as in developing countries, so that lead may have important health effects not only through work but also through environmental exposure. Research priorities have therefore moved from industrial to environmental exposure.

The present study was conducted in a random sample of civil servants who were not professionally exposed to heavy metals. The aim was to examine the determinants of blood lead concentration and, in addition, to investigate whether an association between blood lead and serum creatinine concentrations and blood pressure could be shown.

Methods

The civil servants considered in this report were a sample of men and women drawn from the Department of the Environment offices in London^{4,5} (and the Whitehall, Department of the Environment Study, 1982). The sample was stratified by age and

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employment grade and randomly selected using different sampling fractions in an attempt to provide equal numbers in each age and grade group. The employment grades were classified by four levels from one (low) to four (high).

The subjects completed a detailed health questionnaire and then came to the clinic for measurement of blood pressure and taking of blood. Systolic and phase V diastolic pressures were measured after the subjects had been lying down for five minutes. A standard mercury sphygmomanometer was used and the cuff with an inflatable section of 11×22.5 cm was applied to the right arm. Every observer was trained using the London School of Hygiene tapes of auscultatory sounds until they provided reproducible results.

Blood samples were sent to the Wolfson Research Laboratories, Birmingham, for analysis of serum calcium, creatinine, and gamma-glutamyltranspeptidase, using a Technicon SMA12 analyser, and to Dudley Road Hospital, Birmingham, for analysis of blood lead concentration by atomic absorption spectroscopy.⁶ The intra-assay coefficient of variation for the determination of blood lead was 3.7% and the inter-assay variation 4.6%.

Smoking habits were assessed from the health questionnaire. Current smokers were classified by their total reported daily number of pipes, cigars, and handrolled or manufactured cigarettes. Light smokers were defined as those smoking less than the equivalent of 10 cigarettes of these smoking materials a day, moderate smokers had from 10 to 19 cigarettes a day, and heavy smokers at least the equivalent of 20 cigarettes. Alcohol intake was assessed not only on the basis of the health questionnaire but also by a three day dietary recall. The interviews were administered by trained technicians. The correlation of gamma-glutamyltranspeptidase with alcohol intake quantified by questionnaire was 0.20 ($p < 0.001$) and by dietary recall 0.18 ($p < 0.001$). Subjects were classified as light drinkers if, from both the questionnaire and dietary recall, they appeared to consume less than 25 g alcohol a day. They were designated as heavy drinkers if from the questionnaire or dietary recall they apparently drank more than 50 g a day. This is about 35 units a week, when one unit is defined as a pint of beer, a glass of wine, or a single measure of spirits. The remaining subjects were considered as moderate drinkers, provided that they reported regular alcohol intake.

The distributions of blood lead and serum gamma-glutamyltranspeptidase were normalised by a logarithmic transformation. Statistical methods included t tests for the comparison of means and linear regression analysis. Multiple regression was effected by a step wise procedure, ending when all partial regression coefficients were statistically significant at the 5% level.⁷

Results

DETERMINANTS OF BLOOD LEAD CONCENTRATION

Table 1 shows the characteristics of male and female participants. The blood lead concentration in the total sample averaged $0.54 \mu\text{mol/l}$ and ranged from 0.20 to $1.70 \mu\text{mol/l}$.

Blood lead concentration was higher in men than in women (0.58 versus $0.46 \mu\text{mol/l}$; $p < 0.001$) in post menopausal compared with premenopausal women (0.50 versus $0.42 \mu\text{mol/l}$; $p < 0.002$), in smokers versus non-smokers (0.57 versus $0.53 \mu\text{mol/l}$; $p < 0.005$), and in subjects reporting regular intake of alcohol compared with non-drinkers (0.56 versus $0.47 \mu\text{mol/l}$; $p < 0.001$) (fig 1). The difference in blood lead concentration between never smokers and past smokers, however, was not significant (0.52 versus $0.54 \mu\text{mol/l}$).

Blood lead concentration was positively correlated with age in men ($r = +0.27$; $p = 0.002$) but not in women ($r = +0.04$). In both men ($r = +0.17$; $p < 0.002$) and women ($r = +0.22$; $p = 0.01$) there was a positive relation between blood lead concentration and the number of cigarettes smoked a day. Similarly, in men ($r = +0.34$; $p < 0.001$) and women ($r = +0.23$; $p < 0.01$) blood lead concentration was positively correlated with the reported daily consumption of alcoholic beverages. The correlation coefficient of blood lead concentration with serum gamma-glutamyltranspeptidase was $+0.23$ ($p < 0.01$) in men and $+0.14$ ($p = 0.10$) in women. In contrast, the correlations between blood lead concentration and

Clinical and biochemical measurements

	Men ($n = 398$)	Women ($n = 133$)
Systolic pressure (mm Hg)	128 ± 17 (88 - 192)	123 ± 18 (88 - 176)
Diastolic pressure (mm Hg)	79 ± 12 (50 - 134)	74 ± 12 (50 - 110)
Age (y)	47.8 ± 5.8 (37.0 - 58.0)	47.5 ± 5.7 (38.0 - 57.0)
Pulse rate (bpm)	71 ± 11 (48 - 108)	70 ± 10 (48 - 92)
Body weight (kg)	76.2 ± 10.6 (48.8 - 110.1)	64.4 ± 9.2 (41.7 - 102.8)
Body mass index (kg/m^2)	24.6 ± 2.9 (17.5 - 35.0)	24.1 ± 3.3 (18.5 - 37.0)
Height (cm)	176 ± 7 (152 - 198)	164 ± 7 (142 - 180)
Blood lead ($\mu\text{mol/l}$)	0.60 ± 0.21 (0.30 - 1.70)	0.49 ± 0.19 (0.20 - 1.50)
log 10^*	-0.24 ± 0.14 (0.58)	-0.34 ± 0.15 (0.46)
Serum creatinine ($\mu\text{mol/l}$)	97 ± 26 (66 - 523)	78 ± 11 (53 - 108)
Serum calcium (mmol/l)	2.41 ± 0.92 (2.18 - 2.77)	2.38 ± 0.89 (2.15 - 2.89)
Gamma-glutamyltranspeptidase (U/l)	16.9 ± 14.0 (4.0 - 99.0)	11.2 ± 9.7 (4.0 - 97.0)
log 10^*	1.15 ± 0.24 (14.1)	0.99 ± 0.20 (9.7)

Values are means \pm standard deviation with range between parentheses.

*Arithmetic mean \pm standard deviation after logarithmic transformation (geometric mean between parentheses).

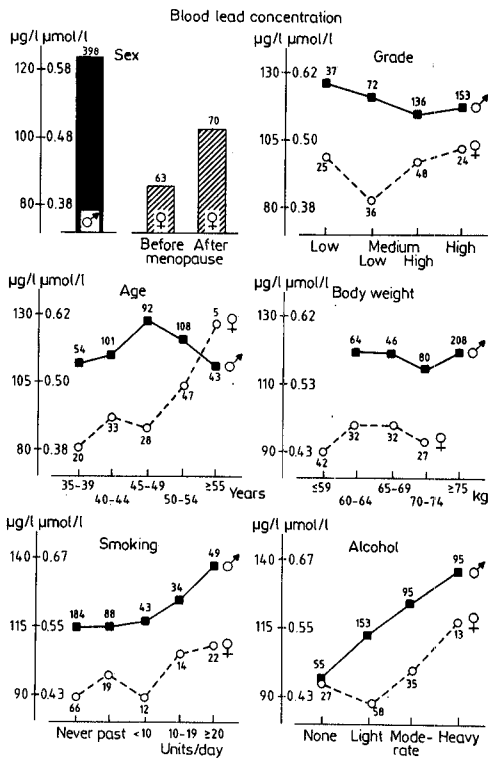


Figure 1 Blood lead concentration according to gender and menstrual status, employment grade, age, body weight, smoking habit, and alcohol intake in 531 civil servants. For each subgroup geometric mean and number of subjects is given.

body weight (men $r = -0.01$ and women $r = +0.01$), body mass index (men $r = +0.02$ and women $r = -0.07$), and employment grade (men $r = +0.05$ and women $r = -0.09$) were not statistically significant.

In men step wise multiple regression showed that blood lead concentration increased significantly and independently with the number of cigarettes smoked a day ($p = 0.02$) and with the reported number of alcoholic beverages consumed a day ($p < 0.001$). With these covariates in the equation, the t-to-enter for age was 0.68 ($p = 0.50$) and for body mass index 0.19 ($p = 0.84$). Current smoking and alcohol intake explained 14% of the variance of blood lead concentration in men. In women blood lead concentration was significantly and independently correlated with age ($p = 0.002$), the number of cigarettes smoked a day ($p = 0.02$), and alcohol intake ($p = 0.005$). The t-to-enter for body mass index was 0.07 ($p = 0.95$). Age, smoking habit, and alcohol intake explained 16% of the variance of blood lead concentration in women. After adjustment for age, current smoking, and alcohol intake, blood lead concentration was still 9% higher in men than in women.

Among current smokers ($n = 174$), 30 smoked a pipe, 19 cigars, and the remainder primarily cigarettes. Blood lead concentration was related to cigarette smoking only. Among the 449 participants reporting regular alcohol intake, 240 consumed beer, 230 wine, and 184 spirits or fortified wine. Blood lead concentration was positively associated with the consumption of beer ($p < 0.001$) and wine ($p = 0.06$) but not with drinking spirits or fortified wine.

SERUM CREATININE AND BLOOD LEAD CONCENTRATION
Serum creatinine was higher in men than in women (97 versus 78 $\mu\text{mol/l}$; $p < 0.001$). In men serum creatinine concentration was significantly related to log blood lead ($r = +0.10$; $p = 0.04$) (fig 2), but not to age ($r = -0.06$) and body mass index ($r = +0.06$). After removing two men with a serum creatinine concentration higher than 180 $\mu\text{mol/l}$, the correlation between serum creatinine and log blood lead concentrations weakened ($r = +0.08$) and significance fell to 0.12. After these exclusions serum creatinine tended to rise by 0.6 $\mu\text{mol/l}$ (95% confidence interval from -0.2 to $+1.36$ $\mu\text{mol/l}$) for each 25% increment in blood lead concentration.

In women serum creatinine concentration correlated with age ($r = +0.15$; $p = 0.07$) and body mass index ($r = +0.24$; $p = 0.005$) but not with log blood lead ($r = +0.03$).

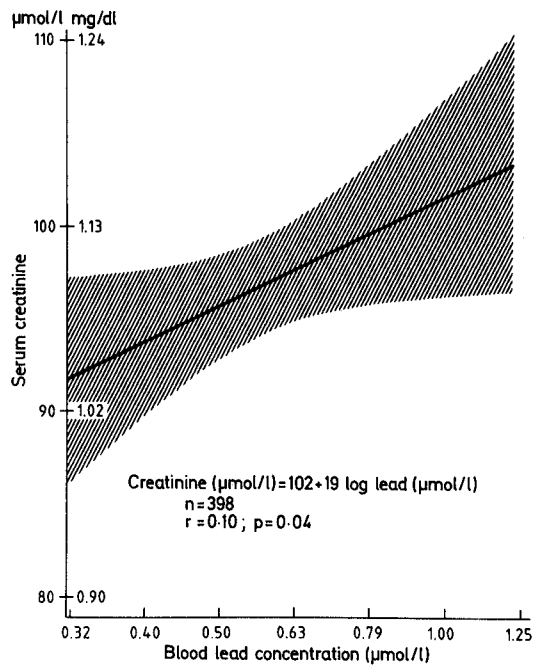


Figure 2 Relation between serum creatinine and log blood lead concentrations in 398 male civil servants. Regression line and 95% confidence limits are drawn.

BLOOD PRESSURE AND BLOOD LEAD CONCENTRATION

The first order correlations of systolic and diastolic pressure with log blood lead concentration were not significant in men (SBP $r=+0.05$ and DBP $r=+0.08$) and in women (SBP $r=+0.12$ and DBP $r=-0.01$) but they were statistically significant ($p < 0.02$) for both sexes together (SBP and DBP $r=+0.11$).

Blood pressure was higher in men than in women ($p < 0.001$). In men and women systolic and diastolic blood pressure were significantly and positively correlated with age, body mass index, pulse rate, log serum gamma-glutamyltranspeptidase, and serum calcium. These covariates and gender explained 19% and 21% of the variance of systolic and diastolic blood pressure, respectively. In step wise multiple regression adding gender and age to the model reduced the partial correlations of systolic and diastolic blood pressure with log blood lead concentration to a low and non-significant level (fig 3).

Discussion

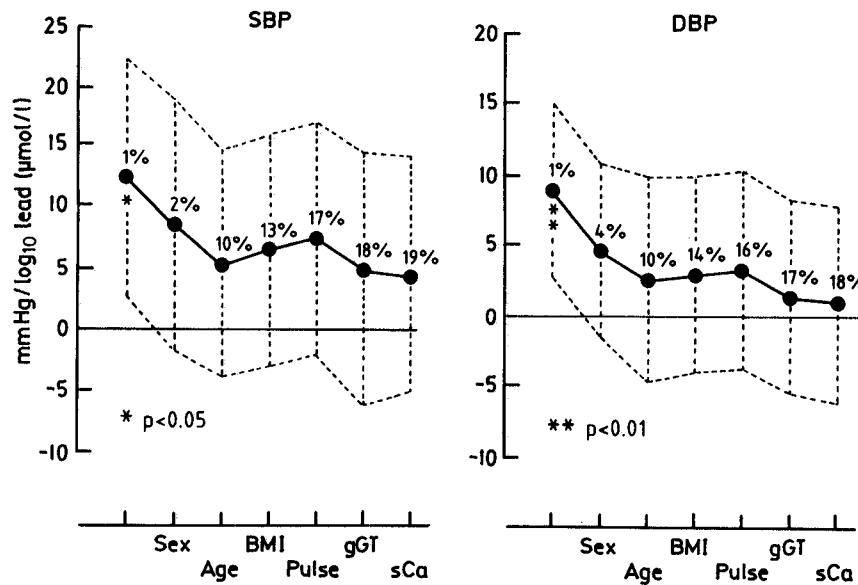
BLOOD LEAD CONCENTRATION

The blood lead concentration is generally considered as a measure of the biologically active metal in the body and reflects environmental exposure of an individual.⁸ The geometric mean concentration of blood lead in the present 1982 study, $0.60 \mu\text{mol/l}$ ($124 \mu\text{g/l}$) in men and $0.49 \mu\text{mol/l}$ ($101 \mu\text{g/l}$) in women, was of the same order of magnitude as in most western populations not exposed to lead at work. In 1984 Pocock and colleagues reported a median blood lead concentration of $0.70 \mu\text{mol/l}$ ($145 \mu\text{g/l}$) in 7735 middle aged men, randomly selected from represen-

tative general practices in 24 British towns.⁹ In earlier studies (1976-80) in Scotland Beever and co-workers¹⁰ found a mean blood lead concentration of $1.05 \mu\text{mol/l}$ ($217 \mu\text{g/l}$) in normotensive subjects and of $1.21 \mu\text{mol/l}$ ($251 \mu\text{g/l}$) in hypertensive patients. In Belgium, in studies published from 1980 to 1987,^{8,11,12} the median blood lead concentration ranged from 0.65 to $1.42 \mu\text{mol/l}$ (135 to $294 \mu\text{g/l}$), whereas in the second National Health and Nutritional Examination Survey (NHANES), conducted in the United States from 1976 to 1980, blood lead concentration averaged $0.67 \mu\text{mol/l}$ ($139 \mu\text{g/l}$).^{13,14} This is almost twice as high as in Scandinavia ($0.37 \mu\text{mol/l}$ or $77 \mu\text{g/l}$ in 1981)¹² and three times as high as in some remote areas, such as Nepal, where the geometric mean was $0.18 \mu\text{mol/l}$ ($38 \mu\text{g/l}$) in men and $0.14 \mu\text{mol/l}$ ($29 \mu\text{g/l}$) in women.¹⁵ Differences in the blood lead concentration not only reflect varying levels of environmental exposure but also the occupation of the subjects and differences in the laboratory techniques. In addition, in Britain,¹⁶ in other west European countries¹² and in the United States¹⁷ blood lead concentration has decreased over time. Elwood reported a 30% drop from 1972 to 1982 in Wales¹⁶ and the NHANES investigators a 37% fall from 1976 to 1980.¹⁷

In the present and in other studies^{3,10,14} blood lead concentration was higher in adult men than in women. The NHANES investigators attributed this sex difference in part to a higher potential for occupational exposure in men.¹⁸ In addition Stuik showed for a similar lead load, a greater increase in blood lead concentration in men than in women.¹⁹ In the present study, where none of the subjects was occupationally exposed, blood lead concentration was higher in men and in postmenopausal women

Figure 3 Slope of relation between systolic (SBP) and diastolic (DBP) blood pressures and log blood lead concentration, unadjusted and after step wise and cumulative adjustments for sex, age, body mass index, pulse rate, log gamma-glutamyltranspeptidase, and serum total calcium. For each adjustment step 95% confidence interval of slope and percentage of explained blood pressure variance are presented.



than in women before the menopause (fig 1). This suggests that the sex trend in middle aged subjects may be related to differences in lead handling by the body, which disappear at an older age. For instance, the lower red blood cell count and haemoglobin concentration in menstruating middle aged women may lead to lower blood levels, as more than 99% of blood lead is bound to the erythrocytes and in particular to haemoglobin HBA2.²⁰

In the present study blood lead concentration increased with age in women. In the NHANES study the blood lead concentration rose between the ages of 15 and 40 in men and from 15 to 50 in women.¹⁸ After these ages the blood lead concentration either levelled off or even slightly decreased.¹⁸ Relation of blood lead concentration with age may be partly due to changing environmental and occupational exposure.

In agreement with previous reports²¹ the present study showed that both beer and wine consumption are associated with an increase in blood lead concentration and that heavy drinkers have a concentration of about 40% higher than non-drinkers (fig 1). European and American wines, with and without lead foil caps, show lead concentrations averaging from 0.48 to 1.45 $\mu\text{mol/l}$ (100 to 300 $\mu\text{g/l}$) which is from 10 to 30 times higher than in most drinking waters.^{22,23} Thus at a consumption of one litre a day, wine may double the total daily intake of lead. Lead concentrations are usually lower in beer, but beer tends to be drunk in higher quantities. Thalacker reported a maximum concentration of 0.39 $\mu\text{mol/l}$ (80 $\mu\text{g/l}$) in several brands of German beer.²⁴

In the present study heavy smokers had about a 20% increase in their blood lead concentration as compared with never smokers. Lead is present in tobacco: a cigarette may contain from 0.01 to 0.06 $\mu\text{mol/l}$ (2–12 $\mu\text{g/l}$) lead, of which 2% may be inhaled by the smoker.^{21,25} Polluted urban air may contain up to 0.005–0.015 $\mu\text{mol/m}^3$ (1–3 $\mu\text{g/m}^3$) lead.²⁶ Thus an urban dweller, who smokes more than a pack of cigarettes a day, may inhale roughly equal amounts of lead from smoking as from breathing polluted urban air.²⁶

RENAL FUNCTION

Lead nephropathy, accompanied by gout and hypertension, is a well known entity and has been described by numerous investigators mainly in exposed workers, among consumers of illicit "moonshine" whisky, or after childhood lead poisoning. By contrast, few studies have been performed to evaluate the possible harmful effects of lead on the kidneys in populations without suspected excessive exposure to lead.

In the present study blood lead and serum creatinine concentrations tended to be positively correlated in men. Campbell and coworkers reported a positive correlation between water lead content and blood

lead and serum urea concentrations among Scottish households consuming drinking water with a lead content in excess of the World Health Organisation recommendation (0.48 $\mu\text{mol/l}$ or 100 $\mu\text{g/l}$).²⁷ In that study the frequency of renal dysfunction in individuals with a raised blood lead concentration (1.98 $\mu\text{mol/l}$ or 410 $\mu\text{g/l}$) was also significantly greater than in age and sex matched controls. By contrast, Pocock and coworkers, after allowing for the influence of alcohol consumption, did not find a substantial association between blood lead and serum creatinine, urea, and urate concentrations.⁹ There was a weak positive trend towards an increased serum urate concentration at a blood lead concentration above 1.79 $\mu\text{mol/l}$ (370 $\mu\text{g/l}$) and a reverse trend for serum urea concentration. Finally, Batuman *et al* studied 48 men diagnosed as having essential hypertension.²⁸ Patients who had a serum creatinine concentration above 132 $\mu\text{mol/l}$ (1.5 mg/dl) had significantly larger amounts of mobilisable lead than did hypertensive patients without renal impairment. The increase in mobilisable lead was not due to the impairment of renal function, since 22 control patients with renal insufficiency from known causes but without a history of essential hypertension, did not excrete more lead during the EDTA tests.²⁸ Thus the positive correlation between blood lead and serum creatinine concentrations may be due to an effect of lead on renal function rather than to an increase of blood lead concentration when renal function is impaired.

BLOOD PRESSURE

Among subjects with excessive exposure to lead the prevalence of hypertension and of cerebrovascular disease has been variously reported to be increased²⁹ or not affected.³⁰ The role of lead in the pathogenesis of hypertension in the general population remains debatable, although there is a growing suspicion that in unexposed individuals a weak positive relation between blood lead concentration and blood pressure may exist. Beattie,³¹ Beevers,^{3,10} and Elwood³² and their coworkers were among the first to suggest a possible association between chronic low grade exposure and the development of hypertension. Weiss and colleagues found in a longitudinal study of Boston policemen that after correction for previous systolic blood pressure, body mass index, age, and smoking, a high concentration of blood lead was a significant predictor of increased systolic pressure.³³ In the NHANES survey a direct relation was found between blood lead concentrations and systolic and diastolic blood pressure, which was independent of the other blood pressure correlates in men but not in women.^{13,14} Similarly, Pocock and coworkers reported a statistically significant association between blood lead concentration and systolic blood pressure ($r = +0.03$) in the British regional heart study.⁹

These investigators, however, concluded that the magnitude of the lead pressure association was not biologically important. The present study also does not support a biologically important relation after adjustment for alcohol intake and other blood pressure covariates (fig 3).

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Appendix

Conversion of units

Calcium : 1 mmol/l = 4.01 mg/dl
 Creatinine: 1 μ mol/l = 0.0113 mg/dl
 Lead : 1 μ mol/l = 207.2 μ g/l

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