Association of Blood Lead to Blood Pressure in Men Aged 55 to 75 Years: Effect of Selected Social and Biochemical Confounders

Antonio Menditto,¹ Gino Morisi,¹ Amedeo Spagnolo,² Alessandro Menotti,² and the NFR Study Group²

¹Laboratorio di Biochimica Clinica, ²Laboratorio di Epidemiologia e Biostatistica, Istituto Superiore di Sanità, Rome, Italy

The association of blood lead (B-Pb) concentration to blood pressure was investigated in men aged 55 to 75 years living in the Rome area, who had no history of exposure to lead in the workplace and who participated between 1989 and 1990 in an epidemiologic survey for coronary heart disease (New Risk Factor Project). Of the 1856 individuals eligible for the study, 59 were excluded from analyses because not all relevant data were available; and 478 were excluded because they were treated for hypertension. In the remaining subjects (n = 1319) the median B-Pb concentration was 113 µg/l (range: 40-442 µg/l). Systolic blood pressure (SBP) averaged 140 ± 18 (standard deviation) mm Hg (range 98-220) and diastolic blood pressure (DBP) 84 ± 9 mm Hg (range 56-118). Median B-Pb values increased significantly from 111 µg/l in subjects with normal blood pressure (n = 668) to 113.5 µg/l in subjects with borderline high blood pressure (n = 373) and to 120 µg/l in subjects with increased blood pressure (n = 278). After log-normal conversion of B-Pb, the linear correlation coefficient between ln[B-Pb(µg/l)] and both SBP and DBP was statistically significant (r = 0.1332, p < 0.001 and r = 0.0737, p = 0.007, respectively). The linear regression coefficient was 6.6 mm Hg/ln(µg/l) for SBP and 1.9 mm Hg/ln(µg/l) for DBP. Multiple regression analyses revealed that, after correction for body mass index (BMI), age, heart rate, skinfold thickness, serum lipids, and glucose levels, blood lead was still a significant predictor of increased SBP and DBP. The adjusted regression coefficient was 5.6 mm Hg/ln(µg/l) for SBP and 1.7 mm Hg/ln(µg/l) for DBP. In further analyses subjects were divided, according to alcohol consumption, into drinkers (n = 1068) and nondrinkers (n = 251). Among nondrinkers the median B-Pb levels was 97 µg/l (2.5th and 97.5th centiles 55-181 µg/l) and SBP and DBP averaged 138 ± 17 and 84 ± 9 mm Hg, respectively. No significant relationship between ln[B-Pb] and blood pressure was found. In drinkers the median B-Pb level was 117 µg/l (2.5th and 97.5th centiles; 63–252 µg/l) and SBP and DBP averaged 141 ± 18 and 84 ± 9 mm Hg, respectively. The linear regression coefficient was 7.5 mm Hg/ln(µg/l) for SBP and 2.6 mm Hg/ln(µg/l) for DBP. In multiple stepwise regressions including BMI, age, heart rate, smoking, skinfold thickness, serum lipids, and glucose levels as covariates—the partial correlation coefficient of systolic and diastolic blood pressure with ln[B-Pb] remained statistically significant. The adjusted regression coefficients were 5.6 mm Hg/ln(µg/l) for SBP and 2.5 mm Hg/ln(µg/l) for DBP. These findings indicate that a slight to moderate positive relationship exists between blood pressure and blood lead concentrations in male drinkers aged 55 to 75 years. —Environ Health Perspect 102(Suppl 9):107–111 (1994)

Key words: blood pressure, lead, hypertension, smoking, alcohol

Introduction

Low to moderate increases in blood lead (B-Pb) concentrations, as those occurring in subjects living in industrialized areas even in the absence of an occupational exposure, have been related to a small or moderate increase in blood pressure (1-10). This positive relationship has not been observed in a large survey conducted in Wales (11).

A number of confounding factors, whose impact has not always been analyzed, have been reported to affect the entity of the blood pressure/B-Pb relation. Grandjean et al. (12) observed that the positive relationship between B-Pb and blood pressure was no longer significant when alcohol intake and hemoglobin were included in a multiple regression analysis. Staessen et al. (13) reported that the addition of gender and age as covariates to models predicting blood pressure reduced the partial correlations of systolic and diastolic blood pressure with B-Pb to a nonsignificant level. Sharp et al. (6) observed that a positive relationship between blood pressure and B-Pb was present in black males but not among nonblack males; the inclusion of alcohol use indicators in multiple regression models did not alter the relationship between blood pressure and B-Pb by more than 10%. In black subjects adjusting for tobacco use markedly increase the association between B-Pb and blood pressure. In addition, the relationship was particularly strong in blacks who were infrequent users of caffeine (6).

The aim of the present study was to examine the relationship between B-Pb and blood pressure in middle-aged and elderly men living within the Rome area, taking into account the potential confounding effect of selected social and biochemical factors associated to blood pressure and B-Pb.

Materials and Methods

Between June 1989 and December 1990, a total of 1856 men aged 55 to 75 years participating in the New Risk Factors (NRF) Survey underwent a comprehensive examination. The primary aim of the project was to identify risk factors which can predict coronary heart disease and total mortality.

Environmental Health Perspectives
Initially between 1979 and 1981, a total of 3395 subjects were seen. They represented the 76.5% of 4438 men enrolled from four occupational groups belonging to defined public companies or agencies located in Rome where the screening was offered at the worksite. At the time of the follow-up (1989–1990) 410 subjects had died; and of the remaining 2985 subjects, 1856 (62.2%) agreed to participate. The examination included a medical history; a physical examination; and measurement of height, weight, various skinfold thicknesses, and blood pressure. Furthermore, a venous blood sample was drawn after overnight fasting.

Diseases, reported by the subjects themselves, were coded according to the International Classification of Diseases (ICD), 9th Revision.

Blood pressure measurements were performed according to World Health Organization Guidelines (14). With the subject seated, systolic blood pressure (SBP) and fifth phase diastolic blood pressure (DBP) were measured twice in the left arm with an ordinary sphygmomanometer to the nearest 2 mm Hg. Increased blood pressure was defined as a SBP at or above 160 mm Hg and/or a DBP at or above 95 mm Hg. Borderline high blood pressure was defined as a SBP below 160 mm Hg but above 140 mm Hg and/or a DBP below 95 mm Hg but above 90 mm Hg. Heart rate (HR, beats/min) was calculated from electrocardiographic traces as an average of rates in lead I and lead V6. Information about alcohol consumption and smoking habits was collected for each subject by direct interview. Alcohol consumption (ALC) was calculated for wine, beer, and spirits separately and the amount of alcohol intake was expressed in grams of absolute ethanol consumed per day. Daily cigarette consumption (CIG/D) was recorded as a measure of tobacco use. Height and weight were compacted into a body mass index (BMI, kg/m²). Triceps, biceps, subscapular, suprascapular, and suprailiac skinfold thicknesses were measured by Harpenden calipers to the nearest millimeter. The variable skinfold thickness (SKF) was defined as the sum of the five measurements.

Venous blood samples for B-Pb determination were drawn into polypropylene tubes containing K₂EDTA as anticoagulant and stored at −20°C until analysis. All the equipment used was free from lead. B-Pb (µg/l) was measured by Atomic Absorption Spectrophotometry (AAS) using a Perkin-Elmer model Zeeman 5000, HGA 500. The method for B-Pb (15) determination has been previously described. The analytical variability of the method has been checked by the adoption of appropriate internal quality controls. Control charts were prepared with measurements carried out on control samples with certified titles, provided by the Community Bureau of Reference, Commission of the European Community. Between-day precision, obtained from B-Pb measurements carried out on our subjects, was 2.7%. Analytic precision and accuracy for B-Pb were also monitored by means of external quality control samples, according to procedures previously described (16,17). Serum levels of cholesterol (CHOL, mg/dl), high-density lipoprotein cholesterol (HDL, mg/dl), triglycerides (TRIG, mg/dl), and glucose (GLU, mg/dl) were determined by automated methods within 12 hr of collection, the samples having been stored at +4°C until analysis. The amount of non-HDL cholesterol (N-HDL) was calculated as the difference between CHOL and HDL.

Subjects were excluded from the present study when not all relevant data were available (n = 59) or if they were treated for hypertension (n = 478). After these exclusions a sample of 1319 subjects was obtained. In further analyses subjects were divided according to alcohol consumption in drinkers (n = 1068) and nondrinkers (n = 251). Log-normal transformation of the B-Pb approached a Gaussian distribution; the use of ln [B-Pb] enabled us to perform parametric analyses of data, i.e. linear correlation and multiple stepwise regression. All statistical analyses of data were carried out using the BMDP Statistical Software package.

Results

In the 1319 subjects the median B-Pb was 113 µg/l (2.5th–97.5th centiles: 62–247 µg/l; range 40–442 µg/l). SBP averaged 140 ± 18 (standard deviation) mm Hg (range 98–220 mm Hg) and DBP 84 ± 9 mm Hg (range 56–118 mm Hg). The mean age was 63 ± 5 years (range 55–75 years). BMI averaged 26.5 ± 3.2 kg/m² and HR 66 ± 11 beats/min. Out of all subjects, 251 (19.0%) were nondrinkers. Among drinkers (n = 1068) the median ethanol intake was 18.4 g/day and more than 90% of total alcohol intake was due to wine. With regard to smoking habits, 72% of subjects were nonsmokers; among current smokers (369 subjects) the median consumption was of 15 cigarettes daily (25th–75th centiles: 8–20).

Median B-Pb levels in relation to blood pressure categories: normal blood pressure, n = 668; borderline blood pressure, n = 373; and increased blood pressure, n = 278, are shown in Table 1. Median B-Pb increased significantly, (p = 0.0004), from 111 µg/l in the normal blood pressure group to 113.5 µg/l in the borderline high blood pressure group, and to 120 µg/l in the increased blood pressure group. In the same table median values of AGE, BMI, HR, CHOL, HDL, GLUC, CIG/D, ALC, and SKF in relation to blood pressure categories are reported; for the variables ALC

| Table 1. Median values (Mdn) of B-Pb, AGE, BMI, HR, N-HDL, HDL, TRIG, GLUC, CIG/D, ALC and SKF in relation to blood pressure categories. |

| Normal blood pressure, n = 668 | Borderline blood pressure, n = 373 | Increased blood pressure, n = 278 |
|---------------------------------|---------------------------------|---------------------------------|
|                                | 97.5th centile | Mdn | 97.5th centile | Mdn | 97.5th centile | K-W | P     |
| B-Pb                           | 111          | 113.5 | 120           | 120 | 17.89           | 0.0004 |
| AGE                            | 62           | 64    | 63.5          | 63.5 | 11.52           | 0.0032 |
| BMI                            | 25.8         | 26.6  | 27.2          | 27.2 | 45.29           | 0.0000 |
| HR                             | 63           | 66    | 67.5          | 67.5 | 42.00           | 0.0000 |
| N-HDL                          | 181          | 191   | 190           | 190 | 13.40           | 0.0012 |
| HDL                            | 46           | 46.5  | 48            | 48  | 7.27            | 0.0264 |
| TRIG                           | 120          | 135   | 135.5         | 135.5 | 17.96          | 0.0001 |
| GLUC                           | 99           | 101   | 100.5         | 100.5 | 9.34           | 0.0084 |
| CIG/D                          | 0            | 28    | 0             | 0   | 29.89           | 0.0000 |
| ALC²                           | 16           | 80    | 16            | 194 | 8.56           | 0.0014 |
| SKF                            | 53           | 53.5  | 56            | 56  | 9.82           | 0.0074 |

Abbreviations: B-Pb, blood lead level (µg/l); BMI, body mass index (kg/m²); HR, heart rate (beats/min); N-HDL, non-HDL cholesterol(mg/dl); HDL, HDL cholesterol (mg/dl); TRIG, triglycerides (mg/dl); GLUC, glucose (mg/dl); CIG/D, cigarettes smoked daily; ALC, alcohol consumption (g/day); SKF, skinfold thickness (mm). For and CIG/D ALC, 97.5th centiles (97.5th) of their distributions are also given. Statistical significance was determined by means of the Kruskal-Wallis test (K-W).
Table 2. Type (+, positive; -, negative) and statistical significance of linear correlations between SBP, DBP, ln[B-Pb], and other variables considered in the analyses (subjects = 1319).

|          | SBP      | DBP      | ln(B-Pb) |
|----------|----------|----------|----------|
| Type     | T-value  | T-value  | T-value  |
| AGE      | +        | 5.432d   | 5.374d   | 2.573p   |
| BMI      | +        | 6.089d   | 10.984d  | 0.780    |
| HR       | +        | 5.826d   | 7.331d   | 0.933    |
| N-HDL    | +        | 4.090d   | 3.011*   | 2.444d   |
| HDL      | +        | 3.566d   | 1.510    | 9.007d   |
| TRIG     | +        | 2.079d   | 3.046d   | 2.250d   |
| GLUC     | +        | 5.432d   | 0.936    | 1.402    |
| CIG/D    | -        | 3.166d   | 5.164d   | 5.389d   |
| ALC      | +        | 4.065d   | 2.744d   | 14.991d  |
| SKF      | +        | 2.305d   | 6.667d   | 5.157d   |

*p<0.05; p<0.02; p<0.01; p<0.001. Abbreviations: BMI: body mass index; HR: heart rate; N-HDL: non-HDL-cholesterol; HDL: HDL-cholesterol; TRIG: triglycerides; GLUC: glucose; CIG/D: cigarettes smoked daily; ALC: alcohol consumption; SKF: skinfold thickness.

and CIG/D, 97.5th centiles of their distributions are also shown.

In the 1319 subjects the linear correlation coefficients between ln[B-Pb] and both SBP and DBP were statistically significant (r = 0.1332, p<0.001 and r = 0.0737, p = 0.007, respectively). The linear regression coefficient was 6.8 mm Hg/ln(µg/l) for SBP and 1.8 mm Hg/ln(µg/l) for DBP. The entity of the association determined by means of Pearson’s correlation coefficient of the other considered variables to ln[B-Pb] and to both SBP and DBP, is reported in Table 2. The variables ALC and N-HDL were positively related to ln[B-Pb] and both SBP and DBP. HDL was related directly to ln[B-Pb] and SBP. TRIG and SKF were related directly to SBP and DBP and inversely to ln[B-Pb]. AGE was related directly to SBP and inversely to both SBP and ln[B-Pb]. CIG/D was related directly to ln[B-Pb] and inversely to both SBP and DBP. As some of these associations might be a possible source of positive or negative confounding bias, multivariate analyses were performed with the aim of estimating the entity and the independence of the relationship between B-Pb and blood pressure. A first set of multiple stepwise regressions analyzed SBP and DBP as dependent variables for the 1319 subjects, with a model including ln[B-Pb], AGE, BMI, HR, N-HDL, HDL, TRIG, GLUC, CIG/D, ALC, and SKF as possible predictors. In these models, 16.06% and 13.14% of SBP and DBP, variances were explained, respectively. BMI, AGE, ln[B-Pb], HR, and HDL were the most significant predictors for SBP, explaining 3.4, 2.8, 2.0, 1.8, and 0.8% of the total variance, respectively.

With regard to DBP the most important predictors were BMI, HR, AGE, CIG/D, and ln[B-Pb], which explained 8.4, 3.0, 1.7, 1.6, and 0.7% of the total variance, respectively. The change in the regression coefficient of ln[B-Pb(µg/l)] with successive addition of covariates to the multiple stepwise regression models predicting SBP and DBP is shown in Figure 1; after the last step of the stepwise analysis the regression coefficients were 5.6 mm Hg/ln(µg/l) for SBP and 1.7 mm Hg/ln(µg/l) for DBP.

In further analyses subjects were divided, according to alcohol consumption, into drinkers and nondrinkers.

Among nondrinkers (n = 251) the median B-Pb was 97 µg/l (2.5th and 97.5th centiles 55–181 µg/l). SBP and DBP averaged 138 ± 17 and 84 ± 9 mm Hg, respectively; in this group no significant relationship between ln[B-Pb] and both SBP (r = 0.0014) and DBP (r = 0.0826) was found.

Among drinkers (n = 1068) the median B-Pb was 117 µg/l (2.5th and 97.5th centiles: 63–252 µg/l) and SBP and DBP averaged 141 ± 18 and 84 ± 9 mm Hg, respectively. In drinkers, the linear correlation between ln[B-Pb] and both SBP (r = 0.1449) and DBP (r = 0.1042) was statistically significant (p<0.001); first order regression coefficient was 7.5 mm Hg/ln(µg/l) for SBP and 2.6 mm Hg/ln(µg/l) for DBP. After correction for BMI, AGE, HR, SKF, serum lipids, CIG/D, and GLU the adjusted regression coefficients were 5.6 mm Hg/ln(µg/l) for SBP and 2.5 mm Hg/ln(µg/l) for DBP.

Discussion

In our sample (n = 1319) B-Pb concentrations were significantly higher among subjects with borderline or increased blood pressure than in subjects with normal blood pressure. This positive association was confirmed by a significant direct linear correlation between B-Pb concentration and both systolic and diastolic blood pressure. The linear regression coefficient was 6.8 mm Hg/ln(µg/l) for SBP and 1.8 mm Hg/ln(µg/l) for DBP. The entity and the independence of these relationships were studied by means of multiple regression analyses. The partial correlation coefficients of systolic and diastolic blood pressure with B-Pb concentration remained statistically significant. Adjusted regression coefficient, after controlling for age, BMI, heart rate, serum lipids, glucose levels, smoking, and skinfold thickness was 5.6 mm Hg/ln(µg/l) for systolic and 1.7 mm Hg/ln(µg/l) for diastolic blood pressure.

The highest negative confounding was due to cigarette consumption. A similar effect of tobacco use on the blood pressure/B-Pb relationship has been reported by Sharp et al. (6).

A negative relationship between tobacco use and blood pressure (18) and a positive one between smoking and B-Pb concentration have been previously described (19). For the cohort under study, we previously reported (20) that the median B-Pb concentration was 29.1% higher in subjects smoking more than 20 cigarettes daily than in nonsmokers. Moreover, the reported smoking status, which explained 2.12% of the total variance, was the second major predictor of B-Pb concentration (20).
A positive confounding from alcohol consumption has been reported by other authors (12). Various studies have shown a direct relation between alcohol consumption and both blood pressure (21) and B-Pb concentration (19,22,23). A highly significant increase in B-Pb with rising alcohol consumption has been previously reported for the subjects examined in the present survey (20). Alcohol consumption, explaining 14.71% of the total variability, was by far the most important predictor of B-Pb concentration; the odds ratio on the risk of having a B-Pb higher than 180 µg/l was proportional to the level of alcohol consumption, with a 27.7-fold increased risk for heavy drinkers (alcohol intake >100 g/day); B-Pb was more specific and sensitive than HDL-cholesterol and γ-glutamyltransferase, commonly considered indexes of alcohol consumption (24,25), in identifying moderate or heavy drinkers (alcohol intake >50 g/day), and also showed the highest positive predictive value.

In spite of these findings, our subjects alleged alcohol consumption, in contrast with results obtained in Denmark (12), failed to alter in a significant manner the relation between B-Pb and blood pressure.

In our subjects, the highest positive confounding was due to HDL-cholesterol. This biochemical indicator of alcohol consumption (24) decreased the systolic blood pressure/B-Pb and diastolic blood pressure/B-Pb regression coefficients by 15 and 23%, respectively.

The strong association of B-Pb concentration to alcohol consumption prompted us to analyze the B-Pb/blood pressure relation separately in drinkers and non-drinkers. Among non-drinkers (n = 251) — for whom 2.5 and 97.5 centiles of blood lead distribution were 55 and 181 µg/l, respectively — no significant relationship between B-Pb and both systolic (r = 0.0014) and diastolic blood pressure (r = -0.0826) was found.

Among drinkers (n = 1068), for whom 2.5 and 97.5 centiles of B-Pb distribution 63 and 252 µg/l, respectively, the linear correlation between B-Pb and both systolic (r = 0.1449) and diastolic blood pressure (r = 0.1042) was statistically significant (p < 0.001). Linear regression coefficient was 7.5 mm Hg/ln(µg/l) for SBP and 2.6 mm Hg/ln(µg/l) for DBP. After correction for body mass index, heart rate, age, HDL-cholesterol, glucose and skinfold thickness the adjusted regression coefficients for SBP was 5.6 mm Hg/ln(µg/l). The adjusted regression coefficients for DBP, after correction for body mass index, heart rate, age, and smoking, was 2.5 mm Hg/ln(µg/l).

In considering our results two main comments can be made. The first comment is that B-Pb as a biochemical index of alcohol intake, at least in the absence of occupational exposure, may be a better indicator of actual alcohol use than alleged alcohol consumption (for which voluntary under-reporting cannot be excluded). According to this B-Pb would be only an indicator of alcohol intake and the effect on blood pressure would be actually due to alcohol consumption.

The second comment is that low levels of lead exposure, such as those, mainly associated to alcohol consumption and occurring in our subjects (20), might cause an increase in blood pressure. Animal data seems to support the hypothesis of a causal link. In fact, both in vitro and in vivo experimental results have strongly suggested a causal relationship between low to moderate levels of lead exposure and increases in blood pressure (26-28).

In conclusion, the adjusted regression coefficient between ln[B-Pb] and blood pressure we have found among drinkers represents an increment of about 6 and 3 mm Hg in systolic and diastolic blood pressure over the range of observed B-Pb levels (i.e., 40–442 µg/l). In terms of a slope of 2 mm Hg for a 100 µg/l change in B-Pb, the decline in B-Pb concentration of about 100 µg/l we have observed in male subjects living in the Rome area since 1979 (20), although not producing significant changes in the relative risk of cardiovascular disease, might have some importance from a public health perspective.

REFERENCES

1. Beevers AD, Erskine E, Robertson M, Beatte AD, Campbell BC, Goldberg A, Moore MR, Hawthorne VM. Blood-lead and hypertension. Lancet 2:1–3 (1976).
2. Pocock SJ, Shaper AG, Ashby D, Delves T, Whitehead TP. Blood lead concentration, blood pressure, and renal function. Br Med J 289:872–874 (1984).
3. Harlan WR, Landis JR, Schmouder RL, Goldstein NG, Harlan LC. Blood lead and blood pressure: relationship in the adolescent and adult US population. JAMA 253:530–534 (1985).
4. Pirkle JL, Schwartz J, Landis R, Harlan WR. The relationship between blood lead levels and blood pressure and its cardiovascular risk implications. Am J Epidemiol 121:246–258 (1985).
5. Orsaaud G, Claude GR, Moureaux T, Lellouch T, Juguet B, Fetsby B. Blood lead concentration and blood pressure. Br Med J 290:244 (1985).
6. Weiss ST, Munoz A, Stein A, Sparrow D, Speizer FE. The relationship of blood lead to blood lead pressure in a longitudinal study of working men. Am J Epidemiol 125:808–808 (1986).
7. EPA. Lead Effects on Cardiovascular Function, Early Development, and Stature: An Addendum to US EPA Air Quality Criteria for Lead. EPA-600/8-83/028aF, Vol. 1. Research Triangle Park, NC:Environmental Protection Agency, 1986.
8. Sharp DS, Benowitz NL, Osterloh JD, Becker CE, Smith AH, Syme SL. Influence of race, tobacco use, and caffeine use on the relation between blood pressure and blood lead concentration. Am J Epidemiol 131:845–854 (1990).
9. Schwartz J. Blood pressure, and cardiovascular disease in men and women. Environ Health Perspect 91:71–75 (1991).
10. Moreau T, Hannaert P, Orsaaud G, Huel G, Garay RP, Claude JR, Juguet B, Fetsby B, Lellouch J. Influence of membrane sodium transport upon the relationship between blood lead and blood pressure in a general male population. Environ Health Perspect 78:47–51 (1988).
11. Elwood PC, Yarnell JWG, Oldham PD, Catford JC, Nutbeam D, Davey-Smith G, and Toothill C. Blood pressure and blood lead in surveys in Wales. Am J Epidemiol 127:942–945 (1988).
12. Grandjean P, Hollnagel H, Hedegaard L, Christensen JM, Larsen S. Blood lead–blood pressure relations: alcohol intake and hemoglobin as confounders. Am J Epidemiol 129:732–739 (1989).
13. Stassen J, Yeoman WB, Fletcher AE, Markowe HJ, Marmot MG, Rose G, Semmence A, Shipley MJ, Bullpit C. Blood lead concentration, renal function, and blood pressure in London civil servants. Br J Ind Med 47:442–447 (1990).
14. Rose GA, Blackburn H. Cardiovascular Survey Methods. Geneva:World Health Organization, 1968.
15. Patriarca M, Morisi G. Metodo raccomandato per la determinazione del piombo nel sangue. G Ital Chim Clin 12:51–56 (1983).
16. Morisi G, Patriarca M, Taggi F. The interlaboratory quality assurance program for blood lead determination: An evaluation of methods and results. Ann Ist Super Sanitá 25:405–416 (1989).
17. Morisi G, Patriarca M, Taggi F. Comparable laboratory perfor-
ASSOCIATION OF BLOOD LEAD TO BLOOD PRESSURE

mannances in the analysis of lead in control samples and in fresh human blood. Ann Ist Super Sanità 25:417-422 (1989).

18. Green MS, Jucha E, Luz Y. Blood pressure in smokers and non-smokers: epidemiologic findings. Am Heart J 111:932-940 (1986).

19. Grandjean P, Olsen NB, Hollnagel H. Influence of smoking and alcohol consumption on blood lead levels. Int Arch Occup Environ Health 48:391–397 (1981).

20. Morisi G, Menditto A, Spagnolo A, Patriarca M, Menotti A. Association of selected social, environmental and constitutional factors to blood levels in men aged 55–75 years. Sci Total Environ 126:209-229 (1992).

21. Puddey IB, Beilin LJ, Vandongen R, Rouse IL, Rogers P. Evidence for a direct effect of alcohol consumption on blood pressure in normotensive men: a randomised controlled trial Hypertension 7:707–713 (1985).

22. Shaper AG, Pocock SJ, Walker M, Wale CJ, Clayton B, Delves H, Hinks L. Effects of alcohol and smoking on blood lead in middle-aged British men. Br Med J 284:299-302 (1982).

23. Elinder CG, Friberg L, Lind B, Jawaid M. Lead and cadmium levels in blood samples from the general population of Sweden. Environ Res 30:233-253 (1983).

24. Giovannucci E, Colditz G, Stampfer MJ, Rimm EB, Litin L, Sampson L, Willett WC. The assessment of alcohol consumption by simple self-administered questionnaire. Am J Epidemiol 133:810–817 (1991).

25. Fex G, Kristenson H, Trelle E. Correlations of serum lipids and lipoproteins with gamma-glutamyltransferase and attitude to alcohol consumption. Ann Clin Biochem 19:345–349 (1982).

26. Webb C, Winquist RJ, Victory W, Vander AJ. In vivo and in vitro effects of lead on vascular reactivity in rats. Am J Physiol 214:H211–216 (1981).

27. Victory W, Vander AJ, Shulak JM, Schoeps P, Julius S. Lead, hypertension, and the renin angiotensin system in rats. J Lab Clin Med 99:354-362 (1982).

28. Sharp DS, Beker CE, Smith AH. Chronic low level lead exposure: its role in the pathogenesis of hypertension. Med Toxicol 2:210-232 (1987).