Briefs

The Association Between Occupational Lead Exposure and Serum Cholesterol and Lipoprotein Levels

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ABSTRACT

Objectives. This study sought to clarify the possible associations between blood lead level and serum cholesterol and lipoprotein levels in subjects occupationally exposed to lead.

Methods. Levels of blood lead, serum total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein cholesterol, and triglycerides in 56 male industrial employees who were exposed to lead were compared with those in 87 unexposed employees.

Results. Mean blood lead levels were 42.3 (± 14.9) μg/dL in the exposed group and 2.7 (± 3.6) μg/dL in the nonexposed group. The exposed subjects had higher mean levels of total cholesterol and HDL cholesterol.

Conclusions. Blood lead levels are positively associated with total and HDL cholesterol. (*Am J Public Health.* 1999;89:1083–1087)

Cardiovascular disease is a leading cause of disability and premature death. Extensive evidence of an association between serum lipid and lipoprotein levels and coronary artery disease has been well documented.[1–4] The positive association is continuous, with no single level of cholesterol separating those who are at risk from those who are not.

Several reports have shown that both acute and chronic lead poisoning cause impairment of heart and vessel function[5,6] and that rates of death from cerebrovascular disease are significantly increased in lead-exposed workers compared with the general population.[7–9] However, no clear data are available demonstrating a higher mortality rate from heart disease in subjects exposed to lead.[10]

An association between atherosclerosis and lead exposure is biologically plausible. Microscopic analysis of lead-intoxicated animals has indicated fatty degeneration of the myocardium and sclerotic changes in the aorta and walls of the small arteries, especially the renal, cerebral, and coronary arteries,[11–14] and atrophy of elastic fibers in the aorta.[15] Thus, it has been suggested that one of the underlying mechanisms in the association between cardiovascular damage and lead exposure is the induction or acceleration of atherosclerosis.[6]

According to Wojtczak-Jaroszowa and Kubow,[6] there are at least 3 pathophysiological mechanisms whereby lead could induce atherosclerosis: (1) inhibition of superoxide dismutase, resulting in the elevation of serum lipid peroxide[16,17]; (2) formation of atherosclerotic plaques from a single mutated proliferating cell (monoclonal hypothesis); and (3) inhibition of the activity of cytochrome P-450,[18] leading to an increase in serum lipids and their accumulation in vessel walls.

There have been few controlled studies of the effects of lead exposure on serum lipids and lipoprotein levels in either animals[13,15,19–29] or humans.[30–35] Increases,[13,19,21,23,25,27,28,31,32,35] decreases,[15,20,22,26,29,30] and no changes[33] in serum cholesterol levels have been reported, and findings specifically for subjects exposed to lead at work have also been inconclusive.[30–33,35] The aim of the present study was to elucidate the effect of occupational lead exposure on serum lipoprotein levels in Israeli workers.

Methods

Study Population

The study population consisted of industrial employees exposed to lead in a battery factory and a recycling factory (exposed group) and factory production workers not exposed to lead or any other nephrotoxic chemicals (nonexposed group). Data were collected in central Israel during 1994 and 1995. Subjects in both groups performed similar physical work (they had nearly identical heart rates, as assessed by Holter monitoring) under similar environmental conditions. To prevent discrimination, all subjects in a single work section were examined, although not all fit our inclusion criteria (male sex, age 25 to 64 years, no history of chronic disease, at least 1 year's tenure, no use of medication other than analgesics during the month preceding data collection, no other activity involving possible occupational exposure to

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chemicals). We excluded men with implausibly high or low total caloric intake (<800 or >4200 kcal/day).

Every employee was offered the examination free of charge. Of 65 eligible exposed workers, 60 agreed to participate, and complete data were available for 56 of those. Of a possible 100 control subjects, 92 agreed to participate, and complete data were available for 87 of those. Before enrollment, all subjects were informed about the risks and discomfort involved in participating in the study. It was explained that they were being asked to volunteer for research purposes only and that their sole compensation would be the receipt of the results of the medical tests. The study was approved by the local Research on Human Subjects Committee.

TABLE 1—Characteristics of Subjects Occupationally Exposed to Lead and Nonexposed Subjects: Central Israel, 1994–1995

	Nonexposed (n = 87)	Exposed (n = 56)	P
Age, mean (SD), y	43.2 (8.3)	43.1 (10.6)	.933
BMI, mean (SD)	25.8 (3.9)	26.3 (3.8)	.432
Energy consumption, mean (SD), kcal/d	2423 (959)	2544 (1250)	.554
Dietary total fat intake, mean (SD), g/d	106.5 (52)	99.4 (92)	.611
Dietary cholesterol intake, mean (SD), mg/d	513 (300)	483 (174)	.448
Dietary calcium intake, mean (SD), mg/d	817.4 (365)	839.2 (414)	.748
Any alcohol consumption, %	51	35	.081
Cigarette smokers[a], %	38	51	.163
Cigarettes/d, mean (SD)[b]	21 (12)	22 (13)	.746
Familial history of CVD, %	14	5	.050
Sports activities ≥1 time/wk, %	37	33	.604
Education ≤12 y, %	44	55	.442
Seniority, y	6 (2)	4 (2)	.341
Air lead, mean (SD), mg/m^3	0.002 (0.009)	0.180 (0.320)	.0010
Blood lead level, mean (SD), μg/dL	2.7 (3.6)	42.3 (14.9)	.0001

Note. The subjects were men who worked in a battery factory or recycling factory (lead-exposed group) and factory production workers who were not exposed to lead or any other nephrotoxic chemicals (nonexposed group). The values shown are summer measures; winter values of all relevant variables were not significantly different (statistically or physiologically) from summer values. BMI = body mass index (weight in kilograms divided by height in meters squared); CVD = cardiovascular disease.
[a]Smokers were defined as subjects who smoked more than 5 cigarettes per day.
[b]Among smokers.

Study Design

The study was carried out on site during regular working days. Data collection and blood sampling of each worker were carried out once in the summer and once in the winter, and not after vacation. Blood samples were taken in a single day for 20 employees in a given work section. Physical examinations were performed on different days; 5 subjects underwent the examination, together with the field tests and personal interview, on each day.

Measurements

Height and weight were measured between 6:00 AM and 9:00 AM, with the subject wearing only light industrial clothes and no shoes. Body weight was measured with the Seca electronic scale, which is accurate to within 100 g. The Quetelet index (weight in kilograms divided by height in meters squared) was used as a measure of body mass index.

Field tests included an examination of working conditions by an expert hygienist and monitoring of environmental lead levels. Environmental lead levels were analyzed by atomic absorption (method NIOSH 7082).

The subjects were interviewed about health-related habits (specific to the time of year of the examination), medical history, demographic information, personal hygiene, and occupational factors. The dietary questionnaire included 112 food items covering more than 80% of the items most frequently eaten by the Israeli population,[36,37] and there was a space at the end of each food subgroup list for volunteered information on unlisted foods consumed. We also sought information about nutritional supplements. We computed nutrient intake by multiplying the frequency of intake of each unit of food by the nutrient composition of the specified portion size. Several types of units were used to quantify portion size (e.g., standard units, commercial container sizes, and natural units such as fruits and vegetables). The face-to-face interview was conducted by a trained interviewer and lasted about 40 minutes.

Venous blood samples were taken in a climate-controlled room before the beginning of a regular workday (between 7:00 AM and 9:00 AM), after the subjects had fasted for 10 hours (subjects were encouraged to drink water during the fasting period). The subjects were seated while samples were drawn. To prevent venostasis, the tourniquet was released immediately after blood began to enter the tube. The samples were placed in vacuum test tubes without additives and with sodium heparin (for lead measures). In the tubes without additives, serum was separated from whole blood within 30 minutes of being drawn. Fresh serum samples were analyzed and tested for blood lipids in the Kodak Ektachem Automated Clinical Chemistry Analyzer. Kodak Ektachem clinical chemistry slides (Eastern Kodak Company, Rochester, NY) were used for all the chemical tests described below.

Cholesterol level was tested with enzymatic colorimetry.[38] High-density lipoprotein (HDL) cholesterol was tested with enzymatic colorimetry[38] after sedimentation of the low-density lipoprotein (LDL) and very low-density lipoprotein in dextran sulfate-Mg^{+2}.[39] Triglycerides were determined in Kodatrol I and II solution (Eastern Kodak Company, Rochester, NY). Blood samples were sent to the Bio-Rad Laboratories (Richmond, Calif) for external control, and a satisfactory rating was obtained. With respect to blood lipids, lyophilized serum samples were sent to the World Health Organization (WHO) Monica Quality Control Center for Lipid Standardization in Prague for external quality control testing.

The coefficients of variation for cholesterol were 0.8% for intra-assay and 1.6% for interassay. Overall coefficients of variation were 1.7% for triglycerides and 1.8% for HDL cholesterol. The average deviations in comparison with the WHO test were +1.6% for cholesterol, +1.2% for triglycerides, and +1.9% for HDL cholesterol. LDL cholesterol was estimated with the formula of Friedwald et al.[40] Blood lead levels were measured by atomic absorption spectroscopy, by a modification of the method described by Fernandez.[41] The coefficient of variation was 5%. Assay quality control was ensured by participation in the UK National External Quality Assessment Schemes for clinical chemistry, with satisfactory results.

Statistical Analysis

Data analyses were carried out with SAS software (version 6; SAS Institute Inc, Cary, NC). All variables were checked for normality with the Wilk-Shapiro test. For normally distributed variables, differences

between means were analyzed by t test; for those not normally distributed, the Kruskal-Wallis one-way analysis of variance (ANOVA) was used. The magnitude of the correlation between paired summer and winter values was assessed by the Pearson coefficient of correlation. Multiple linear regression analysis, controlling for potential confounding variables, was used to test the association between occupational lead exposure or lead level and serum lipids. All independent variables that were significant in a univariate analysis ($P < .10$) were included. All summer and winter values of each subject were averaged before inclusion into the model. All other variables were entered one at a time and removed if they did not add significantly to the model. Results were considered statistically significant at the 5% level.

TABLE 2—Mean Cholesterol and Lipoprotein Values[a] Among Subjects Occupationally Exposed to Lead and Nonexposed Subjects: Central Israel, 1994–1995

	Nonexposed (n = 87)	Exposed (n = 56)	P
Total cholesterol, mean (SE), mg/dL	200.2 (3.01)	212.7 (3.2)	.016
HDL cholesterol, mean (SE), mg/dL	42.5 (0.9)	47.6 (1.2)	.001
LDL cholesterol, mean (SE), mg/dL	127.7 (2.8)	132.3 (3.6)	.345
Triglycerides, mean (SE), mg/dL	162.2 (9.2)	167.3 (12.1)	.740[b]
Ratio of HDL to total cholesterol	0.21	0.22	.156

Note. The subjects were men who worked in a battery factory or recycling factory (lead-exposed group) and factory production workers who were not exposed to lead or any other nephrotoxic chemicals (nonexposed group). HDL = high-density lipoprotein; LDL = low-density lipoprotein.
[a]Adjusted for age, body mass index, season, nutritional variables, sport activities, alcohol intake, cigarette smoking, education, and seniority.
[b]Kruskal-Wallis one-way analysis of variance (also adjusted).

Results

The characteristics of the study groups are shown in Table 1. Age, body mass index, diet, sports activity, education, and seniority were similar in the 2 groups. Both groups had a very rich (higher than recommended) cholesterol and total fat dietary intake. However, the control group contained significantly more subjects with a family history of cardiovascular disease and had a higher percentage of subjects who consumed alcohol. The occupationally exposed subjects had higher blood lead levels than did the nonexposed subjects.

Mean cholesterol and lipoprotein values for both groups, after adjustment for possible confounders, are given in Table 2. Total cholesterol and HDL cholesterol values were significantly higher in the lead-exposed subjects; a similar trend, which did not reach statistical significance, was found for LDL cholesterol and triglycerides. There were no significant differences between groups in the ratio of HDL cholesterol to total cholesterol. The correlation coefficient between summer and winter values was 0.68 ($P<.0001$) for blood lead level and 0.57 ($P<.0001$) for total cholesterol.

Blood lead level was independently associated with both total cholesterol level ($\beta = 0.130$, SE = 0.054; $P = .017$) and HDL cholesterol level ($\beta = 0.543$, SE = 0.173; $P = .002$). (The 2 dependent variables were analyzed in different statistical models. Confounders were age and body mass index [$P < .03$ in both models]. The values used for each subject were the average of summer and winter values.) Adding the nonsignificant variables (including the various subgroups of dietary fats [data not shown]) one at a time did not change the results. In additional statistical models including the same confounders (not shown), we studied the association of blood lead level with LDL cholesterol and with triglycerides ($P = .557$ and .868, respectively).

More subjects in the exposed group than in the nonexposed group had total cholesterol levels higher than 220 mg/dL (44% vs 29%; $P = .014$). In exposed workers, blood lead level was found to be positively associated with serum cholesterol ($P = .028$), demonstrating a dose–response relationship between blood lead level and serum cholesterol (Figure 1). A similar trend (not shown) was found for HDL cholesterol ($P<.0001$), for LDL cholesterol ($P = .558$), and for triglycerides ($P = .729$).

Discussion

The main finding of this study is that serum cholesterol and lipoprotein levels were higher in subjects who were occupationally exposed to lead than in those who were not exposed. There was a dose–response relationship between blood lead and serum cholesterol levels in the exposed subjects, suggesting an altered lipid metabolism related to lead exposure. The assessment of a possible relationship between blood lead levels and lipids is an important step in elucidating the mechanisms underlying the excess cardiovascular morbidity among lead-exposed subjects.[5] The associations between blood lead level and serum cholesterol and HDL cholesterol reached statistical significance, but there were only trends for the associations between blood lead level and LDL cholesterol and triglycerides, possibly owing to larger variances and less statistical power.

Our finding of elevated total cholesterol levels supports 3 previous reports[31,32,35] and disagrees with 2 others.[30,33] In the study by El Gazzar et al.,[32] lipoproteins were not examined, and in the others the results were inconsistent. An increase in HDL cholesterol was reported by Cocco et al.,[33] but this increase was accompanied by reduced total cholesterol levels. Differences between our results and those of the studies cited may be due to differences in sample sizes or to subjects' exposure to other chemicals and an absence of control for confounding variables in the other studies. In our study most possible confounders were taken into consideration, and data were collected twice, in summer and in winter, with similar results. In the study by El Gazzar et al.,[32] high cholesterol levels were seen only in subjects with more than 10 years' seniority. We did not find an effect of seniority on serum cholesterol. However, we cannot reach conclusions about the exposure time needed to effect an increase in lipid levels because subjects with less than 1 year's seniority were not included in our study.

Our results are consistent with the hypothesis that a lead-induced accumulation of serum lipids is one of the underlying mechanisms in the association between lead exposure and cardiovascular damage. Because of the positive and continuous association between serum cholesterol and coronary artery disease,[4] it seems that subjects who are occupationally exposed to lead are at higher risk of coronary artery disease than those who are not exposed. Since we found increased HDL cholesterol levels among lead-exposed subjects, it could be argued that there is a "protective" effect of lead exposure. However, the ratio of HDL cholesterol to total cholesterol did not differ between the groups, and HDL cholesterol levels did not reach the protective value of 60 mg/dL even in subjects with high serum lead levels.

The association between lead exposure and high serum lipid levels is biologically plausible and could be due to either increased synthesis or decreased removal of lipoproteins.

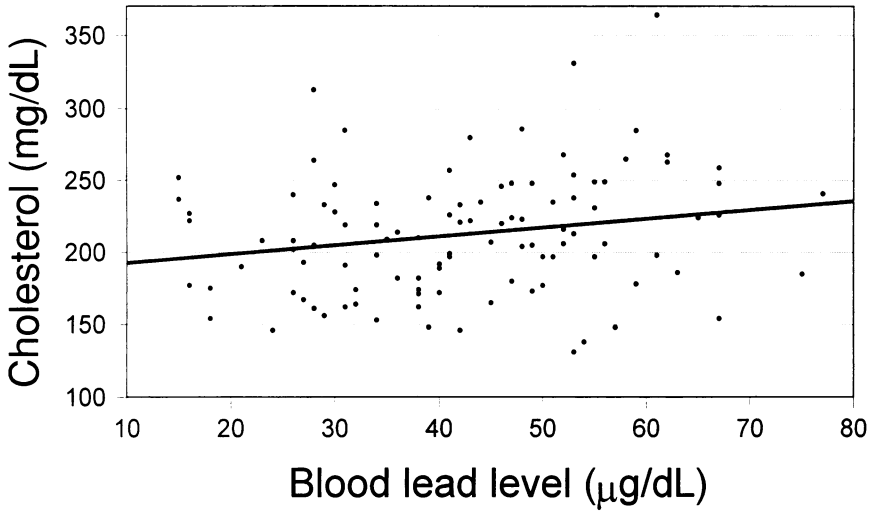

FIGURE 1—Linear regression trend between blood lead level and serum total cholesterol level among industrial workers exposed to lead in the workplace: Central Israel, 1994–1995.

Decreased removal may occur as a result of the alteration of cell-surface receptors for lipoproteins[19] or as a result of the inhibition of hepatic lipoprotein lipase activity.[42] Furthermore, lead has been shown to depress the activity of cytochrome P-450 in man[18,43,44]; this can limit the biosynthesis of bile acids, which is the only significant route for elimination of cholesterol from the body. Increased synthesis may be due to a lead-induced increase in hepatic enzymes at important control points for de novo cholesterol synthesis, as has been found in Wister rats,[45] or it may be due to impaired feedback inhibition.

We conclude that blood lead levels are positively associated with levels of serum cholesterol, HDL cholesterol, and possibly other lipoproteins. The positive association between blood lead level and serum cholesterol among exposed subjects may have important clinical implications. However, caution should be used in extrapolating these results to persons whose blood lead levels are in the lower range, since the cholesterol levels of members of the exposed group with lead levels lower than 25 μg/dL were not higher than those of the unexposed controls. Further carefully controlled cross-sectional studies and longitudinal studies are needed to confirm our results and to establish the causal relationship between lead exposure and elevated cholesterol levels. □

Contributors

E. Kristal-Boneh planned the study, analyzed the data, and wrote the paper. She was assisted by P. Froom. G. Harari was responsible for the statistical analysis. D. Coller designed the questionnaires and examined all the participants. J. Ribak contributed to the writing of this paper.

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References

1. *Report of the 1977 Working Group to Review the 1971 Report by the National Heart, Lung, and Blood Institute Task Force on Arteriosclerosis: Arteriosclerosis.* Washington, DC: National Institutes of Health; 1977. DHEW publication NIH 78-1526.
2. Dawber TR, Kannel WB, Revotskie N, Kagan A. The epidemiology of coronary heart disease. The Framingham inquiry. *Proc R Soc Med.* 1962;58:551–565.
3. Stamler J. Diet, serum lipids, and coronary heart disease: the epidemiologic evidence. In: Levy RI, Rifkind BM, Dennis BH, Ernst N, eds. *Nutrition, Lipids, and Coronary Heart Disease—A Global View.* New York, NY: Raven Press; 1979.
4. Kannel WB, Castelli WP, Gordon T. Cholesterol in the prediction of atherosclerotic disease. New perspectives based on the Framingham Study. *Ann Intern Med.* 1979;90:85–91.
5. Kopp SJ, Barron JT, Tow JP. Cardiovascular action of lead and relationship to hypertension: a review. *Environ Health Perspect.* 1988;78: 91–99.
6. Wojtczak-Jaroszowa J, Kubow S. Carbon monoxide, carbon disulfide, lead and cadmium—four examples of occupational toxic agents linked to cardiovascular disease. *Med Hypotheses.* 1989;30:141–150.
7. Dingwall-Fordyce I, Lane RE. A follow-up study of lead workers. *Br J Indust Med.* 1963; 20:313–315.
8. Malkolm D. Prevention of long-term sequelae following the absorption of lead. *Arch Environ Health.* 1971;23:292–298.
9. Gerhardsson M, Rozenqvist U, Ahlbom A, Carlson LA. Serum cholesterol and cancer—a retrospective case-control study. *Int J Epidemiol.* 1986;15:155–159.
10. Cooper WC, Galley WR. Mortality of lead workers. *J Occup Med.* 1975;17:100–107.
11. Kuzminskaya GN. Effect of lead poisoning on experimental atherosclerosis. *Arkh Patologii.* 1964;26:833–835(T).
12. Kuzminskaya GN. Effect of lead poisoning on experimental atherosclerosis. *Fed Proc.* 1965; 24:833.
13. Revis NW, Horton Y, Majors T. The effects of calcium, magnesium, lead or cadmium on lipoprotein metabolism and atherosclerosis in the pigeon. *J Environ Pathol Toxicol.* 1980;4: 293–303.
14. Hass GM, Brown DVL, Eisenstein R, Hemmens A. Relations between lead poisoning in rabbit and man. *Am J Pathol.* 1964;45:691–693.
15. Skoczynska A, Smolik R, Jelen M. Lipid abnormalities in rats given small doses of lead. *Arch Toxicol.* 1993;67:200–204.
16. Ito Y, Niiya Y, Kurita H, Shima S, Sarai S. Serum lipid peroxide level and blood superoxide dismutase activity in workers with occupational exposure to lead. *Int Arch Occup Environ Health.* 1985;56:119–127.
17. Qinlan GJ, Halliwell B, Moorhouse CP, Gutteridge JM. Action of lead (II) and aluminum (III) ions on iron stimulated lipid peroxidation in liposomes, erythrocytes and rat liver microsomal fractions. *Biochim Biophys Acta.* 1988; 962:196–200.
18. Alvares AP, Fischbein A, Sassa S, Anderson KE, Kappas A. Lead intoxication: effects on cytochrome P-450-mediated hepatic oxidations. *Clin Pharmacol Ther.* 1976;19;183–190.
19. Tarugi P, Calandra S, Borella P, Vivoli GF. Effect of lead intoxication on rabbit plasma lipoproteins. *Atherosclerosis.* 1982;45:221–234.
20. Schroeder HA, Balassa JJ. Influence of chromium, cadmium, and lead on rat aortic lipids and circulating cholesterol. *Am J Physiol.* 1965;209:433–437.
21. Stofen D. Environmental lead and the heart. *J Mol Cell Cardiol.* 1974;6:285–290.
22. Ruparelia SG, Yogendra V, Metha NS, Salyed SR. Lead-induced biochemical changes in freshwater fish *Oreochromis mossambicus. Bull Environ Contam Toxicol.* 1989;43:310–314.
23. Ledda-Columbano GM, Columbano A, Dessi S, et al. Hexose monophosphate shunt and cholesterogenesis in lead-induced kidney hyperplasia. *Chem Biol Interact.* 1987;62:209–215.
24. Columbano A. Ledda GM, Sirigu P, Perra T, Pani P. Liver cell proliferation induced by a single dose of lead nitrate. *Am J Pathol.* 1983;110: 83–88.
25. Xiao GH, Wu JL, Liu YG. The effect of cadmium, mercury and lead in vitro on hepatic microsomal mixed function oxidase and lipid peroxidation. *J Tongji Med Univ.* 1989;9:81–85.
26. Tulasi SJ, Reddy PUM, Ramana Rao JS. Accumulation of lead and effects on total lipids and lipid derivatives in the freshwater fish *Anabas testudineus. Ecotoxicol Environ Safety.* 1992; 23:33–38.
27. Yagminas AP, Franklin CA, Villeneuve DC, Gilman AP, Little PB, Valli VEO. Subchronic

oral toxicity of triethyl lead in the male weanling rat. Clinical, biochemical, hematological and histopathological effects. *Fundam Appl Toxicol.* 1990;15:580–596.
28. Dessi S, Batetta B, Carrucciu A, Pulisci D, Laconi S, Fadda AM, Anchisi C, Pani P. Variations of serum lipoproteins during cell proliferation induced by lead nitrate. *Exp Mol Pathol.* 1989;51:97–102.
29. Khan MZ, Szarek J, Krasnodebska-Depta A, Koncicki A. Effects of concurrent administration of lead and selenium on some haematological and biochemical parameters of broiler chickens. *Acta Vet Hung.* 1993;41:123–137.
30. Cocco PL, Cocco E, Anni MS, Flore C, Salis S. Occupational exposure to lead and blood cholesterol in glucose-6-phosphate dehydrogenase deficient and normal subjects. *Res Commun Chem Pathol Pharmacol.* 1991;72:81–95.
31. Ljubchenko NN, Tishenina RS, Kozlova NI, Drozdova GA. The content of atherogenic lipids in the blood of workers exposed to lead. *Gigiena truda I professional'nye zabolevanija.* 1983;1:21–23.
32. El-Gazzar RM, El-Hefny SA, Noweir KH, Shamy MY. Study of the lipoprotein pattern among workers exposed to lead. *J Egypt Public Health Assoc.* 1989;64:571–585.
33. Cocco P, Salis S, Anni M, Cocco ME, Flore C, Ibba A. Effects of short-term occupational exposure to lead on erythrocyte glucose-6-phosphate dehydrogenase activity and serum cholesterol. *J Appl Toxicol.* 1995;15:373–378.
34. Morisi G, Menditto A, Spagnolo A, Patriarca M, Menotti A. Association of selected social, environm ental and constitutional factors to blood lead levels in men aged 55–75 years. *Sci Total Environ.* 1992;126:209–229.
35. Gatagonova TM. Characteristics of the serum lipids in workers of lead industry. *Med Tr Prom Ekol.* 1994;12:17–21.
36. Modan M, Lubin F, Lusky A, et al. Interrelationships of obesity, habitual diet, physical activity and glucose intolerance in the four main Israeli Jewish ethnic groups. The Israel Glucose Intolerance, Obesity and Hypertension (GOH) Study. In: Berry EM, Blondheim SH, Eliahou HE, Shafrir E, eds. *Recent Advances in Obesity Research.* Vol. 5. London, England: John Libbey & Co; 1986:46–53.
37. Viskoper JR, ed. *Manual of Nonpharmacological Control of Hypertension.* Berlin, Germany: Springer-Verlag; 1990.
38. Allain CC, Poon LS, Chan CSG, Richmond IY, Fu PC. Enzymatic determination of total serum cholesterol. *Clin Chem.* 1974;20:470–475.
39. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-Mg^{+2} precipitation procedure for quantitation of high-density lipoprotein cholesterol. *Clin Chem.* 1983;10:91–99.
40. Friedwald WT, Levy RY, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18:499–502.
41. Fernandez FJ. Micromethod for lead determination in whole blood by atomic absorption with use of the graphite furnace. *Clin Chem.* 1975; 21:558–561.
42. Chajet-Shaul T, Friedman G, Stein O, Shiloni E, Etienne J, Stein Y. Mechanism of the hypertriglyceridemia induced by tumor necrosis factor administration to rats. *Biochim Biophys Acta.* 1989;1001:316–324.
43. Alvares AP, Kapelner S, Sassa S, Kappas A. Drug metabolism in normal children, lead poisoned children and normal adults. *Clin Pharmacol Ther.* 1975;17:179–183.
44. Meredith PA, Campbell BC, Goldberg A. The effect of industrial lead poisoning on cytochrome P-450 mediated phenazone hydroxylation. *Eur J Clin Pharmacol.* 1977;12;235–239.
45. Dessi S, Batetta B, Laconi E, Ennas C, Pani P. Hepatic cholesterol in lead nitrate induced liver hyperplasia. *Chem Biol Interact.* 1984;48: 271–279.