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# CONTRIBUTION OF LEAD POISONING TO RENAL IMPAIRMENT

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The late effects of lead on kidney function and blood pressure were studied in 38 persons occupationally poisoned in the past and in 23 workers exposed to lead. Parameters evaluated in all subjects were: creatinine clearance, hippuran renal flow, blood lead, erythrocyte protoporphyrin, aminolevulinic acid dehydratase, and blood pressure. Out of 11 combined variables, four significant factors were identified by factor analysis. The results showed the presence of the delayed adverse effect of previous occupational lead poisoning on kidney function and blood pressure. This phenomenon is a complex interplay of lead poisoning in the past, overall duration of lead exposure, and age as a major confounding variable related to aging process of the kidneys.

*Key words:*
factor analysis, hypertension, kidney function, occupational lead exposure

Lead is a cumulative poison in man's living and working environment (1–5). Its possible late or delayed effect on kidney has been a subject of discussion for more than a century (6–9). It has been observed that the occurrence of chronic renal failure is often causally related to previous occupational or accidental lead poisoning (10–12).

The introduction of high standards in industrial hygiene led to the virtual disappearance of the previously well-recognized renal complications of chronic lead poisoning (13). On the other hand, the evolution of lead nephropathy is usually an insidious and gradual process and, due to the great renal reserve capacity, clinical manifestations of renal impairment generally do not occur until 50–75% of the nephrons have been destroyed (14). Hence *Landrigan* (15) introduced a new term »subclinical lead toxicity«, which means that low-level lead exposure can cause kidney impairment which cannot be detected by standard clinical examination. The lack of a reliable

biological indicator of early lead-induced kidney damage is the main reason why lead nephropathy is usually detected several years after the beginning of toxic action.

The aim of this study was to evaluate the impact of the chronic lead poisoning on renal functional impairment in persons occupationally poisoned by lead in the past in comparison with currently occupationally exposed subjects with no lead poisoning in the medical history.

## SUBJECTS AND METHODS

The late kidney lead effects were evaluated in 61 occupationally exposed workers. The subjects were chosen randomly from the Register of occupationally lead poisoned patients who were treated at the former Department of Occupational Health and Toxicology of the Institute for Medical Research and Occupational Health in Zagreb over a 37-year period, that is, from 1951 through 1988. All subjects with a history or clinical evidence of previous and/or present renal disease of other etiology were excluded from the study.

Thirty-eight workers experienced at least one episode of acute lead poisoning due to excessive lead exposure during their working life (*Poisoned*). The mean age of subjects in the group herein referred to as *Poisoned* was 48 (ranging from 32 to 72 years) and the mean duration of exposure was 13 years (ranging from several months to 53 years). The patients were poisoned during employment in a glass factory, storage battery industry, and lead glazed ceramics production, while some of them were construction workers and printers. Working conditions in those industries were very bad ten to twenty years ago, with indoor air lead concentrations constantly exceeding threshold limit value (TLV), while the workers lacked proper protective clothing and equipment. Ten of the 38 subjects had been poisoned on several occasions. The diagnosis of lead poisoning in those subjects had been confirmed by a presence of overt clinical symptoms: colic or diffuse abdominal pain, constipation, nausea, weakness, headache, and by increased value of at least one biological index of lead absorption: lead in blood (PbB≥3 mmol/L or 62 μg/100 mL), erythrocyte protoporphyrin (EP>1.6 mmol/LE), and/or aminolevulinic acid dehydratase (ALAD≤10 U/LE).

Twenty-three of 61 occupationally exposed subjects (with PbB=2.0–3.0 mmol/L or 41 μg/100 mL, EP≥1.6 mmol/LE or 90 mg/100 mLE, and ALAD=10–26 U/LE) had never had clinical or biochemical signs of poisoning during their working life (*Exposed*). Most subjects in the group herein referred to as *Exposed* were employed in a lead smeltery and in lead pigments production, where the average concentration of lead in the working environment was 0.8 mg Pb/m$^3$ (range: 0.05–3.25). In Croatia, TLV is 0.1 mg Pb/m$^3$ (16). The mean age of subjects was 41 years (ranging from 29 to 61) and the mean exposure duration 14 years (ranging from 2 to 33 years).

Blood pressure (RR) was measured by a standard sphygmomanometer (mm Hg) on three successive occasions in four different positions: after lying for 10 minutes, after sitting for three minutes, after standing for three minutes, and immediately after reassuming a lying position. The first and the fifth Korotkoff sound were used as indicators of systolic and diastolic blood pressure, respectively. All persons with systolic

blood pressure ≥140 mm Hg and/or diastolic pressure ≥90 mm Hg were considered hypertensive (17).

Blood lead was measured by atomic absorption spectrophotometry (Perkin Elmer® 403, USA) (18,19) at the Clinical Toxicological Laboratory of the Institute for Medical Research and Occupational Health in Zagreb. The accuracy and reliability of PbB determination in that laboratory has constantly been checked by the international quality control. EP and ALAD were measured by spectrofluorometric method (20, 21) on spectrophotometer Perkin Elmer® 551, USA.

Creatinine in serum and urine was determined with a VP automatic analyzer (Abbott, USA). The glomerular filtration rate was evaluated by measuring creatinine clearance corrected to body surface area (ml/min/1.73 $m^2$) (22), and by determining the creatinine index (mg/kg/day) (23). The dependence of glomerular filtration on age (24) was evaluated according to *Giles and Ross* (25). Gradation of kidney function impairment was carried out using the criteria of *Oliver and Wing* (26).

The hippuran renal flow was determined separately for the kidney parenchyma and the whole kidney by quantitative gamma camera radiography using a gamma camera with a large field of view (Searle, the Netherlands) connected to a personal computer (PDP 11/34). Normal flow time for the isotope $^{131}$I-OH (hippuran marked with radioactive iodine) was 2.5–3.5 minutes for the kidney parenchyma, and 4 minutes for the whole kidney (parenchyma and canal system) (27).

The data are presented as arithmetic mean with standard deviation, and the difference between the *Poisoned* and the *Exposed* group was analyzed by the Student's *t*-test.

The significance of the correlations between the examined variables was determined by factor analysis, that is, by principal component analysis (28). By clustering all examined variables and summarizing them into a small number of independent variables called factors, the principal component analysis is able to explain correlations between investigated variables, which makes this statistical method particularly suitable for evaluating and describing the relations between several occurrences. As the principal aim of this study was to investigate such relations and not to examine possible differences between the groups, a control group of unexposed subjects was not needed in this investigation. First the correlation matrix was calculated and then subjected to principal component analysis. By Kaiser criterion (lambda>1) for identifying a number of significant principal components (factors) (28), four dominant factors were established and then rotated orthogonally in Varimax position to simplify the structure of factors. The loadings greater than 0.30 were considered significant.

## RESULTS

Table 1 shows the average values of parameters evaluated in the *Exposed* and the *Poisoned* group. As assessed by creatinine clearance, a significantly lower glomerular filtration rate was found in the *Poisoned* than in the *Exposed* group ($P<0.05$).

Table 1 *Age, duration of lead exposure, renal parameters and blood pressure in Poisoned and Exposed group*

| Variables | Group | | | |
|---|---|---|---|---|
| | Poisoned (N = 38) | | Exposed (N = 23) | |
| | Mean | SD[a] | Mean | SD |
| Age (yrs) | 48.0 | 10.1 | 41.3 | 9.6 |
| Lead exposure (yrs) | 13.4 | 12.1 | 14.2 | 8.4 |
| No of poisonings | 1.4 | 0.7 | 0 | 0 |
| Serum creatinine (mmol/L) | 120.9 | 95.5 | 84.8 | 3.1 |
| Creatinine clearance[b] | 93.2 | 33.0 | 117.9* | 43.9 |
| Hippurane flow (PL)[c] | 3.4 | 1.3 | 3.1 | 0.7 |
| Hippurane flow (PR) | 3.4 | 1.0 | 3.1 | 0.7 |
| Pb blood (mmol/L) | 1.5 | 0.7 | 1.6 | 0.8 |
| EP (mmol/LE) | 4.8 | 5.2 | 2.9 | 3.2 |
| ALAD (U/LE) | 26.6 | 14.2 | 27.0 | 18.2 |
| RR-systolic lying[d] | 144.8 | 22.9 | 142.1 | 18.2 |
| RR-diastolic lying | 87.6 | 12.8 | 84.1 | 11.5 |
| RR-systolic sitting | 150.4 | 22.7 | 143.2 | 17.9 |
| RR-diastolic sitting | 97.8 | 12.5 | 92.0 | 10.0 |
| RR-systolic standing | 148.3 | 24.2 | 145.3 | 19.0 |
| RR-diastolic standing | 98.0 | 13.2 | 95.4 | 11.0 |
| RR-systolic lying | 149.9 | 24.2 | 142.7 | 20.1 |
| RR-diastolic lying | 91.3 | 12.8 | 85.9 | 12.0 |

[a] Standard deviation; [b] Creatinine clearance (mL/min/1.73m$^2$); [c] Hippurane flow: PL – renal parenchyma left, PR – renal parenchyma right (min); [d] Systolic and diastolic blood pressure (mm Hg); * Statistically different ($P<0.05$ by Student's t-test)

Table 2 *Combined variables in Principal component analysis*

| Full description | | Abbreviated description |
|---|---|---|
| $zz_1 = x_1$ | Age (yrs) | Age |
| $zz_2 = x_2$ | Exposure to Pb (yrs) | Lead exposure |
| $zz_3 = x_3$ | Exposure to Pb/Total employment time | Employment |
| $zz_4 = x_4$ | Past occupational lead poisoning | Lead poisoning |
| $zz_5 = x_5$ | Serum creatinine (mmol/L) | Serum creatinine |
| $zz_6 = x_6+x_7$ | Creatinine index (mg/kg/day) + creatinine clearance (mL/min/1.73 m$^2$) | Glomelural filtration |
| $zz_7 = x_8-x_{11}$ | Hipuran renal flow: whole kidney left, whole kidney right, kidney parenchyma left, kidney parenchyma right (min) | Renal flow |
| $zz_8 = x_{12}$ | Pb in blood (mmol/L) | Blood lead |
| $zz_9 = x_{13}$ | Erythrocyte protoporphyrin (mmol/LE) | EPP |
| $zz_{10} = x_{14}$ | Aminolevulinic acid dehydratase (U/LE) | ALAD |
| $zz_{11} = x_{15}-x_{22}$ | Systolic and diastolic blood pressure: lying, sitting, standing, lying (mmHg) | Blood pressure |

Factor analysis was performed to investigate the correlations between past lead poisoning, duration of lead exposure, kidney function, and hypertension. Certain variables with high absolute loadings (>0.7) and the same sign on the same Varimax factor, obtained from the original, untransformed data (i.e. blood pressure measured in 4 different positions), were taken as similar and then combined. Consequently, 11 combined variables were identified by the above method ($z_1$–$z_{11}$) and subjected to principal component analysis (Table 2).

Factor 1 in the Varimax rotation is defined by the following associated variables in descending order: negative correlation age ($zz_1$), blood pressure ($zz_{11}$), serum creatinine ($zz_5$), EP ($zz_9$), number of poisonings ($zz_4$) and the duration of lead exposure ($zz_2$) with positive correlation of creatinine index and clearance ($zz_6$). In this manner the Factor 1 shows well the significant correlation between age, number of poisonings, and the duration of lead exposure on one hand, and the impairment of glomerular filtration rate and hypertension on the other (Table 3).

Table 3 *Varimax rotated factor matrix of combined variables*

| Abbreviated description | | Factor 1 | Factor 2 | Factor 3 | Factor 4 |
|---|---|---|---|---|---|
| Age | $zz_1$ | **−.654** | −.162 | .074 | −.191 |
| Lead exposure | $zz_2$ | **−.348** | .009 | **.931** | −.109 |
| Employment | $zz_3$ | .137 | **.316** | **.781** | .053 |
| Lead poisoning | $zz_4$ | **−.469** | .115 | .061 | **.375** |
| Serum creatinine | $zz_5$ | **−.595** | .173 | .070 | .139 |
| Glomelural filtration | $zz_6$ | **.519** | −.038 | −.040 | −.098 |
| Renal flow | $zz_7$ | .118 | .020 | −.011 | **−.683** |
| Blood lead | $zz_8$ | .026 | **.884** | .194 | −.022 |
| EPP | $zz_9$ | **−.472** | **.465** | .178 | **−.454** |
| ALAD | $zz_{10}$ | .140 | **−.893** | −.066 | .065 |
| Blood pressure | $zz_{11}$ | **−.616** | .050 | −.018 | −.011 |

Significant loadings (>0.30) underlined. For the full description of zz variables please refer to Table 2.

Factor 2 is composed of negative correlation between ALAD ($zz_{10}$) and the following variables: blood lead level ($zz_8$), EP ($zz_9$), and the duration of lead exposure corrected for total employment time ($zz_3$).

Factor 3 encompasses the positive correlation between the variable of lead exposure with ($zz_3$) and without correction for total employment time ($zz_2$). It follows that most subjects spent the greatest part of their working lives exposed to lead at the working place.

Factor 4 consists of the negative variable hippuran renal flow ($zz_7$), EP values ($zz_9$) and the number of poisonings ($zz_4$).

Principal component analysis demonstrated that previous and recurrent lead poisoning in particular can contribute to a decrease in glomerular filtration rate and to an increase in blood pressure (Factor 1). Its influence on a decrease in hippuran renal flow, that is, on the impairment of the proximal tubular cells regardless of age (Factor 4) was also shown in our results. Furthermore, the biological indices of lead exposure

– blood lead level, EP, ALAD – which independently defined the second factor of the Varimax rotated factor matrix were not related either to variables of kidney function or blood pressure.

## DISCUSSION

Our results support the view that kidney impairment depends on the previous duration and magnitude of lead exposure (29, 30). The number of previous lead poisonings, which also determines the magnitude of the lead body burden, is one of the dominant variables in Factor 1 and Factor 4 of the factor analysis and it is significantly related to the variables of kidney function and blood pressure. We assumed that the presence of one or more episodes of acute lead poisonings was associated with an increase of lead body burden, which adversely affects the kidney as a target organ. As suggested in our previous study, the reduction of lead body burden by chelating agents may play a role in the prevention of delayed kidney impairment later in life (31, 32).

Applying the functional clinical classification of the chronic renal insufficiency devised by *Oliver and Wing* (26), we determined that the diminished renal reserve as the first stage in chronic renal failure was frequent in *Poisoned* workers (33). Kidney impairment was more frequent than the increase in systolic and diastolic blood pressure (33). These findings support the view of *Lilis et al.* (34) and of *Batuman et al.* (35) that kidney impairment precedes the appearance of hypertension in workers poisoned with lead.

There is considerable controversy about the possible pathophysiologic mechanisms of lead induced renal injury. In the early sixties, for instance, *Radošević et al.* (9) found an increased incidence of transitory functional renal impairment in persons acutely poisoned by lead, which they ascribed to disordered intrarenal circulation due to the vasoconstrictive effects of lead on intrarenal blood vessels, and to a direct toxic or indirect hypoxic effect of lead on the tubules. The same opinion was reiterated by *Lilis et al.* (34, 36), although later investigations failed to support that hypothesis (37, 38). However, a vasoconstrictive effect of lead seems plausible as some studies have demonstrated that lead interferes with the function mediated by beta-adrenoreceptors (39), induces hyperreactivity of the sympathetic nervous system and affects the renin-angiotenzin system (40). Furthermore, later studies indicate that chronic low-level lead exposure increases susceptibility of the cardiovascular system to epinephrine and norepinephrine (41).

Using a battery of new markers for early lead-induced renal changes, *Cardenas et al.* (42) recently found that a decreased urinary excretion of 6-keto prostaglandin $F_1$ (a vasodilator) was associated with the enhanced excretion of thromboxane $B_2$ which acts as a vasoconstrictor. Such abnormalities in renal metabolism of prostaglandins and thromboxane may contribute to the pathophysiology of renal failure and hypertension, suggesting that the initial result of lead nephropathy might involve vasculature and glomeruli, and not exclusively tubular cells. Although those markers of lead nephrotoxicity were found in workers with low-level lead exposure, their clinical significance remains to be established (42).

Factor 1 of the Varimax rotated matrix encompasses the variables *blood pressure, age, duration of lead exposure, number of previous lead poisonings, creatinine clearance,* and *EP*. As the variable *blood lead level* did not make part of Factor 1, we did not observe a direct relationship between blood lead level, renal impairment and blood pressure. The reason for this is in the fact that blood lead level reflects recent exposure, while the adverse effects of lead on kidney function and blood pressure are the result of a long-term cumulative exposure with increased body burden. Blood lead level as an inadequate marker of chronic cumulative exposure may not reflect the true degree of risk for the target organs. The above reasoning suggests that the "normal" blood lead level, determined in a single moment, does not exclude the presence of lead nephropathy and lead-induced hypertension. We think that in the continuity of events which lead to kidney impairment and hypertension, more than one step separates blood lead level from pathomorphological substrate (end organ failure) induced by previous excessive lead accumulation. This conclusion is in line with other arguments for a reliable and sensitive biological parameter of chronic, cumulative lead exposure both in occupational and environmental conditions (4, 15). Although there are several methods which can give some information on cumulative exposure to lead and lead body burden, their value as useful indices of risk assessment of chronic toxic effects of lead on target organs is yet to be established (43).

With regard to the insidious, gradual and delayed appearance of lead nephropathy, it is possible that some immunological processes are involved in its development (44, 45). This aspect, however, needs thorough investigation.

To conclude, the results of our study show the presence of the delayed adverse effects of previous occupational lead poisoning on kidney function. This phenomenon results from a complex interplay between the past lead poisoning, overall duration of lead exposure, age as a major confounding variable, kidney function impairment, and alteration of blood pressure. Our study shows that the determined occurrence of kidney function impairment related to previous lead poisoning and duration of lead exposure confirms that the kidney is a critical target organ under the conditions of long-term exposure. The confounding variable of age, the lack of a reliable indicator of early lead-induced kidney damage, and the lack of a sensitive biological indicator of cumulative lead exposure are the principal reasons for the conflicting results of studies on the chronic effects of lead on kidney function in the past and, to a certain extent, in the present.

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## REFERENCES

1. *World Health Organization (WHO).* Inorganic lead. Environmental Health Criteria 165, Geneva: WHO, 1995.
2. *Castellino N, Castellino P, Sannolo N, eds.* Inorganic lead exposure. Metabolism and intoxication. Boca Raton, FL: Lewis Publishers/CRC Press, Inc., 1995.

3. *Agency for Toxic Substances and Disease Registry (ATSDR)*. Lead. Toxicological profile for lead: Update. TP-92/12. Atlanta, GO: U.S. Department of Health & Human Services, Public Health Service, ATSDR, 1993.
4. *Bernard BP, Becker CE.* Environmental lead exposure and the kidney. Clin Toxicol 1988; 26:1–34.
5. *Momčilović B.* Lead metabolism with special reference to the problem of population exposure (in Croatian). Arh hig rada toksikol 1973; 24:131–87.
6. *Bennett WM.* Lead nephropathy. Kidney Int 1985;18:212–20.
7. *Buchet JP, Roels H, Bernard A, Lauwerys R.* Assessment of renal function of workers exposed to inorganic lead, cadmium or mercury vapor. J Occup Med 1980;22:741–50.
8. *Lilis R, Fischbein JA, Valciukas JA, Blumberg W, Selikoff IJ.* Kidney function and lead. Relationship in several occupational groups with different levels of exposure. Am J Ind Med 1980;1:405–12.
9. *Radošević Z. Šarić M, Beritić T, Knežević J.* The kidney in lead poisoning. Br J Ind Med 1961;18:222–30.
10. *Hu H.* A 50-year follow-up of childhood plumbism. Hypertension, renal function and hemoglobin levels among survivors. Am J Child Dis 1991;145:681–7.
11. *Koster J, Erhardt A, Stoeppler M, Motil C, Ritz E.* Mobilizable lead in patients with chronic renal failure. Eur J Clin Invest 1989;19:228–33.
12. *Van de Vyver FL, D'Haese PC, Visser WJ, et al.* Bone lead in dialysis patients. Kidney Int 1988;33:601–7.
13. *McMichael AJ, Johnson HM.* Long term mortality profile of heavily-exposed lead smelter workers. J Occup Med 1982;24:375–8.
14. *Landrigan PJ.* Current issues in the epidemiology and toxicology of occupational exposure to lead. Environ Health Perspect 1990;89:61–6.
15. *Landrigan PJ.* Strategies for epidemiologic studies of lead in bone in occupationally exposed population. Environ Health Perspect 1991;91:81–6.
16. *Habuš Z.* The regulations on maximum permissible concentrations of hazardous chemicals in the work atmosphere and biological exposure indices (in Croatian). Laboratory of Analytics and Toxicology, Zagreb, 1993.
17. *Kaplan NM.* Systemic hypertension: Mechanisms and diagnosis. In: E. Braunwald ed. Heart Disease. A textbook of cardiovascular medicine. Philadelphia: Saunders & Co, 1992:817–51.
18. *Stoppler M, Brand K, Rains TC.* Contributions to automated trace analysis. Part II. Rapid method for the automated determination of lead in whole blood by electrothermal atomic absorption spectrophotometry. Analyst 1987;103:714–22.
19. *Prpić-Majić D.* Toxicochemical analysis. (in Croatian) Zagreb: Medicinska knjiga, 1985.
20. *Chisolm JJ, Brown DH.* Microphotofluorometric determination of free erythrocyte porphyrin. Clin Chem 1975;21:1669–82.
21. *Berlin A, Schaller KK.* European standardized method for the determination of delta aminolevulinic acid dehydratase activity in blood. Zeitschr Klin Chem Klin Biochem 1974;12:389–90.
22. *Smyth DH.* The intake of materials – nutrition, metabolism. In: H. Davson, MG Eggleton eds. Starling and Evans principles of human physiology. London: Churchill Ltd, 1968:543.
23. *Levey AS.* Measurement of renal function in chronic disease. Kidney Int 1990; 38:167–84.
24. *Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW.* Age-adjusted standards for creatinine clearance. Ann Intern Med 1976; 84:567–9.
25. *Giles AM, Ross BD.* Normal or reference values for biochemical data. In: DJ Weatherall, JGG Ledingham, BA Warrell, eds. Oxford textbook of medicine. 1st ed. Oxford: Oxford University Press, 1984:27.3–27.8.
26. *Oliver DO, Wing AJ.* Chronic renal failure, dialysis and transplantation. In: DJ Weatherall, JGG Ledingham, DA Warrell, eds. Oxford textbook of medicine. 2nd ed. Oxford: Oxford University Press, 1987:18.134–18.164.

27. *O'Reilly PH, Shields RA, Testa HJ,* eds. Nuclear medicine in urology and nephrology. 2nd ed. London: Butterworths, 1986.
28. *Dillon WR, Goldstein M.* Multivariate analysis. Methods and applications. New York: John Wiley & Son, 1984.
29. *Goyer RA.* Mechanisms of lead and cadmium nephrotoxicity. Toxicol Lett 1989;46:153–62.
30. *Goyer RA.* Lead and the kidney. Curr Top Pathol 1971;55:147–76.
31. *Restek-Samaržija N, Momčilović B.* Delayed renal effects in lead poisoning and chelation therapy (in Croatian). Arh hig rada toksikol 1992;43:321–8.
32. *Restek-Samaržija N, Momčilović B.* Lead body burden and late kidney impairment. In: B. Momčilović ed. Trace elements in man and animal 7. Zagreb: Institute for Medical Research and Occupational Health, 1991:26.3–26.4.
33. *Restek-Samaržija N.* Delayed effects of lead on the kidneys. (M.Sc. Thesis). Zagreb: School of Medicine, University of Zagreb, 1989. pp 88 (in Croatian).
34. *Lilis R, Gavrilescu N, Nestorescu B, Dimitriu C, Roventa A.* Nephropathy in chronic lead poisoning. Br J Ind Med 1968;25:196–202.
35. *Batuman V, Landy E, Maesaka JK, Wedeen RP.* Contribution of lead to hypertension with renal impairment. N Eng J Med 1983;309:17–21.
36. *Lilis R, Dimitriu C, Roventa A, Nestorescu B, Pilat L.* Renal function and chronic lead poisoning. Med Lav 1967;8:506–12.
37. *Beevers DG, Cruickshank JK, Yeoman WB, Carter GF.* Blood-lead and cadmium in human hypertension. J Environ Pathol Toxicol 1980;3:251–60.
38. *Campbell BC, Beattie AD, Elliott HL et al.* Occupational lead exposure and renin release. Arch Environ Health 1979;34:439–43.
39. *Bertel O, Buhler FR, Ott R.* Lead induced hypertension. Blunted beta-adrenoceptor-mediated functions. Br Med J 1978;4:551.
40. *Boscolo P, Carmignani M.* Neurohumoral blood pressure regulation in lead exposure. Environ Health Perspect 1988;78:101–6.
41. *Sharp DS, Smith AH, Holman BL, Fisher JM, Osterloh J, Becker CE.* Elevated blood pressure in treated hypertensives with low-level lead accumulation. Arch Environ Health 1989;44:18–22.
42. *Cardenas A, Roels H, Bernard AM et al.* Markers of early renal changes induced by industrial pollutants. II Application to workers exposed to lead. Br J Ind Med 1993;50:28–36.
43. *Skerfving S, Nilsson U.* Assessment of accumulated body burden of metals. Toxicol Lett 1992;64/65:17–24.
44. *Coscia GC, Discalzi G, Ponzetti C.* Immunological aspects of occupational lead exposure. Med Lav 1987;78:360–4.
45. *Wedeen RP, Mallik DK, Batuman V.* Detection and treatment of occupational lead nephropathy. Arch Intern Med 1979;139:53–7.

*Sažetak*

## UČINCI OLOVA NA BUBREŽNU FUNKCIJU

Kasni učinci olova na bubrežnu funkciju i krvni tlak ispitani su u 38 osoba izloženih i prethodno otrovanih olovom te u 23 osobe izložene olovu, ali bez prethodnog trovanja tim metalom. U svih smo ispitanika odredili kreatininski klirens, bubrežni protok hipurana, olovo u krvi, eritrocitni protoporfirin, dehidratazu aminolevulinske kiseline i krvni tlak. Primjenom faktorske analize na 11 ispitanih varijabla utvrdili smo njihovo grupiranje u četiri značajna faktora. Rezultati faktorske analize potvrdili su pretpostavku o odgođenim štetnim učincima prethodnog trovanja olovom u obliku pada funkcionalnog kapaciteta bubrega i porasta krvnoga tlaka. Opisana pojava posljedica je složene međuovisnosti između prethodnog trovanja olovom, cjelokupnog vremena provedenog u izloženosti olovu, kao i životne dobi ispitanika koja je, zbog normalnih procesa starenja bubrega, osnovni ometajući čimbenik svake analize o kasnim učincima toksičnih tvari na bubrege.

*Ključne riječi:*
analiza faktora, bubrežna funkcija, hipertenzija, profesionalna izloženost olovu

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