Arh hig rada toksikol 1993;44:9-20

Original Scientific Paper
UDC 615.916:611.61:519.241

DELAYED EFFECTS OF LEAD ON THE KIDNEY - FACTOR ANALYSIS

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Received January 10, 1992

A late, i.e. delayed, effect of lead on kidney function and blood pressure was studied in 23 workers with a history of occupational lead poisoning. Twenty lead exposed workers with no known history of lead poisoning were a positive control. Four important factors out of 11 combined variables derived from 22 single variables were identified by factor analysis. The first factor comprised the variables kidney function, blood pressure, age, duration of lead exposure and the number of previous lead poisonings. The second factor comprised the variables duration of lead exposure and biological indicators of lead exposure. The third factor correlated the frequency of previous lead poisonings with the renal blood flow, erythrocytic protoporphyrin and age. The fourth factor comprised the variables length of work service, creatinine clearance and erythrocytic protoporphyrin. The results confirm the presence of the adverse late effect of previous occupational lead poisoning on kidney function regardless of treatment. The phenomenon is not a single event but a complex interplay of past lead poisoning, duration of exposure to lead, »normal« age effect on an increase in systolic and diastolic blood pressure and blood creatinine and a decrease in renal function as revealed by decreased creatinine clearance and a slow down in renal flow time. The complexity of dealing with the confounding variable of age and lack of appropriate classification of renal function impairment may account for the conflicting results of chronic lead effect upon kidney function in the past. The kidney appears to be a critical target organ, reflecting the total lead body burden in chronic lead exposure and poisoning. Therefore monitoring of kidney function in lead exposed workers needs to be mandatory.

Key terms: age, blood pressure, creatinine clearance, delayed kidney impairment, hipurane flow, lead exposure, lead in blood, occupational exposure.

Chronic lead-induced kidney impairment has been the subject of research for more than a hundred years (1). At the beginning of the century several eminent investigators stated that long-term exposure to high lead concentrations could cause chronic kidney damage manifesting later in life (2–5). Other authors considered that there was insufficient evidence that chronic lead nephropathy developed as a result of earlier poisoning or exposure to high concentrations of this metal (6, 7). At the end of the 1940's *Lane* (8) claimed that the serious kidney impairment described in literature was a result of the bad work conditions in industry at the time. At the beginning of the 1960's *Radošević*

and co-workers (9), *Morgan and co-workers* (10) and *Lilis and co-workers* (11, 12) maintained, however, that lead poisoning could cause mainly functional kidney damage as a consequence of a direct spastic effect of lead on intrarenal blood vessels, i.e. direct toxic or indirect hypoxic effect of lead on the renal tubules. In their opinion only long-term exposure to high lead concentrations and repeated poisoning could lead to irreversible organic kidney lesions.

Later results of investigations in humans and animals showed that the pathogenesis of chronic lead nephropathy is a continuum of morphological and functional changes, ranging from the appearance of inclusion bodies, through diffuse interstitial fibrosis to chronic kidney failure (10, 13, 14). According to *Wedeen* (15) occupational lead nephropathy still occurred during the 1970's, although the permissible blood lead level was already significantly decreased (16). In spite of high standards of industrial hygiene major kidney impairment in workers occupationally exposed to lead was reported at the beginning of the 1980's (17, 18). Experts disagree as to whether lead-induced kidney damage can occur at blood lead concentrations of 40 or 60 μg Pb/100 ml (2 or 3 μmol/L) which are still found in industrial workers today (19–21).

As values of 40 μg /100 ml (2 μmol/L) are also occasionally found in non-occupationally exposed persons, there has been increased interest in the chronic influence of lead exposure on hypertension and impaired kidney function in the general population (19, 22–26). It would appear that the detrimental effect of constant 24-hour exposure to low lead concentrations in the human environment on kidney function demands detailed study (27).

In our previous study we demonstrated a significant influence of total lead body burden on delayed renal functional impairment (28).

The aim of this study was to examine possible late effects of lead on kidney function in workers poisoned with this metal and in those exposed to lead, but never poisoned by it. The results were analysed by factor analysis which enabled simultaneous examination of several variables considered to be correlated with the occurrence of delayed lead-induced kidney damage.

SUBJECTS AND METHODS

During the period from 1951 to 1988 125 persons occupationally poisoned by lead, were treated in the Institute for Medical Research and Occupational Health in Zagreb. For the study we succeeded in tracing 79 patients, and the remaining 46 patients were not traced, usually because of change of address or death. To date by random sampling we have examined kidney function in 23 of the above 79 subjects (poisoned).

The oldest poisoned patient was born in 1916, and the youngest in 1956, while the majority of the subjects were born in the 1930's and 1940's. Some of them were poisoned by lead on several occasions. The duration of lead exposure of the poisoned workers ranged from one to forty years. Twelve of these workers still work with lead but some ceased working with this metal 20 years ago (Figure 1).

As a positive control 20 workers occupationally exposed to lead were examined. They had never been poisoned with this metal during their work service, according to the findings of obligatory one-year biological surveillance, physical examination and data from the patient's medical health card (exposed).

The oldest in the group of exposed workers was born in 1933 and the youngest in 1959. The majority of the workers were born in the 1950's. The length of occupational exposure to lead ranged from 2 to 33 years (Figure 2).

No	Code	YEAR OF BIRTH
27	At. Iv.	1916
33	Ga. Fr.	1918
52	Ko. Sr.	1916
92	Ca. Iv.	1929
96	Pa. Sl.	1929
108	Mi. Du.	1930
126	Fa. Jo.	1932
127	Ko. St.	1932
133	Sk. Vl.	1934
142	Ha. Dr.	1937
145	Ha. Mi.	1937
158	Sv. Mi.	1939
161	Re. Iv.	1939
165	De. Jo.	1940
178	Kr. St.	1943
184	Bo. Br.	1945
186	Si. St.	1946
191	Ga. Ra.	1947
195	Sk. Mi.	1948
215	Ru. Jo.	1953
216	Je. Že.	1954
217	Ko. Mi.	1954
221	Ko. Bo.	1956

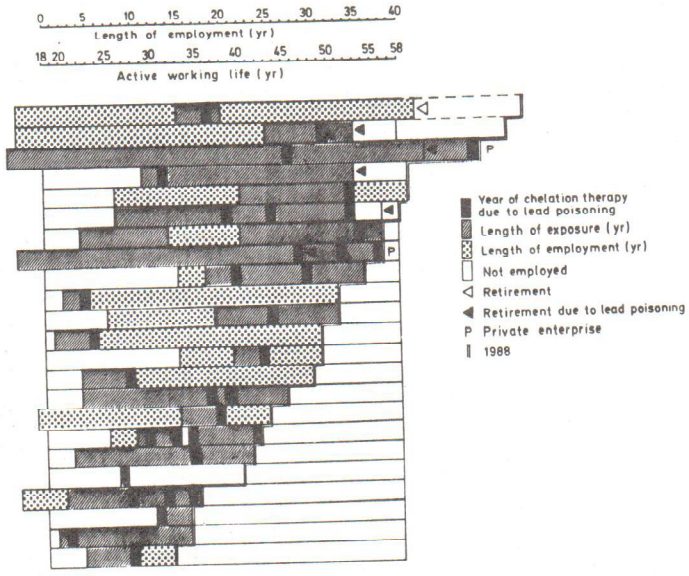

Figure 1 *Employment history of previously treated occupationally lead poisoned workers*

No	Code	YEAR OF BIRTH
2	Mu. Be.	1933
3	Ja. Vi.	1933
4	Kr. Sm.	1935
5	Hr. Ru.	1936
6	Ma. An.	1939
7	To. De.	1941
8	Ja. Iv.	1947
9	Ab. Su.	1949
10	Ra. Že.	1949
11	Ha. Jv.	1950
13	Ho. Jo.	1951
15	Mi. Lju.	1952
16	Ka. Va.	1954
17	Si. Ib.	1954
18	Bu. Sa.	1955
19	Ju. Om.	1956
20	Lu. Cv.	1956
21	Iv. Dr.	1957
22	Do. Iv.	1958
23	Ja. Vl.	1959

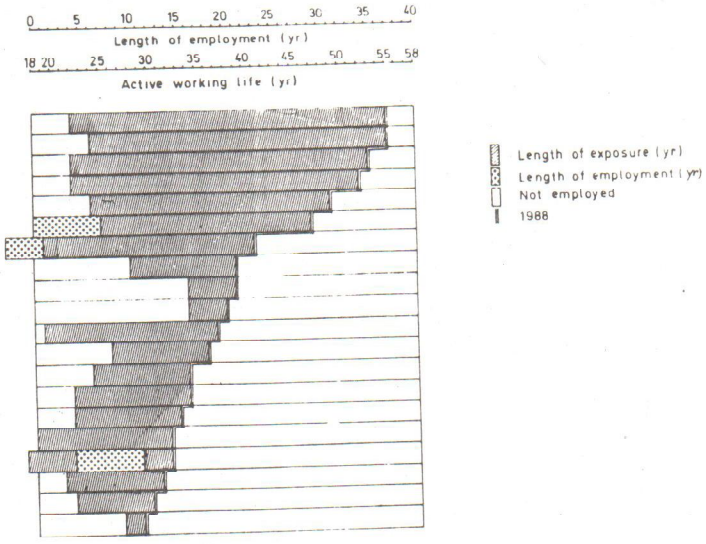

Figure 2 *Employment history of occupationally lead exposed workers*

The following values for blood lead (Pb) are considered normal in occupationally non-exposed populations: ≤1.46 μmol/L and/or delta-aminolaevulinic acid dehydratase (ALAD) ≥26 U/LE and/or erythrocytic protoporphyrin (EP) ≤1.6 μmol/L. We considered values of Pb ≥2 μmol/L to be a sign of increased exposure to lead and values of Pb ≥3.0 μmol/L and/or ALAD ≤10 U/LE to be a sign of lead poisoning (29, 30).

All subjects received normal hospital food (2200 to 2500 KCal). Their height (cm) and weight (kg) were measured immediately on admission. Blood pressure (RR) was measured with a standard sphyngomanometer (mmHg) (31) three times in succession in four different positions: after lying down for 10 minutes, after sitting for three minutes, after standing for three minutes and immediately after lying down again (32). The values of systolic pressure (S) corresponded to the occurrence of a murmur (Ist phase) and of diastolic pressure (D) to its disappearance (Vth phase). According to the criteria of the *World Health Organization* (33) all persons whose systolic blood pressure was ≥160 mmHg and/or diastolic ≥95 mmHg were considered to be hypertensive. Blood lead was determined in the Clinical-toxicological Laboratory of the Institute for Medical Research and Occupational Health, by the method of atomic absorption spectrophotometry (Perkin Elmer 403, USA) (34, 35). The accuracy and reliability of lead determination in this laboratory was constantly checked within the international evaluation of quality control. EP and ALAD were measured by the spectrofluorometric method and spectrophotometry respectively (Perkin Elmer 551, USA) (36, 37).

Creatinine in serum and urine was determined in a laboratory of the Rebro University Hospital by means of a VP automatic analyzer (Abbot, USA). Normal values for creatinine in serum and urine in males were considered to be 53-130 μmol/L i.e. 9–26 μmol/L. The method according to *Schrimeister and co-workers* (38) was used to determine creatinine clearance (CC). The values obtained were corrected to standard body area (ml/min/1.73 m^2) (39), and creatinine index (mg/kg/day) was determined (40). The dependence of glomerular filtration on age (41, 42) was estimated according to the findings of *Giles and Ross* (43) (Table 1). Grading of impaired kidney function was carried out in accordance with the criteria of *Oliver* (44) and *Oliver and Wing* (45) (Table 2).

Table 1 *Dependence of the glomerular filtration rate on age (creatinine clearance) (43)*

Age (years)	Glomerular filtration rate (ml/min/1.73 m^2)
20	105 – 170
50	95 – 138
70	70 – 110

Table 2 *Functional classification of chronic kidney insufficiency (45)*

	Glomerular filtration rate (ml/min)
Diminished renal reserve	70 – 105*
Early renal failure	30
Late renal failure	10
Terminal uraemia	5

* Age dependent (see Table 1)

Table 3 *Correlation matrix of combined variables*

Combined (Z) and individual (X) variables	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}	Z_{11}
Z_1 (X_1) Age	1.0000										
Z_2 (X_2) Lead exposure	0.4667	1.0000									
Z_3 (X_3) X_2 /total employment	–0.3864	0.4374	1.0000								
Z_4 (X_4) Lead poisoning	0.3233	0.2864	–0.0494	1.0000							
Z_5 (X_5) Creatinine (serum)	0.3078	0.2465	0.1303	0.2215	1.0000						
Z_6 (X_6) Creatinine index	–0.3822	–0.1321	0.1868	–0.1226	–0.3897	1.0000					
(X_7) Creatinine clearance											
Z_7 (X_8) Hipurane flow (whole kidney L)	0.1264	0.0022	–0.1568	0.2226	–0.1994	0.2072	1.0000				
(X_9) Hipurane flow (whole kidney R)											
(X_{10}) Hipurane flow (parenchyma L)											
(X_{11}) Hipurane flow (parenchyma R)											
Z_8 (X_{12}) Blood lead	–0.4192	–0.0925	0.3562	–0.2599	–0.0324	0.0352	–0.2144	1.0000			
Z_9 (X_{13}) ALAD	0.2733	0.0226	–0.2451	0.0008	–0.2040	0.2250	0.1419	–0.8129	1.0000		
Z_{10} (X_{14}) EP	0.1269	0.3120	0.2366	0.5196	0.3049	–0.0629	–0.0271	0.2727	–0.4440	1.0000	
Z_{11} (X_{15}) Systolic blood pressure (lying)	0.3752	0.2718	0.0505	0.4376	0.4515	–0.2784	–0.0993	–0.2182	0.0656	0.1589	1.0000
(X_{16}) Diastolic blood pressure (lying)											
(X_{17}) Systolic blood pressure (sitting)											
(X_{18}) Diastolic blood pressure (sitting)											
(X_{19}) Systolic blood pressure (standing)											
(X_{20}) Diastolic blood pressure (standing)											
(X_{21}) Systolic blood pressure ($lying_2$)											
(X_{22}) Diastolic blood pressure ($lying_2$)											

$P<0.05_{\ n=43} \geq 0.2545$ (48)

In the Institute for Nuclear Medicine of the Rebro University Hospital the hipurane renal flow was determined in all subjects by quantitative gamma camera radiography. A gamma camera with a wide field of view was used (Searle, The Netherlands) connected to a personal computer (PDP 11/34). The normal flow-time of isotope ^{131}I-OH (hipurane marked by radioactive iodine) amounted from 2.5 to 3.5 minutes for the kidney parenchyma, i.e. four minutes for the whole kidney (parenchyma and canal system) (46).

The significance of the correlation between 22 of the examined variables (X_1 – X_{22}) was determined by means of factor analysis on an Olivetti M-19 PC computer with the help of Statistical Package for Social Sciences (SPSS/PC 11) (47, 48).

Certain variables which had high absolute values (≥0.7) with the same symbol on the same Varimax factor, were considered similar and were therefore combined by simply adding up their standardized values: $XZ_i=(\overline{X}_i-X_i)/SD_i$ where X_i is individual value, $\overline{X}_i$ arithmetic means of individual values and SD_i standard deviation.

By the above method 11 combined variables (Z_1–Z_{11}) were identified (Table 3) which were suitable for working with a relatively small number of subjects, as was the case in this investigation.

First, the correlation matrix of the combined variables was formed and then subjected to principal component analysis (Table 4). We chose this method for its mathematical elegance and to avoid poorly defined quantity which occurs in simpler forms of factor analysis. The number of significant principal components, i.e. factors, was determined by means of Kaiser criteria (Lambda ≥ 1) and visual examination of a graph of the results. All the combined variables with relatively high communality were estimated to be significant (Table 4) and were taken into account when forming a factor matrix (Table 5).

Table 4 *Principal component analysis of combined variables*

Variable	Communality	Factor	Eigen value*	Variance %	Cumulative %
Z_1 Age	1.0000	1	2.8585	26.0	26.0
Z_2 Lead exposure	1.0000	2	2.5273	23.0	49.0
Z_3 Z_2/total employment	1.0000	3	1.4496	13.2	62.1
Z_4 Lead poisoning	1.0000	4	1.2115	11.0	73.2
Z_5 Creatinine (serum)	1.0000	5	0.8481	7.7	80.9
Z_6 Clearance[a]	1.0000	6	0.6477	5.9	86.7
Z_7 Hipurane flow[b]	1.0000	7	0.5338	4.9	91.6
Z_8 Blood lead	1.0000	8	0.4590	4.2	95.8
Z_9 ALAD	1.0000	9	0.2366	2.2	97.9
Z_{10} EP	1.0000	10	0.1456	1.3	99.2
Z_{11} Blood pressure[c]	1.0000	11	0.0853	0.8	100.0

* Kaiser criteria (Lambda ≥ 1)

[a] creatinine clearance, creatinine index; [b] whole kidney (left), whole kidney (right), kidney parenchyma (left), kidney parenchyma (right); [c] systolic and diastolic (lying), systolic and diastolic (sitting), systolic and diastolic (standing), systolic and diastolic (lying 2).

The solutions for principal components were rotated in Varimax, Quartimax and Equimax positions in order to obtain a simpler factor structure. As rotations of factors basically conformed with one another, only data for the Varimax rotating factor matrix are shown (Table 6). Factor loadings ≥ 0.5 in absolute values were considered significant and those ≥ 0.26 as borderline.

Table 5 *Factor matrix of combined variables*

Variable	Factor 1	Factor 2	Factor 3	Factor 4
Z_1 Age	0.7540	-0.3359	NS	NS
Z_2 Lead exposure	0.5970	NS	0.3793	0.4293
Z_3 Z_2/total employment	NS	0.6122	0.4254	0.5721
Z_4 Lead poisoning	0.6758	NS	0.3843	-0.3747
Z_5 Creatinine (serum)	0.6228	0.3221	-0.3052	NS
Z_6 Clearance[a]	-0.4923	NS	0.6564	NS
Z_7 Hipurane flow[b]	NS	-0.3535	0.5398	-0.4728
Z_8 Blood lead	-0.3826	0.8195	NS	NS
Z_9 ALAD	NS	-0.8563	NS	0.3689
Z_{10} EP	0.4370	0.5896	0.3288	-0.3372
Z_{11} Blood pressure[c]	0.7066	NS	NS	NS

Loadings ≥ 0,5 are considered significant, and those ≥ 0.26 borderline
NS = loadings < 0.26
[a] creatinine clearance, creatinine index; [b] whole kidney (left), whole kidney (right), kidney parenchyma (left), kidney parenchyma (right); [c] systolic and diastolic (lying), systolic and diastolic (sitting), systolic and diastolic (standing), systolic and diastolic (lying 2).

Table 6 *Varimax factor matrix of combined variables*

Variable	Factor 1	Factor 2	Factor 3	Factor 4
Z_1 Age	0.6056	0.4411	0.3638	NS
Z_2 Lead exposure	0.3185	NS	NS	0.7282
Z_3 Z_2/total employment	NS	0.3023	NS	0.8686
Z_4 Lead poisoning	0.2884	NS	0.8044	NS
Z_5 Creatinine (serum)	0.7730	NS	NS	NS
Z_6 Clearance[a]	-0.7838	NS	NS	0.2630
Z_7 Hipurane flow[b]	-0.3887	NS	0.6390	NS
Z_8 Blood lead	NS	-0.8899	NS	NS
Z_9 ALAD	NS	0.9389	NS	NS
Z_{10} EP	NS	-0.5086	0.6074	0.2871
Z_{11} Blood pressure[c]	0.6343	NS	NS	NS

Loadings ≥ 0.5 are considered significant, and those ≥ 0.26 borderline
NS = loadings < 0.26
[a] creatinine clearance, creatinine index; [b] whole kidney (left), whole kidney (right), kidney parenchyma (left), kidney parenchyma (right); [c] systolic and diastolic (lying), systolic and diastolic (sitting), systolic and diastolic (standing), systolic and diastolic (lying 2).

RESULTS

Because of the large number and complexity of data the values for individual variables are not presented but only the results of factor analysis. First the correlation matrix (Table 3) was analysed as a prototype of »unorganized« matrix of data. We then determined the factors (Table 4) and analysed variables within individual factors (Table 5). After that we analysed the factors in the Varimax rotated factor matrix (Table 6).

According to the correlation matrix of combined variables (Table 3) a significant ($P<0.05$) positive correlation of dependence can be seen between the variables of age (Z_1), duration of lead exposure (Z_2), previous lead poisoning (Z_4), serum creatinine (Z_5), ALAD (Z_9) and blood pressure (Z_{11}). At the same time there is a significant negative correlation ($P<0.05$) between the lead exposure corrected to total employment time (Z_3), creatinine clearance (Z_6) and the blood lead level (Z_8). Similarly, the variable of blood pressure (Z_{11}) correlated positively with age (Z_1), lead exposure (Z_2), previous lead poisoning (Z_4) and serum creatinine (Z_5), and negatively with creatinine clearance (Z_6). All the combined variables had well expressed communality (Table 4) and can therefore be considered reliable in our investigation.

The above correlation matrix was analysed according to the principal component and four dominant factors were determined (Table 5). The first and most significant dominant factor correlated with nearly all the examined variables apart from the relation between lead exposure and total employment time (Z_3), hipurane renal flow (Z_7) and ALAD (Z_9). The second factor was significant because it excluded the variables of lead exposure (Z_2), past lead poisoning (Z_4), creatinine clearance (Z_6) and blood pressure (Z_{11}) i.e. variables which were considered to reflect the occurrence of the delayed effect of lead on the kidney. On the other hand, this factor was defined by the variables blood lead level, EP and ALAD as biological indices of lead exposure. In the third factor emphasis was on the connection of the variable of creatinine clearance (Z_6) and renal flow (Z_7) with duration of lead exposure and number of past lead poisonings, while significant age dependence (Z_1) was lost. The fourth factor consisted of the variables connected with work service. However, within this factor there was a negative correlation between the duration of lead exposure (Z_2) and hipurane renal flow (Z_7).

The factor matrix of combined variables was then transformed into the Varimax rotated factor matrix (Table 6).

The first factor was composed, in decreasing order for the same sign, of a negative correlation of creatinine clearance (Z_6) and hipurane flow through the kidney (Z_7) and positive variables serum creatinine (Z_5), blood pressure (Z_{11}), age (1), duration of lead exposure (Z_2) and the number of past lead poisonings (Z_4).

The second factor mainly consisted of variables indicating lead exposure, i.e. a negative correlation of blood lead level and EP to a positive correlation for ALAD. Less important were variables age (Z_1) and lead exposure corrected for total employment time (Z_3).

The third factor was defined explicitly by the frequency of previous lead poisoning (Z_4), hipurane renal flow (Z_7), EP (Z_{10}) and rather less by age (Z_1).

The fourth factor was composed dominantly of the variables lead exposure without (Z_2) or with correction for total employment time (Z_3), and of the less dominant variables creatinine clearance (Z_6) and EP ($_{10}$).

As factor analysis in the field of occupational toxicology has not yet been utilised in this country we will merely discuss its possibilities and limits. Modern methods of statistical analysis, including factor analysis, are a powerful means in the hands of experts. However, during the transformation of variables into factors i.e. from simple into complex information, they may lose certain subtle correlations which can be seen if we compare the empirical correlation of a matrix with factor matrix and separately with the Varimax rotated factor matrix. In the desire for greater homogeneity of the variables which we wish to examine, it is possible to lose insight of the possible poorly comprehensible and still unidentified relations between several complex variables. However, it must be acknowledged that this conditional deficiency is greatly compensated by the better visibility of basic interrelations in examining complex systems.

DISCUSSION

Our results confirm the existence of late, i.e. delayed adverse effects of previous occupational lead poisoning on kidney function later in life. This is certainly not an isolated occurrence, but is a result of the complex interaction of past lead poisoning, duration of lead exposure, age and age dependent physiological increase in blood pressure, serum creatinine and diminished kidney function capacity manifested as a decrease of glomerular filtration rate and tubular secretory function. When interpreting the results of our investigation the relatively small sample should be taken into account, so that the conclusions of this analysis can be considered preliminary.

Our results are in agreement with the assumption that kidney impairment depends on the duration and magnitude of lead exposure and total lead body burden (8, 9, 28, 49). Depending on the »dose rate«, i.e. concentration of lead and the duration of lead exposure, a relevant spectrum of pathomorphological renal changes has been described (10, 13, 14). Although *Lilis and co-workers* (17) believe that the harmful effect of lead on kidney function is not age-dependent the toxicity of xenobiotics is known to increase with age (50). Our findings on the complex interdependence of lead exposure, lead poisoning and age-dependent involutive changes which, due to the presence of lead appear earlier, link these two apparently contradicting claims. According to the modern functional clinical classification (44, 45) applied in this investigation, in poisoned workers we frequently found diminished kidney reserve as the first degree of chronic kidney insufficiency. *Radošević and co-workers* (9) examined kidney function in persons acutely poisoned with lead and found increased incidence of transitory functional damage which they attributed to a hypothetic vasoconstrictive effect of lead. The same standpoint was taken somewhat later by *Lilis and co-workers* (11, 12). More recent investigations on the renin and angiotensin system in acute lead poisoning have not confirmed such a hypothesis (51, 52). However, lead blocks the functions mediating by beta adrenoreceptors (53) and stimulates alpha adrenoreceptors (54). The latest results indicate that chronic exposure to low lead concentrations increases cardiovascular sensitivity to neurogenic mediators of blood pressure (55).

In our subjects kidney function impairment was more frequently present than an increase in systolic and diastolic pressure (33). These findings corroborate the assumptions of *Lilis and co-workers* (12) and *Batuman* (23) that impaired kidney function in lead poisoned workers precedes the late occurrence of hypertension.

We found the variable of blood pressure in factor I of the Varimax rotated matrix together with age, duration of lead exposure, previous lead poisoning, creatinine clearance and the hipurane renal flow. The measured level of blood lead did not belong to this factor, which is an interesting finding with regard to the discussion on the relation between the blood lead level in environmentally exposed populations and the occurrence of increased blood pressure (24, 26).

It can be assumed that in the series of events leading to impaired kidney function and increased blood pressure the present level of lead in blood is one or more steps »further« than the pathomorphological substrate (end organ failure) induced by earlier excessive accumulation of lead. Impaired kidney function can have an insidious onset or may develop as a consequence of gradual exposure to harmful xenobiotics such as lead in the kidney parenchyma. This phenomenon can be seen years after the person has been exposed to lead, which indicates the possibility of immunological involvement (56). According to our investigation a reduction in the total lead body burden is a dominant factor in the prevalence of late kidney impairment (28).

The frequency of kidney function disorders indicates that the kidney is a critical target organ in conditions of chronic exposure to lead (57). We, therefore, consider regular surveillance of kidney function in lead exposed workers to be important part of general health surveillance especially in respect to the prevention of major kidney impairment in later life.

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Sažetak

ODGOĐENI UČINCI OLOVA NA BUBREGE – FAKTORSKA ANALIZA

Pojavu kasnih (odgođenih) oštećenja funkcije bubrega ispitali smo u radnika koji su ranije u životu bili otrovani olovom. Pozitivna kontrola bili su radnici izloženi olovu koji nikada nisu bili otrovani tim metalom. Pomoću faktorske analize dobivena su četiri značajna faktora iz 22 pojedinačne varijable za koje se pretpostavlja da su vezane uz pojavu kasnih (odgođenih) oštećenja funkcije bubrega olovom. Prvi faktor čine varijable funkcije bubrega, krvnog tlaka, dobi, trajanja izloženosti olovu i broja ranijih otrovanja olovom. Drugi faktor dominantno čine varijable trajanja izloženosti olovu i bioloških pokazatelja izloženosti olovu. Treći faktor povezuje učestalost ranijih otrovanja olovom s vremenom protoka hipurana kroz bubrege, eritrocitnog protoporfirina i dobi. Četvrti faktor grupiran je oko varijabli radnog staža, klirensa kreatinina i eritrocitnog protoporfirina. Rezultati potvrđuju pretpostavku kako je ranije preboljelo profesionalno otrovanje olovom kasnije u životu praćeno funkcionalnim oštećenjem bubrega. Kasni (odgođeni) učinci olova na bubrege rezultat su složene interakcije međusobno povezanih varijabli: ranije u životu preboljelog otrovanja olovom, ukupnog vremena provedenog u radu s tim metalom, dobi i dobi pripadajućim promjenama porasta sistoličkog i dijastoličkog krvnog tlaka, porasta sistoličkog i dijastoličkog krvnog tlaka, porasta razine kreatinina u krvi te pada vrijednosti klirensa kreatinina i brzine protoka hipurana kroz bubrege. Stoga se može zaključiti kako je bubreg kritični ciljni organ u metabolizmu ekskrecije olova iz organizma te da praćenje njegove funkcije treba uključiti u skup obaveznih indikatora biološkog nadzora profesionalno izloženih radnika.

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Ključne riječi: dob, izloženost olovu, klirens kreatinina, krvni tlak, odgođeno oštećenje bubrega, olovo u krvi, profesionalna izloženost, protok kipurana