Scand J Work Environ Health 1983;9(5):431-441

<https://doi.org/10.5271/sjweh.2399>

Issue date: Oct 1983

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This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/6143397

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Neurophysiological effects of lead exposure

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ROSÉN I, WILDT K, GULLBERG B, BERLIN M. Neurophysiological effects of lead exposure. *Scand j work environ health* 9 (1983) 431–441. A series of neurophysiological variables was measured for men occupationally exposed to lead. The results were related to the degree of lead exposure and to the concentrations of lead and zinc protoporphyrin in blood. A small but significant correlation was observed between lead exposure and motor and sensory conduction velocities in the lower limbs, the conduction velocities of slow motor fibers in the upper limbs, and also sensory nerve action potentials. It is suggested that a neurophysiological examination should be considered in the surveillance of the health of lead workers.

Key terms: lead in blood, nerve conduction, zinc protoporphyrin in blood.

Several independent groups of investigators have reported that workers exposed to lead, though free from neurological symptoms, may nevertheless show signs of impaired transmission in peripheral nerves (1, 11, 30, 33). This phenomenon may also occur at blood lead (Pb-B) levels that are considered to be free from risk (2, 29, 31, 32). Any connection between such demonstrable changes in the function of peripheral nerves and the possible risk of a subsequent clinically manifest polyneuropathy is arguable (8, 9), but, even if such a connection remains to be established, changes in nerve conduction velocity in individuals exposed to lead are evidence of a biological effect at moderately elevated exposures.

The lead-exposed workers who were the subjects of the present investigation were employed in a Swedish storage battery factory. A health investigation involving kidney function and blood pressure (34) could not establish any adverse changes in these workers. A neurological and neuro-

physiological examination (20) involving a clinical neurological investigation, a determination of motor nerve conduction velocity of the median nerve, and measurement of the sensory vibration threshold gave no support for the presence of any impaired nerve function in these workers.

For some years the surveillance of work conditions in this factory has included regular determinations of lead in air and Pb-B. More recently the measurement of zinc protoporphyrin (ZPP) in blood was included. Since Lamola et al (22, 23) reported a correlation between increased ZPP and Pb-B values among workers exposed to lead, several reports on a correlation between Pb-B levels and increased ZPP values in lead-exposed workers have appeared in the literature. An increase in ZPP is a sign of a deficient incorporation of iron into the heme system, the deficiency depending perhaps on a direct effect of lead on the enzyme ferrochelatase or on a dysfunction of the intramitochondrial transport of iron in the blood-forming tissues (21).

The aim of the present investigation was first to ascertain whether there is any relation between neuronal function and the extent of lead exposure. Second, it seemed of interest to seek a correlation between the measured results and the Pb-B and ZPP values, a comparison that might indicate whether a biological re-

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sponse in the form of a ZPP increase might correspond with changes in nerve function.

Material and methods

Subjects

The storage battery factory had a working population of 260 men and 40 women; this population has been described in more detail elsewhere (36). Exposure to lead has been assessed by regular measurements of lead in air at the workplaces and, for selected individuals, by means of personal samplers. The following grades of lead exposure have been established:

Grade 0: outside manufacturing areas with lead in air within normal urban values.

Grade 1: lead in air never exceeding 0.03 mg/m³.

Grade 2: lead in air occasionally exceeding 0.03 mg/m³, but never as high as 0.1 mg/m³.

Grade 3: lead in air in excess of 0.1 mg/m³. A respiratory filter or fresh air mask is recommended.

Since 1968 the surveillance of the workers has been reinforced by regular Pb-B measurements. If the Pb-B level of a worker exceeded 3.37 $\mu\text{mol/l}$ (70 $\mu\text{g}/100\text{ ml}$), he was removed from exposure until the level fell to 1.92 $\mu\text{mol/l}$ (40 $\mu\text{g}/100\text{ ml}$). A man with a Pb-B value of 2.41 $\mu\text{mol/l}$ (50 $\mu\text{g}/100\text{ ml}$) continued to work while action was taken to limit exposure. After 1977 these limits were reduced to 2.89 $\mu\text{mol/l}$ and 2.17 $\mu\text{mol/l}$ (60 and 45 $\mu\text{g}/100\text{ ml}$, respectively). Since 1977 ZPP has also been recorded.

Determination of blood lead

Venous blood samples were taken in specially cleaned lead-free vacutainers, and the lead content was measured by atomic emission spectroanalysis. Samples were taken for the whole staff at least every other month; for women and workers with a Pb-B value exceeding 2.41 $\mu\text{mol/l}$

(50 $\mu\text{g}/100\text{ ml}$) [2.17 $\mu\text{mol/l}$ (45 $\mu\text{g}/100\text{ ml}$) after 1977] samples were taken monthly. All analyses were performed by a laboratory authorized by the Swedish Labor Protection Board, which requires participation in scheduled national and international controls. Before the start of the present investigation a comparison was made between this laboratory and another authorized laboratory in Sweden; each laboratory analyzed one-half of 441 blood samples drawn from the battery storage factory workers. The results of the lead analyses from the two laboratories corresponded well, and the correlation coefficient was 0.941. When samples were not taken, the background of 14 $\mu\text{g}/100\text{ ml}$ (0.68 $\mu\text{mol/l}$) for an urban population was assumed.

Determination of zinc protoporphyrin in blood

The ZPP concentration of untreated fresh capillary blood on a cover slip was determined by means of a hematofluorometer (AVIV type 133). This apparatus operates according to the "front surface optic" principle with an exciting wavelength of 425 nm, which gives rise to a fluorescence from the ZPP-globin molecule with a wavelength of 595 nm. Further details of the process have been given elsewhere (6, 13, 14, 17, 19).

Groups studied

The workers were selected for the investigation on the basis of their Pb-B values over the two years prior to 1979. Not all of them had been employed in the industry for the same period of time. They were divided into the following three groups:

Group L (low exposure): 16 individuals. Median age 35.5 (range 22–61) years. Exposure time 18–336 months. Mean Pb-B values for the last year not exceeding 1.2 $\mu\text{mol/l}$ (25 $\mu\text{g}/100\text{ ml}$) with no individual value over 1.44 $\mu\text{mol/l}$ (30 $\mu\text{g}/100\text{ ml}$).

Group M (medium exposure): 8 individuals. Median age 35.5 (range 24–61) years. Exposure time 29–312 months. Pb-B values between those of group L and group H. Five members of this group were

selected because they had unusually high ZPP values.

Group H (high exposure): 15 individuals. Median age 36.0 (range 22–55) years. Exposure time 6–318 months. Pb-B for the last year averaging more than 1.92 $\mu\text{mol/l}$ (40 $\mu\text{g}/100\text{ ml}$) with some values exceeding 2.65 $\mu\text{mol/l}$ (55 $\mu\text{g}/100\text{ ml}$).

Table 1 shows the history of the selected groups during the previous eight years.

Clinical investigation

All individuals in the groups were examined clinically according to current Swedish regulations (26) which require monthly tests to be made on those with Pb-B values elevated as previously defined. Those with lower exposure and with no clinical signs of a biological response that might be attributed to lead were subjected to the examination three to six times yearly. All of the employees also had an opportunity to seek medical advice at the company health center; on the average 2.0 visits per individual per year were recorded; this number is somewhat in excess of the average for this occupational health center (1.2 visits). A search was made through the medical records of the subjects and through notes taken during consultations with nurses. Subjects with known alcohol abuse were excluded from the study. One man exposed to lead for five years had worked earlier as a paint-sprayer for seven years. As all clinical records were within the expected range, this subject was not excluded. In five cases a suspicion of a somewhat high alcohol consumption was noted. No record could be found of diseases such as diabetes, chronic kidney insufficiency, etc., that might reasonably be thought to influence the neurophysiological variables. Seven members of the groups had never

required medical treatment, and 12 of them never or only rarely consumed alcohol. Blood samples were taken for the measurement of gamma glutamyl transferase ($\gamma\text{-GT}$) activity by the method of Szasz (35); this parameter is regarded as an indicator of intrahepatic cholestasis, infiltrative liver disease, or chronic alcoholism.

Neurophysiological methods

The 22 neurophysiological variables that were studied are shown in table 2. The group members were subjected to the tests for all these variables on the same occasion at the Department of Clinical Neurophysiology, University Hospital, Lund, during the first quarter of 1979. At the start of each investigation the skin temperature of the hands and feet was measured, and the subjects were warmed by heating pads and heating lamps if the temperature was below 30°C.

The electrophysiological investigations were made with a Disa 1500 electromyographic apparatus, provided with two constant current stimulators with a facility for varying the time interval between stimuli.

Motor conduction studies. The maximal motor conduction velocity was measured for four motor nerves (ulnar, variable 1; median, variable 2; fibular, variable 3; posterior tibial, variable 4). The compound muscle action potential was recorded with surface electrodes over the appropriate distal muscle area (hypotenar, thenar, extensor digitorum brevis, abductor hallucis), and the position of the active electrode was adjusted until the initial phase of the muscle action potential showed a single negative component. In addition the distal latencies were measured for the

Table 1. History of the studied groups in 1971–1979. The figures indicate the number of workers exposed in each group each year. (L = low, M = medium, and H = high exposure)

Group	1979 January– March	1978 July– December	1978	1977	1976	1975	1974	1973	1972	1971
L	16	16	16	16	13	8	6	6	5	5
M	8	8	8	8	7	5	5	3	3	2
H	15	15	15	14	12	9	6	5	5	5

Table 2. Age-adjusted values of the neurophysiological variables. The results of the statistical test, as described in the text, are shown to the right. (NS = not significant, L = low exposure, M = medium exposure, and H = high exposure)

Variable	Unit of measure	Group			Significance
		L	M	H	
1 Motor conduction velocity, ulnar nerve	m/s	58.12	56.40	56.97	NS
2 Motor conduction velocity, median nerve	m/s	56.94	58.09	55.81	NS
3 Motor conduction velocity, fibular nerve	m/s	48.06	47.11	45.71	p = 0.019
4 Motor conduction velocity, posterior tibial nerve	m/s	45.74	46.67	43.95	NS
5 Motor conduction velocity, slow fibers, ulnar nerve	m/s	43.25	39.13	40.73	NS
6 Sensory conduction velocity, median nerve, digit I	m/s	48.67	48.67	48.67	NS
7 Sensory conduction velocity, median nerve, digit III	m/s	53.73	55.37	55.37	NS
8 Sensory nerve action potential, amplitude, median nerve, digit I	μV	32.20	30.62	21.81	p = 0.013
9 Sensory nerve action potential, amplitude, median nerve, digit III	μV	23.18	21.61	15.84	p = 0.023
10 Sensory refractory period, median nerve, digit III	ms	1.01	0.92	0.91	p = 0.048
11 Sensory conduction velocity, sural nerve	m/s	49.11	43.12	43.12	p = 0.022
12 Sensory nerve action potential, amplitude, sural nerve	μV	10.75	8.54	6.92	p = 0.04
13 Warm-cold difference limen, thenar	°C	4.38	5.57	4.17	NS
14 Warm-cold difference limen, chin	°C	2.96	3.76	3.44	NS
15 Warm-cold difference limen, foot	°C	8.56	10.56	9.85	NS
16 Vibration threshold, hand	μm	0.44	0.37	0.49	NS
17 Vibration threshold, foot	μm	0.84	1.58	1.34	NS
18 Difference in motor conduction velocity, fast-slow fibers, ulnar nerve (variables 1–5)	m/s	15.12	17.92	16.05	NS
19 Distal motor latency, median nerve	ms	3.76	3.84	3.72	NS
20 Distal motor latency, ulnar nerve	ms	2.97	2.82	2.82	NS
21 Electromyogram, duration	ms	11.00	11.00	10.46	NS
22 Electromyogram, amplitude	μV	393.5	413.6	370.6	NS

motor nerves of the hand (variables 19 & 20).

The conduction velocity for slow motor nerve fibers (MCV_s), variable 5, was determined for the ulnar nerve by the collision technique (18); the MCV_s was calculated from the expression $MCV_s = d/(T-1)$, where d is the distance between the cathode at the wrist (stimulus 1) and at the elbow (stimulus 2), and T is the time interval between stimuli 1 and 2 at the shortest interval that produces a maximal response after stimulus 2. The refractory period was estimated to be 1 ms. The strength of both stimulus 1 and stimulus 2 was 50 % above the strength producing a maximal response at each stimulus site (7). The difference between the maximal and minimal conduction velocities of the ulnar nerve was determined as a separate variable (variable 18).

Sensory conduction studies. Sensory nerve action potentials were recorded with needle electrodes from the median nerve at

the wrist and with surface electrodes from the sural nerve at the lateral malleolus. The position of the needle electrode in relation to the median nerve was determined by the amount of stimulus current (pulse duration 0.3 ms) required to produce an electromyographic response in the abductor pollicis muscle (0.8–1.1 mA in the present study). Maximal sensory nerve conduction velocities were determined from the latency and distance from the stimulus site at fingers I and III and the calf (variables 6, 7, 11, respectively). In addition the sensory response amplitudes were determined (variables 8, 9, 12).

For the assessment of whether the refractory period for myelinated nerve fibers was related to the degree of exposure to lead, the absolute length of this period in the median nerve (variable 10) was measured by needle sensory neurography and a double stimulus at digit III, the stimulus strength being 50 % in excess of the strength producing a maximal action potential.

Electromyograms were recorded with a concentric needle electrode at three different sites in the anterior tibial muscle during a weak voluntary contraction and also during complete rest. The electromyographic signals were recorded on tape and subsequently analyzed by a computer with automatic motor-unit separation. This procedure gave a measure of the mean discriminated motor-unit potentials (24, 28). Mean amplitudes and mean durations of the discriminated motor-unit potentials were included as variables 21 and 22. The presence of denervation activity in muscle at rest was detected by direct inspection of the playback of the signal on an oscilloscope.

Psychophysical thresholds. Vibrametry was carried out by the method of Goldberg & Lindblom (16) by application of vibrations of 100 Hz to the carpus and tibia on one side (variables 16 & 17). Temperature sensitivity was measured by the assessment of the warm-cold difference limen with the method of Fruhstorfer et al (15). Three different sites were measured (the-
nar, variable 13; chin, variable 14; lateral edge of the foot, variable 15).

Statistical methods

All statistical tests were based on logarithmic neurophysiological data. Age and

γ -GT values were introduced as covariates so that a correction could be made for these variables in regard to normal biological variations and possible toxic effects caused by alcohol. A covariance model with ordered exposure-response alternatives (4) was used in the analysis of differences between the three exposure groups or between the groups based on workplace category. In another approach the grouping was dissolved, and a stepwise multiple regression was applied using each individual Pb-B or ZPP value, as well as the individual effect variables, analysis by a continuous dose-response model on accumulated data thus being enabled. Stepwise discriminant analysis by Wilks' method (25) was applied in the classification of the workers, according to the neurophysiological variables, into their exposure groups.

Results

Blood lead

Fig 1 shows the range of annual mean Pb-B values for individuals in the three exposure groups, these values being derived from six Pb-B measurements taken throughout the year. The columns indicate the group means. It is apparent that the separation between groups L and H is pronounced throughout the whole eight-

Fig 1. Mean blood lead (Pb-B) values of the exposed groups in 1971–1979 (78* = mean values for the last three months of the year). The vertical lines indicate the ranges of individual means; the column heights are group means; the numerals below the columns are the numbers of individuals controlled. (L = low, M = medium, and H = high exposure)

Fig 2. Exposure of groups L, M and H to lead. Columns indicate an estimate of the mean percentage of work time spent by the groups in lead exposure zones 0, 1, 2, 3. (GRP = group)

Fig 3. Mean ZPP (zinc protoporphyrin) values of the exposed groups in 1977–1979 (78* = mean values for the last three months of the year). The vertical lines indicate the ranges of individual log means; the column heights are group log means. (L = low, M = medium and H = high exposure)

year period, while group M shows a considerable overlap with the other two groups. A trend towards increased Pb-B values up to 1978, when the selection was made, is

apparent, presumably due to rather high values in recently employed personnel. The work activities of the three groups have been analyzed over the period 1975–1979, and the time spent in each of the four workplace categories 0, 1, 2, 3, as already defined, has been estimated on the basis of the lead concentration in the air. Residence in category 0 was in some cases due to closure of the plant or to holidays. The distribution shown in fig 2 gives an indication of the mean exposure of the three groups.

Zinc protoporphyrin in blood

The mean annual concentration of ZPP in blood is shown for the three groups in fig 3. As with Pb-B in fig 1, there is a clear separation in 1978 and 1979 of the ranges in groups L and H, while group M shows a considerable overlap with the other two.

Gamma glutamyl transferase activity

The γ -GT assays from blood gave the following median values: 0.39 (range 0.1–1.8) μ kat/l for group L (N = 16), 0.38 (range 0.1–1.2) μ kat/l for group M (N = 7), and 0.39 (range 0.1–1.6) μ kat/l for group H (N = 14). Values exceeding 1.0 μ kat/l were considered pathological. One individual from each of the groups M and H was not available for the test. Pathological values were found for one individual from each group.

Neurophysiological measurements

The results obtained from measurements of the 22 neurophysiological variables are arranged in table 2 according to the three groups of subjects. As age exerts a significant influence on neurophysiological variables, the means have been adjusted to exclude the effect of age. Table 2 includes the adjusted means and the significance of the association between exposure and effect calculated by covariance analysis.

A significant association was found for the following neurophysiological variables: motor conduction velocity, fibular nerve; sensory nerve action potential, amplitude, median nerve, digit I; sensory nerve action potential, amplitude, median

nerve, digit III; sensory refractory period, median nerve, digit III; sensory conduction velocity, sural nerve; sensory nerve action potential, amplitude, sural nerve. The age-adjusted individual values for motor conduction velocity, fibular nerve; sensory nerve action potential, median nerve, digit I; and sensory refractory period, median nerve, digit III, make a significant contribution to the separation between the groups ($p < 0.006$). Of the 15 subjects in group L, 12 were classed correctly into group L, and the number of false positives was consequently 3. Substantially the same exposure-response relationship was obtained when γ -GT values were included as a variable in addition to age. Covariance analysis

Discriminant analysis of the data indicated that motor conduction velocity, fibular nerve; sensory nerve action potential, median nerve, digit I; and sensory refractory period, median nerve, digit III, make a significant contribution to the separation between the groups ($p < 0.006$). Of the 15 subjects in group L, 12 were classed correctly into group L, and the number of false positives was consequently 3. Substantially the same exposure-response relationship was obtained when γ -GT values were included as a variable in addition to age. Covariance analysis

Fig 5. Measured values, corrected for age, for variable 8 [sensory nerve action potential amplitude (SA), median nerve, digit III] of the three lead exposure (exp) groups. The horizontal lines indicate group means.

Fig 4. Measured values, corrected for age, for variable 3 [motor conduction velocity (MVC), fibular nerve] of the three lead exposure (exp) groups. The horizontal lines indicate group means.

Fig 6. Measured values, corrected for age, for variable 10 [sensory refractory (SR) period, median nerve, digit III] of the three lead exposure (exp) groups. The horizontal lines indicate group means.

showed a significant relationship with the following variables: motor conduction velocity, fibular nerve; sensory nerve action potential, amplitude, median nerve, digit I; sensory nerve action potential, amplitude, median nerve, digit III; sensory nerve action potential, amplitude, sural nerve. No such correlation was found with sensory refractory period, median nerve, digit III, or sensory conduction velocity, sural nerve. The falling off of correlation can be attributed to the absence of two individuals from the test, an occurrence which led to a diminished strength for the test.

Covariance analysis showed a significant relationship between the exposure grades 0, 1, 2, and 3 at the workplace and the following variables: motor conduction velocity, slow fibers, ulnar nerve ($p < 0.02$); sensory nerve action potential, amplitude, median nerve, digit I ($p < 0.05$); sensory nerve action potential, amplitude, median nerve, digit III ($p < 0.004$). Stepwise regression analysis enabled an estimate to be made of the cumulative exposure period that gave the greatest weight to the correlation between the mean continuous lead exposure and the neurophysiological measurements. Two years gave the best correlation with the variables motor conduction velocity, fibular nerve ($p < 0.01$), and sensory nerve action potential, amplitude, median nerve, digit III ($p < 0.025$). For the variable sensory nerve action potential, amplitude, sural nerve, three years gave the best correlation ($p < 0.05$); and with the variable sensory nerve action potential, amplitude, median nerve, digit I, the best correlation was found for five years ($p < 0.025$).

When the ZPP measurements were analyzed by stepwise regression techniques, a significant correlation was apparent with the following variables: motor conduction velocity, fibular nerve ($p < 0.05$); motor conduction velocity, slow fibers, ulnar nerve ($p < 0.025$); difference in motor conduction velocity, fast-slow fibers, ulnar nerve ($p < 0.025$). The greatest weight with the last two variables was observed when only the 1978 figures were considered. As the subjects showed fairly stable values for both Pb-B and ZPP over the study periods, there are difficulties in interpreting the significance of the various exposure periods (the so-called multicollinearity).

A significant correlation was also found between the ZPP measurements and the variables warm-cold difference limen, chin ($p < 0.025$), and warm-cold difference limen, foot ($p < 0.05$). No other tendency towards an effect on these variables was observed in this investigation, and it is possible that the apparent effect was due to chance.

As can be seen in table 2, there was no tendency towards neurogenic electromyographic changes, ie, prolongation of duration or increase in the amplitude of the motor potentials with increasing exposure to lead.

Discussion

This investigation on workers occupationally exposed to lead demonstrated a small but significant correlation between Pb-B levels and measured neurophysiological variables for motor and sensory conduction velocities in nerves of the lower limbs, which were the longest of the nerve fibers investigated. This correlation could be demonstrated in spite of the low statistical power of our test, which was due to the moderate number of individuals we were able to examine. A significant connection was also established between an increase in blood ZPP and a decrease in motor conduction velocity in the fibular nerve and in the slow conducting fibers of the ulnar nerve. The upper limbs showed no such changes in maximal motor conduction velocity; this finding is in line with the results of an earlier investigation in the same industry (20) and those of a more recently published study (27). These findings are in agreement with the observation that the nerves of the lower limbs are more vulnerable to the milder forms of polyneuropathy (12).

Our results are somewhat different from those presented by Seppäläinen et al (32) for a similar group of workers. They found significant changes in the distal motor latency, sensory conduction velocity, and motor conduction velocity of slow fibers of the median nerve in addition to a decrease in motor conduction velocity of slow fibers of the ulnar nerve and in the motor conduction velocity of the posterior tibial nerve.

We found a decrease in the motor conduction velocity for the slow ulnar nerve fibers at higher values of ZPP and also at higher concentrations of lead in air at workplaces. As the measured refractory period for the thick myelinated fibers in the median nerve shows a tendency to decrease in exposed groups (fig 6), the reduction in velocity of the slow motor nerve fibers can presumably not be attributed to a lengthening of the refractory period but is probably related to a true reduction in impulse velocity in these fibers.

A variable that, in our investigation, uniformly decreased in magnitude with increasing exposure was the amplitude of the sensory action potential in both the median and the sural nerve. It is customary in clinical neurophysiology to interpret the sensory amplitude as a measure of the population of functioning axons, and a reduction may be an indication of axonal degeneration (10). Nothing, however, in this investigation indicated an axonal degeneration of any significance. No denervation activity emerged from the electromyographic investigation, and no sign of neurogenic changes from the automatic analysis of electromyographic activity. Among the sensory variables no significant changes were recorded in either vibration threshold (function of thick myelinated sensory fibers) or in the temperature discrimination threshold (function of thin myelinated and unmyelinated fibers). As microscopic studies have not revealed any structural myelin changes at the lead exposures under investigation, it has been suggested that the observed neurophysiological changes may derive from functional changes in the properties of the nodal membrane, a phenomenon leading, for example, to a changed time course for the action potential (5, 8, 9). Such a functional change might lead to an increased temporal dispersion of the compound sensory nerve action potential and a decrease in its amplitude, as was observed in the lead-exposed groups of the present investigation. The tendency towards a decrease in the refractory period with increased Pb-B values may provide support for the idea of an underlying functional change. Further support for the observed effects being attributable to functional changes rather than to the first stages of polyneuro-

pathy derives from the observation that the nerve conduction velocity is improved by the reduction of lead exposure (3). A case of lead intoxication that was followed by a rapid increase in conduction velocity after cessation of the previous extremely high intake of lead has also been observed recently in this laboratory. Our results indicate that the outcome of the neurophysiological tests is influenced the most by the lead exposure occurring immediately prior to the examination. We were not able to demonstrate any cumulative effect of earlier exposure. Although the regression analysis was done independently of the primary grouping of the workers, the small number of examined workers and the fact that there was a considerable intra-individual variation in exposure by time are likely to weaken the power of this test.

This investigation has shown that sub-clinical effects on measured neurophysiological variables can be found even at relatively moderate exposure to lead. In our view this conclusion requires that a careful awareness be exercised during all occupational exposures to lead, particular attention being given to the frequency of surveillance and control measures. Neurophysiological examination should be considered in the surveillance of substantial lead exposure. This consideration is of particular importance if it is suspected that individuals are being exposed to other risks, for example, solvents or excessive alcohol consumption. Because the neurophysiological effects are so discrete, it is desirable that the subjects be examined before the start of exposure. On the basis of our results we propose that a neurophysiological examination should include motor neurography of the lower limbs, the measurement of the motor conduction velocity of slow fibers in the upper limbs, and also measurement of sensory action potential amplitudes.

Acknowledgment

The investigation has been supported financially by the Swedish Work Environment Fund, project no 78/64, and the Swedish Medical Research Council, project no B81-14x-00084-17C.

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Received for publication: 25 January 1983