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16. Abstract (Limit: 200 words)

Peripheral neurotoxicity associated with exposure to inorganic mercury (7439976) vapors was investigated. Clinical neurological evaluations, nerve conduction evaluations, and medical questionnaires and interviews were conducted at three chloralkali factories (SIC-2812). Of the 138 workers examined, 77 had significant potential exposures to mercury. All subjects had been in a mercury control program wherein individuals with monthly spot sample urine mercury concentrations exceeding 50 milligrams per liter were removed from exposure. Of 138 workers, 18 had mild sensory disturbances that were evidenced by significantly reduced clinical distal vibratory and pin sensation, reduced distal strength, and reduced muscle stretch reflexes. Significant differences were also see in tests of vibration, touch, and two point discrimination. Affected subjects were older (average age of 43) and had an average of 13 years on the jobs, compared with an average age of 33 and 8 years on the job for normal subjects. Electrodiagnostic abnormalities were more frequent in subjects with polyneuropathy. Subjects with clinical evidence of polyneuropathy had higher mercury urine indexes. The authors conclude that elemental mercury exposure is associated with a clinically significant sensorimotor polyneuropathy. The degree of neurologic impairment is related to the magnitude of exposure.

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ELEMENTAL MERCURY POLYNEUROPATHY

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POLYNEUROPATHY FOLLOWING INDUSTRIAL EXPOSURE TO INORGANIC MERCURY

INTRODUCTION

Mercury peripheral neurotoxicity has been described (1-7) although most previous reports have emphasized central effects (8-11). Electrodiagnostic evaluation of chlor-alkali plant workers has suggested that inorganic mercury vapor exposure can affect both motor and sensory peripheral nerve conduction, the degree of involvement related to time-integrated urine mercury levels (12). Our preliminary study (12), however, did not report clinical evaluation following industrial exposure. The study reported here employed clinical neurological evaluation and more complete nerve conduction evaluation of 138 chlor-alkali plant workers.

METHODS

Subjects

Three chlor-alkali plants which use metallic mercury in the production of chlorine were selected as sites for this study. Employees (both exposed and

non-exposed) completed a medical questionnaire and were interviewed to identify individuals with toxic exposure (other than mercury) or medical disorders potentially associated with neuropathy, including diabetes, renal disease, peripheral vascular disease, excessive alcohol use, or trauma. Employees so identified were excluded from further evaluation. Remaining employees underwent neurologic and electrodiagnostic examination, as part of an evaluation of overall performance.

A total of 138 subjects were examined. Of these, 77 subjects had significant potential exposure to mercury in their jobs. 61 subjects (controls) had no significant exposure. Table 1 gives statistics for exposed and control group urine mercury, age, height and weight. Urine mercury levels shown in Table 1 were determined from spot samples taken on the day subjects were examined.

All subjects had been included in a mercury control program (13, 14) wherein individuals with monthly spot sample urine mercury levels exceeding 0.50 mg/L were removed from mercury exposure. Urine mercury records were available for three years prior to evaluation, or for the duration of employment if less than three years. Examiners had no indication of exposure levels, and different examiners performed neurologic, electrodiagnostic, and urinary mercury evaluations.

For purposes of statistical analysis in this study, urine mercury indices were derived for each subject, based on his history of monthly determinations. Indices for each subject included the following:

- Average urine mercury concentrations over the past 3, 6, 12 or 24 months,
- The number of peak concentrations exceeding 0.25 and 0.5 mg/L in the

previous 6, 12, 24, or 36 months

Such historical indices were used to improve reliability in estimating each subject's long term exposure to metallic mercury.

(Insert Table 1 about here.)

One particular concern with cross-sectional field studies is, of course, the possibility of confounding, and therefore confusing the effects of exposure with effects of extraneous factors such as age. As shown in Table 1, the average age of the exposed group was slightly greater than that of the control group. The exposed group also had a slightly higher average weight. As explained in a later section, potential confounding in student-t test comparisons was controlled by selection and age matching of subjects in case-control studies. Across the entire range of subjects' urine mercury indices, however, there was no evidence of correlation between urine mercury and age, height, weight or reported alcohol intake. Thus there is little reason to suspect confounding in correlation and regression analyses used to explore the relationship between urine mercury and neurologic and electrodiagnostic examination results. Table 2 shows the correlation coefficients between urine mercury indices and potential confounding variables. They are all very low and statistically insignificant.

Urine mercury concentrations were determined using methods which have previously been described (12, 17). Split samples were frequently used in the monthly sampling programs for interlaboratory validation. The correlation between laboratories was generally greater than $r = .95$ (18).

(Insert Table 2 about here.)

Clinical Examination

Neurologic examination was performed on all subjects and graded subjectively by the same examiner. The results of the clinical neurologic examination were reported as normal, equivocal sensory and/or motor abnormality, sensory and/or motor polyneuropathy (mild, moderate, or severe), or other (mononeuropathy, radiculopathy, etc.).

Semi-Quantitative Measure of Neurologic Function

Several quantitative tests of peripheral neurologic function were obtained following the clinical examination including grip strength, two-point discrimination, and vibratory, pin and touch sensation (15).

Dominant upper extremity grip strength was determined using a Jamar hand dynamometer as the maximum force for three - five second trials (kg).

Two-point discrimination was determined for the dorsum of the dominant index finger and dorsal-lateral aspact of the ipsilateral foot. Sweet's two-point compass calibrated in millimeters (mm) was used. Beginning with the index finger, the subject was given a recognizable stimulus of 10 mm. Separation was decreased by 1 mm per trial until three consecutive responses of one point at the measurement. If this was the threshold value, the subject correctly recognized the next increment of 0.5 mm. This was repeated on the foot beginning with a 30 mm separation, decreasing by approximately 2.5 mm per trial as described above. Once the descending threshold was defined, the

subject had to correctly recognize the next increase of 2.5 mm.

Vibratory sensation was determined for the dominant index finger and great toe using a 128 Hz tuning fork. The subject reported when vibration could no longer be felt, and the difference (seconds) between the examiner's and subject's threshold for the index finger was recorded as the average of the last two of four trials. This was repeated recording the difference in the subject's threshold at the toe to the examiner's index finger threshold as described above.

Pin sensation was graded subjectively in the conventional clinical examination. Subjects then determined whether a stimulus at the index finger was equal to, less than, or greater than a stimulus of approximately equal intensity at the upper forearm and asked to subjectively estimate the percentage the smaller response was of the greater, if they were different. This was repeated for the dorsum of the great toe and the upper calf. Responses were recorded as a ratio of the distal to proximal intensity, or 1.00 if the intensities were perceived as equal.

Touch sensation was recorded using a commercially available pressure anesthesiometer (Research Media, Inc.). Stimuli were delivered to the dorsum of the dominant index finger and great toe. Subjects were forced to identify in which of two time intervals the stimulus was delivered beginning with a readily identifiable stimulus. Progressively smaller stimuli were presented until an error was made. That stimulus was repeated (five trials), randomly presenting it either the first or second time interval (forced choice). If all five responses were correct, the next smaller stimulus was used and the sequence repeated until a stimulus was identified for which one or more responses were correct, the next smaller stimulus was used and the sequence

repeated until a stimulus was identified for which one or more responses were incorrectly reported. The next largest stimulus was then repeated and this taken as the threshold value if the subject correctly recognized all five trials.

Nerve conduction studies were performed on the right ulnar (motor and sensory), median (sensory), peroneal (motor), and sural (sensory) nerves using conventional techniques (16). Distal upper and lower extremity surface temperatures were measured for all subjects and the extremities were warmed if less than 31 degrees C. Compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) negative peak amplitude, distal latency, and maximum conduction velocity were measured. If the ulnar SNAP was superimposed upon the motor response, the amplitude was recorded but not used in the statistical analyses. Needle electromyography (EMG) was performed on the right abductor hallucis muscle in all subjects and graded subjectively.

Statistical Analyses

Parametric data obtained for subjects with clinical polyneuropathy were compared to subjects with normal examinations using the student-t test. In student-t comparisons, the objective was to determine if subjects with polyneuropathy had significantly higher urine mercury histories compared to subjects who had normal examinations. Because of the potential confounding effects of age and sex upon case-control comparisons, an age-sex matched control group was randomly selected from subjects having a normal neurologic examination, and the results of their evaluation compared to subjects having polyneuropathy. No subjects older than 55 years of age were included in either

group.

Least square regression analysis was used to correlate the semi-quantitative neurologic measures and the electrodiagnostic measures to the urine mercury indices. Multiple linear regression analysis was used to determine partial correlation coefficients for the relationship between urine mercury indices and clinical and electrodiagnostic measures in a model where the effects of age, height, weight, and alcohol use were accounted for. Subjects were classified into lower ($\leq$ .05 mg/L) and higher (> .05 mg/L) urine mercury groups, and a chi-square analysis performed to determine if there was a greater likelihood of subjects having a polyneuropathy in the higher average exposure group.

RESULTS

Of the 138 subjects evaluated, eighteen had evidence of a mild, sensory greater than motor polyneuropathy based upon the clinical examination. These subjects had significantly ($p < 0.05$) reduced clinical distal vibratory and pin sensation, reduced distal strength, increased sustension tremor of the upper extremities, and reduced muscle stretch reflexes (brachioradialis, knee, and achilles) when compared to remaining subjects. Results of the semi-quantitative examination are shown in Table 3, demonstrating significant differences in tests of vibration, touch, and two-point discrimination. Clinically normal subjects also were significantly younger, (33 versus 43

years) with fewer years in the plant, (8 versus 13 years).

(Insert Table 3 about here.)

Electrodiagnostic abnormalities were more frequent in subjects with polyneuropathy. Abnormal EMG (fibrillation potentials, positive waves, large amplitude motor unit action potentials) was reported for eight of the eighteen subjects with an abnormal clinical examination but for only four of the remaining 120 subjects. Five of the eight had multiple (three or more) abnormalities of nerve conduction studies. None of the four clinically normal subjects with abnormal EMG had conduction study abnormalities. One additional subject with an abnormal clinical examination and six subjects with a normal clinical examination had three conduction study abnormalities. Equivocal abnormalities (one or two conduction study abnormalities) were recorded for nine subjects; two had abnormal and seven had normal clinical examinations. The results are summarized in Table 4.

(Insert Table 4 about here)

Comparison of the electrodiagnostic results for both groups is shown in Table 5. Subjects with polyneuropathy had significantly ($p < 0.05$) prolonged ulnar motor and sensory distal latencies, prolonged median and sural sensory distal latencies, reduced median and sural SNAP amplitudes, and reduced median sensory conduction velocity when compared to those with a normal examination.

(Insert Table 5 about here.)

Results of the comparison between urine mercury index values for normal and polyneuropathy subjects are shown in Table 6. Because the urinary mercury control program removed employees from exposure following a monthly spot sample level exceeding 0.5 mg/L, mercury exposure levels were relatively low. Nevertheless, significant differences existed between the two groups, subjects with clinical evidence of polyneuropathy demonstrating higher mercury indices.

(Insert Table 6 about here.)

The random sex and age matched subset of clinically normal subjects was compared to the male subjects under 55 years of age with clinical polyneuropathy. The control group consisted of 36 subjects and the polyneuropathy group consisted of 6 subjects. Both groups had a mean age of 36 years. The control group was significantly lighter than the polyneuropathy group (181 versus 224 pounds), but no other significant differences were found with regard to education levels, plant number, potential exposure years, alcohol ingestion, etc. The semi-quantitative measures of neurologic function continued to show significant differences between the two groups, similar to those described above. Needle EMG demonstrated abnormality in 4 of 6 subjects with a clinical diagnosis of polyneuropathy and only 2 of the 36 control subjects. Subjects with polyneuropathy had significantly prolonged median and sural SNAP distal latencies and reduced median SNAP amplitude when compared to the control group. The only other significant difference was an increased peroneal CMAP amplitude in subjects with polyneuropathy when compared to control group.

Comparison of urine mercury index values for the sex and age matched

groups demonstrated a trend similar to that shown in Table 6. Although only three of the measures reached statistical significance (number of months > 0.25 mg/L in previous six, twelve, and twenty-four months) 9 of the 11 remaining indices demonstrated higher levels of urine mercury in subjects with polyneuropathy.

Correlation coefficients between urine mercury index values and selected subjective clinical observations, quantitative sensory findings, and nerve conduction tests were determined and many were statistically significant ($p < 0.05$). Table 7 shows correlation coefficients between urine mercury indices and subjective gradings from the clinical examination of items related to neuropathy. Gradings were made on a 5 point scale where 5 represented severe abnormality. Thus, a negative correlation coefficient indicates a trend toward abnormal results as a function of subjects' increasing urine mercury. As shown in Table 7, all of the correlation coefficients are negative. Many are statistically significant. Gradings of vibration sensitivity of the hand and foot, distal strength, and joint position sensitivity show a number of significant correlations with urine mercury indices. All statistical significance levels in Table 7, like others in this report refer to a two-tailed test.

(Insert Table 7 about here.)

Multiple linear regression analysis of clinical and electrodiagnostic variables demonstrated many significant partial correlations for the clinical grading of sensory loss and ulnar and median sensory distal latencies with average urine mercury indices even with age, height, weight and alcohol use

accounted for.

Subjects were divided into two groups based upon average urine mercury values above and below 0.05 mg/L in order to differentiate between exposed and non-exposed subjects. A significantly ($p = 0.03$) larger than expected proportion of subjects with clinical polyneuropathy were in the group with average urine mercury above 0.05 mg/L when averaged over 24 months.

Table 8 shows the correlation between quantitative examination results and subjects' urine mercury indices. There are a number of significant correlations between urine mercury indices and quantitative vibration sensitivity tests of the hand and foot. Since vibration sensitivity was measured as the difference (seconds), between examiner's and subjects' threshold, positive correlations indicate a trend toward reduced vibration sensitivity as a function of increasing urine mercury. The quantitative touch test was performed at only one of the three plants. Because of the reduced number of subjects ($n = 48$), correlation coefficients fail to reach statistical significance. However, they are consistently negative. Grip strength shows no significant correlation with urine mercury indices. The small positive correlations are probably due to the slight tendency for exposed subjects to weigh more, which was mentioned earlier. Table 8 also shows correlations between quantitative pin sensation and urine mercury indices. Few of these are statistically significant, but all are consistently negative, indicating a possible trend toward reduced distal pin sensation as a function of increasing urine mercury.

(Insert Table 8 about here.)

sensory or motor complaints were not more prevalent in these individuals and none were aware of their mild impairment at the time of testing. Based upon subjective and semi-quantitative clinical studies, tests associated with large myelinated nerve fiber function seemed most involved (e.g. joint position and vibratory sensation) although this may simply reflect the sensitivity and reliability of the two measures. Some evidence of negative correlations between urine mercury and distal pin sensation, however, suggests small unmyelinated fibers may also be involved. Subjective examination indicated significantly reduced distal strength in the group of subjects with a clinical diagnosis of polyneuropathy when compared to the remainder of the group. Nevertheless, quantitative measures of grip strength for this same group indicated that they were significantly stronger. The subjective clinical impression likely was based upon reduced strength for size.

Electrodiagnostic studies also demonstrated a significant difference between the clinically abnormal and normal subjects, although the statistically significant differences, by themselves, would have been of questionable clinical significance. Sensory conduction studies were the most discriminative, particularly measures of distal latency. Comparison to normal values for our laboratory, however, indicates that SNAP amplitudes were reduced significantly for both groups of subjects, consistent with the observation that reduced SNAP amplitude is an early finding in toxic polyneuropathy (20). Another possible explanation, aside from mercury exposure, would relate to hand size, the manual laborers studied having larger hands than individuals in the unselected control group (21). This difference also may have existed between the normal and abnormal subjects, the larger individuals being in jobs requiring substantial manual strength and also being in high mercury exposed

areas. This argument cannot readily be extended to explain differences in distal latencies. The peroneal amplitude correlations with urine mercury indices are the opposite of those predicted if peroneal amplitude decreased with mercury exposure but, again may reflect body size, the larger subjects having larger motor evoked responses. Although there is an inverse relationship between body height and conduction velocity (22), the normal and abnormal groups were of equal height.

The relationship between weight and mercury level has not been explained, although large individuals were more likely exposed because of the manual labor component of the work in exposed areas. Mercury is stored in liver, kidney, and bone (9), and it also is conceivable that larger individuals accumulate larger amounts of mercury, producing later symptoms of chronic toxicity.

Electrodiagnostic studies were normal in 7 of the 18 subjects with abnormal clinical examinations and abnormal (abnormality on EMG and/or two or more abnormal nerve conduction studies) in the 11 others. In contrast, only 13 of the remaining 120 workers with normal examinations had abnormal electrodiagnostic studies. These abnormalities were considered mild, or equivocal in all 13. Together, these data suggest little evidence of a "subclinical polyneuropathy". It would appear that both the subjective and semi-quantitative measures were sensitive indicators of neurologic impairment, the electrodiagnostic studies providing collaborative evidence of polyneuropathy, as well as suggesting the underlying pathophysiology.

The electrodiagnostic pattern observed in this study, however, matches patterns observed in previous studies. Barber reported prolonged sensory distal latencies and decreased sensory conduction velocities in two patients with clinically observable signs of inorganic mercury intoxication (3). Vroom

and Greer demonstrated slowed median sensory conduction volocity in addition to other abnormal electrophysiologic results in subjects with exposure to elemental mercury (4). The present investigation demonstrated significant correlations between prolonged sensory distal latencies and slowed sensory conduction velocities and urine mercury indices. Thus, these findings continue to support the hypothesis that elemental mercury can produce measureable effects on peripheral nervous system function.

Employees with disorders associated with polyneuropathy were excluded to the best of our ability. Particular attention was given to alcohol ingestion because of its known association with peripheral neuropathy and because of the possibility of a potentiating affect of alcohol in mercury similar to that seen with arsenic (23). Employees were assured of anonymity and two different questionnaires administered at different times, as well as direct questioning by the neurologist, were used to assess or quantify alcohol consumption. A large number of individuals had either never used alcohol or had used it on only a few occasions during their lifetime. This was in part related to the geographic location of the plants and the social norms for those regions. A smaller group of individuals admitted to using alcohol less than once per week, typically in social settings, and characteristically less than two drinks. All of the correllation studies as well as the age and sex matched control studies used only individuals in the above categories. The responses from both questionnaires correlated highly and the instrument was felt reliable. Several employees known by the plant physician to abuse alcohol were readily identified by the questionnaires and excluded from the study. Long standing company records regarding absenteeism existed and were available to the plant physician in identifying potential alcohol abusers.

The use of the urinary mercury indices in predicting body mercury levels has been reported previously (12). Because of little correlation between spot sample urine mercury concentrations and neurologic findings, urine mercury levels integrated over time were used (19). The program of removing workers with spot urine mercury sample levels exceeding 0.50 mg/L resulted in relatively low exposures. Although urine mercury concentrations greater than 0.50 mg/L may be associated with central nervous system toxicity (17, 19), the present data do not demonstrate substantial differences when considering urine mercury concentrations exceeding 0.25 or 0.50 mg/L. This observation offers little support for a threshold effect in the peripheral nervous system.

We conclude that elemental mercury exposure is associated with a clinically significant sensorimotor polyneuropathy even under conditions of low exposure as measured by integrated urine mercury indices. We further conclude that the degree of neurologic impairment is related to the magnitude of exposure, although only mild sensorimotor polyneuropathies were identified when workers were removed from exposure following monthly urine mercury spot samples exceeding 0.5 mg/L. Electrodiagnostic studies are compatible with an axonal dying back polyneuropathy affecting predominantly sensory fibers consistent with similar observations in other exogenous heavy metal toxins such as arsenic (24).

Table 1: Exposed and Control Group Statistics

	Urine Mercury (mg/l)		Age (years)		Height (inches)		Weight (pounds)	
Group	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.
Exposed (n = 77)	.151	.127	34.2	10.2	70.3	2.9	182	32.3
Control (n = 61)	.019	.036	33.5	10.0	69.9	3.2	176.1	32.3

Total n = 138

Table 2: Correlation of Urine Mercury Indices and Other Independent Variables

Urine Mercury Index	Age	Height	Weight	Alcohol Intake
Spot Sample	- .02	+ .03	0.00	+ .06
3 month average	- .05	+ .02	+ .01	+ .03
6 month average	- .11	+ .04	+ .05	+ .01
12 month average	- .06	+ .05	+ .06	0.00
24 month average	+ .01	+ .06	+ .08	0.00
36 month average	+ .05	+ .07	+ .09	- .03

Table 3: Comparison of Semi-Quantitative Sensory Examinations (1) for Subjects with Normal versus Abnormal (Mild Sensory Polyneuropathy) Clinical Examinations.

Semi-Quantitative Sensory Test	Clinical Neurologic Examination	
	Normal	Mild Polyneuropathy
	(N = 120)	(N = 18)
Vibration sensation (seconds)		
Hand	0.3 + 0.1	1.7 + 0.5***
Foot	3.2 + 0.1	6.1 + 0.5**
Two point discrimination (mm)		
Hand	4.1 + 0.1	4.8 + 0.2***
Foot	19.0 + 0.4	21.9 + 0.9**
Touch (log mg)		
Hand	3.42 + 0.1	3.68 + 0.3
Foot	3.39 + 0.1	3.86 + 0.3**

1. Mean + S.E.M.

Significance level of difference
*** $p < 0.001$
** $p < 0.01$
* $p < 0.05$

Table 4: Observed Frequencies for 138 Workers Classified by Clinical and Electrodiagnostic Evaluation

Electrodiagnostic Evaluation	Clinical Neurologic Examination			
	Normal	Abnormal		
		Equivocal (1)	Mild (2)	Moderate (3)
Normal	107	7	6	0
Mild sensory polyneuropathy	7	2	4	5

1. Two abnormal conduction values, normal EMG.
2. Three abnormal conduction values or abnormal EMG.
3. Three or more abnormal conduction values and anormal EMG.

Table 5: Comparison of Results of Nerve Conduction Studies (1) for Subjects with Normal versus Abnormal (Mild Sensory Polyneuropathy) Clinical Examination.

Nerve	Clinical Neurologic Examination		
	Normal	Mild Polyneuropathy	Normal
	(N = 120)	(N = 18)	values (2)
Ulnar motor			
amplitude (mv)	9.2 + 0.2	9.8 + 0.4	11.6 + 0.2
conduction velocity (m/sec)	62.0 + 0.5	60.0 + 1.4	57.0 + 0.4
distal latency (msec)	2.8 + 0.02	3.0 + 0.09 *	2.8 + 0.02
Peroneal motor			
amplitude (mv)	6.5 + 0.2	7.2 + 0.8	6.4 + 0.2
conduction velocity (m/sec)	48.0 + 0.3	48.0 + 1.2	50.0 + 0.4
distal latency (msec)	4.6 + 0.06	4.6 + 0.16	4.6 + 0.04
Ulnar sensory			
amplitude (uv)	22.0 + 0.8	19.0 + 2.6	32.0 + 1.2
distal latency (msec)	3.3 + 0.02	3.5 + 0.12**	3.3 + 0.04
Median sensory			
amplitude (uv)	27.0 + 0.8	21.0 + 2.0**	38.0 + 1.2
conduction velocity (m/sec)	62.0 + 0.4	58.0 + 1.9**	61.0 + 0.4
distal latency (msec)	3.2 + 0.02	3.6 + 0.16***	3.3 + 0.03
Sural sensory			
amplitude (uv)	16.0 + 0.5	13.0 + 1.3*	17.0 + 0.0
distal latency (msec)	3.6 + 0.03	3.9 + 0.13***	3.7 + 0.0

1. Mean + S.E.M.
2. Normal values for laboratory (Albers, J. W., Willems, W. J., unpublished)

Significance level of difference
*** $p < 0.001$
** $p < 0.01$
* $p < 0.05$

Table 6: Comparison of Urine Mercury Indicies (1) for Subjects with Normal Versus Abnormal (Mild Sensory Polyneuropathy) Clinical Examination

Urinary Mercury (Hg) Index	Clinical Neurologic Examination: Normal (N = 120)	Clinical Neurologic Examination: Mild Polyneuropathy (N = 18)
Average urine Hg (mg/L) in previous:	Group average urine mercury (mg/L)	Group average urine mercury (mg/L)
1 month (spot sample)	0.10 + 0.01	0.13 + 0.03
3 months	0.09 + 0.01	0.13 + 0.03
6 months	0.10 + 0.01	0.14 + 0.03
12 months	0.09 + 0.01	0.13 + 0.03
24 months	0.08 + 0.01	0.12 + 0.02
36 months	0.08 + 0.01	0.12 + 0.02*
No. of months > 0.25 mg/L in previous:		
6 months	0.7 + 0.1	1.5 + 0.5*
12 months	1.3 + 0.2	2.9 + 0.8*
24 months	2.4 + 0.4	5.1 + 1.4*
36 months	3.1 + 0.5	6.2 + 1.8*
No. of months > 0.50 mg/L in previous:		
6 months	0.2 + 0.1	0.3 + 0.2
12 months	0.3 + 0.1	0.7 + 0.4
24 months	0.5 + 0.1	1.3 + 0.5*
36 months	0.7 + 0.1	1.7 + 0.7*

1. Mean + S.E.M.

Significance level of difference
* $p < 0.05$

Table 7: Correlation of Subjective Gradings and Urine Mercury Indices

Urine Mercury (Hg) Index	Vibration Sensitivity (Hand)	Vibration Sensitivity (Foot)	Distal Strength	Hypothenar Strength	Muscle Bulk	Joint Position Great Toe	Pin Sensation	Sweating	Tremor
Average Urine Hg (mg/L) in previous:									
1 month (spot sample)	-.02	-.11	-.27****	-.17**	-.21***	-.17**	-.04	-.15*	-.06
3 months	-.14*	-.16*	-.21***	-.10	-.17**	-.23***	-.03	-.12	-.02
6 months	-.12	-.12	-.14	-.03	-.12	-.16**	-.04	-.08	-.004
12 months	-.17**	-.16**	-.14	-.03	-.14*	-.20**	-.05	-.10	-.02
24 months	-.22**	-.18**	-.15*	+.06	-.05	-.17**	-.06	-.02	-.05
36 months	-.23***	-.18**	-.05	+.08	-.01	-.17**	-.05	-.02	-.05
No. of months .25 mg/L in previous:									
6 months	-.12	-.21**	-.21***	-.06	-.16	-.23***	-.05	-.14	-.05
12 months	-.13	-.22***	-.24***	-.14*	-.18**	-.28***	-.07	-.16	-.04
24 months	-.19**	-.17**	-.12	-.08	-.08	-.22***	-.09	-.06	-.01
36 months	-.22***	-.18**	-.10	-.07	-.04	-.24***	-.08	-.03	-.002
No. of months .50 mg/L in previous:									
6 months	-.14*	-.08	-.12	-.11	-.14*	-.14*	-.01	-.12	-.03
12 months	-.22***	-.18**	-.25***	-.10	-.28****	-.26***	-.03	-.24***	-.02
24 months	-.38****	-.24***	-.15*	-.01	-.18**	-.26***	-.10	-.15*	-.01
36 months	-.43****	-.28***	-.13	-.002	-.13	-.31****	-.10	-.11	+.02

Significance levels:
* $p < .10$
** $p < .05$
*** $p < .01$
**** $p < .001$

Table 8: Correlation of Quantitative Test Results and Urine Mercury Indices

Urine Mercury (Hg) Index	Vibration Hand	Vibration Foot	Pin Sensation Hand	Pin Sensation Foot	Two Point Discrimination Hand	Two Point Discrimination Foot	Quantitative Touch (n = 48) Hand	Quantitative Touch (n = 48) Foot	Grip Strengt
Average Urine Hg (mg/L) in previous:									
1 month	.05	.05	-.12	-.11	.04	.10	.03	.06	.13
3 months	.12	.08	-.16*	-.11	-.01	.02	-.06	-.11	.13
6 months	.08	.09	-.14*	-.12	-.05	-.01	-.16	-.12	.11
12 months	.11	.11	-.15*	-.10	-.05	.03	-.11	-.10	.10
24 months	.15*	.11	-.15*	-.13	-.01	.06	-.05	-.09	.13
36 months	.17*	.12	-.05	-.15*	-.03	.06	-.10	-.13	.16
No. of months > .25 mg/L in previous:									
6 months	.12	.17**	-.13	-.15*	-.01	.03	-.14	-.11	.11
12 months	.12	.18**	-.13	-.15*	-.02	.05	-.09	-.06	.09
24 months	.15	.12	-.12	-.16*	-.03	.07	-.09	-.10	.11
36 months	.17**	.11	-.12	-.16*	-.04	.04	-.11	-.15	.12
No. of months > .50 mg/L in previous:									
6 months	.06	.08	-.11	-.07	-.04	-.08	-.23	-.19	-.03
12 months	.12	.15*	-.09	-.14*	-.02	-.04	-.26*	-.21	-.02
24 months	.26***	.17**	-.15*	-.16*	-.05	.02	-.23	-.22	.01
36 months	.31****	.17**	-.17**	-.11	-.05	.01	-.23	-.25*	.04

Significance levels:
* P < .10
** P < .05
*** P < .01
**** P < .001

Table 9: Correlation of Urine Mercury Indices and Electrodiagnostic Variables

Urine Mercury (Hg) Index	Ulnar Nerve				Median Nerve			Sural Nerve		Peroneal Nerve	
	Sensory Nerve Action Potential	Sensory Distal Latency	Motor Distal Latency	Motor Conduction Velocity	Sensory Nerve Action Potential	Sensory Distal Latency	Sensory Conduction Velocity	Action Potential	Distal Latency	Action Potential	Distal Latency
Average Urine Hg in previous:											
3 months	-.07	.14*	.05	.01	-.12	.24***	-.18**	-.07	.07	.10	-.02
6 months	-.06	.11	.03	.03	-.10	.20**	-.13	-.06	.03	.15*	-.05
12 months	-.09	.18**	.06	-.01	-.11	.21**	-.18**	-.10	.02	.17**	-.06
24 months	-.10	.15*	.01	.07	-.10	.17**	-.17**	-.14	.05	.21***	-.13
36 months	-.11	.12	-.01	.12	-.09	.12	-.14	-.16*	.06	.22***	-.13

Significance levels:
* $p < .10$
** $p < .05$
*** $p < .01$

References

1. Neal, P. A.; Jones, R. R. "A study of Chronic Mercurialism in the Hatter's Fur Cutting Industry" U.S. Public Health Bull. 1937; 237: 1
2. Goldstein, N. P.; McCall, J. T.; Dyck, P. J. Metal Neuropathy (Chap. 61) In: Dyck, P. J.; Thomas, P. K.; Lambert, E. H., eds. Peripheral Neuropathy, Vol. 2 Philadelphia: W. B. Saunders 1975: 1249-1251
3. Barber, T. E. "Inorganic Mercury Intoxication Reminiscent of Amyotrophic Lateral Sclerosis" JOM 1978; 20: 667-669
4. Vroom, F. Q.; Greer, M. "Mercury Vaper Intoxication" Brain 1972; 95: 305-318
5. Ross, A. J. "Mercuric Polyneuropathy with Albumino-Cytologic Dissociation and Eosinophilia" JAMA 1964; 188: 830
6. Greenburg, L. "Diagnosis and Treetment of Occupational Metal Poisoning" JAMA 1949; 139: 815
7. Iyer, K.; Goodgold, J.; Eberstein, A.; Berg, P. "Mercury Poisoning in a Dentist" Arch. Neurol. 1976; 33: 788-490
8. Merritt, H. H. Metallic Poisons (Chap. 7). In: Merritt, H. H. A Testbook of Neurology (4th Ed.) Philadelphia: Lea & Bebiger 1970: 574-575
9. Thienes, C. H.; Haley, T. J. Kidney Poisons (Chap. 18) In: Clinical Toxicology (3rd Ed.) Philadelphia: Lea & Febiger 1955: 172-177
10. Ludwig, G. D. Mercury Poisoning (Chap. 79) In: Goldensohn, E. S.; Appel, S. H., eds. Scientific Approaches to Clinical Neurology, Vol. 2 Philadelphia: Lea & Febiger 1977: 1380-1383
11. Eyl, T. B. "Organic-Mercury Food Poisoning" NEJM 1971; 284: 706-709

12. Levine, S. P.; Cavender, G. D.; Langolf, G. D.; Albers, J. W. "Elemental Mercury Exposure: Peripheral Neurotoxicity" JOM, in press

13. Jacobs, M. B.; Ladd, A. C.; Goldwater, L. J. "Absorption and Excretion of Mercury in Man" Arch. Environ. Health 1964; 9: 454-463

14. Smith, R. G.; Vorwald, A. J.; Mooney, T. F. "Effects of Exposure to Mercury in the Manufacture of jChlorine" Am. Ind. Hyg. Assoc. J. 1970; 31: 687-700

15. Potvin, A. R.; Albers, J. W.; Repa, B. S.; et al. "Quantitative Evaluation of Neuropharmacological Trials" Clin. Pharm. Therap. 1974; 15: 229-238

16. Daube, J. R. Nerve Conduction Studies (Chap. 7) In: Aminoff, M. J., ed. Electrophysiological Approaches to Neurological Diagnosis Edinburgh, Chruchill-Livingstone 1980

17. Henderson, R.; Shotwell, H.P.; Krause, L. A. "Analysis for Total, Ionic, and Elemental Mercury in Urine as a Basis for a Biological Standard" Am. Ind. Hyg. Assoc. J. 1974; 35: 576-580.

18. Langolf, G. D.; Chaffin, D. B.; Henderson, R.; Whittle, H. P. Effects of Elemental Mercury Exposure on Urine Mercury, EMG, and Psychomotor Functions In: Sunderman, W., ed. Clinical Chemistry and Chemical Toxicology of Metals Amsterdam: Elsvier 1977

19. Langolf, G. D.; Chaffin, D. B.; Henderson, R.; Whittle, H. P. "Evaluation of Workers Exposed to Elemental Mercury Using Quantitative Tests of Tremor and Neuromuscular Functions" Am. Ind. Hyg. Assoc. J. 1978; 39: 976-978

20. Asbury, A. K.; Johnson, P. C. Metabolic and Toxic Polyneuropathies (Chap. 4) In: Pathology of Peripheral Nerve W. B. Saunders Co., Philadelphia 1978 72-95

21. Eliason, D. "A Comparison of Median and Ulnar Sensory Conduction Responses in Males and Females" presented at Am. Assoc. of Electromyogrj. Tech. meeting 1979 (unpublished)

22. Swift, T. R.; Ward, L. C.; Soudmand, R. "Height Determines Nerve Conduction Velocity in the Legs" Neurology (NY) 1981; 31: 1057

23. Massey, E. W. "Arsenic" (letter) Neurology (NY) 1981; 31: 1057

24. Feldman, R. G.; Niles, C. A.; Kelley-Hayes, M; et al. "Peripheral Neuropathy in Arsenic Smelter Workers" Neurology (NY) 1979; 29: 939-944