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Residual Neurologic Deficits 30 Years After Occupational Exposure to Elemental Mercury

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Abstract: *A battery of tests of peripheral and central nervous system function was administered to 205 former workers of a large heavy industrial plant, 104 of whom were previously exposed to inorganic mercury. The mean age of those examined was 71 years. Exposed subjects had participated in a urine-mercury exposure monitoring program during the time of operation of a process that required the use of mercury and its subsequent clean-up. Mercury exposure had been high (mean peak urine mercury concentration was >600 µg/l) and had ended 30 years or more prior to the investigation. Peripheral nerve function outcomes that were statistically significantly associated with cumulative mercury exposure after controlling for covariates included classification as having peripheral neuropathy, peroneal motor nerve conduction velocity, ulnar motor nerve conduction velocity, and peroneal motor nerve F-wave latency. Quantitative assessment of resting tremor was nearly significantly associated with cumulative mercury exposure (p=0.07). Among tests of central nervous system function, results of the Handeye Coordination test were significantly associated with cumulative mercury exposure after controlling for covariates. Cumulative mercury exposure was not observed to be associated with a quantitative measure of dementia or with a number of cognitive neurobehavioral test outcomes. The statistically significant associations with mercury exposure were observed in spite of greater mortality among the exposed group than the unexposed group. These results suggest that substantial occupational mercury exposure can have long-term adverse effects on the peripheral nervous system detectable decades after cessation of exposure. Such long-term adverse effects were not observed for a measure of dementia or other measures of cognitive function. © 2000 Intox Press, Inc.*

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INTRODUCTION

Effects of Mercury Exposure

Epidemiological investigations of mercury exposed groups have shown effects on central and peripheral nervous system function. Mercury-related effects on the central nervous system include differences in measures of subjective symptoms and mood (WHO, 1980; Piikivi and Hänninen, 1989) as well as in neurobehavioral function (Roels *et al.*, 1982; Williamson *et al.*, 1982; Piikivi *et al.*, 1984; Smith *et al.*, 1983). Peripheral nervous system function effects, including slowing of nerve conduction velocity, prolongation of distal motor and sensory conduction latency, and diminution of sensory and compound motor amplitudes, have been observed among mercury-exposed workers (Albers *et al.*, 1982; Levine *et al.*, 1982; Singer *et al.*, 1987). In addition, abnormalities on neurological physical examination consistent with peripheral nerve impairment, including diminished sensation, diminished deep tendon reflexes, and impaired postural stability have been found more commonly among mercury-exposed workers than non-exposed comparison workers (Albers *et al.*, 1982; Ehrenberg *et al.*, 1991). Finally, neuromuscular tremor, which has been reported frequently at high levels of occupational

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exposure, is one of the most widely recognized adverse neurological consequences of exposure to mercury. At lower exposures more typical currently, clinically overt tremor has become less common, but some investigations using objective measures of tremor have demonstrated effects on frequency and amplitude of tremor among mercury exposed workers (Ehrenberg *et al.*, 1991, Roels *et al.*, 1982; Roels *et al.*, 1989; Fawer *et al.*, 1983, Chapman *et al.*, 1990).

Past Investigations of Long-Term Effects of Mercury Exposure

While a number of studies of neurological effects of current or recent mercury exposure are available, the long-term, remote effects of substantial occupational mercury exposure have been investigated in only a few studies (He *et al.*, 1984; Albers *et al.*, 1988; Andersen *et al.*, 1993). In all of these studies the mean duration since mercury exposure was greater than 10 years and relatively subtle persistent neurological effects were observed.

The most relevant previous investigation to the present investigation was that of peripheral and central nervous system effects of mercury exposure among a large group of formerly heavily mercury exposed male workers with a long latency (>19 years) since last exposure selected from the same facility as subjects in the current study (Albers *et al.*, 1988). In that study, on neurologic physical examination, "sustension" (i.e., postural) tremor score was significantly associated with two of four measures of mercury exposure. No association was observed between neurologic examination findings demonstrating polyneuropathy and any of the mercury exposure measures. Among the electrophysiologic tests used, statistically significant associations with at least one mercury exposure measure (of 6) were observed only for median sensory nerve distal latency and median sensory nerve amplitude. Near statistically significant associations were observed between ulnar motor nerve conduction velocity and two of the exposure measures.

The results of the investigation of formerly mercury-exposed workers as reported in the peer-reviewed literature (Albers *et al.*, 1988) are somewhat difficult to interpret. The investigators tested a large number of associations between numerous exposure variables and a large number of health outcomes, with separate analyses for different subsets of the exposed group. A number of statistically significant associations were high-lighted, but the associations were not consistent across exposure measures and across subsets of exposed subjects. In addition, neurobehavioral results obtained in that investigation were never reported in the peer-reviewed literature. Neither have the neurobehavioral outcomes obtained in the Norwegian study (Andersen *et al.*, 1993) been reported in the peer-reviewed literature.

Aims of the Current Study

The purpose of the present study was to test whether occupational exposure to elemental mercury was associated with long-term adverse effects on the nervous system in a cohort of men who were previously tested and described (Albers *et al*, 1988). These exposed workers were investigated again one decade after the previous investigation because: (1) this large group of workers had documented high exposure levels and a long latency since last exposure, (2) the previous observation of associations between neurological outcomes and mercury exposure indices in this population (Albers *et al.*, 1988) was inconsistently observed across a large number of exposure measures and a larger number of outcomes, and (3) there was concern that additional age-related declines would unmask even more neurologic dysfunction among this cohort.

The primary aims of the study were: (1) to replicate previous findings of associations between remote past heavy exposure to mercury and physical examination, nerve conduction, and tremor outcomes in the same cohort, (2) to investigate potential associations between remote mercury exposure and cognitive function in old age, and (3) to investigate whether differences in neurologic dysfunction between exposure groups became larger with increasing age of the cohorts.

METHODS

Subjects

Selection of Exposed and Comparison Subjects for Original Study. The original cohort, assembled in 1986, consisted of 502 white males who had worked at least four months in the facility between January 1, 1953, and December 31, 1966, the years during which elemental mercury was used and cleanup operations were performed. The cumulative average quarterly urine mercury measurements (in units of µgHg/L quarter) were calculated for all monitored mercury workers, who were then ranked in descending order of exposure from 8,572 to 2 µgHg/L quarter. To select study subjects for the mercury exposed group, individuals on this rank list were asked to participate beginning with the individual having the highest cumulative exposure and continuing with the individual with the next highest level until approximately 250 individuals had agreed to be tested. The lowest cumulative exposure among previously tested individuals was 2,144 µgHg/L quarter units of mercury.

Unexposed comparison subjects worked in the same facility but were not exposed to mercury. They were frequency matched to the exposed group by five-year birth intervals, active or retired job status, and six categories of job title groupings that corresponded to socioeconomic strata. It is possible that some of the comparison workers could have experienced some exposure to other chemicals. Among the 502 participants in the previous study were 247 exposed workers and 255 unexposed workers.

Composition of Current Study Cohort. All workers who were contacted to participate in the original study (regardless of whether they participated) were contacted to participate in the current study. Since many original study members declined to participate because of advanced age or were deceased, additional members of the plant cohort were selected for inclusion in the current study to increase the number of participants. To choose new exposed subjects for the present study, all individuals having cumulative exposures of at least 2,000 µgHg/L quarter units or known to have one or more times excreted at least 600 µgHg/L were identified (n=34). Comparison subjects were selected for these exposed workers using the same criteria as the original study, and the new eligible exposed and comparison subjects were invited to participate.

Of the 502 men in the original study, 101 were deceased. Of the remaining 401 persons, 42 (10%) were not traceable, and 172 (42%) agreed to participate in the present study. Among the 68 newly-selected persons for the study, 33 (48%) agreed to participate. The vast majority of those who were contacted and did not participate cited advancing age, participation in the previous study, or poor health as the reason for declining to participate.

Interview Questionnaire

The questionnaire included demographic and lifestyle questions, medical status, medications used, occupational history, and symptoms. It was mailed to each study participant prior to his examination and reviewed with him by a trained interviewer at the examination. Information on drinking of alcohol was summarized as a cumulative index, in drinks per day years, defined as the sum over several time periods of the number of drinks per day times the number of years at that consumption level.

Overview of Clinical Examinations

The outcomes obtained in the current examination are listed in Table 1. The current examinations took place between November, 1994, and April, 1995. Written informed consent was obtained from all study participants. Blood was drawn and urine was collected immediately after consent was obtained. All personnel responsible for collecting health outcome results were blind to the exposure status of the subjects.

TABLE 1. Outcome Variables for the Study

OUTCOME:	UNIT:
Peripheral neuropathy *	present/absent
Nerve conduction tests:	
Peroneal motor NCV*	m/s
Peroneal motor amplitude	mV
Peroneal motor F-wave latency *	msec
Ulnar motor NCV*	m/s
Ulnar motor amplitude	mV
Ulnar motor F-wave latency	msec
Ulnar sensory NCV	m/s
Ulnar sensory amplitude	µV
Sensory and other neurologic tests:	
Visual contrast sensitivity (at 1.5,3,6,12 & 18 cpd)	score (1-9)
Quantitative tremor (RMS acceleration)*	$\log_{10}$ mm/sec^2
Index finger, digit 5, and great toe vibrotactile threshold	$\log_{10}$ µm
Hand strength dynamometry (grip, lateral, and palmar)	kg
Postural sway speed with eyes open and closed	cm/sec
Neurobehavioral tests:	
Handeye Coordination *	log RMS error
Simple Reaction Time mean latency	msec
CVLT acquisition	# correct (1-80)
Trails A and B latencies	Sec
Grooved Pegboard latency for each hand	Sec
Finger Tapping (each hand and alternating index fingers)	# of taps
Symbol-Digit Substitution	sec/correct digit
Pattern Memory	# correct (1-25)
Serial Digit Learning	log error
Vocabulary	# correct (6-25)
Mood scales:	
Tension, Depression, Anger, Fatigue, Confusion	avg. score (1-5)
Mattis Dementia Rating Scale	score (0-144)
Dementia (DRS score <128) *	present/absent

* Primary outcome variables

Neurologic Physical Examination

Detailed neurological physical examinations were performed on all study participants by a single board certified neurologist in a standard manner. Cranial nerves, sensory function, motor strength and tone, deep tendon reflexes, coordination, tremor and gait were assessed during the examination. All neurological signs were graded as normal, equivocal, or abnormal, except for motor strength, which was graded on a 5-point scale. Postural tremor on physical examination (Px) was also dichotomized for some analyses with equivocal or abnormal ratings coded as present and normal coded as absent.

Nerve Conduction Testing

Electrophysiologic studies of the ulnar motor and ulnar sensory nerves and the peroneal motor nerve were performed on all subjects enrolled in the study. In addition to evoked response amplitude, distal latency, and segmental conduction velocity, late response (F-wave) latency of the ulnar and peroneal nerves was also obtained (Lachman *et al.*, 1980; Kimura, 1989). All nerve conduction measurements were made a TECA Sapphire (TECA Corp., Pleasantville, NY) electromyograph (EMG) using standard noninvasive techniques. Limb temperature was maintained above 32°C with heat lamps and was continuously monitored with a digital thermometer fixed to the skin with surgical tape.

Visual Contrast Sensitivity Testing

The Functional Acuity Contrast Test using the Optec 1000 (Stereo Optical Co., Inc.; Chicago, IL) was used. Circular 1.7(sine-wave grating patch stimuli were presented. Nine stimuli of decreasing contrast (0.15 log unit change per step) were presented at each of 5 spatial frequencies, i.e., 1.5, 3, 6, 12, and 18 cycles per degree (cpd). Each grating was tilted +15°, 0°, or -15°, and the subject reported which direction each was tilted. The index of the weakest contrast stimulus correctly identified (i.e., threshold) was recorded for each spatial frequency. The threshold at 6 cpd was used as the primary summary measure for this test, as it shows the greatest change in threshold in many visual impairments.

Quantitative Tremor Testing

Tremor was quantified using the Coordination Ability and Tremor System (CATSYS; Danish Product Development, Ltd., Snekkersten, Denmark) (DPD, 1994; Edwards and Beuter, 1997). In this test the subject held a pencil-shaped stylus that contained an accelerometer sensitive to acceleration in two dimensions. Measurements were taken as specified by the instrument manufacturer: "with the elbow in 90° of flexion, the upper arm held loosely at side of body, the stylus grasped approximately 1 cm from the unattached end, and the stylus held approximately horizontal and parallel to the body." Two separate 10-second sampling intervals were recorded for each hand. The root mean square (RMS) of accelerations calculated for the 0.9-15.0 Hz band was calculated for eight seconds of each trial. The primary summary measure used was the mean of the common logarithm-transformed RMS acceleration values of the four trials.

Vibrotactile Threshold (VT) Testing

Cutaneous vibrotactile thresholds were obtained for the index finger and great toe using a portable vibrometer (Vibratron II, Physitemp, Inc., Clifton, NJ) producing sinusoidal oscillation at 120 Hz. A "method of limits" protocol used has been shown reliable and time efficient (Gerr & Letz, 1988; Gerr *et al.*, 1990). The results are reported as the common logarithm of vibration amplitude.

Hand Strength Dynamometry

Bilateral hand strength dynamometry was performed on all study participants to assess neuromuscular function. Grip strength and pinch strength were measured using an adjustable-handle Jamar dynamometer and a B&L pinch gauge (Asimow Engineering Company, Santa Monica, CA). The method and instructions of Mathiowetz *et al.* (1985) were employed.

Standing Steadiness Testing

The instrument employed in this project was the NeuroTest SwayPlot Postural Sway Analyzer (NeuroTest, Inc.; Corona, CA). This device measured the position of the subject's head (in two dimensions) using a sound emitter attached to a lightweight headset worn by the subject and two receivers mounted on a tripod 10-15 cm from the emitter. Timing and data recording were accomplished by a dedicated IBM-PC-compatible laptop computer.

To perform the test, the participant was asked to stand as still as possible in stocking feet with hands at his sides while either fixating visually on a 2-cm diameter circular mark on the wall two meters away or with eyelids closed. Four 60-second trials were performed.

Eyes-opened and eyes-closed trials were alternated. The primary outcome variable analyzed was mean sway speed with eyes closed (Letz and Gerr; 1995).

Neurobehavioral Tests

A combination of computer-administered and manual neuropsychological tests were used in the present study. The neurobehavioral tests included were intended to evaluate a wide range of CNS functions within a relatively brief testing session. The tests administered assessed cognition, memory, psychomotor skills, and mood. The computer-administered tests selected from the Neurobehavioral Evaluation System (NES2; Baker *et al.*, 1985; Letz, 1991) were Finger Tapping, Simple Reaction Time, Handeye Coordination, Symbol-Digit Substitution, Pattern Memory, Serial Digit Learning, Vocabulary, and Mood Scales. Three traditional, manually-administered neuropsychological tests, Grooved Pegboard (Lafayette Instruments), Trails A and B, and the California Verbal Learning Test (Delis *et al.*, 1987), were used. Also, the Mattis Dementia Rating Scale (DRS) was used to assess general intellectual function. The presence of dementia was defined as having a DRS score <128 of 144 (Mattis, 1988).

Peripheral Neuropathy Case Definition

In order to determine whether peripheral neuropathy was associated with mercury exposure, it was necessary to categorize participants as peripheral neuropathy case-positive or case-negative. Two types of health outcome information were used to determine case status: 1) results of selected clinical neurological examination procedures and quantitative functional tests and 2) results of electrophysiologic tests. To facilitate categorization, a *functional test abnormality score* and an *electrophysiologic test abnormality score* were created. Abnormality was assigned for quantitative variables (vibrotactile thresholds, standing stability, and nerve conduction measures) based upon expected performance predicted by the backward-elimination stepwise regression models with several covariates described below.

The functional test abnormality score was incremented by one when (1) proprioception of the great toe on physical examination was abnormal bilaterally or abnormal on one foot and equivocal on the other, (2) the Achilles tendon reflex was similarly scored bilaterally, (3) the vibrotactile threshold for the average score from both toes exceeded the predicted 95th percentile, or (4) the average sway speed from the two eyes-closed trials exceeded the predicted 95th percentile. The maximum possible value for the functional test abnormality score was four.

To construct the electrophysiologic test abnormality score, each of the eight nerve conduction outcomes was assigned a value of 1 for an equivocal result (predicted 95th percentile > observed value > predicted 90th percentile) and a value of 2 for an abnormal result (observed value > predicted 95th percentile). Thus, the electrophysiologic test abnormality score had a possible range of 0 (no test result outside of the 90th percentile) to 16 (all eight test results outside of the 95th percentile).

A study subject was considered to be peripheral neuropathy case definition positive if any of the following four criteria were met:

- Electrophysiologic test abnormality score ≥5 *and* functional test abnormality score ≥0
- Electrophysiologic test abnormality score =3 or 4 *and* functional test abnormality score ≥1
- Electrophysiologic test abnormality score ≥2 *and* functional test abnormality score ≥2
- Electrophysiologic test abnormality score <2 *and* functional test abnormality score ≥3

Biological Samples

Blood and urine samples were obtained at the beginning of the participant's examination session. Blood was analyzed for both hematologic and biochemical constituents. Standard urinalysis was performed on the spot urine samples. These tests allowed for identification of common disorders (e.g., hypothyroidism) known to cause either central or peripheral nervous system impairment.

No biological samples for mercury were obtained in the present study. During the previous study, urine mercury concentrations were very low and not significantly different between the exposure groups.

Mercury Exposure - Exposure Data Source

Data were available from a urine mercury testing program initiated in 1953 by the employer to monitor all workers likely to be exposed to mercury. Measurements were made quarterly. Because some workers with high concentrations of mercury in their urine were found to have multiple tests in a quarter, the average quarterly concentration was used in some of the calculations of summary mercury excretion variables described below. No information is available about the detection limits of the analytical procedures used or quality control activities.

Several summary mercury exposure variables were calculated:

- HgCUM: Cumulative mercury exposure calculated by summing the average urinary concentration for every quarter when monitoring occurred. HgCUM is reported in units of μgHg/L quarter. This variable was used to rank potential study subjects for inclusion in the original study.

- HgDUR: Number of quarters that mercury was detected through urinalysis.

- HgAVG: Average exposure intensity, calculated as the cumulative exposure (HgCUM) divided by number of quarters exposed (HgDUR). HgAVG is expressed in units of μgHg/L.

- Hg300: Number of quarters having urine mercury concentrations ≥ 300 μgHg/L (the "plant action level", the level at which the supervisor was to be notified).

- Hg600: Number of quarters having urine mercury concentrations ≥ 600 μgHg/L (twice the plant action level, the level at which the worker was to be removed from exposure areas).

- HgPEAK: Single highest urine mercury concentration.

Data Analysis

Subjects' data were excluded from analysis for the following reasons (for the types of testing noted): acutely intoxicated with alcohol or drugs (all outcomes), anticonvulsant or major psychiatric medication (neurobehavioral [NB]), admission of regular illicit drug use (NB), prior diagnosis of alcoholism or cumulative drinking of >200 drinks/day years (NB, nerve conduction testing [NCT], vibtotactile thresholds [VT]), history of sustained loss of consciousness due to a blow to the head (NB), history of a stroke (NB), history of psychosis (NB), mental retardation (NB), diabetes (NCT, VT), prior cancer chemotherapy (NCT, VT), history of renal failure (NCV, VT), serious trauma to the limb tested (NCV, VT, Grip), and history of vestibular disease (Sway). In addition, all data were voided for any subject who had grossly incomplete data. The data rejection criteria were applied without reference to exposure status.

Demographic data were initially summarized and described separately for exposed and unexposed study participants. A set of outcome variables calculated from the neurologic and neurobehavioral data collected is provided in Table 1. To the extent feasible, one variable was selected for each test.

In order to minimize the problem of multiple comparisons, a subset of the numerous outcome variables were designated as the primary outcome variables and a subset of the exposure variables were designated as primary exposure variables. The primary outcome variables were selected because they were either significantly associated with mercury exposure in previous investigation of this cohort (Albers *et al.*, 1988) or represent important unanswered questions in the literature. The primary outcome variables selected were ulnar motor nerve conduction velocity, peroneal motor nerve conduction velocity, peroneal nerve F-wave latency, tremor RMS acceleration, Handeye Coordination Test log RMS error, peripheral neuropathy case definition status, and dementia case definition. The four exposure variables selected were exposure group status, cumulative exposure, peak exposure, and duration of exposure.

The primary hypotheses to be tested were whether exposure to mercury was associated with scores on the primary outcome variables listed above. Crude analyses were performed using the two exposure groups: unexposed and exposed. A limited set of variables appropriate for each outcome was considered as potential covariates (e.g., age, sex, race, level of education, and height). Backward elimination stepwise regressions were fitted with the exposure variable forced into the model. Then, the other three exposure variables were substituted for the exposure variable, one at a time. Finally, an interaction term between age and exposure group status was examined. In cases where the dependent variable was dichotomous (i.e., polyneuropathy present/absent and dementia present/absent), logistic modeling of prevalence odds of abnormal outcome was performed.

Additional backward elimination stepwise regression analyses were performed on the subset of participants we examined who were also examined in the previous study (Albers *et al.*, 1988). The analyses were performed only for relevant outcome variables for which there were relatively direct analogous measures in the two studies.

All analyses were performed using SAS software (1990). Separate multivariable models were fitted for each outcome, and models were fitted for each exposure variable separately. The significance levels were not adjusted for these multiple comparisons. Rather, the pattern of results achieving a $p<0.05$ statistical significance level was considered in the context of biological plausibility and consistency for interpreting the results of the data analyses.

RESULTS

Exclusions

A total of 104 exposed and 101 unexposed subjects were examined. Twenty-five (24.0%) of the exposed subjects and 17 (16.8%) of the unexposed subjects met at least one criterion for exclusion from analyses of PNS function. Similarly, 23 (22.1%) of the exposed subjects and 18 (17.8%) of the unexposed subjects met at least one

TABLE 2. Exclusions by Exposure Status Group

	Unexposed		Exposed	
	Yes	No	Yes	No
Current medications:				
Hypoglycemic agents	4	97	8	96
Thyroid medications	5	96	3	101
Benzodiazepines	4	97	8	96
Antidepressants	2	99	6	98
Narcotic analgesics	1	100	0	104
Medical history of:				
Renal failure	1	100	2	102
Head injury	7	94	3	101
Brain tumor	0	101	0	104
Stroke	5	96	7	97
Ear surgery	3	98	7	97
Ear infection (past year)	3	98	5	99
Blood glucose > 300 (non-fasting)	3	97	1	101
TSH > 8.0	3	97	3	99
Lifetime alcohol consumption (>200 drinks/day years)	1	100	2	102
Total # of Exclusions for PNS outcomes	17 (16.8%)	84	25 (24.0%)	79
Total # of Exclusions for CNS outcomes	18 (17.8%)	83	23 (22.1%)	81

criterion for exclusion from analyses of CNS function. The numbers of subjects in the exposed and unexposed groups meeting each of the exclusion criteria are given in Table 2.

Characteristics of Participants

Descriptive statistics for demographic variables and potential confounding variables are presented separately for the two exposure groups in Table 3. Few differences were observed between the exposed and unexposed subjects on the demographic variables. Cumulative alcohol consumption (reported in drinks/day - years) was slightly greater among the unexposed than among the exposed group and height was marginally greater for the exposed group than for the unexposed group.

Descriptive statistics for mercury exposure variables are presented for the exposed subjects only in Table 4. The mean exposure duration was 19.3 quarters (4.8 years) and ranged from less than one year to almost 13 years. The mean cumulative exposure (HgCUM) value was 3,362 µgHg/L-quarters. The mean of the average urine mercury concentration for the entire duration of exposure (HgAVG) for each worker was 201 µgHg/L. The mean number of quarters during which the urine mercury concentration exceeded 300 µgHg/L (Hg300) was 3.6 and ranged from 0 to 11. The mean number of quarters during which the urine mercury concentration exceeded 600 µgHg/L (Hg600) was 0.7 and ranged from 0 to 4. The mean peak urine mercury value (HgPEAK) was 635 µgHg/L and ranged from 187 µgHg/L to 1900 µgHg/L.

Correlations Among the Exposure Variables

Spearman rank order correlation coefficients were calculated for the six exposure variables. Cumulative mercury exposure (HgCUM) was poorly correlated with average urine mercury (HgAVG; r=0.12) and weakly correlated with the peak urine mercury (HgPEAK; r=0.28) and number of occasions that urine mercury exceeded 600 µgHg/L (Hg600; r=0.22). The greatest correlation was observed between the peak mercury value and the number of quarters during which the urine mercury concentration exceeded 600 µgHg/L (r=0.87). Interestingly, duration of mercury exposure was

TABLE 3. Descriptive Statistics for Demographic Variables by Exposure Group for all Nonexcluded Subjects

	Unexposed			Exposed		
	N1	MEAN	S.D.	N	MEAN	S.D.
Age at Last Exam (yrs)	84	71.1	6.56	79	70.3	5.86
Education (yrs)	84	12.1	2.57	79	12.4	2.34
Income: Refused (%)	4	4.8	-	4	5.1	-
$10k-20k	29	34.5	-	24	30.4	-
$20k-30k	19	22.6	-	18	22.8	-
$30k-40k	17	20.2	-	20	25.3	-
$40k-50k	5	6.0	-	9	11.4	-
>$50k	10	11.9	-	4	5.1	-
Alcohol (% current drinker)	51	60.7	-	56	70.9	-
Cumulative alcohol (drinks/day-yrs)	84	18.6	30.66	79	13.3	21.61
Height	84	173.0	5.84	79	174.9	6.54
Weight	84	84.6	13.36	79	88.0	17.27
Body Mass Index (kg/m²)	84	30.4	4.48	79	30.8	5.49
Arm Temperature (°C)	82	33.3	0.79	78	33.3	0.87
Leg Temperature (°C)	81	33.2	0.94	77	33.3	0.91
Visual Acuity (1-8)	83	4.9	1.48	79	5.2	1.31
Video Game/Computer Experience (1-3)	84	1.3	0.50	79	1.3	0.53
Effort on Comp. Tests (1-4)	84	3.4	0.86	79	3.5	0.78

TABLE 4. Descriptive Statistics for Mercury Exposure Variables

Exposure Variable	N	Mean	Std Dev	Median	Minimum	Maximum
HgDUR # quarters exposed	104	19.3	9.1	19	3	51
HgCUM Cumulative exposure	104	3362.2	1177.4	3200	1089	6588
HgAVG Total exposure / # quarters exposed	104	200.6	98.0	180	64	6956
Hg300 # quarters above PAV of 0.3 mg/L	104	3.6	2.25	3	0	11
Hg600 # quarters above 0.6 mg/L	104	0.7	0.9	0	0	4
HgPEAK Highest value	104	635	319.7	568	187	1900

moderately negatively correlated with average mercury exposure (r=-0.67) and weakly correlated with the number of quarters that the mercury concentration exceeded 600 µgHg/L (r=0.21).

Descriptive Statistics for Outcomes

Descriptive statistics for physical examination outcomes are presented for the two exposure groups in Table 5. Of the groups of physical examination signs, only the dichotomized number of sensory abnormalities was statistically significantly associated with exposure group (p=0.04). Interestingly, postural tremor showed a trend toward differences between exposure groups, but intention tremor did not (data not shown).

Unadjusted results of nerve conduction outcome measures obtained in the current study are presented by exposure group in Table 6. Exposure group differences were statistically significant only for ulnar motor nerve

TABLE 5. Descriptive Statistics for Physical Examination Outcomes by Exposure Group

	Unexposed(n = 84)		Exposed(n=79)		
	N	%	N	%	p-value*
Cranial nerve (>2 abn/equiv.)	13	15.5	8	10.1	0.308
Motor strength (>0 abn/equiv.)	2	2.4	4	5.1	0.363
Sensory (>2 abn/equiv.)	9	10.7	18	22.8	0.038
Deep tendon reflexes (>1 abn/equiv.)	16	19.1	15	19.0	0.992
Primitive reflexes (>1 abn/equiv.)	26	31.0	30	38.0	0.345
Coordination (>1 abn/equiv.)	15	17.9	19	24.1	0.331
Postural tremor (abn/equiv.)	15	17.9	22	27.9	0.128
All signs combined (>8 abn/equiv.)	12	14.3	16	23.3	0.313

*p-value associated with chi-square

TABLE 6. Descriptive Statistics for Nerve Conduction Outcomes by Exposure Group

	Unexposed			Exposed			t-test
	N	Mean	S.D.	N	Mean	S.D.	p-value
Peroneal Motor NCV (m/s)	78	43.10	4.06	72	41.96	3.85	0.079
Peroneal Motor Amp. (mV)	80	3.72	2.27	73	3.81	2.08	0.803
Peroneal F-Wave Min (msec)*	67	53.79	4.54	59	55.27	5.60	0.109
Ulnar Motor NCV (m/s)	82	57.67	3.39	77	56.28	4.22	0.024
Ulnar Motor Amp. (mV)	82	9.51	1.74	78	9.96	2.25	0.155
Ulnar F-Wave Min (msec)*	80	30.45	2.03	76	30.98	2.07	0.108
Ulnar Sensory NCV (m/s)	75	50.96	3.78	70	50.81	5.32	0.846
Ulnar Sensory Amp. ((V)	75	13.68	6.09	70	14.85	6.23	0.257

*Higher score indicates poorer performance

TABLE 7. Descriptive Statistics for Sensory-Motor Outcomes by Exposure Group

	Unexposed			Exposed			t-test
	N	Mean	S.D.	N	Mean	S.D.	p-value
Contrast Sensitivity (at 6 cpd)	84	4.23	1.81	79	4.66	1.69	0.017
Vibrotactile Threshold Digit 2 (log μm)*	81	0.51	0.32	68	0.47	0.34	0.418
Vibrotactile Threshold Digit 5 (log μm)*	81	0.50	0.38	68	0.48	0.35	0.699
Vibrotactile Threshold Gr. Toe (log μm)*	81	1.87	0.33	67	1.90	0.40	0.619
Grip Strength (kg)	84	40.35	8.05	79	40.89	9.70	0.702
Lateral Pinch (kg)	84	9.46	1.97	79	9.73	1.77	0.344
Palmar Pinch (kg)	84	8.98	1.99	79	9.24	1.87	0.390
Sway Speed Eyes Open (cm/sec)*	78	1.01	0.50	78	1.02	0.34	0.926
Sway Speed Eyes Closed (cm/sec)*	78	1.61	0.86	77	1.62	0.64	0.893
Tremor Acceleration (log m/sec^2)*	84	2.15	0.19	79	2.19	0.22	0.289

*Higher score indicates poorer performance

TABLE 8. Descriptive Statistics for Neurobehavioral Outcomes by Exposure Group

		Unexposed			Exposed		
	N	Mean	S.D.	N	Mean	S.D.	p-value
Handeye Coordination (mean log RMSE)*	82	2.33	0.33	81	2.41	0.37	0.302
Reaction Time Mean Latency (msec)*	83	263.9	67.32	81	265.0	57.50	0.934
Finger Tapping Preferred Hand (# taps)	82	129.5	37.49	81	128.4	36.92	0.291
Grooved Pegboard (sec)*	82	93.5	25.19	80	93.5	19.71	0.674
Trails A Latency (sec)*	83	41.8	16.26	81	39.9	12.37	0.444
Trails B Latency (sec)*	83	90.5	32.02	81	93.1	34.97	0.727
Symbol-Digit Average Latency (sec)*	81	4.02	1.54	81	3.82	1.00	0.074
Pattern Memory (# correct of 25)	82	6.7	1.81	80	6.4	1.76	0.134
Serial Digit Learning Log Error Score*	82	2.68	1.47	81	2.79	1.50	0.421
CVLT Acquisition (# correct of 80)	83	33.2	9.12	81	34.4	9.45	0.210
DRS Total Score (of 144)	83	134.0	7.73	81	134.3	6.68	0.665
Vocabulary (# correct of 25)	83	15.5	5.86	81	17.0	5.40	0.068
Mood Scales: (1 – 5):* Tension	80	2.22	0.71	79	2.34	0.68	0.389
Depression	80	1.84	0.67	79	1.85	0.60	0.548
Anger	80	1.67	0.59	79	1.64	0.67	0.693
Fatigue	80	2.72	0.74	79	2.86	0.68	0.540
Confusion	80	2.26	0.64	79	2.17	0.54	0.108
Mood Average Score	80	2.14	0.52	79	2.17	0.48	0.928

*Higher score indicates poorer performance

conduction velocity, and there was a nonsignificant tendency toward group differences for peroneal motor nerve conduction velocity (p=0.08).

Crude quantitative sensory-motor test results are presented by exposure group in Table 7. The only statistically significant group difference was for contrast sensitivity, which showed better performance by the exposed group than the unexposed group.

Unadjusted results of the neurobehavioral outcomes obtained in the current study are presented by exposure group in Table 8. There were no statistically significant differences between exposure groups for any of the neurobehavioral outcomes. The trends toward group differences observed for Symbol-Digit and Vocabulary are in the direction of better performance by the exposed than the unexposed group.

Linear Models for Quantitative Outcomes

Exposure parameter estimates and their associated p-values are presented in Table 9 from the final linear regression and logistic regression models fitted. Different models were fitted for each of the selected neurologic outcome variables regressed upon relevant covariates and each of four mercury exposure variables (mercury exposure status [i.e., exposed vs unexposed], cumulative mercury exposure, peak mercury exposure, and exposure duration). All covariates initially included in the each model are listed in the column entitled "Covariates." Those covariates listed inside brackets were not significantly associated with the dependent variable and were therefore not included in the final model. Covariates outside brackets were significantly associated with the dependent variable and were retained in the final model for that dependent variable. Since the units are different for the different exposure variables, standardized regression coefficients are presented. The standardized coefficients represent the estimated change in the dependent variable (in standard deviation units) for a one standard deviation change in the exposure variable. These coefficients can be compared across columns and across rows of the table. The p-values represent a test of the hypothesis that the estimated coefficient is statistically significantly different from zero.

The overall pattern of estimated coefficients and their p-values calculated for the associations between each of the dependent variables and the four exposure variables was similar. Coefficients for the cumulative exposure variable were the largest for all of dependent variables except one. Also, the magnitude of the estimates for each dependent variable were roughly

TABLE 9. Summary of stepwise regression results for primary outcomes.

Dependent Variable	Covariates‡	Standardized Parameter Estimate (& p-value) for Each Exposure Variable			
		Hg Group Status	Cumul. Hg	Peak Hg	Hg Duration
Peroneal NCV (m/s)	Age, height, alcohol, [BMI, leg temperature]	-0.140	-0.150	-0.131	-0.075
		(0.073)	(0.053)	(0.098)	(0.332)
Peroneal F-Wave (msec) *	Age, height, [BMI,leg temperature, alcohol]	+0.123	+0.149	+0.146	+0.063
		(0.112)	(0.049)	(0.057)	(0.411)
Ulnar NCV (m/s)	Age, [height, BMI, arm temperature, alcohol]	-0.208	-0.231	-0.173	-0.205
		(0.006)	(0.002)	(0.022)	(0.006)
Tremor acceleration RMS ($\log_{10}$ mm/sec^2) *	Age, [height, BMI, alcohol]	+0.113	+0.139	+0.033	+0.152
		(0.141)	(0.070)	(0.671)	(0.047)
Handeye Coordination log RMS error*	Age, visual acuity, tryhard, [education, alcohol]	+0.137	+0.141	+0.097	+0.127
		(0.044)	(0.038)	(0.157)	(0.062)
Dx Peripheral Neuropathy †*	Age, [height, BMI, alcohol]	+0.348	+0.250	+0.198	+0.170
		(0.026)	(0.055)	(0.105)	(0.182)
Dementia (DRS<128) †*	Age, education, [alcohol]	+0.066	+0.119	+0.033	+0.116
		(0.647)	(0.391)	(0.822)	(0.393)

* Positive coefficients for this variable indicate worse performance with higher exposure (negative for all others).
† Logistic regression.
‡ All covariates in the original model are listed. Those in brackets were not retained in the final models.

similar across exposure variables. Ulnar motor nerve conduction velocity was the dependent variable most consistently significantly associated with exposure, when controlling for age, height, and alcohol consumption. Peroneal motor nerve conduction velocity and peroneal F-wave latency were each nearly significantly associated with more than one mercury exposure variable when controlling for covariates. Quantitative tremor acceleration, meeting the case definition of peripheral neuropathy, and performance on the Handeye Coordination Test were each statistically significantly associated with one of the exposure variables. Age was a statistically significant covariate of all of the dependent variables. Meeting the case definition of dementia was not associated with any of the four mercury exposure variables.

Age-Exposure Interaction

For each of the dependent variables listed in Table 9, another model was fitted with the statistically significant covariates listed and an age-by-exposure interaction term. The age-by-exposure interaction term was not statistically significant in the models for any of the outcome variables. In a few instances, the interaction term approached statistical significance ($0.05 < p < 0.15$). However, in these cases the sign of the parameter estimate was in the opposite direction from that expected. That is, the estimated effect of exposure was less for the older subjects than for the younger subjects.

Comparison of Participants Examined in Both Studies

A total of 89 exposed and 83 unexposed participants in our study were examined in the previous study of these cohorts (Albers *et al.*, 1988). Descriptive statistics of data from the previous study comparing those examined and those not examined in the two studies are presented separately for the two exposure groups in Table 10. Relative to those not examined in our study, those we examined were younger, somewhat better educated, and somewhat less likely to be a smoker at the time of the previous study. There were no striking differences between those we examined and did not examine in terms of the mercury exposure variables. Among the neurologic variables, those examined had slightly better nerve conduction, less tremor, better handeye coordination, and were less likely to have been classified as

TABLE 10. Comparison of selected demographic, exposure, and outcome variables (measured in 1986) for those examined and not examined in the current study by exposure status

Variable	Unexposed				Exposed			
	Examined (n = 83)		Not Examined (n = 172)		Examined (n = 89)		Not Examined (n = 158)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Demographic:								
Age in 1986	63.3	6.62	64.8	7.69	61.5	5.54	65.6	7.60
Education	11.98	2.45	11.60	2.72	12.45	1.96	11.30	2.58
Vocabulary	17.0	4.68	16.4	4.72	17.8	4.11	15.5	4.73
Current drinker	28.9%	n=24	34.9%	n=60	34.8%	n=31	20.9%	n=33
Drink intensity*	6.8	5.33	6.9	5.14	5.5	3.96	5.9	5.00
Current smoker	19.3%	n=16	22.1%	n=38	20.2%	n=18	27.2%	n=43
Smoke intensity**	2.3	1.00	2.5	1.06	2.2	0.77	2.3	0.97
Exposure:								
HgDUR	-	-	-	-	21.0	8.5	21.1	9.1
HgCUM	-	-	-	-	3600	1094	3592	1245
HgAVG	-	-	-	-	193.3	84.4	203.8	112.0
Hg300	-	-	-	-	3.7	2.3	3.5	2.6
Hg600	-	-	-	-	0.7	0.9	0.8	1.1
HgPEAK	-	-	-	-	617.6	283.6	664.8	410.0
Outcome:								
Tibial Motor NCV	44.7	3.97	43.9	4.48	44.4	4.96	43.5	4.19
Ulnar Motor NCV	58.3	4.39	57.4	4.88	57.4	4.92	57.2	4.48
Tremor Acceleration	0.80	0.33	0.82	0.31	0.78	0.30	0.95	0.57
Polyneuropathy	6.0%	n=5	21.5%	n=37	6.7%	n=6	17.7%	n=28
Handeye Coord. Error	1.80	0.38	1.93	0.40	1.89	0.36	2.05	0.44

*drinks per week
**packs per day
*** Higher score indicates poorer performance

having polyneuropathy in the previous study than those who were not re-examined.

Outcome variables obtained with identical or very similar tests from the two studies were available for analysis for six outcomes. Analyses were restricted to those participants not meeting our exclusion criteria and having valid data for both measurements. Standardized regression coefficients obtained from backward-elimination, stepwise regression of these six pairs of variables on relevant covariates and the cumulative mercury exposure variables are presented in Table 11. The magnitude of the estimated coefficients was roughly consistent between the two studies for lower-extremity nerve conduction velocity, ulnar motor conduction velocity, and Handeye Coordination Test performance. The magnitude of the estimated coefficients was greater in the present study for quantitative tremor, abnormal postural tremor on physical examination, and meeting a case definition of peripheral neuropathy than in the previous study.

DISCUSSION

This study of formerly mercury exposed workers was performed in follow-up to a study of the same cohort performed approximately ten years previously. In the current study, several neurologic outcomes were statistically significantly associated with mercury exposure that had ended 30 years or more prior to evaluation. In this heavily exposed population, the cumulative mercury exposure summary variable was more consistently associated with neurological health outcomes than were the other measures of mercury exposure, including exposed vs. unexposed, average urinary mercury exposure, peak mercury exposure, number of peaks greater than 600 µgHg/L and ever having a peak above 600 µgHg/L.

Among the tests of peripheral nervous system function, classification as having peripheral neuropathy, peroneal motor nerve conduction velocity,

TABLE 11. Comparison of Cumulative Exposure Standardized Regression Coefficients for Key Outcome Variables observed in a Previous Study (UM) and the Present Study for Participants Examined in Both Studies.

Dependent variable	N	Std. Beta	p-value*
UM Tibial NCV	103	+0.023	0.814
Peroneal NCV	103	-0.037	0.688
UM Ulnar Motor NCV	108	-0.225	0.020
Ulnar Motor NCV	108	-0.196	0.028
UM Quantitative Tremor	139	-0.014	0.869
Quantitative Tremor	139	+0.111	0.185
UM Abnormal Postural Tremor (Px)**	140	+0.080	0.467
Abnormal Postural Tremor (Px)**	140	+0.226	0.044
UM Polyneuropathy**	140	-0.084	0.543
PN Case Definition**	140	+0.247	0.082
UM Handeye Coordination	136	-0.165	0.043
Handeye Coordination	136	-0.135	0.076

* P-value testing the hypothesis that the estimated regression coefficient = 0 in stepwise regression models that included the covariates listed in Table 9.

** Logistic regression. Positive coefficient indicates adverse effect of exposure.

ulnar motor nerve conduction velocity, and peroneal motor nerve F-wave latency were all statistically significantly associated with cumulative mercury exposure after controlling for covariates. Among the tests of central nervous system function, only the results of the Handeye Coordination test were significantly associated with cumulative mercury exposure after controlling for covariates. Quantitative assessment of tremor was nearly statistically significantly associated with cumulative mercury exposure. No association was observed between cumulative mercury exposure and a quantitative measure of dementia. No significant age-exposure interactions were observed for any of the outcomes selected as primary ones.

The results of the present investigation are partially consistent with those of the previous investigation of this cohort of formerly mercury exposed workers (Albers *et al.*, 1988). Some difficulty in comparing the results arises because investigators of the previous study did not restrict their exposure-effect analyses to a limited set of exposure measures as was done in the current study, nor did they restrict multivariate analyses to an *a priori* selected set of outcomes.

In both studies, significant associations were observed between mercury exposure and a dichotomized outcome for presence of peripheral neuropathy. In the current study, however, the association was observed between cumulative mercury exposure and this outcome, and in the previous study the association was observed only when subjects with peak exposure in excess of 850 µgHg/L were compared to all other subjects. Several electrophysiological outcomes were associated with cumulative exposure in the current study, including peroneal motor nerve conduction velocity, peroneal F-wave latency and ulnar motor nerve conduction velocity, whereas only the median distal sensory latency and the number of motor nerve abnormalities were significantly associated with mercury exposure in dose-response analyses in the previous study. Cumulative mercury exposure was associated with postural tremor evaluated during the physical examination and nearly significantly associated with a quantitative measure of tremor in the current study, whereas a quantitative measure of postural tremor was associated with mercury exposure in the previous investigation. Comparison of results of tests of central nervous system function is not possible, as neurobehavioral results from the previous investigation have not been published.

The results obtained in the current study are generally consistent with those observed in a study of Norwegian workers formerly exposed to mercury (Andersen *et al.*, 1993). Consistent findings include higher prevalence of abnormalities of distal sensation, postural tremor, and Romberg test (our data not shown) on physical examination and slightly reduced NCVs in the arm among exposed workers than among an unexposed comparison group. We did not observe increased prevalence of impaired coordination or tandem gait abnormalities, as did Andersen *et al.* Relative to our exposed group, theirs was younger (all under 65 vs. all over 65), had a shorter duration since mercury exposure (average of 12.3 years vs. greater than 30 years), and lower exposure (26 of 53 with cumulative urine mercury greater than 500 µgHg/L vs. all greater than 2000 µgHg/L).

We did not observe associations between prior heavy mercury exposure and either a dementia rating scale score or a number of tests of cognitive function. The neurobehavioral tests we used were not insensitive. Expected relationships between these measures and both age and education were observed. The absence of cognitive deficit findings in our study and the absence of published findings of deficits on similar neurobehavioral tests included in the other two long-term follow-up studies (Albers *et al.*, 1988; Andersen *et al.*, 1993) suggest that reported effects on cognitive performance among workers currently or recently exposed to mercury (e.g., Ngim *et al.*, 1992; Smith *et al.*, 1983; Williamson *et al.*, 1982) may not persist many years after exposure has ceased. Alternatively, our ability to observe an association between mercury exposure and persistent impairment of cognitive function would have been attenuated if those with such impairment were less likely to participate than those without impairment.

The authors of the previously published study of this cohort suggested that subclinical damage caused by mercury exposure was most apparent in the oldest workers because "aging may unmask prior subclinical damage" (Albers *et al.*, 1988). In spite of reduced participation in the current study, the relative similarity of the two groups, with the exception of removal of a higher proportion of those who were older in 1986 (when the previous study was performed), offered an excellent opportunity to observe whether highly exposed younger workers showed the same neurologic abnormalities with the passing of time as the older cohort members did in 1986. Contrary to the results of the previous investigation, no age by exposure interaction was observed in the current study. It is possible that the small number of older, heavily exposed subjects who made the major contribution to this effect in the previous study (Albers *et al.*, 1988) were not available for participation in the current study.

The results of numerous statistical tests are reported. No formal correction for these multiple comparisons was made during data analyses. To reduce the magnitude of a potential problem with multiple comparisons, we identified a subset of the outcomes variables as primary. The primary outcome variables were ulnar motor nerve conduction velocity, peroneal motor nerve conduction velocity, peroneal nerve F-wave latency, peripheral neuropathy case definition status, tremor RMS acceleration, Handeye Coordination Test log RMS error, and dementia case definition. We consider the coherence and consistency of the statistically significant results to be of most importance when interpreting the results. In addition, although quite a number of p-values are presented in some tables, most of these p-values were used in a descriptive manner.

Several sources of bias may have influenced the results of the current study. First, errors in estimation of exposure may have occurred. Exposure estimation was based on measurement of urine mercury concentration, which was difficult to perform with high precision during the 1950's and 1960's. No information is currently available about the quality control procedures used in the collection and analyses of these specimens. If error introduced by laboratory procedures was random, then the effect on estimates of association with health outcomes would be toward the null hypothesis. If error was systematic, the effect could be either toward or away from the null hypothesis, depending upon the particular error. In addition, because the half-life of mercury in urine (approximately 50 days) (Berlin, 1986) is a considerable fraction of the sampling interval (i.e., quarterly), urine mercury concentration represents an integrated average of exposure for that period and will therefore underestimate large but short-term exposures. If such exposures were, in fact, causally related to the health outcomes studied, and were randomly distributed across all exposure categories, the resulting bias would be toward the null. If, however, such underestimation occurred preferentially among more heavily exposed individuals, then the resulting bias would lead to an underestimate of the exposure magnitude that produced chronic health effects.

The comparison group was chosen from among former employees who never worked in the departments that processed mercury. The potential for other hazardous exposures still existed for this group of non-mercury exposed workers, however. In addition to mercury, the industrial workers studied were at risk of exposure to lead, beryllium, and uranium. Of these, lead is the only substance known to have significant relationship with neurologic impairment. A lead exposure indicator variable was not selected as a significant covariate for any of the outcomes in stepwise regression analyses. If the neurological function of members of the comparison group was affected adversely by these exposures, the resulting bias would have attenuated observed associations between mercury exposure and neurological function.

Because of its cross-sectional design, the current study is one of surviving workers. If workers who died or became disabled between the previous study and the current study were more affected by exposure to mercury than workers who were able to participate in both studies, then such susceptible workers would be under-represented in the current sample. Evidence was observed that, at the time of the previous study, those who participated in the present study were somewhat healthier than those who did not, although there was not clear evidence that this effect was differential between the two exposure groups. Selective loss of a more susceptible subpopulation from the original cohort would produce a bias towards the null hypothesis.

It is also likely that there was some error in measurement of health effects. Given the use of standard procedures with which the investigators have considerable expertise, such error was not likely to be large. Also, it is not likely that such error was related to exposure, as the examiners were not aware of the exposure status of the participants. The effect of any such error, however, would be to attenuate the observed association between exposure and outcome, if one existed.

In summary, the following conclusions are made from the results of this investigation:

1. Neurologic effects of heavy mercury exposure were still detectable more than 30 years after cessation of that exposure.

2. Effects were observed mainly for the peripheral nervous system, with physical examination and electrodiagnostic evaluation providing results having the best associations with exposure.

3. Postural tremor, assessed by physical examination and accelerometry, was weakly associated with past mercury exposure.

4. No associations were observed between past mercury exposure and either a quantitative measure of dementia or other measures of cognitive function.

5. Of all the summary exposure measures evaluated, the cumulative mercury exposure index was the summary exposure measure most consistently associated with neurological health outcomes.

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