Health Hazard Evaluation Report

HETA 83-465-1674
STACO, INC.
POULTNEY, VERMONT

PREFACE

The Hazard Evaluations and Technical Assistance Branch of NIOSH conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The Hazard Evaluations and Technical Assistance Branch also provides, upon request, medical, nursing, and industrial hygiene technical and consultative assistance (TA) to Federal, state, and local agencies; labor; industry and other groups or individuals to control occupational health hazards and to prevent related trauma and disease.

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I. SUMMARY

In September 1983 the Vermont Department of Health invited the National Institute for Occupational Safety and Health (NIOSH) to assist in an investigation of occupational exposures to elemental mercury at Staco, Inc., Poultney, Vermont. In March 1984, NIOSH and Vermont researchers conducted an environmental/medical survey at the Staco factory. Eighty-four Staco employees participated in this study. In August 1984, a similar survey was conducted using a comparison group of 79 employees of Dowty Electronics, Brandon, Vermont.

A review of previous Vermont OSHA and company measurements of mercury vapor air levels at the plant revealed personal monitoring samples ranging from 24-308 ug/m^3 (time-weighted averages). During the NIOSH survey, personal samples ranged from 25.6-270.6 ug/m^3 for mercury workers. No mercury vapor was detected at the comparison plant. Urine mercury levels among studied Staco workers ranged from 1.3-344.5 ug/g creatinine. Five percent of the study population had levels exceeding 150 ug/g creatinine and three workers exceed 300 ug/g creatinine. These results indicate increased absorption of mercury among the Staco workers. All urine mercury levels among the comparison group were below 10 ug/g creatinine, a value compatible with normal background levels in unexposed adults.

Symptom prevalences among the Staco workers exceeded those among the comparison group for 21 of 28 symptoms. Prevalences of positive neurological findings among the Staco workers also tended to be higher, particularly for the findings of static tremor (19% of Staco workers vs. 10% of Dowty workers) and difficulty with heel-to-toe walk (15% vs. 3%). The prevalences of symptoms or neurological findings, however, could not be unequivocally associated with mercury exposures as measured by urine mercury level or a calculated chronic exposure index.

There was no evidence of a difference in reproductive outcomes in the two groups. Fertility rates in the two populations were similar. The reproductive histories did not suggest group differences in frequencies of adverse reproductive outcomes, although the numbers involved were too small completely to exclude such effects.

There was no clinically important intergroup difference in thyroid status as measured by a calculated free thyroxine index. There were, however, significantly increased prevalences of elevated serum thyroxine levels and decreased triiodothyronine resin uptakes among the comparison group. These results were in a pattern often found with oral contraceptive use but were not explained entirely by differences in hormone usage between the two groups.

There were no intergroup differences for the standard clinical tests of renal function except for a significantly higher mean specific gravity among the Staco workers. Positive dose-response effects were found, however, for urine N-acetyl-b-D-glucosaminidase (NAG) with urine mercury and serum beta-2-microglobulin (B2M) with the chronic exposure index. NAG is an indicator of renal proximal tubule injury. The biological significance of serum B2M is unknown. There was no evidence of differences in proximal tubule function as measured by urinary B2M or retinol binding protein. The intergroup differences were generally at subclinical levels and would reasonably be expected to resolve following cessation of exposure to mercury.

KEYWORDS: SIC 3829 (Measuring and Controlling Devices, not elsewhere classified), mercury, kidney disease, neurological symptoms, thyroid

II. INTRODUCTION

In September 1983 the Vermont Department of Health invited the National Institute for Occupational Safety and Health (NIOSH) to assist in an investigation of occupational exposures to elemental mercury in the thermometer manufacturing process at Staco, Inc. in Poultney, Vermont. The department's concern was prompted by a history of Vermont Occupational Safety and Health Administration (VOSHA) citations to the plant for elevated mercury vapor levels and reports of increasing urine mercury levels among the workers. The plant employed approximately 120 employees, half of whom worked in the thermometer process. The remainder worked in the "glass" plant and produced glass scientific products such as microscope slides, cover slips, and pipettes. In March 1984 a medical/environmental survey was conducted at the Staco facility. In August 1984 a similar survey was conducted on a comparison group at Dowty Electronics in Brandon, Vermont.

III. BACKGROUND

The Staco factory consists of two open, one-story buildings connected by a short hallway. In one building, the thermometer plant, mercury thermometers are produced. In this process, bulb glass is flame-heated and air-blown to form a bulb that is then heat-sealed to lens glass. The tube is next vacuum-injected with mercury and the open end is heat-sealed to form an expansion chamber (head) at the top. Another expansion chamber is heat-formed near the bulb and is subsequently modified by heating to form a check valve constriction. The head is then taken off and the end heat-sealed. After degassing under partial vacuum, the scale is set using the "pointing and grading" machine. The scale is next burned onto the thermometer, which is then sent through quality control, packaged, and shipped. After each application of heat to the glass, the glass is sent through an annealing oven to remove heat-induced stresses. Throughout the process there are numerous opportunities for breakage and the escape of mercury liquid or vapor. Respirators are worn in certain areas with high mercury exposures (e.g., in the mercury room where the mercury is vacuum injected and in the annealing oven room). In the other building, the glass plant, glass scientific equipment including pipettes, capillary tubes, microscope slides and cover slips are processed using a variety of open-flame and cutting techniques. Some glass workers, however, work on processes that are located in the thermometer building.

Review of the results of urine mercury levels obtained from Staco employees from 1978 through 1983 indicated that the percentage of tests with a level of >200 ug mercury/liter on initial screening rose from 5.5% to 48.6% and the percentage with >300 ug/liter rose from 1.1% to 25.0%. Review of environmental sampling from late 1983 (conducted both by the company and VOSHA) showed that several areas of the thermometer plant had average exposures that exceeded the OSHA mercury standard of 100 ug/m^3 as a ceiling concentration. Many additional areas exceeded the NIOSH recommended criterion of 50 ug/m^3 as an 8-hour time-weighted average concentration.

The Dowty also facility consists of a one-story building divided into several large open areas. The company produces a variety of electronic components, circuit boards and cable harnesses. No mercury is used in their processes. Solders containing lead are used in several departments.

IV. METHODS

A. Environmental

We designed the study to document exposures, to identify specific sources for the exposures, and to detect any adverse health effects among the employees. The environmental survey entailed area and personal sampling for mercury vapor levels. This sampling was conducted for seven to eight hours over the work shift and provided 8-hour time-weighted average (TWA) concentrations. The environmental samples were collected on hopcalite sampling medium using low volume gas sampling pumps calibrated at a flow rate of 200 cc/minute. The samples were analyzed for mercury by flameless absorption spectroscopy. In addition, a Mercury Vapor Sniffer was used to pinpoint localized sources of mercury and areas of potential contamination.

B. Medical

The medical portion of the study consisted of a questionnaire and a neurological exam. The questionnaire obtained demographic information, detailed occupational history (with history of potential confounding exposures), past medical history, medication list, symptoms, and a reproductive history. The exam checked for abnormal ocular movements, several types of tremor, several signs of dyscoordination or balance disturbance, and standard deep tendon reflexes. All exams (with one exception) at both sites were performed by the same examiner. We also administered a battery of three neurophysiological tests (for tremor, vibratory sensation, and grip strength) and a panel of serum and urine lab tests to measure renal function. Symptoms of thyroid dysfunction could be mistaken for some symptoms of chronic mercury toxicity. Also, mercury is known to accumulate in the thyroid[1]. For these reasons, we also obtained a blood specimen to assess thyroid function, measuring triiodothyronine (T3) uptake and thyroxine (T4), and calculating the free thyroid index ("T7"). To assess renal function, we measured urine mercury, total protein, albumin, N-acetyl-b-D-glucosaminidase (NAG), beta-2-microglobulin (B2M), and retinol binding protein (RBP) in the urine. We also measured specific gravity and urinary creatinine. In the serum, we measured creatinine, B2M, and RBP for clearance ratio calculations. Finally, we measured urinary levels of cadmium, arsenic, and lead to exclude these other heavy metals as potential confounders. The urine specimen was a morning first-void specimen that was delivered at the start of the work shift.

Participation in the study was offered to all current Staco employees (including several home-workers) and to several recent retirees. The Staco employees were evaluated during March 1984. Difficulties were encountered in identifying an appropriate comparison population, and this group was evaluated in August 1984. The comparison population came from another rural Vermont instrument manufacturer (Dowty Electronics), and we offered participation to all current employees there. No Dowty participants had ever worked at Staco.

Based on industrial hygiene data and the physical layout of the plant, jobs at Staco were divided into four categories--(1) mercury process; (2) glass process and general labor, located in the thermometer building; (3) glass process, in the connected glass building; and (4) other miscellaneous. We also constructed an index to estimate total mercury exposure over time. We assigned to each of the four job categories a weighting factor calculated as the mean urine mercury level for all current workers in that category divided by the mean urine mercury for all employees at Staco. For each employee, we then calculated his or her chronic exposure index by summing the time (in months) spent in each job category multiplied by the weighting factor for that category. Because there was no exposure to mercury at the control plant, this index could not be calculated for the comparison population.

Statistical analysis was performed using the Statistical Analysis System (SAS) programs. Statistical significance was indicated by a p value of less than 0.05 or by 95% confidence intervals.

V. EVALUATION CRITERIA

A. Environmental Criteria

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Criteria Documents and recommendations, 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLV's), and 3) the U.S. Department of Labor (OSHA) occupational health standards. Often, the NIOSH recommendations and ACGIH TLV's are lower than the corresponding OSHA standards. Both NIOSH recommendations and ACGIH TLV's usually are based on more recent information than are the OSHA standards. The OSHA standards also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH-recommended standards, by contrast, are based primarily on concerns relating to the prevention of occupational disease. In evaluating the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet those levels specified by an OSHA standard.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8- to 10-hour workday. Some substances have recommended short-term exposure limits or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high short-term exposures.

NIOSH currently recommends that exposure to inorganic mercury be limited to 50 micrograms per cubic meter (ug/m^3) as an 8-hour time-weighted average (TWA)[6]. The American Conference of Governmental Industrial Hygienists (ACGIH) also recommends that inorganic mercury exposure be limited to 50 ug/m^3 as an 8-hour TWA[7]. The current Occupational Safety and Health Administration (OSHA) standard for inorganic mercury is a ceiling level of 100 ug/m^3[8].

B. Toxicological

Mercury can enter the body through the lungs by inhalation, through the skin by direct contact, or through the digestive system[2].

Acute or short-term exposure to high concentrations of mercury causes tightness and pain in the chest, difficulty in breathing, coughing, inflammation of the mouth and gums, headaches, and fever[2,3]. Acute mercury poisoning is, however, relatively rare in industry today.

Chronic or long-term exposure to lower concentrations of mercury is more common. Chronic mercury poisoning is known to cause kidney damage (nephrosis), tremors and shaking (usually of the hands), inflammation of the mouth and gums, metallic taste, increase in saliva, weakness, fatigue, insomnia, allergic skin rash, loss of appetite and weight, and impaired memory. These symptoms generally occur gradually and may be associated with personality changes such as irritability, temper outbursts, excitability, shyness, and indecision[2,3]. Finally, there is theoretical potential for adverse reproductive effects, but these have not been documented[4,5].

Occupational exposures to mercury are often assessed by monitoring urine mercury levels. The reported correspondence of air levels (in ug/m^3) to urine levels (in ug/L) varies from a 1:1 ratio to a 1:2.6 ratio. There is no generally accepted value, although the World Health Organization currently uses 1:2 (i.e., exposure to an air level of 50 ug/m^3 would tend to result in a urine level of 100 ug/L, on the average)[9].

Traditionally, symptoms would be expected to appear at air levels above 100 ug/m^3. Recent data, however, suggest that early symptoms (both renal and neurobehavioral) may appear with air levels in the 50-100 ug/m^3 range, and there are reports (of uncertain validity) of effects at even lower levels[9]. Similarly, symptoms would classically be expected to appear at urinary levels above 300 ug/L, but recent reports suggest minimal neurobehavioral and subclinical renal effects may be detected with urinary levels as low as 50-100 ug/g creatinine[10] (levels standardized to ug Hg/g creatinine are roughly comparable to those

measured in ug Hg/L urine). It is important to note that with elemental mercury there is great unpredictability in the correspondence of air and urine levels and in the correlation of either of these measures with the appearance of symptoms. This is particularly true
if attempts are made to apply these measures to predict responses in individuals.

VI. INDUSTRIAL HYGIENE RESULTS

The review of recent environmental monitoring (conducted by Vermont OSHA and by the company) at the plant demonstrated area samples ranging from 47-166 ug/m^3 (time-weighted averages) with almost all sites greater than 50 ug/m^3. Personal sampling had ranged from 24-308 ug/m^3, with several jobs consistently above 100 ug/m^3. The current OSHA standard for mercury vapor is 100 ug/m^3 as a ceiling, and NIOSH recommends a level of 50 ug/m^3, as an 8-hour TWA.

During the NIOSH survey at Staco, 40 samples were collected (Table 1). Seventeen were personal samples from mercury workers. These ranged from 25.6 ug/m^3 to 270.6 ug/m^3 with a mean of 75.6 ug/m^3. There were 10 readings from glass workers, which ranged from 2.8 to 24.4 ug/m^3 with a mean of 9.3 ug/m^3. There were 11 area samples from the thermometer building. These ranged from 25.7 to 118.5 ug/m^3 with a mean of 56.7. Seven of 11 (64%) of the area samples exceeded NIOSH recommendations and 1 of 11 (9%) exceeded OSHA criteria. For the personal samples, 9 of 17 (53%) mercury workers were above NIOSH recommendations and 4 of 17 (24%) exceeded the OSHA value. None of the glass plant workers exceeded either criterion. Finally, 2 area samples were obtained from the NIOSH trailer to detect any contamination of the trailer with mercury during the course of the study. These averaged 22.5 ug/m^3 and suggest that, despite the brief duration of the study, some contamination may have occurred from workers inadvertantly bringing mercury in on their shoes and clothes.

Environmental sampling at Dowty Electronics was conducted in October 1985. A direct reading Mercury Vapor Sniffer was used and no mercury was detected on any of the 25 samples taken. In addition, five full-shift area samples for lead were taken in the vicinity of soldering pots. Results were below the limit of detection (2 ug/m^3) in all five samples.

VII. MEDICAL/EPIDEMIOLOGICAL RESULTS

Eighty-four individuals participated in the study at the Staco plant and 79 at Dowty Electronics. Participation rates were 69%

and 81%, respectively. The demographics of the two groups were very similar. The Staco group was 86% female and the Dowty group 87% female. There were no racial differences in the two populations. The Staco group ranged in age from 18-68 with a mean of 34.8 (s.d.=11.6) and comparison group ranged from 17-63 with a mean of 33.1 (s.d=10.9). Each group ranged from 8-16 years of education with a mean of 11.8. The Staco workers had a mean tenure of employment of 65.0 months (s.d.=48.8) and the control group a mean of 62.5 (s.d.=48.1) months. Forty-eight percent of the Staco workers were current smokers compared to 51% of the control workers.

We calculated urine mercuries (standardized to urinary creatinine) for 79 Staco workers and 70 controls. These levels ranged from 1.3-344.5 ug/g creatinine with a mean of 73.2 (s.d.=69.7) for the former and from 0-10.0 ug/g creatinine with a mean of 4.2 (s.d.=2.3) for the latter (p=.0001, t-test). The levels for the control group are all compatible with "normal" levels (>10 ug/ml) in unexposed individuals. The mean urinary mercury at Staco was higher for males than females (96.2 compared with 69.4), but this was not statistically significant. Mean urine mercury was not affected by smoking status, age, educational level, or total duration of employment. There was a strong correlation between the personal environmental monitoring and the urinary mercury values. For the 25 workers from whom we obtained both urinary mercury levels and breathing zone mercury vapor levels, the correlation coefficient for the two measurements was 0.88 (p=.0001) (Figure 1). For these measurements, the ratio of the mean air level (50.1 ug/m^3) to the mean urinary mercury level (65.9 ug/g creatinine) was 1:1.3, which is within the ranges found in other studies[9].

At Staco, the mean urine mercury for the 29 mercury process workers was 118.2 ug/g creatinine (s.d.=87.5) and for 50 non-mercury workers was 47.0 (38.2). This difference was highly significant (p=.0002, t-test). When the cohort was stratified by current job classification into the four categories outlined in the Methods section, mean urinary mercuries were as follows: mercury process, 118.2 (s.d.=87.5); glass process in the thermometer building, 65.4 (s.d.=29.6); glass process in the glass building, 30.3 (32.5); and others, 56.0 (52.2). There were no significant correlations of urinary mercury with tenure in current job, although there was a non-significant negative correlation in the glass workers. There was, however, a modest positive correlation of urine mercury with the calculated exposure index (r=0.23, p=0.05).

Symptoms:

The questionnaire elicited the presence of 28 symptoms (Table 2).

The most frequently reported symptoms in the Staco group were headache (29% of interviewees), difficulty sleeping (25%), nervousness (23%), skin rash/sores (20%), emotional lability (18%) and difficulty with memory or concentration (16%). Headache (24%), nervousness (22%), emotional lability (18%) and skin rash/sores (14%) were also the most frequently reported symptoms in the comparison group. When the prevalences of each symptom in the two groups were compared (see Table 3), the relative risks for each symptom in the Staco group compared to the Dowty group exceeded 1.15 for 21 of the 28 symptoms queried. The relative risks were less than .85 for only 3 symptoms. The comparisons for individual symptoms were statistically significant in only 2 cases (metallic taste and difficulty sleeping), but this overall pattern of elevated relative risks was significant ($p < .02$, normal approximation to binomial). When this analysis is restricted to those symptoms one would expect to be associated with mercury toxicity (see Table 3), a similar, but not significant, pattern was obtained with relative risks exceeding 1.15 for 12 of 17 ($p < .14$, normal approximation to binomial) and less than .85 for only 2 of 17.

In the Staco group, those with each symptom were compared to those without that symptom with respect to their mean urine mercury levels (Table 4) and their mean chronic exposure indices (Table 5). This analysis was restricted to the Staco group because: (1) all Dowty personnel had urine mercury values at or below 10 ug/g creatine, and any symptomatic Dowty worker would necessarily have a low urine mercury and would tend to mask any association of symptoms with high urine mercuries among the Staco employees; and (2) the chronic exposure index cannot be calculated for Dowty workers.

Mean urine mercury levels (Table 4) among symptomatic workers exceeded (by at least 10%) those among non-symptomatic workers for only 6 of 28 symptoms and were less than those of non-symptomatic workers (by more than 10%) in 17 of 28 instances. Considering only symptoms particularly likely to be associated with chronic mercurialism, mean mercury levels were higher among symptomatic workers for only 3 of 17 symptoms and were lower in 12 of 17 instances. As shown in Table 4, only one individual symptom (chest pain/tightness) was associated with a significant difference in mean urine mercury levels (in this instance, lower for symptomatic workers). Overall, there was a tendency for lower mean values among those with positive responses (both for all symptoms queried and for those particularly associated with chronic mercury toxicity), but this trend was not statistically significant.

Mean values for the chronic exposure index for symptomatic individuals exceeded (by more than 10%) those for non-symptomatic workers for 14 of 28 symptoms and were less than those of non-symptomatic workers (by more than 10%) in 8 of 28 (Table 5). When limited to symptoms particularly likely with mercury toxicity, symptomatic individuals had higher mean exposure indices for only 5 of 17 symptoms; they had lower values for the index for 6 symptoms. As shown in Table 5, there was a significantly higher mean index found only for those with shortness of breath, chronic cough, and diarrhea. None of these three symptoms would be particularly associated with chronic mercury toxicity. Those reporting problems with handwriting had a significantly lower mean index. There was no apparent overall pattern of higher or lower values for the exposure index among workers with positive responses for symptoms (either for all symptoms queried or when restricted only to symptoms particularly associated with chronic mercury toxicity).

As an additional part of the analysis, symptoms were grouped (as indicated in Table 2) into the following categories: behavioral, neurological, chest, constitutional/gastrointestinal, and gingival. The mean number of symptoms reported per individual for each category and overall are shown in Table 6. On average, Staco workers reported a significantly greater number of symptoms overall (2.9/person vs. 1.9/person, $p < .05$ by t-test). In each symptom category, Staco workers also reported a higher mean number of symptoms per person than did the control workers, but these differences were not significant and averaged less than one symptom/person in each category. For each symptom category we also performed a dichotamous analysis. All those who reported two or more symptoms in any given category were considered positive responders for that category; those with one or none were considered negative for that grouping. Thus, for example, those who had two or more out of the seven behavioral symptoms were defined as reporting behavioral effects, and so on. In this analysis, Staco workers had relative risks of reporting positive effects that exceeded 1.00 for all five symptom categories (Table 7). Although none of these individual relative risks were statistically significant, again the pattern is suggestive of a difference in symptom prevalences between the Staco and Dowty populations. When positive responders for each symptom group were compared with negative responders (Staco personnel only) with respect to mean urine mercury levels and mean values for the exposure index, no consistent pattern was seen, although those who were positive for constitutional/gastrointestinal effects had a significantly larger mean exposure index (Table 8).

Finally, symptom prevalences in Staco workers (both for individual symptoms and for the symptom groupings) were compared among those who fell above and below cutoff values for urine mercury level and chronic exposure index. The critical values for urine mercury level were set at 100 and 150 ug/g creatinine. These values represent the 75th and 90th percentiles, respectively, for the Staco workers urine mercury levels. The critical values for the exposure index were 120 and 175, which, similarly, represent 75th and 90th percentile values. None of these cutoff values demonstrated any consistent pattern with respect to symptom prevalences.

Neurological Exam:

The prevalences for the two groups of abnormal findings on the neurological exam are shown in Table 9. For the reflexes, we tested the biceps, triceps, patellar, and ankle. The workers were assessed as normoreflexic, hyperreflexic, or hyporeflexic as follows: The eight reflexes tested were checked for asymmetry. In one instance, an individual had an asymmetry of both leg reflexes (one side assessed as normal and one side as absent); this individual was considered normoreflexic in the analysis. Three others had asymmetries of one reflex tested and were also analyzed as normoreflexic. Individuals were considered hyperreflexic if they had at least two reflexes rated increased (e.g., both biceps and both patellar, etc.) and were considered hyporeflexic if they had at least two reflexes diminished or absent (e.g., both patellar and both ankle jerks, etc.).

The most commonly noted abnormalities in the Staco population were hyporeflexia (24% of the 83 examined), static tremor (19%), and difficulty with heel-to-toe gait (15%). Hyporeflexia and static tremor were the only commonly found abnormalities in the Dowty population (Table 9). Comparison of the two groups is seen in Table 10. The Staco workers had a significantly elevated relative risk for an abnormal heel-to-toe gait (p=.01, Fisher's exact) and a significantly diminished relative risk for hyporeflexia (p=.01, Fisher's exact). For the other components of the exam, there were no significant differences in the two groups, but again there was an overall pattern of higher prevalences of abnormal findings in the Staco population.

For the Staco workers, we compared those with and without abnormal findings in terms of their mean urine mercury levels and their mean values for the chronic exposure index. There was no significant difference in mean urine mercury for those with any specific abnormal finding compared to those without that abnormality, nor any overall pattern of higher or lower urine mercury levels for those with abnormal findings (Table 11). Staco workers with rest tremor, dysdiadochokinesis [difficulty performing rapid alternating movements] and hyperreflexia had significantly higher mean values for the exposure index, however, and those with difficulty with heel-to-toe gait had a higher mean index that just failed to reach significance (Table 12). Also, there was a suggestion of an overall pattern of higher mean values for the index in those with abnormal findings.

The results of the neurobehavioral tests were not available at the time of this writing. They will be issued separately as an addendum to this report.

Reproductive Outcomes:

The reproductive history obtained information concerning fertility and pregnancy outcomes.The mean number of pregnancies for Staco workers (or their spouses/partners) was 2.2 per person and for Dowty workers was 2.0. This does not represent a significant difference (p=.39, t-test). For females the comparable values were 2.5/woman in the Staco group compared to 2.0/woman in the Dowty group. For males the values were 1.0/man at Staco and 2.0/man at Dowty. None of these values were significantly different. Eight of 84 (10%) Staco workers and 10 of 79 (13%) Dowty workers reported difficulty conceiving (defined as trying for one year or more to become pregnant or father a child). Five (6%) Staco workers and 11 (14%) Dowty workers reported consulting a physician because of difficulties conceiving. Neither of these differences were significant.

The reported pregnancy outcomes are shown in Table 13a. Among Staco workers, 153 of 190 pregnancies (81%) resulted in term deliveries of normal infants; among Dowty workers, the comparable figures were 124 of 150 (83%). If the Staco workers are separated into those currently in the glass plant and those currently in the thermometer plant, the comparable figures are 103/133 (77%) and 50/55 (91%), respectively (therapeutic abortions excluded). The prevalence of normal outcomes in the thermometer workers does not differ significantly from that for the Dowty workers. Although lower than that for the glass workers, this difference falls just short of statistical significance. The slightly lower percent of normal outcomes among the thermometer workers is accounted for by slightly higher rates of prematurity and spontaneous abortion. When the analysis is limited to female workers, the results are as shown in Table 13b. In general, the findings are similar to those outlined above, except the relative risk of adverse outcomes (prematurity, birth defect or deformity, stillbirth, or spontaneous abortion) in the thermometer workers compared to the glass workers is significantly elevated (OR=3.01, 95% C.I.=1.02-9.51). This was not the case when the female thermometer workers were compared to the female Dowty workers. These findings probably can be accounted for by a relatively low rate of adverse outcomes in the glass plant workers.

The above analysis includes all previous pregnancies reported in both populations. We also analyzed only those pregnancies during any part of which the mother (or spouse) was employed at Staco. These results are shown in Table 14. There were only 17 such pregnancies; 8 of these were in female Staco empoyees. By comparison, there were 57 pregnancies in Dowty workers (employed at Dowty or anywhere else at some point during the pregnancy); 42 of these were in female workers. The numbers involved are too small to permit any valid statistical analysis, but it can be seen that the percentages of normal pregnancy outcomes, premature births and spontaneous abortions among Staco workers (results for thermometer workers and all Staco employees are essentially identical) are similar to those for Dowty workers.

Thyroid Function Studies:

We assessed thyroid function by measuring serum thyroxine (T4), percent triiodothyronine uptake (T3), and calculating the free thyroxine index (T7) from the product of the individual's T4 and T3. T4 is a measure of total circulating thyroid hormone (in forms both bound to serum carrier proteins and unbound). The T3 uptake is an indirect measure of these binding proteins. The T7 is an estimate of the unbound, or metabolically active, thyroid hormone and is the more accurate measure of clinical thyroid status.

As shown in Table 15, the mean level for T4 among Staco workers (9.6 ug/dL) was significantly lower than that for the Dowty group (11.1) (p=.0001, t-test). The mean value for T3 uptake for the Staco workers was 27.4% compared to 27.1% for the Dowty employees. This difference was not significant. Finally, the Staco group had a significantly lower mean T7 (2.7) than did the Dowty group (3.0) (p=.0002, t-test). The prevalences of abnormal thyroid function tests are shown in Table 16. Three (4%) of 83 Staco employees had abnormal (increased) T4 levels, compared to 16 (22%) of 73 Dowty workers (RR=.16; p=.0005, Fisher's exact). Only one (1%) of 83 Staco employees had an abnormal (decreased) T3; 11 (15%) of 73 Dowty employees had abnormal (diminished) T3 uptakes (RR=.08; p=.0015, Fisher's exact). There were no abnormal T7 indices among the Staco group and only one in the Dowty group. This difference was not significant. It should be noted that the T7 is better measure of clinical thyroid status.

Within the Staco group, we analyzed the thyroid function results for associations with either the urine mercury level or the chronic

exposure index. In the Staco workers, there was no apparent association between any of an individual's thyroid function measures and his/her urine mercury level. Correlation coefficients for urine mercury and T4, T3, and T7 were .005, .05 and .04, respectively. Correlations coefficients for the exposure index and T4, T3, and T7 were -.06, -.17. and .-16, respectively. None of these associations were statistically significant.
Because of the significant differences in T4 and T3 (but not T7) results between the two groups and the fact that the pattern of the difference (elevated T4 and decreased T3 uptake) suggested a change (increase) in thyroid binding proteins that can be seen with oral contraceptive (OCP) use (or other female hormones)[11], we analyzed the thyroid results for this factor. In both populations mean T4 levels were significantly higher and mean T3 levels significantly lower among those exposed to OCPs, and there were similar associations of abnormal T4 or T3 levels with OCP use (Table 17). Fourteen (17%) of 83 Staco workers who had their thyroid status measured reported using OCPs (or other female hormones); 13 (18%) of 73 Dowty workers reported the same. Even when the comparison of T4 and T3 results for the two groups was stratified according to OCP use, the intergroup differences persisted (Table 18). Thus, variation in hormone use by the two groups does not account for the T4 and T3 differences, but these intergroup differences seem more attributable to the results for the Dowty group than for the Staco group.

Renal Assessments:

To assess renal function, we measured the urinary and serum levels of chemical markers outlined in the methods section. The results of the renal assessments are shown in Table 19. For NAG there was a minimally higher mean value for the Staco group compared to the Dowty group (0.81 ug/g creatinine vs. 0.71 ug/g) and a relative risk of 2.46 for an elevated level (p=.29, Fisher's exact). For urinary B2M the Staco workers had a non-significantly higher mean (164.2 ug/g vs. 89.9) but a diminished relative risk of 0.27 for an elevated level (p=.33, Fisher's exact). If we eliminate the results for one marked outlier among the Staco workers, however, the difference in the means vanishes. For serum B2M there was a modest, non-significant difference in the means (1613.7 ug/L vs. 1536.2 ug/L) and a relative risk of 6.24 for an elevated level among the Staco workers (p=.07, Fisher's exact). For urinary RBP the mean values for the two groups were identical (0.14 ug/ml), but the relative risk for an elevated value among the Staco workers was 1.52 (p=.47, Fisher's exact). For serum RBP the mean values for the two groups were also identical (6.2 mg/dL), and the relative risk for an elevated level among the Staco workers was 0.93 (p=.75, Fisher's exact). It should be noted that there was a very high prevalence of elevated levels in each group.

The results of standard clinical assessments of renal status are also shown in Table 19. The Staco group had a lower mean total urinary protein (92.0 vs. 148.2 mg/g creatinine) and a relative risk of 0.89 for an elevated value. The Staco workers had a slightly higher mean urinary albumin (8.4 vs. 7.1 mg/g creatinine) and a relative risk of 1.50 for an elevated level. The Staco group had a significantly higher mean urine specific gravity (1.020 vs 1.017; p=.007, t-test), but all results in each group were within normal limits. The Staco group had a non-significantly higher mean urinary creatinine (143.8 vs. 129.2 mg/dL; p=.19, t-test). There is no normal range for this test because reference ranges are based on 24-hour collections, which were not done in this study. Finally, mean serum creatinines were essentially the same in the two groups (0.94 mg/dl vs 0.96 mg/dL). Except as noted above for the specific gravity results, none of group differences among the standard clinical assessments were statistically significant.

When we used urine mercury (standardized to creatinine) as a predictor for renal outcomes, we found the following (Table 20a): There was a significant positive correlation of urinary NAG level with urine mercury. This was true in the total population (r=.36, p=.0002) and when the analysis was restricted to Staco workers only (r=.48, p=.0002). The relationship persisted when diabetics were excluded from the analysis. There were no significant correlations of mercury levels with the serum or urine B2M, the ratio of B2M clearance to creatinine clearance, the serum or urine RBP, the ratio of RBP clearance to creatinine clearance, the total urinary protein, or the urinary albumin. Similarly, there were no correlations with specific gravity, urine creatinine, or serum creatinine. When the analysis was performed comparing mean urine mercury levels in those with and without abnormal values for each lab outcome (Table 21), there were no significant differences found although the results for NAG approached significance.

Next we considered the the renal outcomes in terms of the exposure index (Table 20b). This analysis applies only to the Staco workers as the exposure index is not calculated for the Dowty group. For NAG there was again a positive correlation (r=.30, p=.03), although it was less prominent than that with mercury level. This correlation no longer reached statistical significance, however, following exclusion of diabetics. The urinary B2M level and the ratio of B2M clearance to creatinine clearance both had significant correlations with the exposure index (r=.25, p=.03 and r=.24, p=.03, respectively), but these were no longer statistically significant following exclusion of one prominent outlier. For serum B2M, however, there was a persistent significant correlation (r=.31, p=.005). The urinary RBP and ratio of RBP clearance to creatinine clearance both also showed some correlation with the exposure index (r=.21, p=.06 and r=.24, p=.03, respectively), but much of this correlation can again be explained by one outlier. Serum RBP showed a modest, non-significant negative correlation with the exposure index (r=-.17, p=.13). Total urinary protein also demonstrated a significant correlation with the exposure index (r=.27, p=.02) that vanished with exclusion of one outlier. Urinary albumin did not show a prominent correlation with the exposure index. Significant negative correlations were found for specific gravity (r= -.25, p=.02), urinary creatinine (r= -.31, p=.006), and serum creatinine (r= -.23, p=.04). These negative correlations all persisted following exclusion of diabetics. When the analysis was performed comparing mean exposure indices in those with and without abnormal values for each lab outcome (Table 22), there were no significant differences found. Again, the results for NAG approached significance.

Job category did not predict at a significant level for any lab value. There was, however, a consistent tendency for mean values to be higher in the mercury process compared with the other categories (except in the cases of specific gravity and urine or serum creatinine where the means were lower in the thermometer line). Similarly, although urinary mercury levels were correlated with the IH personal sampling, there were no significant correlations of renal outcomes with the IH results.

Finally, all values for urinary cadmium and lead levels in each group were within normal limits (0.0-5.0 ng/ml and 0.0-80.0 ng/ml, respectively). All values for urinary arsenic levels in each group were also well within normal limits (0.0-80.0 ng/ml) with the exception of two borderline results (65.0 and 75.5) and two elevated results (95.5 and 213.0) in the Staco group. These findings would exclude these heavy metals as likely confounders for any effects otherwise attributable to mercury.

VIII. DISCUSSION

The environmental data, both the historical information obtained from the plant and that acquired by NIOSH researchers during the study, confirm overexposure to inorganic mercury vapor at Staco. Many samples, both personal and area, exceeded the NIOSH recommendation of 50 ug/m^3 (TWA) and/or the OSHA standard of 100 ug/m^3 (ceiling). The measurements obtained in the NIOSH trailer suggested some contamination of the trailer during the short duration of the study and supported the possibility of offsite contamination by mercury inadvertantly brought out of the plant on the workers' shoes, clothing, or persons. This was a concern addressed in a separate State Health Department study. The environmental sampling at the Dowty facility confirmed the absence of any mercury exposures to the comparison population and also indicated the absence of any signficant exposure to lead, a potential confounder for some signs of mercury toxicity.

The results of the urine mercury levels indicated increased absorption of mercury in the exposed population and also demonstrated greater absorption in the presumably more highly exposed thermometer workers (compared to the glass workers) at Staco. The mercury levels for the comparison population were all in a range compatible with normal background levels in unexposed adults (< 10 ug/ml). Despite the documented levels of exposure in the Staco personnel, urine mercury levels were not exceptionally high. Mean (and median) levels were below 100 ug/ml. Although association of mercury levels with signs of chronic mercury toxicity is notoriously inconsistent and unpredictable, effects of mercurialism are commonly expected to start at urinary levels in the range of 150-300 ug/ml or higher. Only 5% of the study population exceeded the lower limit of this range and only three individuals exceeded 300 ug/g creatinine. Finally, it should be noted that urine mercury levels are generally thought to best reflect relatively recent exposures (within two to three months of the sampling time) and are not necessarily reliable indicators of long-term exposure[12].

Symptoms:

The symptom survey revealed only two symptoms suggestive of mercury toxicity that were significantly associated with the Staco group. Mention should be made at this point of a statistical problem encountered when performing multiple comparisons. When, as in this study, many comparisons are made between the results for two different groups, associations or differences that are apparently statistically significant may arise merely by chance. Such chance findings do not necessarily imply a cause and effect association or a true relationship between the findings under study. To attempt to compensate for this phenomenon, we also looked at the overall pattern of the symptom prevalences. This overall pattern of symptom prevalences did suggest higher rates of individual symptoms in the Staco workers. Also, when symptoms were grouped into categories suggestive of behavioral or neurological effects, these categories were not individually associated with the Staco workers at a significant level, but the overall pattern was again one of higher prevalences at Staco. Within the Staco group, however, we could not associate symptoms (individually, in categories, or overall) with exposure to mercury, as estimated either by urine mercury level or the chronic exposure index. Thus, although the Staco workers had higher prevalences for most symptoms and for all symptom groups, this was not a strong difference, and it could not be unequivocally associated with mercury exposures at the levels encountered at the thermometer factory.

Neurological Exam:

For most individuals, the neurological exam had findings that were normal or indicated minor abnormalities unlikely to be of clinical significance. There were, however, increased prevalences in the Staco workers of static tremor, difficulty with heel-to-toe gait (only the latter reached statistical significance) and a significantly decreased prevalence of hyporeflexia, in comparison with the Dowty group. Again, there was an overall tendency for higher rates of positive findings (including other cerebellar signs) in the Staco personnel. The prevalences of positive findings could not be clearly associated with mercury exposure, as measured by urine mercury level, but there was a notable tendency for increased frequencies of findings in association with the exposure index. The increased prevalence of hyporeflexia in the Dowty group and the generally high prevalences in both groups are not readily explained. The intergroup difference may represent some secular trend in the assessment of the examiner, and the overall frequencies may reflect too loose a definition for hyporeflexia. Although the group differences in the prevalences of abnormal neurological findings could not be unequivocally associated with mercury exposure at the levels encountered in this population (as measured by urine mercury), there was a strong suggestion of group differences in cerebellar function compatible with chronic mercury toxicity. According to most of the literature on neurological effects of mercury, prominent neurological abnormalities would not be expected at these levels, although more subtle effects have been reported[10,13].

As stated earlier, the results of the neurobehavioral tests were not available at the time of this writing and will be issued as an addendum to this report when they are available.

Reproductive Outcomes:

The information obtained concerning comparative fertility rates did not suggest any intergroup differences as measured either by mean number of pregnancies per person/spouse or by reported difficulty in conceiving. When all pregnancies (i.e., whether potentially exposed or not) were considered, the Staco personnel had outcomes comparable to the Dowty workers. If only the thermometer process workers are compared to the Dowty group, there was a slight decrease in the percentage of normal outcomes and a slight increase in the total percentage of adverse outcomes, but the percentages of environmental sampling at the Dowty facility confirmed the absence of any mercury exposures to the comparison population and also indicated the absence of any signficant exposure to lead, a potential confounder for some signs of mercury toxicity.

The results of the urine mercury levels indicated increased absorption of mercury in the exposed population and also demonstrated greater absorption in the presumably more highly exposed thermometer workers (compared to the glass workers) at Staco. The mercury levels for the comparison population were all in a range compatible with normal background levels in unexposed adults (< 10 ug/ml). Despite the documented levels of exposure in the Staco personnel, urine mercury levels were not exceptionally high. Mean (and median) levels were below 100 ug/ml. Although association of mercury levels with signs of chronic mercury toxicity is notoriously inconsistent and unpredictable, effects of mercurialism are commonly expected to start at urinary levels in the range of 150-300 ug/ml or higher. Only 5% of the study population exceeded the lower limit of this range and only three individuals exceeded 300 ug/g creatinine. Finally, it should be noted that urine mercury levels are generally thought to best reflect relatively recent exposures (within two to three months of the sampling time) and are not necessarily reliable indicators of long-term exposure[12].

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Thyroid Function Studies:

Thyroid function was assessed for two reasons. Some symptoms of thyroid dysfunction (e.g., tremor, anxiety, or reflex changes) could be confused with classical symptoms of mercury toxicity. Also, mercury is known to accumulate in the thyroid, and the thyroid could, thus, be a target organ; there are little data in the literature to confirm or deny this hypothesis. There was no evidence of clinically significant thyroid dysfunction (as measured by the T7 index) in the Staco group. Thus, any symptoms or neurobehavioral abnormalities cannot be attributed to thyroid disease. Similarly there is no evidence of (clinically measurable) thyroid damage at the levels of mercury exposure encountered, although we could not have detected compensated subclinical damage (that might be detected, for example, by measuring thyroid stimulating hormone levels). We did find significant intergroup differences in T4 levels and T3 uptake in a pattern suggestive of an increase in thyroid binding proteins such as can be seen in pregnancy or with oral contraceptive use. We could not associate variation in the T4 or T3 uptake with mercury exposure (measured by urine mercury or by exposure index). We could associate relative increases in T4 and decreases in T3 with OCP or hormone use (in both populations), but such use was similar in the two groups and did not explain the intergroup differences. These intergroup differences seemed more attributable to variations in the Dowty group than in the Staco group.

Renal Assessments:

Before discussing the results of the renal assessments, some additional background is necessary. Classically, chronic renal toxicity from elemental mercury was thought to consist of albuminuria or a nephrotic syndrome with only minimal or late effects on creatinine clearance or tubular functions. More recently, it has been recognized that there are two types of proteinuria in this condition: a high- and a low-molecular weight proteinuria[15]. The former is primarily a glomerular effect and the mechanism may well be an idiosyncratic immune-complex glomerulnephritis[16]. The latter consists of a variety of smaller proteins, some of which normally are filtered in the glomerulus and then reabsorbed in the proximal tubule. Others are released into the urine when proximal tubule cells are damaged. Thus, this tubular proteinuria may reflect either dysfunction of or damage to proximal tubule cells. B2M and RBP are examples of the former and NAG the latter[15].

Elevated urinary NAG levels have been demonstrated in a variety of clinical states including drug toxicity, early rejection of transplants, and heavy metal toxicity. In addition, urinary NAG may be increased in diabetes and as a function of blood sugar[17]. It is thought to be more indicative of current activity of an injurious process than of chronic damage. Elevated urinary B2M levels have been demonstrated in similar circumstances (except diabetes), but are thought to be more a measure of chronic damage than of acute activity. Also, being freely filtered, urinary B2M levels are more sensitive to serum levels. RBP is thought to behave like B2M, except it is not hydrolized by acid urine and, thus, is less sensitive to destruction in the bladder or following collection.

There were no significant group differences in the standard clinical tests of renal function except for the higher mean specific gravities among the Staco workers (with all still within the normal range). This latter finding is not readily explained, as tubular damage would tend, if anything, to lead to a loss of concentrating ability with a trend toward lower specific gravity. Environmental conditions that would tend to lead to production of more concentrated urine (e.g., warmer ambient temperatures), would have been more likely during the summer and, thus, would have more likely affected the specimens from the Dowty group, which were collected in August. Parenthetically, one Staco worker did have quite high urinary protein measurements that were compatible with significant renal disease, but etiology is not established by this study. The individual was informed of these test results (as were all participants) when they became available.

The data demonstrate a dose-response relationship between urine mercury level and urinary NAG level and suggest an elevated relative risk for an abnormal NAG level among the Staco workers. No such findings were shown for urinary B2M, RBP, or any of the standard clinical measures of renal status. This is not inconsistent toxicologically because urine mercury is a measure of recent exposure and is less reliable as a measure of longstanding exposure or body burden. Thus, current exposure could well be associated with a measure of active damage (NAG) without being associated with measures of chronic damage (B2M, RBP). Similarly, when we considered the long-term index of exposure, we found a less prominent relationship with NAG, which disappeared with exclusion of diabetics. We were unable to demonstrate any consistent effects on urinary B2M or RBP in this population at the levels and duration of exposure
encountered in this population. Thus, even if mercury exposure in the range encountered in this population were sufficient to produce mild tubular damage (as might be indicated by the NAG results), this exposure may not be sufficiently severe to overcome compensatory mechanisms or reserve capacity and manifest itself as tubular dysfunction (as would be indicated by increased excretion of B2M or RBP). These results are consistent with others reported recently [18,19]. We were unable to demonstrate any effects on total urinary protein or albumin. We did see negative correlations of urinary and serum creatinine with increasing exposure index. These are not suggestive of renal disease. There was also negative correlation of specific gravity with increasing exposure index, and this could suggest an increasing difficulty in concentrating urine (in contrast to the intergroup comparison of this measure, which seemed to point to higher specific gravities in the Staco group). This finding requires further analysis.

B2M is normally present in serum, but its precise role is unclear. Its level is thought to be a function of cell turnover and may be elevated in a number of clinical situation such as inflammatory states and certain malignancies. It has also been shown to be elevated in workers exposed to heavy metals like cadmium and uranium[20]. The data demonstrate a similar, consistent dose-response effect using the index of chronic exposure and a non-significant increase in relative risk for elevated serum levels in Staco group. This finding is consistent with findings for other heavy metals, although its biological significance remains obscure.

Finally, it should be emphasized that for these renal effects, we are primarily considering subclinical effects. The correlations of protein levels with indices of exposure are, for the most part, associations within the normal ranges for these outcome measures.

We did not have great numbers of these values fall outside the normal range. Furthermore, it is by no means clear at this time whether such elevations merely represent biochemical abnormalities or whether they have clinical significance to the individual (either currently or as predictors of future, more serious renal disease).

Summary:

In summary, the study showed excess exposure to inorganic mercury vapor at the thermometer plant and documented evidence of absorption. The urine mercury levels, as a group, were elevated and in a range where, classically, minimal symptoms or signs of mercury toxicity would be expected. Nevertheless, the study suggests group differences in the prevalences of symptoms, neurological findings, and subclinical changes in renal status that are compatible with mercury toxicity. We cannot unequivocally associate these findings with mercury exposures, but the overall pattern is quite suggestive. These findings are based on grouped data and cannot reliably be used to determine the status of individuals (although all participants have been informed of their individual lab results). Finally, the overall extent of documented abnormalities was not severe, and findings that were attributable to mercury exposure could reasonably be expected to resolve or diminish following cessation of exposure. The Staco plant was closed down shortly after the field study was conducted so exposures have ceased. For this reason, also, no recommendations to control exposures or improve medical monitoring are made.

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X. DISTRIBUTION AND AVAILABILITY OF REPORT

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Publications Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days, the report will be available through the National Technical Information Service (NTIS), 5285 Port Royal, Springfield, Virginia 22161. Information regarding its availability through NTIS can be obtained from NIOSH Publications Office at the Cincinnati address. Copies of this report have been sent to:

1. Staco, Inc.
2. Dowty Electronics
3. Vermont Department of Health
4. NIOSH, Region I
5. OSHA, Region I

For the purpose of informing affected employees, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calendar days.

FIGURE 1

Urinary Mercury vs. Personal Sampling

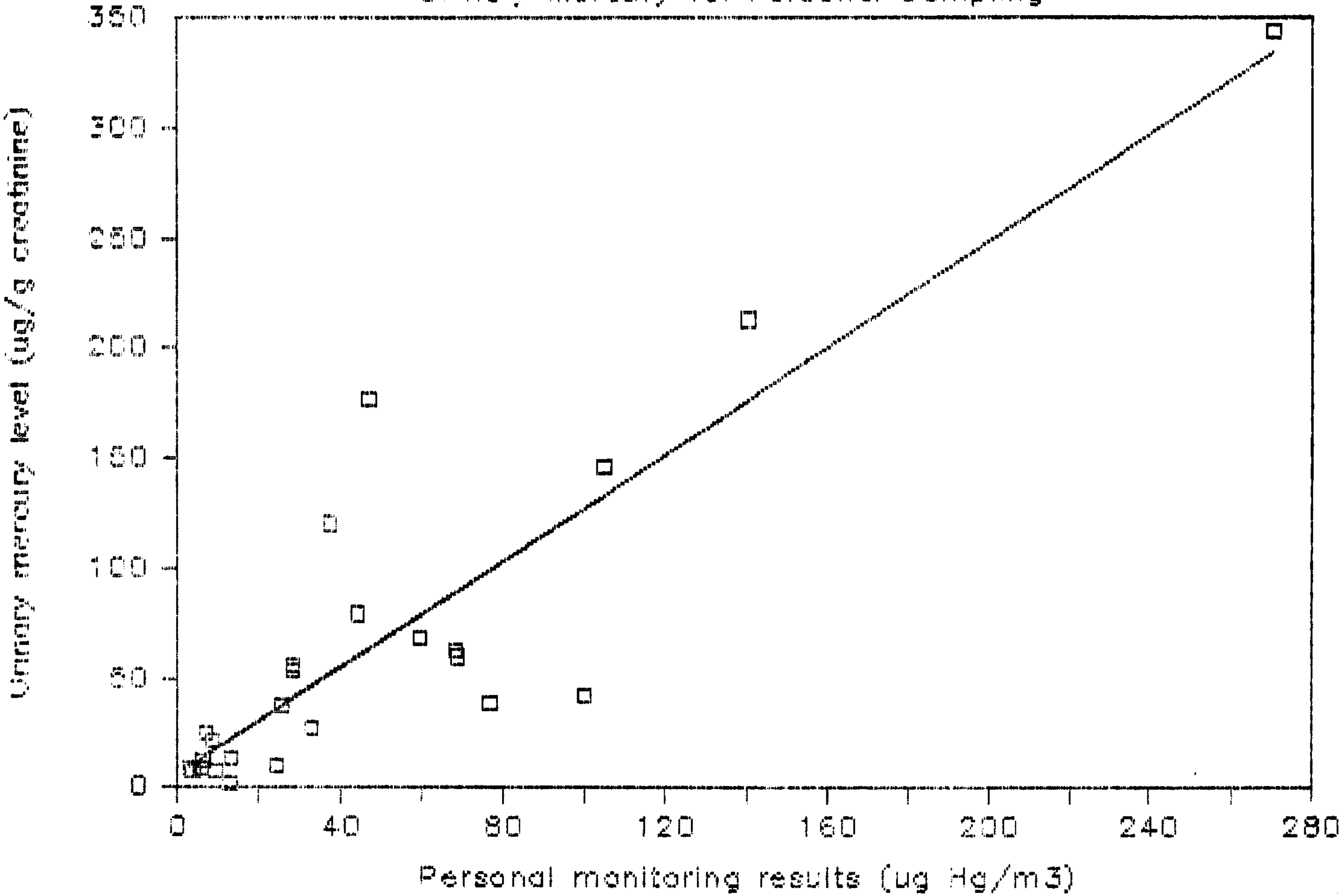

TABLE 1

ENVIRONMENTAL SAMPLING

STACO, INC.

MARCH 1984

MERCURY VAPOR TWA (ug/m^3)

(OSHA Standard = 100 ug/m^3 ceiling   NIOSH Recommendation = 50 ug/m^3 8-hour TWA)

SAMPLE TYPE	RANGE	MEAN	N	#(%)> NIOSH STANDARD
Personal/Thermometer Bldg.	25.6 - 270.6	75.6	17	9 (53%)
Personal/Glass Bldg.	2.8 - 24.4	9.3	10	0 (-)
Area Sample/Thermometer Bldg.	23.7 - 118.5	56.7	11	7 (64%)
Trailer	21.5 - 23.4	22.5	2	0 (-)

TABLE 2

SYMPTOM PREVALENCES

STACO, INC. (March, 1984)
DOWTY ELECTRONIC (August, 1984)

SYMPTOM	Staco (N=84) #	Staco (N=84) %	Dowty (N=79) #	Dowty (N=79) %	SYMPTOM GROUP
1. Skin rash/sores	17	20%	11	14%	
2. Bleeding gums/gum pain*	3	4%	1	1%	Gingival
3. Loose teeth/teeth removed*	1	1%	0	-	Gingival
4. Increased salivation*	2	2%	0	-	Gingival
5. Metallic taste*	9	11%	0	-	
6. Shortness of breath	12	14%	7	9%	Chest
7. Chronic cough	7	8%	3	4%	Chest
8. Chest pain/tightness	6	7%	4	5%	Chest
9. Palpitations	4	5%	5	6%	Chest
10. Anorexia*	3	4%	4	5%	Constitutional/GI
11. Weight Loss*	9	11%	5	6%	Constitutional/GI
12. Diarrhea	4	5%	2	3%	Constitutional/GI
13. Nausea/Vomiting	6	7%	1	1%	Constitutional/GI
14. Blurred vision	6	7%	4	5%	Neurological
15. Dizziness	8	10%	4	5%	Neurological
16. Headache	24	29%	19	24%	Neurological
17. Tremor*	7	8%	3	4%	Neurological
18. Paresthesias*	11	13%	10	13%	Neurological
19. Arm/leg weakness	5	6%	5	6%	Neurological
20. Gait problems*	5	6%	4	5%	Neurological
21. Handwriting*	2	2%	0	-	Neurological
22. Memory/concentration*	13	16%	5	6%	Behavioral
23. Insomnia*	21	25%	7	9%	Behavioral
24. Nervousness/anxiety*	19	23%	17	22%	Behavioral
25. Indecision*	7	8%	2	3%	Behavioral
26. Shyness*	10	12%	3	4%	Behavioral
27. Emotional lability*	15	18%	14	18%	Behavioral
28. Depression*	7	8%	11	14%	Behavioral

*Symptoms particularly suspicious of chronic mercury toxicty

TABLE 3

RELATIVE RISK FOR REPORTING POSITIVE SYMPTOMS

STACO, INC. VS. DOWTY ELECTRONICS

SYMPTOM	# STACO/# DOWTY	RR [Relative Risk]	p^{+} [p-value]
1. Skin rash/sores	17/11	1.45	.31
2. Bleeding gums/gum pain	3/1	2.81	.62
3. Loose teeth/teeth removed	1/0	∞	1.00
4. Increased salivation	2/0	∞	.50
5. Metallic taste	9/0	∞	.003**
6. Shortness of breath	12/7	1.61	.33
7. Chronic cough	7/3	2.19	.33
8. Chest pain/tightness	6/4	1.41	.75
9. Palpitations	4/5	.75	.74
10. Anorexia	3/4	.71	.71
11. Weight loss	9/5	1.69	.41
12. Diarrhea	4/2	1.88	.68
13. Nausea/vomiting	6/1	5.62	.12
14. Blurred vision	6/4	1.41	.75
15. Dizziness	8/4	1.88	.37
16. Headache	24/19	1.19	.59
17. Tremor	7/3	2.19	.33
18. Paresthesias	11/10	1.03	1.00
19. Arm/leg weakness	5/5	.94	1.00
20. Gait problems	5/4	1.18	1.00
21. Handwriting	2/0	∞	.50
22. Memory/concentration	13/5	2.45	.08
23. Insomnia	21/7	2.82	.007**
24. Nervousness/anxiety	19/17	1.05	1.00
25. Indecision	7/2	3.29	.17
26. Shyness	10/3	3.13	.08
27. Emotional/lability	15/14	1.01	1.00
28. Depression.	7/11	.60	.32

\# Symptoms RR >1.15 = 21/28
\# Symptoms RR < .85 = 3/28

\# HG Assoc. Symptoms RR >1.15 = 12/17
\# HG Assoc. Symptoms RR < .85 = 2/17

+ Fisher's exact
** p <.01

TABLE 4

MEAN URINE HG - POSITIVE RESPONDERS VS. NEGATIVE RESPONDERS

STACO, INC - March 1984
(N = 79)

SYMPTOM	# POSITIVE RESPONDERS	MEAN URINE Hg +/MEAN URINE Hg -	t [t statistic]	p
1. Skin rash/sores	15	55.4/77.3	1.69	.10
2. Bleeding gums/gum pain	3	46.5/74.2	.67	.50
3. Loose teeth/teeth removed	1	49.1/73.5	.35	.73
4. Increased salivation	2	51.4/73.7	.44	.66
5. Metallic taste	9	60.4/74.8	.58	.56
6. Shortness of breath	11	75.7/72.7	.13	.90
7. Chronic cough	7	124.0/68.2	1.35	.22
8. Chest pain/tightness	6	31.0/76.6	3.37	.005**
9. Palpitations	4	49.3/74.4	.70	.49
10. Anorexia	3	75.3/73.1	.06	.96
11. Weight loss	7	82.6/72.2	.37	.71
12. Diarrhea	4	81.3/72.7	.24	.81
13. Nausea/vomiting	5	67.2/73.6	.20	.85
14. Blurred vision	6	68.9/73.5	.16	.88
15. Dizziness	8	62.9/74.3	.44	.66
16. Headache	23	58.7/79.1	1.46	.15
17. Tremor	7	56.5/74.8	.66	.51
18. Paresthesias	11	61.0/75.1	.62	.54
19. Arm/leg weakness	5	82.3/72.5	.30	.76
20. Gait problems	5	45.2/75.0	.92	.36
21. Handwriting	2	60.6/73.5	.26	.80
22. Memory/concentration	13	65.1/74.7	.45	.65
23. Insomnia	21	71.8/73.7	.10	.92
24. Nervousness/anxiety	18	79.6/71.2	.45	.66
25. Indecision	7	63.9/74.1	.37	.72
26. Shyness	9	88.6/71.2	.70	.48
27. Emotional lability	13	54.3/76.9	1.51	.14
28. Depression	7	49.0/75.5	1.80	.09

**p<.01

$\frac{\text{Mean Hg + Responders}}{\text{Mean Hg - Responders}} > 1.10 = 6/28$

$\frac{\text{Mean Hg + Responders (merc. assoc. sx)}}{\text{Mean Hg - Responders (merc. assoc. sx)}} > 1.10 = 3/17$

$\frac{\text{Mean Hg + Responders}}{\text{Mean Hg - Responders}} < 0.90 = 17/28$

$\frac{\text{Mean Hg + Responders (merc. assoc. sx)}}{\text{Mean Hg - Responders (merc. assoc. sx)}} < 0.90 = 12/17$

TABLE 5

MEAN EXPOSURE INDEX POSITIVE RESPONDERS VS. NEGATIVE RESPONDERS

STACO, INC
March 1984
(N = 84)

SYMPTOM	# POSTIVE RESPONDERS	MEAN EXPOSURE INDEX +/MEAN EXPOSURE INDEX -	t	p
1. Skin rash/sores	17	85.7/71.7	.74	.46
2. Bleeding gums/gum pain	3	70.9/74.7	.09	93
3. Loose teeth/teeth removed	1	48.2/74.9	.38	.70
4. Increased salivation	2	79.4/74.4	.10	.92
5. Metallic taste	9	87.5/73.0	.59	.56
6. Shortness of breath	12	115.9/67.7	2.29	.02*
7. Chronic cough	7	140.0/68.6	2.71	.008**
8. Chest pain/tightness	6	65.2/75.3	.34	.73
9. Palpitations	4	106.0/73.0	.93	.36
10. Anorexia	3	89.8/74.0	.39	.70
11. Weight loss	9	70.2/75.1	.20	.84
12. Diarrhea	4	156.8/70.4	2.51	.01*
13. Nausea/vomiting	6	107.3/72.0	1.21	.23
14. Blurred vision	6	86.9/73.6	.45	.65
15. Dizziness	8	102.0/71.7	1.18	.24
16. Headache	24	68.7/76.9	.49	.63
17. Tremor	7	75.4/74.5	.03	.97
18. Paresthesias	11	90.8/72.1	.83	.41
19. Arm/leg weakness	5	89.0/73.6	.48	.63
20. Gait problems	5	67.5/75.0	.23	.82
21. Handwriting	2	49.1/75.2	3.35	.001**
22. Memory/concentration	13	84.5/72.7	.56	.58
23. Insomnia	21	78.4/73.3	.29	.77
24. Nervousness/anxiety	19	82.6/72.2	.57	.57
25. Indecision	7	80.1/74.0	.22	.83
26. Shyness	10	65.1/75.8	.46	.65
27. Emotional lability	15	45.9/80.8	1.79	.08
28. Depression	7	56.6/76.2	.71	.48

*p<.05

**p<.01

$\frac{\text{Mean exposure index + Responders}}{\text{Mean exposure index - Responders}}$ > 1.10 = 14/28

$\frac{\text{Mean exposure index + responders (Hg assoc.sx)}}{\text{Mean exposure index - responders (Hg assoc.sx)}}$ >1.10 = 5/17

$\frac{\text{Mean exposure index + responders}}{\text{Mean exposure index - responders}}$ <0.90 = 8/28

$\frac{\text{Mean exposure index + responders (Hg assoc.sx)}}{\text{Mean exposure index - responders (Hg assoc.sx)}}$ <0.90 = 6/17

TABLE 6

MEAN # SYMPTOMS/PERSON IN EACH SYMPTOM GROUP

STACO (N = 84) VS. Dowty (N = 79)

SYMPTOM CATEGORY+	MEAN # SX IN CATEGORY STACO/DOWTY	t	p
1. Gingival Symptoms	.1/0++	1.38	.17
2. Chest symptoms	.3/.2	.95	.34
3. Constitutional/GI symptoms	.3/.2	.97	.25
4. Neurological symptoms	.8/.6	1.17	.33
5. Behavioral symptoms	1.1/.7	1.55	.12

+ see Table 2 for groupings

++ =<0.05/person

TABLE 7

RELATIVE RISK FOR REPORTING EFFECTS IN SYMPTOM GROUPS

(STACO VS. DOWTY)

EFFECTS	# Staco (N=84) / # Dowty (N=79)	RR	p+
1. Gingival effects(>1 gingival sx)	1/ 0	∞	1.00
2. Chest effects(>1 chest sx)	8/ 5	1.50	.57
3. Constitutional effects (>1 const./GI Sx)	7/ 2	3.29	.17
4. Neurological effects (>1 neuro sx)	17/11	1.45	.31
5. Behavioral effects(>1 behavioral sx)	24/15	1.50	.20

+ Fisher's exact

TABLE 8

MEAN URINE HG AND EXPOSURE INDICES: POSITIVE VS. NEGATIVE GROUP EFFECTS

AT STACO

EFFECTS	MEAN URINE Hg + RESP. / MEAN URINE Hg - RESP.	t	p	MEAN EXPOSURE INDEX + RESP. / MEAN EXPOSURE INDEX - RESP.	t	p
1. Gingival effects (>1)	49.1/73.5	.35	.73	48.2/74.9	.38	.70
2. Chest effects (>1)	65.9/74.0	.31	.76	110.3/70.8	1.55	.13
3. Const./GI effects (>1)	83.2/72.3	.37	.72	126.1/69.9	2.10	.04*
4. Neuro. effects (>1)	68.5/74.4	.40	.69	71.9/75.2	.17	.86
5. Behav. effects (>1)	75.9/72.0	.23	.82	73.1/75.1	.12	.90

*p<.05

TABLE 9

PREVALENCES OF NEROLOGICAL FINDINGS

STACO VS. DOWTY

	STACO (N=83)		DOWTY (N=79)	
	#	%	#	%
1. Ocular movements	0	-	0	-
2. Lid lag	0	-	0	-
3. Nystagmus	0	-	0	-
4. Rest tremor	1	1%	0	-
5. Static tremor	16	19%	10	13%
6. Intention tremor	1	1%	0	-
7. Finger-to-nose	0	-	0	-
8. Diadochokinesis	3	4%	0	-
9. Hyporeflexia+	20	24%	34	43%
10. Hyperreflexia+	3	4%	0	-
11. Gait	0	-	0	-
12. Heel-to-toe-walk	12	15%	2	3%
13. Romberg	3	4%	0	-

+ see text for definition

TABLE 10

RELATIVE RISKS FOR ABNORMAL NEUROLOGICAL FINDINGS

(STACO VS. DOWTY)

	# Staco/# Dowty	RR	p^{+}
1. Rest tremor	1/0	∞	1.00
2. Static tremor	16/10	1.52	.29
3. Intention tremor	1/0	∞	1.00
4. Finger-to-nose	0/0	–	–
5. Diadochokinesis	3/0	∞	.25
6. Hyporeflexia	20/34	0.55	.01*
7. Hyperreflexia	3/0	∞	.25
8. Gait	0/0	–	–
9. Heel-to-toe walk	12/2	5.78	.01*
10. Romberg	3/0	∞	.25

+Fisher's exact

*p<.05
*p<.01

TABLE 11

MEAN URINE Hg
ABNORMAL NEURO FINDINGS VS. NORMAL NEURO FINDINGS

AT STACO (N=78)

	# ABNORMAL	MEAN URINE Hg + / MEAN URINE Hg -	t	p
1. Rest tremor	1	42.1/74.1	.45	.65
2. Static tremor	16	94.1/68.4	1.32	.19
3. Intention tremor	1	72.2/73.7	.02	.98
4. Finger-to-nose	0	-	-	-
5. Diadochokinesis	3	78.3/73.5	.12	.91
6. Hyporeflexia	18	59.6/77.2	.94	.35
7. Hyperreflexia	3	159.4/69.7	.97	.43
8. Gait	0	-	-	-
9. Heel-to-toe walk	12	73.7/74.8	.05	.96
10. Romberg	3	56.0/74.4	.44	.66

TABLE 12

MEAN EXPOSURE INDEX POSITIVE NEURO FINDINGS VS. NEGATIVE NEURO FINDINGS

AT STACO (N=83)

	# POSITIVE FINDINGS	MEAN EXPOSURE INDEX +/MEAN EXPOSURE INDEX -	t	p
1. Rest tremor	1	228.2/73.0	2.27	.03*
2. Static tremor	16	99.0/69.1	1.56	.12
3. Intention tremor	1	50.0/75.2	.36	.72
4. Finger-to-nose	0	-	-	-
5. Diadochokinesis	3	195.0/70.4	3.21	.002*
6. Hyporeflexia	20	60.7/78.9	1.02	.31
7. Hyperreflexia	3	127.1/72.6	1.34	.18
8. Gait	0	-	-	-
9. Heel-to-toe walk	12	109.4/68.6	1.89	.06
10. Romberg	3	96.2/74.1	.54	.59

*p<.05
**p<.01

TABLE 13

PREGNANCY OUTCOMES

ALL PREGNANCIES

a. MALE & FEMALE WORKERS

	NORMAL OUTCOME	PREMATURE	BIRTH DEFECTS	STILLBIRTHS	SPONTANEOUS ABORTION	THERAPEUTIC ABORTION	TOTAL
DOWTY	124(83%)	7(5%)	1(1%)	3(2%)	12(8%)	3(2%)	150
STACO (ALL)	153(81%)	13(7%)	3(2%)	5(3%)	14(7%)	2(1%)	190
STACO (GLASS WORKERS)	50(89%)	2(4%)	1(2%)	1(2%)	1(2%)	1(2%)	56
STACO (THERMOMETER WORKERS)	103(77%)	11(8%)	2(1%)	4(3%)	13(10%)	1(1%)	134

b. FEMALE WORKERS ONLY

	NORMAL OUTCOME	PREMATURE	BIRTH DEFECTS	STILLBIRTHS	SPONTANEOUS ABORTION	THERAPEUTIC ABORTION	TOTAL
DOWTY	110(81%)	7(5%)	1(1%)	2(1%)	12(9%)	3(2%)	135
STACO (ALL)	143(80%)	11(6%)	3(2%)	5(3%)	14(8%)	2(1%)	178
STACO (GLASS WORKERS)	50(89%)	2(4%)	1(2%)	1(2%)	1(2%)	1(2%)	56
STACO (THERMOMETER WORKERS)	93(76%)	9(7%)	2(2%)	4(3%)	13(11%)	1(1%)	122

TABLE 14

PREGNANCY OUTCOMES

AT RISK* PREGNANCIES ONLY

a. MALE & FEMALE WORKERS

	NORMAL OUTCOME	PREMATURE	BIRTH DEFECT	STILLBIRTH	SPONTANEOUS ABORTION	THERAPEUTIC ABORTION	TOTAL
DOWTY (AT DOWTY)	13(81%)	1(6%)	0(-)	0(-)	1(6%)	1(6%)	16
DOWTY (AT ANY JOB)	45(79%)	4(7%)	0(-)	1(2%)	5(9%)	2(4%)	57
STACO (ALL)	13(76%)	2(12%)	0(-)	0(-)	1(6%)	1(6%)	17
STACO (GLASS WORKERS)	0(-)	0(-)	0(-)	0(-)	0(-)	1(100%)	1
STACO (THERMOMETER WORKERS)	13(81%)	2(13%)	0(-)	0(-)	1(6%)	0(-)	16

b. FEMALE WORKERS ONLY

	NORMAL OUTCOME	PREMATURE	BIRTH DEFECT	STILLBIRTH	SPONTANEOUS ABORTION	THERAPEUTIC ABORTION	TOTAL
DOWTY (AT DOWTY)	10(77%)	1(8%)	0(-)	0(-)	1(8%)	1(8%)	13
DOWTY (AT ANY JOB)	31(74%)	4(10%)	0(-)	0(-)	5(12%)	2(5%)	42
STACO (ALL)	6(75%)	0(-)	0(-)	0(-)	1(13%)	1(13%)	8
STACO (GLASS WORKERS	0(-)	0(-)	0(-)	0(-)	0(-)	1(100%)	1
STACO (THERMOMETER WORKERS)	6(86%)	0(-)	0(-)	0(-)	1(14%)	0(-)	7

* Parent working during at least part of preegenancy - Staco workers working at Staco during pregnancy

TABLE 15

MEAN VALUES - THYROID FUNCTION TESTS

STACO VS. DOWTY

TEST	MEAN VALUE STACO/MEAN VALUE DOWTY	t	p
Serum thyroxine (T4) [4.5-12.50ug/dl]	9.6/11.1	4.61	.0001***
T3 resin uptake [23.0-34.0%]	27.4/27.1	.68	.49
Free thyroid index [1.00-4.30]	2.7/3.0	3.79	.0002***

***p<.001

TABLE 16

PREVALENCES & RELATIVE RISKS OF ABNORMAL RESULTS

THYROID FUNCTION TESTS

	STACO (N=83)		DOWTY (N=73)			
	#	%	#	%	RR	p+
Serum thyroxine (T4)	3	(4%)	16	(22%)	.16	.0005***
T3 resin uptake	1	(1%)	11	(15%)	.08	.002**
Free thyroid index (T7)	0	(-)	1	(1%)	.0	.47

**p<.01
***p<.001

TABLE 17

ABNORMAL VALUES & MEAN VALUES FOR THYROID FUNCTION TESTS BY FEMALE HORMONE USAGE

STACO & DOWTY

	# ABNORMAL TESTS HORMONE USE +/HORMONE USE -	RR	p+	MEAN VALUE HORMONE USE +/HORMONE USE -	t	p
STACO	N=14 N=69					
Serum thyroxine (T4)	2/1	9.86	.07	11.4/9.2	4.98	.0001***
T3 resin uptake	1/0	∞	.17	25.7/27.7	3.68	.0004***
Free thyroid index (T7)	0/0	-	-	3.1/2.6	3.53	.0007***
DOWTY	N=13 N=60					
Serum thyroxine (T4)	5/11	2.10	.14	12.7/10.7	2.94	.005**
T3 resin uptake	6/5	5.54	.003**	23.2/27.9	5.43	.0001***
Free thyroid index (T7)	0/1	0.0	1.00	2.9/3.0	.44	.66

+Fisher's exact

**p<.01
***p<.001

TABLE 18

MEAN VALUES AND ABNORMAL VALUES FOR THYROID FUNCTION TESTS
STACO VS. DOWTY

STRATIFIED BY HORMONE USAGE

	- HORMONE USE			+ HORMONE USE		
	# ABNORMAL STACO/DOWTY	RR	p+	# ABNORMAL STACO/DOWTY	RR	p+
Serum thyroxine (T4)	1/69 11/60	.08	.001**	2/14 5/13	.37	.21
T3 resin uptake	0/69 5/60	0.0	.02*	1/14 6/13	.15	.03*
Free thyroid index (T7)	0/69 1/60	0.0	.47	0/14 0/13	-	

	MEAN VALUE STACO / MEAN VALUE DOWTY			MEAN VALUE STACO / MEAN VALUE DOWTY	t	p
Serum thyroxine (T4)	9.2/10.7	4.71	.0001***	11.4/12.7	1.59	.13
T3 resin uptake	27.7/27.9	.43	.67	25.7/23.2	2.80	.01*
Free thyroid index (T7)	2.6/3.0	4.26	.0001***	3.1/2.9	.86	.40

+Fisher's exact

*p<.05
**p<.01
***p<.001

TABLE 19

MEAN VALUES OF RENAL FUNCTION STUDIES
STACO VS. DOHTY

TEST (normal range)		RANGE	MEAN (s.d.)	t	p	N	# ELEVATED	RR	p+
NAG (0-1.48ug/g creatinine)	STACO	0.05-3.93	0.81 (0.73)	0.70	.49	56	6	2.46	.29
	DOHTY	0.13-3.97	0.71 (0.65)			46	2		
Urinary B2M (7-2000ug/g creatinine)	STACO	12-7674	164.2 (867.6)	0.75	.46	77	1	0.27	.33
	DOHTY	11-452	89.0 (70.3)			63	3		
Urinary RBP (0.03-0.19ug/ml)	STACO	0.03-2.15	0.14 (0.25)	0.01	.99	78	13	1.52	.47
	DOHTY	0.03-2.32	0.13 (0.25)			64	7		
Serum B2M (<2000-<3100ug/l)#	STACO	946-2955	1613.7 (409.4)	1.33	.18	83	7	6.24	.07
	DOHTY	955-3188	1536.2 (317.1)			74	1		
Serum RBP (3.0-6.0mg/dl)	STACO	3.3-95	6.2 (1.4)	.02	.99	83	44	0.93	>.5
	DOHTY	2.7-100	6.2 (1.5)			74	42		
Total Protein (28-244.8mg/g creatinine)	STACO	39-784	92.0 (99.2)	0.74	.46	79	1	0.89	>.5
	DOHTY	25-3059	148.2 (472.9)			70	1		
Albumin (2.02-12.01mg/g creatinine)	STACO	0.6-89.2	8.4 (11.1)	0.85	.40	77	9	1.50	>.5
	DOHTY	1.6-52.9	7.1 (7.7)			64	5		
Specific Gravity (1.001-1.035)	STACO	1.006-1.035	1.020 (.008)	2.72	.007**	79	0	-	-
	DOHTY	1.006-1.031	1.017 (.006)			70	0		
Urinary Creatinine (N/A)	STACO	30-386	143.8 (69.1)	1.31	.19	79	N/A	-	-
	DOHTY	34-350	129.[illegible] (66.8)			70	N/A		
Serum Creatinine (0.4-1.5mg/DL)	STACO	0.7-1.3	0.94 (.14)	0.89	.37	83	0	-	-
	DOHTY	0.1-1.5	[illegible]			74	0		

Normal range varies with age
+ Fisher's exact
** p<.01

TABLE 20

CORRELATION COEFFICIENTS
RENAL OUTCOMES WITH URINARY MERCURY LEVELS
AND CHRONIC EXPOSURE INDEX

	STACO ONLY		TOTAL COHORT	
	r	p	r	p
a. With Urinary Mercury				
NAG	.48	.0002***	.36	.002**
B2M Urine	-.05	.7	-.01	.9
B2M clearance/creatinine clearance	-.05	.7	-.02	.8
Serum B2M	.02	.9	.08	.3
Urinary RBP	-.05	.7	-.02	.8
RBP clearance/creatinine clearance	-.05	.6	-.03	.7
Serum RBP	-.21	.07	-.11	.2
Urinary protein	-.02	.9	-.05	.7
Urinary albumin	.10	.4	.11	.2
Specific gravity	-.11	.3	.05	.6
Urinary creatinine	-.06	.6	.20	.8
Serum creatinine	-.19	.1	-.13	.1

b. With exposure index (not applicable to control group)

	r	p
NAG	.30	.03*
Urinary B2M	.25	.03*
B2M clearance/creatinine clearance	.24	.03*
Urinary RBP	.21	.06
RBP clearance/creatinine clearance	.24	.03*
Serum B2M	.31	.005*
Serum RBP	-.17	.13
Urinary protein	.26	.02*
Urinary albimin	.16	.2
Specific gravity	-.25	.02*
Urinary creatinine	-.31	.006**
Serum creatinine	-.23	.04*

*p<.05
**p<.01
***p<.001

TABLE 21

MEAN VALUES FOR URINE Hg & RESULTS OF RENAL FUNCTION STUDIES

ABNORMALS VS. NORMALS (STACO ONLY)

TEST	# ABNORMAL/N+	MEAN URINE Hg ABNORMAL/NORMAL	t	p
NAG	6/56	145.0/60.0	1.84	.12
Urinary B2M	1/77	42.1/71.8	.42	.68
Serum B2M	7/78	82.0/72.7	.22	.83
Urinary RBP	13/77	79.3/69.8	.44	.66
Serum RBP	41/78	65.1/83.0	1.10	.28
Total protein	1/79	42.1/73.6	.45	.68
Albumin	9/77	85.0/69.6	.43	.68
Specific gravity#	-	-	-	-
Urinary creatinine#	-	-	-	-
Serum creatinine#	-	-	-	-

None abnormal

+ N's vary with test - not all tests could be completed on all individuals (because of volume of specimen, etc.)

TABLE 22

MEAN VALUES FOR EXPOSURE INDEX AND RESULTS OF RENAL FUNCTION STUDIES

ABNORMALS VS. NORMALS (STACO ONLY)

TEST	# ABNORMAL/N+	MEAN EXPOSURE INDEX ABNORMAL/NORMAL	t	p
NAG	6/56	121.3/74.8	1.61	.11
Urinary B2M	1/77	228.2/76.6	2.22	.03
Serum B2M	7/83	85.8/74.5	.41	.68
Urinary RBP	13/78	74.4/78.5	.19	.85
Serum RBP	44/83	65.2/87.0	1.44	.15
Total protein	1/79	228.2/76.9	2.23	.03*
Albumin	9.77	70.4/79.6	.37	.71
Specific gravity#	-	-	-	-
Urinary creatinine#	-	-	-	-
Serum creatinine#	-	-	-	-

No abnormal results for these tests

+ N's vary with test - not all tests could be completed on all individuals (because of volume of specimen, etc.)

*p<.05

ADDENDUM to HETA 83-465-1674

BEHAVIORAL TESTING OF STACO-CHASE AND REFERENCE WORKERS IN VERMONT

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ABSTRACT

Workers from the Staco-Chase company that manufactured thermometers and other items, and which employed mercury in the process, were compared to workers from an electronics company who were not exposed to mercury (the reference group) using neurobehavioral tests of grip strength, hand tremor, and finger sensitivity. All worker groups had measurable urine mercury concentrations. Group means were 69 (sd = 89.4) and 96 (sd = 66.0) ug mercury/gram of creatinine in female and male workers (respectively) from Staco-Chase, but 10 ug/g was the highest individual concentration reported in the reference group. Grip strength was measured with a dynamometer, finger sensitivity (tactile, vibration) was tested using the Optacon[R], and vertical hand movement or tremor of the type previously associated with mercury exposures was assessed with accelerometers. There were no significant differences in grip strength in younger (<45 years) workers, nor were there differences in measures of tremor between exposed and reference subjects. Older (>45 years) Staco-Chase workers had notably, but not significantly (in statistical terms) less grip strength than comparable reference workers. Staco-Chase females had significantly worse sensitivity in their index and fifth fingers than did referents. Males in the middle age range exhibited deficits of a similar magnitude, but the differences were not significant in this numerically smaller group, despite having higher urine mercury levels than did the females. While individual subjects would probably not notice any loss of finger sensitivity based on the results outlined here, the group results suggest that the earliest stages of polyneuropathy may be present at lower urine mercury levels than previously suspected.

BACKGROUND

The State of Vermont's Department of Health, Epidemiology Division requested National Institute for Occupational Safety and Health (NIOSH) assistance to assess mercury exposure in Poultney, Vermont at the Staco-Chase Company. Behavioral testing was provided by the Neurobehavioral Research Section (NRS) of the Division of Biomedical and Behavioral Science (DBBS). As an unexposed reference group, employees of the Dowty electronics company (Brandon, Vermont) were also identified to determine background urine mercury concentrations and behavioral performance characteristics in a similar community. Tests of tremor, finger sensitivity, and grip strength were administered to Staco-Chase and reference workers to determine if there were differences between these groups. The tests were selected to identify relevant group differences, and it is emphasized that the tests are not tools for individual clinical diagnosis.

Effects of Mercury

Mercury has been mined and used in various human occupations for well over 2000 years. Major nervous system effects were identified soon after humans began using it, because its effects were so serious and obvious at the very high concentrations to which people were then exposed. While the greatest danger of elemental mercury, the form used at Staco-Chase, is from inhaling the vapor, other forms of mercury which produce similar effects can also be absorbed through the skin or through the intestine after ingesting foods containing mercury (Marsh, 1985).

Worksite studies have consistently identified nervous system changes such as slower rates of nerve conduction or psychomotor performance changes in workers with urine mercury concentrations of 400-500 ug/l (reviewed by Anger and Johnson, 1985). Short-term memory losses may occur at urine mercury concentrations of 300 ug/l, but there is mixed evidence regarding mercury's effects at urine mercury concentrations between 100 and 200 ug/l. On the positive side, two recent papers have identified memory deficits at 108 and 130 ug/l in widely different populations (Smith et al., 1983; Williamson et al., 1982). Roels et al. (1985) tested groups with 37 and 52 ug mercury/gram of creatinine (equivalent to ug/l) for short-term memory losses, but did not identify any changes. The development of hand tremor in adults occurs at urine mercury concentrations between 250 and 350 ug/l (Langolf et al., 1981). Hand tremor has historically been one of the most sensitive indicators of mercury overexposure as well as one of its most debilitating effects on day to day human activities. Thus, neuromuscular tremor was assessed in this study since it is sensitive to the effects of mercury, and potentially debilitating in daily activities if exaggerated by mercury. The test of finger sensitivity was used because extremity paresthesias are among the earliest signs of mercury exposure (Marsh, 1985). The test of grip strength was also used for assessment due to strength deficits in people heavily exposed to mercury (Chang, 1980).

METHODS AND MATERIALS

Mercury Determinations

Urine specimens were collected by NIOSH and State of Vermont personnel, and urine mercury concentrations were determined by the clinical chemistry laboratory at the Center for Environmental Health of the Centers for Disease Control.

Test Setting

The subjects in this investigation were tested in a NIOSH/DSHEFS Medicoach (Medical Coaches Inc.; Oneonta, NY), a converted semi-trailer 2.3 m (wide) x 2.1 m (high) x 12 m (long). The Medicoach is divided into front, middle and rear compartments. The neurobehavioral tests were administered to the subjects in the front section, which provided low noise levels and semi-isolation from other phases of the investigation. The internal temperature was maintained in a range between 19-24°C by heating/air conditioning units which were integral to the coach, and which introduced added vibration into the coach at unpredictable times when a unit cycled "on." The Medicoach was parked on level ground located adjacent to the factory, and electrical current was provided by a cable hookup from the company's electrical system.

Apparatus and Procedures

Tremor Test

Wilcoxon Research (Bethesda, MD) tri-axial accelerometers (85 pc/g, +300g, 1-1200 hz, high sensitivity), attached to a Velcro[R] strip, were secured on the subject's dominant hand, such that each of three axes of tremor (vertical, horizontal, and rotational) could be tested. Due to the past mercury literature, only the data from the vertical axis were used in the analyses. The subject was told to extend his/her dominant arm straight out from their side and hold it level for 60 seconds, while looking forward (so that he/she could not observe any visible hand tremor that might have been present). Three second duration samples of accelerometer response were taken at the beginning and again at the end of the 60 seconds.[1]

An Apple[R] IIe microprocessor digitized the analog outputs of the accelerometer (factory calibrated output of 60.3 mV/g) through a Mountain Hardware (Scotts Valley, CA) A/D board, after they were conditioned by a Wilcoxon Research (Bethesda, MD) Model AM-5 low noise amplifier set to 50 dB. An IQS Spectrum Analyst Pak 401 FFT (Fast Fourier Transform) program (5719 Corso Di Napoli; Long Beach, CA) was used to identify the amount of tremor at various frequencies (Hz or cycles per second). A three-second sample (1000 data points) at the beginning (seconds 1-3) and a three-second sample at the end (seconds 57-60) of the 60-second test period were analyzed statistically. These periods are referred to as S1-3 and S57-60 in the remainder of the report. The program sample rate wes set at 1000 Hertz (Hz), the same rate at which the data were collected [but only 333/second for the one tremor axis analyzed, summing to 1000 samples over three seconds], and the 1024 FFT option was used to provide the most fine-grained spectra available in that program. User-written software was developed to access the digital information from this program, store it as a data file, and send it via modem to a mainframe computer, for subsequent analysis, detailed below.[2]

Grip Strength Test

A Stoelting model 19117 Smedley dynamometer was used in this test of grip strength. At a constant handle setting of 9.5 turns, the subject was instructed to squeeze the dynamometer as hard as possible with the arm held at his/her side or other more comfortable position. Three consecutive trials were given on each hand with 10-20 secs between trials for the Experimenter to read and reset the dynamometer, and to record the strength of the squeeze (in kg). The sum of all trials served to reflect absolute strength, and the difference between trial one and three was taken as a measure of fatigue.

Optacon Test

The Optacon[R] is a device that converts visual stimuli to tactile, in the form of 144 vibrating rods which extend above a curved surface; only the vibratory stimulus was utilized in this study. Each Subject placed his/her index finger (or next nearest in the case of absence or injury), and in turn his/her fifth (smallest) finger on the same hand, in the concave surface. The Subject was instructed to use a light pressure, taught and gauged manually by the Experimenter at the outset of the trials, but not monitored thereafter. The vibrating rods were perpendicular to the ventral aspect of the finger and oscillated from side to side in a sweeping motion, much like a windshield wiper. The pins vibrated at 230 Hz (per manual specifications not independently verified), and each pin was in antiphase with its neighbor. The amplitude of vibration was varied by turning a potentiometer dial. The Experimenter increased the vibration from well below threshold until the subject reported that he/she could feel it, and then the vibration was decreased from well above the threshold until the subject stated he or she could not feel it. This defines the method of limits (Engen, 1971), and it was repeated three times (trials) on each subject. White noise presented from a generator through earphones was used to mask the sound of the vibrating rods. (The Experimenter was not blind to which subjects were exposed to mercury at the time of testing.) A Heathkit® Model SM 1210 voltmeter reflected the vibration, and served to provide the data (in volts) from the test.

RESULTS

Data from all three tests from Staco-Chase workers were compared with that from reference subjects to determine if there were significant differences. Age was used as a blocking factor (stratified on age) in all analyses, and males and females were considered separately in the analysis of all three tests. A nonparametric m-ranking procedure (modified Friedman's test) was performed on data from each test. Each test was analyzed separately, and a p-value ≤ 0.05 was considered statistically significant. (Statistical power calculations are not included due to the complexities introduced by the use of blocking factors in the nonparametric analyses.)

Subjects

The mean age of Staco-Chase males was 30.6 years, and that for females was 35.5 years. Comparable mean ages in the reference subjects were 35.0 in males and 32.8 in females. Medians, means, and standard deviations of subject ages, plus minimum and maximum, are listed in Table 1. These data reflect all subjects tested, but ten subjects were dropped from subsequent analyses due to self reports of high alcohol use (arbitrarily defined as 25 or more drinks per week), diabetes, finger injury, or language difficulties bearing on understandability of the instructions. Of these, 8 were from Staco-Chase (5 due to diabetes, 1 each due to language problems, alcohol, and finger injury), and 2 were from the Reference group (1 due to alcohol, 1 due to diabetes). These workers were excluded due to the potential of the indicated problems to produce peripheral neuropathy leading to deficits on the tests that would therefore have been attributable to multiple factors, not just to mercury exposures. Of the remaining subjects, the mean urine mercury concentrations (standardized to urinary creatinine) in Staco-Chase workers were 96.0 ug/g in males and 69.4 ug/g in females. Three of these values exceeded 250 ug/g, the highest being 344 and 343 ug/g in males and females, respectively. Conversely, reference group means were 3.7 and 4.2 ug/g for males and females, with a maximum of 9 and 10 ug/l (See Table 2). An index that combined mercury exposure with duration (roughly, a measure of urine mercury concentrations by one of four job categories divided by the total mean urine mercury concentrations of Staco-Chase workers times the individual's months of exposure) is presented in Table 3. Here, the females have a higher mean index (76.9) than the males (60.2), but the variability is also extremely large, which helps explain why the median index reflects a far greater difference between the groups (50 in females and 20 in males).

<u>Tremor</u>

For tremor analyses, only x axis (vertical) data were used, and all data above 20 Hz were ignored, since such could not reflect human tremor directly. The data were also converted to percent power at frequencies 1-20, again ignoring all numbers above the frequency of 20 Hz. These data are presented in Figure 1, top panel, for all subjects in the Staco-Chase and reference groups. The differences are negligible. Log acceleration was calculated at each frequency, and averaged over subjects.[3] Log acceleration was then graphed for both Staco-Chase and reference (company) group (see Figure 1, bottom panel). Differences between the curves are negligible. For both percent power and log acceleration, graphs from females and males at S1-3 and S57-60 were examined individually and appeared similar in all aspects to the collective graphs presented in Figure 1. For comparison, log acceleration and percent power from previous research is shown in Figure 2.[4] The peaks expected in persons exposed to mercury seen in Figure 2 are not seen in data from the present study, in Figure 1. The mercury literature on adults indicates a peak related to neuromuscular tremor at frequencies of 5.5 to 7.6 Hz. There is a lower frequency peak related to the heart beat (at 1-2 Hz), but that can be ignored. The relationship of acceleration to percent power in previous studies has not been resolved in the literature. A peak in log acceleration data would be expected in the data from the present study, but no such peak is seen. This disparity cannot be explained. However, the analysis of such data varies substantially among studies, and it seems likely that the relatively short sample time may have contributed to the absence of peaks seen in the other studies.

The "median frequency" in (Hz) was determined for each subject by identifying the median of the amplitudes at all frequencies through 20. The mean "median frequency" was similar for all subjects (See Table 4). The amplitude of tremor at each frequency was divided by the sum of the amplitudes at all frequencies (through 20 Hz) to create "percent power" for each frequency. Due to past research, the primary analysis was concerned with the percent power at frequencies 5-8 (Hz): a) The frequency at which the mean percent power between 5 and 8 Hz occurred, referred to as "mean 5-8 frequency;" and b) the percent power associated with the mean 5-8 frequency, referred to as "mean 5-8 power." Males and females were analyzed separately. The mean percent frequency was relatively similar in Staco-Chase and reference groups (as seen in Table 5, top panel), but mean 5-8 power was consistently higher in the reference group than in comparable Staco-Chase subjects, as shown in Table 5, bottom panel.

<u>Grip Strength</u>

Data from all six measures of grip strength were summed and divided by 6 to produce a single measure of strength. Age was divided into three groupings due to the likelihood of reduced strength in older persons. Younger mercury-exposed workers (≤30 years of age) were stronger than their referent counterparts (56 vs. 46 kg in males and 31 vs. 28 kg in females), but the relationship was reversed in the older (>45) female workers (25 vs. 28 kg). There were too few male workers older than 45 to make a statement on them. The data are presented in Table 6. The results of the m-rank procedure indicate that the companies do not differ ($p = 0.47$) for males. For females, the statistical procedure indicates group differences ($p = 0.04$). Further analyses indicate the difference is significant within the 30≤45 age group where the exposed demonstrated <u>greater</u> strength than the reference group. It is of note, however, that strength in the reference group is the same in subjects older than 45 as in the 30≤45 age group, but, in the exposed group, it is 6 kg less (weaker) in subjects over 45 than in the >30≤45 age group, and it is also less than in subjects over 45 in the reference group (by 3 kg).

The measure of fatigue (summing both hands, divided by two) revealed no consistent group differences. The minor differences in the females were not statistically significant; overall, male Staco-Chase subjects demonstrated significantly greater fatigue, but the small sample size makes interpretation difficult. Further, Spearman correlations of grip strength performance with urine mercury were not statistically significant ($p = 0.86$, $n = 18$ for females and $p = 0.89$, $n = 121$ males, combining exposure groups).

<u>Optacon</u>

Data from all twelve measurements (trials) of finger sensitivity were summed together, divided by 12, and treated as a single measure. Data from five persons who reported being diagnosed as diabetic were excluded from the analysis. Age was divided into three groupings, as in the case of grip strength, due to the likelihood of reduced finger sensitivity in older workers. The mean sensitivity was lower (as indicated by higher scores) in mercury-exposed male subjects 31≤45 years of age, and in females in each age range, although the largest differences were seen in the 31≤45 age group. The overall difference, blocked for age, was significant for the females ($p = 0.001$) but not for the smaller group of males ($p = 0.35$), as seen in Table 8.

Since the possibility exists that carpal tunnel problems or callouses as could occur on fingers used extensively in work or leisure activities, analyses of each individual finger tested were also conducted to determine if such biases existed. Using individual analyses (uncorrected for multiple comparisons), male Staco-Chase subjects had higher thresholds on the right index finger, though the differences did not achieve statistical significance ($p = 0.06$). The threshold differences were particularly notable in the middle age range (>30≤45) in the males, and higher thresholds in the other age ranges were equally divided between the reference and exposed groups (see Table 9). In Staco-Chase females, the overall mean thresholds were significantly higher in all four fingers tested (p ≤ 0.002 to 0.001). Again the differences were particularly notable in the middle age groups (see Table 9). Thus, the overall group differences developed from combining the thresholds on all fingers are consistently reflected by the results of comparing the fingers individually.

Further, since the differences were found in the fifth fingers as well as the index fingers, this suggests that neither callouses nor carpal tunnel problems are likely to have been solely responsible for the threshold elevations in this study.

The finger sensitivity scores were significantly correlated (Spearman $r = 0.48$, $N=21$, $p \leq 0.03$ in males, and $r = 0.31$, $N=131$, $p < 0.001$) with age, but not with urine mercury concentrations. Using the index of exposure duration with urine mercury, people with higher index scores also had higher (worse) optacon scores, but the high correlation of this index with age makes it impossible to separate out the effects of exposure duration from the effects of the normal aging process.

DISCUSSION

Group urine mercury concentrations were in the 69-96 ug/g creatinine range in Staco-Chase workers, and were less than 10 ug/g creatinine in all reference subjects. These differences are statistically significant ($p = 0.0001$ when all subjects were included in a t-test as noted in the body of the report; the Staco-Chase mean was 73 ug/g vs. 4.2 ug/g in reference subjects). The urine mercury concentrations were higher in males than in females, but, when duration of exposure was taken into account, females had a higher mean index score than the males. Group differences are apparent, but the mean urine mercury levels are below those previously demonstrated to affect performance in most previous research.

There were no differences in tremor between the Staco-Chase and reference groups. Past literature has demonstrated that, when urine mercury concentrations were above 250 ug/g creatinine, tremor frequency and power can be related more directly to a measure of exposure duration, or with peak urine mercury concentrations above 500 ug/l, than to urine mercury at the time of testing (Roels et al., 1985; Langolf et al., 1981), but such information was not available here. Past studies of workers with urine mercury concentrations in the range of 250-500 ug/l indicate that the percent power and log acceleration in the 5 to 8 Hz range <u>increases</u> as urine mercury <u>increases</u> (Langolf et al., 1981; Roels, 1985). The lack of consistent, compelling, or statistically significant differences in tremor is not surprising due to the fact that all but three individual urine mercury concentrations in this study were below 250 ug/l.

The grip strength data presented no compelling differences (see Tables 6 and 7). While the overall group differences in grip strength for females were statistically significant at $p = 0.04$, further analyses at each age grouping indicated that the cause of the significance was in the middle (>30 $\leq$ 45) age range where the exposed subjects were stronger, not weaker, than the reference subjects. However, Staco-Chase females older than 45 were weaker and demonstrated greater fatigue than the reference subjects, a reversal worth noting.

Staco-Chase females had a significantly higher finger sensitivity threshold than reference subjects; for males (a smaller number of subjects), the direction was similar, but not statistically significant. Reference subject threshold values are close to control values reported in previous research, and the Staco-Chase thresholds are higher (worse) than previous control values (Arezzo et al., 1983). Deficits in finger sensitivity representing a loss of or reductions in large myelinated fibers constitute one of the early indicators of serious mercury exposures (Marsh, 1985), and the slight elevation seen here could be an early indication of mercury overexposures. While other undiagnosed diseases (e.g., diabetes) or differences in work activities in the exposed and reference subjects could also explain these differences, the reference group was chosen to have work tasks similar to those at Staco-Chase. The significant threshold differences in the fifth finger also support the conclusion that the differences are not due to carpal tunnel problems or callouses but reflect a polyneuropathy in which at least two nerves are involved. While the females had lower urine mercury concentrations than the males, the index of duration/exposure which demonstrates a much higher index in females than males supports the finding.

The use of the Optacon® to discriminate the precursor symptoms of peripheral neuropathy has been described by Arezzo and Schaumburg (1980) and more recently by Arezzo et al. (1983). While individual subjects in this study would probably not notice any loss of finger sensitivity based on the results noted here, the group differences would suggest that the earliest stages of peripheral neuropathy (or, alternatively, some more central phenomenon involving this sensory pathway) maybe present at far lower urine mercury concentrations than previously suspected. Further, it gains credibility from and lends support to isolated findings reporting mercury effects (group differences) in measures of intelligence and memory in people exposed to (mean) levels of 83 ug/l and personality differences in people exposed to 50 ug/l (Angotzi et al., 1980). Of course, the Optacon[R] has not been available for use with mercury exposed subjects until recently and it should be noted that improved vibration threshold instruments and test methods (viz., two-alternative forced choice) are now available, and preferred.

In summary, there are no significant differences in tremor or grip strength between Staco-Chase and reference company subjects, but finger sensitivity thresholds were significantly higher (worse) in female subjects exposed to mercury. The results are consistent with the findings in the body of the report in that deficits were clearly present in the mercury-exposed subjects, and the deficits reflected slight, or pre-clinical changes of a similar magnitude.

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DISCLAIMER

Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

FOOTNOTES

1 The brief duration of the samples was due to hardware and software limitations, and these limitations were the main basis for our stated admonition that the results of the study could only be related to group differences and could not be applied to individual clinical diagnosis of tremor.

2 For verification of the accuracy of these manipulations, a Wavetek signal generator was employed to generate a single-frequency signal, which was treated as a transducer input. It was sampled by the IIe, stored, and then run through the 401 FFT program. The graphic output replicated the frequency generated by the signal generator.

3 Log acceleration at each frequency was calculated as follows: Value of FFT program (also referred to as spectra in the apparatus and procedures section) X the program step size re voltage (0.039) - the amplifier gain at 50 db (316.2) - the calibrated acceleration of the accelerometer used (60.3 mV/g). This was g of acceleration, converted to mm/s^2 by multiplying 32 feet x mm per foot (32 x 3048), and then the log of that result was calculated.

4 The photocopies in Figure 2 were taken from copyrighted journals and should not be reproduced without their permission.

TABLE 1. NUMBER, GENDER, AND AGE (in years) OF WORKERS BY GROUP

Group	Gender	Number*	Age			
			Median	Mean (sd)	Min	Max
Mercury	Male	11	29.5	30.6 (7.9)	20	45
Mercury	Female	72	36.0	35.5 (12.0)	18	68
Reference	Male	10	30.5	35.0 (13.6)	20	63
Reference	Female	69	32.0	32.8 (10.6)	17	60

*Data includes all subjects seen in the receiving area and providing history.

TABLE 2. URINE MERCURY CONCENTRATIONS (ug/g creatinine) BY GROUP AND GENDER

Group	Gender	Number*	Urine Mercury Concentrations (ug/g)			
			Median	Mean (sd)	Min	Max
Mercury	Male	11	72	96.0 (89.4)	19	344
Mercury	Female	68	56	69.4 (66.0)	1	343
Reference	Male	7	3	3.7 (2.5)	2	9
Reference	Female	63	4	4.2 (2.3)	0	10

*Subjects excluded due to alcohol use, diabetes, finger injury, language difficulties.

TABLE 3. MERCURY EXPOSURE INDEX OF EXPOSED SUBJECTS

Group	Gender	Number*	Mercury Exposure Index			
			Median	Mean (Sd)	Min	Max
Mercury	Male	12	20	60.2 (64.9)	2	161
Mercury	Female	72	50	76.9 (70.2)	1	239

* Includes subjects ultimately excluded from the analyses.

TABLE 4. MEAN "MEDIAN FREQUENCIES" AT S1-3 AND S57-60 TIME PERIODS FOR STACO-CHASE AND REFERENCE SUBJECTS (Hz ≤ 20)

	Staco-Chase		Reference	
	mean (sd)	median	mean (sd)	median
S1-3				
Male	8.3 (1.3)	8.0	7.4 (1.0)	7.5
Female	7.6 (1.3)	8.0	7.7 (1.1)	8.0
S57-60				
Male	8.0 (1.2)	8.5	8.7 (1.6)	8.5
Female	7.9 (1.3)	8.0	7.7 (1.1)	8.0

TABLE 5. MEAN FREQUENCY (Hz) AND POWER (%) IN THE 5-8 HZ RANGE

Gender	STACO CHASE Mean (sd)	median	REFERENCE Mean (sd)	median
MEAN 5-8 FREQUENCY				
S1-3				
Male	6.7 (0.5)	7	6.7 (0.5)	7
Female	6.4 (0.5)	5	6.7 (0.5)	6
S57-60				
Male	6.4 (0.5)	6	6.7 (0.5)	7
Female	6.5 (0.5)	7	6.7 (0.5)	6
MEAN 5-8 POWER				
S1-3				
Male	6.8 (1.3)	6.4	8.1 (2.0)	7.9
Female	7.6 (1.3)	7.4	7.6 (1.3)	7.6
S57-60				
Male	7.0 (1.2)	6.6	7.2 (1.6)	7.2
Female	7.4 (1.3)	7.2	7.8 (1.4)	7.9

TABLE 6. GRIP STRENGTH IN STACO-CHASE VS. REFERENCE WORKERS

		STACO CHASE			REFERENCE			DIFF PROB
Gender	Age	N	Mean (sd)	Median	N	Mean (sd)	Median	
Male	≤30	7	56 (5)	56	5	46 (6)	45	
Male	>30≤45	4	45 (5)	44.5	3	52 (7)	53	
Male	>45	1	36 -	-	2	45 -	-	p = 0.46
Male	Combined	12	51 (8)	51	10	48 (6)	45	
Female	≤30	30	31 (6)	30	29	28 (5)	28	
Female	>30≤45	24	31 (4)	30	28	28 (4)	28	
Female	>45	12	25 (3)	25	8	28 (6)	27	p = 0.04*
Female	Combined	66	29 (5)	29	65	28 (5)	28	

*Significance is due to differences in >30 ≤45 age group where reference subjects are weaker

TABLE 7. GRIP-STRENGTH FATIGUE IN STACO-CHASE VS. REFERENCE WORKERS

		STACO CHASE			REFERENCE			
Gender	Age	N	Mean (sd)	Median	N	Mean (sd)	Median	
Male	≤30	7	3.3 (2.9)	1.5	5	1.1 (4.0)	0.5	
Male	>30≤ 45	4	1.6 (1.5)	2.0	3	0.7 (1.4)	1.5	
Male	>45	1	1.5 -	2.0	2	0.5 -	-	p = 0.03
Male	Combined	12	2.6 (2.4)	1.8	10	0.8 (2.8)	0.5	
Female	≤30	30	1.2 (1.8)	1.0	29	1.2 (1.9)	1.0	
Female	>30≤45	24	0.6 (2.1)	1.0	28	1.2 (2.4)	1.0	
Female	>45	12	0.7 (1.9)	0.5	8	0.5 (2.8)	0.0	p = 0.90
Female	Combined	66	0.9 (1.9)	1.0	65	1.0 (2.3)	1.0	

TABLE 8. OPTACON THRESHOLD (VOLTS)

		STACO CHASE			REFERENCE		DIFF PROB
Gender	**Age**	**N**	**Mean (sd)**	**Median**	**N**	**Mean (sd)**	**Median**
Male	≤30	7	4.4 (1.6)	4.5	5	4.4 (1.0)	3.8
	>30≤45	3	9.0 (3.6)	6.9	3	4.6 (1.5)	5.3
	>45	1	5.9		2	6.0 (2.6)	6.0
							p = 0.35*
Female	≤30	30	5.0 (1.6)	4.8	30	4.0 (0.9)	4.0
	>30≤45	24	6.4 (2.9)	6.5	28	3.9 (0.9)	3.9
	>45	11	6.7 (2.4)	6.3	8	6.3 (2.4)	6.2
							p = 0.001*

* m-rank procedure p-values

TABLE 9: OPTACON THRESHOLDS (VOLTS) IN MALE AND FEMALE SUBJECTS FOR INDEX AND LITTLE FINGERS

Male Subjects

	Number		Left Index		Right Index[a]		Left Fifth		Right Fifth	
Age	S-C	Ref	S-C	Ref	S-C	Ref	S-C	Ref	S-C	Ref
≤30	7	5	5.3 (6.2)	4.7 (4.3)	4.0 (4.8)	3.2 (3.1)	4.5 (4.7)	5.6 (4.8)	3.6 (3.1)	3.9 (3.9)
>30 ≤45	3	3	8.7 (8.4)	6.2 (6.4)	9.1 (7.2)	4.1 (4.9)	10.3 (7.1)	5.0 (4.9)	8.0 (6.5)	2.5 (1.7)
>45	1	2	7.8	6.3	4.4	4.7	7.6	7.1	2.4	5.3

Female Subjects

	Number		Left Index[b]		Right Index[c]		Left Fifth[c]		Right Fifth[c]	
Age	S-C	Ref	S-C	Ref	S-C	Ref	S-C	Ref	S-C	Ref
≤30	30	29	5.0 (4.5)	4.2 (4.0)	4.9 (4.5)	3.3 (3.3)	5.5 (5.2)	4.6 (4.7)	5.0 (5.2)	3.8 (3.6)
>30≤ 45	24	28	6.1 (5.8)	4.1 (4.0)	6.3 (5.9)	3.4 (3.2)	6.7 (6.5)	4.5 (4.5)	6.9 (7.2)	3.6 (3.5)
>45	11	9	7.7 (7.8)	5.6 (5.8)	6.5 (5.5)	4.8 (4.4)	6.4 (6.4)	7.5 (7.2)	5.7 (5.5)	6.0 (5.2)

[a] $p = 0.06$ [b] $p = 0.002$ [c] $p \leq .001$

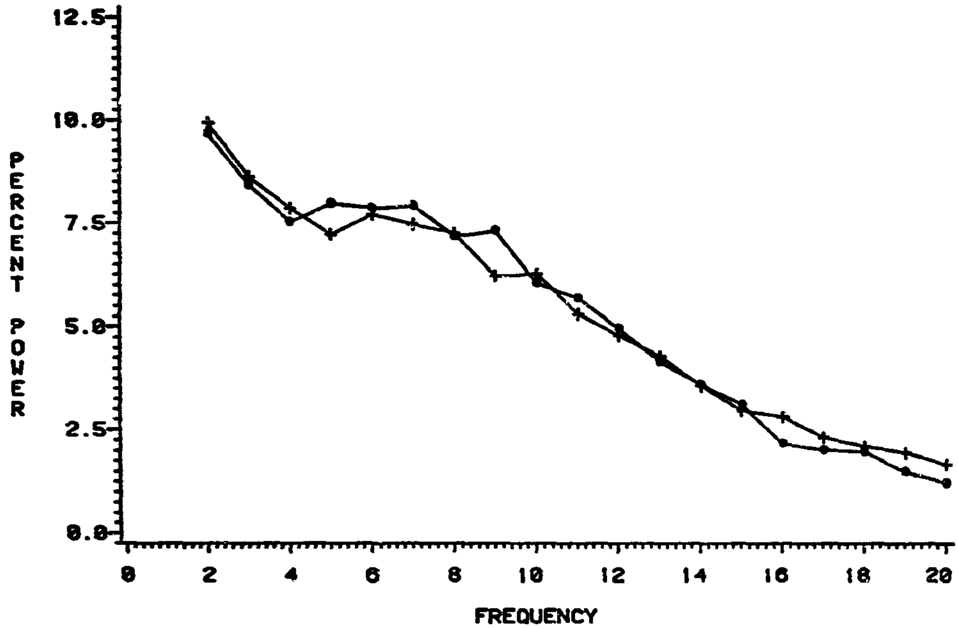
LEGENDS FOR FIGURES

Figure 1. Percent power (top panel) and acceleration (bottom panel) over frequencies 2-20 (Hz) for subjects from Staco-Chase and the reference workers during S1-3 and S57-60.

Figure 2. Percent power over frequencies 1-20 from the Langolf et al. (1981) study using a displacement-type device (top panel) and acceleration (plus velocity and physical displacement in the middle panel) over frequencies 1-25 from the Roels et al. (1985, 1983) studies using an accelerometer (middle and bottom panels).

FREQUENCY VS PERCENT POWER

CONTROL GROUP = + AND EXPOSED GROUP = ●



FREQUENCY VS LOG-ACCELERATION (MM/SEC²)

STACO - CHASE = O DOWTY (CONTROL)= +

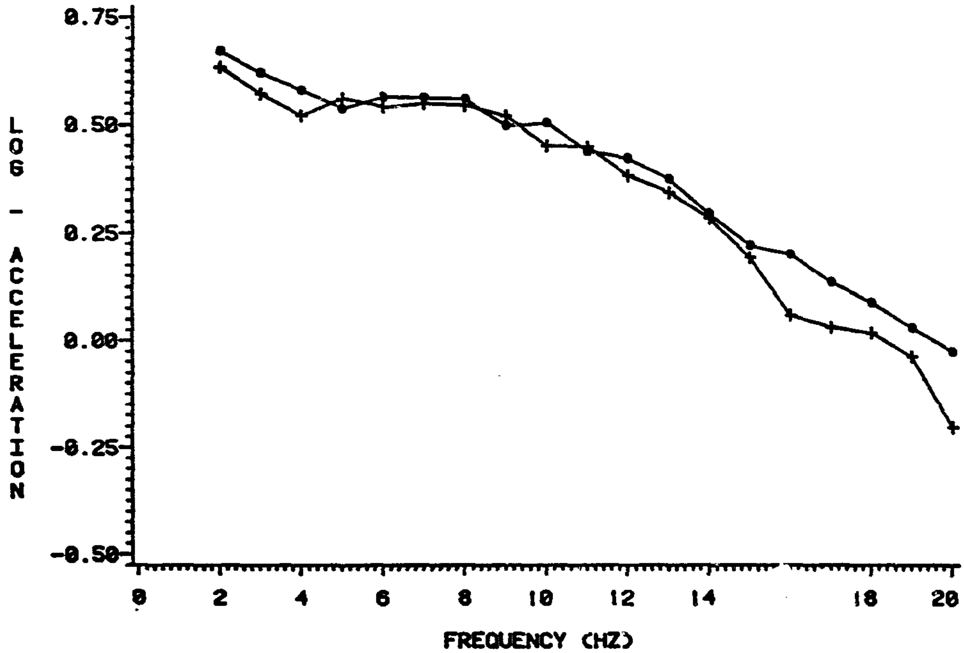
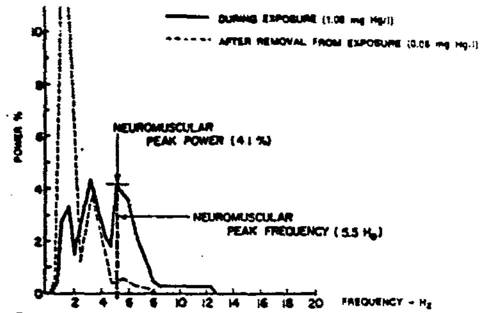
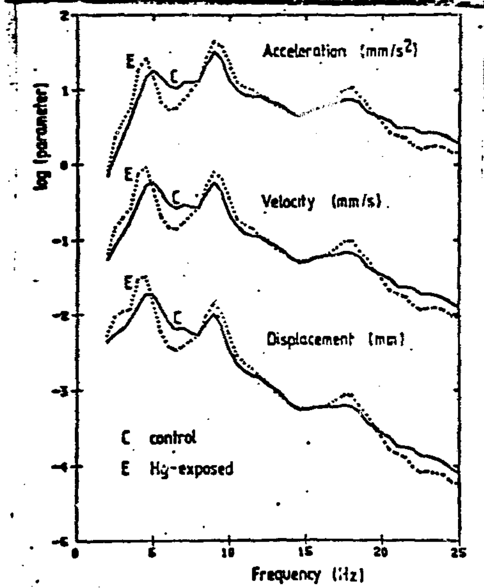


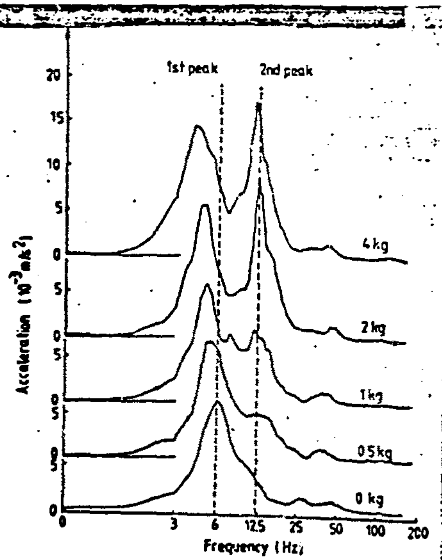
Figure 1



Langolf et al., 1981



Roels et al., 1985



Roels et al., 1983

Figure 2