

# Tactile Vibration Thresholds after Acute Poisonings with Organophosphate Insecticides

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This study evaluated the association between acute poisoning with organophosphate pesticides (OPs) and quantitative tactile vibration thresholds. Thresholds of the dominant index fingers and big toes of 56 men hospitalized for acute poisoning with OPs were measured at hospital discharge (1–24 days after poisoning) and around seven weeks later (24–176 days after poisoning), and compared with those of controls. Thresholds of the big toes of men with severe intentional poisonings due to neuropathic OPs (metamidophos and chlorpyrifos) increased between the first and second examinations. Threshold impairment was not detected in the index finger regardless of poisoning agent or severity. The development of threshold impairment as a consequence of severe intentional poisonings with neuropathic OPs is consistent with other reports indicating that only severe OP poisonings produce sensory peripheral nerve effects. *Key words:* cohort study; organophosphate pesticide poisoning; vibrotactile thresholds; sensory neuropathy.

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Poisonings caused by organophosphate insecticides (OPs) inhibit the enzyme acetylcholinesterase, leading to acute illness characterized by muscarinic and nicotinic effects on the peripheral (PNS) and central nervous systems (CNS).<sup>1</sup>

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Some OPs have persistent effects on the PNS after the acute poisoning resolves.<sup>2</sup> Organophosphate-induced delayed polyneuropathy (OPIDP) develops two to five weeks after the acute poisoning.<sup>3</sup> OPIDP progresses from sensory symptoms (arm and/or leg paresthesias) to leg cramping and weakness, foot drop, and, in severe cases, widespread paralysis of limb muscles.<sup>2,3</sup> The lower extremities are affected.<sup>2,6</sup> Some authors have reported predominantly or exclusively motor OPIDP,<sup>7,8</sup> while others have found mixed sensory-motor OPIDP related to specific pesticides.<sup>9,10</sup> The occurrence of OPIDP may be mediated by the inhibition of a neuronal enzyme, neuropathy target esterase (NTE), which seems to be related to axonal function.<sup>11,12</sup> NTE inhibition results in injury to the CNS as well as axonal degeneration of myelinated peripheral nerves that initially affects the distal portions of the extremities and progresses to the proximal ones (“dying back” effect).<sup>2</sup> Large, long myelinated nerve fibers are especially susceptible to the axonal degeneration induced by OPs.<sup>2</sup>

Among the methods used in epidemiologic studies to assess peripheral nerve function, cutaneous sensory perception thresholds have become increasingly used to measure impairment of large-diameter myelinated sensory fibers. These tests are rapid, noninvasive, inexpensive, and quantitative.<sup>13,14</sup> Moreover, several studies have shown correspondence between vibrotactile thresholds and electrophysiologic measures.<sup>11,14,15</sup> McConnell et al.<sup>16</sup> reported increased vibrotactile thresholds, mainly in the lower extremities, of 36 agricultural workers who had histories of severe poisonings with metamidophos and other OPs. Steenland et al.<sup>15</sup> found significant impairment of vibrotactile sensitivity of the fingers and toes of 128 men who had been poisoned with OPs, including chlorpyrifos, five to seven years earlier. Stokes et al.<sup>17</sup> found impaired vibration thresholds in the hands of 90 male applicators with ongoing exposure to OPs (including chlorpyrifos).

More than 50% of the pesticides used in Nicaragua, as well as in other developing countries, are OPs.<sup>18,19</sup> Not surprisingly, poisonings due to OPs are frequent and are an important public health concern.<sup>18</sup> Methamidophos,<sup>9,16</sup> chlorpyrifos,<sup>10,15</sup> and fenthion<sup>20</sup> are

commonly used in Nicaragua, and are among the OPs reported to result in peripheral neuropathy.

Epidemiologic studies of effects of OP poisonings on the PNS, including sensory threshold evaluations, have been performed on subjects whose poisoning episodes occurred from several months to years earlier.<sup>15,16</sup>

In this study, cutaneous quantitative vibrotactile thresholds were evaluated prospectively on two occasions, soon after poisoning and approximately seven weeks later, in the dominant index finger and great toe of each of 56 poisoned and 38 control men. The purpose was to determine whether organophosphate poisonings cause persistent large-diameter myelinated sensory fiber impairment, and if so, to evaluate the incidence and severity of impairment.

## SUBJECTS AND METHODS

### *Subjects*

Between July 1, 1992, and December 15, 1996, 77 men who had been treated as inpatients for OP poisonings for at least one day at two hospitals in the cities of León and Chinandega, Nicaragua, were identified. Twelve poisoned men were excluded because they were not examined on a second occasion and one because it could not be confirmed that the poisoning agent had been an OP. Six men with severe intentional poisonings died before the first evaluation, and one died before the second evaluation after a second intentional poisoning. One poisoned patient refused to participate. Fifty-six men composed the final poisoned group.

A comparison group consisting of 74 male members of fishing and cattle cooperatives was selected. Of these, 33 were not found for a second examination (in part because this group moved following opportunities for work) and two refused to participate in a second examination, resulting in a final sample of 39 men. Of these, 11 were cattle farmers, some of whom had been occasionally exposed to pesticides, but who had not experienced any poisoning episode requiring medical care, and 28 were members of fishing cooperatives who were not occupationally exposed to, and had never been poisoned by, pesticides.

### *Exposure Assessment*

The pesticide responsible for poisoning was determined from a patient report form completed by the examining physician at hospital admission. Field visits to confirm this report were made for 32 patients (57%), but were not possible for the remaining 24 (43%). In 29 of the cases of patients for whom confirming visits were possible, the pesticides reported to the examining physicians were corroborated by examining the container labels, or by interviewing the dealers. In three cases, where the pesticide could not be

confirmed through the visit, identification was possible through laboratory analysis of samples of the unlabeled pesticide. Data on acetylcholinesterase levels were available for only 23 (38%) of the poisoned men (measured at hospital admission) and ten (28%) of the controls.

### *Neuropathic versus Non-neuropathic OPs*

In accordance with data in the literature, methamidophos,<sup>2,9,16</sup> chlorpyrifos,<sup>10</sup> and fenthion<sup>20</sup> were regarded as "neuropathic" OPs, while terbuphos, ediphenphos, metophox, monocrotophos, and phorate were considered "non-neuropathic" OPs. As there is some indication that poisonings with malathion or parathion may cause peripheral neuropathy,<sup>8,21,22</sup> in separate analyses these pesticides were treated as neuropathic and as non-neuropathic, respectively.

### *Severity of the Poisoning*

Signs and symptoms were obtained through review of hospital records for every poisoned subject. Poisoning severity was classified as: mild if the patient presented weakness, dizziness, headache, or blurred vision and was without other more severe symptoms. None of the participants was included in this category. Severity of the poisoning was moderate if sialorrhoea, vomiting, abdominal pain, diarrhea, miosis, tongue or chest fasciculations, or wheezing or crepitus was reported without altered mental state. The poisoning was considered severe if besides the symptoms regarded as mild and moderate, severe alterations of consciousness occurred. Within this category was also included one of the poisoned patients for whom signs of consciousness were not registered but who had an erythrocyte cholinesterase activity of 2.6 IU/g hemoglobin. This value was 85% below the lower limit of the normal level in the control group (mean > 28.0 IU/g hemoglobin, SD 6.6) measured at hospital admission, using the Testmate OP field kit (EQM Research, Cincinnati, Ohio).<sup>23</sup> Mean cholinesterase level in those 12 moderately poisoned men from whom we had measurements was 11.6 IU/g hemoglobin (range 2.3–24.6, SD 5.9) and in those nine severely poisoned men with measurements it was 8.0 IU/g hemoglobin (range 2.6–17.1, SD 5.5).

### *Cause of Poisoning*

Information about the causes of the poisonings was obtained from the hospital records. Poisonings were classified as intentional and non-intentional. There were six suicide attempts and 50 occupational overexposures.

### *Potential Confounders*

Information concerning potential confounders was obtained from a standardized interview. Age was

treated as a continuous variable. Educational level was categorized into less educated (three years or less in school) and more educated (more than three years in school).

A history of lifetime exposures to the OP pesticides that had been most commonly used in Nicaragua during the preceding 35 years was obtained through an interview questionnaire. Duration of cumulative exposure to OPs was calculated by summing the lifetime numbers of months in which there had been exposures to the individual pesticides investigated. Cumulative exposures to OP pesticides were divided into none, low, and high cumulative exposures to neuropathic OPs, according to the median value of months of exposures among those exposed to these pesticides (60 months). Cumulative exposures to non-neuropathic OPs were classified as none, low, and high according to the median value of months with exposures among those exposed to these pesticides (36 months).

Information about drinking habits was investigated through questions about frequencies of consumption and amounts of beer (5% ethanol) and rum (35% ethanol) consumed monthly. All alcohol consumption came from these two beverages. The total amount in grams of alcohol consumed monthly was obtained by summing the grams of alcohol contained in all alcohol-containing beverages consumed on every occasion, multiplied by the drinking frequency per month. Alcohol consumption was categorized as none, low, and high according to median alcohol consumption (400 grams/month) among those who did drink alcohol.

Participants were questioned about exposures to chemicals (lead, mercury, and solvents), occupational exposures to vibrating machinery, histories of other relevant diseases (diabetes, head trauma with loss of consciousness, neurologic, thyroid and kidney illnesses), and medication intake (substances with suspected adverse effects on the nervous system three months before each evaluation), but none of these exposures or conditions was identified among the participants. Since callus formation has previously been shown to influence vibration threshold,<sup>16</sup> presence of callus in the dominant index finger and toe was examined. Heavy callus formation was qualitatively evaluated at the time of measurement of the vibrotactile threshold, and classified as present or absent. The effects of four different examiners and the time, in number of days, between the poisoning and each of the two examinations, as well as the time between the two examinations, were also evaluated.

### *Testing*

All examinations were carried out at the hospital of the city of León. The participants signed an informed consent before each examination and they were reimbursed for expenses and lost wages on the examination

day. The poisoned subjects were examined for the first time one to 24 days after the poisoning events (median seven days, 81% of the examinations between one and ten days) and for the second time, 24 to 128 days after poisoning (median 50 days and 77% of the examinations between 24 and 80 days). The control subjects were examined over the whole examination period with intervals between the examinations of 28 to 281 days (median 66 days). Four different examiners performed the vibrometry tests, but every individual was tested on the two occasions by the same examiner.

Vibrotactile thresholds were measured using a Vibraton II (Sensortek, Inc: Clifton, NJ) for dominant index finger and big toe. The vibrometer consists of a control box that displays the reading of vibration amplitude units, and two transducer boxes, each with a protruding 1.5-cm vibrating post. The threshold for each digit was determined according to the "method of limits" procedure.<sup>13,14</sup> Briefly, five readings (trials) were made for each digit; after discarding the first, the lowest, and the highest readings, the remaining two readings were averaged. The resulting data (X) were converted into microns of vibration amplitude (A) through the formula  $A = K \cdot (X) \cdot 2.05$ , where K is a constant that represents the peak-to-peak displacement of the stimulator post. The distribution of vibrotactile thresholds was normalized by log transforming A (into log mic).<sup>14</sup> Threshold mean change was calculated as the arithmetic difference between the first and second examinations. Temperatures in the rooms in which the examinations were performed were between 29.4° and 32.4°C for the first examination and between 28.4° and 33.2°C for the second examination.

### *Statistical Analysis*

Multiple linear regression analysis was performed using SPSS for Windows v. 8.0. The exposures (poisonings) were divided into four categories for the analyses: moderate and severe non-neuropathic poisonings and moderate and severe neuropathic poisonings. Indicator variables were created for each level. Vibrotactile thresholds were used as the outcome variables, as well as mean changes in index finger and toe vibrotactile thresholds (difference in vibration thresholds between the two evaluations).

The exposure variables, together with appropriate potential confounder variables (callus, age, height, education, alcohol consumption, days between the poisoning and the examinations, examiner, and OPs cumulative exposure), were entered one at a time in multiple linear regression analyses. Restricting the analyses to those whose first examinations were performed ten days after poisoning also tested the effect of time. The index and toe vibrotactile thresholds at the two examinations were the outcomes. Age was the only independent variable that had a significant impact on

**TABLE 1. General Characteristics of the Study Population**

	Controls (n = 39)	Poisoned (n = 56)
Age, mean (range)	30 years (15–49)	28 years (14–64)
Height, mean (range)	1.63 meters (1.39–1.85)	1.64 meters (1.49–1.77)
Education, mean (range)	4 years (0–10)	4 years (0–11)
Occupation		
Agriculture	0	50 (89%)
Cattle farming	11 (28%)	2 (4%)
Fishing	28 (72%)	0
Other	0	4 (7%)
Long-term exposure to organophosphate pesticides		
None	20 (51%)	3 (5%)
Low (< median*)	9 (23%)	31 (56%)
High (> median*)	10 (26%)	22 (39%)
Heavy callus prevalence		
Hand	8 (21%)	7 (12%)
Foot	11 (28%)	7 (12%)
Alcohol consumption		
None	12 (31%)	20 (36%)
Low (< median†)	9 (23%)	23 (41%)
High (> median†)	18 (46%)	13 (23%)

\*32 days.

†400 g/month.

the regression coefficients for the exposure levels and thus the only confounder entered in the final analyses. A regression coefficient with a *p* value < 0.05 was taken as being statistically significant.

## RESULTS

General characteristics of the study group and distribution of the poisonings are described in Tables 1 and 2, respectively.

*Non-neuropathic poisonings.* Neither moderately nor severely poisoned patients showed differences in index

or toe vibrotactile thresholds in the first or the second examinations as compared with the controls (Table 3). The intra-individual threshold mean changes between first and second index-finger or big-toe vibrometry also were not different from those of the controls (Table 4).

*Neuropathic poisonings.* Neither the moderately nor the severely poisoned patients showed significantly increase in the vibrotactile threshold of the index finger or big toe at the time of hospital discharge or at the second examination as compared with controls (Table 3). Toe-threshold within-person mean change, although not statistically significant, suggested

**TABLE 2. Poisoning Distribution According to Organophosphate Pesticide Type and Severity of Poisoning**

	Moderate Poisonings		Severe Poisonings		Total
	Intentional	Occupational	Intentional	Occupational	
Non-neuropathic OPs					
Methyl parathion	1	3	0	2	6
Malathion	0	0	0	1	1
Terbufos	0	0	0	1	1
Phorate	0	1	0	1	2
Ediphenfos	0	6	0	0	6
Subtotal	1	10	0	5	16
Neuropathic OPs					
Metamisophos	0	9	3	10	22
Chlorpyrifos	0	14	2	1	17
Fenthion	0	1	0	0	1
Subtotal	0	24	5	11	40
TOTAL	1	34	5	16	56

**TABLE 3. Cutaneous Vibrotactile Thresholds in Log Micrometers (log mic) in Individuals Poisoned with Organophosphate Insecticides (OPs) and Control Subjects**

	Threshold of Dominant Index Finger		Threshold of Dominant Big Toe	
	First Examination	Second Examination	First Examination	Second Examination
Controls (n = 39), mean (SD)	0.13 log mic (0.26)	0.07 log mic (0.24)	0.60 log mic (0.35)	0.51 log mic (0.2x)
Poisoned with non-neuropathic OPs				
Moderate poisoning (n = 12)				
Mean (SD)	-0.01 log mic (0.36)	-0.01 log mic (0.28)	0.44 log mic (0.32)	0.48 log mic (0.1x)
RC (CI)*	-0.08 (-0.28, 0.12)	-0.06 (-0.21, 0.09)	-0.08 (-0.29, 0.13)	0.00 (-0.21, 0.21)
Severe poisoning (n = 6)				
Mean (SD)	0.16 log mic (0.32)	-0.05 log mic (0.28)	0.67 log mic (0.26)	0.65 log mic (0.3x)
RC (CI)*	0.08 (-0.18, 0.34)	-0.11 (-0.30, 0.08)	0.12 (-0.16, 0.40)	0.15 (-0.12, 0.42)
Poisoned with neuropathic OPs				
Moderate poisoning (n = 23)				
Mean (SD)	0.19 log mic (0.38)	0.12 log mic (0.23)	0.65 log mic (0.32)	0.60 log mic (0.3x)
RC (CI)*	0.08 (-0.07, 0.24)	0.06 (-0.06, 0.18)	0.07 (-0.09, 0.23)	0.11 (-0.06, 0.28)
Severe poisoning (n = 15)				
Mean (SD)	0.16 log mic (0.23)	0.10 log mic (0.13)	0.57 log mic (0.30)	0.64 log mic (0.4x)
RC (CI)*	0.04 (-0.14, 0.21)	0.07 (-0.07, 0.21)	-0.01 (-0.20, 0.18)	0.17 (-0.02, 0.37)

\*Age-adjusted regression coefficient or difference from controls (RC) with 95% confidence interval (CI).

increases of vibrotactile thresholds between the first and second examinations among the group severely poisoned with neuropathic OPs, compared with the controls (Table 4).

Separate analysis of the group with severe poisonings with neuropathic OPs, revealed elevated index-finger vibrotactile thresholds and significantly increased toe vibrotactile thresholds in the second examinations in the subgroup of intentional poison-

ings, as compared with the controls (Table 5). Mean change difference in the toe thresholds was significantly higher in the intentional-poisonings subgroup as compared with the control group (Table 6).

No effect of cumulative exposure to either neuropathic or non-neuropathic OPs was observed in any of the poisoned groups as compared with the controls.

Including in the analysis the times between the poisonings and the examinations and between the two

**TABLE 4. Changes in Cutaneous Vibrotactile Thresholds in Log Micrometers (log mic) in Individuals Poisoned with Organophosphate Insecticides (OPs) and Control Subjects**

	Change in Threshold of	
	Index Finger	Big Toe
Controls (n = 39), mean (SD)	-0.06 log mic (0.23)	-0.09 log mic (0.34)
Poisoned with non-neuropathic OPs		
Moderate poisoning (n = 12)		
Mean (SD)	0.01 log mic (0.39)	0.04 log mic (0.31)
RC (CI)*	0.05 (-0.15, 0.24)	0.12 (-0.13, 0.38)
Severe poisoning (n = 6)		
Mean (SD)	-0.21 log mic (0.34)	-0.02 log mic (0.32)
RC (CI)*	-0.16 (-0.42, 0.09)	0.06 (-0.27, 0.40)
Poisoned with neuropathic OPs		
Moderate poisoning (n = 23)		
Mean (SD)	-0.08 log mic (0.33)	-0.05 log mic (0.34)
RC (CI)*	-0.03 (-0.18, 0.13)	0.04 (-0.16, 0.24)
Severe poisoning (n = 15)		
Mean (SD)	-0.06 log mic (0.25)	0.08 log mic (0.55)
RC (CI)*	-0.00 (-0.18, 0.18)	0.17 (-0.07, 0.40)

\*Age-adjusted regression coefficient or difference from controls (RC) with 95% confidence interval (CI).

**TABLE 5. Vibrotactile Thresholds in Log Micrometers (log mic) after Severe Occupational and Intentional Poisonings with Neuropathic Organophosphates (OPs)**

	Threshold of Dominant Index Finger		Threshold of Dominant Big Toe	
	First Examination	Second Examination	First Examination	Second Examination
Controls ( <i>n</i> = 39), mean (SD)	0.12 log mic (0.27)	0.07 log mic (0.24)	0.58 log mic (0.36)	0.51 log mic (0.27)
Occupational poisonings ( <i>n</i> = 10)				
Mean (SD)	0.16 log mic (0.28)	0.08 log mic (0.13)	0.58 log mic (0.34)	0.43 log mic (0.28)
RC (CI)*	0.03 (-0.14, 0.21)	0.0 (-0.16, 0.16)	-0.01 (-0.25, 0.22)	-0.08 (-0.29, 0.13)
Intentional poisonings ( <i>n</i> = 5)				
Mean (SD)	0.14 log mic (0.11)	0.24 log mic (0.25)	0.56 log mic (0.21)	1.1 log mic (0.47)
RC (CI)*	0.05 (-0.17, 0.26)	0.18 (-0.02, 0.38)	0.01 (-0.29, 0.29)	0.60 (0.33, 0.86)

\*Age-adjusted regression coefficient or difference from controls (RC) with 95% confidence interval (CI).

examinations did not appreciably change the regression coefficient of the effect, and neither did restricting the analysis to those whose first examinations were performed ten days or less after poisoning.

Non-appreciable differences were detected in the observed effects of poisoning when analyses were performed separately for each of the two main neuropathic pesticides (chlorpyrifos and metamidophos) among either the moderately or the severely poisoned group (data not shown). However, these analyses had limited power due to the small sample size.

Vibration threshold findings among the individuals poisoned with malathion and parathion were similar to those found for the insecticides classified in this study as non-neuropathic.

## DISCUSSION

A marked decrease in toe vibrotactile sensitivity at the second examination was observed in the men who had intentionally severely poisoned themselves with neuropathic OPs, as compared with the controls. Those with intentional poisonings were the most severe cases (five of six required treatment in the intensive care unit, compared with two of ten in the group with severe

occupational poisonings). The men with severe intentional poisonings had worse index-finger vibrotactile thresholds and markedly worse toe vibrotactile thresholds at the second examination as compared with the controls. No effect was detected even from severe occupational poisonings with allegedly neuropathic OPs, but the small size of the study group limits the conclusions that can be drawn from this finding.

Similarities between the comparison group and the poisoned individuals, in terms of education and socioeconomic background, were confirmed through interviews. Moreover, in the first examination there was no difference in vibration thresholds between those individuals in the comparison group who did and did not participate in the second examination. Furthermore, there was no difference in vibrotactile thresholds between cattle farmers and fishermen. Hence the control group used in the analysis seems to have been appropriate. Because sensory thresholds decreased within individuals between the two examinations, it is unlikely that these findings resulted from selection bias.

The high correlation between the pesticides responsible for the poisonings reported in the hospital and in the field visits, as well as the fact that signs and symptoms of OP poisonings are easy to evaluate, renders

**TABLE 6. Changes in Vibrotactile Thresholds in Log Micrometers (log mic) after Severe Occupational and Intentional Poisonings with Neuropathic Organophosphate Insecticides (OPs) and in Control Subjects**

	Change in Threshold of	
	Index Finger	Big Toe
Controls ( <i>n</i> = 39), mean (SD)	-0.06 log mic (0.23)	-0.09 log mic (0.34)
Occupational poisonings ( <i>n</i> = 10)		
Mean (SD)	-0.08 log mic (0.29)	-0.15 log mic (0.34)
RC (CI)*	-0.02 (-0.19, 0.15)	-0.05 (-0.33, 0.22)
Intentional poisonings ( <i>n</i> = 5)		
Mean (SD)	-0.06 log mic (0.14)	0.52 log mic (0.66)
RC (CI)*	0.04 (-0.19, 0.26)	0.60 (0.24, 0.97)*

\*Age-adjusted regression coefficient or difference from controls (RC) with 95% confidence interval (CI).

credibility to the categorization of the pesticides as OPs and as neuropathic and non-neuropathic. Our findings differ from those of McConnell et al.<sup>16</sup> who found persistently impaired vibratory thresholds in the index fingers and, more markedly, in the toes of 36 men who had histories of at least one severe occupational poisoning with methamidophos, between ten and 34 months after the episodes. Also, Steenland et al.<sup>15</sup> found elevated finger and toe vibration thresholds among 128 men who had been occupationally poisoned with different OPs, including chlorpyrifos, between 1982 and 1990. However, in a previously published case report, we found that a young man belonging to this sample had developed OPIDP after ingesting methamidophos, but showed only a mild increase in toe vibrotactile threshold one week after the event and normal thresholds a few weeks later.<sup>24</sup> In accordance with clinical reports, we had assumed maximum effect six weeks after poisoning.<sup>7,9,12,21</sup> We do not have any suitable explanation for this individual finding, unless a longer period for testing could have been needed. The exclusion of this individual from the analysis of the present study caused a significant increase in the mean difference between the thresholds found at the first and second examinations in the big toes of the severe-intentional-poisoning group. This may indicate that this patient was an atypical case within this group, and that the rest of the men did develop vibrotactile threshold impairment.

In another study of the same study population,<sup>25</sup> we have observed a rather marked decrease in grip and pinch strength in the dominant hand among those with severe intentional poisonings. This suggests that motor effects of severe poisonings with neuropathic OPs could be more pronounced than sensory effects.

The absence of an effect from cumulative long-term exposures to neuropathic OPs found in this study agrees with findings of London et al.<sup>26</sup> in the big toes of 164 long-term-exposed OP pesticide applicators in South Africa, and with those of Beach et al.<sup>27</sup> among 20 long-term-OP-exposed sheep farmers who were studied with various sensory examinations, including vibration sensation. However, Stokes et al.<sup>17</sup> found elevated hand vibrotactile thresholds among 90 men with long-term exposures mainly to primarily non-neuropathic OP pesticides. Otto et al.<sup>28</sup> found elevated hand vibrotactile thresholds among 229 men with long-term exposures in a formulation plant. The inconsistency of these findings may be related to differences in the classifications of exposure estimates in the different studies. These exposure estimates vary from comprehensive exposure indexes,<sup>26</sup> to months with exposure (our study) or years of exposure.<sup>17</sup> Recall for past exposures is difficult, and cumulative exposures are likely to be, in general, nondifferentially misclassified in all these studies, which would lead to a bias toward the null hypothesis for the observed effects.

It is often difficult to obtain valid statements about alcohol consumption from those who drink much alcohol. However, our findings concerning the absence of effect from alcohol consumption on vibration thresholds agree with those by Melgaard et al.,<sup>29</sup> who, in a study of a normal population of 468 45-year-old men, found elevated vibration thresholds among individuals diagnosed as alcoholics only. Sosenko et al.,<sup>30</sup> in a study of 156 neuropathy-free individuals, did not find effects on vibration thresholds from alcohol consumption after excluding the individuals diagnosed as alcoholics. Farkkila et al.<sup>31</sup> did not find any association between alcohol consumption and vibration thresholds among 217 forestry workers. This suggests that misclassification of alcohol consumption is unlikely to have markedly biased risk estimates associated with the pesticide exposures under study.

The differences in the findings among the intentional and occupational poisonings could be related to the severity of the poisoning, since the intentional poisonings were probably the most severe cases. However, because of the small sizes of these groups, no firm conclusion should be drawn. Finally, the suicidal subjects and those with severe occupational poisonings showed similar vibration thresholds in the first examination. Hence, to account for the difference in thresholds in the second examination by a depressive state among the suicidal subjects one would have to assume that this depressive state had not been apparent when the suicide was attempted but was present only several weeks later. This seems an unlikely explanation for our results.

## CONCLUSIONS

Big-toe vibrotactile thresholds increased markedly from the first to the second examinations among men with severe intentional poisonings with neuropathic OP poisonings as compared with controls. Although the small sample sizes limited the possibility of detecting small effects, no significant sensory impairment of vibrotactile thresholds was detected in association with occupational poisonings or with less severe intentional poisonings with neuropathic or non-neuropathic insecticides. This suggests that sensory involvement may be related to poisoning severity. However, future follow-up of our study group could be more revealing.

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