Chronic Neurological Sequelae to Organophosphate Pesticide Poisoning

Resource ID# 5137

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A B S T R A C T

Objectives. This work was undertaken to determine whether there are any chronic neurological sequelae to acute organophosphate pesticide poisoning.

Methods. California surveillance data were used in a study of neurological function among 128 men poisoned by organophosphate pesticides in California from 1982 to 1990 and 90 referents. Tests included a neurological physical examination, 5 nerve conduction tests, 2 vibrotactile sensitivity tests, 10 neurobehavioral tests, and 1 postural sway test.

Results. After correcting for confounding, the poisoned group performed significantly worse than the referent group on two neurobehavioral tests (sustained visual attention and mood scales). When the data were restricted to men with documented cholinesterase inhibition (n = 83) or to men who had been hospitalized (n = 36), the poisoned subjects also showed significantly worse vibrotactile sensitivity of finger and toe. Significant trends of increased impairment were found with increased days of disability on a wide spectrum of tests of both central and peripheral nerve function.

Conclusions. While these findings are limited by low response rates and by small sample sizes for specific pesticides, this study was based on a large surveillance database and is the largest study to date of the chronic effects of organophosphate pesticide poisoning. The evidence of some long-term effects of poisoning is consistent with two prior studies. (*Am J Public Health.* 1994;84:731–736)

Introduction

Organophosphate pesticide poisoning results in well-known acute effects, which typically end in a few days. These effects are caused by the binding of cholinesterase and the buildup of acetylcholine. According to data assembled from poison control centers, there are approximately 10 000 cases of organophosphate pesticide poisonings annually in the United States.[1]

Some organophosphates may also cause a delayed-onset peripheral neuropathy several weeks after exposure, which primarily affects the extremities. Symptoms may persist or gradually decrease. This peripheral neuropathy results from severe inhibition of neuropathy target esterase, causing axonal degeneration.[2,3]

The literature is sparse as to whether an acute poisoning followed by apparent recovery has any subsequent chronic neurological effects. Two epidemiological studies with reasonable sample size and control series have indicated deficits among poisoned subjects on various neurobehavioral tests.[4,5] To investigate further the chronic sequelae of acute organophosphate poisoning, we conducted a study of 128 men aged 16 and over who were poisoned by an organophosphate pesticide in California between 1982 and 1990. We studied neurological function via neurobehavioral tests, nerve conduction tests, vibrotactile sensitivity tests, a test of postural sway, and a neurological physical examination.

Methods

Study Population

The state of California requires physicians to report known or suspected cases of organophosphate pesticide poisoning.[6] The pesticide illness reports generated by this system contain detailed information about patients' medical history and exposure; such information was collected from poisoned individuals and their employers during an investigation conducted by the Agriculture Department of the county where the poisoning occurred. Information is available regarding whether a patient was hospitalized as well as the number of days the patient took off from work (disability days) subsequent to the poisoning. In most cases, the report lists the specific pesticide thought to be responsible for the poisoning ("primary" pesticide), as well as any other pesticides to which the patient was exposed at the time of poisoning.

Case subjects (the "exposed" group) were the systemic organophosphate pesticide poisonings between 1982 and 1990 among men aged 16 and older (excluding suicide attempts). Women were not included owing to small numbers (15% of eligibles) and anticipated increased difficulty in tracing. All subjects had been exposed to one or more organophosphate pesticides and had sought medical attention (28% had been hospitalized for at least 1 night). Cases were divided into two types, "definite" and "probable." Definite

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This paper was accepted January 24, 1994.

TABLE 1—Comparison of Poisoned vs Nonpoisoned Subjects

	Poisoned (n = 128)	Nonpoisoned (n = 90)
Mean age, y (SD)	33.8 (9.5)	29.5 (10.9)*
Mean grade level (SD)	9.6 (4.9)	10.6 (3.6)
Mean body mass index (SD)	27.3 (4.4)	26.8 (4.7)
Race[a]		
Hispanic, %	56	56
White, %	41	39
Other, %	3	5
Preferred language[b]		
English, %	70	66
Spanish, %	30	34
Current smokers, %	37	33
Current drinkers, %	66	72
Mean hours of sleep, night before testing (SD)	7.2 (1.7)	7.2 (1.5)
Mean cups of coffee/tea on morning of test (SD)	0.8 (1.1)	0.9 (1.0)
Mean no. of drinks, night before testing (SD)	1.5 (2.7)	1.8 (2.4)
Average year of poisoning	1986	NA
Self-reported solvent exposure, %	20	21
Current employment in agriculture,[c] %	40	19*

Note. NA = not applicable.
[a]Self-reported.
[b]Language chosen for computerized neurobehavioral test; 18 subjects did not take this test.
[c]Nonpoisoned subjects were required to not be currently exposed to pesticides; nonpoisoned men in agriculture denied current exposure.
*Significant difference between groups at $P = .05$.

cases (n = 83) were those reporting one or more symptoms compatible with organophosphate poisoning (flulike symptoms, headaches, nausea, diarrhea, salivation), accompanied by a documented inhibition of red blood cell or plasma cholinesterase. Inhibition had to be at least 20% below the subject's own baseline value or be a value considered below the normal range by the testing laboratory. Probable cases (n = 45) did not have data on cholinesterase inhibition but reported either (1) compatible symptoms accompanied by relative specific physical signs—for example, bradycardia (heart rate less than 60) or miosis (narrowing of pupils to 3 mm or less); or (2) compatible symptoms accompanied by a history of direct exposure to the skin or eye during an application or spill. Virtually all subjects had been exposed occupationally.

Subjects were traced via the address in the pesticide illness report, telephone directory assistance, and current addresses obtained from the Internal Revenue Service. Social security numbers were not available. Subjects were contacted by phone and mail and asked to participate by coming to a central location in California, spending the night in a hotel, and taking a 4-hour battery of tests the following day. They were excluded if they had diabetes, had suffered a stroke, or had experienced trauma that had affected their central nervous system. Subjects were paid $100 for their participation and reimbursed for their expenses.

A nonexposed comparison group consisted of friends of the subjects not currently working with pesticides. The nonexposed individuals were also paid $100 for their participation. Participation was voluntary for all subjects, and consent forms were obtained.

Tests of Neurological Function

All tests were performed by technicians "blind" to exposure status.

Nerve conduction tests for peripheral neuropathy were done on three nerves of the dominant arm (median motor, median sensory, and ulnar sensory) and two nerves of the dominant leg (peroneal motor and sural sensory) using a standard protocol.[7,8] Two measures of nerve function were made: (1) conduction velocity—the amount of time from stimulation to the onset of principal depolarization (latency), divided by distance; and (2) peak amplitude—the size of the maximal response of the compound action potential for sensory studies or the M-wave for motor studies.

All tests were performed with surface electrodes; stimulation consisted of 100 to 200 microsecond square pulses. Motor responses were orthodromic; sensory tests were antidromic. Surface temperature of the limb was maintained at 33.0°C (centigrade) for the upper limb and 32.0°C for the lower limb.

Sensitivity to vibration was tested as a measure of the possible axonal degeneration in the sensory nerves of the index finger and big toe (dominant side, five trials). Vibrotactile thresholds were measured with the Vibration II instrument via the "method of limits."[9]

Eight computerized neurobehavioral tests from the Neurobehavioral Evaluation System (NES2, version 4.22) were conducted.[10] These tests were available in English and Spanish. While generally self-explanatory and requiring little intervention by the investigator, they did require a reading level equivalent to an elementary school education. The eight tests used are listed below:

1. Mood scales (affect test). Measures subjects' self-reported transient states of tension, depression, anxiety, fatigue, and confusion.
2. Finger tapping (motor speed test). Measures how many times a key can be repeatedly struck in 30 seconds, using the preferred hand.
3. Sustained visual attention (continuous performance test). Requires pressing a key quickly when a certain letter appears amid a temporal sequence of various letters; 60 letters appear in 5 minutes.
4. Hand–eye coordination (visuomotor accuracy test). Measures the degree of error in tracing a moving sine curve with a cursor.
5. Simple reaction time (visuomotor speed test). Measures how fast one can respond to a visual stimulus by pushing a button.
6. Symbol digit (coding speed test). Requires matching digits to symbols as fast as possible following an exhibited matched pattern.
7. Pattern memory (visual memory test). Requires selecting a previously seen pattern out of three similar patterns.
8. Serial digit learning (learning/memory test). Requires memorizing and replicating a series of eight digits as quickly as possible.

In addition, two noncomputerized neurobehavioral tests of psychomotor function—the Santa Ana dexterity test and the pursuit aiming test—from the World Health Organization core battery of tests were used.[11] These tests require turning rows of successive pegs 180 de-

TABLE 2—Adjusted Linear Regression Results on a Battery of Tests of Neurological Function for All Poisoned Subjects, Definitely Poisoned Subjects, and Hospitalized Subjects vs Nonpoisoned Control Subjects

Outcome	R^2 Model for All Poisoned[a]	All Poisoned (n = 128)			Definite Poisonings (n = 83)			Hospitalized Poisonings (n = 36)		
		Coefficient	Direction[b]	P[c]	Coefficient	Direction[b]	P[c]	Coefficient	Direction[b]	P[c]
NCV—median sensory	.15	−1.01	−		−1.08	−		0.26	+	
NCV—median motor	.07	−0.58	−		−1.19	−		−0.04	−	
NCV—ulnar sensory	.09	0.26	+		0.07	+		0.12	+	
NCV—peroneal motor	.19	−0.89	−	.09	−1.11	−	.06	−0.43	−	
NCV—sural sensory	.06	−0.04	−		0.41	+		0.22	+	
Amplitude—median sensory	.30	−1.55	−		−2.54	−	.10	−1.41	−	
Amplitude—median motor	.10	0.59	+		0.93	+	.06	1.63	+	.01
Amplitude—ulnar sensory	.12	−2.39	−		−1.65	−		−1.73	−	
Amplitude—peroneal motor	.03	−1.69	−	.06	−1.56	−		−1.35	−	
Amplitude—sural sensory	.21	−1.58	−		−2.04	−		−2.25	−	
Vibration—finger	.08	0.17	−		0.27	−	.03	0.65	−	<.01
Vibration—toe	.33	0.18	−		0.33	−	.05	0.60	−	<.01
Tapping	.18	−1.27	−		−4.89	−		−7.64	−	
Hand–eye coordination	.25	0.00	−		0.03	−		0.00	+	
Simple reaction time	.09	0.01	−		0.01	−		0.02	−	.10
Continuous performance	.13	0.01	−	.05	0.02	−	.01	0.03	−	.01
Symbol digit	.42	0.12	−		0.15	−		0.27	−	.04
Pattern memory	.08	0.78	+		0.63	+		0.18	+	
Serial digit	.27	−0.47	+	.10	−0.03	+		−0.51	+	
Mood scales[d]										
Tension	.03	0.24	−	.02	0.26	−	.03	−0.11	−	
Depression	.01	0.03	−		0.07	−		−0.08	+	
Anger	.02	0.04	−		−0.03	+		0.15	−	
Fatigue	.08	0.30	−		0.27	−		−0.08	+	
Confusion	.20	0.14	−	.01	0.14	−	.02	0.03	−	
Pursuit aiming	.08	0.13	+		0.93	+		−8.48	−	
Santa Ana dexterity	.21	0.53	+		1.21	+		−0.39	−	
Postural sway[e]	.03	0.03	−		0.03	−		0.05	−	

[a]All models had a variable for nonpoisoned vs poisoned. Models for nerve conduction velocity (NCV) and amplitude included age, race, and body mass index. Models for vibrometry included age, weight, race, and height. Models for computerized Neurobehavioral Evaluation System tests included age, education (grade), and test language (Spanish or English). Models for pursuit aiming and Santa Ana tests included race, age, and education. Models for postural sway included race, age, education, height, and weight.

[b]Coefficient represents difference in outcome between poisoned and nonpoisoned. Performance of poisoned vs referents, + = better; − = worse. P values are for tests of the null hypothesis that the coefficient equals 0. The actual values of the outcome variables, adjusted for covariates, may be obtained by request from the authors.

[c]P values reported if ≤ .10.

[d]For mood scales, a higher score meant more tension, depression, etc., interpreted here as a worse performance.

[e]The difference in sway for eyes shut vs eyes open (higher scores represent worse performance).

grees and using a pencil to mark a point inside each of a series of circles as quickly as possible.

A computerized measurement of postural sway (30 seconds), a quantitative analogue of the Romberg clinical exam, was conducted to measure central nervous system function.[12] The outcome is the difference in sway between measurements taken with eyes open and eyes closed.

Finally, a physician conducted a standard neurological physical examination designed to detect gross neurological abnormalities and asked the subject about past medical history. The exam, which screened for primarily motor and cerebellar function, was used primarily to exclude subjects who suffered neuropathies from causes unrelated to pesticides, such as trauma or stroke.

Analysis

Thirty-eight poisoned subjects (30%) did not bring a friend to serve as a nonexposed comparison. Data were analyzed without reference to pair matching both to avoid loss of poisoned cases in the analyses and to facilitate multivariate analyses permitting control of unmatched confounders. All outcome measures were continuous variables; multivariate linear regression was used. Among the potential confounders considered were age, race (self-reported), body mass index (weight in kilograms/height in meters squared), education (grade level), preferred language, hours of sleep and alcohol consumption the evening prior to the test, smoking habits, use of prescription medicine, medical history, current exposure to solvents or pesticides (self-reported), and coffee consumption the morning of the tests. Multivariate models for nerve conduction velocities and amplitudes included race, age, and body mass index. Regressions for computerized neurobehavioral tests included age, grade level, and language in which the test was taken (Spanish or English); those for vibrotactile sensitivity and postural sway included age, race, weight, and height. All models were checked for assumptions of normality of residuals and model fit.

A dichotomous variable indicating poisoned case or referent was the principal exposure variable included in most

TABLE 3—Neurological Outcomes as a Function of Increased Days Taken Off from Work after Poisoning[a]

Outcome	R^2 for Model	Direction of Effect with Increased Days Taken Off from Work[b]	P[c]
NCV—median sensory	.16	+	
NCV—median motor	.08	−	
NCV—ulnar sensory	.08	+	
NCV—peroneal motor	.20	−	
NCV—sural sensory	.08	+	.03
Amplitude—median sensory	.33	−	
Amplitude—median motor	.10	+	.06
Amplitude—ulnar sensory	.13	−	
Amplitude—peroneal motor	.01	−	
Amplitude—sural sensory	.22	−	
Vibration—finger	.11	−	
Vibration—toe	.34	−	<.01
Tapping	.21	−	.03
Hand–eye coordination	.26	−	
Simple reaction time	.11	−	.03
Continuous performance	.16	−	<.01
Symbol digit	.44	−	<.01
Pattern memory	.09	−	.09
Serial digit	.26	−	.03
Mood scales			
Tension	.01	−	
Depression	.01	−	
Anger	.02	−	
Fatigue	.05	−	
Confusion	.18	−	.10
Pursuit aiming	.10	−	
Santa Ana dexterity	.21	−	.06
Postural sway	.02	+	

Note. NCV = nerve conduction velocity.
[a]"Days taken off from work" was entered as a continuous variable in models, replacing the dichotomous (poisoned/nonpoisoned) exposure variable used in other models. There were 18 poisoned men excluded from the analysis because they were missing data for days taken off from work. Referents were assigned "0" for this variable.
Thirty eight poisoned men had 0 days taken off from work and were grouped with the referents; arbitrary assignment of 1 day off from work for these 38 did not change results. Models included days taken off from work and relevant confounders (see Table 2).
[b]Performance of those who took more days off from work: + = better; − = worse.
[c]P values are for tests of the null hypothesis of no trend in outcome with days of work, and are reported if $P \leq .10$.

TABLE 4—Number of Poisoned Cases, by Type of Pesticide[a]

Pesticide	Primary[b]	Some Exposure
Chlorpyrifos	10	17
Diazinon	11	19
Dimethoate	7	14
Demeton methyl/ oxydemeton methyl	3	21
Mevinphos	13	39
Parathion	5	8
Phosalone	20	20
Other—specified	19	NA
Undetermined	38	NA

Note. NA = not available.
[a]Taken from original pesticide illness report.
[b]For most poisoned cases, a primary pesticide suspected of causing the poisoning was listed in the record, but for 38 poisoned subjects no primary pesticide was specified. In addition to the primary pesticide, many men were also exposed concurrently to another organophosphate, which could possibly have contributed to the poisoning (here listed under "some exposure"). All subjects in the category "primary exposure" for a pesticide are included in the category "some exposure" for that pesticide.

models. Analyses were also conducted in which the dichotomous exposure variable was replaced by a variable for number of days taken off from work (disability) subsequent to poisoning, with 0 days assigned to referents.

Although there were numerous outcomes, no formal correction for multiple comparisons was made[13]; instead, statistically significant associations were evaluated for coherence and consistency.

A number of individuals were excluded for all or some tests. The first 16 individuals tested did not have this mood scales test on the computerized neurobehavioral battery since this test was added after the first round of testing. Eighteen subjects (13 poisoned subjects and 5 nonpoisoned subjects, $P = .15$) did not take the computerized neurobehavioral tests, most often because their reading ability was insufficient. Other subjects were excluded in lesser numbers from specific tests for reasons such as malfunction of equipment, trauma affecting the nerves, and frostbite.

Results

We tested 128 poisoned and 90 nonpoisoned subjects. The 128 poisoned men represented 31% of the target population of 416 potential participants. Of the remaining potential participants, 13% refused, 37% could not be located, and 19% could not be contacted. (Although addresses were provided, mailings elicited no response from this latter group, and no phone number was listed with directory assistance.) A comparison of the 128 poisoned participants with the 288 poisoned nonparticipants revealed that nonparticipants were slightly older, were more likely to be Hispanic, and took more days off from work following their poisoning (data not shown).

Table 1 shows that poisoned and nonpoisoned subjects were generally similar but that poisoned subjects were significantly older and somewhat less educated.

Table 2 compares all poisoned subjects, definitely poisoned subjects, and hospitalized subjects with the 90 nonpoisoned subjects. For all poisoned subjects, the only statistically significant differences from the nonexposed group (at the $P = .05$ level) occurred for the test of sustained visual attention (continuous performance) and for two mood scale tests. For the 83 subjects with definite poisonings (documented cholinesterase inhibition), vibrotactile sensitivity for both finger and toe was also significantly worse. For the 36 hospitalized subjects (1 or more nights), vibrotactile sensitivity, the sustained attention test, and the symbol digit test were significantly worse than they were for the referents.

Table 3 shows the results of analyses by days taken off from work (disability days), which ranged from 0 to 32 for poisoned subjects (mean = 3.8, SD = 5.5). Significant trends of increased impairment with increased days of disability were found for peroneal nerve conduction velocity, for finger vibrotactile sensitivity, and for 5 of 10 neurobehavioral tests.

Variables for current employment in jobs with potential pesticide exposure and for years of self-reported past exposure to pesticides were tested but were not generally associated with the outcomes, nor did their inclusion in the model alter results for the effect of poisoning.

Analyses of the data according to year of poisoning did not change results, indicating that observed positive associations were not restricted to those subjects who were poisoned more recently.

Table 4 indicates the distribution of poisonings by pesticide, based on the original pesticide illness reports. As previously noted, these reports list a primary pesticide involved in the poisoning, as well as other pesticides to which a subject was exposed that might have played a role in the poisoning. In some cases, no one pesticide was deemed primary.

Table 5 shows the results of pesticide-specific analysis. For primary pesticides, chlorpyrifos- and phosalone-poisoned subjects showed some decrement in peripheral nerve function.

Table 5 also presents results for subjects exposed to any of seven pesticides at the time of poisoning, regardless of whether that exposure was considered the primary cause of the poisoning. Poisoned men who had been working with demeton methyl (Metasystox) showed a variety of decrements compared with the nonexposed men. (Eighteen of 21 men exposed to demeton methyl or oxydemeton methyl had no primary pesticide listed.) Similar findings for mevinphos may be partly owing to the fact that one third of the men working with mevinphos were also working with demeton methyl (13/39). Findings were unremarkable when analyses were restricted to those whose primary pesticide was mevinphos.

TABLE 5—Significant Associations ($P \leq .05$) in Analyses of Neurological Function, by Primary Pesticide or by Some Exposure to a Pesticide[a]

Primary[b]	
Phosalone[c]	More tension ($P = .05$) and fatigue ($P < .01$) on mood scales, better Santa Ana dexterity test ($P = 05$), worse sural amplitude ($P = .02$)
Diazinon	No associations
Chlorpyrifos	Worse peroneal motor nerve conduction velocity ($P = .04$) and ulnar sensory amplitude ($P = .03$)
Mevinphos	No associations
Some exposure	
Parathion	No associations
Diazinon	More tension on mood scales ($P = .04$)
Chlorpyrifos	More tension on mood scales ($P = .02$, worse finger vibrotactile sensitivity for the definitely poisoned ($P = .003$, n = 8)
Dimethoate	More tension ($P = .02$) and fatigue ($P = .05$) on mood scales
Mevinphos	Worse finger vibrotactile sensitivity ($P = .01$), worse performance on sustained attention test ($P < .01$)
Demeton methyl[d]	Worse finger ($P < .01$) and toe ($P = .01$) vibrotactile sensitivity; worse sustained attention ($P = .03$), simple reaction ($P = .04$), and symbol digit ($P < .01$) tests; more tension ($P = .05$) on mood scales

[a]Models used were the same as those used for Table 3, with same referent group (n = 90). Information on pesticide exposure at time of poisoning came from the original pesticide illness report.
[b]Analyses were restricted to the four primary pesticides with the most cases (nine or more).
[c]Phosalone only occurred as a primary pesticide.
[d]Demeton methyl and oxydemeton methyl (Metasystox and Metasystox-R) combined.

TABLE 6—Comparison of Neurobehavioral Tests in Three Studies of Men Poisoned by Organophosphate Pesticides

	Present Study				
Test	All Poisoned Subjects (n = 128)	Hospitalized Poisonings (n = 36)	Trend with Days Taken Off from Work (n = 110)	Savage et al.[4] (n = 100)	Rosenstock et al.[5] (n = 36)
Tapping	–	–	–*	–*	–
Simple reaction time	–	–	–	NA	–
Sustained attention	–*	–*	–*	NA	–*
Symbol digit	–	–	–*	–*	–*
Pursuit aiming	+	–	–	NA	–*
Santa Ana dexterity	+	+	–	–*	–*

Note. + = better performance; – = worse performance. NA = not available.
*$P < .05$.

Discussion

For the neurobehavioral tests used in this study, we found significantly worse performance on 2 of 10 tests (mood scales and the sustained visual attention test) by poisoned subjects, worse performance on a third test (symbol digit) by hospitalized subjects, and significant trends of worse performance on 5 of 10 tests by those who took more days off from work after poisoning. Increased impairment for those with presumably more severe poisonings (those hospitalized and those who took more days off from work) tends to support the hypothesis that the observed deficits on some of the neurobehavioral tests may be causally related to past poisonings. Two prior studies have also found that poisoned men performed significantly worse on a broad spectrum of neurobehavioral tests.[4,5] Table 6 compares our findings with those of two previous reports for six such tests. Our findings may be viewed as reasonably consistent, although the prior studies found a broader spectrum of deficits among poisoned subjects than we did. As most of the poisoned subjects in these studies had been hospitalized, they may have represented more severe poisonings.

Regarding the peripheral nervous system, nerve conduction velocities and amplitudes were not significantly worse for poisoned men overall. For pesticide-specific analyses, there were some significant deficits in nerve conduction velocity

and/or amplitude observed among men poisoned by chlorpyrifos or phosalone. This is consistent with a case report of delayed-onset neuropathy following poisoning by chlorpyrifos.[14]

Vibrotactile sensitivity of finger and toe was significantly reduced among poisoned men with documented cholinesterase inhibition, among poisoned men who had been hospitalized, and among men who took more days off from work after poisoning. Pesticide-specific analyses suggest that demeton methyl was the pesticide most associated with the vibrotactile sensitivity deficit among the poisoned men. A case report of delayed-onset neuropathy following poisoning by demeton methyl has been previously published.[15] A finding of vibrotactile sensitivity deficit in the absence of significant slowing of nerve conductions may reflect the relative insensitivity of electrophysiologic measures for the detection of a distal axonopathy.[16]

There are a number of limitations in our data. Our relatively low response rate may have affected our results in unpredictable ways. We anticipated difficulty in locating poisoned subjects, a number of whom were migrant Mexican workers. Possible conservative biases could have occurred if those subjects who did not participate were more likely to have had neurological impairment, but the opposite scenario is also possible. The use of friend controls could have also biased our findings toward the null if friends were selected for this similarity to the poisoned subjects regarding the outcomes under study (overmatching); however, a bias in the opposite direction could occur if the friends are more sociable people with better neurobehavioral capability.

Another limitation is the low proportion of variation explained by our predictor variables, indicating that individual heterogeneity or other environmental factors that we did not measure played a large role in determining the neurological outcomes of interest. It is possible that other unmeasured variables may have acted as confounders in our data. It should be noted that other studies using these tests have shown a similar low proportion of variation explained. A final limitation is the small sample size for pesticide-specific analyses, limiting our power to detect significant results.

Despite these limitations, our study is the largest to date of neurological function among both subjects previously poisoned by organophosphate pesticides and appropriate referents. It has the additional advantage of being population based, with a strict definition of cases.

In conclusion, we did not find apparent symptomatic damage to the neurological function of men poisoned in the past by organophosphate pesticides, but we did find some evidence of injury to the peripheral nerves as reflected by decreased vibrotactile sensitivity. We also found some evidence of deficits in central nervous system function as reflected by worse performance on 2 of 10 neurobehavioral tests. Furthermore, performance on a number of neurobehavioral tests was significantly worse for those with more severe poisonings, with severity measured by either hospitalization or number of days taken off from work subsequent to poisoning. □

Acknowledgments

This study was conducted as a collaborative effort between the State of California and the National Institute for Occupational Safety and Health (NIOSH). Financial support was provided partly by the US Environmental Protection Agency.

Drs Joseph Arezzo, Ann Fidler, and Jerry Blondell offered helpful comments on the manuscript. Numerous NIOSH employees contributed to this study: Dr Ray Alderfer, Dr Geoffrey Calvert, Dr Tony Suruda, Karen Davis-King, Nina Baird, Steve Brightwell, Robert Dick, Marie Haring-Sweeney, Kathy Watkins, Chris Gersic, Jean Geiman, Bettie Walpole, Bill Ehling, Rose Watkins, and Patty Gudlewski. Aurelio and Rosa Marta de los Santos recruited subjects and translated. Laura Weiss (Cal EPA) helped collect data. Nada Elmore, Jean Wilhite, and Pat Koenig (Biotrax) performed nerve conduction tests.

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