

# Health Effects Associated With Sulfuryl Fluoride and Methyl Bromide Exposure Among Structural Fumigation Workers

## ABSTRACT

**Objectives.** This study assessed the health effects associated with occupational exposure to methyl bromide and sulfuryl fluoride among structural fumigation workers.

**Methods.** A cross-sectional study of 123 structural fumigation workers and 120 referents in south Florida was conducted. Nerve conduction, vibration, neurobehavioral, visual, olfactory, and renal function testing was included.

**Results.** The median lifetime duration of methyl bromide and sulfuryl fluoride exposure among workers was 1.20 years and 2.85 years, respectively. Sulfuryl fluoride exposure over the year preceding examination was associated with significantly reduced performance on the Pattern Memory Test and on olfactory testing. In addition, fumigation workers had significantly reduced performance on the Santa Ana Dexterity Test of the dominant hand and a nonsignificantly higher prevalence of carpal tunnel syndrome than did the referents.

**Conclusions.** Occupational sulfuryl fluoride exposures may be associated with subclinical effects on the central nervous system, including effects on olfactory and some cognitive functions. However, no widespread pattern of cognitive deficits was observed. The peripheral nerve effects were likely caused by ergonomic stresses experienced by the fumigation workers. (*Am J Public Health.* 1998; 88:1774-1780)

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Methyl bromide and sulfuryl fluoride are commonly used fumigants. Methyl bromide is widely used in Florida and California for agricultural pest control and, until recently, was also widely used in structural pest control. Because of concerns about stratospheric ozone depletion, the US Environmental Protection Agency has proposed a phaseout of methyl bromide production and use by the year 2001.<sup>1</sup> In the early 1990s, sulfuryl fluoride replaced methyl bromide as the fumigant most commonly used in structural termite control.

Methyl bromide is extremely toxic after acute, high-intensity exposure. Neurological manifestations from acute methyl bromide poisoning include ataxia, behavioral changes, seizures, and coma.<sup>2</sup> However, little is known about the effects of chronic, low-level exposure to methyl bromide. Case reports of workers chronically exposed to methyl bromide have described electroencephalogram abnormalities<sup>3</sup> and peripheral neuropathy,<sup>3,4</sup> and a cross-sectional study found that workers with low-level methyl bromide exposures had statistically significant deficits on the Wechsler Memory Scale and on 2-point discrimination at the index finger.<sup>5</sup>

Less is known about the toxicity of sulfuryl fluoride. Fatalities have been reported from acute poisoning.<sup>6,7</sup> In addition, rats exposed to high levels of sulfuryl fluoride experienced neurological, pulmonary, and renal toxicity.<sup>8</sup> A study of workers with low-level sulfuryl fluoride exposures found nonsignificantly reduced performance on all neurobehavioral tests compared with the referent group.<sup>5</sup>

To address the need for additional information on the toxicity of methyl bromide and sulfuryl fluoride, the National Institute for Occupational Safety and Health (NIOSH) and the University of Miami conducted a cross-sectional study in 1992 and 1993 of

123 structural fumigation workers in south Florida. Data were collected and analyzed to determine whether chronic, generally low-level exposure to these fumigants was associated with nervous system (central and peripheral), renal, or pulmonary effects. This is the largest known health study of workers exposed to these fumigants.

## Methods

This study compared health outcomes among workers employed at the time of the study as shooters (individuals who introduced the fumigant into a structure) and tent crew workers (individuals who raised and dismantled the tarps used to cover fumigated structures to prevent fumigant leakage) in the structural fumigation industry with health outcomes in an unexposed referent (comparison) group. Fumigant exposure in this industry is intermittent (generally less than 2 hours per day) and is considered to occur potentially

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when the fumigant is introduced into the building and when the tarps are dismantled.

The workers were employed at the time of the study at one of 40 fumigation companies located in the Miami and Tampa/St. Petersburg, Fla, metropolitan areas. These companies were chosen because they were performing many fumigation jobs and because they used predominantly one type of fumigant. To qualify for participation, workers from these companies had to report in a screening interview that they had been employed in the fumigation industry for at least the preceding 6 months; that they were currently engaged in fumigation activities at least 80% of the time; and that among the fumigation jobs they had ever participated in, the fumigant involved was either (1) sulfuric fluoride on 80% or more of the fumigation jobs or (2) methyl bromide on 50% or more of the fumigation jobs (because use of methyl bromide was declining rapidly at the time of our study, a lower proportion was used). All worker participants were male.

The referent group was recruited by the fumigation workers. Each worker was asked to identify a male friend or neighbor who was a similar age ( $\pm 5$  years), who had never worked as a pesticide applicator or in the fumigation industry, and who had never been poisoned by pesticides. All participants were paid \$150 as compensation for their time and effort. NIOSH Human Subjects Review Board and the University of Miami Institutional Review Board approved the study protocol. Informed consent was obtained from all participants.

Information on each study participant was collected through a comprehensive standardized questionnaire and a set of medical tests. To reduce observer bias, all test administrators were blinded to exposure status. Study instructions, questionnaires, and tests were administered in English or Spanish according to the participant's preference (with the exception of the vocabulary test, which was administered only in English). Lifetime occupational and medical history information was obtained through an interviewer-administered questionnaire. Detailed information on fumigation industry employment was collected for both the year preceding the worker's examination and the worker's entire duration of fumigation industry employment.<sup>9</sup>

### Tests of Neurological Function

Nerve conduction tests to detect peripheral neuropathy were administered by means of documented techniques.<sup>10</sup> Nerve conduction velocities and amplitude were measured on 2 nerves of the nondominant upper limb

(median and ulnar) and 2 nerves of the non-dominant lower limb (peroneal and sural). In addition, latencies were measured on the peroneal motor nerve. All tests were performed with surface electrodes. The surface temperature was maintained at 32°C to 34°C for the upper limb and at 30°C to 33.5°C for the lower limb. If necessary, limb temperature was raised and maintained with an electric heating pad.

Vibration testing consisted of measurement of vibrotactile thresholds in the non-dominant index finger and great toe with the Vibratron II device (Physitemp Instruments, Clifton, NJ) and a "trimmed 2-5 method of limits" protocol.<sup>11,12</sup> Five trials (3 descending and 2 ascending) were performed on each limb. The first trial and the trials with the highest and lowest measurements were discarded. The 2 remaining measurements were averaged and recorded.

Seven supervised, computer-administered neurobehavioral tests from the Neurobehavioral Evaluation System (NES), version 4.33, were conducted.<sup>13</sup> These tests required a reading level equivalent to an elementary school education. The 7 tests are described below:

1. *Hand-eye Coordination*. Measured the degree of error when using a joystick to trace wave patterns projected on the computer screen.

2. *Simple Reaction Time*. Measured the response time for pressing a key when provided a randomly timed visual stimulus.

3. *Continuous Performance Test*. Required the participant to press a key when a certain letter appeared amid a temporal sequence of letters. Response time and non-responses were analyzed.

4. *Symbol Digit Test*. Required rapid pairing of digits to symbols according to an exhibited matched pairing. Immediately following testing, the number of pairings that were memorized was also recorded.

5. *Pattern Memory*. Required selecting a previously seen pattern out of 3 similar patterns. The proportion of correctly identified patterns and the mean recall time were recorded.

6. *Serial Digit Learning*. Required memorizing a series of 8 digits. The number of trials required to memorize the 8 digits was recorded.

7. *Mood Scales*. Evaluated 5 different self-reported mood categories (anger, confusion, depression, fatigue, and tension/anxiety).

In addition, the NES vocabulary test was administered to participants taking the English version of the NES. For each of 25 words, the participant had to select the correct synonym from a list of 4 words.

The Santa Ana Dexterity Test, a non-computerized test of psychomotor function, required turning rows of successive pegs 180 degrees.<sup>14</sup> The total number of pegs turned in two 30-second trials per hand was recorded.

Postural sway testing, a computerized version of the Romberg test, was conducted with a fixed strain-gauge-type force platform (Advanced Mechanical Technologies, Newton, Mass).<sup>15</sup> Four 30-second tests were completed for each participant (standing on a hard surface with his eyes open then repeated with eyes closed, and standing on a soft foam pad with his eyes open then repeated with eyes closed). Ratios between the various measurements were also calculated, as previously described.<sup>16</sup>

Contrast sensitivity, a test of visual function, was assessed with the Pelli-Robson chart, which consists of 16 rows of 3 letters.<sup>17</sup> The rows decrease in contrast from top to bottom. Each eye was tested separately, and a separate chart (with a different arrangement of letters) was used for the left and right eyes. Contrast sensitivity was scored as the row with the faintest contrast in which 2 of the 3 letters were correctly identified. Color vision was assessed with the Farnsworth D-15 panel test.<sup>18</sup> This test consists of 15 movable caps, each of a different color. The participant was asked to line up the caps in sequential color order. Each eye was tested separately. The test was scored as abnormal if the arrangement of caps was consistent with 1 of 3 types of color vision defect. A retroilluminated Snellen letter chart was used to measure visual acuity.

Olfactory function was tested with the University of Pennsylvania Smell Identification Test (UPSIT) (Sensonics, Inc, Haddonfield, NJ).<sup>19</sup> This standardized, self-administered smell test involves 40 microencapsulated odorants. The participant was asked to identify the odor of each odorant from a list of 4 choices. The 4 choices were read to illiterate participants by one of the study staff. The number of correctly identified odors was recorded. Because 28 participants (14 workers and 14 referents) did not provide a response to all 40 odors, all tests were also scored as the proportion of odors responded to that were correctly identified.

### Other Examinations

Spot urine samples were collected and analyzed for total protein, albumin, and adenosine deaminase binding protein. Participants were evaluated for chronic bronchitis with questions recommended by the American Thoracic Society.<sup>20</sup> Finally, a physician completed a physical examination of the

neurological system to detect gross abnormalities of the motor, sensory, and cerebellar systems. The findings from this examination were used to screen for neurological problems unrelated to fumigant exposure (e.g., trauma or stroke).

#### Data Analysis

The Student *t* test was used in the analysis of continuous demographic characteristics. Chi-square statistics were used to compare categorical demographic characteristics and outcomes. (The Fisher exact test was used when any of the expected table frequencies were less than 5.)

Multiple linear regression analyses were performed. Confounders were identified a priori by a review of the literature. Regression models for the nerve conduction tests included age, race, body mass index, and limb surface temperature. Regression models for vibration testing included age, race, and height. Models for the computerized neurobehavioral tests included age, years of education, and the language in which the test was taken. Regression models for the Santa Ana Dexterity Test included age and race. Models for the postural sway data included age, race, number of alcoholic drinks consumed per week, height, and weight. Models for contrast sensitivity included age, visual acuity, and years of education. Regression models for UPSIT included smoking status (current smoker, former smoker, never smoker), years of education, and race. Finally, models for tests of renal function included age, years of education, and race. Findings were similar when premorbid intellectual ability was controlled by using the NES vocabulary test score instead of years of education. However, because the NES vocabulary test score was not available for 17 participants, results are provided only from those models containing years of education.

Several measures of exposure were used in the analyses. Employment as a structural fumigator was used as a dichotomous exposure variable (defined as being a fumigation worker or not). Additionally, separate measures of exposure for each fumigant were created and are described in detail elsewhere.<sup>9</sup> Briefly, the lifetime duration of methyl bromide exposure for each worker was calculated as the product of his self-reported years of fumigation industry employment and his self-reported lifetime proportion of fumigation jobs that used methyl bromide. Methyl bromide-exposed workers were stratified into 2 groups based on the median years of methyl bromide exposure: high methyl bromide years of

exposure and low methyl bromide years of exposure. The lifetime duration of sulfuryl fluoride exposure was calculated in a similar way (sulfuryl fluoride years).

To assess the effect of exposures during the year preceding the worker's examination, workers were defined as having either high sulfuryl fluoride exposure (if the worker used sulfuryl fluoride on more than 50% of jobs during the previous year) or high methyl bromide exposure (if the worker used methyl bromide on 50% or more of jobs during the previous year). These exposure groups were compared with the referent group. Four workers were excluded from the preceding year analyses because they had worked less than 6 months in structural fumigation during that year.

For many of the analyses, some participants were excluded a priori. Nine participants (5 workers, 4 referents) were excluded from analysis of the computerized neurobehavioral data, most ( $n = 7$ ) because of insufficient reading ability. A few participants were excluded from specific tests for reasons such as malfunction of equipment or report of a physician-diagnosed health problem that was unrelated to fumigant exposure but that could affect test performance.

SAS procedures (SAS Institute Inc, Cary, NC) were used for all analyses. A *P* value of .05 or less was considered statistically significant.

## Results

Of the 196 workers employed at the 40 structural fumigation companies chosen for study participation, 49 (25%) were determined by the screening interview to be ineligible for the study. A total of 123 of 147 (84%) of the eligible structural fumigation workers and 120 referents participated. Descriptive information on the study participants is provided in Table 1. The fumigation workers and referents were generally similar, but the referents had significantly longer schooling. Among fumigation workers, the median duration of employment in structural fumigation was 4.0 years. The median lifetime duration of methyl bromide and sulfuryl fluoride exposure was 1.20 years and 2.85 years, respectively.

On average, fumigation workers performed worse on all tests of median nerve function than did the referents, but only 1 of these tests was statistically significant

**TABLE 1—Characteristics of the Study Participants Fumigation Workers: South Florida, 1992–1993**

|   | Fumigation workers<br>(n = 123) | Referents<br>(n = 120) |
|---|---------------------------------|------------------------|
| Mean age, y (range)   | 33 (19–68)                      | 31 (18–58)             |
| Race/ethnicity, no. (%)                                     |                                 |                        |
| White   | 52 (42)                         | 54 (45)                |
| Black   | 44 (36)                         | 42 (35)                |
| Hispanic  | 27 (22)                         | 24 (20)                |
| Mean years of education* (range)                            | 11.5 (0–19)                     | 12.3 (0–17)            |
| Spanish was preferred language, % <sup>a</sup>              | 8.9                             | 5.0                    |
| Mean body mass index (range) <sup>b</sup>                   | 26 (18–41)                      | 26 (18–49)             |
| Mean height, in (range)                                     | 70 (57–76)                      | 70 (57–76)             |
| Smoking status, no. (%)                                     |                                 |                        |
| Current   | 56 (46)                         | 47 (39)                |
| Former  | 13 (11)                         | 10 (8)                 |
| Never   | 54 (44)                         | 63 (53)                |
| Alcohol status, no. (%)                                     |                                 |                        |
| Current   | 92 (75)                         | 84 (70)                |
| Former  | 18 (15)                         | 22 (18)                |
| Never   | 13 (10)                         | 14 (12)                |
| Mean no. of alcoholic drinks consumed per wk (range)        | 13 (0–168)                      | 10 (0–84)              |
| Median years of employment in structural fumigation (range) | 4.00 (0.5–32)                   | 0                      |
| Median methyl bromide years (range) <sup>c</sup>            | 1.20 (0–22.1)                   | 0                      |
| Median sulfuryl fluoride years (range) <sup>d</sup>         | 2.85 (0.11–20.5)                | 0                      |

<sup>a</sup>Language chosen for the computerized neurobehavioral test; 9 participants did not take this test.

<sup>b</sup>Weight in kilograms divided by height in meters squared.

<sup>c</sup>The product of self-reported years of structural fumigation employment and lifetime proportion of fumigation jobs that used methyl bromide.

<sup>d</sup>The product of self-reported years of structural fumigation employment and lifetime proportion of fumigation jobs that used sulfuryl fluoride.

\*Significant difference at the *P* = .05 level.

**TABLE 2—Multiple Linear Regression Results Comparing Nerve Conduction Velocity (NCV), Amplitudes, and Vibration Threshold Among Structural Fumigation Workers vs Unexposed Referents: South Florida, 1992–1993**

| Test  | Fumigation Worker |                            | Referent |                            | P Value for Adjusted Analysis | Direction of Worker Performance <sup>b</sup> | Worse Performance With Increasing Duration of Fumigant Exposure <sup>c</sup> |
|---|-------------------|----------------------------|----------|----------------------------|-------------------------------|--|--|
|   | n                 | Adjusted Mean <sup>a</sup> | n        | Adjusted Mean <sup>a</sup> |                               |  |  |
| <b>Upper limb<sup>d</sup></b>                     |                   |                            |          |                            |                               |  |  |
| NCV (distal): median sensory, m/s                 | 121               | 52.9                       | 120      | 54.3                       | .16                           | –  |  |
| NCV (forearm): median sensory, m/s                | 121               | 60.4                       | 120      | 61.1                       | .41                           | –  |  |
| NCV (forearm): median motor, m/s                  | 121               | 54.6                       | 120      | 55.9                       | .02                           | –  | SF   |
| NCV (distal): ulnar sensory, m/s                  | 122               | 53.2                       | 120      | 51.8                       | .06                           | +  |  |
| Amplitude: median sensory, $\mu$ V                | 121               | 27.0                       | 120      | 29.2                       | .12                           | –  | MB, SF   |
| Amplitude: median motor, mV                       | 120               | 10.6                       | 119      | 11.1                       | .30                           | –  | SF   |
| Amplitude: ulnar sensory, $\mu$ V                 | 122               | 23.8                       | 120      | 23.9                       | .97                           | –  |  |
| Vibration threshold: finger, $\mu$ m peak to peak | 121               | 1.07                       | 120      | 1.10                       | .81                           | +  |  |
| <b>Lower limb<sup>e</sup></b>                     |                   |                            |          |                            |                               |  |  |
| NCV: peroneal motor, m/s                          | 120               | 46.3                       | 115      | 46.6                       | .51                           | –  |  |
| NCV: sural sensory, m/s                           | 119               | 46.0                       | 113      | 44.9                       | .07                           | +  |  |
| Amplitude: peroneal motor, mV                     | 118               | 6.81                       | 115      | 6.78                       | .95                           | +  |  |
| Amplitude: sural sensory, $\mu$ V                 | 118               | 17.3                       | 113      | 15.6                       | .06                           | +  |  |
| f latency: peroneal motor, ms                     | 119               | 49.9                       | 115      | 50.1                       | .64                           | +  |  |
| Vibration threshold: toe, $\mu$ m peak to peak    | 120               | 3.90                       | 114      | 4.28                       | .55                           | +  |  |

<sup>a</sup>Models for nerve conduction tests controlled for age, race, body mass index, and temperature of the limb. Models for vibration threshold controlled for age, race, and height.

<sup>b</sup>+ = Performance of workers was better vs referents based on adjusted means. – = Performance of workers was worse vs referents based on adjusted means.

<sup>c</sup>SF = based on adjusted analyses, as sulfuryl fluoride exposure increased (referent, low sulfuryl fluoride years of exposure, high sulfuryl fluoride years of exposure), monotonically decreasing performance was observed.

MB = based on adjusted analyses, as methyl bromide exposure increased (referent, low methyl bromide years of exposure, high methyl bromide years of exposure), monotonically decreasing performance was observed.

<sup>d</sup>The “distal” measurement is the NCV from the wrist to the interdigital cleft, and the forearm measurement of the median nerve is the NCV from the elbow to the wrist.

<sup>e</sup>NCV of the peroneal nerve was measured from the knees to the ankle, and the sural nerve velocity was measured from the mid-calf to the ankle. The fastest of at least 10 f latency responses was recorded.

(slower nerve conduction velocity of the median motor nerve in the forearm,  $P = .02$ ) (Tables 2 and 3). In addition, 8 workers and 4 referents had nerve conduction velocity findings consistent with carpal tunnel syndrome (the ratio of conduction velocity of the distal ulnar nerve to conduction velocity of the distal median nerve exceeded 1.25, and conduction velocity of the distal median nerve was less than 50 m/sec). All 8 of the fumigation workers with carpal tunnel syndrome were tent crew workers at the time of examination, and all 8 denied ever being a shooter.

Pattern Memory was the only computer-administered neurobehavioral test on which workers had significantly worse performance than did referents. Although this finding was especially evident among workers with high sulfuryl fluoride exposure during the year preceding examination (Table 4), a trend of worse performance with increasing lifetime duration of sulfuryl fluoride exposure was also observed (Table 5). Fumigation workers also had reduced performance on the Santa Ana Dexterity Test when the preferred hand was tested (Table 5), and more specifically among workers with high sulfuryl fluoride exposure in the year preceding examination

(Table 4). This finding may more likely be associated with the ergonomic stresses (e.g., repetition, force, and awkward joint position) among tent crew workers over the year preceding examination than with sulfuryl fluoride exposure. This is because preferred-hand Santa Ana performance was lower among these “currently” employed tent crew workers than among fumigation workers not currently employed as tent crew workers ( $P = .06$ ), whereas no significant difference was found among these 2 groups of fumigation workers in the proportion of jobs that used sulfuryl fluoride in the preceding year ( $P = .31$ ).

Deficits on UPSIT performance were particularly evident among workers with high sulfuryl fluoride exposure over the preceding year (Table 4) (adjusted mean UPSIT score: workers with high sulfuryl fluoride exposure = 33.1, referents = 34.4,  $P = .03$ ), suggesting that sulfuryl fluoride exposure may be associated with adverse effects on olfactory function. No significant differences were found between fumigation workers and referents for chronic bronchitis, for any of the urinary protein concentrations, or for performance on the color vision test or the postural sway tests (data not shown).

## Discussion

This study suggests that employment as a structural fumigation worker is associated with some adverse effects on the central and peripheral nervous systems. With respect to the peripheral nervous system, performance was reduced on the Santa Ana Dexterity Test and on all tests of median nerve function, and the prevalence of carpal tunnel syndrome was higher among workers compared with referents. The median nerve effects experienced by workers are most likely caused by workplace ergonomic factors such as repetitive, forceful squeezing of heavy-duty spring clamps used to fasten tarps that cover a fumigated structure and other repetitive tasks involved in raising and dismantling tarps. The role of these ergonomic factors is supported by the decrements observed in preferred-hand Santa Ana Dexterity Test performance among tent crew workers. Those in occupations that place them at risk for repetitive trauma disorders have reduced performance on Santa Ana testing.<sup>21</sup> In the absence of significant findings involving any of the other upper- or lower-extremity peripheral nerves, it is unlikely that fumigant exposure is responsible for the median nerve

**TABLE 3—Multiple Linear Regression Results Comparing Nerve Conduction Velocity (NCV), Amplitudes, and Vibration Threshold Among Structural Fumigation Workers With High Methyl Bromide Exposure or High Sulfuryl Fluoride Exposure During the Year Preceding Examination vs Unexposed Referents<sup>a</sup>: South Florida, 1992–1993**

| Test                          | Workers With High Methyl Bromide Exposure Over the Year Preceding Examination (n=28)                 |     | Workers With High Sulfuryl Fluoride Exposure Over the Year Preceding Examination (n=91)                 |     |
|-------------------------------|--|-----|---|-----|
|                               | Direction of Workers With High Methyl Bromide Exposure Compared With the Referent Group <sup>b</sup> | P   | Direction of Workers With High Sulfuryl Fluoride Exposure Compared With the Referent Group <sup>b</sup> | P   |
| Upper limb                    |  |     |   |     |
| NCV (distal): median sensory  | –  | .78 | –   | .10 |
| NCV (forearm): median sensory | –  | .20 | –   | .75 |
| NCV (forearm): median motor   | –  | .40 | –   | .02 |
| NCV (distal): ulnar sensory   | +  | .35 | +   | .08 |
| Amplitude: median sensory     | –  | .06 | –   | .34 |
| Amplitude: median motor       | +  | .59 | –   | .09 |
| Amplitude: ulnar sensory      | –  | .21 | +   | .68 |
| Vibration threshold: finger   | +  | .84 | +   | .85 |
| Lower limb                    |  |     |   |     |
| NCV: peroneal motor           | –  | .40 | –   | .77 |
| NCV: sural sensory            | +  | .07 | +   | .21 |
| Amplitude: peroneal motor     | +  | .94 | +   | .88 |
| Amplitude: sural sensory      | +  | .03 | +   | .20 |
| f latency: peroneal motor     | +  | .42 | +   | .86 |
| Vibration threshold: toe      | +  | .56 | +   | .65 |

<sup>a</sup>Workers with high methyl bromide exposure and high sulfuryl fluoride exposure are defined as workers who used each substance on 50% or more of jobs. Models for nerve conduction tests controlled for age, race, body mass index, and temperature of the limb. Models for vibration threshold controlled for age, race, and height.

<sup>b</sup>+ = Performance of fumigation workers was better vs referents based on adjusted means. – = Performance of fumigation workers was worse vs referents based on adjusted means.

findings in our study. Based on the pattern of neurotoxicity produced by high methyl bromide exposure, initial involvement of the nerves in the lower extremity is expected.<sup>22,23</sup> Although one median nerve outcome (nerve conduction velocity of the median motor nerve in the forearm) was associated with exposure to sulfuryl fluoride, this may be an isolated chance finding caused by the large number of comparisons that were performed.

We found limited data to suggest fumigant exposure effects on neurobehavioral function. However, we did find that workers with high sulfuryl fluoride exposure in the previous year had significantly reduced performance on the Pattern Memory Test (Table 4). Because the Pattern Memory Test is a test of cognitive and visual memory,<sup>24</sup> these findings suggest that sulfuryl fluoride exposure may be associated with deficits in this area. Although none of the other memory tests in this study (e.g., Symbol Digit Recall score and Serial Digit Learning score) were associated with sulfuryl fluoride exposure, this may not be unexpected. Sulfuryl fluoride may be altering information-processing abilities that are required only in the Pattern Memory Test. Also, the pattern memory findings may have arisen by chance.

One other study examined neurobehavioral effects among workers with chronic low-level fumigant exposure.<sup>5</sup> Sulfuryl fluoride-exposed workers had nonsignificantly

reduced performance on all cognitive tests compared with the referent group. Methyl bromide exposure was associated with significantly worse performance on the Logical Memory test of the Wechsler Memory Scale (this test measures ability to recall details of a story read aloud). These workers had higher median years of employment in fumigation occupations and may have used methyl bromide on a higher proportion of fumigation jobs compared with the workers we studied. However, this study had several limitations (e.g., significant schooling differences existed between methyl bromide-exposed workers and referents, and the Wechsler Memory Scale was administered only in English even though Mexican Americans constituted a higher proportion of methyl bromide-exposed workers compared with referents [38% vs 7%, respectively]).<sup>5</sup>

Our study found that sulfuryl fluoride exposure may be associated with effects on olfactory function, an outcome not previously assessed in human studies of sulfuryl fluoride exposure. One animal study found that high sulfuryl fluoride exposure is associated with inflammation of nasal tissues<sup>25</sup>; however, effects on olfactory function or olfactory mucosa among animals have not been reported. Further study is needed to determine whether deficits in olfactory function are present in other sulfuryl fluoride-exposed populations and whether these deficits repre-

sent interference of the odor/receptor interaction or a cognitive problem with odor identity. Although small amounts of chloropicrin, an irritant, are used as a warning agent during sulfuryl fluoride and methyl bromide fumigations, chloropicrin is not likely to be responsible for our olfactory findings, because differences in effect from the 2 fumigants should not have been observed.

Note that the intensity of fumigant exposure among structural fumigation workers is low, based on personal airborne sampling conducted by NIOSH in 1991. Among structural fumigation workers, all personal airborne sampling results for sulfuryl fluoride and most for methyl bromide were below the Occupational Safety and Health Administration permissible exposure limits in effect at the time of sampling (20 mg/m<sup>3</sup> time-weighted 8-hour average). Furthermore, more than two thirds of the measurements were below the limit of detection (sulfuryl fluoride = 0.007 mg/sample; methyl bromide = 0.01 mg/sample). However, because the NIOSH-recommended analytic method for measuring methyl bromide may underestimate its concentration,<sup>26</sup> we predict that some fumigation workers may have had periodic short-term exposures to methyl bromide exceeding 80 mg/m<sup>3</sup> (the current permissible exposure limit<sup>27</sup>). No important work process changes have occurred in this industry over the last several decades, suggesting that fumigant exposure has not changed over the

**TABLE 4—Multiple Linear Regression Results Comparing Performance on Neurobehavioral Tests, the UPSIT, and the Contrast Sensitivity Test Among Structural Fumigation Workers With High Methyl Bromide Exposure or High Sulfuryl Fluoride Exposure During the Year Preceding Examination vs Unexposed Referents<sup>a</sup>: South Florida, 1992–1993**

| Test                                       | Workers With High Methyl Bromide Exposure Over the Year Preceding Examination (n = 28)               |     | Workers With High Sulfuryl Fluoride Exposure Over the Year Preceding Examination (n = 91)               |     |
|--|--|-----|---|-----|
|  | Direction of Workers With High Methyl Bromide Exposure Compared With the Referent Group <sup>b</sup> | P   | Direction of Workers with High Sulfuryl Fluoride Exposure Compared With the Referent Group <sup>b</sup> | P   |
| Hand-Eye Coordination                      | +  | .70 | +   | .73 |
| Simple Reaction Time                       | –  | .37 | +   | .48 |
| Continuous Performance Test: response time | +  | .62 | –   | .93 |
| Continuous Performance Test: NR            | +  | .70 | +   | .11 |
| Symbol Digit                               | –  | .83 | –   | .89 |
| Symbol Digit Recall score                  | –  | .51 | +   | .91 |
| Pattern Memory                             | +  | .54 | –   | .05 |
| Pattern Memory recall time                 | –  | .45 | –   | .17 |
| Serial Digit Learning score                | +  | .27 | +   | .70 |
| Mood Scale Score: anger                    | +  | .72 | –   | .47 |
| Mood Scale Score: confusion                | +  | .13 | –   | .73 |
| Mood Scale Score: depression               | +  | .62 | –   | .57 |
| Mood Scale Score: fatigue                  | +  | .80 | –   | .75 |
| Mood Scale Score: tension                  | +  | .86 | –   | .74 |
| Santa Ana: preferred hand                  | –  | .22 | –   | .03 |
| Santa Ana: nonpreferred hand               | –  | .71 | –   | .58 |
| UPSIT (no. correct/40)                     | +  | .21 | –   | .03 |
| UPSIT, %                                   | +  | .67 | –   | .05 |
| Contrast sensitivity: right eye            | –  | .67 | +   | .86 |
| Contrast sensitivity: left eye             | +  | .95 | +   | .64 |

Note. UPSIT = University of Pennsylvania Smell Identification Test; NR = nonresponses.

<sup>a</sup>Workers with high methyl bromide exposure and high sulfuryl fluoride exposure are defined as workers who used each substance on 50% or more of jobs. Models for the computerized neurobehavioral tests controlled for age, years of education, and test language (English or Spanish). Models for the Santa Ana Dexterity Tests controlled for age and race. Models for UPSIT controlled for smoking status (current smoker, former smoker, never smoker), years of education, and race. Models for contrast sensitivity controlled for age, acuity of the examined eye, and years of education.

<sup>b</sup>+ = Performance of fumigation workers was better vs referents based on adjusted means. – = Performance of fumigation workers was worse vs referents based on adjusted means.

last several years. It is unlikely that our findings are limited by inaccurate exposure estimates provided by the workers. The exposure estimates used in this study had adequate agreement with exposure estimates obtained from company records.<sup>9</sup>

Many of the fumigation workers (63%) and referents (41%) were also exposed to other pesticides at work or home. These pesticides included chlorpyrifos, organophosphates, carbamates, pyrethrins, and organochlorines. We found that the pattern memory test and olfactory tests were not significantly associated with any of these classes of pesticides. In addition, chloropicrin is not known to produce neurotoxicity. This information suggests that none of these pesticide classes or chloropicrin is responsible for the findings observed in this study.

Participation bias is unlikely to be responsible for our findings. Of 24 workers who declined to participate, 18 (75%) agreed to be interviewed by telephone. These individuals were asked questions similar to those from the full study, including questions on age, race, years employed in the fumigation industry, and current job title. No significant

differences were found between the examined and refusant workers for these variables (results not shown).

Other potential limitations may be present. Using friends and neighbors as controls may bias findings toward the null or in the opposite direction.<sup>28</sup> There are also limitations due to the cross-sectional design (e.g., temporal sequence of cause and effect, and inclusion of only workers currently employed in the fumigation industry). Finally, all but 11 fumigation workers were exposed to both methyl bromide and sulfuryl fluoride (the 11 were exposed to sulfuryl fluoride only). These concomitant exposures may have limited our ability to distinguish between methyl bromide and sulfuryl fluoride effects. Despite these limitations, this is the largest known study examining neurological function among workers exposed to these fumigants.

In conclusion, this study found some health effects associated with employment in the structural fumigation industry. The peripheral nerve effects were most likely associated with adverse ergonomic factors experienced by tent crew workers. In addition, this study found that sulfuryl fluoride

exposure may be associated with adverse effects on olfactory function and some cognitive functions. Few health effects were associated with methyl bromide exposure, possibly because this study had limited power to assess this exposure. □

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**TABLE 5—Multiple Linear Regression Results Comparing Performance on Neurobehavioral Tests, the UPSIT and the Contrast Sensitivity Test Among Structural Fumigation Workers vs Unexposed Referents: South Florida, 1992–1993**

| Test   | Fumigation Worker |                            | Referent |                            | P for Adjusted Analysis | Direction of Worker Performance <sup>b</sup> | Worse Performance With Increasing Duration of Fumigant Exposure <sup>c</sup> |
|--|-------------------|----------------------------|----------|----------------------------|-------------------------|--|--|
|  | n                 | Adjusted Mean <sup>a</sup> | n        | Adjusted Mean <sup>a</sup> |                         |  |  |
| Hand-Eye Coordination, rmse                    | 118               | 2.21                       | 116      | 2.22                       | .76                     | +  |  |
| Simple Reaction Time, ms                       | 118               | 265.4                      | 116      | 265.3                      | .99                     | –  |  |
| Continuous Performance Test: response time, ms | 118               | 399.3                      | 116      | 397.0                      | .66                     | –  | MB   |
| Continuous Performance Test: NR                | 118               | 0.47                       | 116      | 0.73                       | .19                     | +  |  |
| Symbol Digit, s/digit                          | 118               | 2.26                       | 116      | 2.24                       | .82                     | –  |  |
| Symbol Digit Recall score                      | 118               | 4.67                       | 116      | 4.75                       | .81                     | –  |  |
| Pattern Memory, %                              | 118               | 84.9                       | 116      | 87.3                       | .12                     | –  | SF   |
| Pattern Memory recall time, s                  | 118               | 6.26                       | 116      | 5.93                       | .15                     | –  | MB, SF   |
| Serial Digit Learning score                    | 118               | 4.61                       | 116      | 5.09                       | .40                     | +  |  |
| Mood Scale Score: anger                        | 118               | 1.88                       | 116      | 1.83                       | .58                     | –  | SF   |
| Mood Scale Score: confusion                    | 118               | 2.27                       | 116      | 2.26                       | .92                     | –  |  |
| Mood Scale Score: depression                   | 118               | 1.89                       | 116      | 1.83                       | .56                     | –  |  |
| Mood Scale Score: fatigue                      | 118               | 2.63                       | 116      | 2.60                       | .82                     | –  |  |
| Mood Scale Score: tension                      | 118               | 2.40                       | 116      | 2.35                       | .67                     | –  |  |
| Santa Ana: preferred hand                      | 121               | 39.9                       | 120      | 41.5                       | .02                     | –  | SF   |
| Santa Ana: nonpreferred hand                   | 121               | 36.9                       | 120      | 37.4                       | .50                     | –  | SF   |
| UPSIT (no. correct/40)                         | 109               | 33.6                       | 106      | 34.5                       | .11                     | –  | SF   |
| UPSIT, %                                       | 123               | 82.8                       | 120      | 85.1                       | .10                     | –  | SF   |
| Contrast sensitivity: right eye                | 121               | 12.2                       | 120      | 12.2                       | .83                     | +  |  |
| Contrast sensitivity: left eye                 | 122               | 12.2                       | 119      | 12.1                       | .69                     | +  |  |

Note. UPSIT = University of Pennsylvania Smell Identification Test; rmse = root mean square error; NR = nonresponses.

<sup>a</sup>Models for the computerized neurobehavioral tests controlled for age, years of education, and test language (English or Spanish). Models for the Santa Ana Dexterity Tests controlled for age and race. Models for UPSIT controlled for smoking status (current smoker, former smoker, never smoker), years of education, and race. Models for contrast sensitivity controlled for age, acuity of the examined eye, and years of education.

<sup>b</sup>+ = Performance of workers was better vs referents based on adjusted means. – = Performance of workers was worse vs referents based on adjusted means.

<sup>c</sup>SF = based on adjusted analyses, as sulfuryl fluoride exposure increased (referent, low sulfuryl fluoride years of exposure, high sulfuryl fluoride years of exposure), monotonically decreasing performance was observed.

MB = based on adjusted analyses, as methyl bromide exposure increased (referent, low methyl bromide years of exposure, high methyl bromide years of exposure), monotonically decreasing performance was observed.

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