

# Chemical Sensitivity Attributed to Pesticide Exposure Versus Remodeling

CLAUDIA S. MILLER  
HOWARD C. MITZEL  
Department of Family Practice  
Environmental and Occupational Medicine  
The University of Texas Health Science  
Center at San Antonio  
San Antonio, Texas

**ABSTRACT.** One hundred twelve individuals who reported onset of multiple chemical sensitivity following well-documented exposure to either (1) a cholinesterase-inhibiting organophosphate or carbamate pesticide or (2) remodeling of a building completed mail-out/mail-back questionnaires concerning their exposure, symptoms, sensitivity to ingestants and inhalants, utilization of health-care resources, and impact of their illness on lifestyle. It was hypothesized that if multiple chemical sensitivity resulted from neurotoxic exposure, then organophosphate-exposed respondents should report greater severity of illness resulting from the relatively greater neurotoxicity of this class of chemicals. Pesticide-exposed and remodeling-exposed multiple chemical sensitivity groups reported similar patterns of symptoms and identified similar inhalants and ingestants as triggers for their symptoms; these results suggested a common mechanism (biological and/or psychological) for their conditions. The pesticide-exposed group, however, reported significantly greater symptom severity than did the remodeling-exposed group, especially for neuromuscular, affective, airway, gastrointestinal, and cardiac symptoms. These findings provide evidence for (1) a possible biological basis for multiple chemical sensitivity and (2) a distinct pathophysiology or final common pathway for the condition that, while as yet undefined, appears to be shared by these two groups. Although subjective multisystem health complaints characterize both multiple chemical sensitivity and somatoform disorder, features of this multiple chemical sensitivity sample were inconsistent with somatoform disorder, i.e., onset after 30 y of age in 83%, the predominance of severe cognitive symptoms, and attributions of environmental causation. No group differences were found with respect to lifestyle impact. Eighty-one percent of respondents said they had been working full-time at the time they were exposed, yet at the time of the survey (on average, 7.7 y post exposure) only 12.5% were working full-time. The majority said they had quit their jobs, changed jobs, or changed careers because of their illness. Approximately 40% reported that they had consulted 10 or more medical practitioners. The persistent, disabling neuropsychological symptoms reported by these multiple chemical sensitivity groups are strikingly similar to those reported among individuals exposed occupationally to pesticides and solvents. These parallel findings suggest that the types and levels of exposures associated with extermination and remodeling may not be inconsequential, at least for a subset of the population. Further studies from a variety of perspectives, including human challenge studies and the development of animal models, are needed to define the pathophysiological and psychological mechanisms underlying this costly condition.

MULTIPLE CHEMICAL SENSITIVITY (MCS), the subject of an escalating debate among physicians and environmental specialists, is being diagnosed in a growing number of patients, including industrial workers; occupants of sick buildings; individuals who live near Superfund hazardous waste sites; Gulf War veterans; and others exposed to pesticides, solvents, combustion products, drugs, and consumer products. Some practitioners believe that MCS is a somatoform disorder or, at a minimum, that patients misattribute symptoms from a variety of medical conditions to environmental exposures.<sup>1-4</sup> Others hypothesize that environmental exposures may sensitize certain—perhaps more susceptible—individuals whose symptoms are then perpetuated by a variety of chemically unrelated inhalants and ingestants.<sup>5-7</sup>

Many MCS patients report lifelong symptoms that appear to have no known initial cause. Other patients describe an abrupt onset of illness that follows an identifiable exposure event. In part because of the diverse symptoms associated with the illness and lack of objective markers, there is no agreed upon case definition for MCS. Symptoms ascribed to MCS overlap asthma, chronic fatigue syndrome, fibromyalgia, depression, and somatoform disorders. Another problem is the enormous range of chemicals reported to induce the condition and to subsequently trigger symptoms (solvents, combustion products, pesticides, drugs, etc.).

We chose to compare features of MCS reported by two groups with chemically distinct but well-documented exposures preceding onset of self-reported MCS: one group was initially exposed to an organophosphate or carbamate cholinesterase-inhibiting pesticide (OP), and the other was exposed to the remodeling of a building (RE). Compared with MCS patients with lifelong symptoms, these individuals reported that they became ill at a discrete point in time, and most individuals were working full time when exposure occurred. The authors felt that these two subgroups of MCS patients would be better able to distinguish which symptoms were or were not related to the condition. In addition, OP and RE exposure groups were chosen because (1) many MCS patients have reported that one of the exposures described initiated their condition; (2) such exposures are likely to be readily identifiable; (3) spraying of pesticides and remodeling of buildings occur at discrete times, unlike protracted exposures of industrial workers to solvents; and (4) group differences, if present, should result from differences in potency of the chemical compounds (putatively) inducing the illness.

Most MCS patients report symptoms, triggered by many foods and chemicals, that affect more than one organ system. This nonspecificity has contributed to the biological or physiological implausibility of this illness. Somatization disorder has many features in common with MCS. *The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* diagnostic criteria for somatization disorder include reports of pain at multiple locations, gastrointestinal symptoms, sexual dysfunction, and neurological symptoms; the onset of these symp-

toms occurs in individuals who are under the age of 30 y.<sup>8</sup> Other criteria for somatization disorder include food intolerances, depression, anxiety, and panic attacks.<sup>9</sup> Beliefs that invoke external (e.g., environmental) causes for symptoms are not a reported feature of somatoform disorders, a point that has not been addressed by practitioners who categorize MCS as such. If it is assumed that MCS is entirely a psychologically induced disease state, then MCS groups who attribute their condition to either organophosphates or remodeling should report similar illness severity. In other words, explanations of MCS as a somatoform disorder would not predict differences between MCS patients, based on the inducing exposure, because the nature of the exposure is assumed to be unrelated to the illness.

This stands in contrast to an alternative hypothesis for MCS that suggests that different chemical compounds biologically induce essentially the same illness, although differences in illness severity might exist. Under this schema, individuals who report MCS from organophosphates would be expected to report more severe symptoms on average than remodeling-exposed individuals. This prediction follows from the relatively greater potency of organophosphates and their highly specific effect on the nervous system.

A possible exception might be airway and eye irritation. In sick building syndrome episodes, mucous membrane irritation and airway symptoms occur commonly. Such symptoms, therefore, might be expected to be more severe among MCS respondents exposed to remodeling of a building than among respondents exposed to pesticides. Also, because more women than men report MCS,<sup>2-4,7</sup> women are expected to report higher symptom severity.

Other objectives of this study were to compare the two groups' self-reported responses to inhalants and ingestants; their use of medical resources; number and types of providers visited; and impact on careers, family, and lifestyle. Although mail surveys are expedient and economical, interpretative caution is advised because this study utilized (for purposes of comparison) subgroups of the MCS population, rather than a random sample of MCS patients.

## Materials and Method

Individuals with self-reported MCS were recruited via announcements in MCS patient newsletters to ensure a sample of strictly self-identified MCS respondents. Respondents were sent a mail-out/mail-back questionnaire that covered the exposure event, a brief medical history, and physical and cognitive symptoms that occurred subsequent to their exposures. No payment was offered to subjects. Two hundred three questionnaires of 379 mailed were returned (54%). To be included in the OP group, respondents had to report having developed MCS as a consequence of a pesticide exposure, had to specify the month and year of exposure, and had to provide the name(s) of the organophosphate or carbamate pesticide(s) to which they had been exposed. Inclusion in the RE group was assured only if respon-

**Table 1.—General Characteristics of the Multiple Chemical Sensitivity Study Population**

Variable	Group		
	Organophosphate (n = 37)	Remodeling (n = 75)	Total (n = 112)
Age (y)			
Range	25–63	25–69	25–69
$\bar{X}$	47.7	47.7	47.7
SD	9.5	9.0	9.1
Gender			
Female	29 (78.4%)	60 (80.0%)	89 (79.5%)
Male	8 (21.6%)	15 (20.0%)	23 (20.5%)
Education (y)			
Range	12–20	8–24	8–24
$\bar{X}$	15.3	16.2	15.9
SD	2.9	3.1	3.1
Time elapsed since exposure (y)			
Range	2–18	1–31	1–31
$\bar{X}$	7.2	7.9	7.7
SD	4.3	6.3	5.7
Age at illness onset (y)			
Range	21–61	11–57	11–61
$\bar{X}$	40.5	39.8	40.0
SD	10.6	9.0	9.5

dents reported that they developed MCS as a consequence of exposure to remodeling of a building and if they specified the year and month in which the exposure occurred or began. Those who attributed their MCS to both remodeling and organophosphate exposure, or who did not specify a cause, were not included because our purpose was to compare two groups of MCS patients that identified distinctly different initiating events.

Questionnaires contained (a) items that pertained to the circumstances of the exposure; (b) checklists for 98 common inhalants and 46 common ingestants; (c) severity ratings for 114 symptoms; and (d) questions concerning disability and quality of life issues, number and types of physicians consulted, diagnostic and treatment modalities used, and family history. Treatment modalities used and family history will be reported later. Respondents were directed to check off from lists of inhalants (e.g., diesel exhaust, cigarette smoke, perfume) and ingestants (e.g., chlorinated water, MSG, and foods) any items known to trigger symptoms. Endorsements for each individual and for each item were tallied for both groups. Item frequencies were ordered to form rankings for ingestants and inhalants, thus permitting comparison of the groups' patterns of response.

Symptoms were rated on a four-point severity scale: not a problem, minor problem, moderate problem, and severe problem. Respondents were asked to mark only symptoms that had developed or increased in severity following exposure. One item, "coughing up bright red blood," was included to detect "yea-saying" because this symptom is not associated with MCS. Standard psychometric techniques were used to group items into meaningful subscales and thereby reduce the number of sig-

nificance tests required. Items that showed poor statistical reliability with scale totals were dropped. Eight symptom severity scales were retained for analysis, and such scales comprised 71 of the original 114 items. In addition, a ninth scale was derived heuristically from the clinical experience of one of the authors (CSM). Included in this scale were symptoms reported frequently by patients presenting with MCS. All nine scales have a 0-30 range, with higher values indicating greater severity. A scale total of 0 indicates responses to all items of "not a problem." Scale totals of 10, 20, and 30 indicate consistent responses of "minor problem," "moderate problem," and "severe problem," respectively. The items that were scaled and scale reliability coefficients are listed in the Appendix. Group inferences were drawn from the nine scale totals, using multivariate analysis of variance (MANOVA). Sex and several covariates (i.e., age, education, and years elapsed since exposure) were incorporated initially to control for possible confounding influences associated with these variables.

The proportions of OP and RE respondents who consulted various medical specialists (e.g., internists, allergists, clinical ecologists) were also compared. Finally, effects on quality of life (e.g., illness-forced changes in occupation, locale) were assessed on a four-point scale (i.e., not affected by illness, affected a little, affected moderately, affected a great deal). Percentages of each group that endorsed the most severe category, "affected a great deal," were calculated.

## Results

Thirty-seven questionnaires qualified for inclusion in the OP group and 75 qualified for the RE group. Completed surveys were received from individuals who resided in 33 states and 3 foreign countries. Approximately four times as many females as males returned surveys. There were no statistically significant differences between OP and RE group means for age, education, years elapsed since exposure, or for gender ratios (Table 1). Exposure dates were distributed non-normally and were skewed toward more recent years. The average time between exposure and completion of survey was 7.7 y. The average age at onset of illness (back-calculated from current age and years elapsed since exposure) was 40 y.

OP exposures occurred in the work place in 16 cases (43%), at home in 20 cases (54%), and during outdoor recreation in 1 case. Proportionately more remodeling exposures occurred at work (51 cases, 68%), compared with exposures at home (24 cases, 32%). Twenty-one OP respondents implicated a single pesticide, whereas 16 respondents described mixed-pesticide exposures. Organophosphates or carbamates most frequently named were chlorpyrifos (19), diazinon (9), malathion (6), and carbaryl (4). Although REs were not asked whether new carpeting was laid during the remodeling exposure, 59% mentioned new carpeting in their narrative descriptions. In response to an open-ended question concerning the exposure event, OPs reported approximately twice as frequently as REs that neurolog-

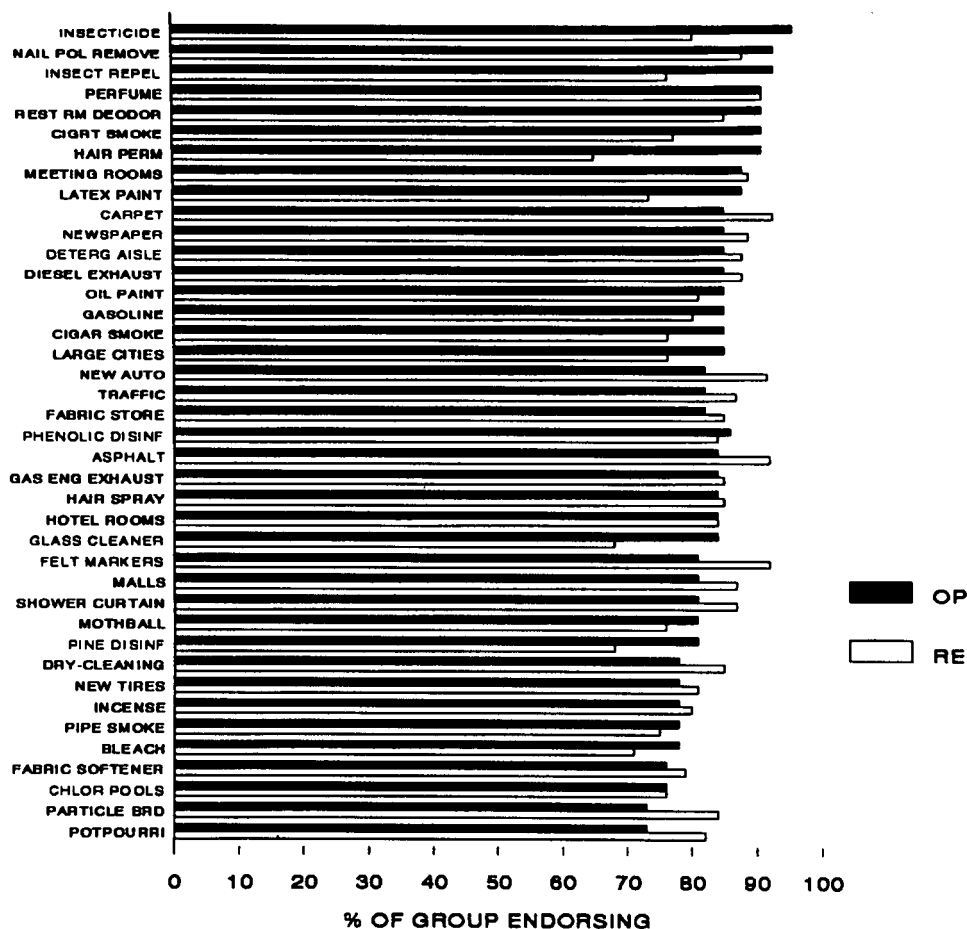


Fig. 1. Organophosphate-exposed (OP) versus remodeling-exposed (RE): comparison of endorsement rates for inhalant items. Items shown were endorsed by more than 75% of the 112 survey respondents.

ical and cardiac symptoms were their earliest symptoms, and REs cited mucous membrane irritation and headache approximately twice as frequently as OPs.

Respondents were asked to identify their current, single, most troublesome exposure. Among the 112 respondents, 28% reported insecticides, 18% reported new carpeting, and 11% reported perfume as their most problematic exposure. Twenty-three (21%) listed more than one exposure as being the "worst." Four respondents named formaldehyde and 3 named diesel exhaust as the "worst" exposure. Only 1 respondent cited cigarette smoke as being most problematic. Not unexpectedly, insecticides were cited by 68% of OP respondents, whereas building-related exposures (i.e., carpet, paint, varnish) were cited by 38% of RE respondents as being their "worst" exposure. None of the OP respondents rated building-related exposures as "worst," but 5 of the RE respondents rated insecticides as causing the most difficulty for them at the time of the survey.

On average, OPs implicated 66.6 (standard deviation [SD] = 26.0) of 98 possible inhalants as triggering symptoms, compared with 63.3 (SD = 21.7) for REs. Similarly, OPs reported that 14.4 (SD = 13.7) of 46 common ingestants caused symptoms, compared with 11.3 (SD = 12.4) for REs. Differences were not statistically signif-

icant. For any given inhalant, there were, on average, 3.4 more endorsements, and for any given ingestant there were 7.2 more endorsements from OPs than from REs. This statistical dissociation indicates more agreement among OPs than among REs with respect to the ingestants they endorsed.

A comparison is made in Figure 1, by group, of problem inhalants cited by at least 75% of the sample. These inhalants include insecticides, solvents, fragrances, fuels, and combustion products. Items cited by one-third or less of the sample included cats, vinegar, cellophane tape, and watching television. Twenty-five of the 112 respondents said that watching television had caused symptoms. Plastic housing, circuit boards, and components associated with televisions, computers, and other electronic equipment, especially if they are new, emit low levels of volatile organic compounds when warm.

A consistently greater number of ingestants were implicated by OPs, compared with REs (see Figure 2). Among the top 15 ingestants for both groups were 4 that are associated with chemical additives: (1) chlorinated tap water, (2) monosodium glutamate (MSG), (3) food dyes, and (4) toothpaste. Foods containing milk products (i.e., milk, cheese, and pizza) were among the

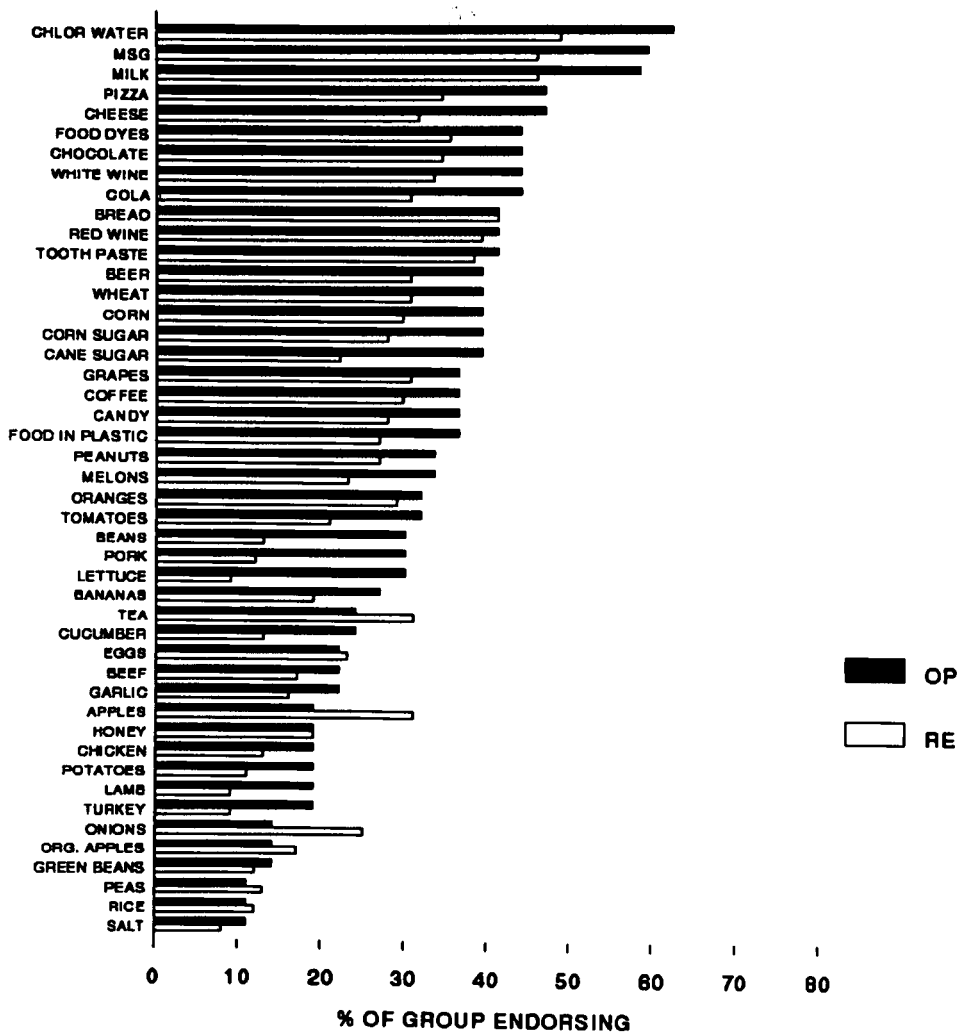


Fig. 2. Organophosphate-exposed (OP) versus remodeling-exposed (RE): comparison of endorsement rates for all ingestant items.

15 most frequently cited items for both groups, as were 3 alcoholic beverages (i.e., white wine, red wine, and beer). Also near the top of both groups' lists were xanthine-containing foods, including chocolate, cola drinks, and coffee. Foods containing or derived from grains (i.e., pizza, bread, beer, corn, and wheat) also appeared near the top of both lists.

The correlation coefficients between the percentage of endorsements by OPs and by REs shown in Figures 1 and 2 were  $r = .91$  ( $p < .0001$ ) for inhalants and  $r = .85$  ( $p < .0001$ ) for ingestants, indicating that the magnitudes of the endorsements for the two groups were quite similar. In addition, the pattern or ordering of items shown in Figures 1 and 2 was nearly identical for the two groups. The similarity in the ranked order of endorsement was examined with Kendall's coefficient of concordance. Agreement between the two groups accounted for 93% of the maximal variance in the inhalant items and for 92% of the maximal variance in the ingestant items. This agreement implies that the two groups were very similar in their patterns of endorsement for chemical and ingestant items.

Not unexpectedly, individuals who noted that a greater number of inhalants caused difficulty also reported that a greater number of ingestants caused problems for them ( $r = .64$ ,  $p < .001$  [Fig. 3]). Similar correlations were found between symptom severity and the number of ingestants and inhalants cited by respondents, i.e., higher symptom severity scores were associated with more chemical and food intolerances.

Symptom severity ratings were compared on the basis of eight factored scales and on the basis of symptoms selected heuristically for their discreteness and frequency in MCS patients. The Appendix contains items included in the nine scales. An overall multivariate  $F$  test of the eight factored scales was significantly different in the groups for exposure type ( $p < .008$ ) but not for gender. The significant overall  $F$  test "protects" the interpretation of the univariate tests reported next.<sup>10</sup> None of the covariates (age, education, years since exposure) originally fit with the model was statistically significant, and all were dropped.

All symptom severity scale means were higher (more severe) for the OP group, compared with the RE group.

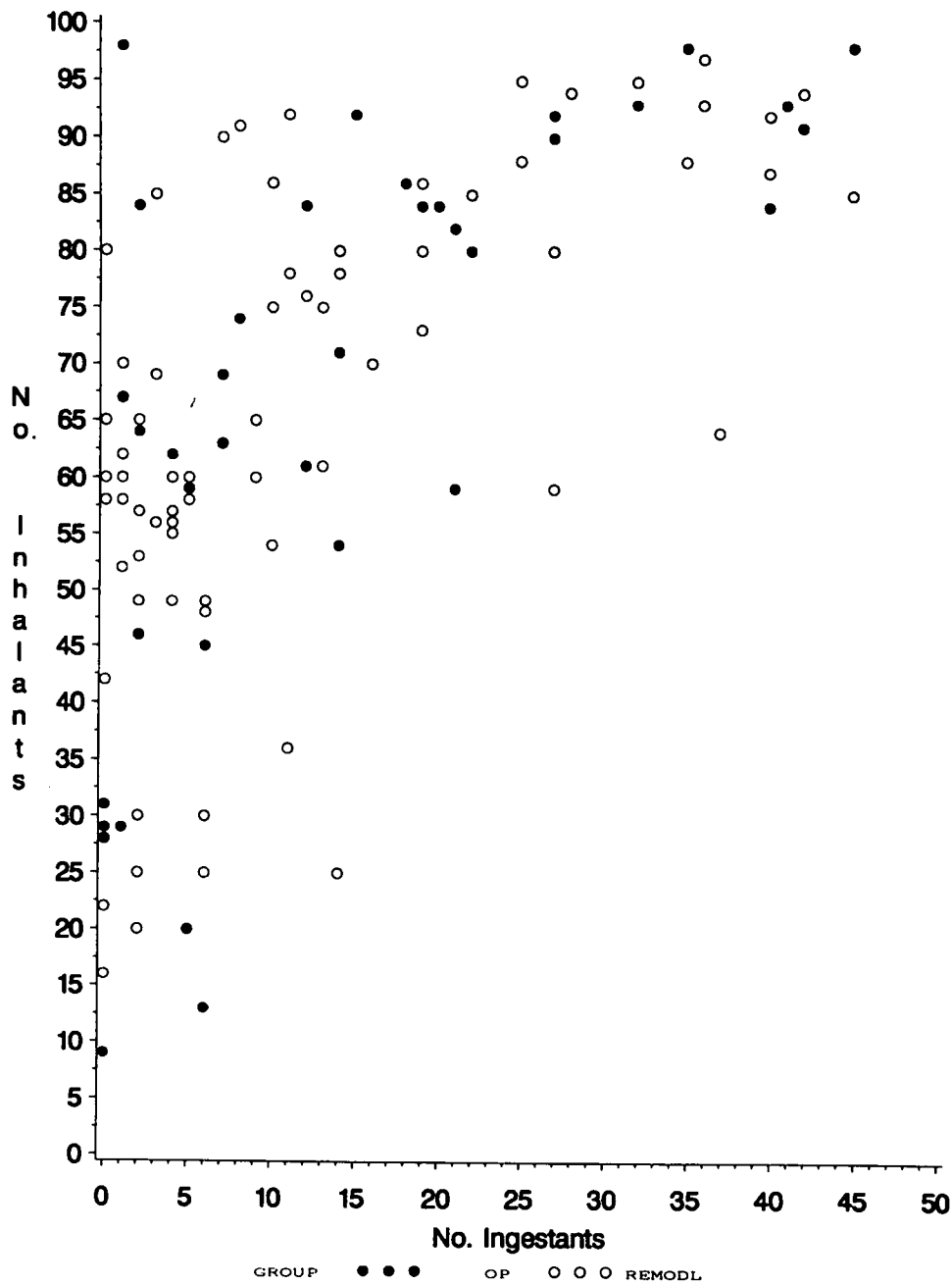


Fig. 3. Scatter plot of endorsement level for inhalants versus ingestants for all 112 respondents.

Symptom severities, based on univariate analyses of variance, differed significantly between OPs and REs for five of the eight factored scales. Statistical significance was reached by about a one-half standard deviation difference between the group means, and this significance corresponded to just under a one-half-unit elevation of average severity from "minor problem" to "moderate problem" for the RE group, compared with the OP (Table 2). Neuromuscular, affective, airway, gastrointestinal, and cardiac symptoms were rated as more severe by OPs than REs. Muscle-related symptoms bordered on significance, with OPs being higher than REs.

Cognitive and head-related symptoms were not significantly different between the two groups. Notably, for both groups, cognitive symptoms attained the highest mean severity, whereas the largest intergroup difference occurred for cardiac symptoms. Presumably, cognitive symptoms caused the most difficulty for these respondents. Airway symptoms were significantly more severe for OPs than for REs, thereby disconfirming one study hypothesis.

In a separate univariate analysis of variance, OPs and REs were compared, using the heuristically derived scale incorporating 15 symptoms commonly associated

**Table 2.—Comparison of Severity of Symptom Scales in Multiple Chemical Sensitivity Exposure Groups**

Symptom scale	Organophosphate	Remodeling	<i>p</i>
Neuromuscular	12.9 (7.5)*	9.0 (6.5)	< .007
Head-related	15.9 (7.6)	13.4 (8.3)	< .12
Muscle-related	17.5 (8.8)	14.2 (8.7)	< .06
Affective	17.7 (7.3)	13.0 (6.8)	< .001
Airway	14.9 (7.5)	12.0 (6.5)	< .04
Cognitive	18.0 (8.3)	15.8 (7.7)	< .17
Gastrointestinal	15.3 (7.9)	11.1 (8.4)	< .01
Cardiac	16.5 (8.2)	9.9 (9.0)	< .001
Fifteen most frequent symptomst	20.8 (6.2)	16.7 (6.0)	.003

\*Values presented as means, accompanied by standard deviations in parentheses.

†Symptom items which comprise the nine scales are reported in the appendix.

with MCS. Age was retained as a significant covariate, suggesting that older respondents tended to report more symptoms on this configuration. Again, symptom severity was statistically significantly greater for the OP group than for the RE group. Furthermore, this scale had the highest severity rating of the nine scales. It is not unexpected that symptoms reported commonly would also be among those rated as most severe. Symptom severity, as determined earlier, did not differ by gender, thus disconfirming another study hypothesis.

The symptom included to detect yea-saying, "coughing up bright red blood," was endorsed by only 4 OP and 2 RE respondents. This item was not included in the factored scales. We sought to determine if these six responses were associated with yea-saying responses to other symptom items; therefore, all 112 respondents were rank-ordered according to the number of symptoms they endorsed (maximum = 114 symptoms). The 6 respondents who reported coughing up blood fell at ranks 25, 33, 80, 96, 98, and 111. A higher ranking connoted more extreme responses. The 25th-ranked respondent had a sum total of 880, out of a maximum of 3 420 points ( $114 \times 30 = 3\,420$ ), and the 111th respondent had 2 760 points. The highest (112th) ranked respondent had a sum total of 2 820, which total included 13 responses of zero ("not a problem") to the severity items. Given this analysis and the caveat that symptom reports of coughing up blood may be associated with bona fide medical conditions (e.g., epistaxis, chronic bronchitis, carcinoma, and tuberculosis), no cases were excluded as probable yea-sayers.

OPs and REs reported that they had consulted similar numbers of medical practitioners (including psychiatrists and psychologists) after exposure occurred: 21.6% consulted 1-4 doctors; 39.6%, 5-9 doctors; 20.7%, 10-14 doctors; 10.8%, 15-19 doctors; and 7.2%, 20 or more doctors. The frequency with which OPs and REs visited internists (95% of OPs and REs combined), allergists (79%), clinical ecologists (67%), psychologists or psychiatrists (63%), occupational medicine doctors

(49%), neurologists (47%), gastroenterologists (24%), and endocrinologists (24%) were comparable. However, OP respondents were more likely to have seen a cardiologist (42% versus 19%,  $p < .02$ ) subsequent to exposure.

There were no significant group or sex differences with respect to quality-of-life ratings. Both OPs and REs reported a major impact upon their ability to work and a substantial lowering of their quality of life. At the time of their exposure, 26 of 37 OP respondents (70%) and 65 of 75 RE respondents (87%) reported that they worked full time (81% of total). At the time of our survey (average of 7.7 y postexposure), 84% of 90 respondents indicated they were no longer able to work full time. Only 2 OPs (5%) and 12 REs (16%) reported that they worked full time (12.5% of total). Seventy-nine percent of those employed full time at the time of their exposure reported that they had quit their jobs, had changed jobs, or had changed careers because of their illness (88% of OPs; 75% of REs).

Both groups reported that many facets of their lives had been affected "a great deal" by their illness: occupation (84%); choice of personal care products (82%); plans for the future (82%); places they go, e.g., shopping, restaurants (80%); income (73%); social activities (73%); ability to travel to other cities (72%); hobbies (68%); home construction, heating, etc. (65%); choice of home furnishings (64%); marriage or family (63%); diet (60%); geographic location (57%); appearance, hairstyle, makeup, etc. (57%); clothing (56%); the car they drove (56%); their ability to do housework (50%); and their decision whether to have more children (28%). The percentage of OPs and REs who reported that they had been involved in litigation related to their exposure were similar: 47% and 43%, respectively.

## Discussion

Recently, some investigators reported symptoms that are similar to those described here among workers exposed to organophosphates and to solvents. For example, Rosenstock et al. noted decrements in neuropsychological performance among Nicaraguan agricultural workers, and that decrement persisted years after accidental organophosphate intoxication.<sup>11</sup> Other authors describe persistent memory difficulties, cognitive problems, motor impairment, mood alterations, feelings of unreality, nervousness, noise sensitivity, and multiple somatic complaints (e.g., fatigue, chest pain, hand tremor, nausea), following an organophosphate exposure.<sup>12-14</sup> Several of our OP respondents reported symptoms consistent with acute OP intoxication minutes to hours following their exposure, e.g., excessive salivation, visual changes, agitation, confusion, and muscle spasms.

Morrow et al. found that solvent workers who had been treated for an acute solvent exposure had persistent cognitive difficulties, and these workers were more likely to show no improvement or to worsen on neuropsychological testing over time than were solvent-exposed workers absent such a history.<sup>15</sup> "Cacosmia"

(i.e., feeling ill from odors), a characteristic complaint of MCS patients, has also been observed among solvent workers who exhibited neurobehavioral dysfunction.<sup>16</sup> Cone and Sult reported on a group of casino workers who were exposed to a mix of carbamate and pyrethrin insecticides and solvents and who subsequently developed persistent multisystem symptoms; cognitive impairment, and sensitivities to the odor of perfumes, gasoline, newsprint, cleaning materials, and pesticides.<sup>17</sup>

The persistent neuropsychological symptoms, including cognitive difficulties and cacosmia, that have been reported in pesticide- and solvent-exposed workers are remarkably similar to symptoms reported by our MCS sample, of whom most were exposed at home or in an office building. This finding suggests that levels of pesticides and solvents associated with remodeling or routine extermination may not be inconsequential, at least for a subset of the population.

The similar rank order for inhalants and ingestants cited by OPs and REs in this study suggests that once MCS develops, similar kinds of substances will trigger symptoms, irrespective of the chemical nature of the original exposure. Comparison of the 8 symptom clusters and 15 most frequent MCS symptoms for both groups suggests that, on average, OPs experience more severe symptoms than do REs, particularly neuromuscular, affective, airway, gastrointestinal, and cardiac symptoms. Group means are most divergent for severity of cardiac symptoms, a result that is consistent with our finding that OPs were much more likely to consult a cardiologist (42%, compared with 19%). The highest mean severity score for both OP and RE groups occurred for cognitive symptoms.

From a toxicologic point of view, one would expect that individuals who become ill from a cholinesterase-inhibiting pesticide or from exposure to remodeling of a building would exhibit different severities of symptoms, assuming that exposures were sufficiently high to induce symptoms: organophosphates and carbamates inhibit acetylcholinesterase.<sup>18</sup> Remodeling involves complex mixtures of solvents (e.g., toluene, butanol, hexane, and xylene) that outgas from paints, adhesives, new carpeting, building materials, and furnishings. Given that air monitoring during remodeling occurs most often after occupants complain, if it occurs at all, peak exposure concentrations are generally unknown. Likewise, cholinesterase levels of more "susceptible" persons during routine extermination have not been studied. These data gaps, coupled with the disabling symptoms reported by these respondents (on average, a highly educated group with nearly 4 y of college), who explicitly attributed onset of illness to extermination or remodeling, suggest that the safety of these common activities warrants further scrutiny. Such familiar exposures must not be presumed harmless solely on the basis of established toxicologic models and exposure limits. New models that might explain unanticipated observations deserve exploration.

Bell et al. hypothesized that MCS results from sensitization (partial kindling) of olfactory-limbic pathways by

environmental chemicals and/or salient stressors.<sup>7</sup> According to this model, strong or repeated low-to-moderate-level stimuli could induce erratic signaling in limbic structures and could reduce the threshold for response to subsequent environmental exposures. Disruption of normal limbic function might affect emotions, short-term memory, endocrine regulation, and autonomic nervous system activity. High levels of acetylcholinesterase in the limbic region may protect against "bizarre sensitivity" by maintaining acetylcholine concentrations at nerve junctions within critical bounds.<sup>19</sup> Notably, organic solvents inhibit acetylcholinesterase activity in the membrane of human red blood cells *in vitro* and, by analogy, are believed to act on nerve cell membranes.<sup>20,21</sup> If both solvents and organophosphates inhibit cholinesterase, this might help explain the similar symptom patterns—but divergent severity—reported by OPs, compared with the REs in this study.

Rosenthal described a retired attorney with depression who developed worsening depression, multisystem symptoms, and odor intolerances after household extermination (organophosphate).<sup>22</sup> Citing a cholinergic theory of depression,<sup>23</sup> Rosenthal suggested that depressed individuals may be particularly sensitive to acetylcholine. Noting that the breakdown of acetylcholine is inhibited by organophosphates, Rosenthal theorized that vulnerability to acetylcholine might explain both environmental sensitivities and an endogenous tendency toward depression. Another hypothesis for MCS offered by Meggs involves neurogenic inflammation that arises from stimulation of chemical-irritant receptors.<sup>24</sup>

Regardless of which mechanism for MCS might be correct, volatile organic compounds outgassing from building materials would be expected to affect the nervous system less specifically and less robustly (solvents "depress" the central nervous system) than would cholinesterase-inhibiting pesticides. Although pesticide formulations include solvent vehicles or carriers, the greater overall severity of symptoms reported by our OP group in the present study suggests relatively greater neurotoxicity or potency for this class of pesticides, compared with remodeling-associated solvent exposures.

Only 3 respondents (1 OP, 2 RE) reported that foods/ingestants did not make them ill. The fact that ingestants containing chemical additives (chlorinated tap water, food additives, MSG) and food-drug combinations (alcoholic beverages and xanthine-containing foods) were frequently implicated by both groups, is consistent with a hypothesis that these individuals exhibit amplified responses to pharmacologic doses of a variety of substances.<sup>7</sup> Although occupational medicine practitioners may feel dietary issues are not a primary concern in their evaluation of MCS patients, participants in this study clearly viewed foods as major factors in their illness, with 60% indicating that their diets had been affected "a great deal."

This survey represents the largest group of MCS patients studied to date. Unlike prior studies, this study

compared two groups that attributed their illnesses to relatively homogeneous, well-characterized antecedent exposures. Limitations of this retrospective survey study include problems with recall bias and uncertain influences of pending litigation on reporting of symptoms. The investigators have not participated in any litigation involving these respondents, and we informed all participants from the outset that they would not be offered any medical advice during or following completion of the survey. The self-selected sample for this study is probably not representative of MCS patients overall; advertising in patient-support newsletters likely disposed the sample toward more severely ill and better "informed" respondents regarding MCS and its manifestations. Patients who are very ill, who are unable to read, or who are less educated may be underrepresented in this sample, whereas nonworking MCS patients who have more time to read newsletters and respond to a survey may be overrepresented.

The finding that pesticide-exposed respondents report similar, but much more severe symptoms than remodeling-exposed respondents is consistent with prior anecdotal observations, and this finding supports the hypothesis that some biological mechanism is operative. A threat to the validity of these findings remains, that of sampling from pre-existing groups, a difficulty always present with retrospective studies. For example, the OP group might have overreported symptoms relative to the RE group because organophosphate exposure is more specific and involves a known neurotoxin, whereas the RE group attributed illness to building remodeling, which most people consider benign. To explain the findings in this study with such a cognitive hypothesis would require that patients hold powerful beliefs regarding the health impact of pesticide versus remodeling exposures that permeate both their symptom reports and their ideas as to which inhalants and ingestants trigger symptoms. Although possible, this explanation seems less parsimonious than the one offered here.

The fact that MCS patients *attribute* their illness to chemical exposure distinguishes MCS from illnesses with overlapping features, such as chronic fatigue syndrome and somatoform disorders. Such attributions may provide fertile ground for future cognitive research. For example, nearly a quarter of our sample indicated that watching television can trigger symptoms, but it seems unlikely that this relatively low-level exposure source was discovered independently by so many respondents. MCS patient support newsletters (via which this sample was recruited) contain much information about potential exposure sources, undoubtedly creating shared "mental models" for MCS. Little is known about how information communicated in this way influences the causal attributions people make toward substances in their environment. Some maintain that MCS patients share an erroneous "belief system." However, shared mental models, if correct, might enable patients to identify problem exposures and cope more successfully with a poorly understood medical condition.

Practitioners who feel that MCS is a somatoform disorder have characterized these patients as "universal

reactors"<sup>25</sup> who have histories of *life-long* illness and childhood abuse.<sup>26</sup> Yet the majority of respondents in this sample reported that they were well and working full time (81%) at the time of their initial exposure. (National full-time employment levels for the past 4 y have ranged from a low of about 61% of eligible women to a high of about 79% of eligible men.<sup>27</sup>) Furthermore, cognitive symptoms among patients with somatoform disorders tend to be far down on the list of complaints, if they appear at all, in contrast to the high severity ratings our MCS sample assigned to cognitive symptoms.<sup>9,28</sup> More concretely, somatoform disorders almost always have an age of onset under 30 y.<sup>8</sup> Only 19 (17%) of our 112 respondents reported onset before age 30 y, a result suggesting that for the majority of MCS patients, somatoform disorder is not applicable as a diagnosis. A diagnosis of somatoform disorder is based on otherwise medically unexplained symptoms; our findings suggest that a biological basis for MCS may indeed exist.

Bell proposes a "synthesis" of biological and psychological explanations for MCS and related illnesses, arguing that a debate centered on premorbid psychopathology (*versus* chemical exposure) as the causal factor in MCS oversimplifies what in reality may be an extremely complex etiology.<sup>7,29,30</sup> The central nervous system (CNS) can be viewed as a transducer of both biological and psychosocial experiences, both of which are integrated into neural activity. In turn, this activity has biological, psychological, and social consequences. Pre-existing psychiatric disorders (e.g., depression and anxiety) involve alterations in brain chemistry and neurotransmitters that may make certain individuals more vulnerable to environmental chemicals (e.g., organophosphates). In recent months, the role of stress and anxiety in Gulf War "syndrome" has been mentioned frequently in press reports and by government spokespersons. At the same time, Gulf War servicemen and women were exposed to complex mixtures of hydrocarbons, including solvents, combustion products, and cholinesterase inhibitors (e.g., pyridostigmine bromide, pesticides, and, possibly, low concentrations of nerve agents<sup>31</sup>).

Complex sociobiological questions concerning the etiology of MCS will not be resolved by retrospective survey studies—perhaps not by retrospective studies of any kind. It may be necessary to develop animal models in which factors, such as stress and chemical exposures, can be manipulated independently. In human studies, stronger scientific inference regarding the roles of chemical exposures and psychological factors may be made by blinded challenges in a controlled environment.<sup>5,6,32</sup> In the longer term, studies from a variety of perspectives are needed from which a picture of the pathophysiological and psychological mechanisms underlying this costly illness may finally emerge.

#### Appendix: Reliability Estimates for the Symptom Severity Scales

Listed below are items that constitute the nine symptom severity scales and the reliability coefficients for each scale. Standard factor analytic techniques were applied to the original 114 symptom items, using the SAS program.<sup>33</sup> Items that were unstable (i.e., facily

changed scale affiliation), loaded negatively, or had standardized coefficients of less than .25 were culled systematically. The remaining 71 symptom items are listed below and appear under each named scale. Scale values were computed for each respondent by simply summing the item and then rescaling to a 0-30 range. Reliability coefficients (also computed with the SAS program<sup>33</sup>) represent the correlation of the item with the scale total, with the item in question removed from the scale. Cronbach's alpha reliability coefficient is reported opposite each of the nine scale names and represents the internal consistency among the items. All of these are quite high, a result of using factor analytic techniques to create the scales. The factor analysis used to derive the scales included all 203 original survey respondents, the result of which increased the stability of the variance-covariance matrix. However, the reliability coefficients presented here are based on the 112 respondents in the OP and RE groups.

<b>Neuromuscular</b>	<b>0.90</b>	<b>Affective</b>	<b>0.87</b>
Loss of consciousness	0.62	Feeling tense/nervous	0.70
Stumbling/dragging foot	0.74	Uncontrollable crying	0.59
Seizures	0.30	Feeling irritable/edgy	0.61
Print moving/vibrating	0.68	Depressed feelings	0.66
Feeling off balance	0.74	Thoughts of suicide	0.66
Tingling in fingers/toes	0.67	Nerves feel like vibrating	0.53
Double vision	0.54	Sudden rage	0.59
Muscle jerking	0.59	Loss of motivation	0.52
Fainting	0.47	Trembling hands	0.50
Numbness in fingers/ toes	0.69	Insomnia	0.47
Clumsiness	0.67	<b>Airway</b>	<b>0.83</b>
Problems focusing eyes	0.67	Cough	0.66
Cold or blue nails/ fingers	0.41	Bronchitis	0.52
Uncontrollable sleepiness	0.52	Asthma or wheezing	0.47
<b>Head-related</b>	<b>0.83</b>	Post nasal drainage	0.52
Head fullness/pressure	0.78	Excessive mucous production	0.53
Tender face/sinuses	0.57	Shortness of breath	0.40
Sinus infections	0.35	Eye burning/irritation	0.52
Tightness in face/scalp	0.74	Susceptible to infections	0.42
Brain feels swollen	0.64	Dry eyes	0.50
Ringing in ears	0.47	Enlarged/tender lymph nodes	0.44
Headache	0.45	Hoarseness	0.56
Feeling groggy	0.44	<b>Cognitive</b>	<b>0.92</b>
<b>Muscle-related</b>	<b>0.88</b>	Memory difficulties	0.76
Joint pain	0.70	Problems with spelling	0.70
Muscle aches	0.73	Slowed responses	0.83
Weak legs	0.58	Problems with arithmetic	0.71
Weak arms	0.68	Problems with handwriting	0.76
General stiffness	0.69	Difficult concentration	0.72
Cramps in toes/legs	0.61	Difficulty making decisions	0.66
Painful trigger points	0.61	Speech difficulty	0.72
<b>Gastrointestinal</b>	<b>0.88</b>	Feeling of unreality/spacey	0.57
Abdominal gas	0.81	<b>Most frequent</b>	<b>0.86</b>
Foul gas	0.75	Feeling tired/lethargic	0.54
Problems digesting food	0.71	Memory difficulties	0.62
Abdominal swelling/ bloating	0.70	Depressed feelings	0.46
Foul burping	0.59	Dizziness/lightheadedness	0.61
Diarrhea	0.47	Feeling of unreality/spacey	0.67
Abdominal pain/ cramping	0.67	Shortness of breath	0.42
Constipation	0.41	Feeling irritable/edgy	0.54
<b>Cardiac</b>	<b>0.83</b>	Problems focusing eyes	0.59
Heart pounding	0.72	Chest discomfort	0.44
Rapid heart rate	0.70	Loss of motivation	0.36
Irregular heart rate	0.71	Problems digesting food	0.38
Chest discomfort	0.51	Muscle aches	0.58
		Tingling in fingers/toes	0.55
		Eye burning/irritation	0.38
		Headache	0.47

\* \* \* \* \*

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Requests for reprints should be sent to Claudia S. Miller, M.D., Department of Family Practice, The University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78284-7794.

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