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Taylor & Francis Group

Archives of Environmental Health: An International Journal

ISSN: 0003-9896 (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/vzeh20

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To cite this article: Ann L. Davidoff & Penelope M. Keyl (1996) Symptoms and Health Status in Individuals with Multiple Chemical Sensitivities Syndrome from Four Reported Sensitizing Exposures and a General Population Comparison Group, Archives of Environmental Health: An International Journal, 51:3, 201-213, DOI: 10.1080/00039896.1996.9936017

To link to this article: https://doi.org/10.1080/00039896.1996.9936017

Symptoms and Health Status in Individuals with Multiple Chemical Sensitivities Syndrome from Four Reported Sensitizing Exposures and a General Population Comparison Group

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ABSTRACT. Self-reported information about health and mental health status and history on (a) three diverse samples of individuals who reported multiple chemical sensitivities syndrome ($n = 60$) and (b) one sample of the general population ($n = 60$) was collected by telephone interview. Subjects from the general population were selected randomly from the telephone directory and were matched for age, gender, and socioeconomic status with index subjects. Data on an additional 10 subjects with multiple chemical sensitivities syndrome were also available for comparison on many of the variables of interest. The four diverse groups of patients with multiple chemical sensitivities syndrome had very similar general and specific indices of illness and sensitivity to chemicals. Members of the general population reported mild sensitivity to chemicals, and even those with more sensitivity differed from the multiple chemical sensitivities syndrome groups with respect to number and types of symptoms reported, duration and frequency of response, and associated features. Multiple chemical sensitivities syndrome was associated consistently with only one psychiatric variable, elevated negative affect scores, which were correlated significantly with the presence of illness. Patients with multiple chemical sensitivities syndrome from the diverse samples had very similar characteristic features, despite whether they had or had not received treatment by clinical ecologists.

ASHFORD AND MILLER[1] postulated that three populations are at special risk for developing a persisting hypersusceptibility to very low levels of environmental chemicals: (1) people who experience nonspecific building-related illnesses, (2) individuals who work in industry, and (3) those who live in contaminated communities. Such an altered response pattern has been called various names, including multiple chemical sensitivities (MCS) syndrome, environmental illness (EI), environmental or chemical hypersusceptibility, chemical hypersensitivity syndrome (CHS), environmentally induced illness, complex allergy, total allergy syndrome, and twentieth-century disease. We refer to the altered response pattern as MCS syndrome.

No case definition of MCS syndrome has gained wide acceptance. Several provisional case definitions have been proposed. In 1985, the Committee on Environmental Hypersensitivity Disorders, commissioned by the Ontario Ministry of Health, advanced the following working definition[2]: "Environmental hypersensitivity is a chronic (i.e., continuing for more than three months) multisystem disorder, usually involving symptoms of the central nervous system and at least one other system. Affected individuals are frequently intolerant to some

foods and they react adversely to some chemicals and to environmental agents, singly or in combination, at levels generally tolerated by the majority. Affected persons have varying degrees of morbidity, from mild discomfort to total disability. Upon physical examination, the patient is normally free from any abnormal objective findings."

The research case definition by Mark Cullen[3] has been used widely in the United States. Cullen asserts that (1) the disorder is acquired relative to some documentable environmental exposure(s), insult(s), or illness(es); (2) symptoms involve more than one organ system; (3) symptoms recur and abate in response to predictable stimuli; (4) symptoms are elicited by exposures to chemicals of diverse structural classes and toxicologic modes of action; (5) symptoms are elicited by exposures that are demonstrable (albeit of low level); (6) exposures that elicit symptoms are very low—below those known to induce health effects; and (7) no single, widely available test of organ-system function can explain the symptoms.

A consensus case definition came from a survey by Nethercott et al.,[4] during which questionnaires were sent to 212 physicians and to other professionals knowledgeable about MCS syndrome by virtue of having contributed to the medical literature on the condition or by having served on a relevant task force, review board, editorial board, and so forth. Five criteria were considered "major" for diagnosing MCS syndrome by more than 50% of the respondents: (1) symptoms are reproducible with exposure, (2) the condition is chronic, (3) symptoms occur at low exposure levels, (4) symptoms resolve when incitants are removed, and (5) individuals respond to multiple unrelated substances.

Given the absence of a well-accepted case definition of MCS syndrome, it is not surprising that published data on prevalence do not exist. Mooser reported that clinician estimates of the prevalence of disruptive forms of MCS syndrome ran as high as 2–10% of the general population.[5] Among 114 individuals who were poisoned by organophosphates in industrial settings and who were diagnosed subsequently by physicians as having occupational disease attributable to organophosphates,[6] 19% of the individuals reported intolerance to low levels of environmental chemicals. With respect to 160 solvent-exposed workers admitted consecutively for clinical services, 13% reported such intolerances.[7]

Mild MCS-like conditions, which may not represent alterations from baseline, are widespread. It was suggested in a research survey, using a random national sample, that 7%–11% of the 600 office workers studied reported that they experienced significant building-related symptoms[8]—considered by some to constitute a less fully expressed pattern of the same syndrome. Sensitivity to chemicals has also been associated with upper and lower respiratory ailments (e.g., sinusitis, asthma, allergies); with metabolic conditions (hypothyroidism, hyperthyroidism, diabetes mellitus); and with drug use.[9,10] Finally, sensitivity to chemicals has been documented in the general population. In a study of male and female undergraduate students enrolled in an introductory class at the University of Arizona, 66% of 643 subjects reported feeling ill from one or more of five chemical odors, and 15% of the students reported being made ill by at least four of five odors.[11]

Although MCS syndrome is often associated with considerable disability,[1,12,13] the basis for the problem has not been elucidated, and controversy about its pathogenesis is widespread. Many observers have reported no evidence that the condition is based on a physiologically mediated response to environmental chemicals, and they have speculated that the symptomatology has a psychogenic etiology.[14–30] Diverse positions about underlying pathophysiology have been stated by other observers who view environmental stimuli as inducers of symptoms in affected persons.[31–49]

To date, the unique features of people who have reported MCS syndrome have been reported in four published and two unpublished studies.[2,23,24,50–52] The Committee on Environmental Hypersensitivity Disorders[2] placed newspaper advertisements in 16 Ontario newspapers, and they solicited testimonials from readers, affected individuals, and organizations and subsequently analyzed the letters received from 130 affected individuals. An unpublished review of 100 patients admitted consecutively to the largest environmental control unit in Carleton, Texas, has also been described.[50] Cone et al.[51] inspected the records of 400 patients who, during a period of approximately 3 y, consulted the Occupational Medicine Clinic at the University of California, San Francisco, after which the researchers published information derived from the case records of 13 clients. Cone and Sult[52] described a cohort of 250 casino workers, exposed to repeated pesticide applications to control a cockroach infestation, who consulted the author or others because of work-related illnesses; 63% of a subsample of 19 workers who were referred to the authors for interview and examination reported a new onset sensitivity or intolerance to perfumes, gasoline, and other solvent-containing materials. Terr[23,24] described the characteristics of patients who were referred for evaluation, primarily by employers or insurance carriers, because of claims of work-related environmental illness (of the 50 subjects in the 1986 study, 43 were included again in the 1989 study).

This article constitutes the first report of a systematic study of extensive self-reported information from standardized interviews with different samples of MCS syndrome subjects and a comparison group that comprised members of the general population. The MCS syndrome samples differed with respect to reported sensitizing exposures. The study enabled us to examine five descriptive questions: (1) Do diverse samples that report MCS syndrome from different sensitizing exposures resemble one another? (2) Do members of the general population report some degree of chemical sensitivity? (3) If so, is the chemical sensitivity in MCS syndrome similar to that observed in the general population? (4) Is MCS syndrome associated with a particular psychiatric history or status? and (5) Do MCS syndrome patients treated by clinical ecologists differ from other MCS syndrome patients? A forthcoming paper will describe dis-

criminant analyses of the interview data that identify a parsimonious set of questions for recognizing individuals with MCS syndrome among the general population.

Material and Method

Information about four sample groups of cases with MCS syndrome (i.e., organic solvent in industry origin, organophosphate pesticide origin, sick building syndrome origin, chlorine dioxide origin) and about one sample group from the general population was used for this study.

Multiple chemical sensitivities syndrome samples. Eligibility requirements for study cases in three of the MCS syndrome groups (i.e., organic solvent in industry origin, organophosphate pesticide origin, and sick building syndrome origin) included (a) having experienced a definite change in perceived sensitivity to chemicals following the exposure specified and (b) having to avoid three or more dissimilar situations involving environmental chemicals to feel good daily. In addition, subjects had to be between the ages of 30 and 60 y, had to have developed MCS syndrome during the previous 5 y, and had to be free of any medications that attenuated their responses to environmental chemicals.

Origin of Cases Identified

Organic solvents in industry. Cases exposed in industrial settings to organic solvents were recruited by enlisting the aid of interested occupational physicians in Baltimore, upstate New York, California, Pennsylvania, and Louisiana. These physicians distributed letters that enlisted volunteers. Letters were also distributed to members of injured workers groups in New York, Massachusetts, and Rhode Island.

Organophosphate pesticide. Cases were recruited by sending letters to persons who were listed on a registry of victims of pesticide poisonings. This registry was maintained by the National Coalition Against the Misuse of Pesticides, a District of Columbia-based organization. The same letters, also distributed to members of support groups, were formulated specifically for people who had identified themselves as being victims of pesticide poisonings.

Sick building syndrome. Cases were recruited by distribution of letters to support groups for injured workers in a private research institute and in a government facility, both of which facilities were associated prominently with outbreaks of sick building syndrome. In some instances, physicians involved in the identification of cases with organic-solvent-in-industry onset referred MCS syndrome patients who had organophosphate pesticide or sick building syndrome onsets.

During the study period, consent forms were received from 201 possible MCS syndrome participants, from which cases were chosen randomly and screened. Subjects who qualified were classified with respect to exposure onset into one of three targeted onsets: (1) sick building syndrome, (2) organic solvent in industry, or (3) organophosphate pesticides. After 20 subjects from a targeted onset history were interviewed, we did not enroll any others with that onset history.

Chlorine dioxide. Ten workers in a potato processing plant in rural Wisconsin were studied. They developed conditions that resembled MCS syndrome after they were exposed chronically and acutely, by accident, to both chlorine dioxide gas and to chloroform, which was formed from the reaction between chlorine dioxide gas and organic material (in this case, potatoes). Pending litigation necessitated evaluation by one of the authors (ALD), who used instruments similar to those used for the other groups. All 10 subjects reported that following, but not before, exposure they were made more than "a little sick" by three or more chemicals.

General population sample. Sixty members from the general population were recruited. A random-number table was used to select 1 000 subjects from several Baltimore-area telephone directories. These subjects received letters that encouraged their participation in a telephone interview on health and common environmental chemical exposures. Subjects were offered an incentive of $25.00 for a completed interview. Respondents were informed that all members of a household who were between the ages of 30 and 60 y had to volunteer for the study, but that only one household member would be selected randomly. Matching was accomplished on the basis of three variables: (1) gender, (2) age, and (3) socioeconomic status (SES). In 55 cases, SES was defined by job status, using seven broad categories based on the 1980 Census Occupational Classification System; for 5 women, we defined SES by educational background (3 cases) or husband's occupational status (2 cases). Forty members of the general population were matched to the index subjects in the SBS onset MCS syndrome group, and 20 members of the general population were matched to the index subjects in the industrial-solvent-onset MCS syndrome group. This was done because these two groups represented the extremes with respect to gender distribution and SES. Members of the general population were not screened for sensitivity to chemicals.

We mailed 1 000 letters, 70 of which were undeliverable and were returned. Thirty-one individuals wrote to disqualify themselves because of their ages. Six individuals who volunteered either could not be reached (n = 4) or declined to be interviewed, despite volunteering initially (n = 2). One letter was returned by a residence that contained a physician's office. Twenty-three eligible households were discarded after the required number of subjects were obtained. The remaining households did not respond to our letter. The total number of respondents was 121. An exact response rate could not be determined because some households may have disqualified themselves on the basis of being "ineligible."

Survey instruments. Items were chosen initially for the questionnaire because pilot data suggested that they discriminated between individuals with MCS syndrome and the general population. Additional items were then chosen to reflect the five criteria of MCS syndrome endorsed by at least 50% of physician participants in the survey described previously. Questionnaires were

adapted for a telephone interview used for the SBS-, organophosphate-pesticide-, and organic-solvent-in-industry-onset cases and in members of the general population. A self-administered questionnaire, derived from the same sources, but with some items deleted and some additional items included, was used for the chlorine-dioxide-onset cases who were studied several months following the study of the original participants.

Telephone interview. The duration of the telephone interview was between 20 and 75 min. Cases were asked 16 questions to ensure that they met the eligibility criteria. Otherwise, cases and controls answered the same questions about the following:

1. Demographic characteristics (e.g., age, gender, occupation, years of education, work setting).
2. Whether and to what degree they would feel sick in 12 situations that involved exposures to various environmental chemicals common in daily life. They were asked first about exposures of 4 h, followed by exposures of 20 min. Outdoor exposures included being near someone who smoked cigarettes, being near a road being tarred, driving a new car, and driving in heavy traffic. Indoor exposures included shopping in an enclosed mall, being in a room newly sprayed with pesticides, being in a newly painted room, being near newly installed wall-to-wall carpet, and being around perfume. Six additional inquiries were made about chemical exposures that occurred for just seconds to several minutes (i.e., using a bathroom newly sprayed with a scented air freshener, reading a freshly printed newspaper, filling a gas tank with gasoline, walking down the detergent row at the grocery, trying on newly dry-cleaned clothing, and drinking a glass of chlorinated water).
3. Changes in tolerance to odors, alcohol, food, medications, and traditional allergens (e.g., pollen, dust, mold, cats).
4. The nature of responses to chemicals (e.g., frequency, consistency, latency, recovery period, time of earliest response).
5. Current symptomatology occurring at least once per week during the previous month and causes of these symptoms.
6. Life histories of medical conditions, including autoimmune, thyroid, and endocrine disorders.
7. Personal and familial mental health history.

At the conclusion of the interview, the interviewer administered the Positive Affect/Negative Affect Scale (PANAS), which consists of 20 adjectives. Ten of the adjectives are toned positively (e.g., interested, excited, strong, active), and 10 are toned negatively (e.g., hostile, scared, guilty). For each adjective, we asked subjects to indicate to what extent during the previous few weeks they had been feeling that way. The positive affect and negative affect scales have been shown to be very consistent internally, largely uncorrelated, and stable at appropriate levels during a 2-mo period.[53] Normative data and factorial and external evidence of convergent and discriminant validity exist for the scales.

All questions were asked in a standardized manner and were closed ended.

Interviewers. Three paid interviewers conducted telephone interviews with members of the general population. One of the paid interviewers and one of the coauthors (ALD) conducted interviews with the MCS syndrome subjects. Given that the interviewers qualified the MCS syndrome subjects for the study, they were not blind to the subjects' group membership.

Statistical analyses. Using the SAS computer software package, we computed frequency distributions on categorical variables, and we computed means and standard deviations on continuous variables for each of the four MCS syndrome groups and for the general population. Pearson product-moment correlations were computed on psychiatric status, medical status, and PANAS data. We used likelihood ratio tests of heterogeneity for categorical data to assess (a) whether the four MCS syndrome samples originated from similar populations and (b) whether the combined MCS syndrome samples and the general population sample came from similar populations. Likelihood ratio tests were used because they could be applied, even with small-cell frequencies.[54] Student *t* tests and likelihood ratio tests were used to assess the likelihood that ecologist-treated and ecologist-untreated subjects were different with respect to continuous and categorical variables, respectively.

Results

Demographic characteristics of the MCS syndrome and general population samples. Demographic characteristics of the samples are shown in Table 1. Females predominated in the general population (75%) and in three of the four MCS syndrome groups (70–90%), whereas males predominated in the organic-solvent-in-industry MCS syndrome group (60%). The mean ages of the MCS syndrome subjects ranged from 42.6 to 51.7 y, and the mean age of the general population was 43.2 y. Professional managerial status predominated in two MCS groups (i.e., SBS-onset, 95%; organophosphate-pesticide-onset, 60%) and in the general population (66.7%). Laborer status predominated in the industrial solvent onset group (85%) and in the chlorine-dioxide-onset group (100%). Correspondingly, education was highest in the MCS, SBS-onset group (mean = 18.1 y); MCS, organophosphate-pesticide-onset group (mean = 16.0 y); and general population group (mean: 15.8 y) group. Education was lowest in the MCS, industrial-solvent-onset group (mean = 13.5 y) and in the chlorine-dioxide-onset group (mean = 11.1 y). Exposure durations before onset of chemical sensitivities ranged from 2.0 to 4.3 y in the three MCS syndrome samples for which data were available. At the time of the evaluation, neither the general population nor chlorine-dioxide-onset MCS syndrome subjects had consulted a clinical ecologist, whereas 30% to 60% of the remaining MCS syndrome subjects had.

General health status. With respect to all health outcomes, negative reports were more characteristic of the MCS syndrome group subjects, compared with subjects in the general population (Tables 2 and 3). Whereas

only 6.7% of the general population sample considered their health to be "fair" or "poor," 75%– 100% of the MCS syndrome samples considered their health to be "fair" or "poor." MCS syndrome subjects did not consider fair to poor health to have always been characteristic of them. Between 80% and 100% of the MCS syndrome subjects felt that their health status had changed, compared with 18.3% of the general population. Consistent with the reports of fair to poor health, 65.0% to 75.0% of the MCS syndrome subjects reported being sick more than 32 h during the preceding week (i.e., equivalent of being sick for all waking hours in any given 2-d period), compared with 8.3% of the general population subjects. On average, the MCS syndrome subjects reported being sick for 59.2–78.6 waking hours during the preceding week, compared with 9 h for the general population subjects. Likewise, 85%–100% of MCS syndrome subjects reported more than 9 symptoms each week during the preceding 2 mo, compared with 21.7% of the general population. On average, the MCS syndrome subjects reported 17.5–19.7 symptoms at least weekly; the general population reported, on average, 5.6 symptoms weekly. A higher percentage of MCS syndrome subjects (80%–90%) had ever been disabled for more than 3 mo, compared with the general population (8.3%), and they experienced limitations on their social lives during much of the time of this study (i.e., MCS = 60%–80%, general population = 2.3%). With respect to all general health and illness status variables, the likelihood ratio tests suggested that the four MCS syndrome groups were not significantly different from one another, but

Table 1.—Demographic Characteristics among Individuals with MCS Syndrome Who Reported Four Different Sensitizing Exposures and a General Population Comparison Group

	MCS syndrome groups				
Characteristic	Sick building syndrome (n = 20)	Organic solvent in industry (n = 20)	Organophosphate pesticide (n = 10)	Chlorine dioxide (n = 10)	General population (n = 60)
Female (%)	75.0	40.0	70.0	90.0	75.0
Professional/managerial status (%)	95.0	10.0	60.0	0.0	66.7
Laborer status (%)	0.0	85.0	10.0	100.0	10.0
Mean age (y)	44.7 (6.7)*	42.6 (7.3)	45.1 (7.3)	51.7 (10.5)	43.2 (8.3)
Mean education (y)	18.1 (1.9)	13.5 (2.5)	16.0 (2.8)	11.1 (1.5)	15.8 (2.9)
Mean exposure duration† (y)	4.3 (2.6)	2.0 (1.1)	3.0 (1.6)	—	—
Sought help from clinical ecologist (%)	30.0	45.0	60.0	0.0	0.0

*All numbers within parentheses are standard deviations.
†Pre-MCS.

Table 2.—General Health and Illness Status (%) among Individuals with MCS Syndrome Who Reported *Four Different Sensitizing Exposures and a General Population Comparison Group*

	MCS syndrome groups					Likelihood ratio tests			
Health/illness status	Sick building syndrome (n = 20)	Organic solvent in industry (n = 20)	Organo-phosphate pesticide (n = 20)	Chlorine dioxide (n = 10)	General population (n = 60)	Within MCS groups	p	Between combined MCS groups and general population	p
Current health rated "fair" or "poor"	75.0	75.0	80.0	100.0	6.7	5.05	> .25	79.95	< .0001
Health status ever changed	85.0	80.0	90.0	100.0	18.3	3.79	> .25	67.89	< .0001
Ever disabled > 3 mo	80.0	90.0	90.0	90.0	8.3	1.19	> .75	92.15	< .0001
Limits on socializing some of the time	60.0	75.0	75.0	80.0	2.3	1.84	> .75	77.57	< .0001
Sick > 32 h during prior wk (max = 112)	75.0	70.0	65.0	—	8.3	0.48	> .90	53.03	< .0001
Experienced > 9 symptoms at least weekly during prior 2 mo	85.0	95.0	95.0	100.0	21.7	3.24	> .50	76.17	< .0001

Table 3.—Symptoms (%) Experienced Weekly During Prior 2 Mo, by System, among Individuals with MCS Syndrome Who Reported Four Different Sensitizing Exposures and a General Population Comparison Group

System	MCS syndrome groups: Sick building syndrome (n = 20)	Organic solvent in industry (n = 20)	Organophosphate pesticide (n = 20)	Chlorine dioxide (n = 10)	General population (n = 60)	Likelihood ratio tests: Within MCS groups	p	Between combined MCS groups and general population	p
ENT (> 1) (max = 7)	95.0	90.0	100.0	100.0	63.3	3.83	> .25	23.69	< .001
GI (2) (max = 2)	95.0	80.0	80.0	40.0	33.3	11.31	.025	28.05	< .001
Systemic (> 1) (max = 6)	90.0	85.0	90.0	60.0	20.0	4.51	> .25	58.17	< .0001
Musculoskeletal (> 0) (max =2)	85.0	100.0	85.0	80.0	31.7	5.93	> .10	47.54	< .0001
CNS, no headache (> 1) (max = 5)	80.0	85.0	80.0	80.0	0.0	0.24	> .975	111.05	< .0001
Headache	80.0	80.0	65.0	100.0	41.7	6.81	> .10	18.96	< .001
Dermatologic (> 0) (max = 2)	60.0	70.0	80.0	80.0	26.7	2.38	> .50	26.80	< .001
Lower respiratory (> 0) (max =2)	75.0	85.0	75.0	100.0	18.3	5.30	> .25	55.64	< .0001
Genitourinary (> 0) (max = 2)	50.0	45.0	65.0	20.0	1.7	5.83	> .20	44.17	< .0001
Circulatory (> 1) (max = 3)	25.0	45.0	40.0	80.0	5.0	8.66	> .05	27.87	< .001
Diagnosed autoimmune condition (%)	40.0	20.0	45.0	00.0	15.0	11.06	< .05	4.21	> .5
Diagnosed thyroid condition (%)	45.0	30.0	55.0	20.0	10.0	4.73	> .25	16.18	< .01

Notes: ENT = eye, nose, throat; GI = gastrointestinal; and CNS = central nervous system.

collectively, they were significantly different from the general population sample.

Current health complaints were aggregated into the systems affected, and symptoms that belonged to every category were reported by larger percentages of MCS syndrome subjects than by general population subjects (Table 3). Systemic, central nervous system (excluding headache), dermatologic, and lower respiratory symptoms were common in MCS syndrome subjects; these symptoms were relatively uncommon in the general population subjects. The symptom categories reported most often by the general population sample were reported much more frequently by the MCS syndrome samples: ear, nose, throat (MCS = 90%–100%, general population = 63.3%); headache (MCS: 65– 100%; general population: 41.7%); musculoskeletal (MCS = 80%–100%, general population = 31.7%); and gastrointestinal (MCS = 40%–95%, general population = 33.3%). Two symptom categories varied greatly in frequency among the MCS syndrome groups, but occurred rarely in the general population group: genitourinary (MCS = 20%–65%, general population = 1.7%); and circulatory (MCS = 25%–80%, general population = 5.0%). In addition, reports by the MCS and general population groups of physician-diagnosed thyroid conditions (20%–55% and 10%, respectively) and autoimmune conditions (20%–45% and 15%, respectively) were elevated in the three MCS syndrome samples. It should be noted that autoimmune conditions were not defined. Participants were simply asked to specify whether a doctor had ever stated that they had an autoimmune condition. Participants who reported affirmatively were asked to specify the conditions they had been told they had. Except for gastrointestinal disorders and diagnosed autoimmune disorders, likelihood ratio tests suggested that the four MCS syndrome groups were not significantly different from one another. Collectively, the MCS syndrome groups were significantly different from the general population sample on all symptom categories, but not with respect to diagnosed autoimmune disorders.

Changed tolerances. All subjects were asked about changes in tolerance for the following: chemical odors; alcoholic beverages; meals; medications; and after-contact with pollen, dust, molds, mildew, animals, grass, leaves, flowers, and other natural allergens. As shown in Table 4, all four groups of MCS syndrome subjects were much more likely than the members of the general population group to say that two or more tolerances had changed (MCS = 90%–95%, general population = 28.8%). Change in odor tolerance was the most common tolerance change reported by MCS syndrome samples (MCS = 85%–100%, general population = 26.7%). Change in tolerance for allergens was also relatively common for all four MCS syndrome groups (70%–85%), but it was much less common (32.2%) in the general population group. The same trend was obtained for changed tolerances for food (MCS =

60%–90%, general population = 20%); alcohol (MCS = 40%–55%, general population = 8.3%); and medication (MCS = 30%–75%, general population = 13.3%). Without exception, likelihood ratio tests suggested that, in terms of changed tolerances, the four MCS syndrome groups were not significantly different from one another. Collectively, however, the MCS syndrome groups were significantly different from the general population sample.

Chemical sensitivity. Responses to questions about chemical sensitivity are shown in Table 5 for all groups. Whereas both MCS syndrome and general population subjects were likely to report chemical sensitivities, the MCS syndrome subjects were more likely to attribute illness to chemical exposures on a *daily* basis (MCS = 70%–80%, general population = 1.7%) and to place recovery from the ill effects of chemical exposures at more than 12 h from onset (MCS = 45%–60%, general population = 0%). These same trends were noted when we compared the MCS syndrome sample with a subset of the general population. This subset contained individuals who reported at least 6 20-min-or-less exposures to environmental chemicals, which made them sick. Without exception, the likelihood ratio tests sug-

Table 4.—Percentage of Group Reporting Changed Tolerances among Individuals with MCS Syndrome Who Reported Four Different Sensitizing Exposures and a General Population Comparison Group

	MCS syndrome groups					Likelihood ratio tests			
	Sick building syndrome (n = 20)	Organic solvent in industry (n = 20)	Organo-phosphate pesticide (n = 20)	Chlorine dioxide (n = 10)	General population (n = 60)	Within MCS groups	p	Between combined MCS groups and general population	p
	Showing changes in tolerance for								
Odor	90.0	100.0	85.0	90.0	26.7	4.54	> .25	62.63	< .001
Allergens	70.0	75.0	80.0	70.0	32.2	0.65	> .90	23.78	< .001
Foods	70.0	60.0	90.0	80.0	20.0	5.44	> .10	40.33	< .001
Alcohol	55.0	50.0	55.0	40.0	8.3	0.75	> .90	30.73	< .001
Medicines	45.0	70.0	75.0	30.0	13.3	8.30	> .05	30.22	< .001
	Showing specified numbers of changed tolerance								
0	0.0	0.0	0.0	0.0	40.7	—		—	
≥ 2	95.0	90.0	90.0	90.0	28.8	0.50	> .90	58.98	< .0001

Table 5.—Occurrence of Chemical Sensitivity (%) among Individuals with MCS Syndrome Who Reported Four Different Sensitizing Exposures and a General Population Comparison Sample

	MCS syndrome groups					Likelihood ratio tests			
Variables	Sick building syndrome (n = 20)	Organic solvent in industry (n = 20)	Organo-phosphate pesticide (n = 20)	Chlorine dioxide (n = 10)	General population (n = 60)	Within MCS groups	p	Between combined MCS groups and general population	p
Illness after chemicals daily	80.0	75.0	70.0	—	1.7	0.54	> .90	81.97	< .0001
Recovery < 2 h after exposure to chemicals	0.0	0.0	0.0	—	86.7	0.00	> .95	117.18	< .0001
Recovery > 12 h after exposure to chemicals	45.0	50.0	60.0	—	0.0	0.94	> .75	54.00	< .0001
More than 4 symptoms/wk from chemical exposure (max = 34)	90.0	100.0	95.0	—	8.3	2.88	> .25	108.08	< .0001
More than 2 systems affected/wk by chemicals (max = 9)	95.0	100.0	95.0	—	8.3	1.66	> .50	114.20	< .0001
More than 6 less-than-21-min chemical exposures rated at least "a little sickening" (max = 18)	95.0	95.0	100.0	80.0	20.0	4.78	> .25	84.27	< .0001

gested that the four MCS syndrome groups were not significantly different from one another on these indices of illness after chemical exposure. Collectively, however, the MCS syndrome subjects were significantly different from the general population sample with respect to these indices.

Indices of illness following exposures that occurred ≤ 20 min were considered relatively sensitive measures of chemical hypersensitivity. The average number of such brief exposures reported to sicken the MCS syndrome subjects ranged from 10.7 to 14.7. The general population subjects reported feeling sick after a mean of 3.8 such brief exposures, and the sensitive subset of the general population reported feeling sick after a mean of 8.9 brief exposures. Eighty to 100% of the MCS syndrome subjects reported that more than 6 chemical exposures of less than 21 min duration made them sick, whereas only 20% of the general population sample reported being made sick by more than 6 brief exposures. Between 90% and 100% of the MCS syndrome subjects reported more than four symptoms weekly that they attributed to chemical exposures (general population = 8.3%). On average, MCS syndrome subjects attributed 11.4 to 14.9 symptoms weekly, on average, to chemical exposures, whereas the general population subjects reported such attributions for 1.0 symptoms; the sensitive subset of the general population reported 1.7 such symptoms. The chemically attributed symptoms of 95% to 100% of the MCS syndrome subjects included symptoms in more than two systems, whereas the chemically attributed symptoms of only 8.3% of the general population sample included symptoms in more than two systems. With respect to the general population, an ear-nose-throat (ENT) symptom and headache were the most commonly reported responses to environmental chemicals; for the sensitive subset of the general population, the most commonly reported response to environmental chemicals was also upper respiratory. In addition to reporting multiple ENT symptoms and headache commonly, the MCS syndrome subjects reported experiencing symptoms in five categories frequently: (1) central nervous system, excluding headache; (2) systemic; (3) lower respiratory; (4) musculoskeletal; and gastrointestinal. Without exception, the likelihood ratio tests suggested that the four MCS syndrome groups were not significantly different from one another on these indices of chemical sensitivity. Collectively, however, the MCS syndrome subjects were significantly different from the general population sample on these indices in every instance.

Psychiatric history and status. Psychiatric data on the MCS syndrome and general population samples are presented in Table 6. Evidence of longstanding somatic complaints or complaints of sickliness in childhood—operationalized in terms of frequency of subjects who reported experiencing three or more chronic health conditions before age 18 y—was seen relatively often (15%–55%) in all three MCS syndrome groups that were asked the questions, but was observed rarely (1.7%) in the general population sample. The difference between the collective MCS groups and the general population was significant ($p < .001$). It is, nonetheless, noteworthy that one or no chronic health conditions in childhood were reported by the majority of subjects in both the general population sample (58%) and in two of the three MCS syndrome groups (50%–80%).

Periods of unusually intense or long-lasting stress before age 18 y were reported relatively frequently by two samples of MCS syndrome subjects: SBS-onset (50%) and organic-solvent-in-industry-onset (30%) groups. However, with respect to the reporting of intense early life stress, two MCS syndrome samples (i.e., organo-

Table 6.—Psychiatric History and Status (%) among Individuals with MCS Syndrome Who Reported Four Different Sensitizing Exposures and a General Population Comparison Group

	MCS syndrome groups					Likelihood ratio tests			
Psychiatric history status	Sick building syndrome (n = 20)	Organic solvent in industry (n = 20)	Organo-phosphate pesticide (n = 20)	Chlorine dioxide (n = 10)	General population (n = 60)	Within MCS groups	p	Between combined MCS groups and general population	p
Chronic childhood conditions, > 2	30.0	15.0	55.0	—	1.7	7.51	> .05	24.64	< .001
Familial psychiatric history	25.0	30.0	15.0	0.0	16.7	6.22	> .10	0.24	> .975
Unusually intense/ long-lasting stress during childhood	50.0	30.0	20.0	0.0	18.3	11.58	> .10	1.90	.75
Treatment of psychiatric condition									
Yes, linked to illness or MCS	15.0	25.0	45.0	—	0.0	4.60	> .25	26.39	< .001
Yes, other	35.0	5.0	10.0	—	21.7	7.23*	> .05	0.49	> .75
No	50.0	70.0	45.0	—	78.3	2.89*	> .10	7.44	< .025

*Percentage in each category compared with other responses.

phosphate-pesticide-onset [20%] and chlorine-dioxide-onset [0%] groups) were comparable with, or lower than, the general population sample (18.3%). A similar pattern was seen for reporting of psychiatric problems among family members. In both cases, the likelihood ratio tests suggested that the four MCS syndrome groups were not significantly different from one another at the .05 level, and, collectively, the MCS syndrome groups were not significantly different from the general population sample.

The three samples of subjects interviewed by telephone were asked, "Has a doctor ever treated you for any kind of condition that s/he considered psychological or psychiatric?" Positive responders were then asked to specify the cause of the condition. A higher percentage of the general population sample (78.3%), compared with the MCS syndrome telephone samples (45–70%), reported never having received psychiatric treatment ($p < .025$). However, 15%–45% of the MCS syndrome telephone samples attributed psychiatric treatment to MCS syndrome or to an associated chemical exposure or illness, whereas none of those in the general population did so. In the case of the telephone-interviewed MCS syndrome subjects, we subtracted from the total number of subjects who had received psychiatric treatment the number of subjects who sought help solely for illness from chemical exposures, illness, and hypersensitivity. We then determined the following estimated percentages of subjects who sought psychiatric help for problems unrelated to physical health: 21.7% of the general sample versus 35% of the SBS-onset MCS syndrome group, 5% of the industrial-onset MCS syndrome group, and 10% of the organophosphate-pesticide-onset MCS syndrome group. Forty percent of the chlorine-dioxide-onset MCS syndrome subjects had sought psychiatric help for unrelated problems, whereas 50% had sought help for MCS syndrome or illness and stress secondary to illness and chemical exposure. In terms of psychiatric treatment for reasons unrelated to illness, the likelihood ratio test results suggested that the MCS syndrome groups that were interviewed over the telephone were not significantly different from one another ($p > .05$). Collectively, the interviewed MCS syndrome groups were not significantly different from the general population sample.

The PANAS yielded estimates of positive affect and negative affect during the few weeks preceding the survey. Positive affect scores were relatively similar for the general population sample (mean = 34.8) and two MCS syndrome groups (i.e., cases of SBS origin [mean = 34.1] and organophosphate pesticide origin [mean = 32.2]). The MCS syndrome subjects in the industrial-solvent- and chlorine-dioxide-onset samples reported less positive affect (means = 28.3 and 26.4, respectively). The negative affect scores of the MCS syndrome samples (means = 21.4–24.5) were all at least slightly higher than those of the general population sample (mean = 18.5). The general population subjects also showed the highest balance of positive to negative affect (mean = 16.3), followed by MCS syndrome subjects in the organophosphate-onset (mean = 11.9) and SBS-onset groups (mean = 10.5). The industrial-solvent-onset group showed the lowest balance of positive to negative affect (mean = 3.8).

In seeking further understanding of the trends observed on the PANAS, we calculated Pearson-product moment correlations between the affect scores and selected psychiatric and illness variables for all subjects interviewed over the telephone. Affect scores were not correlated at a statistically significant level with stress during childhood, personal psychiatric history, or familial psychiatric history. All three affect scores (positive affect, negative affect, balance of positive to negative affect) were correlated at a statistically significant level with number of current symptoms experienced weekly ($r = -.21$, .37, and $-.36$, respectively) and with number of hours sick per week ($r = -.25$, .25, and $-.32$, respectively). Negative affect scores and balance of positive-to-negative affect scores were also associated significantly with total chemical sensitivity score ($r = .27$ and -0.27, respectively).

Clinical ecologist contact and MCS syndrome. Because MCS syndrome is sometimes considered an "invention" of physicians known as clinical ecologists, we examined data on MCS syndrome subjects interviewed by telephone who had and who had not been in contact with a clinical ecologist. We looked for differences between the two groups with respect to selected variables that represented demographics, general health status, changed tolerances, current illness, and chemical sensitivity. Given that the mixed-onset ecologist-treated and -untreated participants were drawn from the same populations, we compared these two groups. There were only two statistically significant differences between the two groups on the variables examined: the ecologist-treated group had more changes in tolerance and more musculoskeletal complaints. The two groups were not differentiated by indicators of general health, illness, and chemical sensitivity, or by mean number of symptoms attributed to chemical exposures that occurred in each system each week during the preceding 2 mo.

Discussion

The MCS syndrome participants who reported four different sensitizing exposures were compared, both with one another and with a general population sample, with respect to self-reported health and mental health history and status variables. The MCS syndrome participants were diverse with respect to gender and education, and prevalence of seeking help from a clinical ecologist also differed among the participants. The five questions that were of interest in this study and our discussion of each follow in the paragraphs below.

Do the Self-Reports of Diverse Samples Alleging MCS Syndrome Resemble One Another?

Despite considerable diversity in SES, education, gender, and reporting of sensitizing exposure, the general health status of the MCS syndrome participants was very similar. Generally, they considered their health status to have changed, and they rated their current health

status as fair or poor (i.e., lowest ratings on a five-point scale). Most claimed to have been disabled at some time in their lives for 3 mo or more, and the majority described limitations regarding socialization with others. On average, MCS syndrome subjects in all four groups reported being ill 59 to 78 h/wk, with 17–20 symptoms. Sickliness before the onset of MCS syndrome, a characteristic of somatization disorder, was reported only by a minority.

Although we expected congruity among diverse MCS syndrome groups with respect to reported health indices of a general nature, we were more surprised to find similarities in reports pertaining to *specific* health status measures. Reports of diagnosed autoimmune and thyroid conditions tended to be elevated in three of the four MCS syndrome groups; this finding is not explained easily by the psychosomatic or conditioning theories of MCS syndrome.

Reports of changes in tolerance for natural substances (e.g., allergens, foods), as well as for alcohol, medicines, and odors, were elevated by about the same amount in all four MCS syndrome groups, with most affected subjects reporting two or more such changes in tolerance. Such changed tolerances cannot be explained easily by the conditioning hypothesis of MCS syndrome. The assumption of this hypothesis is that MCS syndrome is caused primarily by generalizing a conditioned response from a "sensitizing exposure" to stimuli with similar odors. Allergens and foods have very different types of odors than synthetic chemicals, the most commonly reported sensitizing event. Medicines have very little odor. Whatever MCS syndrome is, our data suggest that it is not merely a change in chemical odor tolerance.

We were also surprised to find that the organ systems implicated in MCS syndrome by all four groups of subjects were quite consistent. More than 60% of the subjects in each group reported symptoms that implicated all of the following: upper and lower respiratory, gastrointestinal, musculoskeletal, central nervous system (excluding headache), and dermatologic systems; and, in addition, systemic symptoms and headache. Effects on the genitourinary and circulatory systems were reported less consistently. In contrast, genitourinary symptoms are among those associated prominently with psychosomatic illnesses.

If MCS syndrome were primarily psychosomatic, we would expect more diverse symptoms and consistent signs of illness before age 18 y. If MCS syndrome were primarily a conditioned syndrome, we would expect (a) intolerance primarily to chemicals that resembles a "sensitizing" exposure; (b) more individuality of symptomatology (i.e., resembling responses to the "sensitizing" exposure); and fewer signs of chronic illness. In our opinion, neither the psychosomatic nor conditioning model can easily explain the consistency in symptoms, changed tolerances, and recovery times from illness related to exposure and elevated prevalences of thyroid and autoimmune conditions. In summary, our data appeared less consistent with currently formulated psychogenic models than with a biogenic model.

Do Members of the General Population Report Chemical Sensitivity? Is the Chemical Sensitivity Reported in MCS Syndrome Similar to That Reported in the General Population?

The sensitivity reported by members of the general population was mild, even in a subset of subjects who appeared to be particularly sensitive. As a group, general population subjects reported that an average of four less-than-21-min exposures to chemicals functioned as incitants. General population subjects reported a mean of only one upper respiratory symptom in response to chemical exposures per week; the majority reported that they recovered from chemical exposures within 1 h. Even when we considered the 15 members of the general population who reported that six or more less-than-21-min exposures made them sick, the pattern was similar: for the majority, few symptoms were involved in the response, responses implicated the upper respiratory system, and clearing occurred within 1 h. Only one subject in the general population sample reported daily responses to chemical incitants.

In contrast, the MCS syndrome subjects reported that an average of at least 10 less-than-21-min exposures to chemicals functioned as incitants to illness. The majority of MCS syndrome subjects reported daily illness to chemical exposures, and many indicated that recovery from illness occurred during intervals that exceeded 12 h. In responses occurring weekly, the MCS syndrome subjects implicated 11 or more symptoms that affected a minimum of 5 organ systems; in addition to upper respiratory, lower respiratory, CNS, musculoskeletal, and gastrointestinal systems, systemic symptoms and headache were commonly implicated in weekly symptom reports.

The general population and MCS syndrome subjects also differed substantially in terms of changed tolerance for allergens, odors, foods, and so forth. Although most members of the general population—including the subset of 15 relatively sensitive subjects—tended to report no changes or a single change in tolerance, 90% or more of each MCS syndrome sample reported two or more changes.

These data suggest that although some level of chemical sensitivity is common in the general population, it appears very different from that reported in MCS syndrome.

Is MCS Syndrome Associated with a Particular Type of Psychiatric History or Status?

Striking psychiatric differences between the general population and the MCS syndrome subjects were not observed in this study. The similarities were pronounced. The majority of MCS syndrome and general population subjects did not report potential indicators of psychiatric illness (i.e., having been sickly as children, a familial psychiatric history, intense long-lasting stresses during childhood, and treatment for psychiatric conditions unrelated to chemical exposure). On a standardized test of affect, the majority of general popula-

tion and MCS syndrome subjects reported that they experienced a similar degree of positive affect.

A minority of MCS syndrome subjects reported elevated indicators of psychiatric disturbance, compared with general population subjects (i.e., having been sickly as children [consistent with both true sickliness and with somatizing], unusually intense stress during childhood, familial psychiatric histories, and personal psychiatric treatment for conditions unrelated to illness). These findings suggest that in a minority of MCS subjects, psychiatric variables may precede the condition. To what extent, if any, they contribute to the expression of MCS syndrome cannot be deduced from the data collected for this study.

The MCS syndrome subjects exceeded the general population subjects consistently on one psychiatric index used in this study: negative affect scores. Results of correlational analyses suggested that the differences between the groups on affect scores were more related to illness than to psychiatric history. Number of hours sick each week and number of symptoms and systems affected weekly were associated negatively with positive affect scores and were associated positively with negative affect scores, whereas positive and negative affect scores were not correlated significantly with psychiatric history or psychiatric status variables. These correlations are consistent with the hypothesis that the psychopathology observed in case studies of MCS syndrome subjects are sequelae of illness, rather than indications of preexisting psychopathology or evidence of psychogenic causation. The finding of significant correlations between indices of illness and positive and negative affect scores is consistent with the results of other studies that have shown high negative affect scores and low positive affect scores to be correlated with health complaints in college students.[55,56] The lower negative affect scores in the chlorine-dioxide-onset group, compared with the organic-solvent-onset group, may be an effect of their older age; negative affect has been shown to decrease with age.[57] Collectively, these results are supportive of the notions that chronic medical complaints (a) are burdensome, (b) augment negative affect, and (c) decrease positive affect.

Do the Reports of MCS Syndrome Patients of Clinical Ecologists Differ from Reports of Other MCS Syndrome Patients?

Because MCS syndrome is sometimes considered a figment of the clinical ecologist's imagination, we examined reports by MCS syndrome subjects who had and had not been treated by a clinical ecologist. This comparison was restricted to the telephone interview subjects who attributed their sensitivity to either a sick building, organic solvent in industry, or organophosphate pesticide. The ecologist-treated and ecologist-untreated subjects were similar in gender distribution, education, and age. We found only two statistically significant differences between mixed-onset MCS syndrome subjects who had and had not been treated by a clinical ecologist on the variables under study: (1) number of musculoskeletal symptoms attributed to chemical exposure weekly and (2) mean number of changed tolerances. Simple inspection of the data suggested that consistently larger percentages of ecologist-treated subjects (a) reported more illness and more chemical sensitivity, (b) considered their general health to be fair or poor, (c) reported having been disabled, (d) felt sick more hours each week, and (e) experienced more severe chemical sensitivity outcomes. Psychiatric events did not distinguish ecologist-treated and -untreated MCS syndrome subjects.

The chlorine-dioxide-onset MCS syndrome sample was particularly interesting because of its "naivete." None of the members of this group had been seen by a clinical ecologist. None labeled their health condition MCS syndrome, and none appeared to be aware of media coverage of the condition. Nonetheless, the self-reports of this sample were very similar to those of the ecologist-untreated mixed-onset subjects on indices of general illness, changed tolerances for odors, allergens, foods, alcohol and medicine, number of systems represented in illness episodes after chemical incitants, number of brief-duration incitants, and level of illness ensuing from brief duration incitants.

This finding of overall congruence among diverse samples of ecologist-treated and -untreated MCS syndrome subjects provides evidence that MCS syndrome is not a figment of the clinical ecologists' collective imagination.

Limitations of the Study

The selection methods for recruiting cases and controls were not ideal. The 60 MCS syndrome subjects who reported sensitizing exposures from solvents in industry, SBS, or organophosphate pesticides often originated from the referrals of interested physicians or supportive groups. It is certainly possible that group membership and physicians influenced participants' notions of the condition. This hypothesis was not supported, however, by the congruent data on the chlorine-dioxide-gas-exposed subjects, who were not members of a support group; were not being seen by a sympathetic physician; and did not possess an organizing label, "MCS syndrome." The bias inherent in interviewing volunteers from the general population sample probably worked against finding significant differences between the MCS subjects and the general population (i.e., we suspect that some of our general population subjects may have volunteered because of experiencing some degree of chemical sensitivity). Therefore, the differences that we found were all the more striking.

Using a systematic approach, the investigators found demographically different samples of subjects who attributed MCS syndrome to diverse "sensitizing" exposures to be very similar to one another in symptom presentation and health characteristics and to be very different from members of the general population. Understanding of this puzzling syndrome will be advanced greatly by further systematic research that explores the basis for the similarities that we observed.

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This study was supported, in part, by grant ES03819 from the National Institute for Environmental Health Sciences and by grant OH07090 from the National Institute of Occupational Safety and Health.

Financial assistance in support of this project was provided, in part, by the Johns Hopkins University Center for Occupational and Environmental Health.

Submitted for publication January 12, 1995; revised; accepted for publication October 5, 1995.

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