ABSTRACT

Because no information exists on the prevalence of chemical sensitivity syndromes such as multiple chemical sensitivities, a questionnaire for use in population studies was developed and tested to assess the presence or absence of chemical sensitivity. Seven hundred five individuals attending clinics answered a questionnaire asking whether each of 122 common substances caused symptoms. Results showed that patients with multiple chemical sensitivities and asthma had average total scores that were significantly different from each other and from those of each of the other diagnostic categories. Higher total scores were also reported by female patients. The instrument described here may facilitate meaningful prevalence studies of multiple chemical sensitivities. It will also allow study of chemically induced symptoms in other conditions such as asthma. (Am J Public Health. 1995;85:574-577)

Measuring Chemical Sensitivity Prevalence: A Questionnaire for Population Studies

Howard M. Kipen, MD, MPH, William Hallman, PhD, Kathie Kelly-McNeil, and Nancy Fiedler, PhD

Introduction

Individuals increasingly present for medical care with complaints of symptomatic sensitivity to common agents encountered in modern life, a syndrome commonly known as multiple chemical sensitivities.¹ There are no published, validated population estimates of the prevalence of multiple chemical sensitivities or other forms of chemical sensitivity. A widely cited clinical definition characterizes the multiple chemical sensitivities syndrome as an acquired adult onset syndrome of multiple medically unexplained symptoms triggered by exposure to low levels of common chemical agents.² The unwieldiness of this clinical definition for field surveys necessitated development of an instrument to quantify the salient characteristic of the syndrome: reported symptomaticity from exposure to substances in an individual's personal environment. On the basis of experience at our environmental and occupational health clinical center, we expected that multiple chemical sensitivities patients and, probably, those with asthma would report more symptomatic responses to chemicals than would comparison groups and that there would be a continuum of responsiveness. Therefore, we designed a questionnaire that could be understood by those without chemical sensitivities, did not require positive responders to self-identify as unusual or hypersensitive, and was robust enough to quantitate responses over a broad range, in terms of both number of positive responses and the properties of the agents. We report the development and pilot testing of such an instrument in 705 individuals.

Methods

Development of the Questionnaire

A clinical interview form used to identify environmental exposures in patients' living situations served as the substrate for this questionnaire.³ Instructions were modified to elicit symptomaticity due to exposure rather than the presence or absence of exposure. Outdated items were deleted and new ones (e.g., copy machines) added on the basis of our experience and the comments of colleagues.

The questionnaire used in this study (available from the authors on request) included 122 separate items. Representative items included aerosol deodorant, cigarette smoke, diesel exhaust, fabric softener, marker pens, new carpeting, colognes or perfumes, and recently drycleaned clothes. The following definition of symptom was provided: "A symptom means your awareness of some discomfort or bothersome change. For instance, sneezing, runny eyes, pain, swelling, nausea, or trouble concentrating are examples of symptoms. A word of caution: you may dislike something or find it very unpleasant, but if it does not cause discomfort or a change, it is NOT considered a symptom." Subjects were asked to indicate whether each substance currently caused symptoms when they were exposed to it by providing one of four possible responses: "symptoms"; "no symptoms"; "formerly symptomatic, now avoid"; or "no known exposure/don't know."

The questionnaire was scored by summing the number of responses of "symptoms" and those of "formerly symptomatic, now avoid." The resulting score represented the total number of substances that produced or had produced symptoms.

This paper was accepted December 14, 1994.

Howard M. Kipen, Kathie Kelly-McNeil, and Nancy Fiedler are with University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, Piscataway. William Hallman is with Rutgers, The State University of New Jersey, New Brunswick.

Requests for reprints should be sent to Howard M. Kipen, MD, MPH, Environmental and Occupational Health Sciences Institute, UMDNJ-Robert Wood Johnson Medical School, 681 Frelinghuysen Rd, PO Box 1179, Piscataway, NJ 08855-1179.

Subjects

Subjects were drawn primarily from patients visiting our environmental and occupational health clinical center. The largest subgroup (n = 436) was composed of those referred for routine, prescribed, surveillance, or baseline examinations because of employment as hazardous waste remediation workers (n = 364), laboratory animal handlers (n = 29), biotechnology workers (n = 28), or police officers (n = 15). Symptomatic complaints were uncommon in this group, and examinations were not scheduled on the basis of symptomaticity. The next largest subgroup (n = 219) was composed of clinical center patients referred by employers, physicians, and others with a symptomatic complaint or question related to an environmental or occupational exposure. On the basis of clinical diagnosis, these 219 individuals were further categorized as follows: (1) individuals who met our research protocol definition of multiple chemical sensitivities (n = 28) or those who presented with a clear picture of the syndrome but did not qualify for our concurrent research protocol because they lacked clear symptom onset dates, were in litigation, or were health professionals $(n = 11)^4$; (2) individuals with a diagnosis of asthma or airway hyperreactivity but not a concurrent diagnosis of multiple chemical sensitivities (n = 43); and (3)other patients who had a wide range of occupational and environmental health diagnoses (n = 137). In order to include a nonoccupational medical population, patients presenting to a general medicine clinic at another site were also recruited (n = 41).

Procedure

Ouestionnaires were included in routine intake forms at the clinical center from September 1989 to March 1992. In addition, questionnaires were distributed, in July 1990, in the waiting rooms of selected half-day general-medicine clinics to all arriving patients who were less than 65 years of age. A clinical determination of diagnosis, independent of the questionnaire and based on history, physical, and laboratory studies, was made at the clinical center. Our clinical determination of multiple chemical sensitivities does not involve any quantitative assessment or particular list of symptom-inducing agents. Questionnaire results were kept separate until a diagnosis was established. If individuals qualified for diagnoses of both asthma and multiple chemical sensitivities

TABLE 1—Substance Scores on Questionnaire, by Diagnostic Group and Sex

	Surveillance Patients (n = 436)	Occupa- tional Clinic Referrals (n = 137)	Medical Clinic Patients (n = 41)	Occupa- tional Clinic Patients with Asthma (n = 43)	Patients with Multiple Chemical Sensitivities (n = 39)
Mean age, y (SE)*** Age range, y	35 (0.5)ª 20–68	44 (1) 18–75	51 (3) ^b 25–82	42 (2) 23–65	44 (2) 28–66
Men					
No.	337	93	10	19	12
Symptom score, mean (SE)	3.8 (0.4)	8.3 (1.5)	8.7 (4.0)	18.6 (4.6)	33.8 (6.5)
Women					
No.	99	44	30	24	27
Symptom score, mean (SE)	6.7 (1.1)**	13.9 (2.4)*	12.4 (2.8)	32.8 (4.9)*	41.8 (5.5)
Positive score, % ^c	4	15	20	54	69

^aSignificantly younger than all other groups by Student Newman-Keuls test.

^bSignificantly older than all other groups by Student Newman-Keuls test.

A symptomatic score of \geq 23 was considered positive (see Results section).

*P < .05 (for difference between men and women). **P < .02 (for difference between men and women).

***P < .0001.

(n = 7), they were included with the multiple chemical sensitivities group.

No routine attempt was made to elicit a diagnosis of multiple chemical sensitivities in the surveillance and medical clinic populations; however, such a diagnosis was specifically included or excluded for all 219 symptomatic health clinical center patients. As a means of ascertaining test-retest reliability, 89 consecutive individuals who had completed the questionnaire during a 3-month period were recontacted by mail 4 weeks later and asked to complete a second identical questionnaire at home.

Statistical Analyses

Univariate analyses of variance (ANOVAs) were used to assess group differences for the numbers of substances eliciting symptoms. When the univariate ANOVA was significant, a Student Newman-Keuls test was conducted to determine intergroup differences. Scores were stratified by age and gender. Individual ttests were used to compare scores for men and women in each clinical group. Multiple linear regression analysis was used to calculate partial regression coefficients for age and gender on questionnaire score. Pearson correlations were used to assess test-retest reliability. A receiver operating curve was calculated to examine the trade-off of sensitivity vs specificity. Predictive values were calculated for the combined population.

Results

Of 705 patients approached, none refused participation, and most completed the questionnaire in under 5 minutes. Three individuals could not read English and six questionnaires with no responses to 10 or more items were excluded, leaving 696 questionnaires for analysis.

Table 1 and Figure 1 provide summary statistics for responses. Surveillance patients were significantly younger and medical patients were significantly older than were the referral, asthma, and multiple chemical sensitivities populations. There were also significantly more men in the surveillance and occupational clinic groups than in the other three groups (P < .005).

Since there were no significant differences in substance scores between the 28 multiple chemical sensitivities subjects who qualified for the clinical study and the 11 who did not, these 39 subjects were grouped together in the multiple chemical sensitivities category. Patients with multiple chemical sensitivities reported significantly more substances that elicited symptoms than other groups; those with asthma reported significantly more substances than the surveillance, referral, and medical clinic groups (P < .0001).

Women responded to a significantly greater number of substances overall and in all subgroups tested, although these

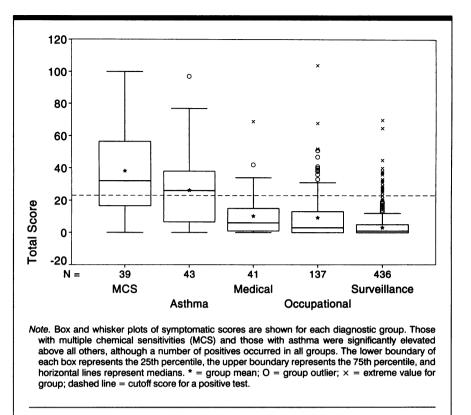


FIGURE 1—Symptomatic substance scores, by diagnostic group.

effects did not reach statistical significance in the smaller multiple chemical sensitivities and medical clinic groups.

Regression analysis was used to partial out the effects of diagnostic category from the effects of gender and age. Entering diagnostic category into the model yielded an R^2 value of .32 (F = 82.22, P < .001). Adding gender to the model improved its predictive value, yielding an R^2 of .34 (Fchange [Fch] = 17.22, P < .001). Adding age to the model raised the R^2 value to .35 (Fch = 7.213, P < .007), suggesting a significant linear relationship between age and total score independent of gender and diagnostic category.

The receiver operating curve suggested that a score of 23 or higher provided adequate sensitivity (69%) and a specificity of 89%. The positive predictive value was 26%, and the negative predictive value was 98%.

Reliability

Of 89 individuals mailed a repeat questionnaire, 56 (63%) responded. Responders consisted of 4 multiple chemical sensitivities patients (100% response), 8 patients with asthma (100% response), 5 other environmental and occupational health clinical center referral patients (56% response), and 39 of the asymptomatic surveillance patients (57% response). The group mean numbers of responses were 13.6 initially and 14.1 on retest. The correlation between initial and repeat scores was .99 (P < .0001).

Discussion

This study demonstrates that individuals with multiple chemical sensitivities report significantly more substances that cause them to become uncomfortably symptomatic than do comparison groups. Epidemiologically, the instrument described here is well suited for refinement to allow delineation of a validated surrogate of the multiple chemical sensitivities syndrome in populations under study. Those with multiple chemical sensitivities were separated from other groups in a highly significant manner. Interestingly, individuals with the syndrome responded symptomatically to fewer than half of the agents. Yet individuals in comparison groups not hypothesized to be sensitive indicated some symptomatic responses, with 4% to 20% having "high" scores characteristic of multiple chemical sensitivities. Since the syndrome represents more than just symptomatic reactivity, we do not suggest that all individuals with high scores have multiple chemical sensitivities. The rate of "high" scores (53%) among those with asthma is particularly striking. The reported sensitivity to nonspecific inhaled irritants of those with asthma has previously shown a high correlation with objective measures of disease severity.⁵ In addition, individuals with active medical complaints who do not have multiple chemical sensitivities indicate more positive responses than individuals being seen as part of routine surveillance.

We chose to examine the greater sensitivity of symptom responses rather than the more specific behavioral changes proposed by others, because behavioral changes probably do not provide a continuum of response but a dichotimization with relatively low sensitivity.6 It is recognized that, for some purposes, such a strict, specific, and less sensitive standard may be desirable, and most likely the approaches are complementary. A limitation of this study is that we are not certain as to whether some of the patients in the medical clinic and surveillance groups would qualify as having multiple chemical sensitivities. However, any true cases there would improve both specificity and predictive values. Female gender was clearly associated with higher scores independent of diagnosis, and women within an age and diagnosis subgroup (data not shown) almost invariably had higher scores than men. Intriguingly, our data suggest a somewhat greater effect of gender in the subgroups of those without multiple chemical sensitivities.

Limitations in the questionnaire's performance probably reflect limitations in an understanding of what the multiple chemical sensitivities syndrome represents. Even detailed clinical diagnoses are based on subjective criteria, and thus higher predictive values may be problematic. The literature suggests substantial overlap, at least behaviorally and psychologically, between individuals who qualify for diagnostic labels of multiple chemical sensitivities, chronic fatigue syndrome, somatization, mood, and anxiety disorder (N. Fiedler, H. M. Kipen, J. DeLuca, and K. Kelly-McNeil, unpublished data, 1994).⁷⁻⁹ Thus, a perfect discrimination may be a false grail. Nevertheless, our questionnaire should enable efficient recruitment of subjects who report the salient features of the multiple chemical sensitivities syndrome to facilitate future studies of its prevalence and causes. \Box

Acknowledgments

Funding for this paper was provided by National Institute of Environmental Health Sciences grants ES00218, ES05022, and ES05955.

We acknowledge the contributions of Carol Natarelli and Carol Roeloffs to the collection of data. The cooperation of Jeff Carson, MD, and the General Internal Medicine Clinic of Robert Wood Johnson Medical School is appreciated. Questionnaire reviews by Cliff Weisel, PhD, and Denis Schusterman, MD, were extremely helpful. Patricia Hutty's expert assistance with manuscript preparation is gratefully acknowledged.

References

- Cullen MR, Cherniack M, Rosenstock L. Occupational medicine. N Engl J Med. 1990;322:675–683.
- Cullen MR. The worker with multiple chemical sensitivities: an overview. Workers Multiple Chem Sensitivities. 1987;2:655–661.
- 3. Randolph TG, Moss RW. An Alternative Approach to Allergies. New York, NY: Harper & Row Publishers Inc; 1989.
- Fiedler N, Maccia C, Kipen H. Evaluation of chemically sensitive patients. J Occup Med. 1992;34:9529–9537.
- 5. Brooks SM, Bernstein IL, Raghuprasad PK, Maccia CA, Mieczkowski L. Assessment of

airway hyperresponsiveness in chronic stable asthma. J Allergy Clin Immunol. 1990;85:17-26.

- Simon GE, Katon WJ, Sparks PJ. Allergic to life: psychological factors in environmental illness. *Am J Psychiatry*. 1990;147:901–906.
- Black DW, Ruthe A, Goldstein RB. Environmental illness: a controlled study of 26 subjects with 20th century disease. *JAMA*. 1990;264:3166–3170.
- Straus SE, Dole JK, Wright R, Metcalfe D. Allergy and the chronic fatigue syndrome. J Allergy Clin Immunol. 1988;81:791–795.
- Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia and multiple chemical sensitivities. Arch Intern Med. 1991;154:2049–2053.

Work-Related Lung Disease Report Available from NIOSH

The National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, has released the *Work-Related Lung Disease (WoRLD) Surveillance Report, 1994.* The report summarizes surveillance data for occupational respiratory diseases such as asbestosis, coal workers' pneumoconiosis, silicosis, byssinosis, hypersensitivity pneumonitis, and occupational asthma. The report contains rate-based surveillance data, age-adjusted mortality rates, geographic distribution of occupational respiratory diseases, and proportionate mortality ratios.

Copies of the 1994 WoRLD report may be obtained by writing to the Surveillance Section, Epidemiological Investigations Branch, DRDS, NIOSH, 1095 Willowdale Rd, Morgantown, WV 26505-2845; fax (304) 285-6111.