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# CHEMICAL SENSITIVITY:

# PERSPECTIVES FROM NORTH AMERICA AND EUROPE

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## ABSTRACT

Chemical sensitivity is a controversial and perplexing illness that has been attributed to low-level chemical exposure in industrial workplaces, indoor environments, and contaminated communities, and to the use of consumer products and pharmaceuticals, first in North America and now in Europe.

This paper explores the different types of sensitivity and the relationship of low-level chemical sensitivity to them. A synopsis of the largest North American study of the condition conducted to date is provided and its findings are contrasted with observations from a recent nine-country European study of chemical sensitivity.

Between-country variations in construction and ventilation practices, choices of furnishings and floor coverings, chemical use (pesticides, fragrances, cleaners), cultural practices (e.g., time spent out-of-doors, window-opening practices), physician awareness/acceptance of the illness, health care systems, compensation practices, and environmental activism may influence the [reported] prevalence and/or recognition of chemical sensitivity.

## INTRODUCTION

"Multiple chemical sensitivity" or "chemical sensitivity" is a perplexing illness that has become the subject of widespread discussion and debate among physicians and scientists in North America. The Canadian government first explored this problem in 1985 in its Thomson Report (Thomson, 1985), and has since sponsored several workshops to help define a research agenda in this area. In the United States, chemical sensitivity has been the focus of three federally-sponsored workshops, and at least five different case

definitions for research on the condition have appeared in the medical literature. The issue has been discussed and examined by state governments (Ashford and Miller, 1989; Bascom, 1989), federal agencies (ATSDR, 1994), the National Academy of Sciences (NRC, 1992), and a number of professional organizations through workshops, conferences, and position papers (AOEC, 1992; ACP, 1989; AMA, 1992). An acrimonious debate between allergists and clinical ecologists in both the United States and Canada concerning this condition and its treatment has been ongoing for nearly a decade in professional meetings, medical journals, and courtrooms.

Recently, Professor Nicholas A. Ashford of the Massachusetts Institute of Technology assembled a team of investigators to explore low-level chemical sensitivity in Europe. While the subject is far more researched and widely known in the United States, this excursion into the European literature and assemblage of clinical observations revealed a broad spectrum of awareness of the condition: In the United Kingdom, where the condition is well known, there is divided opinion in the medical community concerning the reality of the condition, paralleling the situation in North America. On the other hand, in Greece, a country which has no medical advocates for this problem, there is no sharp split in opinion. Indeed, the condition is hardly recognized, although patients seem to present with the problem. Throughout the European countries surveyed, the team consistently found physician reports of illnesses that many academic occupational medicine practitioners in the United States would readily identify as resembling multiple chemical sensitivity.

Even in North America where the condition is widely recognized, research on chemical sensitivity is in its infancy. Most of this research has taken place in the past few years as a consequence of university-based occupational medicine physicians observing onset of the condition in a group of workers following a particular exposure event, for example, application of a pesticide or remodeling of a building (e.g., the U.S. Environmental Protection Agency headquarters building in Washington, D.C.). Prior to 1990, most of the available information on chemical sensitivity was anecdotal in nature, usually involving a single patient attributing onset of illness to a particular exposure. It was only when *groups* of individuals sharing an identifiable exposure at a particular point in time simultaneously reported the condition, that physicians in academic medicine in the United States began to wonder whether a bona fide illness might be occurring and to devise research strategies to understand the problem. When similar problems had occurred prior to 1990, they were generally attributed to psychological causes. In this regard, there is a potentially instructive parallel between chemical sensitivity and sick building syndrome (SBS). When the problem of SBS first emerged in the United States in the 1970's, the National Institute for Occupational Safety and Health (NIOSH) initially viewed it as a form of mass psychogenic illness. Now, of course, SBS is a widely recognized phenomenon, even though the specific mechanism(s) by which very low levels of mixed volatile organic chemicals cause symptoms associated with SBS remain(s) unknown.

Today, we are faced with chemical sensitivity, a similarly ill-defined problem which sometimes, but not always, seems to occur in a subset of those affected by SBS, but unlike SBS, these individuals' problems do not seem to go away when they leave the workplace or even after the building has outgassed. Multiple observers throughout the United States and Canada now have reported similar occurrences in newly constructed or remodeled buildings, with parallel observations in some European countries, as will be discussed.

This paper will explore four topics:

I. The various types of sensitivity and how low-level chemical sensitivity relates to these.

II. A synopsis of the largest North American study of chemical sensitivity conducted to date.

III. Some observations from a nine-country European study of chemical sensitivity.

IV. A comparison of European and American experiences with chemical sensitivity.

The purpose of this paper is *not* to report conclusions of these studies, or to persuade the reader to a particular view, but rather to discuss the approaches that were taken and to share a number of observations and comparisons which may illuminate the path for future studies

to elucidate the nature of this difficult condition. Science is not about "belief." Science is about "guess and test." We are in an early observational stage with respect to chemical sensitivity—as we were with SBS twenty years ago. This is a time for collecting clinical observations and formulating "guesses" or hypotheses based on these observations. The purpose of this paper is to explore some of these preliminary observations and offer some tentative hypotheses.

## I. TYPES OF SENSITIVITY

There is no question that certain chemicals evoke a hypersensitivity response. Recently, however, the term "chemical sensitivity" has been used to describe an intolerance or hyperresponsiveness to low levels of multiple, chemically-unrelated substances, often arising after an identifiable exposure, for example, to a pesticide, solvent, or sick building. Chemicals involved in most such exposures are not those classically considered to be sensitizers. This use of the term "sensitivity" clearly is distinct from its meaning in classical toxicology or in allergy. These different meanings for the term "sensitivity" are at least partially responsible for the confusion surrounding multiple chemical sensitivity.

The underlying causes of inter-individual variability in responses to chemicals include age, sex, and genetic makeup; lifestyle and behavioral factors, including nutritional and dietary factors, alcohol, tobacco and drug use; environmental factors; and preexisting disease (Ashford et al., 1990). In the classical, toxicological use of the word "sensitivity," those individuals who require relatively lower doses to induce a particular response are said to be more sensitive than those who would require relatively higher doses before experiencing the same response (Hattis et al., 1987). A hypothetical distribution of sensitivities, that is, the minimum doses necessary to cause individuals in a population to exhibit a harmful effect, is shown in curve A of Figure 1. This distribution illustrates the traditional toxicological concept of sensitivity. Health effects associated with classical chemical toxins are seen in a significant portion of the normal population as a result of exposure to a relatively "normal" or expected range of doses; the sensitive and resilient populations are found in the tails of the distribution. Of course, different toxins would have different amounts of variance and sizes of tails. For the classically sensitive person, avoidance of low-level exposures generally leads to improvement, or at least to the arrest of the development of the disease.

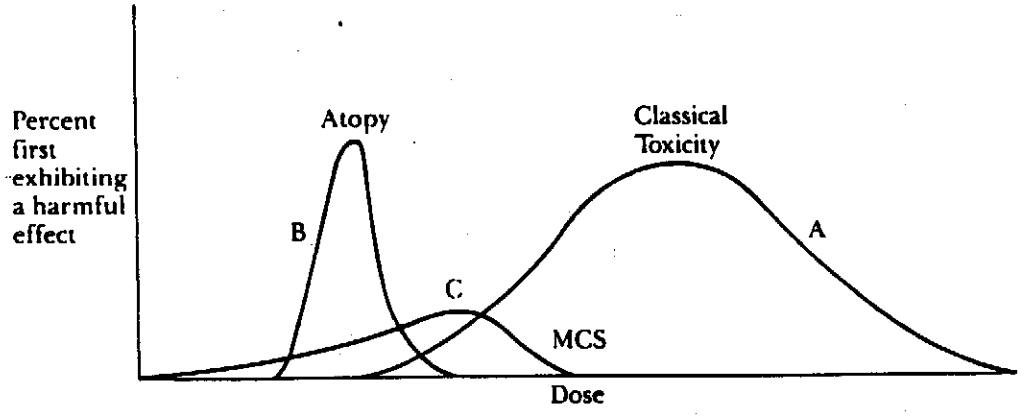


**Figure 1.** Hypothetical distribution of different types of sensitivities as a function of dose. Curve A is a sensitivity distribution for classical toxicity, e.g., to lead or a solvent. Sensitive individuals are found in the left-hand tail of the distribution. Curve B is a sensitivity distribution of atopic or allergic individuals in the population who are sensitive to an allergen, e.g., ragweed or bee venom. Curve C is a sensitivity distribution for individuals with low-level chemical sensitivities who, because they are already sensitized, subsequently respond to particular incitants, e.g., formaldehyde or phenol.

A second meaning of the word "sensitivity" appears in the context of classical IgE-mediated allergy (atopy). The atopic individual exhibits a response to an allergen, whereas non-allergic persons do not, even at the highest doses normally found in the environment. A hypothetical sensitivity distribution for an atopic effect is shown in curve B of Figure 1. Allergists include in the term "allergy" well-characterized immune responses that result from industrial exposure to certain chemicals, such as nickel or platinum salts. Many allergists refer to such responses as *chemical sensitivity*, but reserve this term for responses that have or appear to have a distinct immunological basis. They prefer to use a different term, such as *chemical intolerance*, for nonimmunological responses to chemicals.

Patients suffering from what North Americans call "multiple chemical sensitivity" (Cullen, 1987) may exhibit a third and entirely different type of sensitivity. Their health problems often (but not always) appear to involve a two-step process. The first step originates with some acute or traumatic exposure, after which the triggering of symptoms and observed sensitivities occur at very low levels of chemical exposure (the second step). The inducing chemical or substance may or may not be the same as the substances that thereafter provoke or "trigger" responses. Sometimes the inducing substance is described as "sensitizing" the individual, and the affected person is termed a "sensitized" person. Acute or traumatic exposures are not always necessary. Repeated or continuous lower-level exposures may also lead to sensitization.

These "sensitized individuals" are not those on the tails of a normal distribution. They are thought to make up a distinct subset of the population. The fact that normal persons do not experience even at higher levels of exposure those symptoms that chemically sensitive patients describe at much lower levels of exposure probably helps explain the reluctance of some physicians to believe that the problems are physical in nature. To compound the problem of physician acceptance of this illness, multiple organ systems may be affected, and multiple substances may trigger the effects. Over time, sensitivities seem to spread, in terms of both the types of triggering substances and the systems affected (Randolph, 1962).

Avoidance of the offending substances is reported to be effective but much more difficult to achieve for these patients than for classically sensitive patients because symptoms may occur at extremely low levels and the exposures are ubiquitous. Adaptation to chronic low-level exposure with consequent "masking" of symptoms is alleged to make it exceedingly difficult to discover these sensitivities and unravel the multifactorial triggering of symptoms (Ashford and Miller, 1991). A hypothetical sensitivity distribution for a single symptom for the already chemically sensitive person in response to a single substance trigger is shown in curve C of Figure 1. It should be emphasized that individuals who become chemically sensitive may have been exposed to an initial priming event that was toxic (e.g., neurotoxic) as classically defined. Conceivably, exposure to certain substances, such as formaldehyde, might elicit all three types of sensitivities, although this has not been established.

Mechanisms that have been proposed to explain this third type of chemical sensitivity range from psychological to physiological—including neurological, immunological, and biochemical (or endocrinological) (Ashford and Miller, 1991). Odor conditioning, perhaps involving psychological and physiological mechanisms, has also been suggested (Doty et al., 1988). For reviews in the North American literature on proposed mechanisms, see Ashford and Miller, 1991 and Sparks et al., 1994.

Many cases of chemical sensitivity appear to involve a two-step process (Figure 2) (Ashford and Miller, 1991):

1) *Loss of tolerance* or sensitization, also referred to as initiation, "priming," or "induction." In a sizable number of patients, symptoms appear to develop following a major exposure to any of a wide range of environmental chemicals. The "sensitizing event" may be either an acute high-level exposure, such as a chemical spill, or it may be a chronic (repeated or continuous) exposure, occurring at much lower levels, for example, a sick building. The nature of the events patients say led to their illness is extraordinarily diverse and includes exposures to pesticides, solvents, combustion products, indoor air pollutants, drugs, anesthetics, and, in a few instances, extreme stress without any obvious chemical exposure.

2) *Triggering.* Following loss of tolerance, patients report that extremely low levels of common chemicals tolerated by the majority of the population, for example, tobacco smoke, perfume, and traffic exhaust, trigger severe symptoms. Commonly, they report

that, in addition to the chemicals involved in the original exposure event, over time more and more *chemically unrelated* substances trigger symptoms. Patients refer to the latter as the "spreading phenomenon."

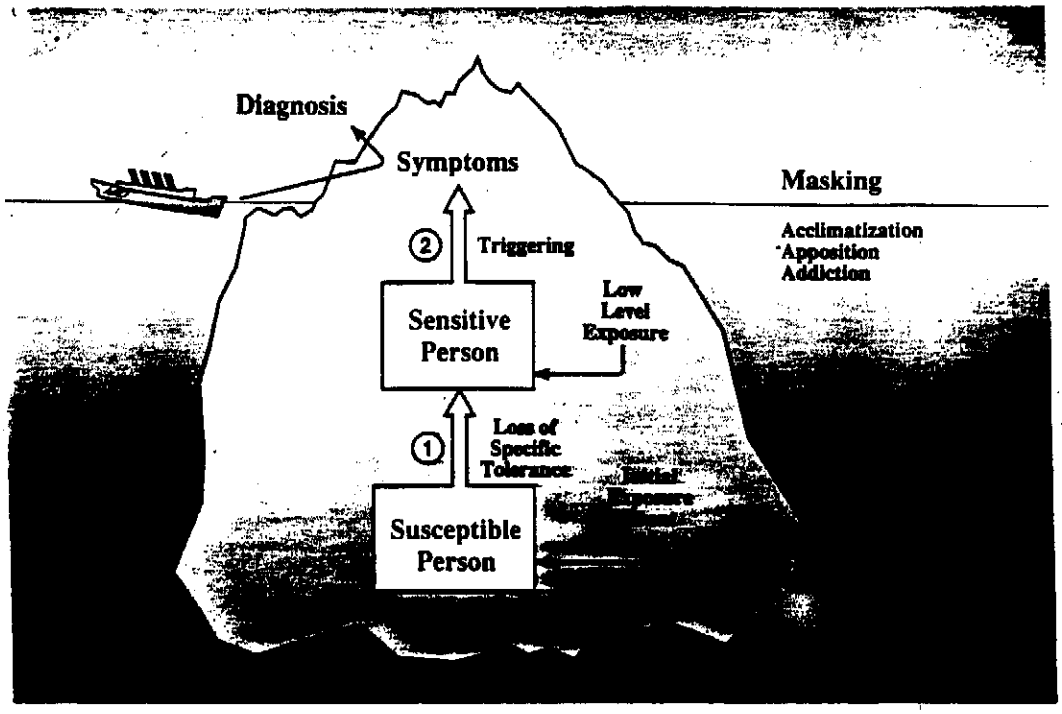


**Figure 2.** Physicians formulate a diagnosis based upon symptoms reported to them by their patients. Because of masking, i.e., acclimatization, addiction, and apposition (overlapping symptoms resulting from temporally overlapping exposures), both physicians and patients may fail to "see" that everyday, low level exposures may be triggering symptoms. Even when such triggers are recognized, an initial exposure event which may have initiated loss of specific tolerance may go unnoticed or may not be linked to the patient's illness.

This two-step process, loss of tolerance and triggering, is reminiscent of allergic sensitization. Indeed, these patients often describe themselves as being allergic. Notably, when von Pirquet first coined the word "allergy" in 1906, he defined it as "altered reactivity" of whatever origin. However, in the 1920s, following the discovery of antibodies, allergy was redefined in immunological terms over the protests of some allergists who cautioned that certain nonimmunologic forms of hypersensitivity might be excluded. The discovery of IgE in 1967 further solidified the immunologic view of allergy.

Low-level chemical sensitivity differs from classical allergies in at least one important respect: IgE formation is exquisitely specific for particular substances, e.g., ragweed or bee venom. In contrast, chemical sensitivity patients report that their sensitivities spread to chemically unrelated substances. This discrepancy has further enhanced many allergists' doubts concerning existence of the condition.

## II. CHEMICAL SENSITIVITY ATTRIBUTED TO PESTICIDE EXPOSURE VERSUS REMODELING—A NORTH AMERICAN STUDY[1]

Dr. Miller, along with Dr. Howard C. Mitzel of the University of Texas Health Science Center at San Antonio, recently completed a study in which they compared features of chemical sensitivity reported by two groups with chemically distinct but well-documented exposures preceding onset of self-reported chemical sensitivity—one group initially exposed to an organophosphate or carbamate cholinesterase-inhibiting pesticide (OP), and the other to remodeling of a building (RE). As opposed to chemical sensitivity patients with lifelong symptoms, these individuals reported becoming ill at a discrete point in time, and most were working full-time at the time of their exposure. It was felt that these two subgroups of patients should 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 chemical sensitivity patients have reported one of these exposures as initiating their condition; (2) such exposures are likely to be readily identifiable; (3) pesticide spraying and building remodeling occur at discrete times, unlike protracted exposures of industrial workers to solvents; and (4) group differences, if present, should be due to differences in potency of the chemical compounds (putatively) inducing the illness.

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

| Variable | Group: Organophosphate (n=37) | Group: Remodeling (n=75) | Total (n=112) |
|---|---|---|---|
| Age (y) | | | |
| Range | 25-63 | 25-69 | 25-69 |
| Mean | 47.7 | 47.7 | 47.7 |
| Standard deviation | 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 |
| Mean | 15.3 | 16.2 | 15.9 |
| Standard deviation | 2.9 | 3.1 | 3.1 |
| Time elapsed since exposure (y) | | | |
| Range | 2-18 | 1-31 | 1-31 |
| Mean | 7.2 | 7.9 | 7.7 |
| Standard deviation | 4.3 | 6.3 | 5.7 |
| Age at illness onset (y) | | | |
| Range | 21-61 | 11-57 | 11-61 |
| Mean | 40.5 | 39.8 | 40.0 |
| Standard deviation | 10.6 | 9.0 | 9.5 |

Individuals with self-reported chemical sensitivity were recruited via announcements in chemical sensitivity patient newsletters to ensure a sample of strictly self-identified chemical sensitivity respondents. Respondents were sent a mail-out/mail-back questionnaire which covered the exposure event, a brief medical history, and physical and

[1] Excerpted from Miller, C.S., and Mitzel, H.C., 1995, Chemical sensitivity attributed to pesticide exposure versus remodeling, *Arch Env Health* 50(2):119.

cognitive symptoms occurring since their exposure. Two hundred-three questionnaires out of 379 mailed were returned (54%). To be included in the OP group, respondents had to report having developed chemical sensitivity as a consequence of a pesticide exposure, specify the month and year of exposure, and provide the name(s) of the organophosphate or carbamate pesticide(s) to which they had been exposed. To be included in the RE group, respondents had to report having developed chemical sensitivity as a consequence of exposure to remodeling of a building and specify the year and month in which the exposure occurred or began. Those who attributed their illness to both remodeling and organophosphate exposure or did not specify a cause were not included, since the purpose was to compare two groups of chemical sensitivity patients that identified distinctly different initiating events.

Questionnaires contained items pertaining to the circumstances of the exposure, checklists for 98 common inhalants and 46 common ingestants, severity ratings for 114 symptoms, questions concerning disability and quality of life issues, and the number and types of physicians consulted.

Thirty-seven questionnaires qualified for inclusion in the OP group and 75 in the RE group. Completed surveys were received from 33 states and 3 foreign countries. Nearly 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). The average time between exposure and survey completion was 7.7 years. Average age at onset of illness was 40 years.

OP exposures occurred in the workplace in 16 cases (43%), home in 20 cases (54%), and during outdoor recreation in 1 case. Proportionately more remodeling exposures occurred at work (51 cases, 68%) versus home (24 cases, 32%). Twenty-one OP respondents implicated a single pesticide, while 16 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 neurological and cardiac symptoms as their earliest symptoms approximately twice as frequently as REs, 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% new carpeting, and 11% perfume as their most problematic exposure. Twenty-three (21%) listed more than one exposure as being "worst." Four named formaldehyde and three diesel exhaust as "worst." Only one cited cigarette smoke as most problematic. Not unexpectedly, insecticides were cited by 68% of OP respondents, while building-related exposures (carpet, paint, varnish) were cited by 38% of RE respondents as their worst exposure. None of the OP respondents rated building-related exposures as "worst," but five 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 (SD 26.0) out of 98 possible inhalants as triggering symptoms versus 63.3 (SD 21.7) for REs. Similarly, OPs reported that 14.4 (SD 13.7) out of 46 common ingestants caused symptoms versus 11.3 (SD 12.4) for REs. Differences are not statistically significant. For any given inhalant there were on average 3.4 more endorsements and for any given ingestant 7.2 more endorsements from OPs than REs.

Figure 3 compares, by group, problem inhalants cited as causing symptoms by 75% or more of the sample. These include insecticides, solvents, fragrances, fuels, and combustion products. Figure 4 illustrates that a consistently greater number of ingestants were implicated by OPs versus REs. Among the top fifteen ingestants for both groups were four associated with chemical additives: Chlorinated tap water, monosodium glutamate (MSG), food dyes, and toothpaste. Foods containing milk products (milk, cheese, and pizza) were among the fifteen most frequently cited items for both groups, as were three alcoholic beverages (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 (pizza, bread, beer, corn, and wheat) also appeared near the top of both lists.

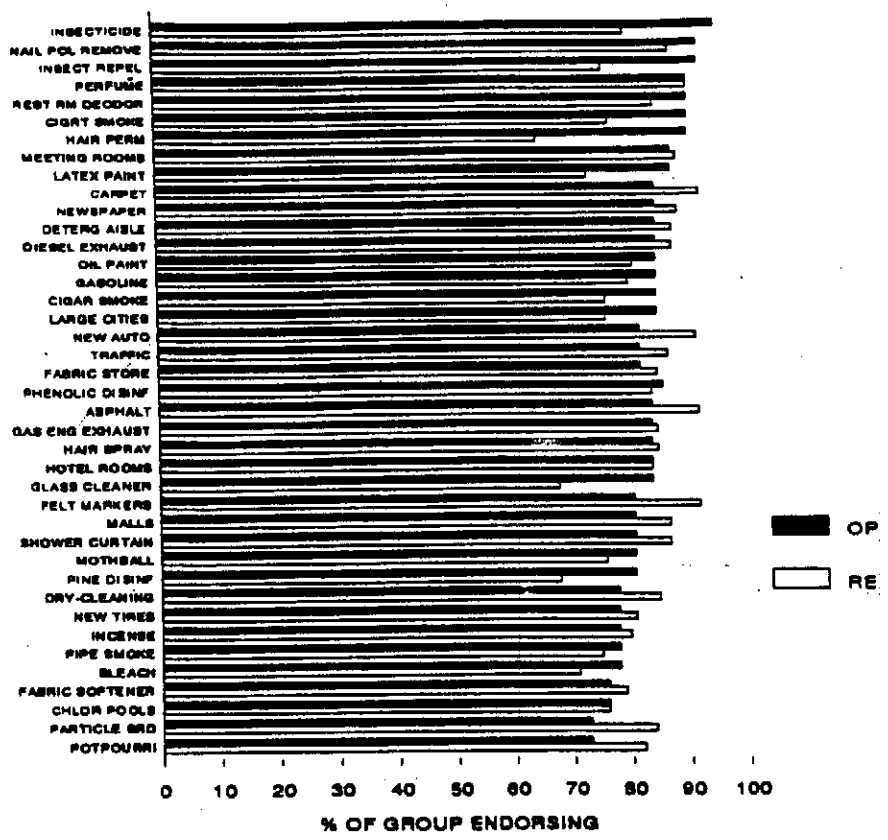


**Figure 3.** Organophosphate-exposed (OP) vs. remodeling-exposed (RE): Comparison of endorsement rates for inhalant items. Items shown were endorsed by more than 75% of the 112 survey respondents.

The correlation coefficients between the percentage of endorsements by OPs and REs shown in Figures 3 and 4 were $r = .91$ ($p<.0001$) for inhalants and $r = .85$ ($p<.0001$) for ingestants, signifying that the magnitudes of the endorsements for the two groups were quite similar. In addition, the pattern or ordering of items shown in Figures 3 and 4 is nearly identical for the two groups. The similarity in the ranked order of endorsement was examined using Kendall's coefficient of concordance. Agreement between the two groups accounted for 93% of the maximal variance in the inhalant items and 92% of the maximal variance in the ingestant items. This implies that the two groups were very similar in their patterns of endorsements for chemical and ingestant items.

Not unexpectedly, individuals who cited more inhalants as causing difficulty also cited more ingestants ($r = .64$, $p<.001$). 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 (1) on the basis of eight factored scales and (2) on the basis of symptoms heuristically selected for their discreteness and frequency in chemical sensitivity patients. The appendix lists items comprising the nine scales. An overall multivariate F-test of the eight factored scales was significantly different for the groups for exposure type ($p<.008$) but not for gender. 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 than the RE group (Table 2). Based on univariate analyses of variance, symptom severities differed significantly between OPs and REs on five of the 8 factored scales: Neuromuscular, affective, airway, gastrointestinal, and cardiac symptoms were rated as more severe by OPs than REs. Muscle-related symptoms bordered on significance, with OPs 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, while the largest inter-group difference occurred for cardiac symptoms. Presumably, cognitive symptoms cause the most difficulty for these respondents. Airway symptoms were significantly more severe for OPs than REs, a finding that was not expected because of the relatively strong association between reports of airway problems and SBS, but not low-level OP exposure.

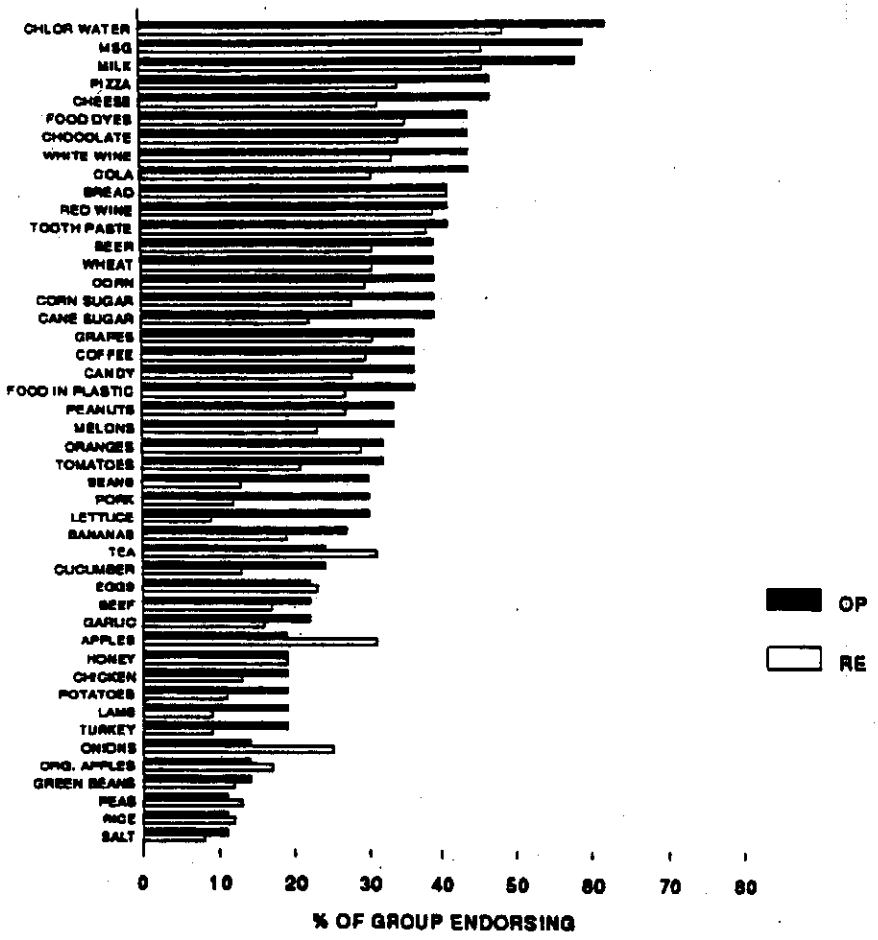


**Figure 4.** Organophosphate-exposed (OP) vs. remodeling-exposed (RE): Comparison of endorsement rates for all ingestant items.

In a separate univariate analysis of variance, OPs and REs were compared using the heuristically-derived scale incorporating fifteen symptoms commonly associated with chemical sensitivity. 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 the RE group. Further, this scale had the highest severity rating of the nine scales. It is not unexpected that symptoms reported commonly also would be among those rated as most severe. As before, symptom severity did not differ by gender.

OPs and REs reported consulting similar numbers of medical practitioners (including psychiatrists and psychologists) following their exposure: 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. 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%) with comparable frequencies. However, OP respondents were more likely to have seen a cardiologist (42% versus 19%, $p < .02$) since their exposure.

**Table 2.** Comparison of Mean (SD) Severity of Symptom Scales in Chemical Sensitivity Exposure Groups.

| Symptom Scale | Organophosphate | Remodeling | p < |
|---|---|---|---|
| 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 symptoms* | 20.8 (6.2) | 16.7 (6.0) | .003 |

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

There were no significant group or sex differences in quality of life ratings. Both OPs and REs reported major impact upon their ability to work and substantial lowering of their quality of life. At the time of their exposure, 26/37 OP respondents (70%) and 65/75 RE respondents (87%) reported working full-time (81% of total). At the time of our survey (7.7 years post-exposure on average), 84% of 90 respondents indicated they were no longer able to work full-time. Only 2 OPs (5%) and 12 REs (16%) reported working 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, changed jobs, or changed careers because of their illness (88% of OPs; 75% of REs).

Both groups felt 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 drive (56%); their ability to do housework (50%); and their decision whether to have more children (28%). Similar percentages of OPs (47%) and REs (43%) reported having been involved in litigation related to their exposure.

This survey represents the largest group of chemical sensitivity patients studied to date. Unlike prior studies, it compares two groups attributing their illness to relatively homogenous, 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 informed all participants from the outset that they would offer no medical advice during or following completion of the survey. The self-selected sample for this study is probably not representative of chemical sensitivity patients overall—advertising in patient support newsletters likely disposed the sample toward more severely ill and better "informed" respondents regarding chemical sensitivity and its manifestations. Patients who are very ill, unable to read, or less educated may be under-represented in this sample, while non-working chemical sensitivity patients with more time to read newsletters and respond to a survey may be over-represented.

The finding that pesticide-exposed respondents report similar, but much more severe symptoms than remodeling-exposed respondents is consistent with prior anecdotal observations, and supports the hypothesis that some biological mechanism is operative. If underlying depression, somatoform disorder, or other psychological factors were the primary cause of chemical sensitivity, one would expect to see no difference between the OP and RE groups in terms of symptom severity (for a more complete discussion of this point, see Miller and Mitzel, 1995). A threat to the validity of these findings remains that of sampling from preexisting groups, a difficulty always present with retrospective studies. For example, the OP group might be over-reporting symptoms relative to the RE group

because organophosphate exposure is more specific and involves a known neurotoxin, while the RE group attributes illness to building remodeling, which most people consider benign. In order to explain the findings in this study, 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. While possible, this explanation seems less parsimonious than the one offered here.

## III. A EUROPEAN STUDY OF CHEMICAL SENSITIVITY [2]

Professor Nicholas Ashford of the Massachusetts Institute of Technology, supported by three teams of investigators, recently completed a study of chemical sensitivity in Europe. The purpose of their investigation was to explore the existence and nature of chemical sensitivity in nine selected countries. To date, no systematic study of the occurrence or magnitude of chemical sensitivity has been undertaken in any European country, and there is no case definition or agreement on the criteria for diagnosis of the condition. However, it was thought that cross-country studies might yield fresh insights into the problem which appears to be influenced by a number of social and cultural factors. In the United States, where chemical sensitivity has received the most attention, some of these social and cultural factors have, to varying degrees, hindered study and understanding of this problem: Partisan biases among physicians concerning the etiology and relevance of chemical sensitivity; disagreements with respect to who should pay for diagnosis and treatment; chemical manufacturers' concerns about liability; the presence of well-informed, networked and activated patient groups; and a citizenry with an acute awareness of and concern for environmental exposures. Not all of these factors are present to the same degree in Europe. Therefore, it was felt that a cross-country investigation in Europe might provide a fresh perspective on the subject, as well as afford an opportunity to examine differences between countries in terms of their pattern and use of various chemicals, building construction and ventilation practices and differing traditions of occupational and environmental medicine.

The study was not designed to test any specific hypothesis, but to collect and compare information from several countries that might suggest hypotheses for future research. Definitive conclusions about the nature and etiology of chemical sensitivity were not sought. Following similar protocols, three teams collected data and reported findings: Denmark, Finland, Norway, Sweden, and the United Kingdom (Team A); Belgium, Germany, and the Netherlands (Team B); and Greece (Team C). A computerized literature search was undertaken and persons thought likely to have some knowledge or experience with chemical sensitivity, including ministries of environmental or public health, environmental groups, labor unions, and professional medical associations were contacted and interviewed according to general guidelines. Anecdotal clinical observations and non-peer-reviewed "gray" literature reports were included in the analysis for the additional insights and opportunities they might provide for future study.

A wide range of terms and definitions were found to be used in European countries to refer to chemical sensitivity or related "overlap" syndromes. Many of these terms closely resemble those used in North America, as depicted in Table 3. However, some are unique. For example, Germans use the novel terms "pseudoallergy" (an abnormal but non-immune reaction to a foreign substance) and "toxicopy" (occurrence of the symptoms of poisoning in the absence of a relevant poison).

The project teams formulated the following taxonomy to guide data collection and analysis. Chemical sensitivity was determined to encompass three relatively distinct categories:

1) The response of *normal* subjects to known exposures in a traditional dose-response fashion. This category includes classical allergy or other immunologically-mediated sensitivity.

2) The response of *normal* subjects to known or unknown exposures, unexplained by classical or known mechanisms. This category includes:

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[2] N. Ashford, B. Heinzow, K. Lütjen, C. Marouli, L. Mølhave, B. Mönch, S. Papadopoulos, K. Rest, D. Rosdahl, P. Siskos and E. Velonakis, 1994, Chemical Sensitivity In Selected European Countries: An Exploratory Study. The investigation was carried out through *Ergonomia, Ltd*, Athens, Greece and was co-financed by the European Union, DG-V. The findings and opinions expressed in this work, however, are those of the authors.

a) Sick building syndrome in which individuals respond to known or unknown exposures but whose symptoms resolve when they are not exposed to the building.
b) Sensitivity, such as that induced by toluene diisocyanate (TDI), which begins as specific hypersensitivity to a single agent (or class of substances) but which may evolve into non-specific hyperresponsiveness described in category 3) below.

3) The heightened, extraordinary, or unusual response of individuals to known or unknown exposures whose symptoms do not completely resolve upon removal from the exposures and/or whose "sensitivities" seem to spread to other agents. These individuals may experience:
   a) a heightened response to agents at the same exposure levels as other individuals;
   b) a response at lower levels than those that affect other individuals; and/or
   c) a response at an earlier time than that experienced by other individuals.

Table 3. Terms Related to Chemical Sensitivity Commonly Used In North America and Selected European Countries

| North American Terms | European Terms |
|---|---|
| Cerebral allergy | Allergy |
| Chemical hypersensitivity syndrome | Chronic fatigue syndrome |
| Chemically-acquired immune deficiency syndrome (chemical AIDS) | Ecological illness/disease; clinical ecology syndrome; eco-syndrome |
| Chemically-induced (or acquired) hypersusceptibility | Environmental somatization syndrome |
| Chemophobia | Environmental stress syndrome |
| Chronic fatigue syndrome | Fibromyalgia |
| Conditioned odor response | Hyperreactivity |
| Ecologic illness | Hypersensitivity |
| Environmental allergy or illness (EI) | Hypersusceptibility |
| Environmental maladaptation syndrome | Intolerance reaction/syndrome |
| Environmentally-induced illness | Multiple chemical sensitivity |
| Fibromyalgia | Non-specific hyper-responsiveness |
| Food and chemical sensitivity | Organic brain syndrome |
| Immune dysfunction or dysregulation | Organic solvent syndrome |
| Mass psychogenic illness | Painters' syndrome |
| Multiple chemical sensitivity | Pseudo-allergy |
| Multiple chemical sensitivity syndrome | Psychoorganic syndrome/organic brain syndrome |
| Multiple symptom complex | Sensitivity |
| Odor conditioning | Sick building syndrome (SBS) |
| Sick building syndrome (SBS) | Solvent intolerance |
| Somatization | Specific chemical hypersensitivity |
| Somatoform disorder | Tight building syndrome |
| The petro-chemical problem | Toxicopy |
| Total allergy syndrome | Wood preservative syndrome/ pentachlorophenol syndrome |
| Twentieth-century illness | |
| Universal allergy (or reactor) | |

The investigation focused primarily on categories 2(b) and 3) above. This focus essentially excluded traditional sick building syndrome, although the study of hypersensitive subsets of populations affected by SBS (that is, those individuals who do not recover, but who manifest persistent sensitivities) might provide useful information on chemical sensitivity.

Despite the potential usefulness of exposure or event-driven information, the research teams were unable to discover many situations or incidents that could provide useful data

relevant to chemical sensitivity as defined above. There is no paucity of events or exposures; there is simply little information available about the *outcomes* in terms of the development of chemical sensitivity. Information on the temporal features of the development and disappearance/waning of the problems would be very important, but was very difficult to obtain. A variety of factors may explain this relative lack of information. For example, the research tended to focus on physicians and the medical literature as sources of data. In general, physicians interact with individual patients and have little reason (and perhaps interest) to recognize that their patient may be part of a larger group of individuals who have experienced a common exposure or event. Second, physicians, researchers, and health authorities who are involved in events or exposure situations (e.g., a "sick building" or exposures at a particular workplace/occupation) do not likely have a focus on chemical sensitivity and thus have little reason to: 1) follow the affected individuals for long periods of time; 2) identify subsequent sensitivities; or 3) distinguish between initiating and subsequent triggering exposures. Despite this, the research teams did identify some exposure or event-driven information that may be suggestive of low-level chemical sensitivity.

The predominant loci of the alleged initiating exposures/events in this investigation were industrial, office, and domestic environments. Agricultural exposures resulting in chemical sensitivity were mentioned in several countries. Hairdressers comprised an occupational group that appeared to be affected in several countries.

A relatively small number of substances were specifically associated with the *onset* of chemical sensitivity (Table 4). The substances most often mentioned as initiators included pesticides, solvents, paints and lacquers, and formaldehyde. Repeated or continuous low-level exposure, rather than a single event, characterized most of the experience. Psychosocial stressors were also mentioned as initiating chemical sensitivity.

**Table 4.** Some Exposures Reported as Associated with the Onset of Chemical Sensitivity in Europe.

| EXPOSURE | Denmark | Sweden | Norway | Finland | Germany | Holland | Belgium | U.K. | Greece |
|---|---|---|---|---|---|---|---|---|---|
| Amalgam/mercury | | ✓ | ✓ | | ✓ | ✓ | | | |
| Anesthetic agents | | | | | | | | | ✓ |
| Carpets | | ✓ | | | | ✓ | | | |
| Diesel exhaust | ✓ | | | | | | | | |
| Formaldehyde | ✓ | | ✓ | | ✓ | | | | ✓ |
| Hairdressing chemicals | ✓ | ✓ | | | | | | | ✓ |
| Indoor climate | ✓ | ✓ | | ✓ | | | | | |
| Industrial degreasers | ✓ | | | | | | | | |
| Methyl methacrylate | | ✓ | ✓ | | | | | | |
| New/renovated buildings | | ✓ | ✓ | | ✓ | | | | |
| Organic solvents | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Paints/lacquers | ✓ | ✓ | | | | | | | ✓ |
| Pentachlorophenol/ wood preservative | | | | | ✓ | ✓ | ✓ | | |
| Pesticides | ✓ | | ✓ | | ✓ | | ✓ | ✓ | ✓ |
| Pharmaceuticals | | | ✓ | | | | | | ✓ |
| Printed material | ✓ | ✓ | | | | | | | |
| Stress/psychosocial factors | ✓ | ✓ | | | ✓ | | | ✓ | |

A unique situation was reported in Germany, where exposure to emissions from treated wood has been associated with its own clinical entity—wood preservative syndrome (or pentachlorophenol syndrome) (Schimmelpfennig, 1994). Some individuals exposed to wood (or rooms with wood) treated with pentachlorophenol (PCP) and lindane (contaminated with dioxins and furans, and dissolved in solvents at a concentration of about 5%) have experienced the multitude of symptoms commonly associated with chemical sensitivity. These include immunologic, dermatologic, neurologic, psychiatric, endocrinologic, and ophthalmologic symptoms (Huber et al., 1992). Many of the physicians surveyed in Germany reported that pentachlorophenol and wood preservatives initiated illness and described subsequent sensitivities (e.g., to odors, solvents, and, sometimes, foods) in their patients.

While these investigations were neither exhaustive nor comprehensive, nevertheless, some interesting observations can be made. Pesticides, organic solvents, formaldehyde, and stress were mentioned as causes of chemical sensitivity in many countries, while anesthetic agents were mentioned repeatedly only in Greece. Problems with hairdressing chemicals were mentioned in Denmark, Sweden, and Greece. Of course, the categories "organic solvents" and "pesticides" are overly-broad. Identification of more specific substances in these categories would be more informative. However, in many cases, more definitive information simply was not available. With the exception of pentachlorophenol, these are the same substances associated with the onset of chemical sensitivity in North America (Ashford and Miller, 1991).

A much larger number of chemically-diverse substances were reported to trigger symptoms in persons who were already alleged to be chemically sensitive (Table 5). These parallel the "triggers" frequently reported in the United States and include perfumes, detergents and cleaners, smoke, cooking odors, car exhaust, new clothing, nail polish, newspaper print, etc. Reactions to these substances were reported in each country. Symptoms frequently include: Mucous membrane irritation, gastrointestinal complaints, joint pain, respiratory complaints, such as chest tightness and rhinitis, fatigue, and central nervous system problems, such as headache, dizziness, memory loss, and difficulty with concentration. Physicians reported a higher occurrence of symptoms associated with chemical sensitivity among women in the age group 30-50 in Scandinavia, Germany, and Greece.

**Table 5.** Some Substances Reported to Trigger Symptoms in Patients with Purported Chemical Sensitivity in Europe.

| | |
|---|---|
| Air fresheners | Gasoline |
| Alcohol | Nail polish |
| Automobile exhaust | New cars |
| Carpets | Newly painted rooms |
| Cleaners/detergents | Newspapers/printed material |
| Clothing stores | Perfumes/fragrances |
| Cooking odors | Solvents |
| Cosmetics | Stress |
| Diesel | Tobacco smoke |
| Drugs/pharmaceuticals | White spirits |
| Foods | |

## IV. COMPARISON OF EUROPEAN AND NORTH AMERICAN EXPERIENCES WITH CHEMICAL SENSITIVITY

The limited data available at this time from North America and Europe suggest that chemical sensitivity is *not* a single, distinct clinical entity. Clinical presentations are extraordinarily diverse, a major reason why consensus on a case definition for the illness has been so difficult to achieve despite numerous attempts (Miller, 1994). Symptoms appear to involve any and every organ system or several systems simultaneously, although central nervous system symptoms such as fatigue, mood changes (irritability, depression), and memory and concentration difficulties predominate (Table 6). Even among persons who have shared the same initiating exposure, symptoms and severity differ markedly.

Ultimately, chemical sensitivity may be more accurately characterized as a *class* of disorders, like infectious diseases, which share a common general mechanism, yet within the class, particular members may involve different symptoms, agents, and specific mechanisms.

**Table 6.** Top 20 Symptoms Reported by Chemical Sensitivity Patients Attributing Their Illness to Pesticides (n = 37) Versus Remodeling (n = 75) (Miller, 1994).

| Symptom | Ranking | | Mean symptom severity** | |
|---|---|---|---|---|
| | Pesticide | Remodel | Pesticide | Remodel |
| Tired or lethargic* | 1 | 1 | 2.49 | 2.44 |
| Fatigue >6 months* | 2 | 3 | 2.43 | 2.10 |
| Memory difficulties* | 3 | 4 | 2.32 | 2.09 |
| Difficulty concentrating* | 4 | 2 | 2.32 | 2.17 |
| Dizziness, lightheadedness* | 5 | 6 | 2.19 | 1.85 |
| Depressed feelings* | 6 | 8 | 2.19 | 1.83 |
| Spacey* | 7 | 12 | 2.19 | 1.74 |
| Groggy* | 8 | 5 | 2.14 | 1.96 |
| Loss of motivation* | 9 | 7 | 2.11 | 1.84 |
| Tense, nervous* | 10 | 15 | 2.11 | 1.64 |
| Short of breath* | 11 | 18 | 2.11 | 1.61 |
| Irritable* | 12 | 10 | 2.03 | 1.79 |
| Problem focusing eyes | 13 | 43 | 2.03 | 1.27 |
| Chest pain | 14 | 52 | 2.00 | 1.19 |
| Muscle aches* | 15 | 11 | 2.00 | 1.79 |
| Problems digesting food | 16 | 33 | 1.97 | 1.35 |
| Joint pain* | 17 | 9 | 1.95 | 1.83 |
| Tingling fingers/toes | 18 | 59 | 1.95 | 1.12 |
| Headache* | 19 | 14 | 1.92 | 1.67 |
| Head fullness or pressure* | 20 | 19 | 1.92 | 1.60 |
| Difficulty making decisions | 21 | 13 | 1.89 | 1.69 |
| Eye irritation | 22 | 16 | 1.89 | 1.64 |
| Slowed responses | 34 | 17 | 1.72 | 1.63 |
| Nausea | 36 | 20 | 1.65 | 1.56 |

* Among top 20 symptoms in both pesticide and remodeling patients.
** Symptoms scored on 0 to 3 scale: 0 = not a problem; 1 = mild; 2 = moderate; 3 = severe.

From European and North American observations, a wide range of environmental exposures appear able to initiate the problem. While implicated chemicals are structurally diverse, certain ones appear again and again on both continents:

(1) Pesticides are frequently cited in North America and Europe, with the exception of Sweden, Finland, and the Netherlands, where indoor use of pesticides may be less frequent as a consequence of cooler temperatures and reduced insect populations. Organophosphate and carbamate pesticides are those most often reported as causing illness in the United States, but this may simply reflect the fact that these are among the agents most commonly applied. The greater symptom severity reported by chemical sensitivity patients exposed to organophosphates versus remodeling, summarized in section II of this paper, suggests that some compounds in this class might be especially potent sensitizers, at least for a subset of the population.

(2) Organic solvent exposure was cited in every European country surveyed and is commonly cited in North America. Such exposures frequently occur in the workplace and are more often chronic than acute in nature.

While there are consistent observations regarding causes of chemical sensitivity between continents, there are also notable differences, for example, the so-called "wood

preservative syndrome' associated with pentachlorophenol use in Germany (described in section III).

Although SBS is widely recognized in the Scandanavian countries where a number of internationally-known researchers are engaged in its study, instances of sick building syndrome *per se* did not generally reveal chemically sensitive subgroups. Conceivably, preoccupation with immediate effects may have obscured their discovery. Certainly, there was no indication of a large problem in those instances. Initiating experiences with carpets were noted, however. If future inquiry were to reveal that chemical sensitivity does not occur in even a subset of individuals in European SBS episodes, this finding might suggest the importance of other factors, for example, the use of wall-to-wall carpeting (common in the United States and relatively infrequent in Europe), or use of certain fragrances, air fresheners, cleaners, and/or extermination practices.

In both Europe and North America, patients report spreading of their sensitivities to an array of common exposures, including fragrances, cleaning agents, engine exhaust, alcoholic beverages, foods, and medications they formerly tolerated without difficulty. The fact that many of these individuals voluntarily forego pizza, chocolate, beer, or other favorite foods because they make them feel so ill warrants consideration—there is little secondary gain to be garnered from such forbearance. Many participants in the North American study reported that drugs, ingestants containing chemical additives (monosodium glutamate, chlorinated tap water), and food-drug combinations (alcoholic beverages or xanthine-containing foods) made them ill, a finding consistent with a hypothesis that these individuals exhibit amplified responses to pharmacologic doses of a variety of substances (Bell at al., 1992).

Generally speaking, awareness of chemical sensitivity may be greater in countries with more environmental activism, but illnesses resembling chemical sensitivity were described in every country that was studied. Clinical ecology's origins in the United States and its spread to other English-speaking nations, including Canada and the United Kingdom, no doubt have influenced the numbers of patients receiving a diagnosis of chemical sensitivity in those countries. Discord among physicians as to what constitutes appropriate diagnostic and therapeutic approaches in these countries permeates professional meetings, medical journals, and court proceedings. Where patients must "prove" a particular exposure caused their illness in order to receive worker's compensation or reimbursement for medical expenses (as in the United States where there is no national health care system), disputes between medical practitioners (who may testify on opposing sides) are most contentious.

Cultural practices may affect the prevalence of chemical sensitivity. In some European countries, the populus typically spends several hours each day out-of-doors, for example, walking to work or shopping, and windows in homes and offices may be left open part or most of the day. In contrast, on average, Americans spend 90% or more of the day indoors, often in tightly-sealed structures, where levels of certain volatile organic air contaminants can be orders of magnitude higher than out-of-doors.

Choices of building construction materials and furnishings also vary greatly between countries, including use of wall-to-wall carpeting versus washable throw rugs or no floor coverings at all; solid hardwood furnishings versus particle board or pressed wood; paint, wallpaper, and adhesive constituents; office equipment, including photocopiers and computers, etc.

Ventilation practices may be similarly diverse. Tightly-constructed buildings with little fresh make-up air built in North America since the oil embargo of the mid 1970's could be a factor that explains the apparent increase in chemical sensitivity cases over the past two decades in the United States and Canada. The experience with SBS, but not chemical sensitivity, in Scandanavia merits closer examination to determine whether the latter condition has thus far escaped attention or whether environmental or perhaps genetic or cultural differences may prevent development of the condition.

Use of chemicals also varies from country to country, in particular, pesticides, cleaners, and personal care products, including fragrances. Comparing differing rates of consumption of these products, as well as pharmaceuticals, and the incidence of chemical sensitivity among countries, could provide further clues.

## CONCLUSION

Complex questions concerning the origins and mechanisms of chemical sensitivity will not be resolved by retrospective survey studies, indeed, probably not by retrospective studies of any kind. Perhaps more informative would be prospective observations on the natural history of chemical sensitivity associated with particular *incidents* or *exposure events* rather than isolated case reports. Nevertheless, enlightening similarities and instructive differences can be gleaned from future, more directed cross-country comparisons of experiences with chemical sensitivity.

In the past five years in the United States, controversies surrounding chemical sensitivity have exploded far beyond the narrow confines of a medical debate into a national debate with far-reaching policy and regulatory implications. Most recently, a number of U.S. Persian Gulf veterans have reported multi-system health problems and new-onset intolerances to chemicals, foods, and other substances since returning from the war. Some have received a diagnosis of chemical sensitivity from private physicians and now seek medical care and compensation for the condition. Such trends in North America could be mirrored in European countries over the next few decades.

Understanding chemical sensitivity is pivotal to establishing sound environmental policy. If there is a subset of the population that is (or can become) especially sensitive to low-level chemical exposures, a strategy for protecting this subset must be found. If it were to be determined that certain chemical exposures can lead to sensitization, then perhaps these exposures could be avoided. Perhaps by preventing chemical accidents, prohibiting occupancy of buildings prior to finish-out or completion, avoiding use of certain cholinesterase-inhibiting pesticides indoors, etc., society could protect more vulnerable individuals from becoming sensitized in the first place. It would make little sense to regulate chemicals at the parts per billion level or lower if what was required was to keep people from becoming sensitized in the first place. Indeed, by understanding the true nature of chemical sensitivity and who is at risk, we may prevent unnecessary and costly overregulation of environmental exposures in the years to come.

Chemical sensitivity could be a new paradigm that has the potential to explain many chronic and costly illnesses, including fatigue, depression, headaches, and asthma, or it could continue to elude definition. Not understanding chemical sensitivity, we take an immense gamble. But knowledge will not come cheaply. Future studies on chemical sensitivity that involve blinded challenges in a controlled environment, that utilize brain imaging, state-of-the-art immunological testing or other sophisticated tests, and that compare adequate numbers of patients and controls, will be costly. Funding agencies will need to invest adequate sums to acquire answers in this area as they have for other diseases, such as breast cancer and AIDS. Until sufficient research funds become available, chemical sensitivity no doubt will continue to pit physician against physician, perplex policy makers, and impoverish patients and corporations alike.

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## APPENDIX: Reliability Estimates for Symptom Severity Scales

Listed below are items comprising the nine symptom severity scales, along with reliability coefficients for each scale.

| Neuromuscular: | 0.90 |
|---|---|
| loss of consciousness | 0.62 |
| stumbling/dragging foot | 0.74 |
| seizures | 0.30 |
| print moving/vibrating | 0.68 |
| feeling off balance | 0.74 |
| tingling in fingers/toes | 0.67 |
| double vision | 0.54 |
| muscle jerking | 0.59 |
| fainting | 0.47 |
| numbness in fingers/toes | 0.69 |
| clumsiness | 0.67 |
| problems focusing eyes | 0.67 |
| cold or blue nails/fingers | 0.41 |
| uncontrollable sleepiness | 0.52 |

| Head-related: | 0.83 |
|---|---|
| head fullness/pressure | 0.78 |
| tender face/sinuses | 0.57 |
| sinus infections | 0.35 |
| tightness in face/scalp | 0.74 |
| brain feels swollen | 0.64 |
| ringing in ears | 0.47 |
| headache | 0.45 |
| feeling groggy | 0.44 |

| Muscle-related: | 0.88 |
|---|---|
| joint pain | 0.70 |
| muscle aches | 0.73 |
| weak legs | 0.58 |
| weak arms | 0.68 |
| general stiffness | 0.69 |
| cramps in toes/legs | 0.61 |
| painful trigger points | 0.61 |

| Gastrointestinal: | 0.88 |
|---|---|
| abdominal gas | 0.81 |
| foul gas | 0.75 |
| problems digesting food | 0.71 |
| abdominal swelling/bloating | 0.70 |
| foul burping | 0.59 |
| diarrhea | 0.47 |
| abdominal pain/cramping | 0.67 |
| constipation | 0.41 |

| Cardiac: | 0.83 |
|---|---|
| heart pounding | 0.72 |
| rapid heart rate | 0.70 |
| irregular heart rate | 0.71 |
| chest discomfort | 0.51 |

| Affective: | 0.87 |
|---|---|
| feeling tense/nervous | 0.70 |
| uncontrollable crying | 0.59 |
| feeling irritable/edgy | 0.61 |
| depressed feelings | 0.66 |
| thoughts of suicide | 0.66 |
| nerves feel like vibrating | 0.53 |
| sudden rage | 0.59 |
| loss of motivation | 0.52 |
| trembling hands | 0.50 |
| insomnia | 0.47 |

| Airway: | 0.83 |
|---|---|
| cough | 0.66 |
| bronchitis | 0.52 |
| asthma or wheezing | 0.47 |
| post nasal drainage | 0.52 |
| excessive mucous production | 0.53 |
| shortness of breath | 0.40 |
| eye burning/irritation | 0.52 |
| susceptible to infections | 0.42 |
| dry eyes | 0.50 |
| enlarged/tender lymph nodes | 0.44 |
| hoarseness | 0.56 |

| Cognitive: | 0.92 |
|---|---|
| memory difficulties | 0.76 |
| problems with spelling | 0.70 |
| slowed responses | 0.83 |
| problems with arithmetic | 0.71 |
| problems with handwriting | 0.76 |
| difficulty concentrating | 0.72 |
| difficulty making decisions | 0.66 |
| speech difficulty | 0.72 |
| feeling of unreality/spacey | 0.57 |

| Most Frequent: | 0.86 |
|---|---|
| feeling tired/lethargic | 0.54 |
| memory difficulties | 0.62 |
| depressed feelings | 0.46 |
| dizziness/lightheadedness | 0.61 |
| feeling of unreality/spacey | 0.67 |
| shortness of breath | 0.42 |
| feeling irritable/edgy | 0.54 |
| problems focusing eyes | 0.59 |
| chest discomfort | 0.44 |
| loss of motivation | 0.36 |
| problems digesting food | 0.38 |
| muscle aches | 0.58 |
| tingling fingers/toes | 0.55 |
| eye burning/irritation | 0.38 |
| headache | 0.47 |