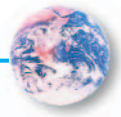
GRAND ROUNDS in Environmental Medicine



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A 37-Year-Old Mechanic with Multiple Chemical Sensitivities

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A 37-year-old heating, ventilation, and air-conditioning mechanic developed respiratory, musculoskeletal, and central nervous system symptoms associated with a variety of odorous environmental chemicals. Organic disease was not evident, but the patient was distressed by these symptoms and was at risk for becoming disabled by them. His symptoms fit broadly into the condition recognized as multiple chemical sensitivity. Multiple chemical sensitivity is a diagnostic term for a group of symptoms without demonstrated organic basis. The symptoms are characteristic of dysfunction in multiple organ systems, they increase and decrease according to exposure to low levels of chemical agents in the patient's environment, and they sometimes occur after a distinct environmental change or insult such as an industrial accident or remodeling. Although traditional medical organizations have not agreed on a definition for this syndrome, it is being increasingly recognized and makes up an increasing percentage of the caseload at occupational and environmental medicine clinics. Although there is often dispute about whether the symptoms have a functional or organic basis, an informed approach to evaluation, diagnosis, and management and a careful assessment of impairment, disability, and work relatedness are necessary. Careful exclusion of organic causes is critical, and this should be followed by a judicious approach to coping with symptoms. ***Key words*****: chemical exposure, multiple chemical sensitivity, psychology.** ***Environ Health Perspect*** **108:377–381 (2000). [Online 9 March 2000]**
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Case Presentation

A 37-year-old white male heating, ventilation, and air-conditioning mechanic was referred in 1992 for further evaluation of headaches and chest tightness. He described excellent health until a day in November 1991, when he removed a panel from an air-conditioning unit and inhaled an unknown gas or vapor, which produced face, nose, and throat irritation. He developed a cough, sore throat, and dizziness, but completed his day at work. Irritation resolved over a long weekend, but shortness of breath progressed until he saw his primary care physician 5 days later. The patient's physician determined that he had symptoms of bronchospasm and a decreased forced vital capacity; he was given bronchodilators and was told to take 2 weeks off from work. Most symptoms resolved; however, after the patient returned to work, he noted that exposure to a number of agents (including cigarette smoke, laundry detergent, ammonia, air fresheners, cleaning sprays, garden sprays, and paint fumes), whether at home or work, gave him the following immediate symptoms: a foul taste in his mouth, gagging, eye irritation, chest tightness, nonproductive cough, myalgias, and arthralgias. After the exposures he noted significant fatigue, a "spacy" feeling, and headaches. Blood work, a repeat spirometry, lung volumes, diffusing capacity, and arterial blood gas were all normal. He purchased a half-face organic vapor respirator that he wore on the job, which resulted in a reduction in negative reactions. His symptoms continued to improve despite stopping all bronchodilator and other medications, although milder systemic reactions persisted.

Past history. In 1990, while taking care of his 5-year-old and 8-month-old children when his wife was hospitalized, he developed a transient anxiety disorder, which responded to anxiolytics. He had no atopic history or history of respiratory disease. He was a nonsmoker and used alcohol infrequently.

Examination. The patient was anxious about his situation; he felt helpless to prevent his sensitivity reactions and he felt that his employer questioned the legitimacy of his condition and his high level of medical expenses. His physical examination and mental status exam were normal. Pulmonary function tests were normal, with no significant response to the bronchodilator. It was determined that formal neurobehavioral or psychiatric testing was not indicated.

We recommended a methacholine challenge, which was declined by the patient; we also recommended counseling to improve his understanding of and his response to his symptoms. We informed the patient that we did not feel he was disabled and that he could continue to work using a respirator as required. We informed his employer that he was able to use a respirator, and should be permitted to wear one on the job at his own discretion.

Discussion

There is no widely accepted definition of multiple chemical sensitivities (MCS) because there is very little agreement on what the symptoms represent. No definition has yet been generally endorsed for clinical use by a recognized body of physicians (*1,2*). Nevertheless, there is a group(s) of patients who present in a way (*3,4*) that leads us to consider this topic; in fact, it is clinically important and useful to recognize their distinctions from and overlaps with other diagnostic categories (*3*). Recognition, evaluation, and treatment can be done from within a perspective of traditional allopathic, scientifically based practice.

MCS is most useful to distinguish persons with medically unexplained symptoms (e.g., fatigue, headache, concentration problems, and respiratory symptoms) when those symptoms are attributed to and are triggered by environmental exposures, as there is no other specific diagnostic label to describe such individuals. Many advocates of the concept of chemical sensitivity, such as the group of environmental physicians formerly

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called "clinical ecologists," espouse a broader definition, which essentially includes all diseases judged by a clinician to be caused or aggravated by chemical exposure (*5*).

It is important to separate a consideration of causes of this clinical picture from a simple question of whether individuals exist who have triggering of otherwise unexplained symptoms. Cullen's effort to define MCS (*6*), primarily for research purposes, is now the most widely used clinical definition for this condition. Objective physiologic or pathologic correlates have not been established. This case definition, if used as stated, is intended to allow physicians to distinguish MCS from other collections of similar commonly experienced symptoms. It relies on four salient characteristics:

- MCS is acquired in relation to some documentable environmental exposure that may initially have produced a demonstrable toxic effect. This aspect serves to exclude patients with long-standing health problems who later attribute certain symptoms to chemical exposure
- Symptoms involve more than one organ system, and recur and abate in response to predictable environmental stimuli. This provides the salient feature of multiple symptoms and multiple chemicals
- Symptoms are elicited by exposures to chemicals that are demonstrable but very low. The exposures eliciting symptoms may be substantially below the typical exposures known to cause toxic or irritant health effects in humans and typically involve chemicals of widely varied structural classes and different mechanisms of toxicologic action
- The manifestations of MCS are subjective. There is no widely available (clinical) test of organ system function that can explain the symptoms, and there is no objective evidence of explanatory organ system damage or dysfunction (*6*).

An alternative and clinically useful definition (*7*) took an operational approach: anyone who endorsed at least three of four items relecting lifestyle changes because of chemicals could be considered to have MCS. There is a reasonably high level of agreement between individuals who, upon clinical evaluation, meet the Cullen criteria (*6*) and those who endorse three or four of these behavioral items (*8*).

A major practical limitation of all available definitions of MCS is the subjectivity and nonspecificity of the available information regarding the predictable and demonstrable attributes of the exposure–symptom relationship. Whereas this relationship might be most meaningfully established by double-blinded and controlled exposure challenge testing, it is usually characterized solely on the basis of the patient's report. Other proposed definitions, and even other names, have been published, but none has been validated, subjected to substantial review, or achieved widespread acknowledgment (*9,10*).

Classification and natural history. Although there is no clear definition for MCS, the available literature suggests useful guides for individual patients, especially in terms of comorbidity and severity. A key consideration is whether or not there is a diagnosable psychiatric condition. Higher rates of diagnosable psychiatric conditions exist when MCS subjects have been compared to controls (*11*). Although rates are not necessarily higher than for other groups of patients with unexplained symptoms, rates of diagnosable psychiatric conditions may reach 50%, sometimes 70%, which is far higher than in the general population. There is also a high correlation between the presence of psychiatric comorbidity and whether the MCS is reported to have a clear, defining onset, as in the first Cullen criterion (lower psychiatric comorbidity), or whether it developed gradually without a sudden overexposure incident (higher psychiatric comorbidity) (*8*).

Patients frequently attribute changes in severity of symptoms to control or lack of exposure, but this has not been carefully studied. One study suggests that self-reported reduction of exposure is an important determinant of well-being, but it was not associated with reduction in actual reported symptoms (*12*). MCS is not known to be progressive in terms of measurable physical dysfunction or development of medical complications. Symptomatic reactions to chemicals tend to persist, although some individuals (such as the patient in this case) learn to cope with such symptoms and achieve relatively normal levels of function, remaining employed.

Epidemiology. No population-based studies have been published on the prevalence or incidence of MCS according to the definitions used here. Neverthess, the prevalence of self-reported sensitivity to chemicals (15%) and the prevalence of self-reported receipt of a physician diagnosis of MCS (6%) has now been reported in a rigorous epidemiologic survey (*4*), confirming earlier reports of high rates of chemical sensitivity symptoms (*13,14*). Studies have documented the presence of chemical sensitivity symptoms in patients with fibromyalgia and chronic fatigue syndrome (CFS) (*16*), Gulf War Illness (*15*), as well as a high prevalence of CFS symptoms in those recruited as having MCS (*8,*).

Etiologic theories. There are a multitude of explanatory mechanisms, most based on fairly limited observations. For simplification, these mechanisms may be grouped into four categories: *a*) pathologic and toxicologic, *b*) psychophysiologic, *c*) psychiatric, and *d*) belief systems. In many individuals more than one of these will seem to be operative; in fact, the idea of complete distinctions between psychophysiologic, pathologic, and psychiatric mechanisms may at times be artificial. The relationship between MCS and environmental chemical exposures has generally not been shown to meet benchmarks for causality in terms of epidemiologic data, dose response, and established mechanisms (*17*).

Pathologic and toxicologic theories. Theories of toxicity or organ damage attributable to immunologic or other dysfunctions remain unsupported (*11,17*). In two studies investigating the olfactory system in MCS patients, it was determined that MCS subjects do not detect odors at lower thresholds, although they may respond more markedly once odors are detected (*11,18*). The relationship of this finding to other reports of nasal pathology and increased nasal resistance is unexplored, and the pathologic findings require confirmation with controlled studies (*18–21*).

Psychophysiologic and psychiatric theories. Some investigators have proposed and have begun to demonstrate that a behaviorally conditioned response to odor could explain some MCS cases (*22–24*). Such a severe chemical exposure may act as an unconditioned stimulus, producing one trial learning of a conditioned psychologic response. For example, exposure to glutaraldehyde, a known irritant, is accompanied by an odor that could act as the conditioned stimulus. The odor, as the conditioned stimulus, then becomes associated with the irritative symptoms of glutaraldehyde, the unconditioned stimulus. Thereafter, the odor (or perhaps other similar odors), paired with lower exposure concentrations, could produce similar symptoms at levels of exposure below a threshold for causing mucosal irritation. On the other hand, an odor may serve as a discriminative stimulus rather than a conditioned stimulus. Some recent data from our laboratory show a dose response in MCS subjects for reported trigeminal symptoms of nasal irritation following exposure to odorants (*25*). This is inconsistent with the conditioned response explanation shown above.

Many physical and emotional stressors produce hyperventilation, as do a variety of pulmonary, renal, cardiovascular, and other disease states. Symptoms of hyperventilation can include some common symptoms of MCS such as headache, dyspnea, palpitations, tremor, panic, pain, and even seizure activity (*26*). There are currently no data on the association of hyperventilation with MCS symptoms, but this is one mechanism for production of symptoms in multiple systems.

Some intriguing case reports have associated organic solvents with panic attacks (*22,27,28*). The substantial importance of panic attacks in some cases of otherwise unexplained symptoms has been recently reviewed by Smoller et al. (*29*). For cases in which one or more chemical odors trigger either typical or limited panic attacks, the designation of "odor-triggered panic attacks or panic disorder" has been proposed (*30*). Other theories of causation of MCS include more complex biologic mechanisms for the conditioning model described above, relying upon interaction between the olfactory, nervous, and endocrine systems to explain odor-triggered symptoms (*17,31*).

Belief systems. In some individuals, MCS is characterized by a belief system (*17*); this is consistent with the increasing concern of the public regarding environmental pollution and health effects of exposure to man-made chemicals (*32,33*). The mechanism by which a set of beliefs might lead to symptoms is not clear, but it is easy to understand how beliefs could affect attribution if symptoms were already present.

Diagnostic evaluation. In clinical practice there may be some confusion between acute and chronic occupational or environmental illnesses associated with objective signs of disease and MCS, although some patients may have both.

From a practical point of view, differential diagnostic problems occur in two settings. The first, as demonstrated with our patient, is when early in the course of the MCS, it is difficult to distinguish the syndrome from a defined occupational disease such as occupational asthma. Later in the course of MCS, diagnosis may be complicated by the development of more severe anxiety and depression as a consequence of having a chronic condition, although this has not been studied. Subsequent exaggeration of psychiatric symptomatology may lead such symptoms to overshadow chemically triggered symptoms. We should be careful to avoid inappropriate diagnosis of MCS in patients who have well-defined toxic or allergic disease or irritant injury (e.g., asthma, lead intoxication, or allergic alveolitis); an incorrect diagnosis could prevent patients from receiving appropriate specific therapy.

Medical history and examination. The keys to diagnosis and clinical management of the individual presenting with suspected or previously diagnosed MCS include a detailed exposure history and a comprehensive medical and psychosocial evaluation.

The baseline medical and psychiatric status of the patient before development of the presenting symptoms should be established. The patient's medical history should include current and previous illnesses, diagnostic evaluations and treatments, and the possibility of a long history of unexplained physical symptoms or excessive medical care. Patients presenting with MCS may have long histories of similar symptoms, but chemical attribution may be lacking (*34*).

The exposure history is fundamental for an understanding of potential causal factors. In addition to establishing the history of symptoms triggered by exposures that are tolerated by most people, it is important to determine the circumstances of the initiating exposure. The exclusion of traditional toxic conditions, particularly irritant-induced asthma and toxic encephalopathy, and the consideration of the toxin-related anxiety syndromes such as post-traumatic stress disorder and toxin-induced panic attacks must be addressed. It must be determined whether the exposure was substantially unusual, such as an accident, the evacuation of a building, or another circumstance, raising the possibility of both chemical damage and psychologic trauma. The physician should estimate concentration and duration of exposures to allow for the determination of the probability that the symptoms are attributable to a known toxic or irritant effect.

Physical examinations are performed largely to identify other medical conditions.

Diagnostic testing. The evaluating and the treating physician must be wary about excessive ordering as well as the misinterpretation of diagnostic tests because these may reinforce a detrimental pattern of illness behavior (*35*). As with other types of unexplained symptoms, the primary physician should function as gate keeper and should order diagnostic tests primarily to identify the presence of other environmental or nonenvironmental illness in the differential. There is currently no test established to actually diagnose MCS. Short-term removal from exposure to the environmental chemical of concern may have diagnostic value; this short-term removal may also have palliative value while interventions that are more suitable for long-term case management are arranged.

Many tests that have been asserted to characterize MCS patients fall into the general realm of neurophysiology or neuroimaging. Although no test of central nervous system effects has been validated to confirm the presence of MCS (*36*), preliminary information indicates that there may be statistically significant but not clinically visable changes in brain single photon emission computed tomography (SPECT) images in individuals with MCS as compared to controls (*37*).

There is a widespread assertion that MCS could be characterized by abnormalities of immune system activation, lymphocyte subtypes, and autoantibodies, which has been studied in a limited number of controlled trials. No form of immunologic testing has been shown to effectively diagnose either exposure to specific chemicals or illness due to exposure in patients with MCS (*11*).

Neuropsychologic testing is dependent on patient cooperation and may be useful to rule out other conditions in the differential diagnosis. At present, neuropsychologic testing does not reveal consistent or specific findings in MCS patients that can be used for diagnosis (*8,38*).

Definitive research on controlled challenge procedures using appropriate controls is necessary before these procedures can be recommended as tools for diagnosis (*39–41*).

Psychiatric evaluation. Psychiatric evaluation may be appropriate for some patients diagnosed with MCS, given the high prevalence of coexisting or preexisting psychiatric disorders in these patients. Unfortunately, many patients given a diagnosis of MCS resist the idea that psychologic factors may play any etiologic role at all in their distress; however, this should not necessarily be interpreted that the patient has a primary psychiatric illness. The stigma placed on psychiatric disorders in our society probably plays a major role in the tendency to somatize. The adamant rejection of psychologic factors in symptom formation and expression by MCS patients is a challenge for the physician, who must establish a workable strategy for approaching this issue that is both sensitive to the patient's feelings and effective in exploring possible emotional contributors to the syndrome (*35*). For psychiatric evaluation to be most useful, it is necessary to ensure that the clinician is familiar with the subtle nature of the toxicologic controversies in MCS, as discussed above.

Clinical management. Very little is known about the proper treatment of MCS. No therapy has been subjected to controlled clinical trials to confirm short- or long-term efficacy with these patients. Approaches to treatment have paralleled etiologic theories, and these have recently been reviewed (*42*). Clinical ecologists and other practitioners who believe that MCS is attributable to immune dysfunction caused by elevated body burdens of xenobiotics champion avoidance of chemical exposure, dietary supplements, antioxidants, chelation therapies, and the use of saunas (*17,42,43*). Many patients do a great deal of independent research about their conditions, and some find support (including information and misinformation) from self-help groups, many of which are on the Internet.

Practitioners who have a more psychologic view of MCS have tried to apply pharmacologic and behavioral techniques (*44*). We have often not found it helpful to directly confront or debate whether chemicals could or could not cause the patient's symptoms.

Rather, as for any organic illness with a behavioral component (e.g., heart disease), we prefer to focus on coping strategies that will improve the quality of life and prevent disability. Specifically, we work collaboratively with the patient to develop prudent avoidance of those substances that cause the most symptoms, and practical guidance (e.g., ventilation, work breaks) to minimize exposure when the patient needs to work or function. Although radical avoidance is inimical to enhancement of function at work, the ability to use judicious avoidance for control of regular and severe symptoms may foster a therapeutic relationship. Balancing the benefits of any avoidance measures with the potential risks of a spiraling pattern of progressively severe environmental restrictions and loss of employment is the ultimate challenge of the MCS patient who is still employed.

We also work with patients to identify symptoms associated with fear or anxiety about exposure. We then use relaxation methods with or without biofeedback to address the anxiety responses. Overall, treatment is behavioral in nature, making use of both cognitive behavioral and physical relaxation techniques. Once litigation or a worker's compensation claim has arisen, the prognosis for behavioral approaches to treatment is less optimistic. An approach to thinking through litigation issues according to the magnitude of the initiating stimulus has been previously outlined (*44*).

Hyperventilation should be identified and approached through breathing control, stress management, and education. More severe symptoms of depression or anxiety should be medically managed with psychotropics. Based on our experience, if psychiatric medications are used, they must be given at very low doses and then titrated up to give these patients time to adjust to potential side effects, which are anecdotally reported to be more problematic in these individuals and others with medically unexplained physical symptoms (*48*).

Cognitive behavioral therapy for medically unexplained symptoms, not specifically including MCS, has been shown to be effective in two randomized trials, with a return-to-work rate of up to 70% in one study (*46,47*). Guglielmi et al. (*48*) identified three MCS patients who met criteria for simple phobia and who were, at least initially, successfully treated by an intensive desensitization program consisting of biofeedback-assisted relaxation training, *in vivo* exposure to offending chemicals, and cognitive restructuring procedures.

Odors and exposure to volatile organic compounds in the workplace and home, which are perceived as irritating or noxious by the symptomatic person, should be reduced and controlled as much as possible.

Conclusions

Although it is often disputed whether the symptoms of MCS have a functional or organic basis, it is necessary to have an informed approach to evaluation, diagnosis, and management and a careful assessment of impairment, disability, and work-relatedness. It is optimal to have an integrated medical and psychologic approach with careful exclusion of organic causes, followed by a judicious approach to coping. Those patients who, after supportive counseling, continue to deny that stress or psychologic factors may play any role at all in their symptoms probably cannot be helped by any of the above behaviorally based therapies. The patient who we described sought counseling at another facility near his home and remained at his job, although various sensitivity reactions continue.

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