# Multiple Chemical Sensitivity Syndrome: A Clinical Perspective

## II. Evaluation, Diagnostic Testing, Treatment, and Social Considerations

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*Multiple chemical sensitivity syndrome (MCS) does not appear to fit established principles of toxicology. Social, political, and economic forces are demanding that MCS be defined medically, even though scientific studies have failed as yet to identify pathogenic mechanisms for the condition or any objective diagnostic criteria. Consequently, a working definition of MCS can only rely on a person's subjective symptoms of distress and attribution to environmental exposures rather than currently measurable objective evidence of disease. Nevertheless, patients labeled with MCS are clearly distressed and many are functionally disabled. Without reconciling the different theories of etiology of MCS discussed in Part I of this report, and recognizing that the cause of the syndrome may be multifactorial, strategies are proposed for clinical evaluation and management of patients with MCS using a biopsychosocial model of illness. The social implications of this illness are also discussed.*

Multiple chemical sensitivity syndrome (MCS) has become a diagnosis increasingly assigned to patients with a variety of symptoms attributed to various environmental chemicals. To distinguish such patients from those reporting similar symptoms (fatigue, malaise, dizziness headache, lack of concentration, memory loss, and "spaciness") but labeled with other diagnoses such as chronic fatigue syndrome, an attempt has been made to define MCS in terms of attribution of symptoms to environmental exposures.

Cullen's[1] attempt to define MCS, primarily for research purposes, is now the most widely used clinical definition for this condition and states: "MCS syndrome is an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects. No single widely accepted test of physiologic function can be shown to correlate with symptoms" (Table 1).[1]

Despite the absence of "objective" findings of disease to explain symptoms in patients diagnosed with MCS, *the syndrome may be severely distressing and functionally disabling*, even as patients increasingly avoid universally present chemical exposures.

There are four major views about the etiology of this syndrome, although more than one of these proposed mechanisms are likely to be operating in different cases. These theories of etiology were discussed in Part I of this study. There is overlap among

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**TABLE 1**
Cullen's Definition of Multiple Chemical Sensitivity Syndrome*

1. Acquired in relation to documentable environmental exposure(s), insult(s), or illness(es).
2. Symptoms involve more than one organ system.
3. Symptoms recur and abate in response to predictable stimuli.
4. Symptoms elicited by exposure to chemicals or diverse structural classes and toxicologic modes of action.
5. Symptoms are elicited by exposures that are demonstrable (albeit of low level).
6. Exposures that elicit symptoms must be very low (several standard deviations below levels known to cause adverse human responses).
7. No single widely available text of organ system function can explain symptoms.

* From ref 1.

the views of pathogenesis. For example, is possible that preexisting or concurrent psychiatric illness, particular health belief models, and psychologic stress may produce a vulnerable group of people who then develop a sensitivity to odors or low-level chemical irritants that occurs as a result of one or more of the physiologic mechanisms discussed in Part I.

Because none of current views of etiology of MCS is universally accepted on the basis of substantial scientific evidence, dogmatic adherence to one of them is unwise as a basis for managing individual patients with an MCS diagnosis. Furthermore, one could postulate still other theories or some combination of them. In the face of uncertainty regarding the etiology of symptoms in an individual patient, it is prudent for the clinician not to substitute his or her own beliefs about etiology for the patient's observations. *The fact that there is no agreement upon any one etiology for most patients with MCS does not prevent clinicians from helping affected patients with their symptoms.*

Clinicians with different views about the pathogenesis of MCS still may agree on clinical management programs aimed at symptom control and improved functional ability rather than "cure" of MCS. Further research is needed to refine such strategies, to develop new and more effective approaches, and to address the issue of prevention.

## Diagnostic Evaluation

### The History and Physical 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 of the patient. It is critical to rule out the presence of a physical disease caused by defined occupational or environmental factors. *A pitfall to avoid* is to diagnose inappropriately those patients with well-defined toxic or allergic disease or irritant injury, such as asthma, lead intoxication, or allergic alveolitis with MCS, and thus possibly fail to provide appropriate treatment. There also may be some overlap of these conditions and MCS syndrome.

The clinical evaluation of MCS is challenging enough for the occupational and environmental physician specialist with formal training and experience in exposure assessment and clinical toxicology, and therefore may be extremely difficult for the primary care physician who usually is not trained to evaluate the clinical significance of the patient's exposure history. In most cases, consultation with a physician who is board-certified in occupational and environmental medicine should be obtained. The evaluation of a patient presenting with MCS may take several hours and it is necessary to allot sufficient time, even if inadequately reimbursed.

Industrial hygiene data regarding the patient's exposures should be obtained whenever possible. If the exposure occurred in the workplace, the relevant Material Safety Data Sheets should be obtained from the patient or employer. Many chemicals are well-established potential causes of the symptoms that MCS patients describe (ie, toluene diisocyanate and chest tightness, or headache and nausea from exposure to lead or organic solvents). Clearly, it is the physician's job to *estimate the dose* of environmental exposure, and to determine the probability that a patient's symptoms are due to a known toxic or irritant effect of exposure.

Some clinicians have suggested having the patient keep a symptom diary throughout the day, along with information regarding activities and environmental exposures. If, however, culturally and physician-shaped belief systems or misdiagnosed psychiatric or physical illness are operative, this could tend to reinforce the patient's perception of the relationship between symptoms and chemical exposures rather than other potential psychologic stressors, for example. Thus this approach is probably not appropriate for all MCS patients, and there is a fine line between urging the patient to pay attention to the effect of various environmental exposures on their symptoms and promoting symptom attribution by suggestion.

It is essential that the physician rule out other nonenvironmental illness or disease in the differential diagnosis. The physician should take a detailed medical history regarding current and previous illnesses, previous diagnostic evaluations and treatments, and a possible historical pattern of many unexplained physical symptoms with onset early in adulthood or frequent utilization of medical care. Access to prior medical and psychiatric records and their thorough review is particularly important. Physical examination and laboratory evaluation should be sufficiently comprehensive to establish or rule out all other occupational and nonoccupational disease conditions in the differential diagnosis.

Psychiatric evaluation of the patient diagnosed with MCS may be appropriate for some persons, given the high prevalence of coexisting or preexisting psychiatric disorders in these patients. Unfortunately, most 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 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 still effective in exploring possible emotional contributors to the syndrome. Rather than labeling the patient with a psychiatric diagnosis, if the physician merely queries the patient as to the effect the illness has had on lifestyle and mood, most patients report and discuss symptoms of depression and anxiety freely.

Trial removal from the environmental chemical exposure of concern for a short time may have diagnostic value; short-term removal may also have palliative value while arranging interventions that are more suitable for long-term case management. If the exposure of concern is in the workplace, the physician and employer should encourage the patient to continue to work as much as possible but in another place, such as at home. Whether or not prolonged removal from exposure situations ameliorates the symptoms of MCS has not been studied adequately.

These recommendations are summarized in Table 2.

**TABLE 2**
Diagnostic Evaluation for Multiple Chemical Sensitivity

A. History
- Detailed exposure history (workplace and other environmental exposures)
- Industrial hygiene data (Material Safety Data Sheets, results of exposure monitoring, etc.)
- Current and past medical illnesses, and results of previous diagnostic work-ups and treatments
- Review of prior medical records

B. Physical examination
- Rule out other illnesses in the differential diagnosis

C. Consultation
- Occupational and environmental medicine specialist
- Psychiatrist
- Other specialists as appropriate to rule out other medical conditions in the differential diagnosis

D. Other
- Symptom diary
- Short-term removal from exposure

## Diagnostic Testing in MCS

Because there is *no* established and widely available test to use to diagnose MCS, the physician must be extremely cautious about excessive or inappropriate testing or the misinterpretation of such tests. This may merely reinforce a detrimental pattern of illness behavior.

At this time, it is important to separate the issue of whether MCS exists from the issue of appropriate diagnostic testing in these patients.

Diagnostic testing in patients expressing symptoms of MCS is necessary to rule out the presence of other environmental or nonenvironmental illness or treatable disease conditions in the differential diagnosis. For example, if the patient has prominent respiratory tract complaints, appropriate pulmonary function tests are needed, as a minimum, to rule out the presence of reactive airway disease. Biological monitoring might be used in some cases to assess exposure to specific chemical substances where there is known to be good correlation of the specific exposure with measured blood or urine levels and health effect (e.g., heavy metals). However, results of diagnostic tests should not be presumed to explain multiorgan symptoms. For example, if pulmonary function tests show airway reactivity, this does not explain central nervous system, gastrointestinal, dermal, visual or other organ system complaints. In addition, subtle variations in physiologic testing may be hard to distinguish from normal variability in a heterogeneous population, and caution is necessary so as not to overinterpret results as an explanation for the patient's symptoms.

Definitive research on controlled challenge procedures is necessary before they can be recommended as useful tools for diagnosis.[2,3] The clinical use of environmental challenge units for diagnosing MCS remains controversial. The problems with this approach are that we usually do not know the actual level of environmental exposure causing symptoms, testing of substances having distinct odors or irritant properties cannot be done in a blinded fashion, and proper controls and objective measures of response that are relevant to the patient's symptoms are unavailable. This approach to diagnosis is currently unreliable. Successfully blinded chemical challenges have reportedly resulted in both high false-positive and false-negative rates of response.[2,4,5]

Quantitative EEG, brain electrical activity mapping, evoked potentials, as well as positron emission tomography and single photon emission computed tomography scans, which measure regional blood flow or brain metabolic function, are procedures that have sometimes been misapplied in an effort to provide "objective findings" for patients with MCS. Any technique for investigating the central nervous system effects of low-level exposure to chemical substances should take place only in a research setting with proper controls to validate its clinical use as a diagnostic tool to confirm the presence of MCS.[6,7]

At present, no form of immunologic testing has been shown to be diagnostic of either exposure to specific chemicals or illness due to exposure in patients with MCS.[8-21] For example, low titers of antibodies to formaldehyde have not been correlated either with exposure or with disease due to exposure to formaldehyde.[9-12] Nontraditional tests such as provocation-neutralization show no correlation with exposure or disease resulting from specific chemicals,[13-15] and cannot be justified because of lack of evidence of symptom provocation by subneutralizing concentrations.[13]

Some commercial laboratories offer measurements of part per billion concentrations of various organic solvents or other exogenous chemicals in blood. Often the chemicals are reported to be present at concentrations in the range of error noise of mass spectrometer analysis and have no clinical relevance. Unfortunately, some physicians have misinterpreted such measures as evidence of unusual chemical exposure and/or toxicity or as an explanation for the symptoms of MCS. Clinical misuse and misinterpretation of such testing is to be avoided.

Neuropsychologic testing is dependent on patient cooperation and might be useful to rule out other conditions in the differential diagnosis, but currently does not reveal consistent or specific findings in MCS patients that may be used for diagnosis of this condition.

These recommendations are summarized in Table 3.

*Reinforcement of illness behavior by unjustifiably giving a patient the diagnosis of a disease due to toxic, immunologic, or neurologic mechanisms based on diagnostic testing that is clinically unsubstantiated or invalid may actually perpetuate illness, prolong disability, and delay effective therapy.*

## Treatment Recommendations

*Even if the etiologies of the symptoms in patients diagnosed with MCS are controversial and unknown in most patients, these patients can still be helped with their symptoms.* Haller[16] has demonstrated some success with a small series of patients using supportive therapy. Her experience is corroborated by that of several of the reviewers of this manuscript. Haller's is a nonjudgmental approach to evaluation and treatment, based on the assumption that the patient's symptoms are "real" and distressing regardless of the presence or absence of observable organic pathology. The physician may affirm the illness experience without affirming the attribution for it. It is counterproductive to instruct patients that their symptoms are not present on the basis of exposure to various environmental chemical exposures when that is their perception of what they are experiencing. The absence of positive findings on physical examination or diagnostic testing is not presented to the patient as absence of an organic etiology of symptoms. The goal of therapy is control of symptoms, and success is not dependent upon a specific organic diagnosis or etiology but rather on the patient's improved understanding of the role of stress on his or her illness and the acquisition of skills for coping with the impact of the illness on daily life.

A multidisciplinary and behavioral medicine approach similar to that taken in the treatment of chronic pain,[17] which also may or may not have objective physical correlates, may help the patient cope better with his or her symptoms.

Enhancing the patient's sense of control over workplace or home stressors, including environmental chemical exposures, is likely to be effective in managing symptoms.[18,19] A variety of approaches to reducing stress in the MCS patient exist, and many do not involve treatment by a mental health professional or physician. These may include massage, physical therapy, prayer, meditation, or regular exercise, for example.

Systematic changes in the organization of work may be needed to reduce organizational stress. 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. This should be attempted even if levels of exposure are below government-mandated or -recommended permissible exposure limits; these standards may be inadequate to prevent symptoms in unusually sensitive workers. It is necessary, although challenging, to balance the benefits of the above recommendations with the potential risks of a spiraling pattern of progressively severe environmental restrictions and loss of employment.

A definite medical recommendation for complete avoidance of chemical exposures is not indicated at this time. In fact, because there is no evidence for a cumulative toxic injury underlying MCS, recommendation for long-term avoidance of chemical exposures is contraindicated. It is also impossible to accomplish. Without negating the patient's symptoms, reassurance should be given that MCS is not associated with signs of progressive disease nor is it fatal. The physician should engage the patient in a cost-benefit discussion of avoidance.

The avoidance issue is a major dilemma. Human exposure to toxic levels of any chemical should be avoided by employing engineering controls, personal protective equipment, work practices, and, in some cases, job modification or removal. To those who believe that MCS is primarily due to toxic mechanisms, such as immunologic injury or neurotoxicity, these forms of avoidance seem appropriate even for very low exposure levels. Those who support total avoidance believe that treating symptoms rather than the possible root cause of MCS might be harmful. However, there is currently no proof that such exposure exacerbates any underlying disease process or produces pathologic damage, and there are no data showing that long-term withdrawal from exposure produces an improvement in symptoms. Because major lifestyle modifications frequently lead to substantial and deleterious consequences such as loss of work and social support, which may exacerbate or produce depression and anxiety, the burden of proof rests with the proponents of avoidance that it is effective in reducing symptoms and is necessary to prevent toxic injury.

As stated by Terr in a recent editorial,[20] ". . . firm recommendations for specific treatment modalities must await results of definitive clinical trials." However, cognitive and behav-

**TABLE 3**
Diagnostic Testing for Multiple Chemical Sensitivity (MCS)

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| No established diagnostic test for MCS |
| Done primarily to rule out other illnesses in the differential diagnosis |
| Results of test should not be presumed to explain multiorgan symptoms |
| The following tests are currently not validated for clinical use to confirm the diagnosis of MCS: |
| Environmental challenge testing (uncontrolled, unblinded) |
| Quantitative electroencephalography |
| Brain electrical activity mapping |
| Evoked potentials (brainstem, visual, sensory) |
| Position emission tomography scan |
| Single photon emission computed tomography scan |
| Immunologic testing |
| Measurements of trace concentrations of volatile organic compounds or pesticides in blood (parts per billion) |
| Neuropsychologic testing |

ioral interventions to achieve symptomatic desensitization may be effective treatment for some persons with MCS.[21] This requires patient acceptance and cooperation. The fundamental principle of behavioral approaches is symptom desensitization by gradually increasing exposure in an organized program allowing for accommodation and increasing tolerance. This should not be confused with allergic desensitization, which works by well-established immunologic methods. Biofeedback may be useful in modifying body sensations. Any behavioral program should also promote an overall increase in physical and social activity. There is no published experience related to such desensitization treatments for MCS, but clinical experiences suggest that the efficacy of this approach warrants controlled study.[18,21,22] This approach assumes that an important contributing factor to the manifestation of MCS is primarily behavioral without associated objective or progressive physiologic impairment, dysfunction and disease.

Importantly, treatment of coexisting psychiatric manifestations, such as depression and panic attacks, is likely to reduce symptoms and disability.[21,22] Psychiatric treatments may be helpful in controlling symptoms *regardless* of etiology. Even if specific immunologic or neurophysiologic or neurotoxic mechanisms ultimately are discovered to be operative in some patients with MCS, treatment of psychiatric symptoms may still be a most effective approach to palliation. Social workers and master's-level psychologists seem to do a better job than do psychiatrists in helping patients cope with their illness.[23]

Because most patients given a diagnosis of MCS resist the idea that psychologic factors may play any role at all in their distress, it may be more helpful to comanage such patients with a primary care physician experienced in the diagnosis and treatment of depression, anxiety, and somatoform disorders, rather than a psychiatrist. The goal of treatment at this time must be relief of symptoms, rather than expectation of cure, which must await firm knowledge of etiology.[21]

Pharmacologic treatment may be a helpful adjunct in relief of the psychophysiologic symptoms that accompany chemical sensitivity such as depression and mood swings, chronic fatigue, difficulty sleeping, and anxiety, regardless of the etiology of those symptoms. Certainly, those who meet *Diagnostic and Statistical Manual*, 3rd edition, revised, criteria for major depression should be considered for a trial of antidepressant medication, but psychopharmacologic drugs should be prescribed only as part of an overall treatment program, ideally involving an expert in mental health. However, many patients with MCS report intolerance to relatively low doses of any medication or "chemical" intervention, and this needs to be considered in initiating antidepressant therapy. Despite these obvious challenges, the rewards from successfully uncovering and relieving depression, anxiety, and mood swings justify the effort.

Those patients who deny that stress or psychologic factors might play any role at all in their symptoms, and who perceive their locus of control outside themselves, probably cannot be helped by any of the above medical therapies.

Some MCS patients have attempted to pursue bizarre and costly treatments and may appear desperate as they seek unorthodox therapies such as sublingual neutralization, or various "detoxification" treatment programs. This does not prove the psychologic origin of their symptom; many patients with chronic arthritis, for example, have also sought unorthodox therapies when conventional medical therapy has failed to meet their expectations. While remaining nonjudgmental about the patient's motivation to seek such therapies, it is the physician's responsibility to educate the patient about their lack of efficacy.[13,15]

Finally, MCS has been recognized as a potentially disabling condition by some governmental agencies such as the Social Security Administration and the US Department of Housing and Urban Development. Political or social definitions of MCS as work-related or disabling, however, should not cloud the physician's judgment regarding the diagnosis and treatment of symptoms associated with MCS in the individual patient.

Recommendations for treatment are summarized in Table 4.

## Social and Political Implications of the MCS Phenomenon

There are substantial ways in which the administrative recognition of MCS as an occupational or environmental illness may interfere with the objective study of this phenomenon as a clinical condition.[24] Recognition of this syndrome as an illness with potential to cause permanent disability could necessitate changes in health care coverage and delivery, awarding of workers' compensation benefits, and the regulation of chemicals in the workplace and the environment in the United States. There are also social implications for the increasing human and economic costs of disability in this country.

There is current pressure to answer several questions of social policy regarding MCS. First, there is the issue of whether compensation should be awarded for a condition that relies entirely on a patient's report of subjective symptoms for diagnosis without an objective basis for confirming the diagnosis or rating its severity.[24] It is noteworthy that this compensation issue is not unique to the MCS, and

**TABLE 4**
Treatment Recommendations for Multiple Chemical Sensitivity

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| Treatment should be individualized but may include the following: |
| Nonjudgmental, supportive therapy |
| Enhance patient's sense of control |
| Reduce psychosocial stress and/or patient's response to stress |
| Biofeedback, relaxation response |
| Treatment of coexisting psychiatric illness |
| Behavioral desensitization to *low-level* chemical exposures |
| Pharmacologic treatments to control symptoms |
| Increase in physical and social activity |
| Treatment of other coexisting medical illnesses |

disability determination policies that address MCS differently from other subjectively defined conditions, such as chronic low back pain, may be challenged as potentially discriminatory. As a related issue, should it be established that chemical exposure precipitates a psychiatric disorder (either due to aggravation of a preexisting psychiatric disorder or initiation of a new condition), should this be a compensable injury?

Second, how would the expanded recognition of the phenomenon of MCS impact regulation and exposure control? Should employers attempt to reduce specific chemical exposures or to investigate organizational factors that may put an employee in a workplace at risk of expressing this type of illness? At this point, it is unclear whether controlling exposure to chemical substances far below levels associated with known toxic effects would have any positive impact on symptom expression or the natural history of MCS. In addition, the economic burden posed by widespread reductions of exposure to protect even the most "sensitive" members of the population at orders of magnitude below levels considered "safe" for most people may be more than society can or wishes to bear. The economic costs of such an approach could be enormous.

Third, there is the perceived need to regulate and control nontraditional unproven medical practices, such as those that have been promoted by clinical ecologists and other "environmental physicians" as part of the normal vigilance that the medical profession exercises to limit potentially dangerous or misleading practices and iatrogenic chronic disability.[24] This effort has angered many MCS patients who view this effort as an attempt by mainstream medicine to negate the existence of MCS as an illness.

*MCS is rapidly becoming a politically defined illness* in the vacuum created by lack of data. Some legislators, administrators of government bodies, and several in the legal profession believe or fear that the current controversy surrounding MCS is similar to that which existed several decades ago regarding asbestos-related lung disease and that medical science simply has not yet found a way to link environmental chemical exposure causally with the illness or to measure the impairment and disability of patients given an MCS diagnosis. Physicians who question or are agnostic about its relationship to workplace or environmental exposure have been targeted by hostile attack from MCS support groups or others with an economic stake in the outcome of the debate: in some cases even being removed from government jobs for the expression of their views (*Seattle Times*. July 17, 1993:A1–A5). In the future, MCS may increasingly impact the country's total burden of chronic disability, much as low back pain and cumulative trauma disorders of the upper extremities do now. It would thus be appropriate to obtain the data necessary to define this condition and its relationship to environmental chemical exposure medically, *before medical science becomes irrelevant to the diagnosis, treatment, and social policy decisions relating to MCS.*

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### A Risk of the Affluent

Midlife crises are an affliction of the relatively affluent: rosy illusions are easier to maintain when a person is already somewhat shielded from reality. Just as childhood is often constricted among the poor, who early in life face adult realities and burdens, so middle age may be eclipsed by a premature old age brought on by poverty and poor health. Among working-class people, for whom strength and stamina mean earning power, middle age may begin at thirty-five rather than the forty-five often cited in studies by respondents drawn from the sedentary middle class. Because any fanciful notions that poor and blue-collar people might have are rigorously tested by daily life, [Ronald] Kessler says, they rarely dwell in fantasy. "In terms of career, factory workers are likelier to be wherever they're going to be at thirty than executives," he says. "In terms of mental health, being disappointed at what *is* is a better kind of problem to have than being anxious about what will be. Once you know the reality, you can say, 'I can't afford to buy a boat, so I'll rent one for vacations.' Being up in the air is the big problem."

From "Midlife Myths," by W. Gallagher in *The Atlantic*, May 1993, pp 51–68