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Multiple chemical sensitivities

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In 1987 Cullen¹ proposed the term *multiple chemical sensitivities* to define a condition that he described as “An acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to 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.”

“Multiple chemical sensitivities” is a renaming of a condition previously known as “environmental

illness.”² The newer term first appeared in a published volume that contained 12 chapters written by different physicians with widely differing views of “environmental illness.”¹ The *total allergy syndrome*, *twentieth century disease*, *cerebral allergy*, and *chemically induced immune dysregulation* are a few of the many other names used to describe the same condition.³

The concept of “multiple chemical sensitivities” as a physical illness is central to the alternative form of medical practice known as clinical ecology.^{4 5} During the past 40 years the small group of physicians who practice clinical ecology have brought forth the idea that some persons are made sick because of the toxic effects of environmental synthetic chemicals. These persons have polysystemic, multiple symptomatic complaints without any objective evidence of physical disease.⁶ In most cases the symptoms are attributed to ordinary low-level exposure to chemicals that are generally considered safe and do not appear to affect the rest of the population. In some cases the disease is attributed to a particular exposure incident, and in other cases it is attributed to long-term accumulated exposure. Clinical ecologists often use the concept of multiple chemical sensitivities to explain several otherwise well-defined diseases, particularly autoimmune and allergic diseases, migraine headaches,^{7 8} dysmenorrhea,⁹ and cancer.¹⁰

The Clinical Spectrum of Multiple Chemical Sensitivities

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In accord with the definition, the illness is almost always subjective. The patient describes numerous symptoms that could encompass virtually any and in some cases all anatomic areas and physiologic systems of the body. The most common complaints are nonspecific and include fatigue, malaise, disorientation, poor memory, and disability for both occupational and domestic activities.⁶ Although patients with medically unexplained symptomatology have always accounted for a significant number of those seeking treatment from doctors, patients with “multiple chemical sensitivities” present the unique story that their symptoms are triggered, provoked, or worsened by “chemicals.” The specific chemicals identified as symptom-provoking are often common ones that have a characteristic odor, such as the ingredients or components in perfumes, paints, cleaning solvents, new carpeting, construction materials, gasoline, exhaust fumes, office machines, formaldehyde, and ammonia.^{6 11} The patients generally are intolerant of clothing stores and supermarkets. The provoking exposures, like the symptoms, are multiple. They are variable in chemical structure but are almost always detectable by odor.

Typically the patient's history includes an inability to tolerate a large variety of foods, drugs, and environmental chemicals. Intolerance in these cases contrasts strikingly to food or drug allergy, in which an immunologically specific sensitivity can be demonstrated and in which exposure to the allergen causes objective evidence of target organ inflammation. Intolerance in “multiple chemical sensitivities” is subjective. Many different foods and medications evoke multiple symptoms that do not correspond to either recognized allergic responses or the known toxicities of the particular agents.

No pathognomonic (or even typical) abnormalities are found on physical examination.⁶ No single abnormality or combination of abnormalities is revealed by laboratory testing. Although proponents

of multiple chemical sensitivities have claimed that tests of immune function will show defects that correlate with this diagnosis, published reports to date indicate that these patients as a group are immunologically normal.¹² In keeping with the subjective character of the condition, there have been no reports of tissue pathology by either biopsy or autopsy.

Most patients with a diagnosis of multiple chemical sensitivities are women, and they are almost exclusively adults. No epidemiologic surveys have been performed to estimate prevalence, incidence, or geographic clustering. However, such a survey would be virtually impossible to carry out in the absence of a clear case definition. No information is available about prognosis, although the published cases and series reports describe a chronic and progressively increasing symptomatic condition.

Theories of Pathogenesis

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The concept that “multiple chemical sensitivities” is an illness of solely subjective complaints caused by environmental chemicals is highly controversial. There are strongly held opinions on all sides. A recurring theme of the controversy is the debate about whether these persons have a physical or a psychiatric illness. Clinical ecologists and others who favor a physical explanation theorize that “multiple chemical sensitivities” is caused by toxic damage to the immune system from environmental chemicals, foods, and drugs.^{5 10 13 14} Within this immunotoxic framework the manifestations of disease are variously classified as allergic, autoimmune, immunodeficient, or some combination of these. Critical evaluation of the clinical manifestations as reported by the patients, however, reveals that the symptomatology and absence of objective evidence for immunologic abnormality clearly distinguishes these patients from those with well-recognized allergic disorders, autoimmune diseases, and the spectrum of congenital and acquired immunodeficiencies.^{6 15}

In spite of compelling evidence to the contrary, the prevailing opinion among proponents of “multiple chemical sensitivities” and their patients is that this illness results from unspecified “damage” to the immune system by a wide range of environmental chemicals.

A new concept of multiple chemical sensitivities as a neurologically mediated disease has recently emerged.¹⁴ This theory postulates that odorant chemicals travel through the olfactory nerve, which in turn communicates with the hypothalamus and other parts of the limbic system. This theory also postulates that the numerous symptoms that are often accompanied by changes in mood and feelings are caused by chemical stimulation of the olfactory-hypothalamic-limbic pathway in the brain. To date no experimental proof has been provided in support of this idea.

A third theory proposes the concept that these patients fail to detoxify environmental chemicals because of an unspecified defect in appropriate enzymes, possibly linked to functional deficiencies in vitamins and minerals.¹⁶ Although this theory also lacks any experimental or clinical verification, it has led to the idea that patients with multiple chemical sensitivities carry an excessive body burden of xenobiotic chemicals. This theory has spawned a recommendation of therapeutic “detoxification,” which will be described later.

There is considerable sentiment among physicians who evaluate patients diagnosed by clinical ecologists as having “multiple chemical sensitivities” that the diagnosis is most consistent with a psychiatric illness.¹⁷ The clinical presentation is virtually identical to a condition described in the nineteenth century as “neurasthenia.”³ Thus the illness was recognized by physicians well before the era of synthetic chemistry, widespread pollution, chemical pesticides, food additives, and synthetic drugs. Even today, conditions that have been labeled chronic fatigue syndrome, chronic Epstein-Barr virus syndrome, Candida hypersensitivity,¹⁸ and others have a pattern of symptomatology very similar to if not indistinguishable from that of “multiple chemical sensitivities.” The distinguishing feature of “multiple chemical sensitivities” is the presumptive causal relationship to the chemical environment. Psychiatric evaluations of patients with “multiple chemical sensitivities” reveal a strong background of mental and emotional disorders.^{17, 19-21} These patients have been found to have the necessary diagnostic criteria for specific psychiatric illnesses such as somatoform disorders, affective disorders, major depression, and, occasionally, mass psychogenic illness. In addition, “multiple chemical sensitivities” has been viewed as a form of learned response to the odors of chemicals. It has also been considered by some investigators to be an iatrogenic illness. Finally, some students of the phenomenon believe that “multiple chemical sensitivities” is neither a physical disease nor a psychiatric disease but rather a belief system fostered by an unreasonable fear of chemicals.

Diagnosis

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In keeping with the fact that “multiple chemical sensitivities” by definition is a subjective phenomenon, the diagnosis rests entirely on the patient's own description of symptoms and the presumed relationship of these symptoms to environmental chemical exposure.⁶ Because the range of symptoms and provoking chemicals are both without limit as to either number or type, the diagnosis requires merely the acceptance of the concept of “multiple chemical sensitivities” as an illness and reliance on the patient for establishing the exposure-symptom relationship. Physical examination is neither revealing nor necessary, because neither the presence nor absence of a specific physical finding is diagnostic or exclusionary. Proponents of “multiple chemical sensitivities” have nonetheless used a variety of testing methods with these patients. The provocation-neutralization procedure, which uses intradermal, sublingual, or subcutaneous exposure to test substances, has traditionally been the procedure most often used.^{4, 5} Details of the method are described elsewhere.²² The methodology, however, has been investigated under controlled conditions and has been found incapable of distinguishing test chemicals from placebos.²³ Environmental test exposures in special challenge booths are performed in a few environmental control units, but to date no controlled studies have established diagnostic efficacy of this procedure. Scientific evaluation of this form of testing, which would be critical to the entire concept of the disease, is hampered if not made impossible by the fact that the chemicals that these patients identify as provocative of their symptoms must be detectable by smell, thereby precluding a double-blind protocol for definitive study.

As mentioned previously, the diagnostic workup often includes extensive measurements of various products of the immune system, such as the circulating levels of immunoglobulins, presence of circulating autoantibodies, and the blood concentrations of lymphocytes bearing a variety of surface

markers. Some practitioners include measurement of blood, urine, and hair samples for concentrations of both foreign and natural chemicals, vitamins, minerals, amino acids, enzymes, and many other substances. Many of these analytes have no established normal or expected reference ranges for comparison, and no proof exists that such tests distinguish persons with “multiple chemical sensitivities” from others.

Treatment

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The primary recommended form of treatment is avoidance of environmental chemicals. Although avoiding the agents that cause an illness might seem logical, this recommendation needs to be examined closely. First, many investigators who have evaluated patients with presumed “multiple chemical sensitivities” do not question the fact that these persons experience the symptoms that they report. It is the relationship between symptoms and environmental exposure that is in question. If the condition is in fact based on a different cause, such as underlying psychopathology, environmental chemical avoidance would be both ineffective and detrimental because of a missed opportunity for effective treatment. This appears to be the case, because most persons with multiple chemical sensitivities experience an ever-expanding range of symptoms and causes in spite of (or perhaps because of) chemical avoidance.^{[6](#)} No prospective clinical trial of avoidance therapy in this disease has been published. There are no limiting parameters to the avoidance recommendation. In general, patients are advised to avoid all perceived causes and all items tested by provocation-neutralization. In many instances this results in extreme social, psychological, and nutritional deprivation. Without demonstrated efficacy, the results are sometimes tragic.

Other recommendations to supplement environmental chemical avoidance are numerous. Most patients are prescribed some form of elimination diet, usually a program of rotating foods on a regular schedule and the complete elimination of food additives.^{[5](#), [24](#), [25](#)} Injections or sublingual drop therapy with solutions of chemicals, antigens, food extracts, hormones, or other items are often recommended based on provocation-neutralization testing. The theory for this recommendation is not clear, but the expectation is “neutralization,” that is, prevention or disappearance of symptoms. A variety of vitamins, minerals, and nutritional supplements, as well as oxygen, γ -globulin injections, and oral salt mixtures are prescribed based on such rationales as “neutralization of the allergic reaction,” boosting the immune system, and strengthening detoxification pathways. A regimen of exercise, sauna treatments, niacin and other vitamins, and induced sweating has recently become a popular procedure advertised as “detoxification.”^{[26](#)} Not one of these forms of treatment has been subjected to proper clinical trials for efficacy and safety.

Relationship of Multiple Chemical Sensitivities to the Sick Building Syndrome

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The concept of “multiple chemical sensitivities,” its presumed theoretic basis, and the clinical diagnosis and management of the condition are not consistent with current, scientifically based clinical practice. Nevertheless, there is a small group of physicians with strong beliefs in this form of practice who reject the results of studies that fail to support their ideas and practices. The controversy surrounding “multiple chemical sensitivities” is heightened by confusion about the relationship of multiple chemical sensitivities to the sick building syndrome, building-related illnesses, occupational illness, hypersensitivity diseases, and toxicity from present-day

environmental pollution. The ideas that are put forth to support “multiple chemical sensitivities” as a toxic disease caused by environmental chemicals are very different from the accepted principles of toxicology and immunologic hypersensitivity. The extensive published results of scientifically valid biochemical and immunologic research, epidemiologic surveys, and clinical evaluations that are the framework for our modern understanding of the causes, diagnoses, and management of toxic and allergic diseases offer no support for the concept of “multiple chemical sensitivities.”

Building-related illnesses encompass a variety of diseases that affect occupants of buildings that harbor agents of disease. A detailed description of these illnesses is included in the other articles in this supplement. The allergic, infectious, and toxic diseases that can be attributed to agents contaminating a building are similar to the same diseases that can be acquired from outdoor sources. However, in some cases a particular disease-causing agent, such as the bacterium *Legionella pneumophila*, has growth requirements that are peculiarly suitable for certain types of buildings. In contrast to multiple chemical sensitivities, building-related illnesses cluster within a particular building because of a defect in the building construction, maintenance, or usage that permits a particular infectious microorganism, allergen, or toxic chemical to contaminate that building.

The sick building syndrome, a special category of building-related illness, is most likely to be confused with “multiple chemical sensitivities.” Clinical manifestations of the sick building syndrome include systemic symptoms such as fatigue, but there are also characteristic localizing symptoms of mucus membrane and conjunctival irritation. In contrast to “multiple chemical sensitivities,” however, patients with sick building syndrome become ill promptly when they enter the building and improve rapidly after they leave the building. They do not have intolerance to environmental exposures elsewhere. In some cases, the cause of the sick building syndrome in a particular building can be traced to impaired air quality.

Conclusion

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“Multiple chemical sensitivities” or “environmental illness” are terms used to describe a condition in which multiple subjective symptoms are attributed to a large number of environmental chemicals, foods, and drugs. This condition is not associated with any evidence for anatomic or physiologic illness, but it can be disabling. The cause is highly controversial, because scientific evidence linking environmental factors with symptoms in these persons is lacking. The diagnosis of “multiple chemical sensitivities” is often made on the basis of diagnostic procedures that are either unproved or shown to be based on suggestion only. Treatment of symptoms by extensive environmental avoidances, diets, detoxification, and neutralization has been shown to be ineffective. “Multiple chemical sensitivities” should not be confused with the sick building syndrome or other building-related illnesses, allergic diseases, or toxic illnesses.

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[ABSTRACT](#)

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