Clinical Ecology

Council on Scientific Affairs, American Medical Association

PHYSICIANS who practice clinical ecology believe that exposure to low levels of environmental substances present in the air or ingested from food and liquids causes in susceptible individuals a variety of ill-defined symptoms affecting nearly every organ system.

MULTIPLE CHEMICAL SENSITIVITY SYNDROME

Most physicians who practice clinical ecology (clinical ecologists) maintain that a number of patients have the multiple chemical sensitivity syndrome (MCSS) (also called clinical ecological illness, environmental illness, chemical AIDS [acquired immunodeficiency syndrome], 20th-century disease, environmental hypersensitivity disease, total allergy syndrome, and cerebral allergy]. Clinical ecology has been defined as the orientation in medicine in which physicians primarily work with patients to uncover the cause-and-effect relationship between their ill health and food or low-level chemical exposure.

Other definitions have been offered and no general agreement exists that clinical ecology and MCSS are synonymous. The lack of a clear definition or diagnostic test for MCSS has made it difficult to estimate its prevalence in the United States.

Clinical ecologists report that significant numbers of people have immune system derangements that increase their sensitivity to low levels of substances in the environment that are innocuous to normal people and are either inhaled (eg, the outside air, the workplace, or home) or ingested as liquids, foods, or drugs. Exposure to such substances in susceptible individuals is alleged to produce a polysymptomatic disorder that may involve any organ or many organ systems. Predisposing risk factors are said to include infection due to Candida albicans, a deficient or inadequate diet, and/or food intolerance. The primary complaints of such patients include allergy-like symptoms, food and chemical intolerance, rhinitis, difficulty in breathing, depression, headache, fatigue, irritability, insomnia, palpitations, and other cardiovascular symptoms.

A subset of MCSS is the Candida hypersensitivity syndrome. Some patients fit the criteria for chronic fatigue syndrome (CFS). Multiple chemical sensitivity is also claimed to be a cause or a contributing factor in the development of a number of recognized diseases and disorders (eg, migraine, various psychiatric illnesses, urticaria, anaphylaxis, atopic dermatitis, allergic rhinitis, asthma, learning disabilities, arthritis, and susceptibility to cancer).

Clinical ecologists propose a series of events to explain the development of MCSS. Low concentrations of a number of different chemicals over time are purported to damage the immune system and produce symptoms and sensitivity to other substances. The total load (body burden) of environmental insult is considered critical for the induction of illness. The concept of total load was introduced to explain inconsistent development of symptoms and variable dose-response findings after experimental exposure to chemicals and food.

Changes in the frequency of exposure and intervals between exposures to a specific antigen may delay the onset of symptoms and alter the sensitivity of a patient to the offending substance. Clinical ecologists report that unrecognized immune system dysregulation develops over a long period after cumulative exposure to certain chemicals. Further, overt manifestations are purported to be triggered by a single serious viral infection, major stress, or fungal infection (particularly C. albicans). One currently popular hypothesis suggests that damage to T cells by chemicals or other agents causes inversion of the normal helper/suppressor T-cell ratio, and as a result alters antibody production by B cells. To assess immune dysfunction, some investigators have reported that analysis of T- and B-cell surface markers and assay of a variety of specific antibodies (eg, formaldehyde and isocyanates) could be useful in diagnostic testing.

THERAPEUTIC APPROACHES

Avoidance is a major aspect of therapy; patients are often told to ingest a defined or restricted diet or use a rotation diet, to move to another location, to create an environmentally "safe" room in their home, or in severe cases to be placed temporarily in special environmental isolation units (such units are used primarily for investigational purposes and are rarely used for treatment).

A major technique used by many practitioners of clinical ecology is sublingual or intradermal provocation-neutralization. It is used for diagnostic purposes (provocation) or for therapy to relieve symptoms (neutralization). With this procedure, a diluted extract of the suspected antigen is administered sublingually or intradermally. The prompt development of symptoms confirms the substance as causative. Once the dose that elicits symptoms has been determined, decreasing doses of the antigen are administered until symptoms disappear; this is the neutralization dose. The mechanisms for these effects are unknown. Although a large number of uncontrolled studies have been conducted and a large body of anecdotal evidence is available, no well-controlled studies have demonstrated either diagnostic or therapeutic value for provo-

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This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all the facts and circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and patterns of practice evolve. This report reflects the views of scientific literature as of December 1991.

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jection. In one recent double-blind trial of provocation-neutralization, placebo was as effective as injection of food extracts to induce either symptoms or neutralization. In contrast, two other studies supported the value of these techniques for diagnosis and treatment. These three studies and other reports have been criticized for design and methodologic flaws.

Two models have been reported that might permit controlled studies of provocation-neutralization.

**CANDIDA HYPERSENSITIVITY SYNDROME**

Many clinical ecologists believe that the fungus *Candida* is a major cause of symptoms associated with MCSS. It is claimed that repeated use of antibiotics, birth control pills, corticosteroids, and/or an improper or defective diet can lead to overgrowth and a systemic infection by this organism. Clinical ecologists also claim that *Candida* produces a toxin or other substances that disrupt bowel chemistry and immune function in susceptible patients. However, *Candida* is a constituent of the normal gastrointestinal tract in many healthy individuals. Because reliable tests to detect *Candida* or its putative toxin systemically in levels postulated to exist by clinical ecologists are unavailable, diagnosis is by exclusion and the only proof of *Candida*-related disease is response to therapy. Although considerable anecdotal evidence supports the existence of *Candida* hypersensitivity syndrome through its response to therapy with antifungal agents, nutritional supplements, and dietary manipulation, scientific proof from well-controlled studies has not been provided.

**CHRONIC FATIGUE SYNDROME**

Considerable controversy exists over whether this alleged syndrome is a specific disease entity. Patients diagnosed as having CFS suffer from a disabling weakness and exhaustion that may continue for months or even years. Some patients lose the ability to think clearly, to concentrate, and to retain memory; confusion, depression, insomnia, and/or hypsomnria often are present. Flu-like symptoms also may be present and include sore throat, headache, fever, and muscle/joint pain. Diagnostic criteria for this syndrome have been proposed. However, no definitive laboratory tests exist. No single cause for this syndrome appears likely. An infectious or immunological mechanism has been investigated with few tangible results. In particular, suggestions have been made that infection (eg, Epstein-Barr virus, human herpesvirus 6, human T-cell leukemia virus II [HTLV-II], or other environmental insults [eg, chemicals]) may stimulate cells involved in the immune response and trigger cytokines such as interferon or interleukin 2 as well as other endogenous inflammatory mediators. In a well-controlled study, evidence was presented for the presence of serum antibodies to HTLV-II, a retrovirus, by Western blot in patients with CFS. This finding awaits confirmation by other laboratories. Another well-controlled study demonstrates activation of cytotoxic CD8 cells in up to 50% of patients with CFS.

More than two thirds of patients with CFS appear to have an associated psychiatric disorder. Management is difficult although depression and other psychiatric disorders may be treated with drugs and/or psychotherapy. Other treatment is symptomatic and generally not helpful.

**SICK-BUILDING SYNDROME**

Air quality is poor in many newly constructed buildings, and low levels of toxic agents, allergens, chemicals, or contamination with microorganisms circulating in a closed environment can produce a building-related illness for which a causative agent can be identified (eg, legionnaires' disease, humidifier fever, hypersensitivity pneumonia, and building-related asthma). In contrast to building-related illness, no specific causative agent has been identified for the symptoms occurring in patients with the sick-building syndrome. Symptoms reported in patients with the sick-building syndrome include chest tightness, fatigue, headache, malaise, and cough, as well as eye and mucus membrane irritation. The MCSS should not be confused with the sick-building syndrome. The lack of agreement by workers in this field over the definition of the sick-building syndrome and inclusion and exclusion criteria for patients suspected of having this syndrome has hampered efforts to design well-controlled studies. Evidence that this syndrome exists as a separate disease entity is weak. Some have claimed that mass hysteria and other psychosocial factors are responsible for symptoms. A few reports discuss building-related illness and the sick-building syndrome and provide a basis for studying the latter.

**ASSESSMENT OF CLINICAL ECOLOGY**

Validation of MCSS is complicated by the number and variety of symptoms and the lack of objective signs, and by the overlapping of symptoms in a number of alleged clinical ecological illnesses (eg, *Candida* hypersensitivity and CFS) with those of recognized disorders (eg, depression and polymyalgia rheumatica). The proposed immune imbalance associated with MCSS has not been identified. No evidence based on well-controlled clinical trials is available that supports a cause-and-effect relationship between exposure to very low levels of substances and the myriad symptoms purported by clinical ecologists to result from such exposure. Several articles and books are available that seek to provide a scientific basis for such an association. Such publications, while thought-provoking and interesting, fail to provide proof based on well-controlled clinical studies.

The view that some patients are allergic to or intolerant of environmental substances is not in itself controversial. Rarely, some individuals are known to be hypersensitive to minute concentrations of a food, drug, or inhalant allergen, causing objective illness; on the other hand, clinical ecologists claim that such occurrences are common and not rare and that manifestations are subjective only. Controversy revolves around the minimum concentration of the offending substance that causes adverse reactions, the nature of such adverse effects, and the mechanisms involved.

Although malingering or hypochondriasis may be responsible for symptoms, such a cause appears unlikely in most patients. A number of clinicians have reported that the majority of patients have a definite psychosomatic disorder that could be responsible for symptoms.

The fact that the diagnostic tests and therapy recommended by clinical ecologists are largely unproven by controlled clinical studies does not necessarily establish the lack of scientific validity. Well-controlled studies could validate and provide a scientific basis for many of the tests and therapies associated with multiple chemical sensitivity. Attempts to design and carry out such controlled studies have been discussed at a recent 2-day National Academy of Sciences workshop, a Canadian environmental workshop, in a recent book, and in review articles.

**CONCLUSIONS**

Some patients present to physicians with symptoms that cannot be attributed to any known condition, disorder, or disease. Further, they may have no physical findings or laboratory abnormalities to support a standard diagnosis. The constellation of symptoms presented (eg, depression, fatigue, irritability, difficulty in breathing, headache, gastrointestinal distress, and food intolerance) resemble those seen in many illnesses. Physicians who practice
clinical ecology associate these symptoms with repeated exposure of susceptible individuals to very low levels of substances that exist in the environment or are ingested as food or liquids. After these substances have accumulated to a threshold concentration in the body, they are purported to produce immune dysfunction and result in a generalized clinical disorder—MCSS. Subsets of this syndrome include Candida hypersensitivity syndrome and CFS. Some patients diagnosed as having MCSS have an associated psychiatric disorder that could be responsible for many of the symptoms. Other patients are presumed to have a physical basis for symptoms that result from an unrecognized or undefined organic disorder.

Two medical societies have issued position papers and one has issued an informative report on clinical ecology. The position papers reported that no scientific evidence supports the contentions that MCSS is a significant cause of disease, that the diagnostic tests and the treatments used have any therapeutic value. Until such accurate, reproducible, and well-controlled studies are available, the American Medical Association Council on Scientific Affairs believes that multiple chemical sensitivity should not be considered a recognized clinical syndrome.

Based on the reports in the peer-reviewed scientific literature, the Council on Scientific Affairs finds that at this time (1) there are no well-controlled studies establishing a clear mechanism or cause for MCSS; and (2) there are no well-controlled studies providing confirmation of the efficacy of the diagnostic and therapeutic modalities relied on by those who practice clinical ecology.

**RECOMMENDATIONS**

The Council on Scientific Affairs recognizes that the above findings are those existing at one point in time, and encourages the opportunity to review well-controlled studies as they become available. It recommends the following:

1. That the American Medical Association continue to monitor the published literature on clinical ecology and report on it as appropriate.

2. That those who support a new test, procedure, or treatment must prove by appropriately controlled peer-reviewed trials that it is effective for the purposes for which it is used and that the burden should not be shifted to opponents to prove that a new test or therapy is invalid.

**References**


6. Black DW, Rathe A. Total environmental aller-...