Position Statement

Idiopathic environmental intolerances
AAAAI Board of Directors
January 1999

AAAAI Position Statements and Work Group Reports are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. For reference only.

The statement below is not to be construed as dictating an exclusive course of action nor is it intended to replace the medical judgment of healthcare professionals. The unique circumstances of individual patients and environments are to be taken into account in any diagnosis and treatment plan. The above statement reflects clinical and scientific advances as of the date of publication and is subject to change.

The condition now called idiopathic environmental intolerances (IEI)⁴-⁵ and formerly known as multiple chemical sensitivities (MCS)⁴ or environmental illness was addressed in the AAAAI Position Statement on Clinical Ecology published in 1986.⁴ Since then, additional research and clinical studies have been reported. This updated position by the AAAAI reflects the current status of this condition as documented in the published scientific literature.

Definition and Terminology
The term environmental illness was used for many years to refer to a subjective illness in certain persons who typically describe multiple symptoms, which they attribute to numerous and varied environmental chemical exposures, in the absence of objective diagnostic physical findings or laboratory test abnormalities that define an illness. Other terms, such as universal allergy, 20th-century disease, chemical hypersensitivity syndrome, total allergy syndrome, and cerebral allergy have also been used to describe the same condition. Since the last AAAAI position statement on this subject, the name multiple chemical sensitivities has largely supplant these names. In February 1996, the invited experts forming a workshop organized by the International Programme on Chemical Safety of the World Health Organization and other organizations, recommended a new name-idiopathic environmental intolerances—because the term MCS "makes an unsupported judgment on causation" (ie, environmental chemicals), does not refer to "a clinically defined disease," and is not based on "accepted theories of underlying mechanisms nor validated clinical criteria for diagnosis."¹,³ Furthermore, the "relationship between exposures and symptoms is unproven."¹,³

History of the IEI Phenomenon
The existence of IEI as a medical illness was first proposed by Randolph,⁶-¹⁰ who founded a movement known as clinical ecology. He published his theories and numerous case reports in a series of books and articles beginning in the 1950s. He and others¹⁰-¹⁵ attributed the illness to a failure of human adaptation to virtually all modern-day (20th century) synthetic chemicals. However, more than a century ago, Beard¹⁶ described the same clinical condition, which he in turn ascribed to certain items and activities introduced into 19th-century living, specifically the telegraph, the sciences, industry, the periodical press, and female education. Shorter¹⁷ has written an excellent treatise with a unique historical and social perspective about related symptom complexes from the late 18th century to the present.

Clinical Description of IEI
Because of the varied and subjective nature of the illness, no precise case definition or diagnostic criteria exist. Nevertheless, reports of individual cases and series of cases reveal that the diagnosis is made almost exclusively in adults and primarily in women.¹²,¹⁸-²⁸ Although the "typical" patient has numerous symptoms that appear to involve many organ systems,⁴ careful review of case material reveals that IEI has been diagnosed sometimes in persons with few or no symptoms.²⁶

Abbreviations used:
IEI: Idiopathic environmental intolerances
MCS: Multiple chemical sensitivities
The central focus of the diagnosis is the fact that the patient describes symptoms in relation to environmental exposures. As mentioned earlier, there are no physical examination abnormalities in IEI.

The list of environmental chemical exposures triggering symptoms is virtually unlimited. They are usually, although not always, identified by odor. The more common ones cited are perfumes and scented products, pesticides, domestic and industrial solvents, new carpets, car exhaust, gasoline and diesel fumes, urban air pollution, cigarette smoke, plastics, and formaldehyde. In many patients symptoms are triggered also by certain foods, food additives, and drugs and in some cases by electromagnetic fields and mercury in dental fillings. There have been no dose-response studies of this phenomenon, but patients report that these materials provoke symptoms at concentrations at or below commonly encountered ambient levels. Furthermore, symptoms bear no relationship to established toxic effects of the specific chemical and occur at concentrations far below those expected to elicit toxicity. The latent period for response varies considerably.

Certain environmental irritants, including some of those mentioned above, are recognized as triggers for patients with asthma and rhinitis. However, this phenomenon differs from that of IEI in that objective changes of bronchial or nasal obstruction and hypersecretion occur rather than subjective symptoms only.

The patient may not be able to identify the circumstances surrounding the onset of illness. In those cases involving litigation for workers-compensation benefits or alleged personal injury caused by the actions of a third party, however, the patient typically attributes the disease to a specific initiating exposure event. IEI has been claimed to arise from silicone breast implants and has been attributed to military service in southwest Asia during the brief 1991 hostilities (Gulf War Syndrome).

**IEI Theories**

Over the past 40 years, a number of theories have been put forward to address the cause of IEI and the mechanism by which diverse environmental exposures produce symptoms. Immunologic, toxicologic, psychologic, and sociologic theories predominate. Opinions about etiology and pathogenesis are sharply divided.

Immunologic and toxicologic explanations of IEI are favored by clinical ecologists. These physicians place emphasis on the disease being a previously unrecognized form of allergy or immunologic hypersensitivity. This concept was gradually replaced by various immunotoxic theories in which environmental chemicals are believed to cause autoimmunity or immunodeficiency. More recently, a neurotoxic theory of IEI has been introduced. According to this theory, symptoms arise from stimulation of the olfactory-limbic system of the brain and the hypothalamus. The condition has also been ascribed to the effects of oxidative damage to unspecified tissues.

IEI has been interpreted by some as an overly sensitive state of the respiratory or nasal mucosa. Many physicians have proposed that IEI is a manifestation of a psychiatric disease or personality disorder. A comparison with somatoform illness has been noted by some and with panic disorder or mass hysteria by others. Additional psychologic interpretations include atypical posttraumatic stress disorder, behavioral conditioning, and adult manifestation of childhood abuse. Several investigators have observed a high prevalence of several different psychiatric diagnoses among patient with IEI. Clinical ecologists often interpret the presence of psychopathology in patients with IEI to be the result and not the cause of the illness.

**Diagnostic Methods**

The diagnosis of IEI is typically made on the basis of the patient's history, without any defining criteria. There are no diagnostic symptoms, and there are no diagnostic objective physical signs. Many different tests and procedures have been proposed, but no single test or combination of tests has been validated as diagnostic. The tests most frequently used by practitioners who diagnose IEI are provocation-neutralization and a panel of immunologic tests. The latter encompasses measurements of serum immunoglobulins, complement levels, blood lymphocyte subset counts, autoantibodies, and serum antibodies to chemicals. Some practitioners obtain blood, urine, or fat levels of environmental chemicals, as well as brain imaging studies, neuropsychologic testing, and
psychologic/psychiatric interviews.\textsuperscript{26,50,52,82-84} Studies to date have failed to confirm that any immunologic tests are diagnostic for chemically induced symptomatology.\textsuperscript{76,79} The diagnostic validity of the other procedures has yet to be tested.

**Position Statements**
Several medical societies and organizations have issued position statements pointing out the shortcomings of the IEI diagnosis, the unreliability and misuse of certain diagnostic procedures, and the lack of scientific support for and clinical evidence of the alleged toxic effects from environmental chemicals in these particular patients. In 1986, the AAAI was the first to do so.\textsuperscript{5} The American College of Physicians published a position paper in 1989,\textsuperscript{84} which was later adopted by the American College of Occupational and Environmental Medicine. The Council on Scientific Affairs of the American Medical Association published a critical review in 1992.\textsuperscript{85} The Ministry of Health of the Province of Ontario\textsuperscript{86} and the California Medical Association\textsuperscript{65} have published results of their investigations of the IEI phenomenon. The US National Academy of Sciences,\textsuperscript{87} the World Health Organization,\textsuperscript{1} and the International Society of Regulatory Toxicology and Pharmacology\textsuperscript{88} have held symposia on the subject. The American Council on Science and Health\textsuperscript{65} and the Royal College of Physicians and Royal College of Pathologists in Great Britain\textsuperscript{90} have also published reports detailing the unscientific basis for IEI.

**Treatment Recommendations for Patients with the Diagnosis of IEI**
Those physicians who view the symptoms of IEI as arising from the toxic effect of environmental chemicals (and foods) stress an avoidance program that is sometimes extreme. This is usually supplemented with vitamins and minerals, occasionally with intravenous gamma globulin, and often with "neutralizing" administration of chemical and food extracts by injection or sublingual drops. To date, no controlled clinical trial has been carried out to evaluate this approach. There is evidence that such a program may make the patient worse.\textsuperscript{26} Others advocate an undocumented form of "detoxification" through induced sweating and the administration of oral minerals and oils.\textsuperscript{91}

A psychotherapeutic approach is recommended by those who find evidence for current psychopathology in the patient's history. One study found short-term benefit from a brief course of inpatient psychotherapy,\textsuperscript{95} but no long-term studies have yet been reported.

**Comparison with Other Illness**
Some observers have interpreted IEI as part of a spectrum of nonphysical illnesses characterized by multiple somatic complaints. Others see it as a distinct entity. The so-called Candida hypersensitivity syndrome has been claimed to be a similar illness,\textsuperscript{93} but there is no scientific proof that Candida albicans causes such a condition.\textsuperscript{94}

Some psychiatrists have pointed out the similarity of IEI to the somatoform/conversion disorders,\textsuperscript{19,28,50,51,83} which in the past were called neurasthenia. Myalgic encephalomyelitis and the chronic fatigue syndrome\textsuperscript{95} share features in common with IEI, but these patients do not attribute their symptoms to environmental exposures. The influence of social and cultural factors in shaping the interpretation of unexplained somatic symptoms has been discussed\textsuperscript{84,96} and could be relevant to IEI because of the current widespread concern about environmental pollution.

IEI is distinct from true environmentally caused diseases. Infectious microorganisms, allergens, toxins, and irritants are responsible for diseases that are clinically well characterized and for which specific diagnostic procedures are available. In a few situations these pathogens have been proven to cause certain building-related illnesses, such as Legionnaire's disease\textsuperscript{97} and hypersensitivity pneumonitis.\textsuperscript{98} The term sick building syndrome has been applied to a condition of mucous membrane irritation caused by inadequate air-handling systems in new, energy-efficient office buildings.\textsuperscript{99} Unlike IEI, however, these patients experience a limited range of symptoms, and they occur in the affected building only. Reactive airways dysfunction syndrome is a persisting asthma-like illness that arises in some persons with no preexisting asthma after an acute exposure to a toxic substance sufficient to induce a chemical bronchitis.\textsuperscript{100}
Summary
IEI—also called environmental illness and multiple chemical sensitivities—has been postulated to be a
disease unique to modern industrial society in which certain persons are said to acquire exquisite
sensitivity to numerous chemically unrelated environmental substances. The patient experiences wide-
ranging symptoms, but evidence of pathology or physiologic dysfunction in such patients has been
lacking in studies to date. Because of the subjective nature of the illness, an objective case definition is
not possible. Allergic, immunotoxic, neurotoxic, cytoxic, psychologic, sociologic, and iatrogenic theories
have been postulated for both etiology and production of symptoms, but there is an absence of scientific
evidence to establish any of these mechanisms as definitive. Most studies to date, however, have found
an excess of current and past psychopathology in patients with this diagnosis. The relationship of these
findings to the patient's symptoms is also not apparent. Rigorously controlled studies to verify the patient's
reported subjective sensitivity to specific environmental chemicals have yet to be done. Moreover, there is
no evidence that these patients have any immunologic or neurologic abnormalities. In addition, no form of
therapy has yet been shown to alter the patient's illness in a favorable way. A causal connection between
environmental chemicals, foods, and/or drugs and the patient's symptoms continues to be speculative
and cannot be based on the results of currently published scientific studies.

References
1. Conclusions and recommendations of a workshop on multiple chemical sensitivities (MCS). Reg
2. Lessof M. Meetings report: Report of multiple chemical sensitivities (MCS) workshop, Berlin,
Germany, 21-23 February 1996. PCS/96.29 IPCS, Geneva, Switzerland. Human Exp Toxicol
Safety (IPCS)/German workshop on multiple chemical sensitivities: Berlin, Germany, 21-23
5. American Academy of Allergy and Clinical Immunology Executive Committee. Position statement:
7. Randolph TG. Human ecology and susceptibility to the chemical environment. Springfield (IL):
Charles C Thomas; 1962.
1980.
Reinhold; 1991.
15. Levin AS, Byers VS. Multiple chemical sensitivities: a practicing clinician's point of view. Clinical
16. Beard GM. American nervousness, its causes and consequences: a supplement to nervous
exhaustion (neurasthenia). New York: GP Putnam's Sons; 1881.
17. Shorter E. From paralysis to fatigue: a history of psychosomatic illness in the modern era. New
18. Black DW, Rathe A, Goldstein RB. Environmental illness. A controlled study of 26 subjects with


57. Davidoff LL. Models of multiple chemical sensitivities (MCS) syndrome: using empirical data (especially interview data) to focus investigations. Toxicol Ind Health 1992;8:229-47.


AAAAI Position Statements and Work Group Reports are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. For reference only. January 1999.