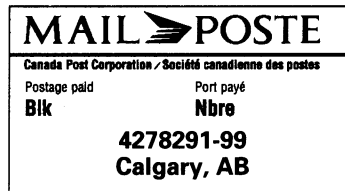
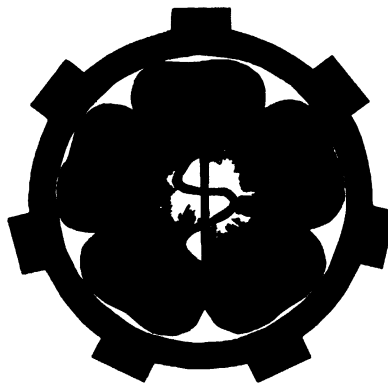


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ALBERTA OCCUPATIONAL MEDICINE NEWSLETTER

EDITORIAL COMMENTS

This edition of the Occupational and Environmental newsletter contains an article submitted by Dr. Murray Young about Multiple Chemical Sensitivities (MCS). The article provides a good overview of the issue. Dr. Young is an Occupational Medicine Health Consultant.

The number of people diagnosed with MCS is growing every year. It is quite a controversial area of medicine. People familiar with it usually believe it exists completely or else put no credibility in it what so ever. There area not many who take the middle ground.

I would like to pass on some pieces of information that have crossed my desk lately.

The British Columbia Workers Compensation Board publishes the *Worksafe* magazine every other month with various articles in it of interest to physicians who deal with work-related issues. The March/April 2001 and 2002 issues contain articles about injuries arising from repetitive activities, and provide some ideas on how to determine, and control some risk factors. Several other recent additions have some information in this area.

The Jan/Feb 2002 edition of *Worksafe* contains an article about protecting workers from radiation. This may be of

interest to some of you since Xrays and other radiation-producing tests are used so often. The magazine is available online, for no charge, at www.worksafebc.com.

It is with regret that I inform you that Kim Blaikie is no longer involved with the publication of the newsletter as she has taken on a new job with the Alberta Cancer Board. Her contributions have been very valuable and I will miss her input. Thank you Kim, and good luck in your new position.

Ken Fryatt, MD, FRCPC
Editor

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IDIOPATHIC ENVIRONMENTAL INTOLERANCE

aka MULTIPLE CHEMICAL SENSITIVITY

Murray Young, MD, PhD*

Introduction:

There is currently considerable controversy among physicians, scientists and the general public regarding a phenomenon known as Idiopathic Environmental Intolerance (IEI) or more commonly Multiple Chemical Sensitivity (MCS). Although widely used, the term "multiple chemical

sensitivity" is an unsatisfactory label because it implies causation. Nevertheless, the two terms will be used interchangeably in this paper.

A contribution to the confusion surrounding IEI is the fact that there is significant overlap of symptoms between it and a number of other conditions, notably chronic fatigue syndrome and fibromyalgia. Further confusion has resulted from the fact that a number of other labels have been used to describe environmental illnesses (see Table I). A panel convened by the World Health Organization after their 1996 workshop on MCS recommended the term Idiopathic Environmental Intolerance (IEI). Several scientific and medical organizations have adopted IEI as the most appropriate designation. IEI was suggested because, as stated by Staudenmayer (1999), it more accurately describes the condition as an acquired disorder with multiple recurrent symptoms, associated with diverse environmental factors tolerated by the majority of people and not explained by any known medical or psychiatric or physiological disorder.

By way of a very brief history, in 1962 Theron Randolph published "Human Ecology and Susceptibility to the Chemical Environment." The "Environmental Health Center" in Dallas was opened in 1974. Dr. William Rea, a thoracic surgeon associated with the Dallas Clinic,

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and the Section of Occupational Medicine, Alberta Medical Association

Table I
IEI Alternate Names

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|---|---|---------------------------------|
| 1. Multiple Chemical Sensitivity | 10. Toxicant-induced Loss of Tolerance (TILT) | 20. Toxic Response Syndrome |
| 2. Multiple Chemical Sensitivity Syndrome | 11. Total Environment Allergy | 21. Universal Reactivity |
| 3. Cerebral Allergy | 12. Total Immune Disorder Syndrome | 22. Ecological Illness |
| 4. Chemical Allergy | 13. Chronic Toxic Encephalopathy | 23. 20th Century Disease |
| 5. Chemical Sensitivity | 14. Environmental Illness | 24. Universal Allergy |
| 6. Chemical Hypersensitivity Syndrome | 15. Multi-organ Dysesthesia | 25. Ecological Illness |
| 7. Chemically Induced Hypersensitivity Syndrome | 16. Environmental Hypersensitivity | 26. Chemical AIDS |
| 8. Chemical Intolerance | 17. Environmental Irritant Syndrome | 27. Allergic Toxemia |
| 9. Total Allergy Syndrome | 18. Environmental Maladaptation Syndrome | 28. Functional Somatic Syndrome |
| | 19. Generalized Immune Deficiency | |

published 4 volumes on "Chemical Sensitivity" during the years 1992-1997. Dr. Mark Cullen of Yale University coined the phrase "multiple chemical sensitivity" in his 1987 publication "Workers with Multiple Chemical Sensitivities." There was an outbreak of multiple chemical sensitivity complaints at the Camp Hill Hospital in Halifax, Nova Scotia in 1988-1989. The Nova Scotia Environmental Health Centre, patterned after the Dallas clinic, was established in 1989 and became associated with Dalhousie University in 1994. The Nova Scotia Government instituted a perfume ban in public places in 2000. Other jurisdictions have done so as well. Over the years there has been a gradual increase in MCS-related litigation in both the USA and Canada.

Cullen has stated that "although still lacking a widely agreed upon definition or designation, the disorder idiosyncratically occurs in individuals who have experienced a single episode or recurring episodes of a typical chemical intoxication or injury such as solvent or pesticide poisoning. Subsequently, an expansive array of divergent environmental contaminants in air, food or water may elicit a wide

range of symptoms at doses far below those that typically produce toxic reactions. Although these symptoms are not associated with objective impairment of the organs to which they are referable, the complaints may be impressive, causing considerable dysfunction and disability".

Proponents and critics of the concept of multiple chemical sensitivity essentially represent two factions that appear to be at opposite ends of a spectrum of clinical and scientific approaches and/or beliefs. Each side has produced extensive literature purporting to prove their respective points of view. Neither faction has much credibility with the other. Consensus, be it scientific, clinical, regulatory or legal has therefore been difficult to achieve. MCS patients are often within a politically active advocacy group with fixed belief symptoms. Unfortunately, the controversy surrounding this condition has often placed these patients, who can be quite ill, in a position where they are not served well.

Several professional medical and scientific organizations (including ACOEM and the AMA) have published position statements critical of MCS as a

distinct condition (Table 2). On the other hand, the Americans with Disabilities Act (ADA) recognizes MCS as a disability as does the US Department of Housing and Urban Development. MCS is a compensable injury in the German WCB system. Those who do not subscribe to the concept of MCS consider it to be in the spectrum of known conditions such as odour aversion and somatoform disorders. The Alberta Heritage Foundation for Medical Research (1999) concluded that "the reviewed literature suggests that at this point in time there is insufficient scientific evidence to justify the existence of MCS as a distinct syndrome or disease entity but the available limited evidence cannot be ignored and warrants further investigation."

Clinical Presentation:

Typical intolerances include sensitivity to various classes of chemicals (e.g. solvents, pesticides, formaldehyde, perfumes, body odours), certain foods, electromagnetic fields (electrical hypersensitivity or electric allergy), infections (yeast or bacteria) and metals. "Spreading" to include a variety of environmental factors often occurs. The

Table II
Organizations Critical Of IEI Concept

- | | |
|--|--|
| 1. American Academy of Asthma, Allergy and Immunology | 4. American Medical Association |
| 2. American College of Occupational and Environmental Medicine | 5. American Academy of Toxicology |
| 3. American College of Physicians | 6. International Society of Regulatory Toxicology and Pharmacology |
| | 7. American Council on Science and Health |

incidence of IEI is high in western countries (especially the USA and Canada) and has been reported as ranging from 2–10% of the general population. Electrical Hypersensitivity is primarily a Scandinavian phenomenon. Both industrial and white-collar workers can be effected. There is a preponderance of female patients (up to 80% in some studies). Patients age 40-49 represent 37% of cases. Only 28% have completed university. There is a higher incidence of IEI in individuals who have been separated or divorced or are of low socioeconomic status.

IEI patients report extensive, perplexing, medically unexplained, complexes of symptoms referable to many organ systems, without correlation to objective laboratory or physical findings. Symptoms can occur in different patterns in different individuals in response to repeated perceived exposures. Onset can be gradual or sudden and symptoms can come and go. There may or may not be linkage to a specific exposure or event. Symptoms may be systemic, respiratory, musculoskeletal, or gastrointestinal. They are most frequently referable to the central nervous system. They include fatigue, weakness, headache, skin rash, aching muscles, joint pain, abdominal pain, nausea, bloating, diarrhea, impairment of attention or concentration, speech problems, light-headedness, depressed mood, dry or itchy eyes and sore throat.

Supporters of the IEI/MCS condition believe that the condition is attributable to exposure to very low doses of chemicals – amounts so low as to defy proven scientific and medical principles. Therein lies the problem: IEI and its variants consist of diffuse, nonspecific and ambiguous symptoms that are very common in healthy, non-patient populations. There is no laboratory evidence of disease. Those with the MCS label do not exhibit progression of the disease or have shortened lives. The condition is not fatal.

Theories of Causation:

Sparkes (2000) has recently proposed 4 hypothetical models for IEI with the comment that “no single, replicated,

peer-reviewed study proves any of these models to a definitive degree.”

1. Direct biological effects of chemicals on the body.
2. Psychosomatic effects of chemicals on the body.
3. Misattribution of symptoms of psychiatric disorders to chemicals.
4. Delusions of chemically caused symptoms.

Repeated attempts to explain the cause of IEI on the basis of current clinical and scientific knowledge have been unsuccessful to date. A few examples follow.

1. Immunological Basis. Allergies, autoimmune diseases and immune deficiencies are associated with well-characterized disorders. IEI does not resemble any of the recognized immune disorders. There are severely atopic individuals who have symptoms and signs that can not always be adequately explained by the current understanding of the immune system. The suggestion that atopy could represent a mechanism applicable to MCS has not been shown to have scientific basis. Since individuals with MCS do not by definition have positive allergen tests, an MCS immune mechanism would have to differ in its immunopathology from known immune disorders. Individuals who are allergic to formaldehyde, chromium, isocyanates, or other well-known allergens, do not have MCS. They have a classic allergy. Although there has been much speculation about the possible role of the immune system in the etiology of IEI, there is little or no substantiated evidence supporting such a role.

2. Inflammatory Basis. The hypothesis has been suggested that a significant exposure could be followed by the development of chronic intolerance to low doses of chemicals on an inflammatory basis. The analogy is that of hyper-reactive airways. The cellular mediators (cytokines and neuropeptides) released upon exposure to the offending chemicals are hypothesized to cause the symptoms of MCS. Studies to date have not provided support for this hypothesis.

3. Neurological Basis. Models and descriptions of recognized brain processes such as limbic kindling,

sensitization, conditioning, and time-dependent sensitization have been incorporated into toxicogenic theories as possible explanatory mechanisms. The most interesting possibility is partial kindling. Kindling refers to the experimental induction of seizures by repeated, low level electrical stimulation. Partial limbic kindling hypothesizes the same process as limbic kindling with the qualification that subjective complaints substitute for seizure activity. A proposed theory is that smells can trigger a response in the brain in a way that results in the brain responding to lower and lower levels of the odour. Space does not permit a review of other proposed neurological mechanisms. However, to date no replicated, peer-reviewed study has substantiated a neurological basis to IEI.

4. Psychological Basis. There are two basic psychological categories related to possible causation in IEI/MCS. First is the presence of a primary psychiatric disorder such as classic anxiety disorders, panic attacks and phobias, and secondly, a conditioned response perhaps more appropriately described as a “learned sensitivity.” CCK is brain-gut neuropeptide and a well-recognized panicogenic agent. Binkley (2001) has demonstrated an association of specific CCK-B receptor alleles in patients with both IEI and panic disorder, suggesting they may share a common neurogenic basis. MCS patients are reported to have a greater prevalence of traumatic early life experiences, such as abuse. Secondly, researchers studying odours have concluded that MCS patients have many of the features of a conditioned response (odour aversion). Simon et al (1990) concluded that psychological factors strongly influence the development of environmental illness. They stated “for some subjects, exposures to chemicals does not appear to precipitate new symptoms as much as provide a new explanation for chronic physical symptoms and/or psychological distress.”

5. Toxicological Basis. Some MCS practitioners attribute their patients’ symptoms to low levels of chemicals, especially mixtures of chemicals, to which most humans are exposed without effect. They directly or implicitly attribute the symptoms of their patients to the additive, synergistic, and

potentiation factors of all the compounds in the MCS patient's environment. There have not, as yet, been any scientific studies supporting MCS that meet Hill's globally accepted epidemiological criteria for toxicologic disease. Staudenmayer (1999) evaluated 20 MCS cases by individual double-blind placebo-controlled studies. A total of 145 challenges were conducted – 62 active chemical agents combined with an olfactory masker and 83 placebo with only the olfactory masker. Each challenge was classified as a response or non-response based on the individual's appraisal of a reaction and an increase in personal symptom ratings pre- to post-exposure. Both individual and group appraisals were no different from chance performance. The authors felt that this study clearly demonstrated that personal toxicogenic hypotheses were unreliable and that appraisals were cognitively mediated.

Some MCS patients feel that they are sensitive to odorous chemicals at levels well below the odour threshold of most individuals. Several studies designed to investigate this possibility have clearly demonstrated that this is not the case. However it was demonstrated that subjects could acquire somatic symptoms and altered respiratory behaviour in response to harmless but odorous chemical substances, especially if these odours had been associated with a physiological challenge that originally had caused their symptoms.

Rea (1992-1997) first proposed the concept of Total Body Load. Repeated exposures are seen as contributing to a "load" which may exceed the body's capacity to handle the environment in which it lives. To explain, Rea has used the analogy of a barrel filled to overflowing with environmental insults. Proponents feel that individuals suffering from the MCS condition represent the most sensitive (smaller barrel) of the population. The hypothesis is that exceeding the "total body load" accounts for the myriad of symptoms and non-conventional responses that cannot be explained by conventional science and medicine. The language of clinical ecologists includes one-molecule effects, subsensory threshold, unmasking, craving the offending agent, adaptation,

switching, bipolarity, biochemical individuality, kindling, hyperarousal and hypoarousal, natural versus synthetic chemicals, and spreading of effects to multiple triggers. Spreading is a well-known phenomenon in clinical medicine, but not at the extremely low doses that is claimed by the MCS community. The toxicogenic theory of MCS causation does not adhere to generally accepted medical and scientific norms and has been ruled as unacceptable in several legal decisions.

Lonne-Rahm et al (2000) carried out provocation studies on 24 MCS patients with self-reported "sensitivity to electricity." These patients reported increased skin symptoms when exposed to electromagnetic fields. Using matched controls, both groups were exposed to low and high stress situations with and without exposure to electromagnetic fields. Symptoms were documented and a number of stress-related blood tests (prolactin, cortisol and dehydroepiandrosterone) were carried out. The conclusion of the authors was that the patients did not react to electromagnetic fields.

Diagnostic Tests:

There is no single or combination of widely accepted tests for IEL. The main purpose of diagnostic testing in MCS should be to rule out other, treatable, environmental or non-environmental illnesses. Immunological testing has not proven useful (Margolick, 2000). The presence of small traces of exogenous chemicals in the blood is almost the norm in many healthy populations. Apart from known toxic reactions, a link between extremely low levels of chemicals and causation of MCS has not been established. PET Scans and CT Scans have not as yet proven useful for either diagnostic or therapeutic purposes. Sparks (2000) states that quantitative EEG, brain electric activity mapping (BEAM), evoked potentials, and photon emission computed spectrometry (SPECT) scans have been misapplied in an effort to obtain objective findings for patients with IEL. SPECT does not distinguish IEL patients from patients with anxiety, depression, or obsessive compulsive disorders. Neuropsychological testing has not identified consistent or specific findings in IEL patients that may be used for

diagnostic purposes. Blood enzyme assays for porphyria have numerous limitations and there is no scientific evidence supporting a causal link between any of the porphyrias and IEL. Sparks (2000) made the following comment regarding diagnostic evaluation: "Reinforcement of illness behavior by unjustifiably giving a patient the diagnosis of a disease due to toxic, immunological, metabolic or neurological mechanisms based on diagnostic testing that is clinically unsubstantiated or invalid may actually perpetuate the illness, prolong disability, and delay effective therapy."

Treatment:

Unfortunately, as there is no consensus regarding the etiology of MCS, there equally is no consensus regarding its treatment. Some of the approaches advocated by the MCS community include elimination and rotation diets; supportive care; fasting followed by using organically grown foods only with gradual exposure to environmental substances to determine which cause symptoms; antifungal therapy; detoxification procedures including sauna treatments, showers, massage, herbal wraps, megavitamin therapy and self-administered desensitization injections; and complete avoidance of the suspected environmental agents. The approach most favored by clinical ecologists emphasizes avoidance of suspected substances. There is currently no data showing that long-term withdrawal from chemical exposure produces a lasting improvement in symptoms. It is also impossible to accomplish. Sparks (2000) states that "a definite medical recommendation for complete avoidance of chemical exposure is not indicated at this time."

Treatment recommendations include:

- provide nonjudgmental support
- enhance patient's sense of control
- reduce psychosocial stress and/or patient's response to stress
- consider biofeedback, relaxation techniques
- treat coexisting psychiatric illness
- try behavioral desensitization to low-level chemical exposures

- use pharmacological treatment to control symptoms
- increase physical and social activity
- treat coexisting medical illnesses

The Workplace:

Employees with IEI present a difficult challenge for both physicians and employers. Negative attitudes to such employees by supervisors and co-workers can easily contribute to the problem. Every effort should be made to keep the employee at work through accommodation, understanding, encouragement and assistance. Perhaps most importantly, the employee should be given some control as an active participant in determining workplace adjustments. Job satisfaction is extremely important. A job that is both manageable and rewarding will have a positive effect. The relationship with the supervisor is crucial. It appears to be the main determining factor in how well chronically ill employees do at work. The quality of the professional and social relationship with co-workers is also crucial. Physicians should advocate "reasonable" accommodation. Drastic changes that create a very unique workspace are inappropriate. If odours are an issue, an attempt should be made to at least reduce odours and volatile organics perceived by the employee as irritating or noxious. A balance has to be achieved between avoidance and the potential damage of creating such severe environmental restrictions that

isolation and loss of employment are inevitable outcomes. Some form of telecommuting may be worth a try - as a last resort.

Those individuals experiencing the symptoms associated with the MCS condition should not be regarded as having an illness any less real because of the controversy over the etiology of IEI/MCS. The distress of these patients can be very disabling. The goal of treatment should be the control of symptoms and should focus on the patient's acquisition of skills for coping with the impact of their illness on their daily life. Practitioners should avoid ineffective, potentially hazardous, unproven, costly, diagnostic and treatment procedures that may increase a patient's distress and symptoms. Even though medical practitioners may vary greatly in their beliefs regarding the phenomenon of IEI, the approach to the patient should always be the same - compassion and understanding.

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WEB NEWS

Helpful Magazines and Newsletters available on line:

- *Alberta Occupational Medicine Newsletter*
www.med.ucalgary.ca/oemweb
- The British Columbia WCB's *Worksafe* magazine
www.worksafebc.com
- The WCB Alberta's *Insight* and *WCB Health Care Matters*
www.wcb.ab.ca/news/insight.html
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Occupational and Environmental Medical Association of Canada

Annual Conference will be held in Montreal, Quebec, during the first weekend of October, 2002

Please check the OEMAC website for updates as they are available

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